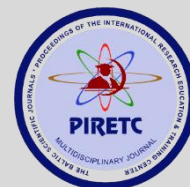


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REENGINEERING AS A MODERN TYPE OF BUSINESS MANAGEMENT

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ABSTRACT

Modern companies can increase their efficiency and competitiveness by implementing reengineering, which involves restructuring their business activities. First of all, existing business procedures within the enterprise are completely reviewed and built using this methodology. Customer satisfaction, methodical research and in-depth analysis constitute the methodological cornerstones of reengineering. The first step should be to define the organization's vision and strategic goals. It describes the goals of the reengineering and the path it will take to get there. First, the strategic goals are defined, and then the current business processes are analyzed. At this point, all operations are thoroughly examined, focusing on assessing their effectiveness, value creation potential, and customer experience.

After the analysis phase, a plan for reorganizing business processes is presented. These adjustments usually relate to how technology is implemented, how work is automated, and how resources are managed. At this point, employees' responsibilities are clarified and training is provided to familiarize them with the new procedures. For reengineering to be successful, it is important to gain the support of management and employees. Given that there may be internal opposition within the organization to a complete overhaul of business procedures. To overcome this opposition, management must use strong leadership and communication techniques. The next stage of reengineering is the implementation of a new business process. At this stage, new systems are gradually implemented, tested and optimized as necessary. The results of these procedures are regularly monitored and the results obtained are compared with the initial strategic goals. When implementing new business methods, the selection of technological solutions and their integration into the company are of great importance.

Reengineering can be more successfully implemented by using modern information technologies such as business automation tools and ERP systems. There is a lot of potential with these technologies to reduce errors, improve work and speed up the flow of information. The main goals of reengineering are to increase the competitiveness of the company and optimize its management. This can only be achieved by constantly taking into account the needs and expectations of the consumer. The effective completion of this process helps the organization to be recognized in the market as a more adaptable, creative enterprise.

Keywords: management, competitiveness in enterprises, strategy, competitive advantages, business operations, investment opportunities, innovation potential of reengineering.

XÜLASƏ

Müasir şirkətlər biznes fəaliyyətlərinin yenidən qurulmasını nəzərdə tutan reinjiniinqi həyata keçirməklə öz səmərəliliyini və rəqabət qabiliyyətini artırma bilərlər. İlk növbədə, bu metodologiyadan istifadə etməklə müəssisə daxilində mövcud biznes prosedurları tamamilə

nəzərdən keçirilir və qurulur. Müştəri məmnuniyyəti, metodik araşdırma və dərin təhlil reinjiniringin metodoloji təməl daşlarını təşkil edir. İlk addım təşkilatın vizyonunu və strateji məqsədlərini müəyyən etmək olmalıdır. O, reinjiniringin məqsədlərini və oraya çatmaq üçün keçəcəyi yolu təsvir edir. Əvvəlcə strateji hədəflər müəyyən edilir, sonra isə cari biznes prosesləri təhlil edilir. Bu nöqtədə, bütün əməliyyatlar hərtərəfli araşdırılır, onların effektivliyinin, dəyər yaratma potensialının və müştəri təcrübəsinin qiymətləndirilməsinə diqqət yetirilir. Təhlil mərhələsindən sonra biznes proseslərinin yenidən təşkili planı təqdim olunur. Bu düzəlişlər adətən texnologiyanın necə həyata keçirildiyi, işin avtomatlaşdırılması və resursların necə idarə olunması ilə əlaqədardır. Bu zaman işçilərin vəzifələri aydınlaşdırılır və onları yeni prosedurlarla tanış etmək üçün təlimlər keçirilir. Reinjiniringin uğurlu olması üçün rəhbərliyin və işçilərin dəstəyini qazanmaq vacibdir. Nəzərə alsaq ki, biznes prosedurlarının tam yenidən qurulmasına təşkilat daxilində daxili müxalifət ola bilər. Bu qarşıdurmanı aradan qaldırmaq üçün rəhbərlik güclü liderlik və ünsiyyət üsullarından istifadə etməlidir. Reinjiniringin növbəti mərhələsi yeni biznes prosesinin həyata keçirilməsidir. Bu mərhələdə yeni sistemlər tədricən tətbiq olunur, sınaqdan keçirilir və lazım gəldikdə optimallaşdırılır. Bu prosedurların nəticələri mütəmadi olaraq monitorinq edilir və əldə edilən nəticələr ilkin strateji hədəflərlə müqayisə edilir.

Yeni biznes metodlarını tətbiq edərkən texnoloji həllərin seçilməsi və onların şirkətə integrasiyası böyük əhəmiyyət kəsb edir. Biznesin avtomatlaşdırılması vasitələri və ERP sistemləri kimi müasir informasiya texnologiyalarından istifadə etməklə yenidən mühəndislik daha uğurla həyata keçirilə bilər. Səhvləri azaltmaq, işi yaxşılaşdırmaq və məlumat axınıni sürətləndirmək üçün bu texnologiyaların böyük potensialı var. Reinjiniringin əsas məqsədləri şirkətin rəqabət qabiliyyətini artırmaq və idarəetməni optimallaşdırmaqdır. Buna yalnız istehlakçının ehtiyac və gözləntilərini daim nəzərə almaqla nail olmaq olar. Bu prosesin effektiv şəkildə başa çatdırılması təşkilatın bazarda daha uyğunlaşa bilən, yaradıcı müəssisə kimi tanınmasına kömək edir.

Açar sözlər: idarəetmə, müəssisələrdə rəqabət qabiliyyəti, strategiya, rəqabət üstünlükləri, biznes əməliyyatları, investisiya imkanları, reinjiniringin innovasiya potensialı.

Introduction

One of the most effective innovations in the world economy in recent years is reengineering. It is among the important management tools and is widely used in many countries of the world. Reengineering involves the identification of processes - inputs and outputs - within a business unit and the continuous improvement and refinement of the sequence of steps. M. Hammer is considered the founder of the reengineering theory. In his book "Corporate Reengineering: A Manifesto for a Business Revolution," published with J. Ciampi, it is stated that reengineering is a fundamental rethinking and radical change of decisions in business processes in order to achieve dramatic improvements in critical performance indicators such as costs, quality, service, and speed. In other words, reengineering is understood as a fundamental rethinking and reorganization of a business in order to achieve improvements in important indicators such as the value of the firm, the level of service, the speed of its activities, the structure of its finance, marketing, and information systems. Reengineering is the reorganization of business processes in order to achieve radical, breakthrough-like improvements in the company's activities. The goal of reengineering is to change and fundamentally improve the current direction of the enterprise's activities. For this, the following principles are preferred: mobilization of the maximum number of employees; participation of consumers in projects; involvement of suppliers; reduction of the number of elements interfering with the process.

Reengineering has the following characteristics:

1. abandoning outdated rules and approaches, restructuring the business process. This allows you to free the existing enterprise from its negative impact;
2. radical change in the activities of companies, neglecting their existing systems and structures.

The realization of reengineering activities accelerates the restructuring process in enterprises. The necessity of restructuring in many processing industry enterprises of Azerbaijan was conditioned by the influence of a number of organizational, economic and technical-technological factors.

The following can be attributed to organizational and economic factors:

- slow implementation of innovation;
- incomplete use of progressive forms of management;
- imperfection of the existing management structure;
- failure to establish a functional hierarchical model of the innovation system in the field
- failure to develop a long-term innovation program;
- lack of strategic plans for innovation activities;

Aim

Business process reengineering has made a significant contribution to economic science and has become an advanced and rapidly developing field of industrial technology. Reengineering reflects a deep understanding and radical restructuring of such business indicators as value, quality, finance, marketing, etc. Reorganization of industrial enterprises implies changing the fixed assets, organizational structure, and management system of the enterprise. When implementing reengineering in enterprises, several questions should be answered.

1. Why is the business doing this now?
2. What does the business want to be?
3. Why is the business doing it this way?

To answer these questions, we must first consider the two main paths of reengineering.

1. Radical reengineering is a method for completely re-evaluating and creating an organization's business processes. With this method, existing business processes are created from scratch to build more productive, customer-oriented and efficient systems. The following ideas and methods form the basis of radical reengineering:
 - a. Analysis of existing procedures: The organization's current operating procedures and processes are thoroughly examined.
 - b. Establishment and redesign: Existing operations in enterprises are comprehensively reviewed, revised and organized in more productive, transparent methods.
 - c. Use of technology: The use of modern technologies to introduce automation and improve efficiency in processes.
 - d. Breakthrough reengineering – this type of reengineering is not only applied to improve and increase the performance of an enterprise (20-100%). As a rule, business process reengineering is applied when it is necessary to replace the old management methods (500-1000%) with new ones.

The methodological foundation of the business process makes the company more customer-oriented and efficient, while ensuring its readiness for future developments and changes in the market. The main goals of reengineering are to make the company more competitive, satisfy customers and thrive in the current market conditions. When these operations are carried out

correctly, they not only improve the internal efficiency of the organization, but also strengthen its relations with the outside world and create the basis for sustainable success. Increased competition and globalization force most enterprises to be innovative and embrace change.

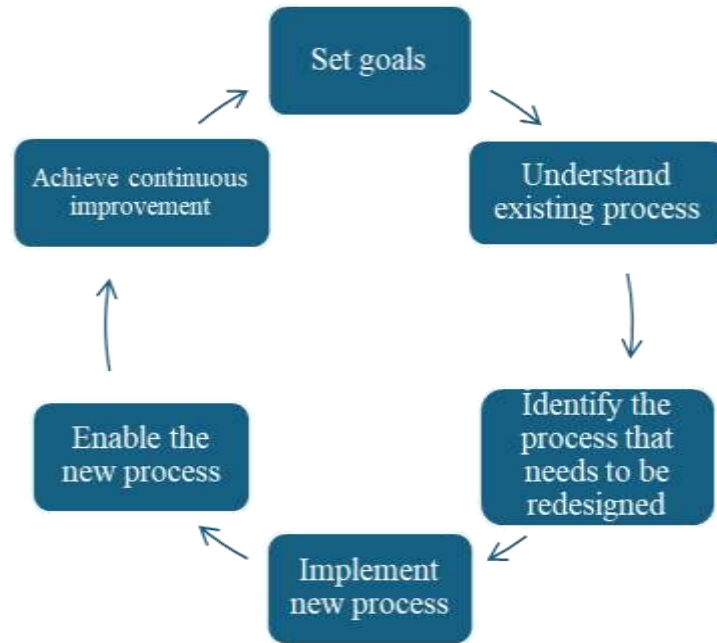
Business process reengineering is one of the approaches that brings incredible solutions to corporations. BPR has emerged as a solution for companies to improve their capabilities, the main goal of which is to increase their competitive advantage and efficiency in a changing and developing world.

Companies implement Business Process Reengineering (BPR) mainly for the following reasons:

1. To increase efficiency – When existing processes are too complex and time-consuming, productivity and efficiency are increased by redesigning them.
2. To reduce costs – Operating costs are minimized by eliminating unnecessary procedures and cost-increasing barriers.
3. To improve quality – The quality of services and products is improved to increase customer satisfaction.
4. To adapt to technological innovations – The company's competitiveness is increased by using new digital solutions and automation capabilities.
5. To be customer-centric – Business processes are optimized to respond more flexibly and effectively to customer needs.
6. To gain competitive advantage – New strategies are implemented to be more agile and sustainable compared to other companies in the industry.
7. To comply with legislation and regulations – When government requirements and regulations change, processes are updated to adapt.
8. Adapting to crisis or unstable economic conditions – For example, during a pandemic or financial crisis, companies transition to new business models.

Method

As we know, reengineering in companies is carried out simultaneously with business processes. Business processes are a broad and comprehensive concept in enterprises. In their basic meaning, business processes are a set of "internal and external steps" that an enterprise takes to produce a product. The main goal of business processes in enterprises is to create a product that satisfies customers in terms of price, quality, and service. One of the long-term results of reengineering is that an organization can innovate more. Adopting new technologies and workflows allows a company to develop an innovative culture and respond more quickly and effectively to market needs.

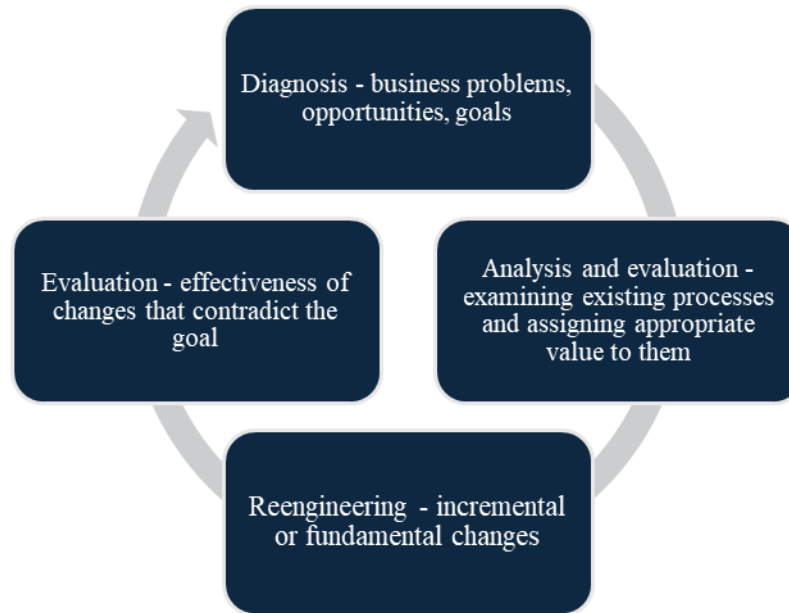


Şəkil 1. The sequence of application of reengineering in industrial enterprises.

As we can see in the picture, in the modern world, an industrial enterprise sets a long-term goal for its sustainable operation. The goal is a set of logical decisions that exist in the enterprise. It is mainly developed by professional specialists in the enterprises. After determining the goal in the enterprise, there is a need to understand the processes. Thirdly, the processes necessary for reengineering are determined.

The fourth shows what tools and factors will be involved in implementing that reengineering in the enterprise. In the fifth stage, the restructuring is implemented by the enterprise. In the sixth stage, the reengineering is put into operation.

The 4 main phases of a business reengineering initiative are diagnosis, analysis, reengineering, analysis, and evaluation. This is a virtuous cycle that must be started over. We can easily see this cycle of activity in the following figure:



Şekil 2. Stages of establishing business process reengineering.

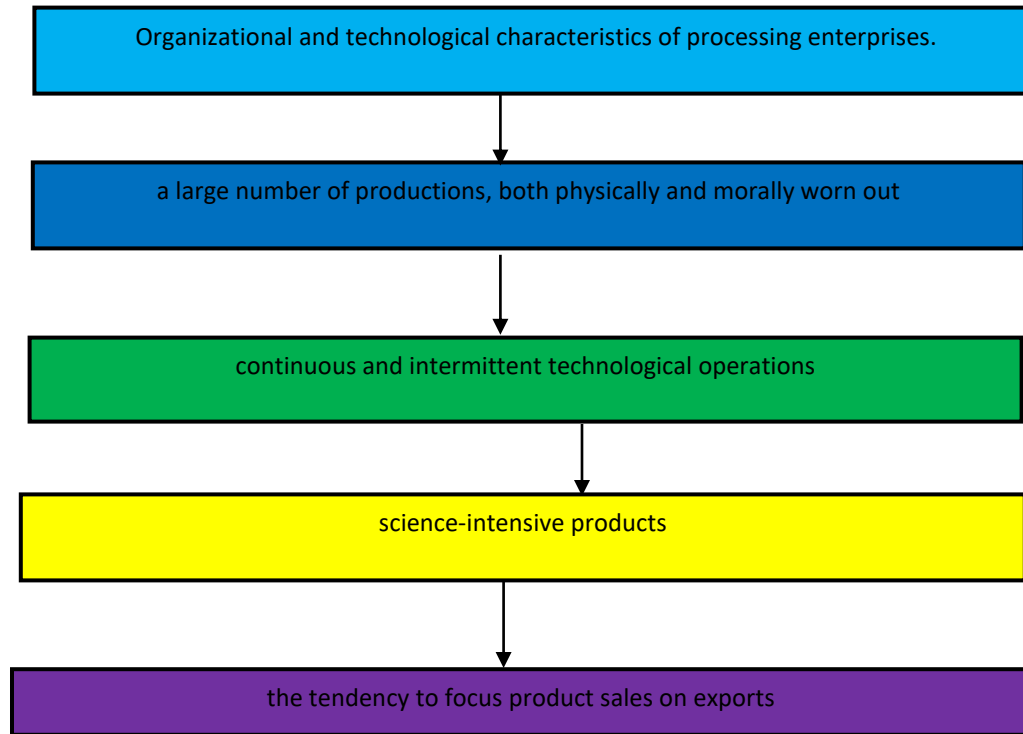
Diagnosing Problems and Opportunities - This stage analyzes current business processes to identify areas that need improvement. This involves gathering information about current processes, understanding how they work, and identifying areas of inefficiency, redundancy, or waste.

Analysis and Evaluation of the Current Process - Once the diagnosis phase is complete, the analysis phase begins. In this phase, the data collected in the diagnosis phase is analyzed to identify the root causes of problems in the current processes. The analysis phase involves breaking down the current processes into component parts, identifying process bottlenecks, and analyzing the workflow in the organization. If the process performance is measured using KPIs, they are the main input to uncovering where the problems lie.

Process Reengineering and Redesign - The reengineering phase involves redesigning business processes to eliminate inefficiencies, streamline workflows, and reduce costs. This can include reorganizing work activities, implementing new technology, changing job responsibilities, and changing business rules and policies. No-code technologies play a key role here, allowing processes to be quickly modeled, tested, and deployed in production. Avoiding coding and complex configurations in software for process automation significantly reduces the time and associated costs and motivates the team by quickly showing tangible results.

Business process reengineering is essential because it helps organizations achieve significant improvements in efficiency, productivity, and service quality. By fundamentally rethinking and redesigning business processes, BPR eliminates inefficiencies and redundancies, and promotes streamlined operations.

The elimination of the identified shortcomings in the processing infrastructure of any country indicates the need for radical reengineering there. The classification of elements that determine its necessity is given in Figure 3.



Şekil 3. Characteristics of economic and technical factors that determine the importance of reengineering in industrial enterprises.

This section examines how business process reengineering can lead to resource savings, waste reduction, and operational efficiency improvements in industrial enterprises. Business process reengineering (BPR) is an approach to improving organizational performance in an enterprise. It has developed mainly in the private sector to maintain a successful business model despite increasing global competition. BPR provides a fundamental improvement in the basic organizational design. This scientific paper identifies the success factors of BPR projects and their relationship to the people-technology-organization (HTO) framework.

Conclusion

The formal establishment of a reengineering structure ensures the effective and transparent implementation of a project, product or process. This is a form of management in which an organization can better meet the goals it wants to achieve and work efficiently. This structure goes through a number of stages, starting from setting goals, to drawing up an implementation plan, ensuring cooperation and establishing control. In the future, advanced technologies and equipment should be involved in enterprises of particular importance in the economy, the production harmony of enterprises that have ceased to operate should be restored, and work should be carried out in the field of restructuring, de-monopolization and rehabilitation of large, medium and small state-owned enterprises that perform the functions of the economy. Reengineering in enterprises can be considered the best technological strategy for business. This strategy provides long-term competitive advantages. Most enterprises have long had all the changes in all laws and regulations

of business. Therefore, all changes in it, as a rule, occur within the framework of reengineering of business operations. Reengineering is of essential and effective importance for enterprises and various economic entities. They achieve high levels of success in production by applying reengineering in their daily activities.

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ASSESSMENT OF ECHOCARDIOGRAPHIC PARAMETERS OF RIGHT VENTRICLE DYSFUNCTION AND ITS RELATION TO THE PARAMETERS OF PULMONARY HYPERTENSION (PULMONARY ARTERY PRESSURE, SYSTOLIC PULMONARY ARTERY PRESSURE, MEAN PULMONARY ARTERY PRESSURE, TAPSE/SPAP RATIO, PULMONARY VASCULAR RESISTANCE) IN PATIENTS WITH CHRONIC HEART FAILURE WITH PRESERVED LEFT VENTRICULAR CONTRACTILITY

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ABSTRACT

Chronic heart failure with the preserved LV ejection fraction and associated pulmonary hypertension (PH) is one of the most frequent and attentive cardio-vascular conditions that occur among a specific group of patients.

The exact reasons for PH are generally complicated and fully undetected. Nevertheless, remodeling the left cavities, especially the left atrium, the elevated LV filling pressure and the final involvement of RV, emerge the irreversible lesions in the pulmonary capillary vessels that caused the development of pos-capillary or combined PH.

We tried to elucidate the frequency of PH among the HFpEF patients, the types of PH and its severity despite the presence of normal sinus rhythm or atrial fibrillation. Additionally, we looked for that transthoracic echocardiographic parameter that would better point out the existence of PH, its severity, RV dysfunction and its association with PH.

Keywords: Chronic heart failure with the preserved LV ejection fraction (HFpEF), sinus rhythm, atrial fibrillation, right ventricular dysfunction, pulmonary hypertension.

Intruduction

Pulmonary hypertension is a pathological condition that contains multiple cardiovascular and respiratory problems and complications.

Pulmonary hypertension (PH) is defined as an elevation of mean pulmonary artery pressure (mPAP) > 20mmHgⁱ. PH associated with the left heart complication is well known among all PH patients and this condition is noted as post-capillary pulmonary hypertension (pcPH)ⁱⁱ. Regardless of the acknowledgment that left heart failure is an important reason for PH, the exact cause of the development of pulmonary hypertension and the mechanism of its progression are different and face lots of questionsⁱⁱⁱ.

When we speak about post-capillary pulmonary hypertension, initially we should better perceive its meaning. Post-capillary pulmonary hypertension (pc-PH) might be associated with left-side heart failure regardless contractile function of the left ventricle. Hence, chronic heart failure with preserved LV function (HFpEF) might cause pc-PH.

Based on 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, pc-PH should be defined as: 1. Elevation of mean pulmonary artery pressure (mPAP) $> 20\text{mmHg}$. 2. Elevation of pulmonary capillary wedge pressure (PCWP) $> 15\text{mmHg}$ in the resting condition. 3. Pulmonary vascular resistance (PVR) $\leq 2\text{WU}^{\text{iv}}$. The most significant factor among these parameters is pulmonary capillary wedge pressure (PCWP). Its elevation especially linked PH with left-side cardiac complications. Besides the elevation of PCWP in these patients, end-diastolic pressure of the heart's left sides is increased, which is also associated with the presence of diastolic dysfunction^v.

Carolyn S. P. Lam described the problem of pc-PH among patients with HFpEF in her article. Based on the author, PH especially spreads among elderly subjects suffering from HFpEF. The severity of PH in HFpEF patients is determined by diastolic dysfunction and elevation of end-diastolic pressure of LV (as well as in any cases of left-heart failure, despite the LV contractile function). The more prominent restrictive filling pressure was among the patient, the more severe the pc-PH was. Since LVEDP and PCWP have a significant direct relation, the assessment of both parameters might give us an important clue in the foundation of reasons for PH^{vi}.

Other authors also pointed out the remodeling of the left atrium, and elevation of left-side pressure as significant supportive factors for development the of pulmonary hypertension in HFpEF patients. Some of them emphasize the presence of concomitant mitral regurgitation, which reinforces the severity of PH in HFpEF subjects despite the presence of sinus rhythm or atrial fibrillation^{vii}.

Bradley Maron interestingly described the classification of pulmonary hypertension associated with LV dysfunction in his scientific article. The author reminded us that PH might be divided into isolated post-capillary pulmonary hypertension (ipcPH) and combined pulmonary hypertension (cpcPH) based on the mechanism of development of this pathological condition. In patients with cpcPH both, pre-capillary and post-capillary mechanisms are met. The author specifies that elevation of mPAP $> 20\text{mmHg}$ is a main echocardiographic marker for PH, despite the mechanism of development. Hence, pulmonary vascular resistance (PVR) might be the hemodynamic principal marker, which assists in the delineation of ipcPH and cpcPH. $\text{PVR} > 2\text{WU}$ is a separate and independent risk factor that increases hospitalization possibility and mortality rate in HF patients. In conclusion, $\text{PVR} > 2\text{WU}$ should be considered as a main dividing line between the isolated post-capillary and combined pulmonary hypertension^{viii}.

Ideally, PVR should be calculated using invasive methods. Nevertheless, these methods are not achievable in all patients. Hence, the scientists offered us alternative transthoracic echocardiographic techniques which assist with the estimation of pulmonary vascular resistance without any intervention. Per Lindqvist discussed one of those methods in his article. Regardless author's warning, that invasive methods for measurement of PVR cannot be replaced with the TTE technique, the alternative way might be used for massive screening of the population. The author suggested using the formula $\text{PVR} = \text{PAMPecho} - \text{PCWP}/\text{COecho}$. In this formula, PAMPecho means the mean pulmonary artery pressure (mPAP) calculated as $\text{PASPecho} \times 0.61 + 2 \text{ mmHg}$. Per Lindqvist emphasized that the PVR cutoff for delineation of IpcPH and CpcPH should be considered as $> 3\text{WU}$ if this parameter is assessed with the TTE technique^{ix}.

Pulmonary vascular resistance might be measured with other alternative TTE techniques, besides that described by Per Lindqvist. For instance, during our trial, we used the Abbas formula. This formula will be described in detail in the appropriate section below.

When we talk about PRV, we should mention that regardless elevation of PCWP and PAP in HFpEF patients, PVR will be possibly in norm. On the other hand, if PVR is elevated, it does not mean that primary diseases of the respiratory system and pulmonary vasculature should persist. Hence, the pre-capillary mechanism mightn't be involved in the pathological chain of development of PH at the initial stage. The fact is that in patients with HFpEF suffering from PH, pulmonary capillary circulation might experience secondary damage. It causes the further elevation of PVR and transpulmonic gradient. As a result, the pre-capillary mechanism is activated by the secondary ways and PH is transferred from IpcPH to CpcPH. Thenappan Thenappan well describes this attractive mechanism.

Based on the author, in comparison to patients with primary pulmonary hypertension, those subjects for whom PH is developed due to HFpEF, are mostly adult and elderly populations with the frequent existence of different cardiovascular risk factors (arterial hypertension, diabetes mellitus, obesity, coronary artery disease). Those subjects with PH and HFpEF are distinguished with dilation of the left atrium rather than the right cavities. Unlike the primary PH patients, mPAP and PVR are also elevated less in PH-HFpEF subjects. Meanwhile, mean right atrial pressure (mRAP) might be increased much more significantly in that population. Thenappan Thenappan keeps away from the description of the exact reasons; nevertheless, he assumes that more pronounced right-side dysfunction, lesser dilation of the right atrium and associated hemodynamic disturbances could explain this interesting fact^x.

We should emphasize that PWCP and its elevation $> 15\text{mmHg}$ is an important marker that might assist with the differentiation of PH-HFpEF from the primary PAH. Additionally, PWCP is a principal marker of left-side hypertension and dysfunction. However, Thenappan Thenappan pointed out the reduction of PWCP in patients with significant RV dysfunction and decline of preload, regardless undoubted existence of HFpEF. In conclusion, the author suggested assessing the PCWP with caution in the appropriate population of patients with HFpEF^{xi}.

Marco Guazzi also discussed the problems related to PH in patients with HFpEF. The author identified those patients with PH-HFpEF as elderly, obese subjects with significant metabolic disorders. Coronary artery disease, atrial fibrillation, chronic kidney disease and COPD were assumed as the additional risk factors among those patients^{xii}.

Pulmonary hypertension in patients with chronic heart failure with the preserved ejection function of the left ventricle generally determined the risk of further hospitalization and mortality. For example, Vaishnavi Aradhyula wrote that in the association of PH with the HFpEF condition, the five-year risk of mortality is 60% and the six-year risk of hospitalization is equal to 50%. Pulmonary systolic artery pressure (sPAP) $\geq 44\text{mmHg}$ is called one of the important echocardiographic markers of this association. Based on the author, in such elevation of CPAP, the mortality range might be exceeded 5 times^{xiii}.

Marco Guazzi published lots of articles related to PH in association with HFpEF patients. The author described those conditions which frequently met among PH-HFpEF patients and emphasized that PH, RV hypertrophy and RA dilation are usually observed in elderly subjects, with several cardio-vascular complications, chronic kidney disease and left heart dysfunction. In difference with chronic heart failure with the reduced ejection fraction (HFrEF), subjects with HFpEF, are commonly women with significantly deteriorated RV / RA functions^{xiv}.

Marco Guazzi broadly discussed the echocardiographic parameters, which might be used in PH-HFpEF patients for evaluation of the RV/RA functions. Based on the author, the decline of tricuspid tissue Doppler S' prime and Fractional Area Change (FAC) were not rare findings.

However, in comparison with HFrEF subjects, those parameters deviated from the normal ranges not so importantly rather than in subjects with HFpEF. The decline of tricuspid Annular Plane Systolic Excursion (TAPSE) $< 14\text{mm}$ was rarely observed in patients with HFpEF (19%), rather the subjects with HFrEF (39%)^{xv}.

According to Jiawang Xiao, the tricuspid regurgitation jet and its velocity should be considered as one of the important echocardiographic parameters with TAPSE for better evaluation of the PH, especially sPAP and the severity of PH. However, the author mentioned that the more severe the TR jet and its velocity and the more declined the TAPSE parameter is, the less reliable sPAP findings are using the TR velocity. Hence, Jiawang Xiao concluded that in the presence of a prominent TR jet, especially in association with a low TAPSE range, other alternative ways should be sought for evaluation of the sPAP and PH, rather than rely on TR velocity only^{xvi}. One of the alternative methods might be the elevation of mean pulmonary artery pressure (mPAP), using the pulmonary acceleration time (PVAT). Rachael Cordina mentioned that method in her article. The author concluded that a decline PVAT $< 90\text{msec}$ indicates the presence of pulmonary hypertension and elevation of PRV more than 3WU ^{xvii}.

When we investigate the PH and its severity, the evaluation of TR velocity with TTE is considered one of the most frequent and important methods. This parameter might be applied for the calculation of sPAP, mPAP, PVR and other valuable findings. Nevertheless, based on Rachael Cordina, the estimation of TR velocity might face lots of obstacles and disadvantages in consideration significant decline of RV function. Therefore, the competent estimation of the TR jet and its velocity should be performed with caution^{xviii}.

Pulmonary circulation adaptation is strictly necessary for maintaining the RV's normal function. In a common situation, an RV tries to extend its energy to the pulmonary artery. This kind of adaptation is known as right ventricle-pulmonary artery coupling (RV-PA coupling)^{xix}. The modern echocardiography examination allows us to use a relatively new parameter, called the TAPSE/sPAP ratio. That parameter assists with the calculation of the RV-PA coupling. On the other hand, RV-PA coupling gives us information about the presence of pulmonary hypertension, and its severity, describing the risk of hospitalization and mortality in PH subjects. Zied Ltaief wrote that the TAPSE/sPAP ratio is the most significant prognostic marker for the evaluation of the RV-PA coupling. This parameter determines the severity of heart failure and assists us with an estimation of the HF NYHA class. Additionally, it gives us information about possible mortality scores. Based on the author the estimated cutoff for the TAPSE/sPAP ratio should be considered 0.36mm/mmHg , regardless of the LV function and its contractility^{xx}.

Yanan Zhai investigated those echocardiographic parameters, which might be applied in the diagnostic chain of pre-capillary pulmonary hypertension. The author paid attention to measurements of RVOT, its tissue Doppler parameters, S' prime, TAPSE, and FAC. In conclusion of his article, Yanan Zhai wrote that FAC is the less reproductive parameter, than TAPSE and S', for instance. In addition, the measurements and volume of RVOT might be considered as well when evaluating the RV function^{xxi}.

The significance of RV-PA coupling is well described in Amalia Colalillo's article. Based on the author, the progression of PH severity leads to the remodeling of pulmonary vessels. As a result, the pulmonary capillary resistance increases and RV-PA coupling malfunctions. TAPSE/sPAP ratio will assist us with an estimation of the above-mentioned disturbances and finally give us a clue for the diagnostic approach of PH and its severity. Amalia Colalillo described several parameters of the TAPSE/sPAP ratio based on the differences in the patients' population.

Nevertheless, in the conclusion of that article, there is documented that the TAPSE/sPAP ratio $< 36\text{mmHg}$, clearly indicates the deterioration of RV-PA coupling in PH-HF patients. Meanwhile, TAPSE/sPAP ratio $< 55\text{mm/mmHg}$ might be considered as a separate marker of PH in its deterioration^{xxii}.

Based on Paul Palacios-Moguel, the calculation of TAPSE/sPAP facilitates better delineation of the presence of PH and describes its seriousness. Additionally, this parameter might valuably indicate the risk of further hospitalization and mortality range in PH patients^{xxiii}.

RV-PA coupling was interestingly examined by Guangjie Lv. The author describes the RV-PA coupling as an RV force to overcome the pressure in the pulmonary artery. If the post load in PA decreases and RV-PA coupling malfunctions, RV function will deteriorate, and it will worsen the prognostic features of patients. RV-PA coupling might be estimated using some interventional methods and, in this scenario, the results would be the best. Nevertheless, the interventional techniques are not always available. Hence, TAPSE/sPAP ratio might be a better alternative way and this opinion was proved by this author also. Additionally, in the conclusion of the article, Guangjie Lv described the relationship between TAPSE/sPAP ratio and RV-PA coupling as not consecutive and directly proportional. It was explained with several factors. TAPSE is the angle-depending, one-dimensional factor, that does not ideally describe the RV contractility function. On the other hand, sPAP does not fluently indicate the RV post-load parameter, especially while severe PH, when PRV increases and sPAP declines in parallel with decreasing contractility forces. Finally, the TR jet and its velocity are one of the problems also. It does not appropriately describe the sPAP value. Hence, based on all these obstacles, Guangjie Lv concludes that TAPSE/sPAP might be used for the calculation of the RV-PA coupling. Nevertheless, lots of impedance influence those two parameters and TAPSE/sPAP separately will never fluently gain the RV-PA coupling condition, especially in patients with severe PH and deterioration of LF function^{xxiv}.

Based on the description above, we examined almost all echocardiographic TTE parameters of PH during our trial. We analyzed the presence of any statistical relation among those parameters in HFpEF regardless of sinus rhythm or atrial fibrillation.

Description of investigated population

This prospective trial tried to investigate transthoracic echocardiographic parameters of pulmonary hypertension (pulmonary artery pressure, systolic pulmonary artery pressure, mean pulmonary artery pressure, TAPSE/sPAP ratio, pulmonary vascular resistance) in patients with chronic heart failure and preserved LV ejection fraction. Received results were compared between two groups of patients with normal sinus rhythm and atrial fibrillation.

The trial was held between January 2025 and February 2025. 62 subjects were examined. This trial was conducted at the cardiology department of the clinic Jerarsi.

The basic demographic parameters were investigated in all patients, including gender, age, height, weight and body mass index.

The subjects were divided into two categories: those with normal sinus rhythm and those with atrial fibrillation.

All the subjects involved in that trial, satisfied the subjective and objective criteria, laboratory and echocardiographic requirements of HFpEF. We used the H2FpEF scale to prove the presence of HFpEF. That scale was suggested to be completed by the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Based on the H2FpEF scale, we investigated the subjects' age, BMI, presence of atrial fibrillation, information about antihypertensive treatment,

clues for pulmonary hypertension and its severity and parameters of filling pressure of the left cavities. About the results, we calculated the final score for HFpEF. That diagnosis was proved if the score was 4 points. The Maximal H2FpEF scale score was 9 points. None of the patients from our trial had an H2FpEF scale score below 4.

Since the examination of pro-BNP is the most important chain link in the diagnostic approach for HFpEF patients, we attentively evaluated laboratory analyses among all subjects. Based on the international guidelines, in HFpEF patients with normal sinus rhythm, the cutoff level of pro-BNP was 220pg/ml; for the AF patients, the cutoff of the same lab test was 660pg/ml. None of the patients involved in our trial deviated from those requirements.

We also applied several formulas and equations for calculation the of pulmonary hypertension. Pulmonary artery pressure (PAP) was quantified by the tracing of the tricuspid regurgitation curve and receiving the mean gradient (PGmean) in mmHg. Nevertheless, PAP was not considered as an important and decisive value in the evaluation of pulmonary hypertension and its severity.

Systolic pulmonary artery pressure (sPAP) was calculated from the formula $sPAP = 4 \times (TR\ vel)^2 + RAP$. TR Vel was the maximal velocity of the tricuspid regurgitation jet and RAP was the right atrial pressure. In turn, RAP was quantified based on the volume of the inferior vena cava and its collapsibility index. Hence, if IVC was < 15mm and its collapsibility index (CI) was > 50%, RAP was considered as 0-5mmHg. If IVC was 15-25mm and CI was > 50%, RAP was considered as 5-10mmHg. If IVC was > 25mm and CI was < 50%, RAP was equal to 10-15mmHg. Finally, if IVC was < 25, without any collapsibility and additionally hepatic veins were dilated, RAP was equal to > 20mmHg. In conclusion, aimed at sPAP, we described the presence of PH and its seriousness: the normal range of sPAP was < 25mmHg. If sPAP was 40-50mmHg, we considered the PH as mild. In case sPAP was > 50-60mmHg, the PH was equal to moderate severity and finally, if sPAP was > 60mmHg, PH was considered as severe. Should be emphasized that sPAP was applied as an additional method for the diagnosis of PH and its seriousness because we focused on the level of mean pulmonary artery pressure.

For evaluation of the mean pulmonary artery pressure (mPAP), we used the formula $mPAP = (sPAP \times 0.61) + 2mmHg$. Hence, the PH was considered normal if mPAP was < 20mmHg. In case mPAP was 20-40mmHg, PH was equal to mild. If mPAP was 41-55mmHg, PH was considered as moderate severity and if mPAP was > 55mmHg, PH was equal to severe.

When we investigated the presence of PH, we also relied on pulmonary acceleration time (PVAT). Its cutoff range was the following: the normal range of PVAT was considered > 130msec; in this situation, the presence of PH was excluded. If PVAT was 100-130msec, we concluded the presence of mild PH. In case PVAT was 80-100msec, PH was equal to moderate severity and finally, if PVAT was < 80msec, PH was considered as severe.

One of the main questions of our investigation was to determine whether the patients had the real post-capillary PH of the combined PH. Hence, we examined the pulmonary vascular resistance applied to the Abbas Formula: $PVR = (TRV_{max} / VTI_{RVOT}) \times 10 + 0.16$. TRV_{max} was the maximal regurgitant jet velocity of the tricuspid valve. VTI_{RVOT} was the velocity-time integral of the right ventricular outflow tract. Since PVR was quantified with the TTE method, we aimed at the cutoff as 3 Wood. Therefore, if PVR exceeded 3 WU, we were speaking about elevating the PVR and the PH was considered as combined.

Pulmonary capillary wedge pressure (PCWP) was used for confirmation of the post-capillary PH. The normal range for that parameter was < 15mmHg. If PCWP was elevated, it proved the

presence of high filling pressure of the left cavities and therefore, PH was reckoned as post-capillary genesis. PCWP was quantified from the Nagueh Formula: $PCWP = 1.24 \times (E/e') + 1.9$. We attentively examined the tricuspid regurgitation jet, especially its maximal velocity (TR V max). Based on recommendations, if TR V max was $\leq 2.8\text{m/sec}$ the existence of PH was unlikely. If TR V max was $2.9\text{-}3.4\text{m/sec}$, PH might be considered as possible and finally, if TR V max was $> 3.4\text{m/sec}$, the presence of PH was undoubted.

Additionally, we investigated TAPSE/sPAP ratio among all included patients. Despite the different cutoffs of this ratio in various articles, the scientists concluded that the most significant prognostic and valuable range of the TAPSE/sPAP ratio was $< 0.36\text{mm/mmHg}$. Therefore, this value was taken into consideration for our subjects.

Besides the mentioned parameters of PH, we also examined the echocardiographic aspects of systolic and diastolic function of the right ventricle, including fractional area change (FAC), tricuspid annular plane systolic excursion (TAPSE), tissue doppler S' wave of the RV (TDI RV S'), and RV index of myocardial performance (RIMP). Normal ranges for those parameters were the following: $FAC < 35\%$, $RIMP > 0.54$, $TAPSE < 20\text{ mm}$, $RV S' < 10$.

The transthoracic echocardiographic examination was performed with a MINDRAY Resona I9 echo machine. The linear and volumetric measurements of heart cavities were executed based on the 2015, Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. The right ventricle was investigated based on the 2010 Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography and 2020 Guideline of Echocardiographic Assessment of the Right Heart in Adults: A Practical Guideline from the British Society of Echocardiography. Diastolic function was calculated by 2016 Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Pulmonary hypertension was evaluated based on 2022, ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension, AHA, 2013, Echocardiography in Pulmonary Arterial Hypertension: from Diagnosis to Prognosis, 2022 ESC/ERS Guidelines for Pulmonary Hypertension and 2010 BSE Guidelines for Pulmonary Hypertension.

About all obtained data, we made the appropriate conclusions which will be described below in the appropriate section of this article.

Statistical analyses

We used Levene's Test for Equality of Variances and the t-test for Equality of Means for the statistical processing of the results received from the patients involved in our trial. These statistical tests were applied to conduct comparative analyses.

Pearson Chi-Square Tests and Fisher's Exact Test were used for correlational and cross-sectional analysis.

We judged the reliability of the obtained data based on the P-value. If P was $< .05$, the result was considered statistically reliable. If P was $> .05$, we did not have any statistically reliable answer.

Results

Demographic and clinical findings

62 patients were enrolled in our trial. 47 subjects were female among them (75.8%) and 15 patients were male (24.2%).

Table 1. Distribution of patients by gender.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	47	75.8	75.8	75.8
	Male	15	24.2	24.2	100.0
	Total	62	100.0	100.0	

Table 2. Distribution of patients by heart rate.

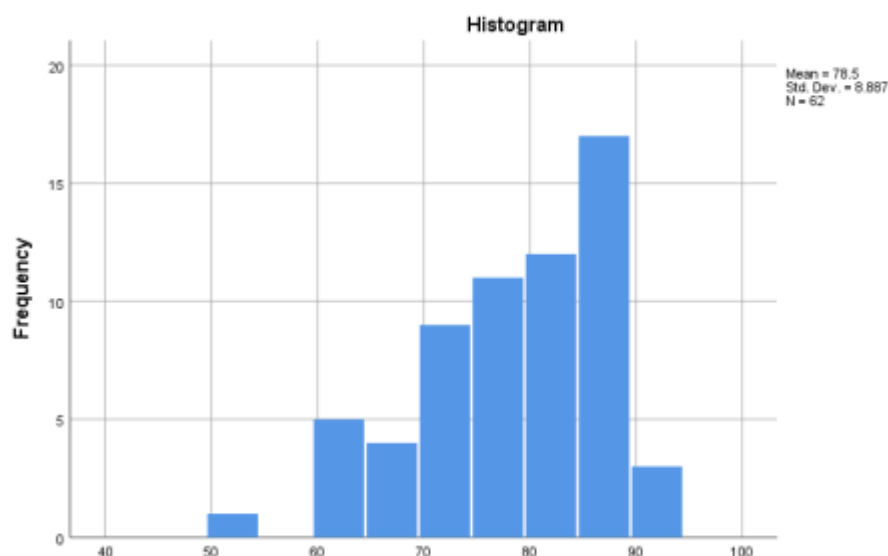
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Sinus rhythm	35	56.5	56.5	56.5
	Atrial fibrillation	27	43.5	43.5	100.0
	Total	62	100.0	100.0	

Among 62 examined patients, 35 subjects had normal sinus rhythm (56.5%) and 27 patients had ECG clues of permanent atrial fibrillation or a history of paroxysmal Afib (43.5%).

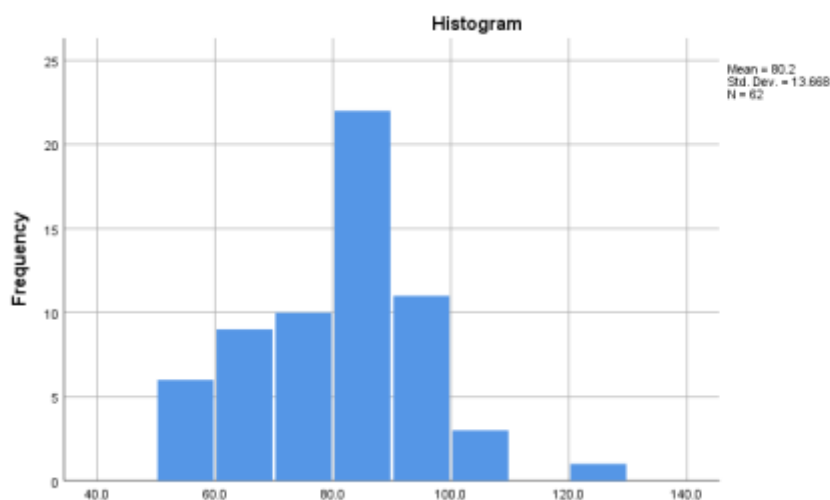
We investigated the following demographic parameters: maximal, minimal and average age. We attentively examined the patients' weight also because overweight and obesity are some of the important diagnostic parameters for HFpEF. Hence, we investigated the maximal, minimal and average weight. After the assessment of the results, we concluded that the average age among the enrolled patients was 78 (M = 78,50; SD = 8,88), the minimal age was 52 and the maximal parameter was 93.

Regarding the age, the average result was 80kg (M = 80,19; SD = 13,66). The maximal weight was 120kg and the minimal parameter was 55kg.

<i>Age</i>			<i>Weight (kg)</i>		
N	Valid	62	N	Valid	62
	Missing	0		Missing	0
Mean		78.50	Mean		80.198
Std. Deviation		8.887	Std. Deviation		13.6680
Minimum		52	Minimum		55.0
Maximum		93	Maximum		120.0
Table 3 Patients' minimal, maximal and average age.			Table 4. Patients' minimal, maximal and average weight.		



Scheme 1. Patients` minimal, maximal and average age.



Scheme 2. Patients` minimal, maximal and average weight.

Since HFpEF should have been diagnosed for all enrolled patients we attentively examined the basic chronic concomitant cardio-vascular and extracardial diseases. Information about those conditions should have been retrieved because they were assisting with the HFpEF diagnostic approach. We did not choose either of the subjects for our trial with congenital heart disease, infiltrative disease, for instance, Amiloidosis, or systemic disease. Those conditions were not considered as exclusion criteria for our trial. Nevertheless, none of them were officially diagnosed for either of the patients. Regarding cardio-vascular and extracardiac conditions, we frequently met arterial hypertension, a history of acquired vascular disease, a history of different types of arrhythmia, coronary artery disease, a history of endocrine disease, anemia, chronic kidney disease and other associated pathologies. The exact information regarding concomitant illnesses is

described in table # 5. The main difference between the groups with normal sinus rhythm and Afib was revealed in the presence of distinct types of arrhythmia ($P < .05$). That was explained by the presence of Afib directly among 27 patients in the second group.

Table 5. The frequency of cardiovascular and extracardiac diseases in patients with normal sinus rhythm and atrial fibrillations.

	Sinus rhythm	Atrial fibrillation	Sum	Sig
History of coronary artery disease	18 (64,3%)	10 (35,7%)	28	$P > .05$
History of arterial hypertension	35 (56,5%)	27 (43,5%)	62	$P > .05$
History of heart valvular diseases	34 (55,7%)	27 (44,3%)	61	$P > .05$
History of the different types of arrhythmias	8 (22,9%)	27 (77,1%)	35	$P < .05$
History of chronic infective conditions	1 (100%)	0	1	$P > .05$
History of pericardial diseases	1 (50%)	1 (50%)	2	$P > .05$
History of endocrine illnesses	15 (65,2%)	8 (34,8%)	23	$P > .05$
Anemia	14 (58,3%)	10 (41,7%)	24	$P > .05$
History of chemotherapy treatment	1 (20%)	4 (80%)	5	$P > .05$
CKD	13 (59,1%)	9 (40,9%)	22	$P > .05$
Other concomitant conditions	11 (47,8%)	12 (52,2%)	23	$P > .05$

We attentively investigated subjective and objective symptoms for all patients (see Table #6). It assisted us with a better diagnostic approach for HFpEF on the one hand and with the evaluation of the HF NYHA class on the other. Later, we compared the HF NYHA class with the severity of PH. We concluded the direct correlation between the worsening of the NYHA class and the severity of PH (see Table #18). It should be emphasized that neither of the subjects complained about blurred mind, elevation of jugular venous pressure, hepato-jugular reflux, significant loss or increase of weight, hepatomegaly, ascites, or oliguria. On the contrary, the most frequent symptoms that occurred among 100% or at least 100% of patients were the following: difficulty breathing, decreased physical activity, tiredness, decreased working capacity, swelling in the ankle area, heart murmur while auscultation, and peripheral edema. Additionally, the statistical differences between the patients with normal sinus rhythm and atrial fibrillation were observed in some symptoms, especially nighttime paroxysmal dyspnea, night-time cough, wheezing while breathing, and heart palpitation ($P < .05$).

Table 6. The frequency of subjective and objective symptoms in patients with normal sinus rhythm and atrial fibrillation.

	Sinus rhythm	Atrial fibrillation	Sum	Sig
Difficult breathing	35 (56,5%)	27 (43,5%)	62	$P > .05$
Orthopnea	12 (46,2%)	14 (53,8%)	26	$P > .05$
Nighttime paroxysmal dyspnea	5 (25%)	15 (75%)	20	$P < .05$
Decreased physical activity	35 (56,5%)	27 (43,5%)	62	$P > .05$

Tiredness and decreased working capacity	35 (56,5%)	27 (43,5%)	62	P > .05
Swelling in the ankle area	34 (55,7%)	27 (44,3%)	61	P > .05
Nighttime cough	8 (38,1%)	13 (61,9%)	21	P < .05
Wheezing while breathing	10 (40%)	15 (60%)	25	P < .05
Loss of appetite	19 (51,4%)	18 (48,6%)	37	P > .05
Depression	8 (72,7%)	3 (27,3%)	11	P > .05
Heart palpitation	9 (25%)	27 (75%)	36	P < .05
Dizziness	24 (50%)	24 (50%)	48	P > .05
Syncope	0 (0%)	1 (100%)	1	P > .05
Bendopnoe	19 (51,4%)	18 (48,6%)	37	P > .05
So-called gallop rhythm	0 (0%)	2 (100%)	2	P > .05
Lateral deviation of the cardiac apex	6 (40%)	9 (60%)	15	P > .05
Heart murmur while auscultation	34 (55,7%)	27 (44,3%)	61	P > .05
Peripheral edema	33 (55%)	27 (45%)	60	P > .05
Crepitation while lung auscultation	3 (75%)	1 (25%)	4	P > .05
Pleural effusion	12 (44,4%)	15 (55,6%)	27	P > .05

Laboratory findings

Pro-BNP analyses are one of the important laboratory measurements in the diagnostic approach of HFpEF. Hence, that laboratory test was evaluated among our patients. Statistical analysis uncovered that those patients with atrial fibrillation tended to have a pronounced elevation of pro-BNP rather than subjects with normal sinus rhythm. The average value of pro-BNP among the Afib patients was more elevated (M = 5720.3; SD = 7445.7). Despite this result, we did not receive any statistically reliable differences between those two groups (P > .05).

Table 7. The minimal, maximal, and average levels of pro-BNP in patients with sinus rhythm and atrial fibrillation.

AF	Mean	N	Std. Deviation	Minimum	Maximum
Sinus rhythm	2788.97	35	4285.810	475	24757
Atrial fibrillation	5720.38	26	7445.746	1274	35000
Total	4038.42	61	5970.328	475	35000

Table 8. Differences in elevation of pro-BNP in patients with sinus rhythm and atrial fibrillation.

	Leven e's Test for Equality of Variances		t-test for Equality of Means						
	F	Sig.		df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
								L	U

									ower	pper	
T- proBNP (pg/ml)	Eq ual variances assumed	.806	.032	.940	9	5	.057	1.409	1.367	92.829	55.647
	Eq ual variances not assumed			.798	7.165	3	.080	1.409	0.055	370.900	33.718

Echocardiographic findings

The main goal of our investigation was to uncover the presence of pulmonary hypertension between two separate groups of patients. We used the different echocardiographic parameters to achieve that goal. Taking into account the ESC 2022 guideline for the diagnosis and management of PH, where the main attention was paid to the mean pulmonary artery pressure (mPAP), we also applied to that echocardiographic marker for the development of the PH and its severity. If we consider that the normal range for mPAP is < 20 mmHg, we can conclude that PH was observed almost for all enrolled patients (96%). However, we did not meet the statistically reliable differences between the patients with sinus rhythm or Afib ($P > .05$).

Table 9. The spreading of PH based on mPAP value in patients with sinus rhythm and atrial fibrillation.

			Pulmonay hypertension		To tal
			Mpap < 20	Mpap > 20	
AF	Sinus rhythm	Count	1	34	35
		Expected Count	1.1	33.9	35
		% within AF	2.9%	97.1%	.0
	Atrial fibrillation	Count	1	26	27
		Expected Count	.9	26.1	27
		% within AF	3.7%	96.3%	.0
	Total	Count	2	60	62
Expected Count		2.0	60.0	62	
% within AF		3.2%	96.8%	.0	
Chi-Square Tests					
	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.035a	1	.852		

Continuity Correction ^b	.00	1	1.000		
Likelihood Ratio	.35	1	.852		
Fisher's Exact Test				1.000	.685
Linear-by-Linear Association	.34	1	.853		
N of Valid Cases	62				
a. 2 cells (50.0%) have an expected count of less than 5. The minimum expected count is .87.					
b. Computed only for a 2x2 table					

mPAP was also used for evaluating the severity of PH and its division among patients with sinus rhythm and Afib. After the results statistical assessment, we concluded that severe PH, when mPAP was > 55 mmHg, was observed for neither of the patients. The redistribution of patients with mild and moderate PH was almost the same, despite the heart rhythm. However, in Afib patients, we pointed out a slight tendency towards a predominance of moderate PH (19%). Meanwhile, in sinus rhythm subjects, the same finding was 11.8%. The statistical differences were not reliable ($P > .05$).

Table 10. The redistribution of mild and moderate PH based on mPAP value in patients with sinus rhythm and atrial fibrillation.

			Pulmonary Hypertension		otal
			Mild PH	Moderate PH	
F	Sinus rhythm	Count	30	4	4
		Expect ed Count	28.9	5.1	4.0
		% within AF	88.2%	11.8%	00.0 %
	Atrial fibrillation.	Count	21	5	6
		Expect ed Count	22.1	3.9	6.0
		% within AF	80.8%	19.2%	00.0 %
	Total	Count	51	9	0
		Expect ed Count	51.0	9.0	0.0
		% within AF	85.0%	15.0%	00.0 %
Chi-Square Tests					
	Value	df	Asympt otic	Exact Sig. (2-sided)	Exact Sig. (1-sided)

			Significance (2-sided)		
Pearson Chi-Square	.6	1	.422		
Continuity Correction ^b	.1	1	.662		
Likelihood Ratio	.6	1	.424		
Fisher's Exact Test				.482	.328
Linear-by-Linear Association	.6	1	.426		
N of Valid Cases	60				

Slightly different information was received while investigating the severity of PH and its distribution among both groups based on systolic pulmonary artery pressure (sPAP). Its normal range was 40–50 mmHg. Taking into account that value, we uncovered some patients in the sinus and Afib population with severe PH when sPAP was > 60 mmHg. In the sinus rhythm, we had 6 patients with severe PH (23.1%), and in the Afib population, we had 5 subjects (26.3%). These results were also not statistically reliable ($P > .05$).

Table 11. The redistribution of mild and moderate PH based on sPAP value in patients with sinus rhythm and atrial fibrillation.

			RVSP_Groups			Total
			Mild PH	Moderate PH	Severe PH	
F	Sinus rhythm	Count	14	6	6	26
		Expected Count	14.4	5.2	6.	26.0
		% within AF	53.8 %	23.1% %	23 .1%	1 00.0%
	Atrial fibrillation.	Count	11	3	5	19
		Expected Count	10.6	3.8	4.	19.0
		% within AF	57.9 %	15.8% %	26 .3%	1 00.0%
	Total	Count	25	9	11	45
		Expected Count	25.0	9.0	11	45.0
		% within AF	55.6 %	20.0% %	24 .4%	1 00.0%
Chi-Square Tests						
	Value	df	Asymptotic Significance (2- sided)			
Pearson Chi-Square	.371a	2	.831			
Likelihood Ratio	.378	2	.828			

Linear-by-Linear Association	.001	1	.975
N of Valid Cases	45		
2 cells (33.3%) have an expected count of less than 5. The minimum expected count is 3.80.			

Tricuspid regurgitation jet maximal velocity (TR Vmax) was one of the additional parameters that was used for the evaluation of PH and its severity. The normal range for TR Vmax was considered ≤ 2.8 m/sec when the presence of PH was unlikely. We examined the possible relation between the degree of elevation of TR Vmax and the severity of PH, which in turn was estimated by the mPAP value. The statistical analyses showed the more TR Vmax was elevated, the more severe the PH degree was. If TR Vmax was in the normal range (≤ 2.8 m/sec), moderate and especially severe PH was not detected at all. Additionally, we pointed out 12 patients in both groups (75%) for whom the elevation of TR Vmax simultaneously caused the worsening of PH severity from mild to moderate. Interestingly, the statistical results were reliable ($P < .05$).

Table 12. Correlation relation between TR Vmax and severity of PH in both groups of patients.

			mPAP_Groups		Total
			Mild PH	Moderate PH	
Velocity	TR norm	Count	18	0	18
		Expected Count	15.3	2.7	18.0
		% within TR_Velocity	100.0%	0.0%	100.0%
	TR mild elevation	Count	30	0	30
		Expected Count	25.5	4.5	30.0
		% within TR_Velocity	100.0%	0.0%	100.0%
	TR significant elevation	Count	3	9	12
		Expected Count	10.2	1.8	12.0
		% within TR_Velocity	25.0%	75.0%	100.0%
Total		Count	51	9	60
		Expected Count	51.0	9.0	60.0
		% within TR_Velocity	85.0%	15.0%	100.0%
Chi-Square Tests					
	Value	df	Asymptotic		

			Significance (2-sided)
Pearson Chi-Square	4 2.353 ^a		0.000
Likelihood Ratio	3 7.229		0.000
Linear-by-Linear Association	2 5.711		0.000
N of Valid Cases	6 0		
a. 3 cells (50.0%) have an expected count of less than 5. The minimum expected count is 1.80.			

Pulmonary acceleration time (PVAT) was also applied to better estimate the presence of PH and its severity. PVAT > 130 msec was reckoned as a normal range of PVAT. We were also interested in the possible relationship between the decline of PVAT value and the severity of PH calculated from mPAP. We found a statistically reliable relation between the PVAT and PH ranges as well as its severity ($P < .05$). We did not meet any moderate/severe PH among those patients for whom the PVAT value was slightly decreased (100-130 msec). In cases of moderate decline of PVAT (80-100 msec), a moderate elevation of PH was detected in 6.7%. Meanwhile, in significantly decreasing PVATs of more than 80 msec, moderate PH was noted in 33.3% of patients.

Table 13. Correlative relation between PVAT and PH in both groups of patients.

			mPAP_Groups		T otal	
			Mild PH	Moderate PH		
PvaT_ Group	PVAT mild	Count	9	0	9	
		Expected Count	7.7	1.4	9. 0	
		% within PvaT_Group	100.0%	0.0%	10 0.0%	
	PVAT moderate	Count	28	2	30	
		Expected Count	25.5	4.5	30 .0	
		% within PvaT_Group	93.3%	6.7%	10 0.0%	
	PVAT severe	Count	14	7	21	
		Expected Count	17.9	3.2	21 .0	
		% within PvaT_Group	66.7%	33.3%	10 0.0%	
	Total		Count	51	9	60
			Expected Count	51.0	9.0	60 .0
			% within PvaT_Group	85.0%	15.0%	10 0.0%
Chi-Square Tests						

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	8.758 ^a	2	0.013
Likelihood Ratio	9.296	2	0.010
Linear-by-Linear Association	7.556	1	0.006
N of Valid Cases	60		

a. 3 cells (50.0%) have an expected count of less than 5. The minimum expected count is 1.35.

			RVOT VTI		Total		
			Norm	Deviation (less than < 14)			
mPAP_Groups	Mild PH	Count	24	27	51		
		Expected Count	22	28.9	51		
		% within mPAP_Groups	.1	52.9%	.0		
	Moderate PH	Count	47	7	10		
		Expected Count	.1%	5.1	0.0%		
		% within mPAP_Groups	22	77.8%	10		
		Total			.2%	56.7%	0.0%
		Count	26	34	60		
Expected Count	26	34.0	60				
			.0		.0		
			43		10		
			.3%		0.0%		

Correlations				
		PVAT (msec)	RVOT VTI (cm)	mPAP
PVAT (msec)	Pearson Correlation	1	0.377**	-
	Sig. (2-tailed)		0.003	0.278*
	N	62	62	62
RVOT VTI (cm)	Pearson Correlation	* 0.377*	1	-
	Sig. (2-tailed)	0.003		0.254*
	N	62	62	62
mPAP	Pearson Correlation	- 0.278*	-0.254*	1
	Sig. (2-tailed)	0.029	0.046	
	N	62	62	62

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

Table 14. Statistical correlation between RVOT VTI and PVAT in both groups of patients.

We were also interested in determining the frequency of post-capillary and combined pulmonary hypertension in both groups of subjects. Besides mPAP calculation, we used TTE methods as well for calculating the pulmonary vascular resistance (PVR) and pulmonary capillary wedge pressure (PCWP). Normal range was PVR was considered $< 3\text{WU}$, and for PCWP $< 15\text{ mmHg}$. After cross-tabulation analysis, we concluded that in patients with normal sinus rhythm, the post-capillary PH occurred in 57.1% of cases. In Afib subjects, the post-capillary PH was met in 44.4%. Despite the slight pronouncement of post-capillary PH among the sinus rhythm subjects, statistically reliable differences were not detected ($P > .05$).

			Post-capillary PH		Total
			No	Yes	
F	Sinus rhythm	Count	15	20	35
		Expected	16.9	18.1	35
		Count			.0
		% within AF	42.9%	57.1%	100.0%
	Atrial fibrillation	Count	15	12	27
		Expected	13.1	13.9	27
		Count			.0
		% within AF	55.6%	44.4%	100.0%
Total		Count	30	32	62
		Expected	30.0	32.0	62
		Count			.0
		% within AF	48.4%	51.6%	100.0%
Chi-Square Tests					
	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.984 ^a	1	0.321		
Continuity Correction ^b	.41	1	0.462		
Likelihood Ratio	.986	1	0.321		
Fisher's Exact Test				0.443	0.231
Linear-by-Linear Association	.68	1	0.325		
N of Valid Cases	62				
0 cells (0.0%) have an expected count of less than5. The minimum expected count is 13.06.					

Table 15. Spreading of post-capillary PH in both groups of patients.

We have received interesting information regarding the combined form of PH. Mainly, combined PH was observed for 11 subjects only among all 62 investigated patients and statistical dereference between the sinus rhythm and Afib groups was reliable ($P < .05$). In sinus rhythm patients, the combined PH occurred in 8.6% of cases, nevertheless in Afib patients the same case was observed in 29.6%. This fact might be explained by more pronounced remodeling of the left atrium in individuals with AFiB, with higher filling pressures of the left ventricle, which secondarily involves the pulmonary blood vessels in the pathological process. All those lesions finally caused the transformation of post-capillary PH into the combined form of PH.

			Combined PH		T
			No	Yes	otal
F	Sinus rhythm	Count	32	3	35
		Expected Count	28.8	6.2	35.0
		% within AF	91.4%	8.6%	100.0%
	Atrial fibrillation	Count	19	8	27
		Expected Count	22.2	4.8	27.0
		% within AF	70.4%	29.6%	100.0%
	Total	Count	51	11	62
			Expected Count	11.0	62.0
			% within AF	17.7%	100.0%
Chi-Square Tests					
	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4.631 ^a	1	.031		
Continuity Correction ^b	.301	1	.069		
Likelihood Ratio	4.674	1	.031		
Fisher's Exact Test				.045	.035
Linear-by-Linear Association	4.557	1	.033		
N of Valid Cases	62				
a. 1 cells (25.0%) have an expected count of less than 5. The minimum expected count is 4.79.					
b. Computed only for a 2x2 table					

Table 16. The spreading of combined PH in both groups of patients.

We additionally examined the TAPSE/sPAP ratio for all the enrolled patients. The normal range for that parameter was considered 0.36mmHg. All data below that range was considered pathological. We investigated the correlation of the TAPSE/sPAP ratio with the different heart rhythms. Finally, the statistical analyses showed that TAPSE/sPAP ratio decreased almost with a similar range in both groups: at least 34.3% in sinus rhythm subjects and 48.1% in Afib patients. Additionally, the maximal norm of that parameter was detected in 65.7% of cases in the sinus rhythm group and 51.9% of the Afib group.

			Tapse_Groups		To tal
			Decrease of TAPSE/sPAP	The maximal norm of TAPSE/sPAP	
F	Sinus rhythm	Count	12	23	35
		Expected	14.1	20.9	35
		Count			.0
		% within AF	34.3%	65.7%	10 0.0%
	Atrial fibrillation	Count	13	14	27
		Expected	10.9	16.1	27
		Count			.0
		% within AF	48.1%	51.9%	10 0.0%
Total		Count	25	37	62
		Expected	25.0	37.0	62
		Count			.0
		% within AF	40.3%	59.7%	10 0.0%
Chi-Square Tests					
	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.217 ^a	1	.270		
Continuity Correction ^b	.709	1	.400		
Likelihood Ratio	1.216	1	.270		
Fisher's Exact Test				.306	.200
Linear-by-Linear Association	1.198	1	.274		
N of Valid Cases	62				
a. 0 cells (0.0%) have an expected count of less than 5. The minimum expected count is 10.89.					
Computed only for a 2x2 table					

Table 17. Decline of TAPSE/sPAP ratio in sinus rhythm and Afib patients.

We also investigated the relationship between our subjects' HF NYHA class and PH severity. We were guided by the New York HF classification on the one hand and the mPAP value on the other. After statistical analyses, we received reliable differences ($P < .05$). The more severe the PH degree was, the more advanced the HF NYHA class we had. For example, neither of the patients with HF NYHA I class had moderate PH. Among the patients with NYHA II class, the moderate PH was met in 3.4% of cases. NYHA III class was associated with moderate PH in 20% of cases. Finally, among the patients with NYHA IV class, moderate PH was detected in 60%.

			mPAP_Groups		Total	
			Mild PH	Moderate PH		
Class	NY HA - I	Count	2	0	2	
		Expected	1.7	.3	2.0	
		Count				
	NY HA - II	% within Class	100.0%	0.0%	100.0%	
		Count	28	1	29	
		Expected	24.7	4.4	29.0	
	NY HA - III	Count				
		% within Class	96.6%	3.4%	100.0%	
		Count	19	5	24	
	NY HA - IV	Expected	20.4	3.6	24.0	
		Count				
		% within Class	79.2%	20.8%	100.0%	
	NY HA - IV	Count	2	3	5	
		Expected	4.3	.8	5.0	
		Count				
	Total	% within Class	40.0%	60.0%	100.0%	
Count		51	9	60		
Expected		51.0	9.0	60.0		
Total	Count					
	% within Class	85.0%	15.0%	100.0%		
	Count					

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	11.970 ^a	3	.007
Likelihood Ratio	10.732	3	.013
Linear-by-Linear Association	10.246	1	.001
N of Valid Cases	60		

a. 6 cells (75.0%) have an expected count of less than 5. The minimum expected count is .30.

Table 18. The correlation of HF NYHA class with the severity of PH among both groups of patients.

After the statistical assessment of all results, we aimed to receive information about the possible correlation between the PH and its severity and echocardiographic parameters of RV dysfunction, such as TAPSE, FAC, S` and RIMP. For the assessment of PH and its severity, we also used the mPAP value. The variability of FAC parameters was unimportant in both groups. Deviation of FAC from the normal range was observed in 6.4% among mild PH patients, but in moderate PH subjects, FAC was not deviated at all (0%). TAPSE variation from the normal range in the mild PH group was observed in 61.7% of cases and 77.8% among moderate PH patients. Examination of the S` parameter uncovered an interesting association between the mild and moderate PH groups: in mild PH subjects deviated in 34%, meanwhile in moderate PH patients that parameter was variated from the normal range in 88.9% of cases. Finally, RIMP deviated from the norm in 91.5% of mild PH patients and in 100% of cases among the moderated PH cases. After the attentive evaluation of those four RV dysfunction parameters, we met the statistically reliable variation for S` ($P < .05$). As for FAC, TAPSE, and RIMP, none of the results were statistically reliable ($P > .05$).

			Disfunction of RV				otal	
			Fac _Factor	Rim p_factor	Tapse _Factor	S _factor		
mPAP_ Groups	Mild PH	Count	3	43	29	1	7	
		% within mPAP_Groups	6.4 %	91.5 %	61.7% 4.0%	3		
	PH	Moderate	Count	0	9	7	8	
		% within mPAP_Groups	0.0 %	100. 0%	77.8% 8.9%	8		
Total		Count	3	52	36	2	6	
					4			

Percentages and totals are based on respondents.

a. Dichotomy group tabulated at value 1.

Chi-Square Tests

	V alue	df	Asympto tic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1 0.545 ^a	1	.001		
Continuity Correction ^b	8. 284	1	.004		
Likelihood Ratio	1 1.033	1	.001		
Fisher's Exact Test				.002	.002
Linear-by-Linear Association	1 0.369	1	.001		
N of Valid Cases	6 0				

a. 1 cells (25.0%) have an expected count of less than 5. The minimum expected count is 3.60. Computed only for a 2x2 table
--

Table 19. The correlation between PH and its severity and RV dysfunction parameters (TAPSE, FAC, S', RIMP) among both groups of patients.

Discussion

Chronic heart failure with preserved LV ejection fraction associated with pulmonary hypertension is one of the important and frequent pathological conditions that, on the one hand, causes RV involvement, deterioration of its systolic and diastolic functions, and worsening of HF NYHA class, or exaggerates the subjective and objective symptoms on the other one. Interestingly, among PH-HFpEF patients, post-capillary and combined PH might be met. This assassination might be explained by the frequent remodeling of LA, elevation of LV filling pressure, and secondary lesions in the pulmonary circulation, especially among Afib patients. Finally, all those changes might provoke the transformation of post-capillary PH into the combined form of PH.

We examined the presence of PH and its severity during our trial using several echocardiographic parameters, including PAP, sPAP, mPAP, PVAT, and TR Vmax. However, the attention especially was paid to the mPAP value.

To evaluate the reasons for PH and its division into the post-capillary and combined forms, we used some TTE parameters. Those methods assisted us in the calculation of PVR and PCWP.

After the final assessment, we investigated the differences in several echocardiographic parameters between two groups of patients: those with normal sinus rhythm and those with atrial fibrillation.

Additionally, we examined the correlation of different parameters among each other. It assisted us in revealing the connection between RV dysfunction and PH with its severity and uncovering the most sensitive and informative TTE methods and parameters.

In conclusion, we attentively investigated the TTE parameters of RV dysfunction and their relation to PH and its severity. We revealed the most principal diagnostic values and criteria of TEE examination of PH-HFpEF patients.

Conclusion

62 patients were enrolled in this trial, 47 female subjects and 15 male patients among them. 35 patients had normal sinus rhythm, and 27 subjects had atrial fibrillation.

It was uncovered that a history of arterial hypertension and heart valvular disease were the most frequent concomitant conditions that were met among all enrolled patients. Therefore, those diseases might be declared as the most persistent supportive factors for the development of PH-HFpEF. Moreover, in AFib patients, the history of different types of arrhythmias was an additional and frequent associated condition that was met among all subjects (100%) and showed statistical reliability ($P < .05$).

Regarding clinical symptoms and objective findings, some important issues were uncovered that were met in 100% or almost 100% of PH-HFpEF patients, despite the presence of sinus rhythm of AFib. Those symptoms and findings were the following: difficulty breathing, decreased physical activity, tiredness and decreased working capacity, swelling in the ankle area, heart murmur while auscultation, and peripheral edema. Moreover, the statistically reliable differences ($P < .05$) were

met regarding some symptoms that were observed in AFib PH-HFpEF patients: nighttime paroxysmal dyspnea, nighttime cough, wheezing while breathing and heart palpitation.

We revealed the important association between the severity of PH and HF NYHA class. The more severe the PH degree was, the more advanced the HF NYHA class was. None of the subjects in the NYHA I class had moderate/severe PH. On the contrary, HF NYHA IV class subjects suffered from a more advanced stage of PH, especially moderate PH. The sum of those patients was 60%. The largest share was in patients with HF NYHA III class. 19 patients (79.2%) in this group had mild PH, and 5 subjects (20.8%) had moderate PH. Those differences were statistically reliable ($P < .05$).

Surveying the HFpEF patients, we concluded that PH was met almost for all subjects ($> 96\%$). Assessing the PH and its severity, we considered the mPAP value, and all conclusions were made based on that parameter. When we were interested in the severity of PH, we finally uncovered that mild and moderate PH were approximately met equally among sinus rhythm and AFib patients. Meanwhile, based on the mPAP value, none of our patients had a severe degree of PH.

Similar results were received investigating the PH severity based on TR Vmax. Based on TR Vmax, did not uncover either of the subjects with severe PH. The mild elevation of TR Vmax (2.9 – 3.4m/sec) was observed in 30 patients (despite the heart rhythm) and none of those cases were associated with moderate PH. As for the moderate elevation of TR Vmax ($> 3.4\text{m/sec}$), that abnormal value was met in 3 patients with mild and 9 patients with moderate PH (75%). Considering the reliable statistical differences ($P < .05$), we can conclude that the correlation of TR Vmax with PH severity is an important echocardiographic parameter in the diagnostic approach of PH-HFpEF patients.

An almost identical correlation was shown regarding the additional diagnostic criteria of PH, such as PVAT and RVOT VTI. Among the patients with moderate PH calculation by mPAP, the mild decline of PVAT (100-130 msec) was not met for either subject. PVAT was moderately (80-100msec) or significantly declined ($< 80\text{msec}$) among that population. As for the mild PH patients, moderate PVAT decline was frequently met (54.9%); PVAT severe decline was found in 27.5%, and finally, its minimal decrease was met among 17.6% of subjects. Based on statistically reliable differences ($P < .05$), we can conclude that correction between PH severity and PVAT decline range might seriously assist us with the diagnostic approach in PH-HFpEF subjects.

The relation between PH severity and RVOT VTI was visible also. Decline RVOT VTI $< 14\text{mm}$ was detected in 52.9% of patients with mild PH and 77.8% of patients with moderate PH. It appears that the relationship between RVOT VTI and the degree of PH is also pronounced, although. Nevertheless, the results were not statistically reliable ($P > .05$). Hence, that correlation might be used as an additional diagnostic method associated with other, statistically confirmed and reliable techniques.

The statistical data in association with postcapillary and mixed PH are noteworthy. In 35 patients with a normal sinus rhythm and 27 patients with Afib, post-capillary PH was noted in 20 subjects (57.1%) and 12 subjects (44.4%), respectively. In turn, the combined PH occurred in 3 patients among 35 subjects with sinus rhythm (8.6%). In the sinus rhythm group, PCWP was not elevated $> 15\text{mmHg}$ at all among 11 patients (31.4% of this population). Hence, elevation of LV filling pressure was not found despite the presence of mild PH. Only one patient was met in the sinus rhythm group (2.9%) for whom neither elevated PCWP nor PH was detected at all. As for the Afib group, combined PH was detected in 8 patients (29.6%). Meanwhile, we did not observe an elevation of PCWP of more than 15mmHg in 4 subjects in that population (14.8%) despite the

presence of PH; 1 subject in this group did not have either elevated PCWP or PH at all (3.7%). mPAP was less than 20mmHg; however, other, additional signs of mild PH were observed. Should be emphasized that differences in spreading the post-capillary and combined PH in sinus rhythm and Afib patients were statistically reliable ($p < .05$). By all statistical data, we should conclude again that the calculation of PCWP and PVR for evaluation of the post-capillary or combined PH as well as pre-capillary PH, is better to perform with invasive methods rather than TTE. In this scenario, we might avoid receiving any controversial results. The TTE approach might be used as a screening method but not for the final and proper diagnosis.

Based on the results of our examination, we uncovered some interesting data regarding the relation between RV dysfunction markers (TAPSE, S' , RIMP, FAC) and the severity of PH. If we try to reach a conclusion considering the FAC parameter, we might face an obstacle because FAC did not decline more than 35% in either of subjects with moderate PH; but in mild PH patients, FAC declined in 6.4% only. Hence, FAC does not have to be considered the best echocardiographic parameter for evaluating RV function, at least among patients with PH-HFpEF. TAPSE showed a quite high sensitivity. Its decline $< 20\text{mm}$ was observed in 61.7% of mild PH and 77.8% of moderate PH cases. Regarding PH severity, an important correlation showed the S' . A decline of $S' < 10\text{mm}$ was met in 77.8% of moderate PH and 61.7% of mild PH cases. Additionally, differences in S' values were statistically reliable ($P < .05$). Finally, the elevation of $\text{RIMP} > 0.54$ was the most specific and sensitive parameter for evaluation of RV function either in mild or moderate PH patients: its elevation was met in 91.5% and 100% of subjects, respectively. Nevertheless, RIMP differences did not show statistically reliable values ($P > .05$). In sum, RIMP, S' and TAPSE might be considered the best and most informative TTE parameters for evaluation of the RV systolic and diastolic function in PH-HFpEF patients.

The main limitations

The main limitations during this trial were the following: 1. For evaluation of the PH and its severity, we relied on mPAP only and basically, we disregarded the PAP and sPAP values. 2. For the evaluation of the PVR, we used the TTE methods and the Abbass formula. None of the subjects were investigated by the invasive methods. Hence, the PVR value might have been somewhat deviated from the real data that could have been obtained during an invasive study. 3. For the evaluation of the PCWP, we used the TTE methods and the Nagueh Formula. None of the subjects were investigated by the invasive methods. Hence, the PCWP value might have been somewhat deviated from the real data that could have been obtained during an invasive study.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

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Competing Interests

The authors declare no competing interests.

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Ethical Standards

The research meets all ethical guidelines, including adherence to the legal requirements of the study country.

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MICRONUTRIENTS AND THE MIND: HOW ZINC AND VITAMIN D AFFECT CHILD DEVELOPMENT

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ABSTRACT

Long-term abnormal levels of micronutrients may be involved in the etiopathogenesis of some neurological diseases^[xxv].

Methods: Participants included 226 children, almost evenly split between 109 males (48.2%) and 117 females (51.8%). The study patients and involved four patient groups. The groups monitored the growth and mental health of children aged 3-10 (mean age = 7.43 years). Group 1 consisted of individuals with micronutrient levels within the normal range; Group 2 included those with Vitamin D deficiency but normal Zinc levels; Group 3 comprised patients with Zinc deficiency and normal Vitamin D levels; and Group 4 included those with deficiencies in both micronutrients.

In these groups we studied demographic, anthropometric, laboratory data and clinical characteristics. IQ was determined according to Raven's Progressive Matrices Test.

Results: The analysis revealed a high prevalence of micronutrient deficiencies: only 30.5% of participants had normal levels of both Vitamin D and Zinc, while 23.5% had only Vitamin D deficiency, and a significant 44.7% suffered from both Vitamin D and Zinc deficiency. Only 1.3% had isolated Zinc deficiency.

The clinical characteristics observed in children with low IQ closely resemble those associated with Vitamin D and Zinc deficiencies. Specifically, these children show a significantly higher prevalence - Hair loss (66.67% vs. 13.37%, $p < 0.0001$); Dry kin (62.50% vs. 36.14%, $p = 0.0122$); Skin rush (50.00% vs. 15.35%, $p < 0.0001$); Growth delay (33.33% vs. 12.87%, $p = 0.0079$); Physicalactivity (37.50% vs. 68.32%, $p = 0.0026$); Positive good (45.83% vs. 81.19%, $p = 0.0001$); Emotional instability (58.33% vs. 22.28%, $p = 0.0001$); Feeling if weakness (54.17% vs. 18.81%, $p = 0.0001$); Synthetic fluids (79.17% vs. 55.94%, $p = 0.0291$);

Conclusions: This study revealed compelling evidence of a significant correlation between deficiencies in Vitamin D and Zinc and both mental health outcomes and physical clinical characteristics in children.

The results highlight the urgent need for early detection of deficiencies and the implementation of targeted nutritional interventions as part of routine pediatric care.

Keywords: Vitamin D and Zinc deficiencies, IQ, physical development.

Introduction

The divalent cation zinc is an integral requirement for optimal cellular processes, whereby it contributes to the function of over 300 enzymes, regulates intracellular signal transduction, and contributes to efficient synaptic transmission in the central nervous system^[xxvi]. Zinc is a nutritional trace element that has an essential role in neuronal activity and, consequently, in brain development. Zinc is considered essential for oligodendrogenesis, neurogenesis, neuronal differentiation, thitemattergroeth, and multiple biological and physiological roles in neurobiology. Zinc is found in

the brain, where it contributes to the structural development and proper functioning of the brain. It is directly involved in the process of neuron myelination and impulse conduction^[xxvii]. Zinc has an essential role in neuronal activity and, consequently, in brain development^[xxviii]. Neurons containing “free ionic zinc” (Zn²⁺) are found in various areas of the brain, including the cortex, amygdala, olfactory bulb, and hippocampal neurons, which appear to have the highest concentration of zinc in the brain. Studies show that zinc has been found to influence N-methyl-D-aspartate (NMDA) and gamma aminobutyric acid (GABA), neurotransmitter systems believed to be involved in obsessive-compulsive disorder (OCD)^[xxix] and in anxiety disorders^{[xxx][xxxi]}. Zinc deficiency contributes to the development of severe diseases in the intranatal period, such as: hydrocephalus, microcephaly, anencephaly. And in pediatric age children, cognitive development delay, symptoms of ADHD, motor development delay, attention deficit, behavioral problems, spatial perception.

Mental health disorders, such as depression, anxiety, and cognitive decline, have become increasingly prevalent worldwide. While genetic, environmental, and psychosocial factors contribute to these conditions, nutritional status—especially the sufficiency of micronutrients like Vitamin D—has gained considerable attention. Vitamin D receptors (VDR) and enzymes responsible for its activation are present in many areas of the brain, including the hippocampus, which is critical for mood regulation and cognitive function^[xxxii]. Epidemiological data suggests that adolescents with insufficient Vitamin D levels are at increased risk for cognitive impairment. The vitamin D receptor (VDR) and the 1-alpha-hydroxylase enzyme that converts vitamin D to its active form are expressed in the human brain^[xxxiii]. Through its effects on neuronal proliferation, differentiation, migration, and apoptosis, vitamin D may play an important role in brain development^{[xxxiv][xxxv]}.

Vitamin D exerts neuroprotective effects by:

- Regulating the synthesis of neurotrophic factors such as nerve growth factor (NGF)
- Modulating neurotransmitters, including serotonin and dopamine
- Reducing inflammation and oxidative stress in the central nervous system ^{[xxxvi][xxxvii]}

Studies have shown that Vitamin D enhances neuroplasticity and supports the survival of neurons. It also participates in calcium homeostasis within neural tissues, which is essential for synaptic function and neurotransmission. However, emerging research has demonstrated a significant link between Vitamin D levels and various aspects of mental health, including depression, anxiety, and cognitive function. In addition, it has been proposed that prenatal vitamin D deficiency may increase the risk of neuropsychiatric disorders, such as schizophrenia^[xxxviii]. There are inconsistent small effects of vitamin D deficiency on postnatal brain function^[xxxix]. Low levels of 25-hydroxyvitamin D (25[OH]D) are frequently found in patients with depression or Alzheimer disease^{[xl][xli][xlii]}, and a meta-analysis of observational studies showed lower Mini-Mental State Examination scores in patients with lower serum vitamin D concentrations (25[OH]D <20 versus ≥20 ng/mL)^[xliii].

Methods: Participants included 226 children, almost evenly split between 109 males (48.2%) and 117 females (51.8%). The study patients and involved four patient groups. The groups monitored the growth and mental health of children aged 3-10 (mean age = 7.43 years). Group 1 consisted of individuals with micronutrient levels within the normal range; Group 2 included those with Vitamin D deficiency but normal Zinc levels; Group 3 comprised patients with Zinc deficiency and normal Vitamin D levels; and Group 4 included those with deficiencies in both micronutrients.

In these groups we studied demographic, anthropometric, laboratory data and clinical characteristics. Anthropometric data were studied: by studying the physical characteristics of the children, measuring, weighing and calculating BMI. IQ was determined according to Raven’s Progressive Matrices Test. Statistical analysis for quantitative indicators, the mean (Mean) and standard deviation (SD) were

calculated. For qualitative indicators - absolute and percentage values. The difference between the groups was determined: for quantitative indicators - using the Student's t criterion; for qualitative indicators - using the Fisher's exact criteria, the relationship between quantitative factors was determined by correlation analysis - Pearson's test; for qualitative indicators - Spearman's test

Results: The analysis revealed a high prevalence of micronutrient deficiencies: only 30.5% of participants had normal levels of both Vitamin D and Zinc, while 23.5% had only Vitamin D deficiency, and a significant 44.7% suffered from both Vitamin D and Zinc deficiency. Only 1.3% had isolated Zinc deficiency.

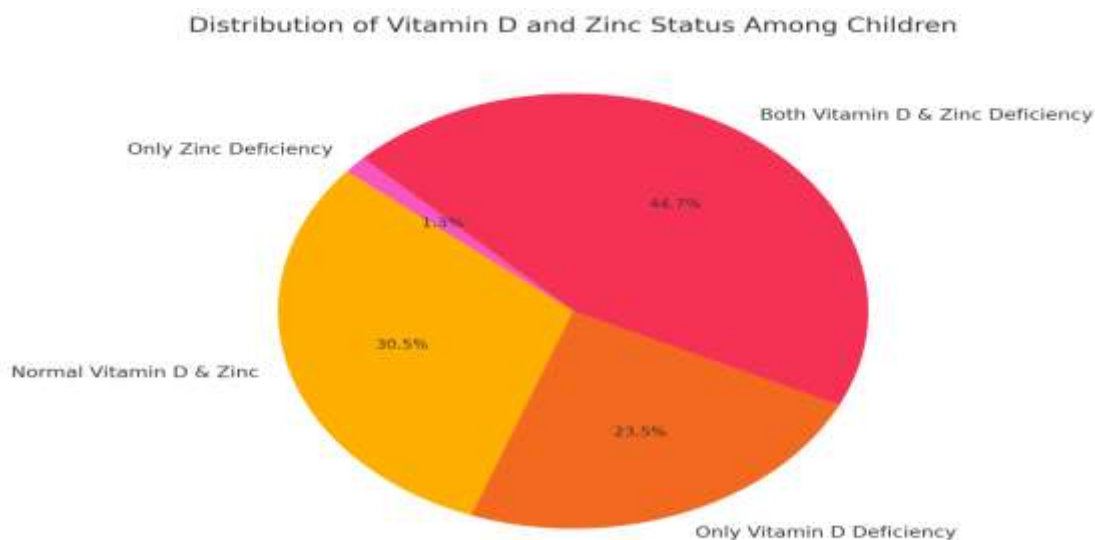


Figure 1. Distribution of Vitamin D and Zinc Status Among Children

We obtained interesting results and correlational links between Vitamin D and Zinc deficiencies and both mental health and various clinical characteristics. In the case of high IQ, the average values of vitamin D and zinc are significantly higher, while the values of zinc are lower than normal in the case of low IQ. These data allowed us to consider vitamin D and zinc concentrations as a predictive factor for low IQ in children.

The clinical characteristics observed in children with low IQ closely resemble those associated with Vitamin D and Zinc deficiencies. Specifically, these children show a significantly higher prevalence of excessive sweating, dry skin, skin rashes, brittle nails, dental caries, growth retardation, emotional lability, and sensations of weakness.

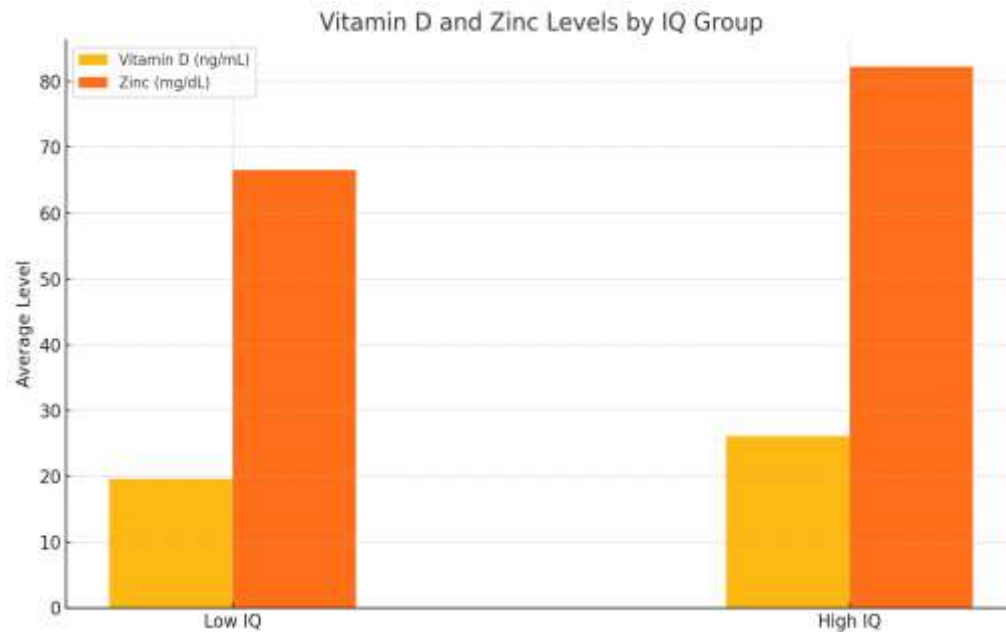


Figure 2. Vitamin D and Zinc Levels by IQ Group

The clinical characteristics observed in children with low IQ closely resemble those associated with Vitamin D and Zinc deficiencies. Specifically, these children show a significantly higher prevalence of excessive sweating, dry skin, skin rashes, brittle nails, dental caries, growth retardation, emotional lability, and sensations of weakness.

Factors	Low IQ N=24		High IQ N=202		F	p
	n	%	n	%		
Social status (+)	13	54.17	174	86.14	16.33	0.0001
Gen. Thyreiod pathology	12	50.00	70	34.65	2.19	0.1406
Gen. Obesity	9	37.50	77	38.12	0.00	0.9532
Gen. Diabetes	11	45.83	81	40.10	0.29	0.5907
Hirsutism	5	20.83	66	32.67	1.39	0.2393
Hair loss	16	66.67	27	13.37	47.52	<0.0001
Hyperhidrosis	15	62.50	87	43.07	3.29	0.0711
Dry skin	15	62.50	73	36.14	6.39	0.0122
Skin rush	12	50.00	31	15.35	17.90	<0.0001
Brittle nails	8	33.33	22	10.89	9.70	0.0021
Dental caries	13	54.17	39	19.31	15.60	0.0001
Growth delay	8	33.33	26	12.87	7.19	0.0079
Physical activity	9	37.50	138	68.32	9.25	0.0026
Positive mood	11	45.83	164	81.19	16.32	0.0001
Dizziness	4	16.67	15	7.43	2.38	0.1241
Emotional instability	14	58.33	45	22.28	15.31	0.0001

Feeling of weakness	13	54.17	38	18.81	16.32	0.0001
Increased appetite	7	29.17	56	27.72	0.02	0.8821
Balanced nutrition	5	20.83	81	40.10	3.40	0.0666
Synthetic fluids	19	79.17	113	55.94	4.82	0.0291

Table 1. Comparison of clinical characteristics by IQ

Case report: A 5-year-old boy was referred to our endocrinology department due to assess endocrine status. He was born in a family with normal psychosocial development, at 42 weeks, from the first pregnancy, with a birth weight of 3.5 kg and a length of 51 cm. His Apgar scores were 9-10, and his medical history is unremarkable, with no known genetic diseases. He was breastfed for only a month. According to his parents, he could stand independently at 9 months and started walking at 15 months. He has a younger sister with normal mental and physical health for her age. The patient's IQ is low Raven's Progressive Matrices Test. Among of Wechsler Preschool and Primary Scale of Intelligence (WPPSI) IQ was score of 85, and his bone age corresponds to her chronological age of years. According to his parents, he has diffuse hair loss, delayed wound healing, frequent diarrhea, decreased immunity, growth failure with delay, sweating, symptoms of ADHD, emotional dysregulation, anxiety, learning/memory problems, obsession with food (he feeds mainly on carbohydrates), and attachment issues.

- Weight: 19 kg (50th percentile)
- Height: 101 cm (8th percentile)
- BMI: 18.6 kg/m² (88th percentile)
- Target height: 167 cm (10th percentile)
- Tanner stage: 1 (ax: 1; testies1:1.5; penis: 2cm.)

Consulted by a neurologist: The patient's IQ is low according to Raven's Progressive Matrices Test. The assessment score according to the Wechsler scale is 85. No pathology is evident in the cranial nerves. The patient walks in a straight line, and full range of motion is present in the limbs. Strength is preserved. The patient stands firmly in the Romberg posture. Coordination tests are performed. Reflexes are symmetrical (S=D). No pathological reflexes are evident.

Test	Result
TSH/FT ₄ /anti-Tpo	Normal Range
Total IgA; tTG IgA, tTG IgG	Normal Range
Ca/K/Na/Mg/Fe	Normal Range
Zn (NR: 80-120 µg/dL)	61.00 µg/dL
25OHD (NR: 30-100 ng/ml)	19.2 ng/ml

Table 2. Blood test.

Blood test result shows, that the thyroid gland is functioning ideally, and the patient does not have any absorption problems. Microelements are normal, except for zinc and vitamin D, which are in deficient levels.

Discussion: The findings of this study provide important insights into the complex and interconnected role that micronutrients—specifically Vitamin D and Zinc—play in both the physical and mental

health of children. The observed associations between deficiencies in these micronutrients and various clinical symptoms, including low IQ, emotional lability, growth retardation, and dermatological issues, highlight the systemic impact of nutritional imbalance.

Vitamin D has long been recognized for its role in calcium regulation and bone health, but emerging evidence increasingly points to its involvement in neurodevelopment and mood regulation. Its receptors are widely distributed in the brain, particularly in regions responsible for emotion and cognition, such as the hippocampus. Similarly, Zinc is involved in over 2,000 enzymatic reactions and plays a crucial role in neurotransmission, synaptic plasticity, and immune function. The strong positive correlation observed between Vitamin D and Zinc levels in this study ($r = 0.696$, $p < 0.001$) suggests not only shared dietary sources but also potential biological synergy in developmental pathways.

Children with combined deficiencies showed significantly worse clinical outcomes compared to those with adequate micronutrient levels. These children exhibited more frequent occurrences of skin disorders (e.g., dryness, rash, brittle nails), metabolic concerns (e.g., increased BMI), and psychological symptoms (e.g., fatigue, emotional instability, lower IQ). Such manifestations are consistent with known mechanisms by which Vitamin D and Zinc influence inflammation, oxidative stress, and neuroendocrine function.

Conclusions: This study revealed compelling evidence of a significant correlation between deficiencies in Vitamin D and Zinc and both mental health outcomes and physical clinical characteristics in children. Children with lower levels of these micronutrients were more likely to experience emotional instability, lower IQ scores, and physical symptoms such as excessive sweating, dry skin, brittle nails, and growth delays.

These findings emphasize the synergistic role of Vitamin D and Zinc in supporting not only proper physical development but also cognitive and emotional well-being. Maintaining adequate levels of both nutrients is therefore essential for ensuring optimal child health. The results highlight the urgent need for early detection of deficiencies and the implementation of targeted nutritional interventions as part of routine pediatric care.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

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Competing Interests

The authors declare no competing interests.

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Ethical Standards

The research meets all ethical guidelines, including adherence to the legal requirements of the study country.

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DYSTROPHIC EPIDERMOLYSIS BULLOSA TREATMENT WITH FIBROBLAST: (REVIEW)

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The genetic abnormalities that cause blisters on the skin and mucosa are called epidermolysis bullosa (EB). EB has four primary types: acquired, simple, junctional, and dystrophic, each with many variants [1]. Mutations in the COL7A1 gene produce Recessive Dystrophic Epidermolysis Bullosa (RDEB), an EB variation that can be treated using fibroblast engineering. Lack of type VII collagen and anchoring fibrils in the dermal-epidermal junction (DEJ) causes blisters and soft tissue scarring. RDEB has no cure, so researchers have investigated fibroblasts, which make type VII collagen, as a treatment. In the realm of cell-based therapies for RDEB, two prominent types are considered: allogeneic fibroblasts, which are cultured from parents or unrelated individuals, and autologous fibroblasts, which are cultured directly from patients themselves. So, in the first clinical study, Wong et al. utilized allogeneic fibroblasts as potential type VII collagen producers. They injected allogeneic fibroblast into the non-wounded skin of 5 subjects with RDEB [2]. 2 to 3 months of follow-up were required. Type VII collagen at the DEJ demonstrated a 1.5- to 2-fold increase, while anchoring fibrils showed a 1.5-fold increase. Autoantibodies to collagen VII were not developed in any of the patients, and skin biopsies showed no significant immune reactions despite their abnormal morphology. Furthermore, they indicate that allogeneic fibroblasts have a significant impact on elevating the recipients' own COL7A1 mRNA levels, resulting in more significant deposition of mutant type-VII collagen at the DEJ and the development of additional rudimentary anchoring fibrils. This mutant protein may possess some functionality and improve adhesion at the DEJ [3]. The injection of allogeneic fibroblasts into chronic wounds in RDEB patients may be a feasible and beneficial therapy for wound healing. However, in cell-based therapy, some clinical trials prefer to employ products that have already been approved. For instance, a suspension of allogeneic human dermal fibroblasts (ICX-RHY-013) has been presented in a sterile solution and contains HypoThermosol-FRS (BioLife Solutions Inc., Bothell, WA, United States). According to the European Medicines Agency, ICX-RHY-013 is classified as an orphan medicinal product designed to treat EB [4]. In a clinical study, ICX-RHY-013 increased initial healing in RDEB wounds. Results showed that a single injection of fibroblasts improved erosion healing within 28 days but not after that. During the other trial, fibroblasts and vehicle injections resulted in a 50% reduction in the area of chronic ulcers after 12 weeks. Other clinical studies have also investigated the benefits of ICX-RHY-013 in improving RDEB wounds, but the results have not been published as an original paper [5]. Possible explanations for these differences are that the two trials used different types of wounds, varied doses and frequencies of injections, varied outcome measures, and different patient populations. The epidermis is affected by erosions, which are superficial wounds, whereas ulcers are deeper wounds that extend into the

dermis or subcutaneous tissue. Erosions may heal faster than ulcers but also be more prone to recurrence. In a comparative study, Moravvej et al. investigated the efficacy of cultured allogeneic fibroblasts administered via intradermal injection for the treatment of RDEB wounds, juxtaposed against the effects of fibroblasts situated on scaffolds constructed from amniotic membranes (FAMS). Following periods of 2 and 12 weeks, it was observed that the intradermal injection of fibroblasts demonstrated superior performance in promoting wound healing compared to FAMS. These findings underscore the potential of fibroblast injection as a viable and promising therapeutic strategy for augmenting recovery in RDEB wounds. It is well known that cell and gene engineering approaches are one of the most promising approaches for treating incurable diseases [6]. This vision has led to the design of some clinical trials for treating EB, especially RDEB. Considering this, Lwin et al. designed a self-inactivating lentiviral platform for phase I assessment that carries a codon-optimized COL7A1 cDNA controlled by a human phosphoglycerate kinase promoter [7]. In this open-label trial, four grownups with RDEB were inoculated with modified autologous fibroblasts intradermal three times and followed for a year. Safety, autoimmune responses to recombinant type VII collagen, expression of type VII collagen, and the presence of transgenes were evaluated. Modified fibroblasts showed good tolerance, with no severe adverse reactions or autoimmune responses to recombinant type VII collagen. Regarding efficacy, three out of four subjects showed a significant increase in type VII collagen expression in the injected skin, with two maintaining elevated levels for up to 12 months. Despite the absence of fully mature AFs, transgenes were detected in the subjects' injected skin after a year. In this innovative human study, lentiviral fibroblast gene therapy is proven harmless and possibly effective, as evidenced by the presence of COL7A1 transgene and the renovation of type VII collagen in treated skin one year after gene therapy. As a result of these findings, phase II clinical trials can advance clinical assessment [8]. Our literature review serves as the basis for conducting clinical studies involving more significant numbers of fibroblast cells and participants in individuals with RDEB, paving the way for further research in this area. However, further research is required to clarify the most effective procedures for fibroblast therapy, such as determining the best cell sources, delivery systems, and treatment schedules. To summarize, dermal fibroblast therapy has significant potential as a beneficial tool in cell-based therapies and regenerative treatments for skin disorders.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

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BURN WOUNDS TREATMENT WITH FIBROBLASTS: (REVIEW)

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The skin burns can result from flames, hot liquids, chemicals, and hot surfaces. Intricacy and elevated morbidity make burn wounds hard to cure [1]. Recent research shows that burns kill 180,000 people annually. Burns are defined by intensity and skin and tissue damage. Epidermis injuries are first-degree. Second-degree burns affect the dermis. But third-degree burns destroy all skin layers and the underlying structures. Fourth-degree burns, which penetrate the epidermis and dermis, can cause necrosis and damage muscle and bone in the subcutaneous area [2]. Burn wounds can cause mental, emotional, and physical problems and death from bacterial infections. Researchers are studying regenerative medicine and cell therapy to enhance burn treatments by promoting wound healing and skin regeneration, enhancing the quality of life for burn patients, and reducing the need for invasive procedures. In vitro tissue engineering and human skin allografts, especially those from living first-degree relatives, have improved wound healing, decreased microbial wound contamination, and reduced burned individual deaths. Additionally, 3D bioprinting and employing stem cells or fibroblasts to treat and regenerate burn wounds are being studied [3]. Research in regenerative medicine, cell-based therapy, and tissue engineering may improve burn treatment and patient outcomes. Based on our scoping review, fibroblast therapy has been used in clinical trials for healing burn wounds in two published clinical studies and one letter [4]. The extracellular matrix components such as collagen and elastin, growth factors, and cytokines are produced by fibroblasts and promote cell proliferation, migration, and differentiation. Fibroblasts are being studied as a potential therapy for skin regeneration and burn wound healing [5]. Fibroblasts can be obtained from the patient's skin or a donor source, such as a tissue bank. Allogeneic fibroblasts are a better option than autologous fibroblasts due to a decreased likelihood of donor site morbidity and the ability to obtain many cells for transplantation. Fetal fibroblasts exhibit superior proliferation, extracellular matrix component synthesis, and senescence resistance compared to adult fibroblasts. A study evaluated the safety, feasibility, and potential efficacy of using amniotic membranes seeded with fetal fibroblasts for burn patients to heal their donor sites faster. Ten patients with burns covering 10–55% of their body were enrolled in the study. Each patient's donor site was divided into three equal parts and treated with Vaseline gauze (control group), amniotic membrane (AM group), or amniotic membrane seeded with fetal fibroblasts (AM-F group). According to the results, using amniotic membrane seeded with fetal fibroblasts for treating burn patients' donor sites was safe and significantly sped up the healing process compared to the control group. Fetal fibroblasts have been found to be a promising therapeutic approach for skin disorders, such as burn wounds. Nevertheless, additional research is required to comprehend their effectiveness and safety entirely. More extensive trials are needed with larger populations to draw accurate conclusions [6]. The

effectiveness of low-level laser therapy (LLLT) and autologous fibroblast transplantation for healing grade 3 burn wounds in diabetic patients was evaluated in an open-label study. Patients with grade 3 burn wounds and diabetes were enrolled in the study. The treatment protocol involved LLLT and autologous fibroblast transplantation, and the results showed complete healing of wounds within 4–6 weeks without any adverse events. According to the study, using LLLT and autologous fibroblast transplantation together is a secure and efficient cure for grade 3 burn injuries among diabetics. The study indicates that the treatment protocol could be a hopeful therapeutic method for healing burn wounds, especially for diabetic patients who are more prone to complications [7]. Mobility and unsightly appearance are caused by burn contractures, which result from the tightening of the skin and underlying tissues during healing [8].

The United States phase 1/2 clinical trial (NCT01564407) is assessing the safety of ICX-RHY-013 for treating stable, restrictive scars in burn victims [9]. Allogeneic human dermal fibroblasts were utilized to address burn contractures by administering fibroblast injections near the joints. While patients experienced an enhanced range of motion in the contracted joint after 12 weeks, the improvement was not statistically significant in this study. The study suggested that allogeneic human dermal fibroblast injection is safe and well-tolerated, offering a potential nonsurgical treatment for burn scar contractures. Allogeneic fibroblasts, sourced from donors, can be genetically engineered to enhance their potential for wound healing. This approach eliminates the need for harvesting fibroblasts from the patient's skin, making it highly valuable for burn wound treatment [10]. Clinical trials have demonstrated that fibroblast therapy is a more effective treatment for healing burn wounds compared to other approaches, including, low-level laser treatment, pressure garment therapy, hyperbaric oxygen therapy, moist exposed burn ointment (MEBO), and evaluation of adipose-derived mesenchymal stem cells. However, further investigation is needed to determine the protection and effectiveness of fibroblast therapy in various wound-healing contexts.

Declarations

The manuscript has not been submitted to any other journal or conference.

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FIBROBLASTS THERAPY AND DERMAL COSMETICS: (REVIEW)

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Fibroblast cells have the ability to improve skin conditions through regenerative medicine and cell-based therapies. The purpose of this scoping review is to assess the contribution of fibroblast cells to skin homeostasis and extracellular matrix deposition in clinical trials involving skin disorders and cosmetic applications. Age-related physiological changes include skin texture and function. Wrinkles, folds, and diminished elasticity characterize skin aging. These cosmetic issues can be addressed with various fillers [1]. Some fillers may be more dangerous and ineffective than others. Thus, before using fillers, one must grasp their properties and injection procedures. With the use of fibroblasts, skin cells that produce collagen and elastin, fillers have improved. Fibroblasts have been cultured and injected as fillers to enhance skin quality and reduce aging signs [2]. Owing to the simplicity of the direct fibroblast injection technique, it has been the subject of extensive research, particularly for its potential to enhance facial aesthetics. Table 4 presents a comprehensive list of published clinical trials on fibroblast therapy for aesthetic purposes, including the number of studies and the time frame of the research. For example, Weiss and colleagues investigated the effectiveness and potential side effects of injecting autologous live fibroblasts to address facial contour defects like acne scars and nasolabial folds. They administered live fibroblasts in three doses, spaced 1 to 2 weeks apart, and assessed the results at 1, 2, 4, 6, 9, and 12 months after the initial injection and compared with placebo. The results show that using live fibroblasts improved skin problems and acne scars more than the placebo. The statistical connotation of this difference was observed at the 6-month mark. Patients who received live fibroblast treatment experienced ongoing positive outcomes, with answer degrees of 75.0% and 81.6% at the 9-month and 12-month check-ins, respectively. Crucially, over 12 months, no severe side effects were reported as a consequence of the treatment [3]. Nevertheless, it is crucial to acknowledge that further research and clinical trials may be necessary to validate and extrapolate these findings to a broader population. Consequently, additional studies focusing on nasolabial folds [4], acne scars, and nasojugal grooves have been designed to corroborate the applicability of fibroblast injections. Moreover, a separate study comparing autologous cultured fibroblast injections with HA fillers revealed superior improvements in the fibroblast groups without any associated side effects, consistently enhancing aesthetic appearance [5]. These findings have encouraged researchers to explore alternative delivery methods, including combining fibroblasts with other molecules. As a case in point, Geldenhuys and his team combined platelet-rich plasma (PRP) with cultured fibroblasts. They administered a single dose to twenty adults with nasolabial folds and tracked their progress for nine months. The results included an impressive 80% increase in skin thickness adjacent to the nasolabial fold, heightened dermal density, enhanced skin hydration, improved sebum quality, and reduced wrinkle depth.

This study underscores the potential of PRP combined with cultured fibroblasts as a viable, long-lasting, and well-received option for non-invasive facial rejuvenation and wrinkle reduction, although direct comparisons with single PRP or fibroblast injections were not made [6]. Expanding upon the investigation of novel combinations, Wang and colleagues conducted a study in which they compared a blend of fibroblast and keratin to HA as a control for the treatment of neck wrinkles in 30 individuals. They administered two doses at two-week intervals and gathered data at multiple time points up to 12 months post-treatment. The findings demonstrated that the fibroblast and keratin mixture maintained a substantial filling effect, ranging from 70 to 90%, even at 12-months. In contrast, HA effects persist for approximately 6 months. These findings indicate that a mixture of fibroblasts and keratin could be a more practical option for reducing neck wrinkles than traditional HA fillers. These results emphasize the importance of continued aesthetic medicine research [7]. A summary of the literature indicates that fibroblasts, alone or in combination with other molecules, significantly affect durable and reliable aesthetic outcomes. Furthermore, fibroblasts have been reported to be safe and well-tolerated without adverse reactions or immunological responses. Additional research is necessary to establish the ideal quantity and dosage of cells for each treatment, compare fibroblasts with approved drugs as control groups, and track patients' long-term outcomes and treatment results [8]. Our article highlights the advantages of fibroblast therapy in treating skin conditions such as skin alterations and cosmetic reasons. Fibroblasts possess remarkable regenerating capabilities, making dermal fibroblast therapy crucial in cell-based and skin regenerative treatments. Nevertheless, additional research is required for more disorders and cosmetic applications.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

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THE PSYCHOLOGICAL EFFECT OF THE COVID-19 PANDEMIC ON THE NEXT GENERATION

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ABSTRACT

The World Health Organization's declaration of COVID-19 as a pandemic has become the most important challenge of 2020, which has had a huge impact on almost every area in the world. The spread of the virus has proved to be an important challenge both in terms of economic and legal and health, life in social isolation has been associated with stress for many people.

This article is about the psychosomatic impact of the pandemic on people's mental health, in particular on the next generation. Discussing this issue in the light of the widespread spread of the pandemic is undoubtedly extremely interesting and relevant.

The potential long-term psychological impact of the pandemic on the mental and emotional development of the next generation is interesting. This article is about the challenge that COVID-19 has created for the next generation and what it can mean for their future lives.

Keywords: COVID-19, mental health, awareness of microbes.

In the spring of 2020, the declaration of a state of emergency affected the emotional state of people in order to prevent the spread of COVID-19.

"Mental health is part of physical health. We don't have the luxury of continuing to perceive him from another perspective.

The pandemic has brought unprecedented changes for everyone, especially in children's lives, the closure of kindergartens and schools, and social isolation, watching parents stress. "Due to the pandemic restrictions of movement, lockdowns, children have spent important years of their lives away from family, friends, kindergartens, school classrooms, which are integral elements of childhood 'impact is important and this is just the tip of the iceberg'.

Even before the pandemic, a number of children were faced with mental health problems. The actions taken by governments to meet these critical needs are very small. The fact is that inadequate importance is the relationship between children's mental health and their future life achievements."

The impact on the mental health and well-being of children and young people is evidenced by the UNICEF study, which found that at least one in every seven children had a direct impact on lockdowns, the cessation of daily life routines, education, recreational activities, and incites many young people to fear the future. This is evidenced by an online study conducted in China in 2020 on "On the Sensitivity of the World's Children", which states that a third of respondents experienced fear and anxiety.

The UN Committee on the Rights of the Child recommends that countries should unambiguously take care of the protection of primary rights of children, such as education, physical and mental health, protection against violence, etc. In Georgia, where all 5 children are starving the state, the state does not have a social security system that will help families overcome unexpected strikes, such as the situation caused by the pandemic.

The closure of educational spaces "staying" in the new generation homes significantly had a negative impact on their psycho-emotional state, since these spaces are not only a place for academic knowledge, but they are recognized spaces for the social and emotional development of children.

Numerous studies have shown that children's psychological problems have been identified as new behavioral problems, as well as worsening existing behavioral disorders; Also with somatic symptoms such as headache, sleep disturbance, fear, arousal, nervousness, stress, appetite, abdominal pain, dizziness, muscle pain, difficulty breathing, air failure, heart rate, nightmares; restlessness; Symptoms such as nausea, vomiting, heart leaving, mind-boggling...

During the pandemic, uncertainty, lockdown, remote learning, social distancing have created an unpredictable environment that has helped to raise anxiety levels in children.

Roasting the next generation of psychoemotional states during a pandemic can be conditionally divided into several aspects:

1. With the loss of social interaction, young children missed critical years of face-to-face communication, which was necessary for the development of social skills, compassion and emotional intelligence, such as establishing early friendships and participating in group games.

2. In terms of academic context, school closures and remote learning have led to a gap in the educational progress of many children, influenced their academic performance and, in some cases, reduced interest in learning. Possible symptoms in this regard include problems with learning motivation and concentration and refusal to go to school. Distance learning and lack of structured routines have hampered skills such as attention, focus, and self-discipline.

3. Changing family dynamics, the observation of children, stressed parents affected their sense of safety, which led to a sense of hyperresponsibility or, conversely, distrust of stability.

However, it should also be said that despite these challenges, I read in studies that some children have shown excellent adaptability, as a number of families have been able to contribute to the emotional resilience of children, the supportive family environment has been able to provide potential psychological assistance in the fight against the impact of external factors on them.

4. An important point is the increased awareness of microbes and hygiene, which has developed enhanced concerns about illness and cleanliness in children raised during the pandemic, leading to potential health anxiety. As a long-term effect, we will see how this increased alertness to hygiene in adulthood can potentially lead to obsessive-compulsive predispositions, germaphobia, or increased anxiety about health risks.

5. Increased screen time and increased dependence on it during school, socialization and entertainment, children have developed new digital attitudes that can have a lasting impact on their attention range, communication skills, and mental health risks such as depression.

To do this, as a digital detox strategy, to reduce on-screen addiction, schools, parents and mental health professionals can play an important role in setting healthy boundaries around the use of technology.

According to a study conducted in the United States, 27% of parents and about 14% of children have mental health problems during the pandemic, there was a higher degree of distress in families of single parents and in families where small children could no longer receive social services such as nanny services, or preschool points, e.g. a garden.

Due to the presence of economic difficulties in Georgia, these percentages may be higher, unfortunately the research in this regard has not yet been conducted in our country.

Development delays, academic failures, disruptions in communication and social skills can affect future interpersonal relationships, self-confidence and adaptation to the social environment.

There is a need for programs that have been implemented on social-Emotional Learning Curriculum, To help children recover their social and emotional skills lost during the pandemic, To address and support the post-COVID-19 pandemic of a child, the need for child-friendly mental health services is needed to alleviate the problem in the post-pandemic psychological problems and challenges, parenting programmes are important., Which Support Heartfelt, Attentive environment and promotes the mental health of the parent and caregiver, Which Provides mental health support in schools, Through quality service and positive relationships. Investing in the mental health of children and adolescents in the sectors is also important, To prevent, Introduction of an entirely public approach to incentives and treatment. Disruption of silence around mental health, By coping with existing stigmas and promoting a better understanding of mental health and paying more attention to the experiences of children and young people.

In conclusion, we can say that there is no doubt that the pandemic has opened a completely new dynamic, which allows us to achieve a significant orientation of psychosomatic policy to counter the pandemic, so that we can create an effective model of psychosocial regulation in the context of the crisis caused by such a pandemic, because children of the "pandemic" face unique psychological obstacles. Standing, but they also develop resilience that can serve them in the future challenges of life.

While the psychological impact of the pandemic on the next generation may continue, awareness, support and the right appeal of resources by families, schools and mental health specialists, through collective efforts, we can work to create a future where these children They will be successful despite the difficulties they face.

Declarations

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CLASSICAL AND CONTEMPORARY APPROACHES TO THE IMPACT OF QUALITY MANAGEMENT ON FINANCIAL PERFORMANCE IN THE FOOD INDUSTRY

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ABSTRACT

This article explores the evolving relationship between quality management systems (QMS) and financial performance in the food industry, using Azerbaijan as a case study. Drawing on both classical and contemporary quality management theories, the study examines how frameworks such as ISO 22000, HACCP, and Total Quality Management have transitioned from technical tools to strategic assets. The paper reviews theoretical foundations from classical thinkers like Taylor and Fayol and contrasts them with modern quality systems that incorporate risk-based thinking, customer satisfaction, and digital traceability. Empirical analysis focuses on Azerbaijan's food exports between 2017 and 2025, highlighting how the adoption of international quality standards contributed to increased export volumes, product diversification, and resilience amid global disruptions such as COVID-19. The findings demonstrate that quality management not only ensures compliance and operational efficiency but also serves as a key enabler of export competitiveness and financial sustainability. The article concludes that in emerging markets, strategic quality investments supported by institutional frameworks can drive significant economic returns.

Keywords: Quality Management, Financial Performance, ISO 22000, HACCP, Azerbaijan Food Exports, Total Quality Management, Strategic Compliance

XÜLASƏ

Bu məqalədə Azərbaycan nümunəsi əsasında qida sənayesində keyfiyyət idarəetmə sistemləri (QİS) ilə maliyyə göstəriciləri arasında inkişaf edən qarşılıqlı əlaqə araşdırılır. Tədqiqat həm klassik, həm də müasir keyfiyyət idarəetmə nəzəriyyələrinə əsaslanaraq, ISO 22000, HACCP və Ümumi Keyfiyyət İdarəetməsi (TQM) kimi çərçivələrin texniki vasitədən strateji resursa çevrilmə prosesini təhlil edir. Məqalədə Taylor və Fayol kimi klassik nəzəriyyəçilərin nəzəri əsasları araşdırılır və bunlar risk əsaslı düşüncə, müştəri məmnuniyyəti və rəqəmsal izlenebilirlik kimi elementləri özündə birləşdirən müasir keyfiyyət sistemləri ilə müqayisə olunur. Empirik analiz 2017–2025-ci illər ərzində Azərbaycanın qida məhsulları ixracına yönəlmişdir və göstərir ki, beynəlxalq keyfiyyət standartlarının tətbiqi ixrac həcmlərinin artmasına, məhsul çeşidlərinin diversifikasiyasına və COVID-19 kimi global pozuntular qarşısında dayanıqlılığın möhkəmlənməsinə töhfə verib. Tədqiqatın nəticələri sübut edir ki, keyfiyyət idarəetməsi yalnız uyğunluq və əməliyyat səmərəliliyi deyil, həm də ixrac rəqabət qabiliyyəti və maliyyə dayanıqlılığı üçün əsas hərəkətverici qüvvədir. Məqalə belə qənaətə gəlir ki, inkişaf etməkdə olan bazarlarda institusional çərçivələrlə dəstəklənən strateji keyfiyyət yatırımları əhəmiyyətli iqtisadi nəticələr verə bilər.

Açar sözlər: Keyfiyyət İdarəetməsi, Maliyyə Göstəriciləri, ISO 22000, HACCP, Azərbaycanın Qida İxracı, Ümumi Keyfiyyət İdarəetməsi, Strateji Uyğunluq

Introduction

The dynamic interplay between quality management systems (QMS) and enterprise-level financial performance has long captured the interest of economists, policymakers, and food industry professionals. In today's globalized and highly regulated food sector, the strategic application of quality standards is no longer viewed as an operational choice but as a key determinant of competitiveness, sustainability, and market access. From early total quality management (TQM) doctrines to modern ISO 22000 and HACCP-based food safety frameworks, the quality-performance linkage has evolved to reflect not only internal efficiencies but also broader reputational, regulatory, and economic implications.

Despite significant advancements in business management thought over the past century, many foundational concepts about quality, cost, and output efficiency continue to influence how organizations view their investment in quality control systems. Classical theories have laid the groundwork for understanding value creation and resource optimization, while contemporary approaches incorporate risk-based thinking, customer focus, and digital transformation.

The purpose of this article is to examine classical and contemporary approaches to the quality–financial performance relationship, with a particular focus on empirical developments in Azerbaijan's food industry between 2017 and 2025. Using this hybrid theoretical lens, the article aims to provide a nuanced framework for understanding how quality strategies influence profitability, market penetration, and long-term enterprise resilience.

Theoretical Foundations of Quality Management and Financial Linkages

The connection between quality management and financial outcomes has been shaped by multiple theoretical perspectives over time. In early classical economic thought, profitability was seen as a direct result of efficient resource allocation and production optimization. For instance, Adam Smith emphasized the division of labor as a key factor in increasing productivity and economic prosperity. While structured quality systems were absent in Smith's era, his focus on efficiency and minimizing waste aligns closely with the principles found in modern methodologies like Lean Manufacturing and Six Sigma [1, p. 35].

By the mid-20th century, quality management emerged as a specialized discipline. Pioneers such as W. Edwards Deming, Joseph M. Juran, and Kaoru Ishikawa played a pivotal role in linking quality practices to strategic business outcomes. Deming's System of Profound Knowledge promoted the reduction of variation and continuous improvement cycles (PDCA), which proved essential in driving operational excellence [1, p. 105]. Juran, in turn, introduced the "Cost of Quality" framework, which categorized quality-related costs into prevention, appraisal, and failure types (internal and external) [2, p. 241]. These models helped clarify how quality investment could reduce waste and increase profitability through fewer defects and stronger customer satisfaction.

In the context of the food industry, contemporary standards such as ISO 9001, ISO 22000, and HACCP have formalized quality control processes. These systems promote proactive risk management, enhanced traceability, and full regulatory compliance. Research has confirmed that companies adopting these frameworks typically see reductions in product recalls, improvements in customer trust, and broader access to export markets [4, p. 110; 5, p. 672].

From a financial perspective, quality management delivers value on two fronts. First, superior product quality often allows firms to charge premium prices, attract loyal customers, and gain entry to high-standard markets. Second, streamlined processes and reduced defects directly lower production costs and resource waste. In this way, quality acts as both a catalyst for revenue growth and a tool for cost efficiency.

More recent studies have further broadened the scope of this relationship by highlighting the role of intangible assets—such as brand reputation and consumer trust—in the quality–finance dynamic. In an increasingly interconnected global market, the cost of poor quality now includes reputational harm, declining investor confidence, and legal or regulatory repercussions. This has elevated quality management from a compliance function to a strategic instrument for long-term value creation and enterprise resilience [3, p. 75].

Classical Foundations: Efficiency, Control, and Standardization

The classical school of management emerged during the Industrial Revolution, a period marked by the rise of factory-based production systems, mechanization, and increasing demand for efficiency in organizational operations. As businesses scaled up, it became essential to find systematic ways to manage labor, streamline production, and maximize output. It was in this context that foundational thinkers such as Frederick W. Taylor, Henri Fayol, and Henry Ford developed their theories. These classical approaches laid the groundwork for what would eventually evolve into modern quality management systems, particularly within industrial sectors like food manufacturing, where structure, predictability, and measurable outcomes are essential.

Frederick W. Taylor: Scientific management and process optimization

Frederick Winslow Taylor is often referred to as the father of Scientific Management. His theory was rooted in the belief that labor productivity could be drastically improved through scientific analysis and optimization of tasks. Taylor introduced time-motion studies to identify inefficiencies in manual labor and developed standardized methods for task performance. According to Taylor, there exists "one best way" to perform any given task, and this optimal method should be determined scientifically rather than through tradition or guesswork [1, p. 45].

Taylor's contribution to quality management is profound. The concepts of standard operating procedures (SOPs), task sequencing, and performance measurement—all critical components of quality control systems—stem from his original framework. By reducing variation and emphasizing precision, Taylor's system sought to enhance predictability and efficiency on the factory floor. In modern food production, these principles are reflected in the strict adherence to SOPs, the use of production flow charts, and the enforcement of performance benchmarks. Taylor believed that when workers clearly understood their roles and followed structured processes, the results would be fewer errors, reduced waste, and higher output—all of which contribute to improved financial performance [1, p. 49].

Moreover, Taylor's ideas influenced the development of Lean Manufacturing and Six Sigma practices. Lean emphasizes eliminating waste (*muda*), while Six Sigma focuses on reducing process variability—both deeply aligned with Taylor's emphasis on measurable efficiency. Though Taylor did not explicitly link his work to quality systems as defined today, his principles are embedded in virtually every modern approach to operational quality.

Henri Fayol: Administrative theory and managerial control

While Taylor focused on task-level efficiency, Henri Fayol brought attention to the structural and administrative elements of management. Fayol, a French mining engineer and executive, proposed that management should be viewed as a universal function applicable across industries. He outlined five core functions of management: planning, organizing, commanding, coordinating, and controlling [2, p. 132]. These elements provide a comprehensive framework for organizing enterprise activities, ensuring accountability, and maintaining system coherence.

Fayol's influence on quality management lies in his emphasis on structure and coordination. Today's quality management systems, particularly those aligned with ISO 9001 or ISO 22000, reflect Fayol's model in their demand for documented procedures, defined roles and responsibilities, and hierarchical accountability. In the food industry, where compliance with safety regulations is paramount, Fayol's principles provide the scaffolding for systematic oversight and traceability.

Furthermore, Fayol championed the idea that effective management requires both technical expertise and moral integrity. He argued that managerial behavior should be guided by discipline, equity, and esprit de corps (team spirit)—ideas that remain vital in today's quality-focused organizations. Fayol's insistence on control as a managerial function directly correlates with internal auditing practices found in modern quality management frameworks.

Henry Ford: Standardization and mass production

Henry Ford, the American industrialist and founder of the Ford Motor Company, introduced transformative practices in manufacturing that profoundly influenced quality thinking. Ford's implementation of the moving assembly line in 1913 allowed for the mass production of automobiles at unprecedented speed and consistency. His approach to standardization—using interchangeable parts and uniform processes—created a production environment where quality could be systematically built into each product [3, p. 88].

Ford's focus on simplification and repeatability has become central to modern quality systems. In food production, similar principles are applied through batch production, automated packaging lines, and rigorous monitoring of critical control points. Ford's practices anticipated the principles later formalized in Lean Production, which emphasizes continuous flow, takt time, and elimination of non-value-added activities. Additionally, his legacy resonates in Six Sigma's focus on consistency and data-driven improvement.

Financially, Ford's model demonstrated how standardization reduces costs, improves throughput, and enhances product reliability. These benefits are particularly relevant to export-oriented food enterprises that must maintain consistent quality across large volumes and diverse markets. The predictability of standardized operations aligns with customer expectations and regulatory requirements, both of which are fundamental to financial sustainability.

Integrative Reflections: Classical theory in contemporary context

While Taylor, Fayol, and Ford developed their ideas in the early 20th century, the relevance of their theories endures. Each offered distinct but complementary perspectives: Taylor emphasized operational precision, Fayol stressed administrative structure, and Ford demonstrated the economic benefits of production consistency. Together, their contributions laid the intellectual and practical foundation for modern quality management systems.

However, it is also important to recognize the limitations of classical theory. These approaches primarily focused on internal efficiency and control, often neglecting external factors such as customer satisfaction, environmental sustainability, and stakeholder engagement. Concepts such as adaptability, organizational learning, and systems thinking were not part of their original frameworks.

In today's dynamic food industry, classical principles serve as a foundation, but they must be supplemented with contemporary approaches that incorporate risk-based thinking, digital traceability, and customer-centric strategies. Nonetheless, the classical emphasis on structure, discipline, and accountability remains embedded in the DNA of modern quality systems, ensuring that these early insights continue to shape how enterprises pursue operational excellence and financial performance.

Transition to quality-centric thinking: post-war developments

Following World War II, the concept of quality management underwent a profound transformation—from a purely technical process to a strategic and organization-wide function. Thought leaders such as W. Edwards Deming, Joseph M. Juran, and Kaoru Ishikawa were instrumental in reshaping quality into a philosophy deeply rooted in systems thinking, leadership responsibility, and employee involvement.

W. Edwards Deming emphasized a holistic view of organizational performance through the Plan-Do-Check-Act (PDCA) cycle and his renowned 14 Points for Management [1, p. 125]. He argued that improving quality should not be limited to inspections but rather achieved through process improvement and statistical control. His approach showed that reducing variability and rework could generate significant financial advantages over time.

Joseph Juran further advanced this thinking by introducing the concept of the Cost of Quality, which classified quality-related expenditures into prevention, appraisal, and failure categories. He also developed the Juran Trilogy—planning, control, and improvement—which linked quality management practices directly to operational and financial success [2, p. 241].

Kaoru Ishikawa contributed significantly by developing quality tools such as the cause-and-effect diagram (also known as the fishbone or Ishikawa diagram) [3, p. 78]. He emphasized root cause analysis and active employee participation in quality improvement efforts. Ishikawa's contributions supported the idea that quality is not solely a managerial concern, but a collective organizational responsibility.

These post-war developments greatly expanded the scope of quality management to include customer satisfaction, workforce engagement, and continuous improvement as essential dimensions of organizational performance. The financial impact was no longer confined to cost reduction; it extended to areas such as enhanced brand equity, reduced legal liability, and stronger market competitiveness. This shift laid the foundation for many of the principles that underpin today's international quality standards.

Contemporary Concepts: Systems thinking, risk management, and digital integration

Modern quality management has evolved into a multidimensional discipline that addresses not only product control but also broader system reliability, risk mitigation, and stakeholder trust. Key frameworks such as ISO 9001, ISO 22000, HACCP, and FSSC 22000 reflect this evolution, embedding holistic principles into quality strategies. These standards emphasize traceability,

accountability, preventive actions, and continual improvement—all of which are particularly vital in the food industry where public health, legal compliance, and brand reputation are at stake.

ISO 22000, specifically designed for food safety, integrates the structure of traditional quality management systems with Codex Alimentarius-based food hazard controls [1, p. 12]. It provides a harmonized system that eliminates duplication, enhances transparency, and supports both domestic and international trade. Its implementation improves operational consistency and reduces risks associated with foodborne diseases, thereby contributing to improved financial resilience and market access [2, p. 328].

HACCP (Hazard Analysis and Critical Control Points), originally developed by NASA and later codified by international food authorities, focuses on identifying biological, chemical, and physical hazards at every stage of food processing. It mandates monitoring at critical control points and corrective actions to mitigate risk [3, p. 16]. Although initial implementation costs can be high, the long-term benefits from reduced recalls, legal liabilities, and reputational risks have been well documented.

FSSC 22000, which builds upon ISO 22000 and incorporates additional sector-specific criteria, addresses the growing demand for supply chain transparency and food traceability. It is particularly advantageous in global trade environments where proof of rigorous food safety compliance is a prerequisite for supplier selection [4, p. 71].

Total Quality Management (TQM) provides a broader cultural and strategic layer to quality initiatives. It promotes company-wide commitment, customer-centric thinking, and employee empowerment. TQM programs are directly associated with long-term financial performance through increased innovation, reduced operational errors, higher employee retention, and improved customer loyalty [5, p. 673].

Comparative Analysis: Classical vs. Contemporary Approaches

Criteria	Classical Approaches	Contemporary Approaches
Focus	Efficiency, standardization	Risk-based thinking, stakeholder value
Orientation	Internal (production-centric)	External and holistic (entire value chain)
Role of Employees	Task execution	Active participation and innovation
Customer Consideration	Minimal	Central to quality definition
Technology Integration	Absent	High (automation, AI, data analytics)
Compliance and Governance	Informal or absent	Formalized through global standards

Implications for financial performance

Empirical research increasingly supports the view that advanced quality management systems significantly enhance financial outcomes. Organizations that implement ISO, HACCP, or TQM frameworks consistently report:

- Cost reductions through minimized waste, efficient use of resources, and lower defect rates
- Revenue growth from better market access, higher customer satisfaction, and quicker delivery times
- Risk mitigation by reducing the likelihood of recalls, legal sanctions, and reputational crises
- Brand equity via internationally recognized certifications that serve as competitive differentiators

Enterprises that align quality management with strategic goals frequently achieve higher returns on investment (ROI), enhanced investor confidence, and improved alignment with sustainability and ESG objectives [5, p. 676].

The Azerbaijani Context: observations and practical findings (2017–2025)

Azerbaijan’s food export trajectory from 2017 to 2025 serves as a compelling case study in how quality management systems (QMS) can shape financial performance and global market access. Over this nine-year period, the country experienced sustained growth in its non-oil exports, particularly in agricultural and food products. This expansion was made possible through the adoption of internationally recognized standards, supportive government programs, and modernization efforts across the sector.

In 2017, the country recorded a sharp rise in food exports, with fresh tomatoes leading at USD 151.6 million, followed by shelled hazelnuts at USD 114.5 million [6]. This growth was driven by the development of greenhouse infrastructure and policy-driven incentives for agribusinesses. The following year, tomato exports climbed to USD 177.4 million, and hazelnuts reached USD 125.7 million, reflecting sustained momentum and supply chain optimization.

Despite global supply chain disruptions in 2020 due to the COVID-19 pandemic, Azerbaijan’s fruit and vegetable exports remained stable at over USD 400 million [6]. The continued application of ISO 22000 and HACCP systems helped maintain food safety compliance and mitigate operational risks. By 2024, tomato exports increased to USD 188.2 million and shelled hazelnuts to USD 141.7 million. Moreover, the export portfolio expanded to include larger volumes of persimmons, apples, sugar, tea, and dairy products. Notably, dairy exports more than tripled in value compared to 2017, indicating diversification and improved production capacity [6].

Export destinations were led by Russia, Turkey, Switzerland, Georgia, and Italy, all of which maintained stable trade partnerships. Recent efforts also focused on opening new corridors into Central Asia and the Middle East, further diversifying Azerbaijan’s export geography [6].

Strategic government initiatives played a vital role in supporting this expansion. The “Made in Azerbaijan” program, under the Ministry of Economy, provided branding, exhibition support, and subsidized access to international markets such as Gulfood Dubai [8]. Additionally, the “One-Stop Export Support Center” streamlined certification, logistics, and documentation processes through a unified digital platform, reducing bureaucratic friction and promoting faster market entry [7].

These figures clearly indicate that the strategic implementation of QMS standards and institutional support have enhanced both export volumes and financial performance. The Azerbaijani experience validates the practical relevance of both classical efficiency-driven models and contemporary risk-based approaches in emerging economies.

The following table summarizes the export values of key food products from 2017 to early 2025:

Year	Tomatoes	Hazelnuts	Persimmons	Apples	Tea	Sugar	Dairy Products
2017	151.6	114.5	20.9	18.0	10.0	39.0	4.0
2018	177.4	125.7	39.2	27.6	7.1	39.0	4.5
2019	141.5	120.3	38.0	25.5	7.5	20.1	4.7
2020	167.8	120.8	29.5	22.6	8.5	21.4	5.0
2021	167.0	124.4	33.8	28.0	9.7	19.9	10.5
2022	173.7	133.3	42.4	39.3	8.5	35.3	12.4
2023	182.0	139.5	47.1	40.6	9.2	37.8	13.3
2024	188.2	141.7	49.5	41.8	9.0	38.6	13.9
2025	15.4	13.6	7.5	6.2	1.5	5.4	2.3

*Note: 2025 data reflects January–March results only.

Conclusion

The intricate relationship between quality management and financial performance has undergone a significant transformation over the last century. Classical approaches, rooted in the industrial revolution, emphasized standardization, efficiency, and control. These foundational concepts laid the groundwork for operational discipline, but were limited in scope, often neglecting broader concerns such as customer satisfaction, environmental responsibility, and systemic risk.

Contemporary quality frameworks—notably ISO 22000, HACCP, FSSC 22000, and Total Quality Management—represent an evolution of these early ideas. They incorporate risk-based thinking, technological integration, and stakeholder-focused governance, making them more responsive to today's dynamic and globalized food markets. These systems not only ensure product safety but also contribute to cost reduction, improved brand reputation, and expanded market access, all of which have direct and indirect implications for financial performance.

The empirical evidence from Azerbaijan's food export sector between 2017 and 2025 substantiates the theoretical claims. Despite global disruptions such as the COVID-19 pandemic, the country sustained growth in food exports by embracing internationally recognized quality systems, enhancing logistical capacities, and benefiting from coordinated government support. The consistent increase in export volumes and diversification into higher-value and processed goods reflect the maturation of Azerbaijan's food industry and its alignment with international standards.

Several key conclusions emerge:

- Quality management is no longer a reactive function but a strategic driver of competitiveness and resilience.
- There is a strong correlation between the adoption of QMS and improved financial outcomes in export-oriented food enterprises.
- Government intervention, in the form of support programs, certification incentives, and infrastructure investment, is critical in enabling firms to meet international benchmarks.
- The Azerbaijani case demonstrates that emerging economies can leverage quality standards not only for compliance but for market expansion and brand building.

As the global food economy becomes increasingly interconnected and regulated, firms that invest in robust quality management systems will be better positioned to adapt, compete, and grow. For

Azerbaijan, continued emphasis on workforce development, digital traceability, and institutional transparency will be essential to sustain and deepen the gains made thus far. Future research could further explore the microeconomic impacts of quality investment at the firm level, particularly focusing on profitability, productivity, and market share evolution. Additionally, comparative studies across neighboring countries may yield valuable insights into regional best practices and collaborative export strategies. The integration of classical principles with contemporary practices has created a new paradigm in quality management—one that supports both economic performance and public trust in the food industry. Azerbaijan's experience provides a compelling example of this paradigm in action.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

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Competing Interests

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Ethical Standards

The research meets all ethical guidelines, including adherence to the legal requirements of the study country.

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THE SCIENTIFIC EXPLORATION OF MANIFESTATION OF KEY ISSUE ASPECTS OF ECHOCARDIOGRAPHY AS AN INITIAL DIAGNOSTIC APPROACH FOR RARE EXTRA-CARDIAC CONDITIONS: A FOCUS ON IDIOPATHIC ACHALASIA AND PHARMACOTHERAPY MANAGEMENT CHALLENGES STRATEGICS IN MODERN MEDICINE IN GENERAL

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ABSTRACT

Echocardiography has long been a cornerstone in diagnosing cardiovascular diseases, offering a non-invasive, real-time view of the heart's structure and function. While primarily used to evaluate heart conditions, echocardiography has also been identified as a valuable diagnostic tool for rare extracardiac conditions. One such condition is idiopathic achalasia, a rare disorder affecting the esophagus that can present with nonspecific symptoms like chest pain, dysphagia (difficulty swallowing), and weight loss. The challenges in diagnosing achalasia often arise due to its overlapping symptoms with other cardiac conditions, making the role of echocardiography even more critical. This article explores the scientific implications of using echocardiography as

an initial diagnostic approach for identifying extracardiac abnormalities, focusing on idiopathic achalasia, and also examines the challenges clinicians face in managing pharmacotherapy for such conditions. Transthoracic echocardiography (TTE) is a non-invasive imaging technique commonly used to assess the anatomical structure and function of the heart. Although its diagnostic accuracy is slightly lower compared to computed tomography (CT) and magnetic resonance imaging (MRI), TTE remains valuable for detecting extracardiac abnormalities. This case report highlights a rare and significant finding identified through TTE. A 61-year-old male patient presented with chest pain, dyspnea, cough, dysphagia, and weight loss. Initial cardiologic evaluation with TTE revealed left atrial compression due to an inhomogeneous mass, along with accelerated flow in the left atrium. The echocardiographic findings suggested the presence of an extracardiac lesion, prompting further investigations. Subsequent X-ray with barium swallow and endoscopy confirmed the diagnosis of idiopathic achalasia. This case demonstrates the importance of routine TTE in identifying extracardiac conditions, leading to a crucial diagnosis and guiding treatment decisions, including referral for surgical intervention. It underscores the necessity of enhancing echocardiographic training to improve the detection of extracardiac manifestations and establish guidelines for comprehensive diagnostic protocols. The use of echocardiography as an initial diagnostic approach for rare extracardiac conditions like idiopathic achalasia has the potential to transform clinical practices. Early detection of extracardiac abnormalities, including left atrial compression due to esophageal dilation, can expedite the diagnosis and improve the management of these patients. Moreover, echocardiography's ability to monitor cardiac involvement in achalasia can guide pharmacotherapy decisions and inform the need for further interventions. The challenges associated with pharmacotherapy for idiopathic achalasia underscore the need for a comprehensive, multidisciplinary approach to patient care. While pharmacological treatments provide symptomatic relief for many patients, the role of surgical interventions and ongoing monitoring is crucial for those with more severe forms of the disease. As echocardiography continues to demonstrate its value in identifying and managing extracardiac conditions, ongoing research, training, and clinical awareness are essential to fully harness its diagnostic and management potential. Managing idiopathic achalasia presents unique challenges, particularly when it comes to pharmacotherapy. The primary goal of treatment is to reduce the pressure in the lower esophageal sphincter and improve esophageal motility. Pharmacological therapies, including calcium channel blockers and nitrates, are commonly used to relax the lower esophageal sphincter temporarily. However, these medications often provide only short-term relief and may not be effective for all patients. Additionally, the variability in patient responses to pharmacotherapy complicates treatment management. While some patients may experience significant symptom relief, others may require additional interventions, such as botulinum toxin injections, balloon dilation, or surgical myotomy (the Heller myotomy procedure). The decision to proceed with these interventions often depends on the severity of the disease, patient preference, and response to initial treatments. Echocardiography can also play an indirect role in pharmacotherapy management by helping assess the effects of treatment on the heart. For instance, if left atrial compression is alleviated as the esophagus is treated, echocardiography can monitor changes in atrial size and flow dynamics, offering valuable feedback on the success of pharmacological or surgical interventions. Transthoracic echocardiography is a noninvasive primarily initial imaging modality in evaluating the anatomic structure and function of the heart. With widespread availability, portability, low cost and safety TTE presents a mainstay of cardiac imaging. In some cases, it may also present as a diagnostic tool to identify different non-cardiac

structures within multiple anatomical areas. Incidental extra cardiac findings (INCF) are chiefly investigated and described by cardiac computed tomography and magnetic resonance imaging. The literature in this field about the role of TTE is very sparse. The majority of incidental findings are clinically insignificant; however, some may cause symptoms or require further investigation and management.

Keywords: Echocardiography, Diagnostic, Extra-Cardiac Conditions, Idiopathic Achalasia Pharmacotherapy Management, Modern Medicine.

Introduction

Echocardiography, a non-invasive imaging technique, has been widely used in cardiovascular diagnostics but holds significant potential in identifying rare extracardiac conditions. This scientific exploration focuses on the role of echocardiography as an initial diagnostic tool for detecting conditions that are typically outside its traditional scope, with a particular emphasis on idiopathic achalasia. The case of idiopathic achalasia highlights the challenges in diagnosing this rare esophageal disorder, which often presents with nonspecific symptoms such as chest pain, dysphagia, and weight loss. This study investigates how transthoracic echocardiography (TTE) can assist in identifying extracardiac abnormalities that may be missed in routine clinical evaluations. In addition, the abstract delves into the complexities of pharmacotherapy management for patients diagnosed with idiopathic achalasia, addressing the challenges clinicians face in optimizing treatment strategies. The integration of echocardiography into the diagnostic process for extracardiac conditions like achalasia underscores the need for advanced training and awareness in echocardiography, promoting its broader application in clinical practice. The article further emphasizes the importance of a comprehensive diagnostic approach, including pharmacological management and surgical intervention, to effectively manage these rare conditions.

Many patients with refractory achalasia or terminal achalasia, characterized by a barium-like esophagus with severe dilation (>6 cm in width) and complex anatomical deformity (concha trap), experience severe symptoms and complications, potentially fatal. Therefore, measures should be taken to prevent aspiration and malnutrition. And the dead. Unfortunately, esophagectomy is associated with a high complication rate and a real risk of death. Additionally, quality of life is reduced after esophagectomy, so this approach should be considered a last resort, and most patients and doctors prefer a more conservative treatment attempt. For patients in whom PD and POEM methods have failed, attempting Heller myotomy may still be reasonable before resorting to esophagectomy, given the number of cases in which severely terminally ill patients may respond to surgery. You should know that the success rate still remains much lower than that of patients with a more favorable anatomy and without prior radical treatment. A comprehensive evaluation including assessment of esophageal anatomy with barium, upper esophageal endoscopy to assess for esophagitis and strictures, and possibly manometry or FLIP to assess LES function may provide evidence that a disease-targeted level of WIS therapy can be effective. Patients with severe anatomy, significant bolus delay, and evidence of complete myotomy may be referred for esophagectomy, while patients with evidence of incomplete myotomy may undergo Heller myotomy. Ultimately, this decision is extremely complex and this approach requires careful assessment and informed discussion, focused on risks and benefits. Patients requiring esophageal resection should be referred to specialized centers with a large number of patients, because the results directly depend on the number of patients and their experience [20-23].

Patients with symptoms suggestive of achalasia should undergo upper gastrointestinal endoscopy to ensure the absence of other pathologies and to rule out possible pseudo achalasia. Heart rate management and timed barium swallows should be used to confirm the diagnosis. The choice between treatment modalities depends on the manometric subtypes of achalasia, patient preference, and institutional experience. PD, HM and POEM are good choices for people with achalasia type I and II. PD should be performed gradually, starting with the smallest balloon (3.0 cm), except in young men (<45 years) who require one initial 3.0 cm to 3.5 cm balloon or surgical myotomy. Patients who do not respond to Parkinson's disease should undergo surgical myotomy. Individual CM or POEM can be used in patients with type III achalasia. If patients are not suitable for radical treatment due to comorbidities, treatment with botulinum toxin and smooth muscle relaxants should be offered. To maximize patient outcomes, all definitive treatments should be offered in centers of excellence with sufficient capacity and experience. Patients should be monitored for recurrence of GERD symptoms and complications after the procedure. CE and endoscopy can be complementary in assessing disease recurrence versus inflammation or stenosis associated with reflux. Repeat PD, CM, or POEM may be performed in individuals with recurrent disease, and antacid therapy should be offered to individuals with symptoms due to GERD. People with a dilated esophagus (more than 8 cm) and an unsatisfactory response to the initial myotomy may require an esophagectomy [24-26].

Transthoracic echocardiography is a noninvasive primarily initial imaging modality in evaluating the anatomic structure and function of the heart. With widespread availability, portability, low cost and safety TTE presents a mainstay of cardiac imaging. In some cases, it may also present as a diagnostic tool to identify different non-cardiac structures within multiple anatomical areas [1, 2]. Incidental extra cardiac findings (INCF) are chiefly investigated and described by cardiac computed tomography and magnetic resonance imaging. The literature in this field about the role of TTE is very sparse. The majority of incidental findings are clinically insignificant; however, some may cause symptoms or require further investigation and management [3, 4].

Our case shows the role of routine TTE in identifying extra cardiac structure – esophageal achalasia, leading to important diagnosis and indication for further surgical intervention.

Achalasia is a motility disorder of the esophagus, characterized by impaired peristalsis and inadequate relaxation of the lower esophageal sphincter. Patients most commonly experience dysphagia with solids and liquids, regurgitation, and intermittent chest pain with or without weight loss. Using high-resolution manometry, three subtypes of achalasia have been identified that differ in pressure and contraction patterns. Important diagnostic signs are endoscopic findings of saliva residues with folds at the esophagogastric junction or findings of a dilated esophagus with a bird's beak [13-15].

Cardiac achalasia, a form of dynamic esophageal disorder, is a relatively rare primary esophageal movement disorder characterized by loss of function of ganglion plexus cells in the distal esophagus and lower esophageal sphincter. Loss of distal and lower esophageal sphincter ganglion cell function is a major cause of cardiac achalasia and is more common in older adults. Histological changes in the esophageal mucosa are considered pathogenic; However, research has shown that inflammation and genetic changes at the molecular level can also cause cardiac achalasia, leading to dysphagia, reflux, aspiration, chest pain and weight loss. Current treatment options for achalasia aim to reduce the resting pressure of the lower esophageal sphincter, which helps empty the esophagus and relieve symptoms. Treatment options include botulinum toxin injection, inflatable dilatation, stenting, and surgical myotomy (open or laparoscopic). Surgical

procedures are often controversial due to concerns about their safety and effectiveness, especially in older patients. Here, we review clinical, epidemiological, and experimental data to determine the prevalence, pathogenesis, clinical presentation, diagnostic criteria, and treatment options for achalasia to aid clinical management [28-30].

As an important part of the digestive system, the esophagus plays an important role in transporting nutrients. Diseases of the esophagus can be classified into anatomical lesions of the organic cavity (e.g.: digestive or eosinophilic stenosis) or severe dysphagia with progressive injection of the digestive tract (e.g.: severe dysphagia of neurological origin or cardiac achalasia). Esophageal achalasia is a form of dynamic esophageal disorder (DED). It refers to obstruction of the esophageal outflow tract due to impaired relaxation of the lower esophageal sphincter (LES) and loss of esophageal motility or spasmodic contraction when the esophageal body or esophagogastric junction (EGJ) is not structurally blocked. There are primary and secondary types of achalasia. Cardiac achalasia is characterized by a loss of functional muscle ganglion cells in the distal esophagus and LES. Although histological changes in the esophageal mucosa have long been considered part of the pathogenesis of cardiac achalasia, recent studies have shown that inflammation and genetic changes may also contribute to achalasia at the molecular level. Currently, achalasia is an incurable chronic disease. Different subtypes of achalasia respond differently to medications and surgery, after which some patients develop submucosal fibrosis. This may recur and require additional treatment [32-34].

Achalasia is one of the most studied esophageal motility disorders. In this guide, we discuss the diagnosis, treatment, and general management of adult patients with achalasia. This guidance includes recommendations, key concepts and a summary of the evidence. Each recommendation statement is accompanied by an assessment of the quality of the evidence and the strength of the recommendation based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) process. Key concepts are statements that do not meet the requirements of the GRADE process due to the structure of the statement or the available evidence. In some cases, key concepts rely on the extrapolation of evidence and/or expert opinion. Although the nature of the symptom may influence clinical judgment, it may be difficult to determine which of these causes is affecting the patient. Therefore, additional diagnostic testing is necessary unless the patient is experiencing heartburn and a PPI is attempted. High-resolution manometry allows you to assess the integrity of the myotomy, as well as determine the presence of spasmodic contractions after treatment; However, it is not possible to accurately determine bolus delay and assess the contribution of GERD, and the procedure can be difficult due to obstruction and abnormal anatomy [16-19].

Results and Discussion

Echocardiography's role as an initial diagnostic approach for rare extra-cardiac conditions like idiopathic achalasia highlights the intersection between diagnostic imaging and treatment strategies in modern medicine. Although pharmacotherapy remains a cornerstone of management for conditions like achalasia, it faces inherent challenges, including limited effectiveness, side effects, and the need for ongoing adjustments. In light of these challenges, a more comprehensive approach involving precise diagnostics, individualized treatment regimens, and coordinated care is essential to improving patient outcomes. Continued research into both diagnostic tools and therapeutic strategies will be critical in addressing the complexities of rare diseases and ensuring effective care for patients in the future.

The treatment of achalasia is the result of an evidence-based approach and international interdisciplinary efforts. The guidelines provide advice on key aspects of the diagnosis and treatment of achalasia, as well as commentary based on the best available literature and the opinions of leading European achalasia experts. The main aim of these recommendations is to reduce variations in practice and improve patient outcomes in Europe. Careful and widespread dissemination of these recommendations is therefore necessary to ensure high compliance in clinical practice. It is important to promote counseling and education. Future well-designed clinical trials should address the knowledge gaps and unmet needs that emerged during the development of these guidelines.

Achalasia symptomatic consequence the motility disorder is the classic form of solid-liquid dysphagia associated with regurgitation of soft undigested food or saliva. Substernal pain while eating, associated with dysphagia, weight loss, and even heartburn, can accompany symptoms that often lead to achalasia being misdiagnosed as gastroesophageal reflux disease (GERD). Achalasia should be suspected in individuals with solid-liquid dysphagia and in those with ineffective regurgitation after the first use of proton pump inhibitor (PPI) therapy. Endoscopic evidence of retention of saliva, fluids and food into the esophagus without mechanical obstruction due to stenosis. or the mass should arouse suspicion of achalasia. In contrast, other diseases can mimic achalasia both clinically and manometrically. These include pseudoachalasia due to tumors of the gastric cardia or tumors infiltrating the myenteric plexus (adenocarcinoma of the gastroesophageal junction, pancreatic, breast, lung or hepatocellular carcinoma) or secondary achalasia due to external processes such as anterior dense fundoplication or laparoscopic adjustable gastric banding [36-38].

Achalasia is a primary movement disorder of the esophagus, characterized by lack of peristalsis and insufficient relaxation of the lower esophageal sphincter. Given new advances and developments in the treatment of achalasia, there is a growing need for comprehensive evidence-based guidelines to assist clinicians in treating patients with achalasia. Achalasia is a relatively rare primary esophageal motility disorder characterized by loss of function of the ganglion cells of the distal esophageal plexus and the lower esophageal sphincter. Histological changes in the esophageal mucosa are considered pathogenic; However, research has shown that inflammation and genetic changes at the molecular level can also cause cardiac achalasia, leading to dysphagia, reflux, aspiration, chest pain, and weight loss. The aim of this review article is to provide a comprehensive overview of the literature and to present the current state of knowledge on the subject of achalasia.

Currently, the etiology and pathogenesis of cardiac achalasia remain unclear; However, it is generally accepted that histological changes in the esophageal mucosa caused by loss of esophageal nerve cell function play a fundamental role in the pathophysiology. Autoimmune attack on the esophageal intermuscular nerves by cell-mediated mechanisms and possibly by antibodies can lead to inhibition of esophageal smooth muscle, resulting in loss of nerve function and degeneration of nerve fibers.

Several pathological mechanisms have been proposed as possible triggers of this immunodeficiency process, including underlying viral infections, idiopathic autoimmune triggers, and genetic predisposition. Herpes zoster virus, herpes simplex virus, measles virus, and human papillomavirus may influence the regulation of functional esophageal movement and control of LES in patients with achalasia, but not in all patients with viral infections. Many patients with achalasia have varicella-zoster virus DNA in their saliva. Limited evidence suggests that

eosinophils and mast cells may play a role in the development of achalasia and obstructive esophageal motility disorders. Aggregation of eosinophils and mast cells in the esophagus leads to increased levels of inflammatory cytokines; This leads to fibrous remodeling of the esophageal wall, which ultimately leads to esophageal dysfunction and associated symptoms. Dysphagia (solid or liquid) is a common symptom in patients with achalasia. Initially, this symptom appears sporadically; However, as the disease progresses, the esophagus enlarges significantly, resulting in burning and decompensation of the sigmoid colon with corresponding clinical symptoms. Additionally, patients with achalasia may experience chest pain [5]. There is also a risk of long-term aspiration pneumonia and esophageal squamous cell carcinoma [17]. A study using UK hospital and primary care databases found that patients with achalasia had high morbidity and mortality from oesophageal cancer, aspiration pneumonia and lower respiratory infections [37-39] Additionally, other studies have shown that patients with achalasia suffer from acute respiratory failure and hemodynamic instability. The final stage of achalasia with hypertrophy of the thoraco-esophageal region can manifest as an acute illness. Achalasia often presents insidiously, with many subclinical features before a definitive diagnosis is made, which can result in a delay between symptom onset and diagnosis.

Echocardiography has long been a cornerstone in diagnosing cardiovascular diseases, offering a non-invasive, real-time view of the heart's structure and function. While primarily used to evaluate heart conditions, echocardiography has also been identified as a valuable diagnostic tool for rare extracardiac conditions. One such condition is **idiopathic achalasia**, a rare disorder affecting the esophagus that can present with nonspecific symptoms like chest pain, dysphagia (difficulty swallowing), and weight loss. The challenges in diagnosing achalasia often arise due to its overlapping symptoms with other cardiac conditions, making the role of echocardiography even more critical. This article explores the scientific implications of using echocardiography as an initial diagnostic approach for identifying extracardiac abnormalities, focusing on idiopathic achalasia, and also examines the challenges clinicians face in managing pharmacotherapy for such conditions.

Currently, cardiac achalasia is mainly diagnosed by high-resolution manometry (HRM), endoscopy, and barium meal examination. Temporary barium swallow esophagography or functional luminal imaging probe (FLIP) is only used if achalasia cannot be diagnosed.

Manometry plays an important role in the differential diagnosis of dynamic esophageal diseases. Human resources management is the gold standard in the diagnosis of achalasia cardiaca. HRM typically involves performing a pressure test using a minimum of pressure sensors distributed throughout the catheter. Each pressure sensor is spaced 1 cm apart to obtain baseline values at rest. The probe enters through the nose and passes through the esophagus into the esophagus, allowing the entire esophagus to be examined. In fact, HRM can not only confirm the diagnosis of achalasia, but also identify specific subtypes demonstrating significantly different therapeutic outcomes. Correct diagnosis of intraoperative HRM can help guide therapeutic approaches and predict therapeutic outcomes. Endoscopy is necessary in patients with digestive disorders, although it is not very sensitive to achalasia. Studies have shown that only a third of patients can be diagnosed with achalasia via endoscopy. Endoscopy is commonly used to evaluate patients with gastrointestinal symptoms and to exclude luminal neoplasms of the esophagus and proximal stomach.

Drugs are usually prescribed to patients who cannot undergo or refuse endoscopic or surgical treatment, as well as to those in whom endoscopic or surgical treatment has failed. Calcium

channel blockers, nitrates, and proton pump inhibitors are commonly used to control acid reflux; However, they provide only short-term relief and are less effective [31].

In the early stages of the disease, dysphagia may be very subtle and may be misinterpreted as dyspepsia, poor gastric emptying, or stress. Heartburn due to stagnant food can increase this confusion. As the disease progresses, difficulty swallowing solid and liquid food usually occurs. Dysphagia affects solid foods more than liquids. To facilitate the flow of food, patients usually change their eating habits: They eat more slowly or resort to certain maneuvers, such as raising their arms or arching their backs. The most common misdiagnosis of achalasia is GERD, as many patients misinterpret regurgitation symptoms as reflux.⁸ It is important to ask about dysphagia or shutdown symptoms and to be alert to the possible diagnosis of achalasia in patients whose condition does not improve. . Treatment with PPIs after initial suspicion of GERD.

In this section, an algorithm for the individual treatment of patients with achalasia is presented. Symptomatic patients with achalasia who are good candidates for surgery should be provided with information about the risks and benefits of equally effective treatment options such as MP and myotomy. The choice between procedures should depend on patient preference and facility experience. However, to achieve maximum results for patients, both procedures must be performed in centers of excellence with sufficient size and experience. PD should be performed gradually, starting with the smallest balloon (3.0 cm), except in younger men (<45 years), in whom initial placement of a 3.5 cm balloon or surgical myotomy may be beneficial. Patients who do not respond to PD should undergo surgical myotomy. Surgical candidates with poor indications should initially inject botulinum toxin into the LES and be aware that retreatment is often required. Other treatments based on nitrates or calcium channel blockers may be offered if there is no clinical response to botulinum toxin injection. Individuals with a dilated esophagus (>8 cm) and a poor response to the initial myotomy may require an esophagectomy.

Achalasia is a relatively rare disorder of esophageal motility. The main clinical manifestations are dysphagia, reflux, chest pain and weight loss; They can significantly affect the patient's quality of life. Treatment for achalasia cardiaca is primarily aimed at relieving symptoms, as there is no cure for the disease. POEM is expected to be an ideal treatment for cardiac achalasia due to its effectiveness and safety. Individual treatment should be carried out taking into account the clinical characteristics of each patient. Currently, clinical studies on cardiac achalasia suggest the possibility of infectious events associated with certain genetic factors triggering the autoimmune mechanism. However, further research is needed in related areas to determine optimal treatment regimens [11,25].

The clinical care of patients with achalasia has changed significantly in the past decade under influence of new developments such as high-resolution manometry, per-oral endoscopic myotomy and studies providing new insights regarding achalasia subtypes, cancer risk and follow-up. Given the substantial growth of knowledge in the past years, there is need for a comprehensive, evidence-based European guideline covering all aspects of the disease. This multidisciplinary guideline aims to provide an evidence-based framework with recommendations on the diagnosis, treatment and followup of adult achalasia patients. Chagas disease and achalasia secondary to other disorders, as can be seen after fundoplication, bariatric surgery, sarcoid infiltration, opiate usage or malignancy, is not covered by this guideline. This guideline is intended for clinicians involved in their management, including gastroenterologists, endoscopists, radiologists, gastrointestinal surgeons, dietitians and primary care practitioners [12,29,36].

The diagnosis of achalasia should be considered when patients present with dysphagia associated with other esophageal symptoms and when upper gastrointestinal endoscopy can exclude other conditions. Barium esophagography may reveal the classic bird's beak sign, esophageal dilation, or free fall. Esophageal manometry is the gold standard for diagnosing achalasia; A diagnostic sign is incomplete relaxation of the VOC, expressed by an increase in integrative relaxation pressure in the absence of normal peristalsis. The use of high-resolution manometry (HRM) has led to the classification of achalasia into three clinically relevant groups based on esophageal contractility patterns.

Malignant pseudoachalasia is a condition in which a patient is initially diagnosed and sometimes even treated for achalasia, but is later found to have a malignant disease as the underlying cause. This may occur with submucosal adenocarcinoma of the cardia, locally advanced pancreatic cancer, submucosal metastases, or anti-Hu-producing small cell carcinomas (most commonly lung carcinoma). All Patients diagnosed with achalasia should under no circumstances undergo additional tests such as: B. undergo a CT scan or endoscopy. Ultrasound to exclude malignancy. Interpretation of temporary barium esophagus. In a patient with achalasia, radiographs were taken at 0, 1, 2, and 5 minutes in the left posterior oblique position after ingestion of 100 to 200 ml of low-density barium suspension. Measurement of the height and width of a barium column measured from the OGJ to the barium-foam interface. A barium height > 5 cm at 1 minute and > 2 cm at 5 minutes indicates achalasia. The time is lost if malignant disease is not recognized at an early stage. Only two studies have addressed the question of how to identify patients with malignant pseudoachalasia. significant duration of weight loss and aging. A study by Ponds et al. also identified difficulties inserting the endoscope into the stomach, which endoscopists identified as a risk factor. A model was developed in which the presence of fewer than two risk factors did not increase the risk of malignancy, whereas the presence of two or more risk factors increased the risk [14,18,26,35].

Idiopathic achalasia is a primary esophageal motor disorder characterized by loss of esophageal motility and inadequate relaxation of the lower esophageal sphincter in response to swallowing. Patients with achalasia often complain of solid and liquid dysphagia, mild regurgitation that often does not respond adequately to proton pump inhibitors, and chest pain. Many, but not all, patients experience weight loss. Although the exact etiology is unknown, it is often thought to be an autoimmune disease, viral immune disease, or neurodegenerative disease. Diagnosis is based on history, barium esophagus, and esophageal motility studies. To exclude malignancy, endoscopic evaluation of the gastroesophageal junction and gastric cardia is necessary. New diagnostic techniques such as high-resolution manometry help predict treatment response in achalasia based on esophageal pressure topography patterns that identify three achalasia phenotypes (I-III), and studies of Results show improved treatment response in Types I and II compared to Types III. Although achalasia cannot be completely cured, excellent results are obtained in more than 90% of patients. Modern medical and surgical treatments (pneumatic dilatation, endoscopic and surgical myotomy and pharmacological agents) aim to reduce the pressure of the LES and facilitate emptying of the esophagus under the influence of gravity and hydrostatic pressure of food debris and liquids. Staged pneumatic dilatation or laparoscopic surgical myotomy with partial fundoplication is recommended as initial treatment, depending on the patient's age, gender, preference, and local experience. The prognosis of patients with achalasia is excellent. Most patients who receive adequate treatment have a normal life expectancy, but the disease recurs and the patient may require periodic treatment.

The increased prevalence of circulating antibodies against the myenteric plexus in some patients with achalasia suggests that autoantibodies play a role in the pathogenesis of this disease. It has been suggested that these circulating antibodies are likely the result of a nonspecific reaction to the disease process rather than its cause. This idea was supported by the discovery of similar antibodies in patients without achalasia. Ultrastructural studies of esophageal tissue in patients with achalasia also revealed inflammatory infiltrates around myenteric neurons, whereas controls showed a normal myenteric plexus without infiltration. Several case-control studies have reported a significant association with HLA class II antigens in idiopathic achalasia. Patients with achalasia and its associated HLA allele were found to have a higher prevalence of circulating antimyenteric autoantibodies, suggesting an autoimmune etiology. HLA association also suggests immunogenetic susceptibility to idiopathic achalasia; However, this should be treated with caution since not all patients with achalasia have associated HLA antigens. Recent genetic association in patients with achalasia revealed classical HLA haplotypes and amino acid polymorphisms, suggesting immune-mediated processes in idiopathic achalasia [4,9,23].

The presence of familial cases may indicate that achalasia is, in some cases, a hereditary disease. Such familial cases have been observed mainly in children, between siblings and, in some cases, in identical twins. There are also reports of a parent-child association in achalasia.⁶¹ Although these data suggest an autosomal recessive mode of inheritance for this disorder, the rarity of familial occurrence does not support the hypothesis that genetic inheritance occurs in most cases. Case of achalasia. Instead, it is suggested that genetic predisposition in these individuals likely increases their susceptibility to acquiring achalasia following exposure to common environmental factors that may play a role in pathogenesis [28,35,38].

The Role of Echocardiography in Diagnosing Rare Extra-Cardiac Conditions.

Echocardiography, particularly transthoracic echocardiography (TTE), provides clinicians with detailed images of the heart and surrounding structures. While it is conventionally used to assess heart function and detect cardiovascular diseases, its ability to identify extracardiac conditions has garnered growing attention. In patients presenting with chest pain, dyspnea, or other symptoms mimicking cardiac disease, TTE can reveal abnormal findings outside the heart, such as masses or compression of surrounding structures.

In the case of **idiopathic achalasia**, TTE can identify indirect signs that suggest esophageal involvement. One of the key echocardiographic findings in such cases is **left atrial compression** caused by the dilated esophagus. This compression may alter the flow dynamics in the left atrium, which could be detected as an abnormal pattern on the echocardiogram. Additionally, other signs, such as changes in atrial size, may prompt clinicians to consider further imaging or diagnostic tests, like X-rays or endoscopy, to confirm the diagnosis.

The importance of using echocardiography in diagnosing such extracardiac conditions is clear: it can help avoid misdiagnosis, initiate further testing, and ultimately guide clinicians toward an appropriate treatment plan.

Idiopathic Achalasia: Diagnostic Challenges

Idiopathic achalasia is a condition in which the esophagus fails to move food properly due to the loss of muscle coordination and relaxation of the lower esophageal sphincter. The disease is characterized by dysphagia, regurgitation, chest pain, and weight loss, often leading to a delayed diagnosis as these symptoms overlap with more common conditions, including heart disease and

gastroesophageal reflux disease (GERD). The difficulty in diagnosing idiopathic achalasia early in the disease process stems from its nonspecific presentation, which often leads to the pursuit of cardiology consultations before gastrointestinal conditions are considered.

While barium swallow and endoscopy are the gold standards for diagnosing achalasia, echocardiography can play a crucial role in identifying signs of extracardiac involvement, such as left atrial compression, that suggest a broader diagnostic evaluation. Identifying these signs early may prompt clinicians to investigate further with esophageal imaging, reducing the time to diagnosis and improving patient outcomes.

The advancement of medical diagnostics and treatments has revolutionized the landscape of modern medicine, allowing for more accurate identification and management of complex conditions. One significant area of this progress is the use of **echocardiography** as an initial diagnostic tool, particularly in identifying rare extra-cardiac conditions that may have previously gone undetected or misdiagnosed. Idiopathic achalasia, a rare esophageal disorder, presents a unique challenge in clinical practice due to its overlapping symptoms with various cardiac and gastrointestinal conditions. This essay delves into the use of echocardiography in diagnosing rare non-cardiac conditions, with a special focus on idiopathic achalasia and the associated pharmacotherapy management challenges in contemporary medical practice.

Echocardiography in Modern Diagnostics

Echocardiography is a widely used, non-invasive imaging technique primarily employed to assess cardiac structure and function. However, its utility extends beyond the heart, as it can also reveal manifestations of extra-cardiac conditions that may not be immediately obvious. These conditions often present with nonspecific symptoms that mimic those of cardiovascular diseases, leading to diagnostic confusion. For example, patients with idiopathic achalasia frequently experience chest pain, dysphagia (difficulty swallowing), and regurgitation—symptoms that are sometimes mistaken for heart disease. This underscores the importance of using echocardiography as a complementary diagnostic tool in the initial work-up of such patients.

Idiopathic Achalasia: A Rare Extra-Cardiac Condition

Idiopathic achalasia is a rare motility disorder of the esophagus, characterized by the loss of normal peristalsis and impaired relaxation of the lower esophageal sphincter (LES). This results in progressive difficulty in swallowing and, if left untreated, can lead to significant complications such as esophageal dilation, aspiration pneumonia, and even cancer. The pathophysiology remains unclear, with several theories suggesting autoimmune, neurodegenerative, or genetic causes.

In clinical practice, idiopathic achalasia often presents with symptoms that overlap with cardiovascular conditions, such as chest pain and regurgitation. Therefore, physicians must distinguish between cardiac and gastrointestinal origins. Echocardiography serves a crucial role in this diagnostic process by ruling out cardiac etiologies and prompting further investigation into esophageal disorders. In some cases, an esophagram, manometry, or endoscopy might follow echocardiography to confirm the diagnosis.

Challenges in Pharmacotherapy Management of Idiopathic Achalasia

Once diagnosed, the management of idiopathic achalasia presents additional challenges. Pharmacotherapy is often employed as an initial treatment approach, aiming to relieve symptoms and improve esophageal motility. Common medications include calcium channel blockers,

nitrates, and botulinum toxin injections, which work by relaxing the LES and enhancing esophageal transit. However, these treatments are not curative, and their effectiveness can be limited, with some patients experiencing inadequate relief or developing tolerance over time.

Additionally, long-term pharmacotherapy management can present complications, such as side effects (e.g., hypotension from nitrates), and the need for ongoing adjustments to medication regimens. In some cases, pharmacotherapy may be insufficient, necessitating more invasive interventions like pneumatic dilation or surgical myotomy.

The limited efficacy and potential adverse effects of pharmacological treatments underscore the importance of a multidisciplinary approach to managing idiopathic achalasia. Incorporating diagnostic tools like echocardiography, which allows for early identification and differentiation of extra-cardiac conditions, can help guide therapy and minimize complications.

Pharmacotherapy and Strategic Management in Modern Medicine

The challenges of pharmacotherapy management in modern medicine extend beyond idiopathic achalasia and can be observed across various rare and complex conditions. Precision medicine, which tailors treatment based on individual genetic, environmental, and lifestyle factors, is emerging as a powerful tool in overcoming some of these challenges. However, access to such treatments and the ongoing development of personalized therapies remain issues for many patients, particularly in under-resourced healthcare settings.

The growing prevalence of polypharmacy—especially among elderly patients—also presents a significant obstacle in managing rare and complex conditions. With multiple medications prescribed for comorbidities, patients may face drug-drug interactions, diminished adherence to regimens, and increased risk of adverse effects. Strategic management of pharmacotherapy requires careful monitoring, patient education, and sometimes coordination with specialists across different fields.

Case report

A 61-year-old man with unremarkable past medical history presented to the hospital with a 6-month history of chest pain, dyspnea, cough, dysphagia and weight loss (about 15kg). Chest pain, dyspnea and cough were worsening in the postprandial period, with regurgitation of undigested food.

Physical examination revealed irregular heartbeat, without appreciable heart murmurs, clear lung sounds.

Electrocardiography showed sinus rhythm with supraventricular extra heart beats and nonspecific ST Segment and T-wave changes in leads V3-6.

Echocardiography revealed mild hypertrophy of the left ventricle with normal systolic function, without regional wall motion abnormalities, diastolic dysfunction – grade I (abnormal relaxation), right ventricular systolic function was preserved; Estimated pulmonary artery systolic pressure (PASP) was normal of 28mm/Hg. The valves were without significant structural changes; 2D and color Doppler echocardiography revealed left atrial compression by an inhomogeneous mass in close relation to the pulmonary veins and accelerated flow in LA (Figure 1, figure 2).

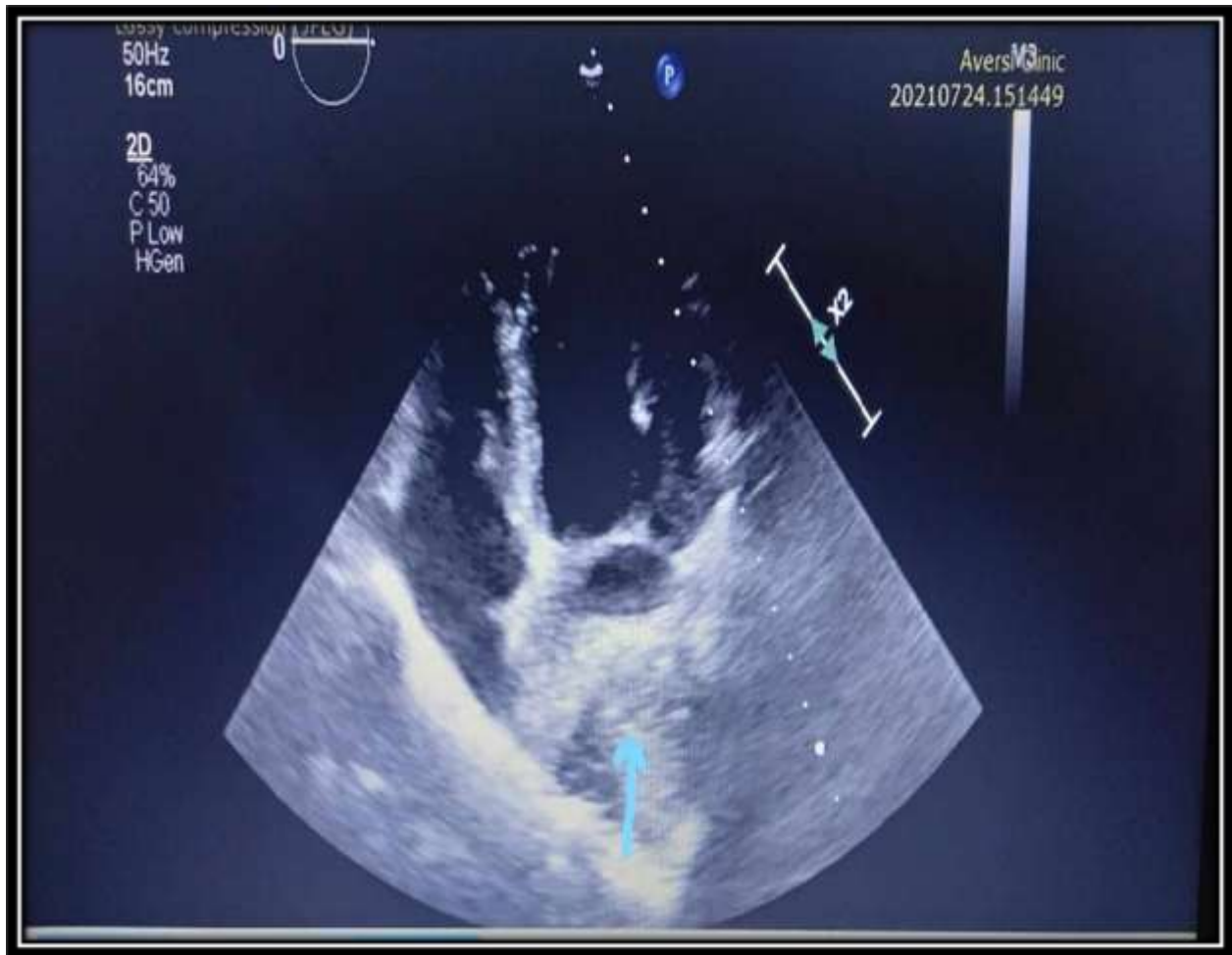


Figure 1. Apical 4-chamber view. Left atrial compression with extra cardiac structure (blue arrow)

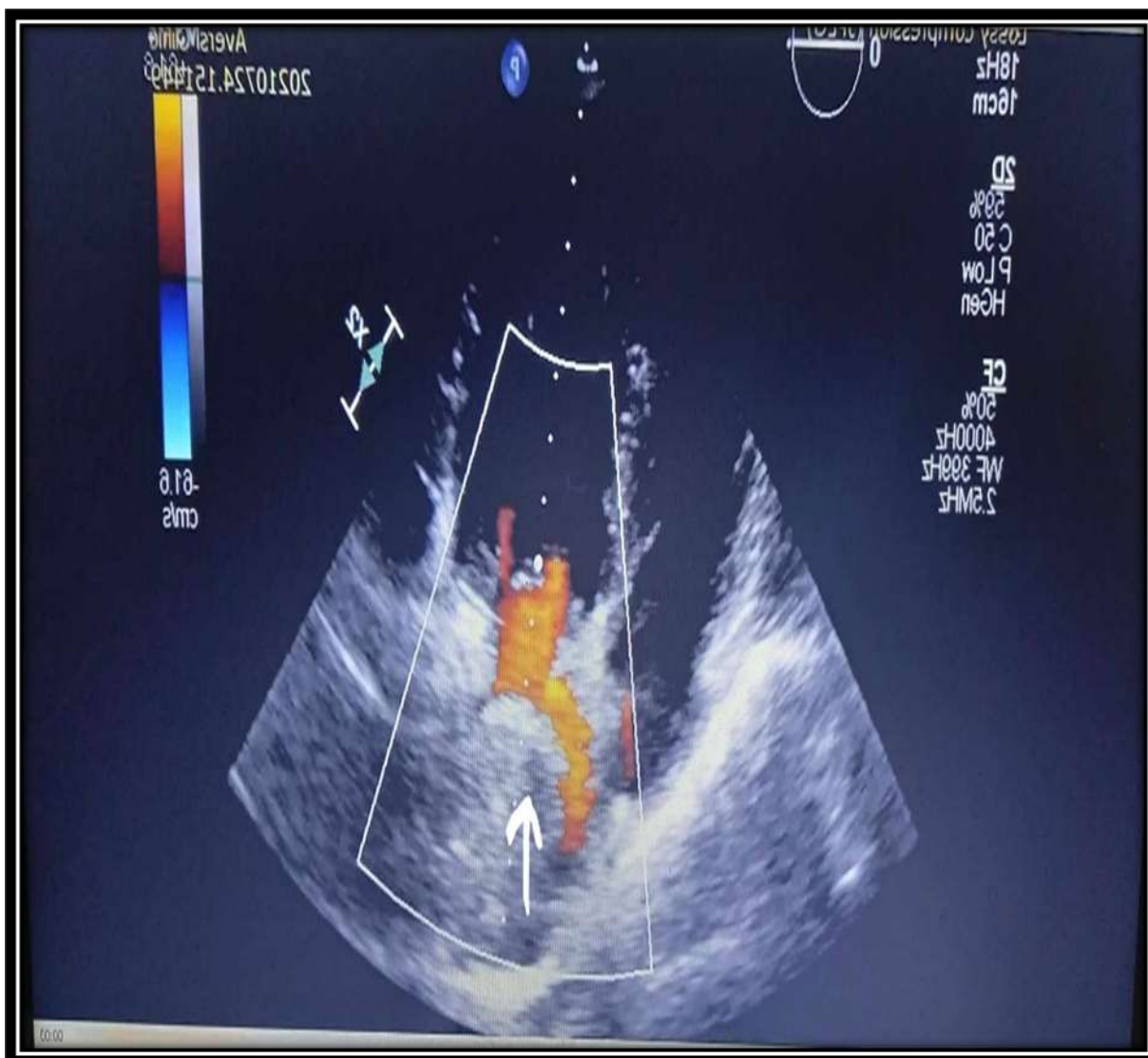


Figure 2. Apical 4-chamber view with color Doppler. Left atrial and pulmonary vein compression with extra cardiac structure (white arrow)

Esophageal pathology was suspected and the patient was referred to the barium swallow study to confirm the diagnosis. The x-ray showed the typical “bird’s beak” sign, esophageal dilatation with failure of normal peristalsis, incomplete lower esophageal sphincter relaxation that did not coordinate with esophageal contraction, stasis of barium in the esophagus (figure 3).

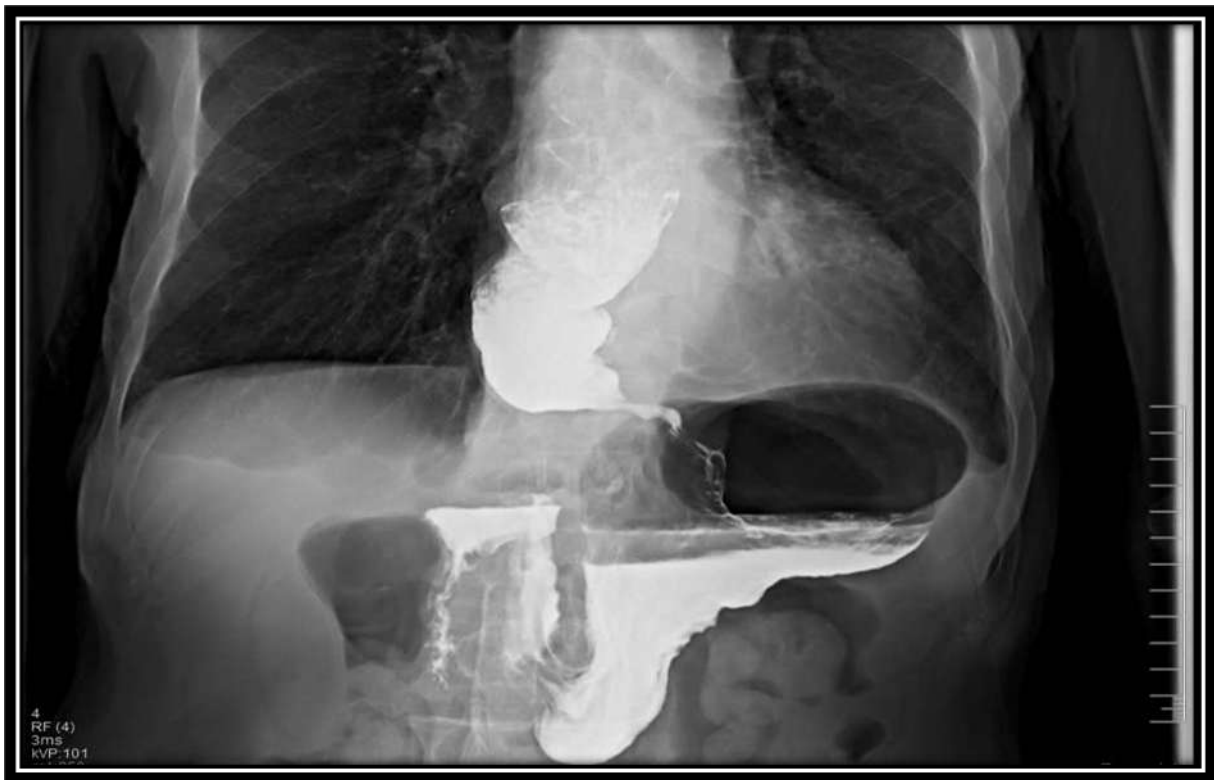


Figure 3. The x-ray shows the typical “bird’s beak” sign, esophageal dilatation.

Endoscopy showed dilation of the esophagus with food remnants, whitish coating of the mucosa caused by adhesion of the remained food inside of the esophagus and thickening of the mucosa. Endoscopy excluded esophageal and gastric cancer.

Secondary causes of achalasia, such as: esophageal malignancy and stricture, gastric carcinoma, Chagas disease, systemic sclerosis was excluded.

Coronary angiography was unremarkable and has been performed 1 years ago due to unexplained acute chest pain.

As soon as diagnosis was established, the patient was referred to the laparoscopic Heller myotomy with fundoplication, after which his complaints disappeared and patient fully recovered. Thus, it is very important to train, improve knowledge, focus on extra cardiac manifestations on echocardiography and establish appropriate guidelines for conducting a comprehensive study.

Discussion

Idiopathic achalasia (IA) is a primary esophageal motility disorder characterized by aperistalsis and lower esophageal sphincter dysfunction, with an annual incidence of approximately 1.6 cases per 100,000 individuals and prevalence of 10 cases per 100,000 individuals [5].

IA results from inflammation and degeneration of inhibitory neurons in the esophageal wall that primarily release vasoactive intestinal peptide and nitric oxide. A localized decrease of these substances causes failure of lower esophageal sphincter relaxation and disruption of esophageal peristalsis [6]. The cause of the inflammatory degeneration of neurons in primary achalasia is not

known [7]. IA is most frequently seen in middle and late adulthood (age 30 to 70 years) with no gender and racial predisposition.

Left atrial compression by achalasia is a rare presentation and may cause hemodynamic compromises [8].

Patients with achalasia may suffer symptoms for a long time before being diagnosed. The most common symptoms are: dysphagia, regurgitation, chest pain, difficulty swallowing both liquids and solids and thus weight loss. Some patients may have a cough due to aspiration of food particles into their airways [9].

Several diagnostic tests are routinely utilized for the diagnosis of achalasia: Barium swallow, esophageal manometry, esophagogastroduodenoscopy, prolonged esophageal pH monitoring, endoscopic ultrasonography.

Because conservative treatment of achalasia is not curative, therapeutic success is determined by the improvement in symptoms as reported by patients. All available treatments are hence palliative [10].

Management of achalasia involves improving the esophageal outflow in order to provide symptomatic relief to patients [11].

The treatment modalities employed for this purpose included pharmacological therapy (e.g., Calcium channel blockers, long-acting nitrates), endoscopic interventions (e.g., botulinum toxin injection to lower esophageal sphincter, pneumatic dilation, paroral endoscopic myotomy) and surgical interventions (surgical myotomy, esophagectomy) [12].

Our case shows the role of routine TTE in identifying extra cardiac structure – esophageal achalasia, leading to important diagnosis and indication for further surgical intervention.

Incidental echocardiographic extra cardiac findings in the clinical case presented by us led to a new diagnosis, referral of patients to surgeons and, accordingly, changed the treatment strategy.

Pharmacotherapy Management Challenges

Managing idiopathic achalasia presents unique challenges, particularly when it comes to pharmacotherapy. The primary goal of treatment is to reduce the pressure in the lower esophageal sphincter and improve esophageal motility. Pharmacological therapies, including calcium channel blockers and nitrates, are commonly used to relax the lower esophageal sphincter temporarily. However, these medications often provide only short-term relief and may not be effective for all patients.

Additionally, the variability in patient responses to pharmacotherapy complicates treatment management. While some patients may experience significant symptom relief, others may require additional interventions, such as botulinum toxin injections, balloon dilation, or surgical myotomy (the Heller myotomy procedure). The decision to proceed with these interventions often depends on the severity of the disease, patient preference, and response to initial treatments.

Echocardiography can also play an indirect role in pharmacotherapy management by helping assess the effects of treatment on the heart. For instance, if left atrial compression is alleviated as the esophagus is treated, echocardiography can monitor changes in atrial size and flow dynamics, offering valuable feedback on the success of pharmacological or surgical interventions.

Future research should explore the refinement of echocardiographic techniques to better identify and characterize extracardiac abnormalities, as well as the development of guidelines for incorporating echocardiography into the diagnostic pathway for rare conditions like achalasia. Additionally, continued investigation into pharmacological treatments and their integration with

echocardiographic monitoring could lead to improved management strategies and patient outcomes.

In summary, echocardiography plays a critical, yet often underappreciated, role in diagnosing and managing rare extracardiac conditions. Its application in diagnosing idiopathic achalasia exemplifies the potential for cardiac imaging to impact broader medical fields and underscores the need for more focused research and clinical training to unlock its full potential.

Conclusion

The use of echocardiography as an initial diagnostic approach for rare extracardiac conditions like idiopathic achalasia has the potential to transform clinical practices. Early detection of extracardiac abnormalities, including left atrial compression due to esophageal dilation, can expedite the diagnosis and improve the management of these patients. Moreover, echocardiography's ability to monitor cardiac involvement in achalasia can guide pharmacotherapy decisions and inform the need for further interventions. The challenges associated with pharmacotherapy for idiopathic achalasia underscore the need for a comprehensive, multidisciplinary approach to patient care. While pharmacological treatments provide symptomatic relief for many patients, the role of surgical interventions and ongoing monitoring is crucial for those with more severe forms of the disease. As echocardiography continues to demonstrate its value in identifying and managing extracardiac conditions, ongoing research, training, and clinical awareness are essential to fully harness its diagnostic and management potential.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

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Competing Interests

The authors declare no competing interests.

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Ethical Standards

The research meets all ethical guidelines, including adherence to the legal requirements of the study country.

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THE SCIENTIFIC TALKS OF A COMPREHENSIVE REVIEW OF MANIFESTATION OF FEATURES OF ASSESSING THE HEALTH RISKS OF ELECTRONIC CIGARETTES

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ABSTRACT

Electronic cigarettes (e-cigarettes) have gained significant popularity worldwide as an alternative to conventional tobacco products, sparking widespread scientific inquiry into their health risks and benefits. This review aims to provide a comprehensive assessment of the current evidence on the health risks associated with e-cigarettes. By synthesizing findings from toxicological studies, clinical research, and epidemiological analyses, we explore the chemical composition of e-cigarette aerosols, their potential for addiction, and their short- and long-term effects on respiratory, cardiovascular, and other organ systems. The review highlights critical risk factors, including variability in device designs, e-liquid formulations, and patterns of use. Additionally, the potential role of e-cigarettes in smoking cessation versus their impact on youth and nonsmoker initiation is critically evaluated. The paper identifies gaps in the existing literature, emphasizing the need for long-term studies to guide public health policy and regulatory frameworks. This comprehensive review serves as a resource for researchers, healthcare professionals, and policymakers aiming to navigate the complex health implications of e-cigarette use. The burgeoning popularity of electronic cigarettes (e-cigarettes) has sparked intense scrutiny over their potential health effects, particularly concerning respiratory, cardiovascular and mental well-being. This review consolidates current scientific knowledge on the subject, shedding light on the multifaceted impacts of vaping. Respiratory concerns, including the risk of E-cigarette or Vaping Use-Associated Lung Injury (EVALI), popcorn lung, and exacerbation of asthma and allergies, are discussed alongside cardiovascular risks associated with long-term e-cigarette use. Additionally, the threat of nicotine poisoning, particularly among children, is highlighted. Moreover, the potential impact of vaping on mental health, including its association with depression, anxiety, and suicidal thoughts, is explored. Despite their perception as a safer alternative to traditional tobacco products, e-cigarettes contain harmful substances with the potential to damage DNA and contribute to cancer risk, though definitive evidence remains elusive. As e-cigarette usage continues to evolve, further research is essential to comprehensively

assess their risks and benefits, informing evidence-based policies and public health interventions. Additionally, insights into the diverse landscape of e-cigarette varieties underscore the importance of informed decision-making and adherence to safety protocols among users. In light of these findings, it is imperative to adopt evidence-based regulatory measures to mitigate the potential risks associated with e-cigarette use. Additionally, further research is warranted to elucidate the long-term health impacts of vaping and inform targeted interventions. Moving forward, a holistic approach that considers the interplay between individual behaviors, regulatory frameworks, and public health initiatives is essential to safeguarding the well-being of populations worldwide in the era of e-cigarettes.

Keywords: assessing, health risks, electronic cigarettes.

Exploring the Effects of Vaping on Your Well-being

Considering using an e-cigarette? It is crucial to be aware of potential health impacts, especially if you have allergies or asthma. Here is a rundown of the health risks associated with vaping [6].

Respiratory Concerns

Vaping poses risks to your lungs, potentially leading to various respiratory issues. One significant worry is EVALI, a condition linked to prolonged e-cigarette use, causing acute lung injury. Reports indicate numerous fatalities and hospitalizations due to EVALI. Additionally, vaping may contribute to popcorn lung, a rare condition resulting from inhaling a chemical found in certain e-cigarette flavors, possibly causing permanent lung damage. Furthermore, vaping could lead to a collapsed lung. The safest approach is to avoid e-cigarettes altogether [7].

Aggravating Allergies and Asthma

For individuals with asthma or allergies, vaping can worsen symptoms. Inhaling vapor can irritate the respiratory system, triggering inflammation and leading to coughing, wheezing, and breathing difficulties. Using e-cigarettes with asthma might even trigger an asthma attack. Allergy sufferers may experience heightened symptoms after vaping, such as congestion, sneezing, and watery eyes [8].

Cardiovascular Risks

Research suggests that long-term e-cigarette use harms blood vessels, elevating the risk of heart disease, stroke, and other cardiovascular issues. Nicotine in e-cigarettes also contributes to cardiovascular problems by increasing blood pressure and heart rate, constricting blood vessels, and potentially reducing oxygen-rich blood flow to organs and tissues. Chemicals present in vape products further compound these risks [9].

Nicotine Overdose

Nicotine poisoning is a grave concern, especially for children and inexperienced smokers. E-cigarettes contain highly concentrated nicotine, and accidental ingestion or exposure to high levels can lead to symptoms like nausea, vomiting, increased blood pressure, arrhythmia, and convulsions. Some vape products have higher nicotine levels than traditional cigarettes, posing particular risks to young users. Prompt medical attention is crucial if you suspect nicotine poisoning [10].

Impact on Mental Health

Vaping is associated with mental health issues, including suicidal thoughts, depression, and anxiety. Nicotine affects the brain's reward system, potentially exacerbating existing mental health conditions or precipitating new ones. Seeking support from mental health professionals is vital during times of stress or emotional distress, rather than resorting to vaping [11].

The ongoing discussion surrounding the possible cancer-causing effects of electronic cigarettes (e-cigarettes) continues to be a pertinent topic. E-cigarettes function through the heating of a liquid comprising nicotine, flavorings, and assorted chemicals. Upon heating, users inhale an aerosol substance into their lungs (4). While they are often considered safer than traditional tobacco products, e-cigarettes still contain harmful substances that have the potential to damage DNA and cause cancer. Numerous studies have delved into the potential cancer risks associated with e-cigarette usage, with some indicating that the aerosol emitted by e-cigarettes may contain carcinogenic compounds that could heighten the likelihood of lung and bladder cancer in humans. Nonetheless, these investigations are constrained in scope and fail to furnish definitive evidence. The overarching uncertainty regarding the long-term cancer risks attributed to e-cigarette use underscores the imperative for further research to comprehensively grasp the potential hazards and advantages of e-cigarettes. Nonetheless, this assessment will facilitate the researcher in accessing more recent insights concerning e-cigarettes [1].

In 2003, Lik Hong, a chemist hailing from Hong Kong, introduced the inaugural commercially viable electronic cigarette (e-cigarette). Unlike traditional tobacco products, this device functions by heating a nicotine solution to liberate nicotine without the emission of tobacco smoke. E-cigarettes and vaping devices commonly utilize a solution comprising nicotine, moisturizers, and flavorings for inhalation purposes. The appeal of e-cigarettes among young adults stems from assertions suggesting their potential efficacy in aiding smokers to quit. This inclination among young adults could be attributed to their susceptibility to novel trends, particularly if they perceive such trends as conducive to breaking the habit of cigarette smoking [12]. Moreover, the diverse array of flavors contributes significantly to their popularity among users. Smokers who struggle to quit often view e-cigarettes as a preferable alternative with fewer health implications. Across various European countries, the lifetime prevalence of e-cigarette vaping stands at 43.7%, with notable gender disparities: 51.3% among men and 40.5% among women. Noteworthy prevalence rates of e-cigarette usage include France (25.46%), Mexico (42.22%), China (24.44%), Australia (12.5%), and the United States (13%), as indicated by multiple studies. Furthermore, research findings suggest a potential association between e-cigarette use and increased risks of cardiovascular and respiratory diseases [13].

Cigarette Varieties

The world of e-cigarettes is diverse, with various monikers such as mods, e-hookahs, e-cigs, vapes, vape pens, and tank systems. Each variant comes with its own set of pros and cons, catering to individual preferences, experience levels, and vaping routines. It is crucial to opt for a high-caliber e-cigarette crafted by a reputable manufacturer and adhere to safety protocols during usage.

E-Cigarette Classifications:

1. Electronic Nicotine Delivery Systems (ENDS): These devices house flavored solutions typically infused with nicotine.

2. Electronic Non-Nicotine Delivery Systems (ENNDS): Contrarily, these devices contain flavored solutions devoid of nicotine [15].

Through the heating of liquids, these systems generate aerosols for inhalation by users. These "e-liquids" may or may not incorporate nicotine, but frequently do, alongside flavors, additives, and potentially harmful substances [3]. E-cigarettes or vaping apparatus can transport various compounds like nicotine, cannabis, flavors, and chemicals, posing health risks. Known by diverse aliases like electronic cigarettes, vapes, vape pens, dab pens, dab rigs, tanks, mods, and pod mods, they are commonly associated with activities such as "juuling" or "vaping." Occasionally, the term "dabbing" pens is used in reference to electronic cigarettes or vaping products utilized for dabbing purposes.

E-Cigarette Components

E-cigarette encompasses several integral parts: a mouthpiece, a sensor or button facilitating the activation of the battery's heating coil, an atomizer or heating coil, and a reservoir or tank. Activation of the heating coil occurs upon user inhalation through the mouthpiece, thereby transforming the e-cigarette solution into an aerosol, commonly referred to as vapor-liquid, contained within the cartridge. Cartridges may come pre-filled or be refillable, typically utilized alongside a nebulizer [12].

Atomizer: This component serves as an electrical heating element, aiding in the conversion of e-liquid into aerosolized microscopic air droplets [16].

E-cigarettes featuring sensors, rather than buttons, activate upon user inhalation. Regardless of button presence, sensors require activation in electronic cigarettes [17].

Battery: Facilitating the rapid heating of the atomizer to approximately 400 degrees Fahrenheit, this rechargeable lithium-ion battery powers the device [18].

Different Generations of E-Cigarettes:

First-Generation ECs: These devices, often resembling traditional cigarettes, feature fixed low-voltage batteries. The three primary configurations include:

1. The three-piece original EC type, comprising a separate injector, battery, and liquid tank.
2. A one-piece disposable variant integrating the nebulizer, liquid reservoir, and battery into a single unit.
3. A two-piece model with a combined injector and liquid tank, distinct from the battery [19].

Second-Generation ECs: Referred to as advanced personal vaporizers or mod systems, second-generation electronic cigarettes (ECs) offer enhanced potency and adaptability compared to their first-generation counterparts. These devices, sometimes termed cigarlike, feature larger, variable-voltage batteries, also known as pen-type batteries. Commonly known as "clearomisers," second-generation ECs boast detachable nozzles housing a filament enclosed within a casing that screws into the liquid tank and batteries. Unlike cigarette-like ECs, clearomisers are transparent and accommodate larger liquid reservoirs. They can be refilled with any available refill liquid [20].

Third-Generation ECs: Third-generation ECs, commonly referred to as "Mods," feature customizable batteries allowing users to adjust voltage, capacity, and other parameters. Some models even offer additional functionalities like the ability to charge a mobile phone. Notably, third-generation ECs are capable of producing substantial vapor clouds, which appeal to experienced vapers. However, users must exercise caution to avoid excessive nicotine intake due to the heightened vapor production [21].

Fourth Generation Electronic Cigarettes (ECs): Given its rapid evolution and introduction of numerous new products, the fourth iteration of ECs features a battery-powered stack with preset voltage and diverse configurations, including USB or teardrop designs [22].

Constituents of Electronic Cigarettes (E-Cigarettes)

E-cigarettes function by heating a liquid blend containing multiple ingredients, producing an aerosol. Users inhale this aerosol into their lungs, potentially exposing bystanders when exhaled into the surrounding air. Vapers emit an aerosol comprising liquid droplet mixtures, with reported indoor aerosol sizes typically under 50 nm. Due to the extensive surface area of the alveolar airways, a substantial portion of inhaled e-cigarette aerosol is expected to penetrate and settle in the deep lung. The deposited dose serves as the precursor to the internal dose, accounting for respiratory clearance and absorption rates. Consequently, the deposited amount of e-cigarette aerosol may serve as a key indicator of the health risks associated with passive vaping. Nonetheless, previous research has relied on numerical models or partial human airway replicas due to limitations in traditional experimental methods [23].

Electronic Cigarette Fluids

Commonly referred to as vape juice or e-juice, e-liquids are the solutions used in electronic cigarettes (ECs) to generate vapor. These solutions typically contain glycerol, propylene glycol, flavors, nicotine, formaldehyde, and other chemicals, which undergo heating, aerosolization, and inhalation. Recent findings suggest that e-liquids often harbor various potentially hazardous chemicals. Propylene glycol (PG) and Vegetable glycerin (VG) serve as carriers for flavorings and nicotine in e-liquids. PG, being thinner, provides a stronger throat hit and more intense flavor, while VG, thicker in consistency, yields more vapor and a sweeter taste. The PG-to-VG ratio in e-liquids impacts overall flavor, throat hit, and vapor production. Flavorings are incorporated to offer a wide array of tastes and scents, ranging from fruit and candy to dessert and menthol. Some e-liquids also contain nicotine, an addictive substance found in tobacco. Nicotine concentration in e-liquids varies, allowing users to select strengths based on preference. Users should exercise caution regarding e-liquid ingredients and opt for high-quality products from reputable manufacturers. Inferior e-liquids may contain harmful impurities or incorrect nicotine levels, posing potential risks. Proper storage of e-liquids away from children and pets, along with adherence to manufacturer instructions, is crucial. According to the American Cancer Society, formaldehyde, a carcinogen, may form when e-liquid overheats or when insufficient liquid reaches the heating element, known as "dry puff" [24].

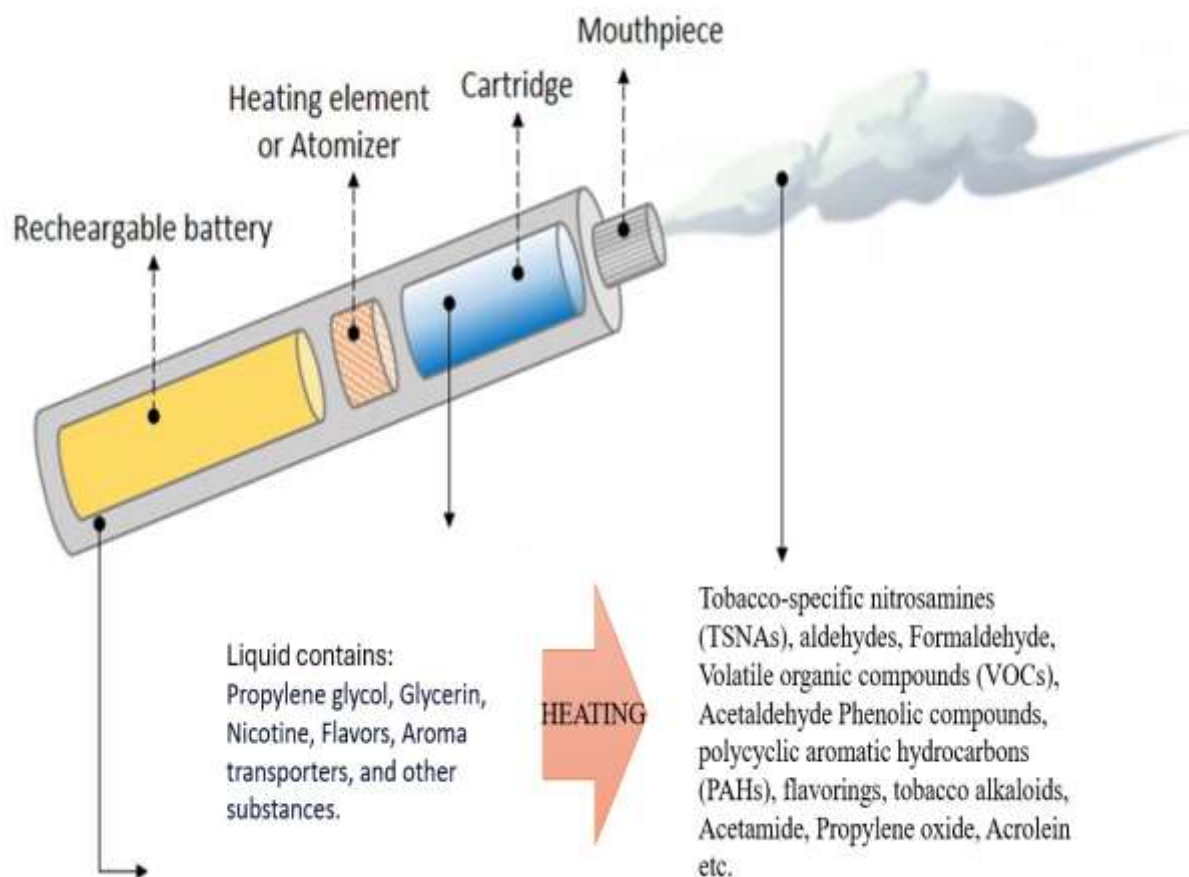


Figure 1: E-cigarette and its constituents.

The impact of the heating process on aerosol composition is notable, revealing various harmful effects. E-cigarette aerosols contain several compounds that are absent in e-liquids, with device materials contributing to the presence of metal and silicate particles in these aerosols. The heating conditions, particularly concerning humectants, flavorings, and the quality of materials utilized, have been pinpointed as the primary sources of these new compounds in aerosols. Certain compounds derived from humectants such as propylene glycol and glycerol, along with flavorings, have been linked to respiratory issues, inflammation, cardiovascular dysfunction, and toxicity. Additionally, some of these compounds possess carcinogenic properties or exhibit potential carcinogenicity (28).

Electronic Cigarette Aerosol

The cloud of particles, termed vapor, emitted by electronic cigarettes (ECs) when e-liquid is heated and transformed into a gas is known as EC aerosol. Typically, EC aerosol comprises water, propylene glycol, vegetable glycerin, flavorings, and occasionally nicotine [2]. The composition of EC aerosol varies based on the specific e-liquid and heating device employed. Particle quantity and size in the aerosol can be influenced by factors like device voltage, heating element temperature, and user inhalation technique. While EC aerosol is generally perceived as less harmful than traditional cigarette smoke, it is not entirely innocuous. Unlike cigarette smoke,

which contains thousands of known toxic and potentially hazardous elements, EC aerosol is notably simpler in composition, albeit present at significantly lower levels than in cigarette smoke. According to the research, glycerol, propylene glycol, water, and nicotine constitute 89–99% of the e-cigarette aerosol composition, with additional minor components comprising about 3% (figure 1) [2].

Chemical Components in E-Liquids

Contrary to popular belief, electronic nicotine delivery systems do not burn tobacco frequently, which prevents the release of harmful compounds. Instead, the elevated temperatures ($>200^{\circ}\text{C}$) reached by e-cigarette solutions are specific to tobacco. Acetaldehyde, a potential carcinogen, along with metals, nitrosamines, and carbonyl compounds such as acrolein and formaldehyde, identified as human carcinogens by the International Agency for Research on Cancer, are produced. Although the quantities generated by e-cigarettes are lower than those in tobacco smoke, they are sufficient to contribute to carcinogenesis due to the presence of recognized carcinogens like formaldehyde and acrolein (26).

Formaldehyde, a Carbonyl Compound

Formaldehyde-containing hemiacetals were detected through Nuclear Magnetic Resonance spectroscopy during the evaporation process, with its chemical structure depicted in Figure 1. Propylene glycol and glycerol act as formaldehyde releasers. According to an analysis of a commercial e-liquid utilized in a "tank system" e-cigarette with a variable voltage battery, formaldehyde-releasing compounds averaged 38,090 g per sample (10 puffs) at high voltage (5.0 V). It may accumulate in the respiratory system faster than gaseous formaldehyde, potentially heightening the risk of cancer development, which is five times greater than that of chronic smoking [27].

Acetaldehyde

Acetaldehyde, labeled by the Institute of Medicine as the foremost cardiovascular (CV) toxin in tobacco smoke. Acetaldehyde exposure carries a potential cancer risk. Prolonged use of ECs may significantly amplify this risk, as recurring exposure to the compound can result in DNA damage accumulation and other cellular alterations linked to cancer susceptibility. Studies indicate variable acetaldehyde levels in EC aerosols, are influenced by EC device type, power settings, and other factors. Even at minimal concentrations, acetaldehyde demonstrates carcinogenic properties and correlates with an elevated cancer risk, particularly affecting the upper respiratory tract and head and neck regions. Acetaldehyde, a carcinogen, may catalyze cancer development via multiple mechanisms, including DNA replication interference, DNA damage induction, and DNA adduct formation [29].

Acrolein

Identified by the Institute of Medicine as the primary cardiovascular (CV) toxin in tobacco smoke. Acrolein, a hazardous chemical, is present in both tobacco smoke and e-cigarette aerosol. It forms when glycerin, a common e-liquid ingredient, undergoes heating during vaping. Acrolein serves as a known respiratory irritant and has the potential to induce DNA damage, thereby contributing to cancer development. Research exploring the cancer risk associated with acrolein exposure from e-cigarette use has been undertaken. Some studies suggest that e-cigarette aerosol may contain

higher levels of acrolein compared to tobacco smoke. Numerous investigations have highlighted that chronic exposure to acrolein exacerbates cardiovascular disease (CVD). Even low-level acute exposure to acrolein can lead to dyslipidemia, vascular damage, endothelial dysfunction, and platelet activation. Animal studies have also implicated acrolein in cancer development [30].

Menthol

Menthol's potential to induce cancer is primarily attributed to its modulation of nicotine metabolism and its direct carcinogenic and pro-inflammatory effects. Menthol is intertwined with nicotine effects, both indirectly—by influencing the body's responses to nicotine, such as through altering nicotinic receptor expression—and directly—by reducing throat irritation and increasing tolerance to tobacco smoke (ECS), thereby contributing to heightened addiction prevalence. Various aromatic e-liquids containing menthol, increased the invasiveness and metastatic potential of lung cancer cells [31].

Ethyl Maltol

Ethyl maltol (EM), a commonly used flavoring agent in food, is generally considered safe for consumption. However, it has been detected in the aerosols of various commercial e-cigarette vaping liquids. EM has been observed to generate radicals when interacting with iron and copper, typically found in the heating element or as impurities. Moreover, EM has been associated with increased pro-inflammatory effects, heightened systemic exposure to inhaled chemicals, inflammatory responses, altered local immune function, and impaired epithelial barrier function and integrity. These findings strongly suggest the carcinogenic potential of ethyl maltol, given the known oncogenicity of free radicals, both individually and collectively [32].

Ethanol

Labeled as a carcinogen by the International Agency for Research on Cancer. While regulations in other countries mandate the disclosure of substances like ethanol in e-liquids, ethanol has been identified as an undisclosed ingredient in nicotine-containing e-liquids sold in the United States. EtOH influences epigenetics by modifying DNA and histone methylation and acetylation, potentially impacting gene expression regulation even following transplacental exposure. However, evidence regarding the carcinogenicity of EtOH in laboratory animals remains inconclusive. There is currently no definitive evidence linking ethanol in e-liquids to cancer [12].

Tocopherol

Vitamin E, particularly acetate, is a viscous substance used as a diluent and thickener in some formulations, particularly those involving cannabis derivatives. Vitamin E acetate, an oil-based additive, was occasionally included in EC e-liquids to enhance viscosity. Inhalation of this oil can coat the lungs and lead to respiratory issues, implicated in a series of recent cases of e-cigarette-related lung injury. The thermal decomposition of vitamin E generates highly toxic and irritating ketene gas (by removing the aryl acetate group) and various other toxic and reactive chemicals, including benzene and several alkenes, with identifiable carcinogenic properties [33].

Metals

According to certain studies, hazardous heavy metals such as cadmium and lead are found in both cigarette smoke and the aerosol generated by e-cigarettes. A recent investigation by the California

Department of Public Health reveals that toxic heavy metals like lead, chromium, nickel, manganese, and nickel are present in higher concentrations in e-cigarette aerosols and e-liquids compared to cigarettes. Exposure to heavy metals through e-cigarettes can have adverse health effects. Certain e-cigarette brands containing chromium and nickel have been associated with respiratory conditions like lung cancer. Chromium and nickel compounds are commonly used in welding, electroplating, and other industrial processes. Lead and manganese exposure can lead to neurological and developmental issues, with manganese compounds being utilized in batteries, insecticides, and steel manufacturing. Lead compounds are found in batteries, ammunition, metal products, paints, and ceramics. Cadmium exposure is linked to lung cancer and kidney damage, with cadmium compounds used in nickel-cadmium batteries and in the production of coatings, plastics, ceramics, glass coloring pigments, and polymers. The cancer risk associated with e-cigarettes is not solely due to heavy metals; compounds like formaldehyde and acetaldehyde, also carcinogens, pose additional risks to e-cigarette users. In summary, e-cigarettes contain numerous components that may increase the likelihood of cancer among users [34].

Cancer Risks Associated with E-Cigarettes

The full spectrum of long-term health consequences stemming from electronic cigarette (EC) use remains incompletely understood, given the relative novelty of the technology and ongoing research endeavors. Nonetheless, emerging evidence suggests a potential elevation in the risk of certain cancer types among EC users. The presence of carcinogens in the bodily fluids of e-cigarette users inherently exposes cells to the possibility of oncogenic transformations. While nicotine itself may not directly cause cancer, it remains a highly addictive substance with various adverse health effects, including heightened heart rate and blood pressure, narrowed blood vessels, and compromised lung function. Nicotine residues from aerosols or e-liquid persist on surfaces for extended periods, reacting with environmental elements to produce nitrates and tobacco-specific nitrosamine compounds. This process increases the likelihood of inhalation, ingestion, or dermal exposure to carcinogens [35].

Head and Neck Findings

Research involving various brands of electronic vapor, with or without nicotine, alongside heavy metals like cadmium, lead, nickel, and nitrosamines, demonstrated diminished cell viability and increased apoptosis compared to unexposed controls. Notably, there was substantial evidence of necrosis observed in head and neck squamous cell carcinoma and normal epithelial cell lines. Additionally, exposed cell lines exhibited heightened expression of H2A histone family member X (-H2AX), a recognized marker of double-stranded DNA breakage. Significant DNA double-strand breaks were noted in cells exposed to e-cigarette aerosols (0.5–2% volume) over periods ranging from 24 hours to 4 weeks. Furthermore, e-cigarette treatment led to increased migration of head and neck cancer cells along with upregulation of EMT-promoting genes [36].

Lung Health Concerns

Lung cancer (LC) is widely recognized as a prevalent form of cancer worldwide. Various studies have highlighted the associations between E-cigarette, or vaping, products (EVPs) and several established environmental toxins in the development of LC. While tobacco smoke remains the primary culprit for LC, there is a growing worry that the use of EVPs could amplify the risk of contracting the disease. The consumption of EVPs has seen a significant surge globally, especially among youth and non-smokers. Consequently, EVPs present a substantial risk factor for LC and

pose a substantial concern for the future. Given the established links between these factors and LC development, further investigation is required to elucidate the mechanisms through which they impact lung pathology. Uncovering the pathophysiology of EVP use and exposure to environmental toxins in LC development can aid in the implementation of strategies to reduce exposure [37].

Breast Cancer Concerns

Breast cancer (BC) stands as the most common cancer among women in the United States, comprising nearly one-third of all cancer diagnoses in this demographic and accounting for over 18–20% of all cancer-related female deaths. There is growing evidence indicating that e-cigarettes contribute to the lung metastasis of human breast cancer cells, highlighting significant concerns for human health that warrant further investigation [38].

As ongoing research continues to explore the long-term impacts of e-cigarette usage, emerging evidence indicates a potential link between e-cigarette use and heightened cancer risk, alongside other health complications such as cardiovascular and respiratory diseases. This heightened risk stems from the presence of harmful chemicals and flavorings present in e-cigarette aerosols. Consequently, exercising caution during e-cigarette use and contemplating alternative smoking cessation methods are pivotal considerations. The safest approach remains to abstain from e-cigarette use entirely.

Beyond the cancer risk associated with e-cigarette usage, there are broader health implications to ponder. E-cigarettes harbor nicotine, an addictive substance capable of impairing adolescent brain development. Moreover, nicotine intake can elevate blood pressure, accelerate heart rate, and constrict blood vessels, thereby amplifying the likelihood of heart disease. Although e-cigarettes may offer limited benefits as smoking cessation aids, the potential hazards, including cancer susceptibility, necessitate careful evaluation before adoption.

Moreover, according to insights from the European Respiratory Society, prolonged inhalation of any substance carries inherent risks to lung health.

Conclusion

The widespread adoption of electronic cigarettes (e-cigarettes) has ushered in a complex landscape of potential health implications, prompting a critical appraisal of their safety and efficacy. While e-cigarettes have been touted as a safer alternative to traditional tobacco smoking, accumulating evidence suggests that they are not without risks. Our review underscores the diverse array of health concerns associated with vaping, ranging from respiratory and cardiovascular issues to mental health impacts and potential carcinogenicity.

Respiratory complications, including the risk of EVALI, popcorn lung, and exacerbation of asthma and allergies, pose significant threats to e-cigarette users. Moreover, long-term e-cigarette use has been linked to cardiovascular diseases, potentially stemming from nicotine's adverse effects on blood vessels and the cardiovascular system. The risk of nicotine poisoning, especially among children, highlights the need for stringent regulation and public awareness campaigns.

Furthermore, the association between vaping and mental health issues, such as depression, anxiety, and suicidal thoughts, underscores the need for comprehensive support systems and mental health interventions. Despite assertions of harm reduction, the presence of harmful chemicals in e-cigarette aerosols raises concerns about their potential carcinogenicity and long-term health effects.

In light of these findings, it is imperative to adopt evidence-based regulatory measures to mitigate the potential risks associated with e-cigarette use. Additionally, further research is warranted to elucidate the long-term health impacts of vaping and inform targeted interventions. Moving forward, a holistic approach that considers the interplay between individual behaviors, regulatory frameworks, and public health initiatives is essential to safeguarding the well-being of populations worldwide in the era of e-cigarettes.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

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Competing Interests

The authors declare no competing interests.

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Ethical Standards

The research meets all ethical guidelines, including adherence to the legal requirements of the study country.

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THE SCIENTIFIC TALKS OF MANIFESTATION OF EXPLORING SOME KEY ISSUE ASPECTS OF SCHOLARLY DISCOURSE OF APPRAISING INDICATORS ALTERING PHARMACISTS' PROFESSIONAL EXPANSION, PROGNOSIS, ACHIEVEMENT, AND CHALLENGES AND VOCATIONAL OBSTACLES IN GEORGIA

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ABSTRACT

The primary objective of this research was to evaluate of some key issue aspects of scholarly discourse of appraising indicators altering pharmacists' professional expansion and vocational obstacles in Georgia in general. This study employed a quantitative approach to investigate the core determinants shaping pharmacists' career progression and vocational setbacks, using structured questionnaires as the primary data collection tool. A survey study was conducted, complemented by in-depth interviews with respondents. The research utilized validated questionnaires (with randomly selected participants) and employed systematic, sociological inquiry alongside comparative, mathematical-statistical, and graphical analyses. Data processing and analysis were carried out using the SPSS software. Descriptive statistics and regression analyses were conducted to explore relationships between variables, with statistical tests performed using SPSS version 11.0. The Chi-square test was applied to determine statistical significance, with a threshold of $p < 0.05$ considered significant for all analyses. The study comprised several sub-studies aimed at evaluating the principal factors affecting pharmacists' professional growth and the challenges within their occupational scope in Georgia. The findings highlight the critical need to address key factors influencing pharmacists' career advancement and workplace challenges, identifying crucial areas for improvement. Addressing these issues necessitates a comprehensive strategy that encompasses educational reform, modernization of regulatory frameworks, enhanced inter professional collaboration, and strengthened workplace support systems. These measures would better position the pharmacy profession in Georgia to adapt to the evolving demands of healthcare and improve patient outcomes significantly. In many developing nations, the pharmacy profession is subject to stringent regulatory oversight, similar to family medicine. Chi-square test of independent has been performed in order to compare the attitude of different sides to the necessity of pharmacists' certification regulation by Government. The opinion that certification of pharmacists should be mandatory was more common among public health specialists, than among managers (Chi-square = 45.2, $p < 0.001$) and pharmacists (Chi-square = 68.9, $p < 0.001$), but there was not statistically significant difference between chiefs and pharmacists. It was more common also among patients than in pharmacists (Chi-square = 44.2, $p < 0.001$). The necessity of pharmacists' certification was stated more often by employed students, than by pharmacists (Chi-square = 57.3, $p < 0.001$). Present pharmaceutical services connected to self-health care and the significance that pharmacist professionals drive the health care frame systems in the new modern direction. Collaboration between physicians and pharmacists in treatment is gaining moment and has shown positive effects on patients' health. So according study results found, that drug-drug interactions, adverse drug reactions and treatment costs are reduced by involving pharmacists in the drug therapy process. Study showed that when pharmacists' interventions were taken into account, the therapeutic effect improved in majority of patients and adverse drug reactions were prevented in many of cases. The professional development of pharmacists in Georgia faces several critical challenges, particularly in education, job satisfaction, and professional recognition. Addressing these issues will require concerted efforts from the government, educational institutions, and healthcare organizations. By aligning the profession more closely with global standards and enhancing opportunities for continuous education, Georgia can ensure that its pharmacists are equipped to meet the growing demands of the healthcare system. Pharmacists in Georgia face a unique set of challenges compared to their counterparts in Western countries. In many developed countries, the profession of pharmacy is

regulated similarly to other healthcare professions, such as family medicine. Pharmacists undergo rigorous training, continuous education, and periodic licensing reviews to maintain professional standards. However, in Georgia, the profession has not yet reached the same level of integration into the healthcare system. Many pharmacists report feeling underappreciated, both in terms of professional recognition and compensation. Moreover, the lack of continuing education programs and the absence of a cohesive professional body to advocate for pharmacists' rights and responsibilities has further limited their role. The global pharmaceutical industry continues to evolve, with pharmacists taking on more specialized roles, especially in clinical settings. This paper seeks to identify the gaps between Georgian pharmacists and their international counterparts, emphasizing the importance of reforms in education, licensing, and professional integration.

Keywords: pharmacists', professional expansion, vocational obstacles, Georgia, general.

Introduction

Pharmacy practice in Georgia, as in many regions, has undergone significant transformations in recent years, driven by advancements in healthcare, changes in educational frameworks, and evolving regulatory environments. Pharmacists, once seen primarily as dispensers of medications, now play a critical role in patient care through collaborative practice models, disease management, and preventive healthcare initiatives. However, despite these opportunities for professional expansion, numerous vocational obstacles continue to challenge the workforce in Georgia.

The article seeks to explore and critically examine the key issues influencing the professional growth and development of pharmacists in Georgia. It addresses the complex array of factors—educational, economic, regulatory, and societal—that impact the practice of pharmacy in the state. These factors shape not only the scope of the profession but also the opportunities available for professional expansion. At the same time, they create barriers that hinder pharmacists' ability to fully engage in these expanded roles.

The article provides an in-depth analysis of the indicators that alter pharmacists' professional trajectories. By examining both the positive advancements and persistent challenges within the profession, the study aims to offer insights into potential solutions and policy recommendations for overcoming these vocational obstacles. Ultimately, the goal is to contribute to the ongoing discourse on enhancing the role of pharmacists in Georgia's healthcare system, ensuring that the profession continues to evolve in ways that benefit both practitioners and the communities they serve. The evaluation of key determinants affecting pharmacists' professional formation and occupational setbacks in Georgia highlights significant areas for improvement. Addressing these issues requires a multifaceted approach involving educational reform, regulatory updates, enhanced inter professional collaboration, and adequate workplace support. By focusing on these aspects, the pharmacy profession in Georgia can better align itself with the evolving demands of healthcare and ultimately improve patient outcomes. The role of a pharmacist as a health profession provider requires not only higher education but also postgraduate and continuous professional development in pharmacy. Pharmacists must obtain a license and undergo periodic accreditation to maintain their professional standing. In Western nations, only individuals with accredited higher pharmaceutical education are permitted to practice. The process of opening a pharmacy is also strictly regulated, with permits granted exclusively to those who have completed recognized pharmacy programs and earned the credentials necessary to operate a pharmacy. It is

important to note that in both developed and developing nations, pharmacy is a tightly regulated profession, akin to family medicine. Pharmacists, viewed as family healthcare providers, must possess advanced pharmaceutical education, a diploma, ongoing professional training, a pharmaceutical license, and undergo regular accreditation. These regulations ensure the highest standards of care and accountability in the profession.

On the basis of theoretical analysis of the process of professional development will be developed by a set of common criteria for the effectiveness of this process, which will be based on the regularities of formation, reflecting its focus and dynamics: an interest in their chosen profession, changing choice motives, increased satisfaction of occupational choice and labor, increasing the motivation to knowledge and professional development, change career planning purposes. The goal, purpose and objectives of the planned research. The main aim is to develop a methodological approach to study and improve the process of professional development specialists' pharmaceutical profile, regulation requirements for pharmaceutical staff in drugstore professional career improvement strategy and jobsatisfaction among pharmacists. A systematic analysis identified factors which had influence the formation of personal-professional position of a pharmaceutical professional and realization of their personal resources. On the basis of theoretical analysis of the process of professional development there will be developed a set of common criteria for the assessment of the effectiveness of this process, based on which will be identified the regularities of formation, reflecting its focus and dynamics: their interest in profession of choice, changes in choice making motivation, growing job satisfaction, increasing the desire to acquire more knowledge and professional skills and making appropriate adjustments in their career goals. Based on the theoretical analysis of the main approaches to the study of the process of professional development, taking account the concept of pharmaceutical assistance, a set of related criteria for the effectiveness of this process. Based on common performance criteria, the patterns of formation are revealed, reflecting its direction and dynamics: interest in the chosen profession, changing the determinants of choice motives, increasing satisfaction with choice of profession and work, increasing motivation for cognition and continuous professional development, changing career planning goals. On the basis of specific criteria, the specifics of the formation are revealed, which include: incomplete correlation of the internal resources of the individual with the needs of the pharmacist/pharmacist profession, insufficient awareness of individual aspects of future activities, the difficulties of production adaptation, and low satisfaction with the work of pharmaceutical professionals [11-13].

Deficiency of knowledge and functions of pharmaceutical professions in Georgia is not exists only in the non-medical section of the society, but also in the medical staff like health-care specialists. Developing a continuous pharmaceutical education system, will enhance the professionalism of pharmaceutical personnel. We also measure the perception of job satisfaction among Georgian pharmacists and future proposals to improve pharmacists' job satisfaction. Using described above questionnaire, the purpose of our study was: To obtain data on job satisfaction retail environment; To distinguish aspects of the community of practice that have the greatest contribution to work gratification; To investigate the precision and reliability of the questionnaire in a study sample community pharmacies. We have been studied "the peculiarities of professional pharmacists, career satisfaction and service improvement strategy". It is necessary to obtain a grade of key issue factors influence of pharmacists' professional development according occupational vision of health care professionals and pharmacy students in Georgia. [14-16].

Development of organizational and functional models for licensing pharmaceutical activities, is considered as one of the mechanisms to improve the efficiency of public administration, and has great relevance and scientific and practical value. An integral part of the state system of measures to implement the rights of citizens to protect their health is pharmaceutical care, the quality of the provision which is largely dependent on the qualifications of the personnel pharmacist. In this regard, the professional qualification of experts is under the control of the state and is one of the objects of state regulation of relations in the field of drug- medicine, whose purpose - maintaining the competence of expert specialists on throughout their careers with varying requirements for professional quality [17-18].

The modern system of pharmaceutical care to improve the quality of life of patients depends on highly skilled professionals in drug-store whose competence has been growing in the process of professional development. The pharmacists require not only the use of earned at the institution of knowledge and skills, but also the willingness to professional self-development. Since the scope of drug treatment is one of the most socially significant areas of state regulation, the sequence in carrying out reform measures, conservation experience, and smooth introduction of new methods become crucial. However, comprehensive studies aimed at understanding the process of professional formation pharmaceutical worker, for to provide quality pharmaceutical care has not yet been carried out. Development of organizational and functional model of the licensing of pharmaceutical activities, pharmacists job as one of the mechanisms to improve the efficiency of public pharmaceutical and public administration, has great relevance, scientific and practical value [19-21].

- **High Workload and Stress:** Increased responsibilities, coupled with staffing shortages, can lead to overwhelming workloads, resulting in stress and burnout.
- **Public Perception:** Misunderstandings regarding the role of pharmacists can limit their recognition as vital healthcare providers, impacting job satisfaction and career advancement.
- **Regulatory Constraints:** Overly stringent regulations can stifle innovation and restrict pharmacists from fully utilizing their training to enhance patient care.
- **Economic Factors:** Financial pressures within healthcare systems can lead to resource constraints, affecting the availability of training and professional development opportunities for pharmacists.

Pharmacist profession has undergone significant changes in recent years, particularly in the realm of clinical responsibilities and patient care. Traditional roles, where pharmacists primarily dispensed medication, have expanded globally, with pharmacists now playing a crucial part in healthcare teams. In Georgia, however, pharmacists still face challenges in professional recognition, continuing education, and collaboration with other healthcare professionals. This paper aims to explore the professional development of pharmacists in Georgia and suggest areas for improvement by comparing local trends with global advancements [1-3].

The advent of online pharmacies and other technological developments has further shifted the landscape of the profession. While these changes meet consumer demand, they have also impacted the direct, personal connection pharmacists traditionally had with patients. This erosion of pharmacist-patient relationships, coupled with inadequate government support for pharmacists' professional development, has raised concerns about the future of the profession in Georgia. Globally, the role of pharmacists is increasingly being recognized, particularly in fields such as pharmacotherapy and clinical pharmacy. This paper will examine the Georgian context and

evaluate how pharmacists' roles can be enhanced through targeted reforms in education, regulation, and professional collaboration [4-6].

The role of pharmacists has evolved significantly in recent years, with increasing responsibilities that extend beyond traditional dispensing duties. In Georgia, as elsewhere, pharmacists are now expected to contribute actively to patient care, medication management, and public health initiatives. However, the professional formation of pharmacists faces various challenges that can hinder their effectiveness and the overall impact they have within the healthcare system [7-8].

A systematic analysis will identify factors which influence the formation of personal-professional position of a pharmaceutical professional and realization of their personal resources. On the basis of theoretical analysis of the process of professional development there will be developed a set of common criteria for the assessment of the effectiveness of this process, based on which will be identified the regularities of formation, reflecting its focus and dynamics: their interest in profession of choice, changes in choice making motivation, growing job satisfaction, increasing the desire to acquire more knowledge and professional skills and making appropriate adjustments in their career goals. The stage of professional development of specialists is the adaptation to work activity: the beginning of an independent professional activity and the accumulation of experience by young specialists. This stage reflects the student's transition to a new type of activity - to professional work in its various forms in the conditions of real situation, performance of official duties, production relations, finding oneself in the system of work collectives. In the course of adaptation, the system of professional knowledge and skills is acquired in the required volume; the emergence of interest in the work, which begins to play an increasingly important role in life, a sense of the connection between success and the profession, is self-determination for professional development [9-10].

Goal

The main aim of the study was to analyze and grade the key issue aspects of scholarly discourse of appraising indicators altering pharmacists' professional expansion and vocational obstacles in Georgia.

Methodology

Research objectives are materials of sociological research: the study was quantitative investigation by using survey (Questionnaire). The study was quantitative investigation by using survey (Questionnaire). The in-depth interview method of the respondents was used in the study. The approved questionnaires were used (Respondents were randomly selected. Were used methods of systematic, sociological (surveying), comparative, segmentation, mathematical-statistical, graphical analysis. Research objectives are materials of sociological research: the study was quantitative investigation by using survey – questionnaire. The in-depth interview method of the respondents was used in the study. Different types of approved questionnaires were used (respondents were randomly selected), e.g.

- Questionnaire for chief pharmacists: 410 chief pharmacists;
- Questionnaire for patients: 1506 patients (customers of drug-stores);
- Questionnaire for employed pharmacy faculty-students: 222 employed students;
- Questionnaire for health-care specialists: 307 public health specialists;
- Questionnaire for pharmacist specialists: 810 pharmacist specialists.

Totally 3888 respondents were interviewed in Georgia.

The data was processed and analyzed with the SPSS program. Results and discussion: Questions and answers are given in the tables. On each question are attached diagrams or table. Questionnaire and diagrams are numbered. Study of the data was processed and analyzed with the SPSS program. We conducted descriptive statistics and regression analyses to detect an association between variables. Statistical analysis was done in SPSS version 11.0. A Chi-square test was applied to estimate the statistical significance and differences. We defined $p < 0.05$ as significant for all analyses. The study's ethical items. In order to provide the study's ethical character each participant of it was informed about the study's goal and suggested of willingness of the work to be done. So, the respondents' written or oral compliance was got on that issue. All the studies were carried out by the selected organizations administrations' previous compliance. Were used Informed consent form for each respondent to participate in an anonymous survey. During the whole period of research, the participants incognita was also provided. For the international rules and criteria' conformity this human subject comprising given study was discussed and confirmed on the Bioethics Committee sessions of the YSMU. In order to meet the objectives, set in the research we also used the results obtained through analysis of available official information, studies and opinions about pharmacists, as well as the methods of quantitative studies. We conducted descriptive statistics and regression analyses to detect an association between variables. Statistical analysis was done in SPSS version 11.0. A Chi-square test was applied to estimate the statistical significance and differences. The research implementation required the following sub studies: The key issue aspects of scholarly discourse of appraising indicators altering pharmacists' professional expansion and vocational obstacles in Georgia.

Results and discussion

Pharmacists, as healthcare providers, require not only advanced education but also postgraduate and continuous professional training. They must obtain licenses and undergo periodic accreditation to maintain professional status. In Western countries, only individuals with accredited pharmaceutical education can practice pharmacy. The establishment of a pharmacy is also strictly regulated, with permits granted solely to those holding recognized qualifications. Whether in developed or developing countries, the pharmacy profession remains highly regulated, akin to family medicine. Pharmacists, regarded as providers of family healthcare, must possess advanced pharmaceutical education, professional diplomas, continuous training, valid licenses, and regular accreditation to ensure the highest standards of practice and accountability. In Georgia, pharmacists face significant challenges in professional development, particularly in areas such as education, job satisfaction, and professional recognition. Overcoming these barriers will require collaborative efforts among government bodies, academic institutions, and healthcare organizations. By aligning the pharmacy profession in Georgia with global standards and expanding opportunities for continuous education, the country can ensure that its pharmacists are well-equipped to meet the growing demands of the healthcare system.

On the question what is your interest in regard of your future work (workplace)? (You can indicate several answers) pharmacy faculty students' 34.2% answer content (essence) of the work, pharmacy faculty students' 35.7% answer labor conditions, necessary equipment, pharmacy faculty students' 66.8% answer the system of labor and rate of wage (salary of labor), pharmacy faculty students' 23.5% answer peculiarities of team of collective, where I have to work,

pharmacy faculty students' 17.6% answer employment opportunities, pharmacy faculty students' 31% answer demand for such specialist at the labor market. See Illustration 1.

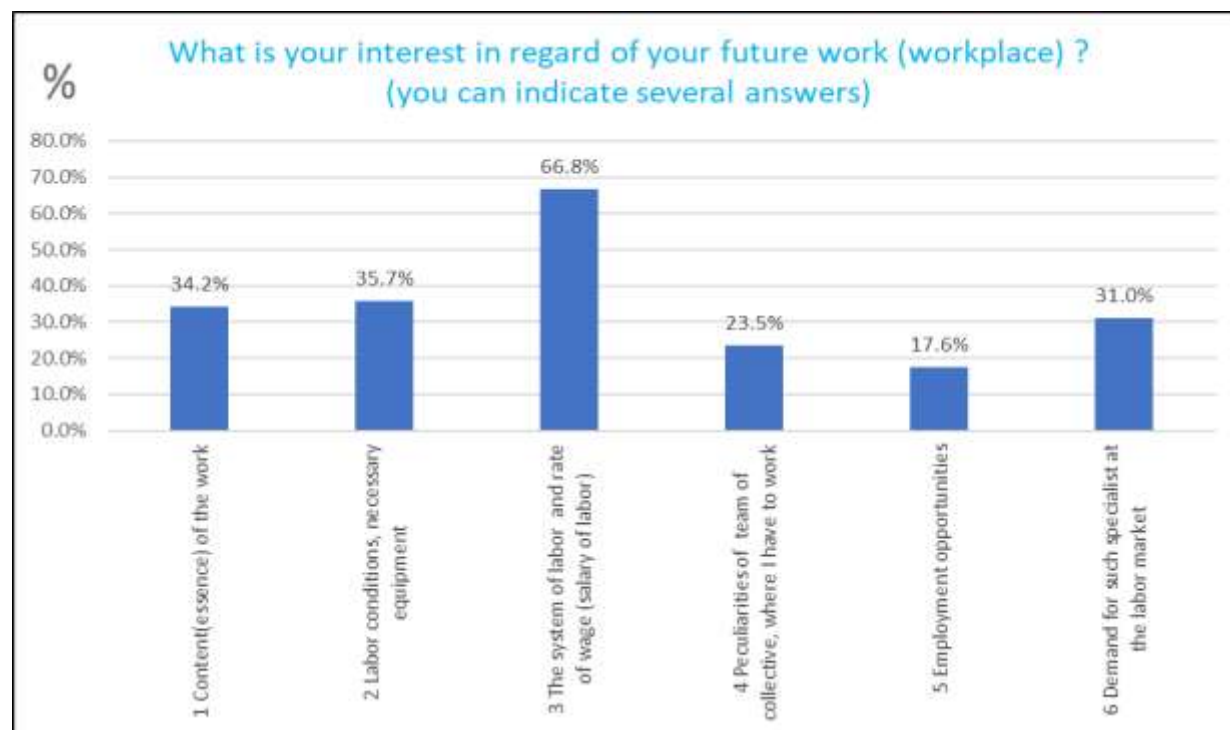


Illustration 1. Respondents interest issues regarding of future work (workplace).

Source – study results.

Would you like to change your chosen specialty? On the question would you like to change your chosen specialty? Pharmacy faculty students' 13.2% answer yes, pharmacy faculty students' 86.8% answers no.

What is main reason for change your direction of learning? On the question- What is main reason for change your direction of learning? Pharmacy faculty students' 31.7% answer I understand that the given work is not interesting to me, pharmacy faculty students' 46.3% answer future work will not correspond to my aspirations, and inclinations (affections), pharmacy faculty students' 9.8% answer I am not satisfied with the quality of education, pharmacy faculty students' 7.3% answer I do not like the quality of teaching, pharmacy faculty students' 4.9% answer other reason.

On the question do you know where to work after graduating? Pharmacy faculty students' 40.8% answer yes, pharmacy faculty students' 17.9% answer no, pharmacy faculty students' 41.4% answer I know roughly, but it may be change.

On the question -Are you engaged in the search of your future work by specialty (training)? Pharmacy faculty students' 63.3% answer yes, pharmacy faculty students' 36.7% answers no. See Illustration 2.



Illustration 2. If respondents are you engaged in the search of future work by specialty (training).
 Source – study results.

On the question-What goals do you want to achieve as a result through professional career? - Obtain more power and authority-pharmacists' 7.5% evaluate by 1 point, pharmacists' 11.2% evaluate by 2 points, pharmacists' 16.8% evaluate by 3 points, pharmacists' 31.1% evaluate by 4 points, pharmacists' 33.3% evaluate by 5 points. See Table-1.

Table 1. Obtain more power and authority of respondents, as goals to achieve as a result through professional career, evaluated by 5 points scale system.

What goals do you want to achieve as a result through professional career? -Obtain more power and authority					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	61	7.5	7.5	7.5
	2	91	11.2	11.2	18.8
	3	136	16.8	16.8	35.6
	4	252	31.1	31.1	66.7
	5	270	33.3	33.3	100.0
	T otal	810	100. 0	100.0	

Source – study results

On the question-What goals do you want to achieve as a result through professional career? - Much higher status-pharmacists' 6.7% evaluate by 1 point, pharmacists' 8.8% evaluate by 2 points, pharmacists' 15.2% evaluate by 3 points, pharmacists' 32.6% evaluate by 4 points, pharmacists' 36.8% evaluate by 5 points. See Ill.-3.

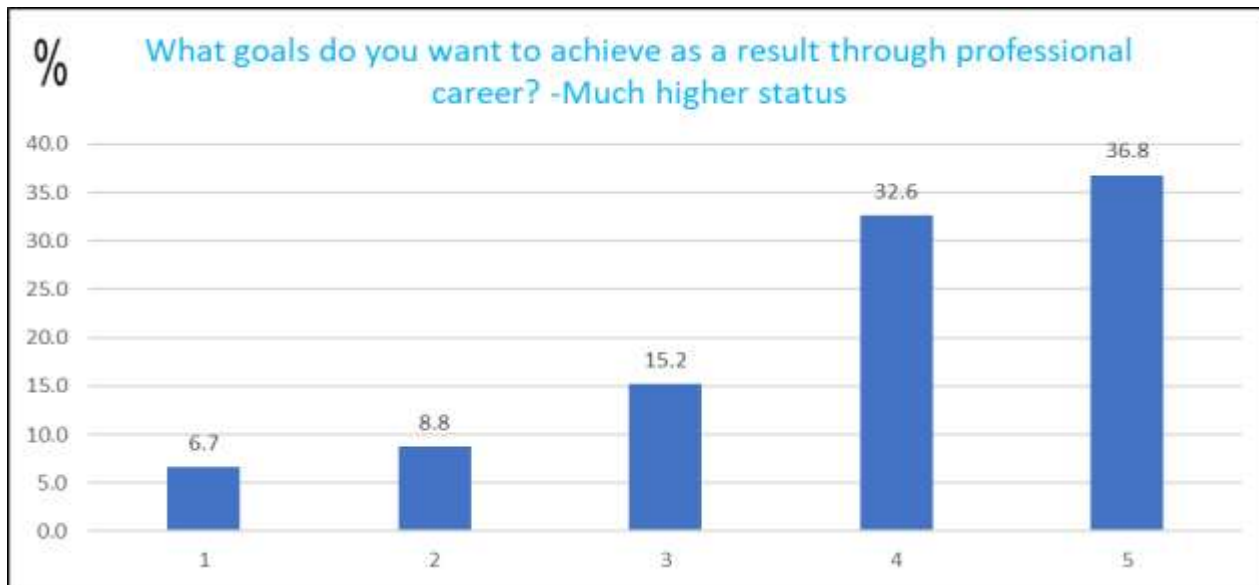


Illustration 3. Much higher status of respondents, as goals to achieve as a result through professional career, evaluated by 5 points scale system.

Source – study results.

On the question-What goals do you want to achieve as a result through professional career? – Independence-pharmacists' 7.8% evaluate by 1 point, pharmacists' 8.1% evaluate by 2 points, pharmacists' 14.2% evaluate by 3 points, pharmacists' 28.4% evaluate by 4 points, pharmacists' 41.5% evaluate by 5 points. See illustration-4.



Illustration 4. Independence of respondents', as goals to achieve as a result through professional career, evaluated by 5 points scale system.

Source – study results.

On the question-What goals do you want to achieve as a result through professional career? -Self-realization-pharmacists' 5.9% evaluate by 1 point, pharmacists 6.9% evaluate by 2 points, pharmacists' 12.3% evaluate by 3 points, pharmacists' 23.1% evaluate by 4 points, pharmacists' 51.7% evaluate by 5 points [46-47]. See Table-2.

Table 2. Self-realization of respondents', as goals to achieve as a result through professional career, evaluated by 5 points scale system.

What goals do you want to achieve as a result through professional career? -Self-realization					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	48	5.9	5.9	5.9
	2	56	6.9	6.9	12.8
	3	100	12.3	12.3	25.2
	4	187	23.1	23.1	48.3
	5	419	51.7	51.7	100.0
	Total	810	100.0	100.0	

Source – study results

On the question-What goals do you want to achieve as a result through professional career? – Power-pharmacists' 20.5% evaluate by 1 point, pharmacists' 13.7% evaluate by 2 points, pharmacists' 18% evaluate by 3 points, pharmacists' 24.8% evaluate by 4 points, pharmacists' 23% evaluate by 5 points. See Table-3.

Table 3. Power of respondents, as goals to achieve as a result through professional career, evaluated by 5 points scale system.

What goals do you want to achieve as a result through professional career? -Power					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	166	20.5	20.5	20.5
	2	111	13.7	13.7	34.2
	3	146	18.0	18.0	52.2
	4	201	24.8	24.8	77.0
	5	186	23.0	23.0	100.0
	Total	810	100.0	100.0	

Source – study results

On the question-What goals do you want to achieve as a result through professional career? -Economic (material) welfare-pharmacists' 2.2% evaluate by 1 point, pharmacists' 2.3% evaluate by 2 points, pharmacists' 5.6% evaluate by 3 points, pharmacists 21.5% evaluate by 4 points, pharmacists' 68.4% evaluate by 5 points. See Ill.-5.

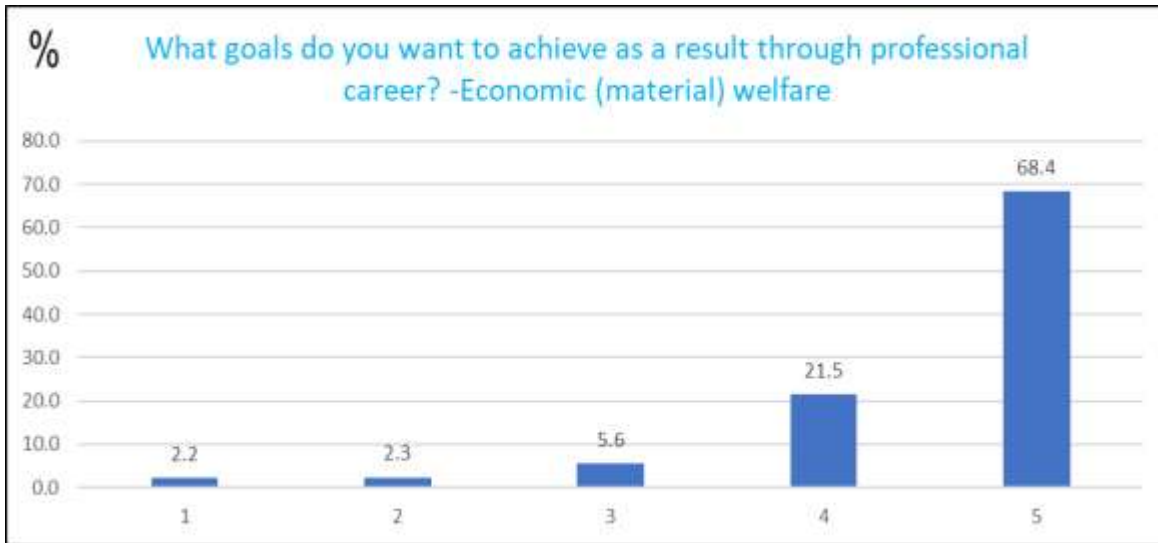


Illustration 5. Economic (material) welfare of respondents', as goals to achieve as a result through professional career, evaluated by 5 points scale system.

Source – study results.

On the question-What goals do you want to achieve as a result through professional career? - Professional growth-pharmacists' 2.1% evaluate by 1 point, pharmacists' 1.7% evaluate by 2 points, pharmacists' 6.5% evaluate by 3 points, Pharmacists' 18.9% evaluate by 4 points, pharmacists' 70.7% evaluate by 5 points. See Ill-6.



Illustration 6. Professional growth of respondents, as goals to achieve as a result through professional career, evaluated by 5 points scale system.
 Source – study results.

On the question-What goals do you want to achieve as a result through professional career? - Career advancement (growth)-pharmacists' 2.8% evaluate by 1 point, pharmacists' 2.7% evaluate by 2 points, Pharmacists' 6.2% evaluate by 3 points, Pharmacists' 18.5% evaluate by 4 points, Pharmacists' 69.8% evaluate by 5 points [21,23,29]. See Table-4.

Table 4 . Career advancement (growth) of respondents, as goals to achieve as a result through professional career, evaluated by 5 points scale system.

What goals do you want to achieve as a result through professional career? -Career advancement					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	23	2.8	2.8	2.8
	2	22	2.7	2.7	5.6
	3	50	6.2	6.2	11.7
	4	150	18.5	18.5	30.2
	5	565	69.8	69.8	100.0
	Total	810	100.0	100.0	

Source – study results

Report on the question - What goals do you want to achieve as a result through professional career? (Please evaluate each of the chosen option by 5 points scale system). See Table-5.

Table 5. Report of respondents on the question – “What goals do you want to achieve as a result through professional career?”

What goals do you want to achieve as a result through professional career? (Please evaluate each of the chosen option by 5 points scale system)			
	Mean	Median	Std. Deviation
What goals do you want to achieve as a result through professional career? -Obtain more power and authority	.71	4.00	1.245
What goals do you want to achieve as a result through professional career? -Much higher status	.84	4.00	1.203
What goals do you want to achieve as a result through professional career? - Independence	.88	4.00	1.253
What goals do you want to achieve as a result through professional career? -Self-realization	.08	5.00	1.203
What goals do you want to achieve as a result through professional career? -Power	.16	3.00	1.449
What goals do you want to achieve as a result through professional career? - Economic (material) welfare	.51	5.00	.877

What goals do you want to achieve as a result through professional career? - Professional growth	.54	5.00	.858
What goals do you want to achieve as a result through professional career? -Career advancement (growth)	.50	5.00	.937

Source – study results

On the question- Are you satisfied with the balance between the workload and your personal life? Pharmacists' 28.6 % answer yes, pharmacists' 37.2% answer partially, pharmacists' 34.2% answer no.

In many developing countries in the field of pharmacy are regulated, as well as family medicine. The pharmacist as family doctor needs of higher education, post-graduate and continuing education in pharmacy, a pharmacist license and periodic accreditation. In western countries in pharmacy, allowed to work only with higher pharmaceutical education specialists who have graduated from state-recognized and accredited colleges. The opening of a pharmacy permit is issued only to a person of higher pharmaceutical education, who passed the diploma courses in pharmacy and earned the right to open the pharmacy. It should be noted that in developed countries and in many developing countries pharmaceuticals are regulated profession, as well as family medicine, pharmacist as a family doctor, need higher pharmaceutical education, diploma and continuous pharmaceutical education, pharmaceutical license and periodic accreditation. Only pharmacists with higher pharmaceutical education have the right to work as pharmacists in pharmacies, who have graduated from universities recognized and accredited by the state [54-55]. Despite the significant contributions pharmacists can make, they encounter various setbacks that impact their occupational effectiveness [26,38].

Statistically significant was association between the buyers' educational level and their opinion about the necessity of pharmacists' certification ($p < 0.04$): customers with higher education considered certification of pharmacists as mandatory more often, than did buyers (patients) with secondary education. The respondents' vast majority considered that the issues to for pharmacists were in need of the further regular studies or trainings in the following fields: new medications, issues of pharmacotherapy of certain diseases, pharmacology and pharmacotherapy, drugs toxicity. From study results it is obvious that in the higher pharmaceutical institutions' pharmaceutical educational programs and curriculum need upgrade, renewal, modernization and adaptation to the new modern medical challenges. Therefore, continuous pharmaceutical educational programs should be created. These programs should be more focused on new medications, pharmacotherapy, drugs toxicity and dosage, routes of drug administration, selection of OTC drugs, cost-effectiveness and cost-benefits of drugs. Pharmacist provide contribution and assistance in teaching of patients to understand the prescribed drugs intake rules, pharmacists need in deep knowledge in basics of medicine, pharmacology, pharmacotherapy, pharmaceutical chemistry, pharmaceutical care, clinical pharmacy and other pharmaceutical disciplines. Properly educated pharmacists have great importance and value for the provision higher quality health care services, for the provision higher quality pharmaceutical care and very essential for patient's safety. The respondents' vast majority considered that the Government should make the certification of pharmacists. It is very essential and important that higher pharmaceutical educated pharmacists to have pharmacist license issued by the Government. The vast majority of the public

health specialists considered that the professional activity of pharmacist is very important for the society [22-23].

It is necessary to provide a deep cooperation between pharmacists and physicians on the issues of pharmacotherapy and healthcare to ensure the patients' health state effective improvement, and also to provide the best feedback regulation and revision in the healthcare specialists' team work. Pharmacists also should be responsible for registration of the drugs' side effect, as well as be attentive in case of improperness and professional defects of drugs they provide. To achieve that it is necessary to raise awareness of specialists on the essence of pharmacists' profession and functions among the medical personnel and general public [26-27].

On the question is a pharmacist responsible for treatment together with a physician? Health care specialists' 25.4% answer yes, health care specialists' 54.1% answer no, health care specialists' 20.2% answer partially, health care specialists' 0.3% answer cannot say. See Illustration 7.

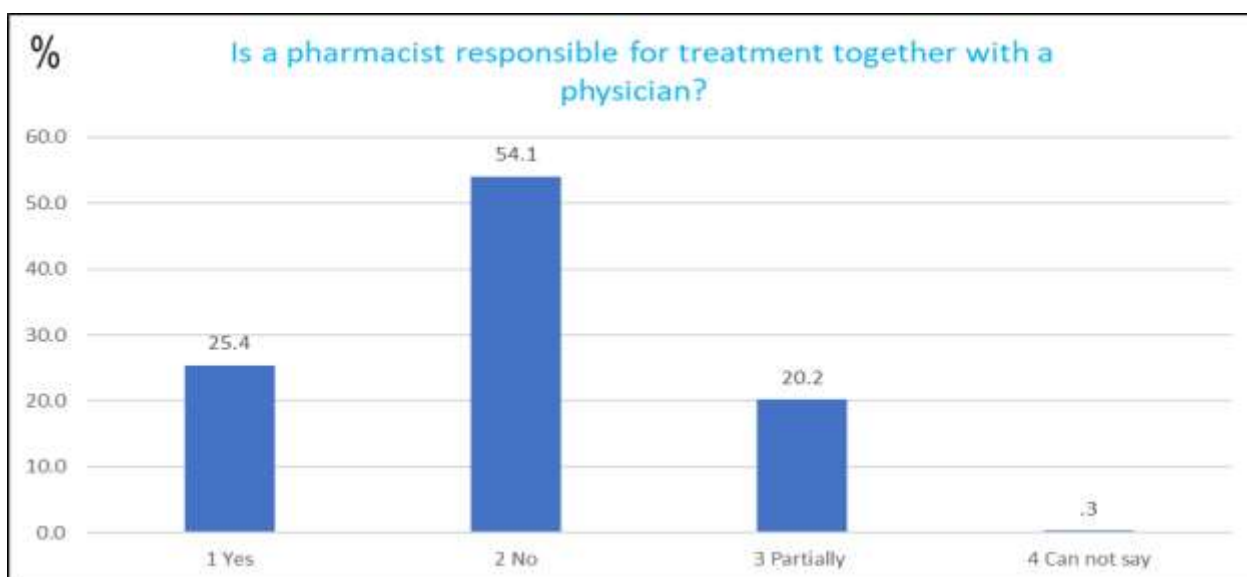


Illustration 7. Respondents' opinion if pharmacist responsible for treatment together with a physician.

Source – study results.

On the question- Should a pharmacist provide assistance in teach patients to understand rules of intake of prescribed drugs (medications)? Health care specialists' 79.5% answer yes, health care specialists' 6.5% answer no, health care specialists' 14% answer partially [28-29].

On the question - Is the pharmacist responsible for registration of side (adverse) effects of the drug (medication)? Health care specialists' 30.6% answer yes, health care specialists' 49.5% answer no, health care specialists' 14.3% answer partially, health care specialists' 5.5% answer cannot say.

On the question- Do you think that the government should make the certification of pharmacists? Health care specialists' 94.8% answer I agree, health care specialists' 4.6% answer I partly agree, health care specialists' 0.7% answer I do not agree [30-31].

On the question -what most of all had influence on your professional (occupational) choice (indicate only one answer)? Pharmacy faculty students' 25.7% answer parents' advice (or will),

pharmacy faculty students' 4.4% answer teachers' advices , pharmacy faculty students' 7.2% answer worker-specialist's advice, pharmacy faculty students' 3.8% answer friends advice, pharmacy faculty students' 3.4% answer relatives or acquaintances' advice, pharmacy faculty students' 29.2% answer this profession corresponds to my aspiration, and inclination (affection) , pharmacy faculty students' 26.3% answer interest in profession [32-33].

On the question-What underlying motives did you have while selection of the given direction of education? (Indicate no more than 5 answers) pharmacy faculty students' 53.6% answer desire to obtain high-quality professional training, pharmacy faculty students' 26.3% answer prestige of specialty, pharmacy faculty students' 22.9% answer the existence of abilities to this (the given) type of activity, pharmacy faculty students' 8.8% answer family tradition, pharmacy faculty students' 39.8% answer desire to develop own capabilities, aspirations, and inclinations (affections), pharmacy faculty students' 29.8% answer the desire (ambition) to be included in a student community as a special social environment, pharmacy faculty students' 36.1% answer the desire to expand horizons (desire to widen sense of vision), pharmacy faculty students' 18.5% answer desire to extend (lengthen) carefree period of life, pharmacy faculty students' 16% answer opportunity to take high social position, pharmacy faculty students' 49.8% answer guarantee to be employed, pharmacy faculty students' 27% answer desire to get high level to material well-being (security) , pharmacy faculty students' 28.5% answer the possibility to develop further (future) social promotion , pharmacy faculty students' 10.7% answer desire to obtain self-respect in the eyes of others who are close to me , pharmacy faculty students' 10% answer the desire (ambition) and interests to obtain certain circle of contacts, connections with friends and acquaintance, pharmacy faculty students' 1.9% answer deferring from military service , pharmacy faculty students' 13.5% answer desire to have needful social well-being, pharmacy faculty students' 39.8% answer interest in a profession, pharmacy faculty students' 21.6% answer desire to be useful to people [34-35]. See Table 6.

Table 6. Underlying motives of respondents, while electing of the given direction of education.

What underlying motives did you have while selection of the given direction of education? (indicate no more than 5 answers)		
Answers:	Count	Column N %
1 Desire to obtain high-quality professional training	71	53.6%
2 Prestige of specialty	84	26.3%
3 The existence of abilities to this (the given) type of activity	73	22.9%
4 Family tradition	28	8.8%
5 Desire to develop own capabilities, aspirations, and inclinations (affections)	27	39.8%
6 The desire (ambition) to be included in a student community as a special social environment	95	29.8%
7 The desire to expand horizons (desire to widen sense of vision)	15	36.1%
8 Desire to extend (lengthen) carefree period of life	9	18.5%
9 Opportunity to take high social position	51	16.0%

10 Guarantee to be employed	59	49.8%
11 Desire to get high level to material well-being (security)	86	27.0%
12 The possibility to develop further (future) social promotion	91	28.5%
13 Desire to obtain self-respect in the eyes of others who are close to me	34	10.7%
14 The desire (ambition) and interests to obtain certain circle of contacts, connections with friends and acquaintance	32	10.0%
15 Deferring from military service	6	1.9%
16 Desire to have needful social well-being	43	13.5%
17 Interest in a profession	27	39.8%
18 Desire to be useful to people	69	21.6%

Source – study results

On the question- Are you satisfied with your professional (occupational) choice? Pharmacy faculty students' 77.4% answer yes, I am satisfied with my professional choice, pharmacy faculty students' 9.1% answer in general, I am satisfied, but I have some doubts about the preciseness of my professional (occupational) choice, pharmacy faculty students' 8.5% answer I am partly satisfied with my professional choice, pharmacy faculty students' 3.8% answer I am mostly disappointed with my professional choice, pharmacy faculty students' 1.3% answer I am not satisfied with my professional choice [36-37]. See Illustration 8.



Illustration 8. Satisfaction of respondents with professional (occupational) choice.

Source – study results.

Key determinants of pharmacists' professional formation several principal determinants influence the professional formation of pharmacists in Georgia. These include:

- ✓ **Educational Framework:** The quality and relevance of pharmacy education play a crucial role in shaping the competencies of future pharmacists. Continuous updates to curricula that reflect current practices and technologies are essential.
- ✓ **Regulatory Environment:** The legal and regulatory framework governing pharmacy practice significantly affects how pharmacists operate. Regulations can either empower pharmacists to expand their roles or create barriers that limit their scope of practice.
- ✓ **Interprofessional Collaboration:** Effective teamwork among healthcare professionals is vital for optimizing patient care. Barriers to communication and collaboration can impede pharmacists' contributions to the healthcare team.
- ✓ **Technological Integration:** The integration of advanced technologies, such as electronic health records and tele pharmacy, is critical in modernizing pharmacy practice. However, insufficient training and resources can limit pharmacists' ability to utilize these technologies effectively.
- ✓ **Workplace Support and Resources:** Adequate support from healthcare institutions, including access to continuing education and professional development opportunities, is essential for pharmacists to thrive in their roles.

This article explores the key factors influencing the professional growth and vocational challenges of pharmacists in Georgia. It aims to present a scholarly discourse on the evolving nature of pharmacy practice, focusing on the various indicators that shape professional expansion within the state. The study examines how educational frameworks, policy changes, and industry shifts have altered the landscape for pharmacists, highlighting both opportunities for growth and the obstacles hindering their advancement. Through a comprehensive review of existing literature and professional experiences, the article appraises the socio-economic and regulatory factors impacting the profession. It also explores the role of continuing education, professional development, and the integration of pharmacists into collaborative healthcare practices. The findings underscore the importance of addressing these barriers to facilitate a more robust and inclusive professional environment in Georgia's pharmaceutical sector.

Conclusion

Chi-square test of independent has been performed in order to compare the attitude of different sides to the necessity of pharmacists' certification regulation by Government. The opinion that certification of pharmacists should be mandatory was more common among public health specialists, than among managers (Chi-square = 45.2, $p < 0.001$) and pharmacists (Chi-square = 68.9, $p < 0.001$), but there was not statistically significant difference between chiefs and pharmacists. It was more common also among patients than in pharmacists (Chi-square = 44.2, $p < 0.001$). The necessity of pharmacists' certification was stated more often by employed students, than by pharmacists (Chi-square = 57.3, $p < 0.001$). Present pharmaceutical services connected to self-health care and the significance that pharmacist professionals drive the health care frame systems in the new modern direction. Collaboration between physicians and pharmacists in treatment is gaining moment and has shown positive effects on patients' health. So according study results found, that drug-drug interactions, adverse drug reactions and treatment

costs are reduced by involving pharmacists in the drug therapy process. Study showed that when pharmacists' interventions were taken into account, the therapeutic effect improved in majority of patients and adverse drug reactions were prevented in many of cases. The professional development of pharmacists in Georgia faces several critical challenges, particularly in education, job satisfaction, and professional recognition. Addressing these issues will require concerted efforts from the government, educational institutions, and healthcare organizations. By aligning the profession more closely with global standards and enhancing opportunities for continuous education, Georgia can ensure that its pharmacists are equipped to meet the growing demands of the healthcare system.

Pharmacists in Georgia face a unique set of challenges compared to their counterparts in Western countries. In many developed countries, the profession of pharmacy is regulated similarly to other healthcare professions, such as family medicine. Pharmacists undergo rigorous training, continuous education, and periodic licensing reviews to maintain professional standards. However, in Georgia, the profession has not yet reached the same level of integration into the healthcare system. Many pharmacists report feeling underappreciated, both in terms of professional recognition and compensation. Moreover, the lack of continuing education programs and the absence of a cohesive professional body to advocate for pharmacists' rights and responsibilities has further limited their role. The global pharmaceutical industry continues to evolve, with pharmacists taking on more specialized roles, especially in clinical settings. This paper seeks to identify the gaps between Georgian pharmacists and their international counterparts, emphasizing the importance of reforms in education, licensing, and professional integration.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

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Competing Interests

The authors declare no competing interests.

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Ethical Standards

The research meets all ethical guidelines, including adherence to the legal requirements of the study country.

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THE SCIENTIFIC TALKS OF KEY ISSUE ASPECTS OF PROGNOSIS, ACHIEVEMENT, AND CHALLENGES OF GENERAL PRINCIPLES OF TREATMENT OF PERIODONTAL DISEASES IN MODERN MEDICINE IN GENERAL

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ABSTRACT

Periodontal diseases represent a significant public health challenge, characterized by complex interactions between microbial biofilms, host immune responses, and environmental factors. The treatment of periodontal diseases is anchored in general principles that emphasize microbial control, host modulation, and tissue regeneration. This review highlights key issues surrounding these principles, integrating current research on non-surgical and surgical interventions, systemic risk management, and emerging therapies. Non-surgical strategies, including scaling and root planning, adjunctive antimicrobial therapies, and host modulation, form the first line of defense. Surgical approaches, such as flap surgery, guided tissue regeneration, and biomimetic materials, aim to restore periodontal structure and function. Additionally, systemic links between

periodontitis and conditions like diabetes, cardiovascular disease, and osteoporosis underscore the importance of personalized treatment plans. Recent advancements in regenerative medicine, including the use of growth factors, stem cells, and biomaterials, hold promise for more effective outcomes. The role of innovative technologies, such as laser therapy and probiotics, in enhancing traditional therapies is also explored. This comprehensive discussion underscores the need for multidisciplinary collaboration to advance periodontal treatment strategies, improve patient outcomes, and address the broader health implications of periodontal disease. Periodontal diseases, characterized by complex interactions between microbial biofilms, host immune responses, and environmental factors, demand a multifaceted approach to treatment. The review delves into the fundamental principles of periodontal therapy, encompassing microbial control, host modulation, and tissue regeneration. Non-surgical methods, including scaling and root planning with adjunctive antimicrobials, form the foundation of initial therapy, while surgical approaches like guided tissue regeneration and biomimetic applications aim to restore periodontal integrity. The review also addresses systemic connections with conditions such as diabetes and cardiovascular disease, emphasizing the need for personalized, holistic care. Emerging trends, including laser therapy, probiotics, and stem-cell-based regenerative techniques, offer promising advancements but also present challenges in clinical application. This discussion highlights the need to bridge current knowledge gaps, improve patient compliance, and develop cost-effective solutions. By exploring key controversies and advancements, this analysis advocates for an interdisciplinary approach to advancing periodontal treatment and improving patient outcomes. The treatment of periodontal diseases is rooted in well-established principles that aim to restore oral health by controlling microbial factors, modulating host responses, and regenerating periodontal tissues. Advances in our understanding of the pathogenesis of these diseases have paved the way for innovative approaches, from non-surgical therapies to regenerative techniques incorporating biomaterials and stem cells. These developments, coupled with the integration of personalized and interdisciplinary care, have significantly improved treatment outcomes. Despite these advancements, challenges such as patient compliance, cost-effectiveness, and the complexity of systemic associations remain hurdles to be addressed. Continued research is necessary to optimize treatment protocols, enhance accessibility, and explore emerging technologies, such as laser therapies and biotechnological innovations, for widespread application. By bridging existing knowledge gaps and fostering collaboration between disciplines, the field of periodontology can continue to make strides toward more effective, efficient, and holistic care for patients with periodontal diseases. This effort is vital not only for improving oral health but also for addressing the broader systemic implications of these conditions. The treatment of periodontal diseases is anchored in three overarching principles: the control of microbial factors, modulation of host responses, and regeneration of lost periodontal tissues. Traditional approaches, such as scaling and root planning, remain central to initial therapy, while advancements in surgical techniques and regenerative therapies have expanded the scope of periodontal treatment. At the same time, growing recognition of the systemic links between periodontal diseases and conditions like diabetes, cardiovascular diseases, and osteoporosis underscores the importance of personalized and interdisciplinary approaches to care.

Keywords: Key, issue, aspects, general principles, treatment, periodontal diseases.

Introduction

Periodontal diseases are among the most prevalent chronic inflammatory conditions affecting the oral cavity, with profound implications for overall health and well-being. These diseases, primarily initiated by microbial biofilms, result in the destruction of the supporting structures of the teeth, including the gingiva, periodontal ligament, and alveolar bone. Despite their widespread occurrence, the management of periodontal diseases has undergone significant evolution, guided by a deeper understanding of their multifactorial etiology and the interplay between microbial and host factors.

The treatment of periodontal diseases is anchored in three overarching principles: the control of microbial factors, modulation of host responses, and regeneration of lost periodontal tissues. Traditional approaches, such as scaling and root planning, remain central to initial therapy, while advancements in surgical techniques and regenerative therapies have expanded the scope of periodontal treatment. At the same time, growing recognition of the systemic links between periodontal diseases and conditions like diabetes, cardiovascular diseases, and osteoporosis underscores the importance of personalized and interdisciplinary approaches to care.

Recent years have witnessed significant innovations in periodontal therapy, including the use of biomaterials, stem cells, and advanced diagnostic tools. However, challenges such as patient compliance, cost, and the varying predictability of therapeutic outcomes highlight the need for ongoing research and refinement of treatment protocols. This paper explores the scientific advancements, controversies, and emerging strategies in the treatment of periodontal diseases, offering a comprehensive review of the principles underpinning contemporary periodontal care.

Progress and development in endodontics and endodontology, in common with other medical or dental disciplines, has been driven by the coalescence of numerous independent driving forces in society. The key driver for any healthcare profession is the societal imperative to improve the health of the population as cost-effectively as possible, without imposing an economic burden. These aims are coupled with the desire for both efficacy and efficiency in treatment delivery. Support industries grow up around these global aims to service the delivery needs of health professionals by developing tools and materials suitable for the purpose, at the price of manufacture and profit for the business. Given that healthcare professionals may deliver their remits within different funding frameworks, they too may become embroiled in the business element. There has therefore evolved a complex dynamic between endodontic healthcare, business, and service delivery. That publicly funded healthcare bodies and private business willingly invest in root canal treatment is tacit indication by the system that the procedure works and serves a useful purpose.

All components of this complex delivery system must have a vested interest in improving their respective contributions to enhance their measures of success, therefore requiring close interaction amongst them through partnerships in research and development and propagation of protocols, devices, and materials. The proposed model assumes that the key measures of efficacy and efficient service delivery are product-based, although that may not entirely hold true for root canal treatment because of the biological nature of the problem it seeks to resolve. Added to this are the facts that root canal system complexity and clinician expertise may be confounding factors. Nevertheless, endodontics has become a gadget-oriented discipline, with dentists keen to adopt new technology in the interests of efficiency, efficacy and economy.

The dental pulp is a sterile connective tissue protected by enamel, dentin, and cementum. Significant injury of the pulp chamber leads to inflammation and may result in pulp necrosis if left untreated. Possible scenarios that can result in periapical radiolucencies are commonly

initiated either by trauma, caries, or tooth wear. Microorganisms might colonize the pulp tissue after it loses its blood supply as a consequence of trauma, resulting in periradicular pathosis. Pulp exposures can lead to pulp necrosis and periradicular pathosis. Microorganisms and their products have a pivotal role in the initiation, progression, and establishment of periradicular conditions. With the progression of inflammation due to carious pulp exposure and invasion of microorganisms, the most likely result would be pulp necrosis. Once root canal infection is established, and pulp necrosis occurs, neither host defense nor systemic antibiotic therapy would be effective in restricting the infection due to the absence of local blood supply. It is possible to prevent their spread successfully through non-surgical endodontic treatment. It has been reported that the majority of endodontic bacteria are suspended in the fluids found within the root canal(s); however, bacterial aggregates and biofilms tend to adhere to the root canal walls to form concentrated bacterial centers. Infections might spread into dentinal tubules and root canal complexities. Root canal infections can be treated through professional intervention, using endodontic procedures or extraction.

Microorganisms residing in the root canal play an essential role in the initiation and establishment of periradicular lesions, which has been proved by studies performed on rats and monkeys. Considering the role of microorganisms in the presence of apical periodontitis, clinicians should be aware that endodontic therapy is the management of infective disease.

The predominance and prevalence of inflammatory changes, such as granulomas and periapical cysts induced by root canal infection, have been assessed by examining periapical biopsy specimens. Attempts to accurately assess the nature of the periapical pathosis and diagnose the lesion have limited success before performing surgery. Although several methods have been proposed, such as periapical radiographs, contrast media, Papanicolaou smears, real-time ultrasound imaging, and albumin tests, these have proved inaccurate. Although the postoperative histopathological examination has remained the standard for the evaluation of the nature of the lesion, the use of other imaging systems, such as cone beam computed tomography (CBCT) with high specificity and excellent accuracy, can enhance the chance of a more accurate preoperative diagnosis.

All dentists and endodontists must be able to manage patients who present with a dental emergency. Emergencies usually involve pain as a result of inflammation, but they can also involve swelling and other signs of infection. The aim of this review is to provide an overview of endodontic emergencies. The details of the mechanical aspects of endodontic treatment of emergencies and their outcomes will not be discussed as these can be found in numerous textbooks and journal articles. In this review, the term ‘endodontic treatment’ has been used to include all possible treatments for pulp, root canal and periradicular conditions—these include indirect pulp capping, direct pulp capping, partial pulpotomy, pulpotomy, pulpectomy with root canal treatment, root canal re-treatment and periradicular surgery. The term ‘root canal treatment’ has been used to specifically refer to pulpectomy and its associated procedures to clean, disinfect and fill the root canals.

An endodontic emergency can be defined as occurring when a patient has pain associated with inflammation of the pulp and/or periradicular tissues, or when there is pain (with or without swelling) caused by infection of the root canal system and/or the periradicular tissues. The endodontic emergency was defined as “pain and/or swelling caused by inflammation or infection of the pulp and/or periapical tissues”. However, their definition is limited since it does not include teeth that do not have pulps (e.g. a tooth with a pulpless infected root canal system; a tooth with a

root canal filling, etc.), and it does not include all of the periradicular tissues (e.g. acute lateral periodontitis associated with a lateral canal or with a tooth that has external lateral inflammatory resorption). Hence, the above broader description is proposed as it is more comprehensive and representative of all possible emergencies that may occur as a result of endodontically related conditions.

The various pulp, root canal and periapical conditions that may present as endodontic emergencies, it is essential to have a clear and concise classification of these conditions. There has been debate in the literature regarding the terminology used in classifications of these conditions with little, if any, agreement. The terms used in most diagnostic classifications for pulp, root canal and periradicular conditions have not been based on, or do not adequately describe, what is happening (or has already happened) within the tissues or the anatomical location even though this is arguably the most important requirement of a classification system. Other requirements are that the classification system and terminology are possible to use in the clinical setting, useful, clear and universal. In order to be possible to use, the diagnosis has to be able to be formulated by considering the information obtained from the patient via the history, symptoms, clinical signs, results of diagnostic tests and the radiographic findings. To be useful, a diagnosis using the classification system should indicate the management options for the presenting condition and to be clear, the terminology should be understood by all relevant clinicians. Ideally, there should be one universal classification for any group of diseases or conditions so clinicians throughout the world can communicate effectively, educators can teach effectively and researchers can report in a consistent manner.

Goal

Aim of the research was to study key issue aspects of general principles of treatment of periodontal diseases.

Result and Discussion

When starting the treatment of periodontal diseases, it is necessary to take into account Here are some requirements:

1) Removal of the cause of the disease, which consists in removing soft and hard dental plaques, as well as their causative factors (carious cavities, replacement of poor-quality dentures, restoration of interdental contacts). We use local antimicrobial medicines. It is necessary to remove super contacts. Replacement of low-quality artificial crowns and orthopedic constructions. We advise the patient to maintain oral hygiene.

2) Pathogenic treatment provides for elimination of inflammation by various means and methods In periodontitis and gingivitis, causal factors are long-term. Disintegration of cloud cells, lysis of polymorphonuclear leukocytes is activated. Against this background, numerous enzymes (proteases, hydrolases, pepsidases, cathepsins, heparin, histamine and serotonin) are released. At the first stage, these substances lead to an increase in vascular permeability, they are actively left by polymorphonuclear leukocytes, which participate in phagocytosis and destroy microorganisms. A large amount of enzymes accumulates in the marginal tissues of the gums, the connective tissue structures are decomposed.

Derivatives of arachnoid acid - prostacyclins, prostaglandins - are mediators and modulators of inflammation. At the first stage of the inflammatory process, they create a condition for an active

vascular reaction. The accumulation of these substances causes damage to the connective tissue structure, activates osteoclasts and bone resorption of the alveolar ridge.

During the acute inflammatory phase, the immune mechanisms of the inflammatory reaction are involved and become especially important during the chronic course. The long-term course of the local inflammatory process causes the body's immune response and leads to the phenomenon of hypersensitivity.

Tissue swelling develops not only as a result of failure of the lymphatic system, but also occurs due to increased permeability of capillaries.

The treatment measures carried out by us should first of all take into account the removal of the causal factor. The following drugs can be used in local treatment: prostaglandin inhibitors, kallikrein-kinin systems, antioxidants, vasoactive and anti-edema drugs, correctors of trophic and immune disorders.

Each medication is prescribed taking into account the clinical picture, after removing microbial and traumatic factors.

3) The center of local infection chronically affects the state of the body. It is necessary to carry out general therapy.

Local treatment of some periodontal diseases

Treatment of gingivitis

In acute catarrhal gingivitis, bleeding and pain symptoms predominate. Therefore, after applying or infiltrating anesthesia (2% dicain solution, numbing gels; 2% novocaine, trimecaine, ultracain and other solutions), we remove soft and cool dental plaques. We can remove soft plaques with cotton swabs soaked in antiseptic, treat the spaces between the teeth with turunds soaked in the same antiseptic, then wash the pathological center under pressure with a directed stream from the syringe. After removing dental plaque, we treat the gums with hydrogen peroxide, 0.06% chlorhexidine solution, 1% iodinol solution.

At home, we prescribe antiseptics (chemical preparations or medicinal plant decoctions) for the patient's mouth.

After a week, we perform a control examination of the patient's oral cavity. We determine the hygienic index and the condition of the mucous membrane of the gums. In case of unsatisfactory results, we teach the patient how to properly brush his teeth. Sometimes, if necessary, we use healing bandages containing 3% acetylsalicylic acid, 5% butadione, 10% debunol ointments and others. When preparing the bandage, we mix zinc oxide and artificial dentine in equal amounts until we get a mass of thick sour cream consistency. We place the latter on the pre-medicated and well-dried gum for 2-2.5 hours. In addition to wrapping, we can also use the application of this or that drug.

We begin the treatment of chronic catarrhal gingivitis by removing dental plaque, eliminating carious foci, replacing poor-quality dentures, encouraging the patient to maintain oral hygiene. We conduct anti-inflammatory therapy. In order to regulate the processes of change in the gum, after eliminating the inflammation, we apply physioprocedures that activate hemodynamics. It is desirable for the patient to perform automassage of the periodontal tissues.

Treatment of the swelling form of hypertrophic gingivitis involves the removal of the causative factor and after reducing the inflammatory reaction in the gum, the use of anti-swelling agents. We use a 10% hypertonic solution of sodium chloride for oral baths. A good effect is given by applications of 5% solution of SO₄ or SO₄. Heparin has the best antiproliferative effect, it

regulates tissue turnover. We can use heparin extract or ointment as applications. During treatment, it should be taken into account that the swollen form of gingivitis rarely occurs independently. In almost all cases, swelling of the gum edge is accompanied by excessive development of connective tissue. In the treatment of local hypertrophic gingivitis, we can use sclerosing agents: for example, after preliminary pain relief, a 50% solution of glucose or a 25% solution of magnesium sulfate is injected into the gum cavity.

In the treatment of the fibrous form of hypertrophic gingivitis, we use antiproliferative drugs locally. Heparin is prescribed every day for 6-10 days according to the above scheme. Hydrocortisone ointment or suspension applications may be used. Heparin electrophoresis also gives good results. We use Vagotil from burning agents, Maraslavin is allowed as an application. Cryotherapy gives good results in the treatment of hypertrophic gingivitis. In case of significant hypertrophy of the gum, surgical intervention is indicated.

The treatment of ulcerative gingivitis is characterized by its genesis. Initially, we remove necrotic masses, locally treat the tissues with antiseptic and antimicrobial drugs. We carry out any manipulation against the background of applied pain relief (trimecaine, ultracaine ointment, hiromecaine ointment). Enzymes can be used to wash away necrotic masses (trypsin, chymopsin, lysozyme, teralitin, etc.). We remove necrotic masses to healthy gum tissue. We remove tartar with an excavator, staples or an ultrastoma. After mechanical treatment, we use 1% sanguine solution, trichopol (trichopol tablets are dissolved in 0.3% chlorhexidine solution) for application on the gums. We prescribe tinidazole to the patient.

At home, we prescribe the following antiseptics for a sick person's oral bath: weak solution of potassium permanganate, furcilin, 0.1% chlorhexidine solution, 0.25% chloramine, chamomile tincture, lysozyme in 0.5% ecmolin solution, lysol and others. After removal of necrotic masses and elimination of the inflammatory process, in order to improve epithelization, the patient is prescribed an oily solution of carotolin, panthenol, methyluracil ointment.

Treatment of periodontitis

General plan of periodontal diseases treatment

- ❖ General principles:
 - ✓ Aetiological treatment
 - ✓ Pathogenetic treatment
 - ✓ Symptomatic treatment
 - ✓ Local treatment
 - ✓ Removal of local irritation factors-
 - ✓ Removal of dental deposits
 - ✓ Oral hygiene
 - ✓ Treatment of caries and its complications
 - ✓ Orthodontic treatment
 - ✓ Prosthetic treatme
 - ✓ Anti-inflammatory treatment
 - ✓ Pharmacotherapy of microcirculatory disorders
 - ✓ Influence on tissue' metabolism
 - ✓ Stimulation of regeneration processes
 - ✓ Antibacterial treatment
 - ✓ Physiotherapy treatment

- ✓ Electropathy
- ✓ Hydro-treatment
- ✓ Massages
- ✓ Laser-treatment

- ❖ General treatment
 - To stimulate immune defense of organism
 - General-strengthening treatment
 - General treatment of major diseases of the body
 - Diet-therapy
 - Deep Cleaning (Scaling and Root Planing)

Is aimed to remove local factors of irritation- dental deposits, carious cavities, and traumatic occlusion. Elimination of traumatic occlusion - selective teeth grinding, temporary or permanent teeth splinting.

In the local treatment of periodontitis, first of all, our goal is to eliminate unfavorable exogenous factors; Medicinal treatment of the pathological focus, reduction of the inflammatory process in the soft tissues of the periodontium and, accordingly, the depth of the tooth-gingival pockets.

We start the local therapy of generalized periodontitis with oral cavity sanitation: we remove dental plaque, carious teeth, perform extraction of tooth roots, and correct individual low-quality artificial crowns or orthopedic constructions. After removing soft and cool plaques, we polish the surface of the treated crown, after which we cover the tooth with fluorine-containing preparations. We treat tooth-gingival and periodontal pockets with antiseptics. This, in turn, represents the first stage of medicinal, anti-inflammatory therapy.

The goal of local anti-inflammatory therapy is to eliminate pathogenic microflora and granulations; Coping with the inflammatory process in the gum and bone tissue of the alveolar ridge. If the inflammation is strongly expressed, we additionally prescribe prostaglandin inhibitors; Stabilizers of cellular and lysosomal membranes.

At the first stage of treatment, we prescribe antimicrobial agents. Chlorhexidine is more or less effective among numerous drugs, which is effective against all types of microorganisms except the simplest ones; Trichopol acts on the simplest. Therefore, after removing dental plaque and antiseptic treatment, a mixture of chlorhexidine 3% solution and trichopol is injected into the periodontal pockets.

Local anti-inflammatory treatment is carried out with various antimicrobial agents, such as Iodinol, Microcid, Sanguiritin, 5% solution of aminocaproic acid, Kalanchoe juice, etc. Let's consider some drugs: polymineralol is a solution containing macro and microelements, colloids, biostimulants. It is a good anti-inflammatory, regeneration stimulating drug. Activates phagocytosis and immunogenesis.

Maraslavin is an extract of medicinal plants, it suppresses the growth of granulation tissue, the action of bacterial flora.

Lutenurin is a herbal antibiotic that has an anti-inflammatory effect. Reduces vascular permeability.

Kernosan is a herbal remedy. It is characterized by anti-inflammatory, antiseptic action. It should be noted that sometimes even intensive antimicrobial therapy does not give positive results. This is explained by the fact that during chronic periodontitis, the activity of physiological mechanisms is significantly increased, which play a protective role in the initial stage of inflammation and in

the conditions of the action of pathogenic factors and disruption of hemodynamics, determine the vitality of periodontal tissues.

After antiseptic treatment and antimicrobial therapy, we can treat the pathological focus with enzymes (trypsin, chymotrypsin, lysozyme, etc.), which lead to the lysis of the remaining necrotic masses. Enzymes are used both as solutions and as crystals.

At the next stage of treatment, if the inflammatory reaction persists, we use: a) prostaglandin inhibitors, such as aspirin solution, 3% aspirin and butadione ointments; b) antioxidants - suspensions, emulsions, dibunol ointment; c) cell membrane stabilizers - corticosteroids, such as hydrocortisone, prednisolone; Dexazone in the form of ointment, suspension or joint. How effective the action of these drugs is, is determined by the clinical condition of the periodontal tissues. Establish a treatment plan for each patient individually. In case of slight exudation, we place the latter in the periodontal pockets under the dressing in order to prolong the effect of antimicrobial agents. If there is abundant pus, the use of a bandage often leads to the formation of abscesses.

It is preferable to use antioxidants, prostaglandin inhibitors and corticosteroids in combination with the bandage. In practice, there are cases when, despite the successful anti-inflammatory treatment, swelling of the gums is still maintained. In this case, the use of anti-edematous agents is shown, such as: Maraslavin, musclerosing mixtures, heparin, polymineralol, 5% ascorbic acid solution.

The final stage of treatment is the appointment of keratoplastic and tissue change stimulators. For example, 10% Metacil ointment, Vagotil, Retinol and others.

In the case of a mild form of periodontitis, the treatment with the mentioned scheme is completely satisfactory. In the case of moderate and severe periodontitis, it is used only at the initial stage of treatment, as a result of which we resort to surgical methods.

General treatment of periodontal diseases

1) Antibacterial treatment

Periodontal disease has a microbial nature. Therefore, it is treated with the use of antimicrobial drugs. When using antibiotics in periodontology, their properties are of great importance, in particular, they should be biologically compatible and well absorbed in the gastrointestinal tract. The main place is given to the pharmacokinetics of the drug. In periodontology, the main parameter of an antibiotic is its concentration in the gingival fluid.

When prescribing antibiotics, we must take into account the risk factor and adverse effects of taking them. The negative effect is manifested by immunological and non-immunological reactions, the first of which includes allergic reactions. Allergic reaction to antibiotics develops in 1 to 7% of cases. The group of non-immunological reactions includes superinfections caused by other pathogenic resistant microorganisms and fungi. Against them, we prescribe other antibiotics according to the antibiotic chart.

Candidiasis mainly develops in a weakened body, and 10-14 days after the appointment of antibiotic therapy, it will appear on the mucous membrane of the oral cavity and genitals. It is easily fixed by prescribing nystatin group of drugs.

Prescribed under the age of 8. After 12 years, 0.3g 2-4 times a day. Contraindication: liver and kidney diseases, leukopenia.

- a) Erythromycin is a bacteriostatic drug. For 6-8 years, 0.25 g is prescribed, from 12 years, 1 g once every 4 hours. Contraindication: severe liver disease.

- b) Monomycin is a bactericidal drug. We prescribe 10-15 mg per body weight.
 Contraindication: auditory nerve neuritis, liver disease.
- c) Tetracycline Hch - 250 mg is prescribed once every 8 hours for 14 - 21 days.
- d) Amoxicillin – 375 mg once every 8 hours.
- e) Metronidazole – 250 mg once every 8 hours.
- f) Augmentin - 250-500 mg every 8 hours.
- g) Clindamycin - 150 mg every 6 hours.
- h) Ofloxacin - 100-200 mg every 12 hours.
- i) k) In the treatment of periodontal diseases, we use such effective drugs as Rulid, Sumamed and others.

After carrying out antibacterial therapy, we control the effectiveness of the treatment, both microbiologically and clinically.

2) Therapy stimulating the body's reactivity

In the general treatment of periodontal diseases, the greatest importance is given to stimulating therapy, the indication of which is 1). The initial stage of the pathological process; 2). A pathological process occurring at a young age, when the treatment is ineffective; 3). This method is also used in patients who are weakened due to one or another operative intervention or transfer of a general disease.

Contraindications to the mentioned treatment are: the presence of new formations, Qhormonal disorders, the period of pregnancy, the period of menstruation, the active inflammatory process in periodontium with abscesses.

We use both specific and non-specific means to stimulate the body's reactivity. So, for example, biostimulators, aloe, fibs, splenin use both in the form of injections and electrophoresis.

Aloe is prescribed as a subcutaneous injection of 2 ml. Every day for 10 days. Aloe electrophoresis is also quite effective. For Phibs, we prescribe 2 ml subcutaneously, a total of 15 injections per day. Microbial polysaccharides stimulate the reticulo-endothelial system. The amount of globulin in the blood increases, which in turn contributes to the activation of humoral immunity. So, for example, we prescribe prodigiosan injection once every 5 days. In total, we prescribe 5-10 injections per course. It is also effective to perform autohemotherapy, namely 5 ml once every 2-3 days. We pour blood. The course of treatment consists of 5-10 injections.

Specific stimulants are, for example, anabolic steroids such as Nerabol, Retabolil. The latter regulate the exchange of protein, calcium and phosphorus, cause the activation of osteoblasts, against the background of which bone formation takes place.

Retabolil is prescribed in the form of a 5% oily solution of 1 ml in the muscle, once every 3 weeks we carry out a total of at least 5, at most 7 injections.

Nerabol is prescribed in the form of pills - 1 pill twice a day. The total duration of treatment is one month, one and a half months.

Desensitizing therapy

One of the stages of general treatment is desensitization therapy: for this purpose we use such drugs as Suprastin, Tavegil, Diphenhydramine, Pipolfen, Semprex, Diazolin, Calcium Chloride and others.

Suprastin is prescribed 0.025 g 2 times a day with food or as an injection of 2% solution in 1-2 ml of muscles.

We prescribe Tavegil 0.001 g 2 times a day in the form of pills.

Diphenhydramine is prescribed in the form of pills 0.025 g 1-3 times a day or 1 ml of a 1% solution in the muscles, or as an intravenous injection.

Pipolfen is prescribed in the form of pills 0.025 g 2-3 times a day or 2 ml of 2.5% solution intramuscularly.

Semprex - we prescribe 1 tablet (0.8 g) once every 12 hours. Its advantage is that the drug does not have a sedative effect.

Diazolin - we prescribe 0.05 g 2 times a day in the form of pills. Nor does this drug have a sedative effect. Contraindications: gastric or duodenal ulcer and inflammatory diseases of the gastrointestinal tract.

We prescribe a 10% solution of calcium chloride 1 tablespoon per day 3 times a day. The appointment of this drug is also effective with electrophoresis. Contraindication: the body's disposition towards atherosclerosis, thrombosis.

We prescribe calcium gluconate and calcium glycerophosphate both in the form of pills 0.5 g 3 times a day, and 5-10% solution of these drugs in the form of electrophoresis.

4) Regeneration accelerators

Methyluratsul (Metacil) has anti-inflammatory and regeneration-accelerating action. We prescribe 0.3 g of powder 3 times a day for 10 days. We also use 10% ointment of this drug as an application.

P Pentoxyl stimulates the reticulo-endothelial system and the phagocytic activity of leukocytes. We prescribe 0.2 g 3 times a day.

P Brephosteoplast is a germinal bone in a sterile state, which stimulates the proliferation of osteogenic ungraded elements and the formation of new bone structures. Hydroxyapatite - it has a mineral that stimulates reparative osteogenesis

5. Therapy with vasoactive agents

For this purpose, we use Trental (pentoxifylline) - it is a vasoactive agent of angioprotective action. Improves borrower circulation. We prescribe 1 dragee 3 times a day. Contraindications are severe diarrhea, hemorrhages. Heparin (Vetren) is a direct-acting anticoagulant. We prescribe ointment in the form of applications. Electrophoresis of heparin

6) General health therapy

In periodontal disease, the greatest attention is paid to vitamin therapy.

We prescribe vitamin C in the form of powder or pills 0.2-0.3 g 3 times a day, for 20 days, if there are no contraindications. We often prescribe vitamin C in combination with vitamin P (rutin) in the form of ascorutin, 0.1 g 2-3 times a day. 2 ml of a 5% solution of vitamin C can be prescribed as an injection or injected into the periodontal tissues with electroforms.

B group vitamins enhance protein biosynthesis, tissue oxygen supply. Improves the trophism of periodontal tissues.

Vitamin B1 can be prescribed in the form of powder 0.01 g 3 times a day; with 2 ml injections of 6% solution (the course contains 15 injections). Vitamin B1 can be introduced into periodontal tissues by iontophoresis.

Vitamin B2 is prescribed together with other vitamins in a complex of 0.003 g 3 times a day.

Vitamin B6 (pyridoxine) is prescribed at 0.1 g 1-3 times a day for 10 days.

We can prescribe 2 ml of 2.5% solution of B6 as an injection for 15-20 days.

B12 (cincobalamin) is prescribed by injection 1 ml of 0.01% solution every 2-3 days. A total of eight injections. Good results are given by prescribing vitamin B12 together with other vitamins of group B, vitamin C and ATP for 15 days.

We prescribe vitamin P in the form of powder 0.1 g 2 times a day. Electrophoresis of 1% solution also gives good results (10 procedures in total).

We prescribe 0.01 g of PP vitamin powder per day, and iontophoresis of 1% solution is also effective.

50 mg of vitamin E (oil solution) is prescribed 3 times a day at a distance of three cubits. Vitamin EE is in large quantities in castor oil, it is recommended to prescribe a combination of vitamin A and E (Aevit) to stimulate the growth of the fetus. We prescribe 1 capsule 3 times a day for 2 weeks.

Vitamin A can be prescribed 10 drops once a day for three weeks.

Dihydrotachysterol - contains vitamin DD, causes regulation of osteogenesis. We prescribe 10 drops 3 times a day for 10 days. We can prescribe polyvitamins. For example, Undevit, Gendevit, 7) Sedatives

We use tranquilizers to relieve stress: Tazepam - 0.02 g 2 times a day; Rudotel (Mezapam) - 0.01 g 2 times a day Elenium 0.005 2 times a day Sibazon (Relanium, Seduxin) - 0.005 g 3 times a day Trioxazin - 0.3 g 2 times a day.

Among the sedatives, we prescribe: potassium bromide 0.1 g - 1 g day-night (in the form of powders). Bromkafur - in the form of powders 0.5 g 2 times a day.

Novopassit - 1 tablespoon (5 ml) 3 times a day and etc

We can also consider the method of neurotropic therapy - electric power. The treatment course consists of a total of 10-15 sessions.

Diet therapy

The diet should be balanced, it is necessary to eat raw fruits and vegetables, unseasoned meat, which leads to massage and manual cleaning of the periodontal tissues. Calcium deficiency can be compensated by consuming dairy products.

Physical treatment of periodontal diseases methods

The use of physical methods plays an important role in the complex treatment of periodontal diseases. Consider each of them.

Medicinal electrophoresis is one of the methods of physiotherapy, when drugs are injected into the body by means of direct current. The latter, during electrophoresis, are split into positive and negative ions, accumulate in the mucous membrane, and form a depot, from where their prolonged transition into the blood takes place. During medicinal electrophoresis, we use low-concentration substances from 1 to 6%. The lower the concentration of the substance - the faster the ionization occurs, the negative effect of the medicine and allergic reactions are reduced.

Fluctuation

This physical method involves the use of alternating sinusoidal, pulsed current for healing purposes. It has an analgesic, anti-inflammatory effect that accelerates wound healing.

Apparatus АНÁ-2 is used. In bipolar, the chaotically moving impulses cause afferent impulse blocking, due to which the pain is weakened or completely disappears. We use the following doses for fluctuating:

1. Small dose - current strength is up to 1 mA. At this time, the patient indicates a tingling and burning sensation. This dose is used for pain relief.

2. Average dose – current strength is up to 1-2 mA. The patient indicates the vibration of the superficial muscles. This dose has an analgesic and anti-inflammatory effect.

3. Large dose – current strength is 2 and more than 2 ma. At this time, the patient has deep muscle vibration. We use a large dose to treat inflammatory processes located in the groin.

Duration of procedures is 10 minutes. The course of treatment consists of 5-7 procedures.

Contraindications for fluctuating are: malignant tumors, pregnancy, bleeding tendency.

UMSD - therapy

At this time, we use a current of 40 MHz frequency for healing purposes, mechanical energy is transformed into heat energy. We use 3 doses during treatment:

- a) During a small or athermic dose - no heat is released. Has an anti-inflammatory effect.
- b) Medium or oligothermic dose - used for anti-inflammatory and trophic improvement.
- c) Thermal dose - at this time heat is released.
- d) Contraindications to UMSD therapy are: cardiovascular diseases; pregnancy; benign and malignant tumors; lung, liver, kidney failure; Bleeding tendency.

Darsonalization

Darsonvalization is a physical method where alternating current (high voltage and low amperage) is used for healing purposes. During darsonvalization, 100-microsecond-long quenching pulses travel 50 times per second. The latter is brought to the tissues by means of vacuum capacitor electrodes, which in turn causes the irritation of nerve receptors, from which the excitation moves to the CNS in an afferent way. After that, the impulses coming in the efferent way will reach the tissues, causing a reflex action.

Darsonvalization helps to increase the tone of vascular walls of periodontal tissues, improves trophism and metabolism. The duration of the procedure is 10 minutes. The treatment course consists of 10-15 procedures. Darsonvalization is mainly used in the initial stage of the disease. Contraindications to the method are: malignant tumors, pregnancy, and tendency to bleeding.

Diathermocoagulation

A dental diathermocoagulator is a high-frequency generator whose electromagnetic rays pass through an active metal electrode and are converted into heat. During diathermocoagulation, when the active electrode is in contact with the tissue at a high temperature, 60-800 C, protein coagulation takes place. This method is designed to stop bleeding, burn granulation tissue on the gum, hypertrophied mucosa. Active electrodes of different shapes are used, depending on the area in which coagulation is performed. Exposure time is 1-3 seconds.

Contraindications for diathermocoagulation are: malignant and benign tumors, pregnancy, and tendency to bleeding.

Helium-neon laser treatment

A laser is a generator of the optical range of electromagnetic radiation, the operation of which is based on forced radiation or scattering of a light beam. We use the JTM-01 physiotherapy device. This device is safe, convenient and reliable for working both in the polyclinic and in the hospital. The wavelength of the laser device JTM_01_ is 0.63 μm. HNL is used as a source of monochromatic coherent radiation. It has an output tube (cable) through which we can perform treatment in any area of the oral cavity. Electrodes are of different shapes and their use depends

on which area we are irradiating. Exposure time of laser therapy is 2-3 min. Power density 100-200 mW/cm² Number of sessions 5-7.

Using this method, the microcirculation of the irradiated area is regulated, it reduces vascular permeability, it stimulates reparative regeneration, it has an analgesic effect, and it has a desensitizing effect. Increases cell resistance to pathogenic agents, thereby shortening treatment sessions.

Contraindications to HNL therapy are: 1) severe cardiovascular system diseases - 1) heart rhythm disturbance; Atherosclerotic cardiosclerosis, with coronary blood circulation disorders; aortic aneurysm;

- 2) Diseases of the nervous system with sharp excitability.
- 3) Blood diseases.
- 4) Hyperthyroidism.
- 5) Pulmonary emphysema in a pronounced and severe form.
- 6) Functional failure of kidneys.
- 7) Malignant tumors.
- 8) Severe form of pulmonary tuberculosis.
- 9) Severe form of diabetes.
- 10) Pregnancy.

When working on the laser, it is not allowed to look directly at the beam coming out of the radiation source or at the reflected beam. Protective glasses must be used by both the doctor and the patient.

Magnetotherapy

Treatment with a magnetic field is highly effective, causes the excitation of nerve receptors, improves the hemodynamics of the body, accelerates regeneration, promotes the expansion of arterial blood vessels, regulates EDS, and activates tissue tropism.

We choose constant and variable magnetic field. Magnetic bracelets, chains and magnetophore are used as permanent magnetic field. The latter is a rubber plate in which magnetic powder is placed. Magnetophor is used to treat inflammatory processes, fractures, wound healing; In order to improve microcirculation.

In the form of a variable magnetic field, we use the device ПОЛЛОС-1, which is intended for magnetotherapy with a frequency of 50 Hz. The intensity of the magnetic field is from 12.5 to 19.5 millitesla. Magnetotherapy improves microcirculation, normalizes vascular tone, regulates metabolism, enzyme activity.

Before conducting physical procedures, it is necessary to medically treat the surfaces of the teeth. We should remove both soft and cold plaques.

The round indicator of the magnetic field ends 0.5 cm away from the oral cavity. The duration of the procedure is 20 minutes. The treatment course consists of an average of 10 procedures. This method has an advantage compared to other procedures. Because it does not heat the patient's body and does not cause the generation of endogenous heat. The patient has no sensation.

We can also conduct magnetophoresis by means of a magnetic field. Calcium salts, sodium fluoride or any other substance are introduced into the periodontal tissues under the action of a magnetic field, which in turn promotes the activity of metabolic processes in the bone tissue. During the procedure, from the vestibular side, we place pieces of dolband paper soaked in this or that medicinal substance. We close the patient's mouth, we place the magnetic field inductor at a

distance of 0.5 cm from the cleft of the mouth. The duration of the procedure is 20 minutes. Contraindication of this method is pregnancy.

Icroplasma scalpel - radiation treatment

In therapeutic dentistry, as the best means of physio-procedures, we used for the first time a microplasma scalpel-irradiator.

Plasma is an ionized, high-temperature gas. In laboratory conditions, plasma is obtained by electric discharge. When inert gas argon is released into the electric charge between 2 electrodes, the gas is ionized, heated and exits from the nozzle of the microplasmatron in the form of a plasma stream. The length of the illuminated or ionized part of this flow reaches 10-15 cm on average. At a distance of 2-3 cm from it, the temperature does not exceed 300 °C. We irradiate the pathological focus with a distance of 7-12 cm with the output cable of the plasmatron. The patient will feel heat, in case of burning we increase the distance between the electrode and the tissue. Exposure time is 3-5 minutes. The number of procedures is on average 3-5.

Plasma is a polychromatic beam. It is a "little sun". Plasma therapy has many advantages. It causes significant stimulation of the body's immune system, has a bactericidal effect, anti-inflammatory, analgesic effect, causes dilation of blood vessels, which in turn improves tissue trophism, activates vitamin synthesis, and stimulates reparative regeneration.

In order to determine the effectiveness of plasma therapy, both an experimental and a clinical study were conducted by us on the basis of the NN4 clinical hospital of the city. The method reduces the duration of treatment, it is economical and we use less expensive means. Contraindications of this method are: benign and malignant tumors, pregnancy.

Massage

Massage is mechanical irritation of periodontal tissues, improves lymph and blood circulation, metabolism, and reduces congestive changes. Indications for massage are catarrhal gingivitis of any degree and the period following the resolution of acute inflammatory events. Contraindications: purulent exudation from periodontal pockets, hemorrhagic diathesis, hemophilia.

There are various types of massage - finger, vibration, vacuum massage, hydromassage.

Hydromassage - involves irrigation of the oral cavity with water under pressure. At this time, in addition to mechanical irritation, food waste, bacteria, and scraped epithelium are washed out of the mouth.

Vacuum therapy

This method is widely used in the complex treatment of periodontal diseases. V. A vacuum machine was provided by Kulazhenko for treatment.

During the procedure, we take a glass tube (cuvette) connected to the device, place it in the vicinity of the transitional fold on the mucous membrane of the alveolar ridge. Under the influence of the negative pressure created in the device, negative tissue pressure develops. When the cuvette is touched, the tissue will be pumped, blood vessels will break, blood will enter and hematoma will be formed. The latter is given diagnostic value. If the hematoma is formed in 5-15 seconds, the patient has severe periodontitis; when a hematoma is formed within 20-30 seconds, periodontitis of medium severity; if a hematoma forms in 40-45 seconds - the patient has mild periodontitis; And in 50-60 seconds, a healthy periodontist answers.

We start the vacuum therapy from the back teeth, we place a sterile glass tube on the transition wrinkle, and we do not get a hematoma when the device is turned on, but we perform superficial massage both on the upper and lower jaw. During vacuum therapy, there is an improvement of collateral blood circulation at this time, there is a splitting of thin capillaries, complex proteins are also divided, the final products of which are biologically active substances - histamine, serotonin hyaluronidase and others, which in turn stimulate the body's defense system.

The duration of the procedure is not determined by time, and the course of individual treatment includes 10 procedures.

Vacuum therapy can be used for curettage. With a cuvette, we drain out the contents (the scraped epithelium of the blood pus) from the pathological pockets.

Oxygen therapy

This method leads to the saturation of periodontal tissues with oxygen, which leads to a decrease in hypoxia. Bobrov, Novik Mironenko, and others provided an apparatus by which oxygen could be injected into the gum tissues. 5.0 cm³ of oxygen is delivered per injection. 2-3 injections per session are provided. The treatment course consists of 12-15 sessions.

Balneotherapy (mud and water treatment)

At this time, we use natural and artificial mineral water and mud in the form of oral baths. During their long-term use, tooth-gum pockets are washed out, teeth are cleaned of plaque. By the action of some mineral water, dental plaques are removed, ions of microelements, salts, gases penetrate into the tissues, in which they increase the metabolism in the periodontium.

During balneotherapy, before each session, we clean the surface of the teeth with a brush. When treating with mud.

Relevance of the topic

Observation of the regeneration of damaged human bone has a long history. There are many treatments or methods for regulating and stimulating reparative osteogenesis, but the search for their perfection continues. In dentistry, the full treatment of diseases such as periodontitis is very relevant, because solving the mentioned problems goes beyond the scope of dentistry. Periodontitis is the most common among dental diseases in the population and they may have both.

Despite the many antibacterial drugs currently available, the issue of treatment of forms of periodontitis is still unresolved, which is manifested by immediate and later complications after treatment.

Full treatment of periodontitis is problematic. Moreover, according to the data of the International Health Organization, the prevalence of periodontal diseases is detected in 80% of cases in children, and up to 100% in adults. The digestion process is disturbed, the psychogenic status changes, the body becomes sensitized, etc. Well-known methods of periodontitis treatment give positive results to some extent, but most of them are still unable to normalize immune reactions.

Periodontal diseases, complex inflammatory conditions of the oral cavity, demand a comprehensive and multi-faceted approach to treatment. Key principles in managing these diseases include the reduction of microbial biofilms, modulation of host immune responses, and regeneration of damaged periodontal tissues. Initial therapy often involves non-surgical methods like scaling and root planning, complemented by antimicrobial agents. For more severe cases,

surgical interventions, including guided tissue regeneration and biomaterial applications, aim to restore periodontal structures.

Recent advancements, such as the integration of biomaterials, stem cell therapies, laser technologies, and probiotics, have revolutionized the field. Additionally, the systemic links between periodontal diseases and chronic conditions like diabetes and cardiovascular diseases underscore the need for personalized and interdisciplinary care.

However, challenges remain in ensuring patient compliance, cost-effectiveness, and the predictability of outcomes. Continued research and innovation are critical to overcoming these barriers and advancing periodontal therapy. By addressing these challenges, periodontal care can achieve its goal of improving both oral health and overall systemic well-being.

The complex picture of factors influencing the outcomes of root canal (re)treatment ultimately distils down to a very simple principle, which explains all the apparently surprising findings.

The net effect of all the various root canal treatment protocols ever used has been the same, to enable control of infection in the instrumented root canals. The single most important intra-operative factor is the proximity to the canal terminus of apical extent of debridement and the apical extent of root-filling (without periapical extrusion). Extrusion of root filling material consistently delays or prevents periapical healing. However effective the protocol is in exerting control over the microbiota within the instrumented parts of the root canal system, the complex apical anatomy remains infected (Nair et al., 2005). Interaction between this residual apical infection and host defences (original cause of apical periodontitis) continues beyond the completion of the root canal treatment procedure, but with an altered dynamic in all healing cases. The root canal treatment induced sufficient bacterial control in the instrumented part of the root canal system to dampen apical inflammation without completely switching it off. This is because of the residual bacteria in the apical anatomy, which do however, progressively become inactive or die because their nutritional source, the inflammatory exudate, reduces in concert with the dying bacteria. Completion of active root canal treatment (or sometimes chemo-mechanical debridement) marks the beginning of a new phase in the dynamic apical encounter, in which the apical immune mechanisms gradually re-exert control over the surviving intra-radicular apical infection. The precise dynamic may vary from tooth to tooth, and host to host, dependent on the relative strength of the two arms (infection versus host defences) of the interaction, resulting in the typically variable but nearly-always extended periapical healing period (1–4 years plus).

The rates of periapical healing over the previous century show no significant differences because the principles of root canal treatment had remained the same over that period, despite conceptual and protocol variations. Whilst the protocol changes have improved the efficiency and predictability of the technical outcome, they have not altered the efficacy of periodical healing. This is perfectly logical because none of the root canal treatment protocols over the last century have altered the nature of the intra-operative or postoperative apical host/microbial dynamic. It should therefore not be expected that the biological outcomes would be any different by chronological (decade of treatment) or geographic (location in the world) distribution.

All the factors that have a direct effect on the apical host/microbial dynamic have a powerful prognostic effect on periapical healing (preoperative periapical status including signs and symptoms of infection and size of lesion, patency to canal terminus, apical extent of canal instrumentation and root-filling, quality of restoration and remaining tooth structure). Whilst all the factors that have no or only an indirect influence on the apical host-microbial dynamic exert no or only a weak prognostic effect on periapical healing (age, sex, general health, tooth type,

rubber dam use, magnification and illumination use, access cavity design, root canal instrumentation choice and technique, dimensions of canal preparation, root canal irrigation choice and technique, root filling material choice and technique). Effective apical root canal irrigation and medication can have an impact on the apical dynamic, as may the genetic expression of host immunity, and are yet likely to emerge as important influencing contenders in future studies.

Root canal treatment may be summarized as the management of pulpal or periapical infected wounds through the application of age-old surgical principles of wound management, debridement and dressing (obturation) to allow healing. Put simply, once the dynamic host/microbial interaction is established at the periapex, it is sustained across the pre-operative, intra-operative and postoperative phases of root canal treatment. Adequate root canal treatment “actively” shifts the ecological balance in favour of the host immune defences, dampening the inflammation and commencing a new phase in the interaction. Breaches in the tooth (cracks) or marginal integrity (leakage) may “passively” allow reversal of the targeted microbial demise and host interaction, hence the remarkably powerful impact of this factor on outcomes. This then is the reframed and re-stated principle of root canal treatment. It strongly and logically argues for a two-stage (two-visit) management of teeth with apical periodontitis, in which the debridement phase only is ideally completed within one visit.

Prognostication should therefore take account of the feasibility of both biological (periapical lesion size and symptoms) and technical (root canal system complexity and operator competency) control of the root canal infection, as well as the prospect of sustaining any root-canal-treatment-induced microbial control through tooth and restorative interface integrity. The endodontist must, therefore, also have insight about factors influencing tooth restoration and survival.

Although histopathology is still the standard for the diagnosis of PA lesions, technologies such as CBCT, MRI, and echography show promising results in differentiating granulomas and cyst, which can affect the treatment strategy. There are several new treatment options available for eliminating periradicular lesions or enhancing the healing process to save teeth with persistent periapical lesions. Albeit several treatment modalities have been proposed for these teeth which have failed endodontically, there is a need for less invasive methods with more predictable outcomes. It is highly recommended that with technological advances, further minimally invasive approaches must be considered for resolving the issue of persistent apical periodontitis and true cysts to reduce the burden for patients.

Conclusion

The treatment of periodontal diseases is rooted in well-established principles that aim to restore oral health by controlling microbial factors, modulating host responses, and regenerating periodontal tissues. Advances in our understanding of the pathogenesis of these diseases have paved the way for innovative approaches, from non-surgical therapies to regenerative techniques incorporating biomaterials and stem cells. These developments, coupled with the integration of personalized and interdisciplinary care, have significantly improved treatment outcomes. Despite these advancements, challenges such as patient compliance, cost-effectiveness, and the complexity of systemic associations remain hurdles to be addressed. Continued research is necessary to optimize treatment protocols, enhance accessibility, and explore emerging technologies, such as laser therapies and biotechnological innovations, for widespread application. By bridging existing knowledge gaps and fostering collaboration between disciplines, the field of

periodontology can continue to make strides toward more effective, efficient, and holistic care for patients with periodontal diseases. This effort is vital not only for improving oral health but also for addressing the broader systemic implications of these conditions.

Declarations

The manuscript has not been submitted to any other journal or conference.

Study Limitations

There are no limitations that could affect the results of the study.

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Competing Interests

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Ethical Standards

The research meets all ethical guidelines, including adherence to the legal requirements of the study country.

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- In the "Summary" give: 1) relevant background information, 2) why the work was done, 3) what were the significant results, 4) possible explanation of the results.
- Only give the significant results of your study and give their possible explanation.
- Do not compare your results with other studies.
- Do not give references in the "Summary" section. First reference should start in main text of your manuscript from the "Introduction" section.

Introduction (Times New Roman, 12)

Mostly Papers starts with introduction. It contains the brief idea of work, requirement for this research work, problem statement, and Authors contribution towards their research. Sufficient recent reference citation [1] from last 2 years should be included for showing the existing challenges and importance of current work. This section should be succinct, with no subheadings unless unavoidable [2, 3]. State the objectives of the work and provide an adequate background related to your work, avoiding a detailed literature survey or a summary of the results.

Research Methodology (Times New Roman, 12)

This part should contain sufficient detail to reproduce reported data. It can be divided into subsections if several methods are described. Methods already published should be indicated by a reference [4], only relevant modifications should be described. Methodology should be written concisely in detail by maintaining continuity of the texts.

Theory and Calculation (Times New Roman, 12)

A Theory section should extend, not repeat, the background to the article already dealt with in the Introduction and lay the foundation for further work. In contrast, a Calculation section represents a practical development from a theoretical basis. Do not add extensive basic definitions or well-known theories, instead highlight theoretical background and its specific usages in view of your work only.

Mathematical Expressions and Symbols (Times New Roman, 12)

Mathematical expressions and symbols should be inserted using **equation tool** of Microsoft word. References may be added for used equations to support its authenticity, e.g. this result has been analysed using Fourier series [5].

$$f(x) = a_0 + \sum_{n=1}^{\infty} \left(a_n \cos \frac{n\pi x}{L} + b_n \sin \frac{n\pi x}{L} \right) \quad (1)$$

Results and Discussion (Times New Roman, 12)

This section may each be divided by subheadings or may be combined. A combined Results and Discussion section is often appropriate. This should explore the significance of the results of the work, don't repeat them. Avoid extensive citations and discussion of published literature only, instead discuss recent literature for comparing your work to highlight novelty of the work in view of recent development and challenges in the field.

Preparation of Figures and Tables (Times New Roman, 12)

Authors are supposed to embed all figures and tables at appropriate place within manuscript. Figures and tables should neither be submitted in separate files nor add at the end of manuscript. Figures and Tables should be numbered properly with descriptive title. Each Figure/Table must be explained within the text by referring to corresponding figure/table number. Any unexplained or unnumbered Figure/Table may cause rejection of the paper without being reviewed.

Formatting Tables (Times New Roman, 12)

Table should be prepare using table tool within the Microsoft word and cited consecutively in the text. Every table must have a descriptive title and if numerical measurements are given, the units should be included in the column heading. Formatting requirement has been summarized in the Table 1.

Table 1: Summary of formatting requirement for submitting paper in this journal. (Times New Roman, 12)

Layout	Size	Margin (Normal)	Header	Footer	
Single column	A4 (8.27" X 11.69")	Top=1" Bottom=1" Left=1" Right=1"	Do not add anything in the header	So not add anything in the footer	
Font	Article Title	Headings	Subheadings	Reference list	Text
	Times New Roman, 16 pt, Bold, centred	Times New Roman, 11 pt, Bold, Left aligned	Times New Roman, 10 pt, Bold, Left aligned	Times New Roman, 8 pt, Justified	Garamond, 11 pt, Justified
Line Spacing	1.15	1.15	1.15	1.15	1.15
Page number	We will format and assign page numbers				

(Times New Roman, 10)

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All figures should be cited in the paper in a consecutive order, author may be asked to provide separate files of the figure. Figures should be used in bitmap formats (TIFF, GIF, JPEG, etc.) with 300 dpi resolution at least unless the resolution is intentionally set to a lower level for scientific reasons. If a bitmap image has labels, the image and labels should be embedded in separate layer. Figure 1 shows the logo of IRETC Publisher.

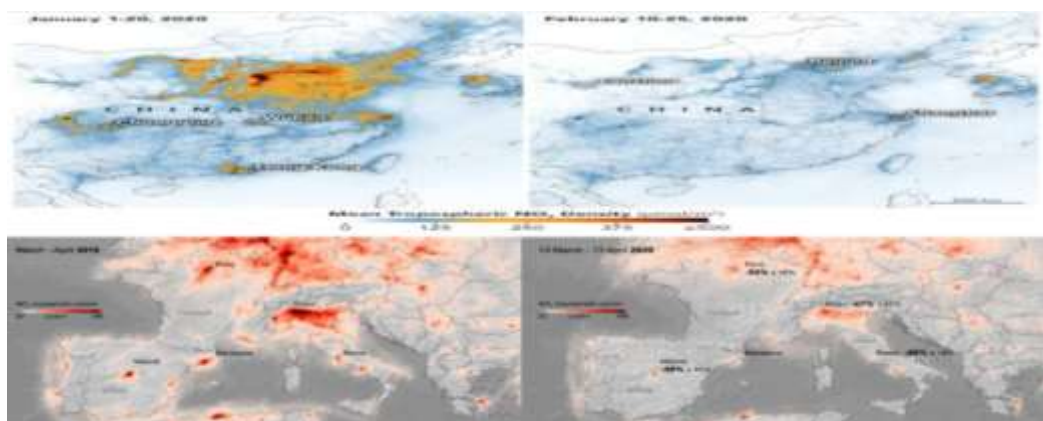


Figure 1: Logo of the IRETC Publisher (Times New Roman, 12)

Conclusions (Times New Roman, 12)

Each manuscript should contain a conclusion section within 250-450 words which may contain the major outcome of the work, highlighting its importance, limitation, relevance, application and recommendation. Conclusion should be written in continuous manner with running sentences which normally includes main outcome of the research work, its application, limitation and recommendation. Do not use any subheading, citation, references to other part of the manuscript, or point list within the conclusion.

Declarations (Times New Roman, 12)

Study Limitations (Times New Roman, 12)

Provide all possible limitation faced in the study which might significantly affect research outcome, If not applicable write, none.

Acknowledgements (Times New Roman, 12)

All acknowledgments (if any) should be included in a separate section before the references and may include list of peoples who contributed to the work in the manuscript but not listed in the author list.

Funding source (Times New Roman, 12)

Provide funding source, supporting grants with grant number. The name of funding agencies should be written in full, if no funding source exist, write, none.

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Declare any potential conflict of interest exist in this publication.

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If the work involves the use of human/animal subjects, each manuscript should contain the following subheadings under the declarations section-

Ethical Approval (Times New Roman, 12)

Provide ethical approval authority name with the reference number. If ethical approval is not required, provide an ethical exemption letter of not required. The author should send scan copy (in pdf) of the ethical approval/exemption letter obtained from IRB/ethical committee or institutional head.

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Write a statement of informed consent taken from the participants to publish this research work. The editor may ask to upload scan copy if required.

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Author(s) are responsible for ensuring that the information in each reference is complete and accurate. **Do not use grey literature (unauthentic website, news portal, social media, Wikipedia etc) as reference, only scholarly literature (Journal, online books, proceedings, patents, authentic websites with permanent archival policy) are acceptable references.** Author should include sufficient recent (last 2 years) references in the article. All references must be numbered consecutively and citations of references in the text should be identified using numbers in square brackets (e.g., “as explained by AIJR [1]”; “as discussed in many reports [2]-[6]”). All references should be cited within the text correctly; do not add only list of references without citation within the text. All cited references should be listed after declarations section in the following style-

1. W. S. Author, “Title of paper,” Name of Journal in italic, vol. x, no. x, pp. xxx-xxx, Abbrev. Month, year. <https://doi.org/10.21467/ajgr>
2. Bahishti, “Peer Review; Critical Process of a Scholarly Publication”, J. Mod. Mater., vol. 2, no. 1, pp. 1.1-1.2, Oct. 2016. <https://doi.org/10.21467/jmm.2.1.1.1-1.2>
3. Bahishti, “A New Multidisciplinary Journal; International Annals of Science”, Int. Ann. Sci., vol. 1, no. 1, pp. 1.1-1.2, Feb. 2017. <https://journals.aijr.in/index.php/ias/article/view/163>
4. W. S. Author, “Title of paper,” Name of Journal in italic, vol. x, no. x, pp. xxx-xxx, Abbrev. Month, year. Access online on 20 March 2018 at <https://www.aijr.in/journal-list/advanced-journal-graduate-research/>
5. W. S. Author, “Title of paper,” Name of Journal in italic, vol. x, no. x, pp. xxx-xxx, Abbrev. Month, year. Access online on 5 March 2018 at <https://www.aijr.in/about/publication-ethics/>
6. M. Ahmad, “Importance of Modeling and Simulation of Materials in Research”, J. Mod. Sim. Mater., vol. 1, no. 1, pp. 1-2, Jan. 2018. DOI: <https://doi.org/10.21467/jmsm.1.1.1-2>

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