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## Estimating the clinical needs for tissues and cells in the Republic of Moldova

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### Abstract

**Background:** Safe and sustainable supply of tissues and cells for human application is an essential pillar in modern medical assistance and a priority for the health authorities both at national and international level.

**Material and methods:** The study protocol for the needs assessment in tissue and cell grafts for the healthcare system was approved by the Ethic Committee. The survey of 161 surgeons was carried out in 24 institutions, through specially developed questionnaires. In order to validate some data obtained through questionnaires, the analysis of already existing national data and sources was performed.

**Results:** Most surgeons (93.4%) declare that the institution they work at has been provided with a sufficient number of grafts for all patients needing transplantation. Despite this, the estimation of surgeons' opinion regarding the need for grafts showed that 59.4% of respondents consider that they have enough grafts, 21.7% of respondents deal with exceptional cases of lack of grafts, 13.2% respondents consider that there are sufficient grafts for urgent patients and, sometimes, for non-urgent patients.

**Conclusions:** The study revealed that increasing the number of tissue transplantations will contribute to improve the patients' life quality and increasing the number of transplanted patients over the next 5 years is a priority measure in the management of the institutions included in the survey.

**Key words:** tissue and cell grafts, clinical needs, transplantation, transplant services.

### Cite this article

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### Introduction

Transplantology as a medical science and transplantation per se have recorded a significant progress over the past decades. In analysts' opinion, transplantation is an indicator of the level of development of medical industry, the scientific and practical potential of a state and the level of maturity of society [1]. As to organs, the demand for certain types of tissues and cells to be transplanted goes beyond the available supply.

World Health Organization (WHO) presented two reports – First and Second Global Consultation on Regulatory Requirements for Human Cells and Tissues for Transplantation (2004 and 2006, respectively) providing an overview regarding the relevance and development of this field in different countries. The First WHO Report defines the tissue and cell grafts as a specific class of medical products with an important therapeutic value where almost no substitutes for restoring vital functions exist [2]. Many countries face a deficit of standards and regulations relevant for this field and they also face a lack of necessary grafts, for instance corneal grafts. The other Report highlights the importance of systems safe for traceability and biovigilance, underlining the fact that, for instance, annually, in Spain almost 10.000 patients get bone, tendon or corneal grafts [3].

The American Association of Tissue Banks (AATB),

which includes more than 120 accredited tissue banks, says that the tissue banks have been established to satisfy critical medical needs for tissue grafts in order to save or to improve life of more than a million Americans yearly [4].

AATB's Activity Report for 2017 shows that over the last 10 years there has been noted a general increase in donors and grafts procurement. The total number of actual tissue donors (both alive and deceased ones) has rapidly increased by 92%: from 30.380 in 2007 up to 58.339 in 2015. The total number of grafts distributed has also gone up from 2.496.010 in 2007 up to 3.294.066 in 2015, representing 32% [4, 5]. The musculoskeletal grafts remain to be the most requested ones and represent 71% of the total number of tissues distributed in 2015. In the period 2012-2015, the number of grafts distributed registered a rise in those 5 categories out of six in whole, except for cardiac tissues: musculoskeletal, skin, soft tissues, vessel, tissues from alive donors have increased up to 122%.

Spain has the highest number of deceased donors. If in the middle of the '90's, it counted 27 donors per million populations (pmp), in 2017 this rate went up to 46.9 pmp [6, 7]. Tissue donation has increased in the period 2011 – 2016: cornea – from 60 pmp up to 82.4 pmp, musculoskeletal tissue – from 44.8 pmp up to 57 pmp, skin tissue – from 4.5 pmp up to 7.3 pmp [8, 9].

Croatia has successfully introduced different elements of the best European practices (Spanish model, Eurotransplant system, etc.) and recorded a sustainable increase in the rate of pmp donors, registering in 2017 a rate of 33 donors pmp [10]. In 2011 – 2016, the corneal tissue donors have increased significantly from 2.7 pmp up to 69.9 pmp [8, 9].

In other European Union countries (EU countries), the number of donors and tissues transplants have also increased. For instance, in France, in the period 2011-2016, the tissue donation has significantly increased, namely the musculoskeletal tissue from 1.3 pmp up to 402 pmp, the number of grafts distributed for transplantation has risen from 27997 up to 47528, representing 41% [8, 9].

The increase in possibility to use human material in various forms for the others' benefit during the medical treatment has put significant pressure on the EU countries to satisfy this demand. The demand of human material is obviously variable as scientific developments make available more forms of treatment, it is likely that demand for such treatment to go up, meanwhile the development of alternate forms of treatment could result in decrease of demand. People's expectations as to what the medical sciences could reach put additional pressure on that supply [11].

Safe and sustainable supply of tissues and cells is an essential pillar in modern medical assistance in the EU countries and a priority for the health authorities both at national and the EU level [12-14]. In more situations, a tissue or cell transplant is the best or the single therapeutic option for patients. The supply and offer of human tissues and cells is a task of management during which medical, financial and social aspects should be constantly balanced as for the organization to continue to work and to be accepted by society [15].

The history in different types of tissue and cell banks underscore the complicated and interconnected ways the tissues and cells donated by one person may be used to help others or themselves [16, 17].

The main aim to preserve human material for transplantation in a bank is to satisfy the clinical demand of tissues and cells [18, 19]. The national health authorities are responsible to ensure that the patients' needs are satisfied with a safe, qualitative and appropriate source of tissues and cells [20].

The goal of this study was to assess the needs for tissue and cell grafts for the healthcare system in order to ensure the functioning of the transplant services provided to the population.

### Material and methods

The study was performed to evaluate the opinions of the doctors of surgical profile, whether or not involved in the transplant services, regarding the needs for tissue and cell grafts for the healthcare system, through specially developed questionnaires, consisting of 35 questions. The volume of the representative sample of the doctors of surgical profile was calculated based on the classical formula, proposed for

the random non-repetitive survey with an admitted error of 5% and a non-response rate of 10.0%. In order to validate some data obtained through questionnaires, we used the case studies and the analysis of already existing national data and sources. The study protocol was approved by the Ethic Committee of the Nicolae Testemitsanu State University of Medicine and Pharmacy, Chisinau (No. 2, 27.10.2016).

The survey of 161 doctors of surgical profile aged 25 – 81 was carried out in 24 medical-sanitary institutions, including 20 public institutions (9 republican, 2 municipal and 9 district) and 4 private institutions. In order to carry out the tissue and cell donation and transplantation activities, 10 from 24 medical-sanitary institutions are authorized by the Ministry of Health: 8 public and 2 private institutions. Their annual activity reports submitted to the Transplant Agency were used for the analysis.

In the group of doctors of surgical profile were included: 24 (14.9%) transplant coordinators and persons in charge of transplantation from medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation, 52 (32.3%) orthopaedic traumatologists, 27 (16.8%) general surgeons, 15 (9.3%) ophthalmologists, 7 (4.3%) combustiologists, 36 (22.4%) doctors with another surgical profile – oncologists, neurosurgeons, gynecologists, urologists.

Of the total number of surgeons, 125 (77.6%) were men and 36 (22.4%) were women. Depending on age and gender, the respondents in the study group were distributed as follows: 25 (15.5%) persons were aged within 25 – 34 years (15 – 60.0% men and 10 – 40.0% women), 93 (57.8%) persons – within 35 – 54 years (73 – 78.5% men and 20 – 21.5% women), 43 (26.7%) persons – within 55 – 81 years (37 – 86.0% men and 6 – 14.0% women). The average age of surgeons was  $46.84 \pm 0.9$  years. The average age was statistically significantly higher in men –  $47.78 \pm 0.9$  years, compared with women –  $43.58 \pm 2.1$  years (from 25 to 70 years;  $p < 0.05$ ).

Statistical processing of the material was based on the special files elaborated where the primary data were coded – the results of the questionnaires, the data from the primary documents of the medical-sanitary institutions and the data from the databases of the Transplant Agency. The primary materials of the study were computerized using the software "Statistical Package for the Social Science" version 20.0 for Windows (SPSS, Inc., Chicago, IL, 2011) by methods of variation, correlation and discriminant analysis. Differences with the bilateral p-value  $< 0.05$  were considered statistically significant.

### Results and discussion

To assess the needs for tissue and cell grafts, 139 (86.3%) surgeons from the public medical-sanitary institutions and 22 (13.7%) surgeons from the private medical-sanitary institutions have been interviewed. Out of the mentioned surgeons, 106 (65.8%) respondents were from the medical-sanitary institutions with activities in the field of tissues and

cells donation and transplantation, and 55 (34.2%) respondents were from the medical-sanitary institutions without activities in this field.

The survey showed that to carry out donation and transplantation activities does not depend on the type of financing, legal form of medical institution: 13 (59.1%) respondents confirmed that transplant services are provided in private institutions and 93 (66.9%) respondents – in public institutions ( $p > 0,05$ ).

The estimate of frequency of different transplant types made was taken from the annual activity reports by the medical-sanitary institutions and based on the opinion of surgeons from the medical-sanitary institutions included in the survey.

Most surgeons – 99 (93.4%) – say that the institution they work at has been provided with a sufficient number of tissue grafts for all patients needing transplantation. Only 7 (6.6%) respondents consider that the provided tissue grafts are insufficient. Respondents from the public medical-sanitary institutions say that they are provided with sufficient tissue grafts to cover all patients needing transplant, statistically more frequently compared to respondents from private institutions: 91 (97.8%) and 8 (61.5%), respectively;  $p < 0.001$ .

Despite this, the estimation of surgeons' opinion regarding the need for grafts showed the following: 63 (59.4%) respondents consider that their institutions have enough grafts, 23 (21.7%) respondents consider that their institutions deal with exceptional cases of lack of grafts, 14 (13.2%) respondents consider that there are sufficient grafts for urgent patients and, sometimes, for non-urgent patients, and 6 (5.7%) respondents consider that grafts are enough only for patients in emergency need (fig. 1).

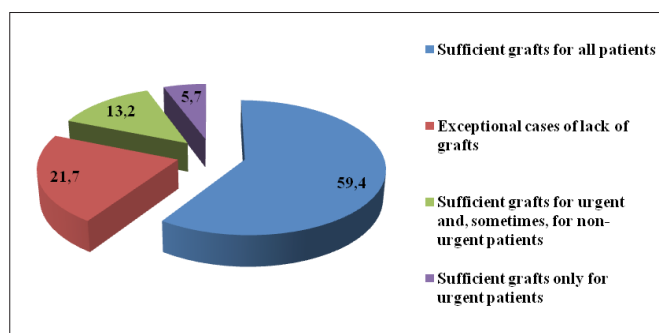


Fig. 1. Surgeons' opinion regarding the need for grafts (%).

The need to develop the tissue transplantation, especially the cornea transplant, results from the analysis of further increase in the cornea transplant waiting list that is presently performed in 5 medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation [21]. The total annual number of cornea transplantations in average is  $7.2 \pm 3.34$  (from 1 up to 19 corneal grafting surgeries) (fig. 2).

Over 1/2 (24 – 51.1%) of surgeons would perform more corneal grafting surgeries if such grafts were provided by

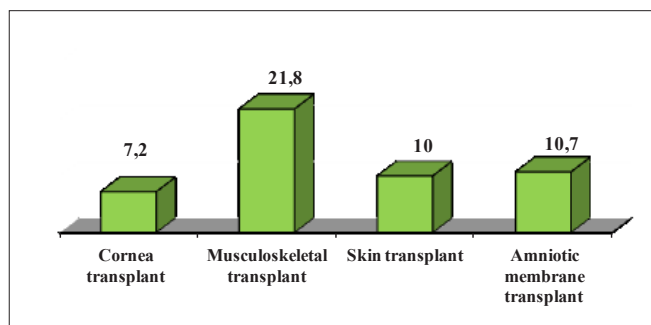


Fig. 2. Annual number of tissue and cell transplants performed (average value).

the tissue bank – in average  $12.33 \pm 1.86$  (from 4 up to 15 corneal grafts). In the private medical-sanitary institutions, this parameter is statistically more frequently encountered (6 – 100.0%) compared to the municipal medical-sanitary institutions (1 – 16.7%;  $p < 0.001$ ) and the republican medical-sanitary institutions (17 – 48.6%;  $p < 0.001$ ).

One of the reasons why the donation and transplantation activities are not performed is that there is no qualified medical personnel and appropriate medical equipment. The main reasons why the corneal grafting is not performed in the public and private medical-sanitary institutions is the lack of qualified medical staff and adequate medical equipment, problem that was highlighted by 28 (24.6%) surgeons, the lack of qualified medical staff – by 16 (14.0%) surgeons, the lack of adequate medical equipment – by 16 (14.0%) surgeons and other reasons (the institution is focused on other type of transplantation of human tissues or is not authorized to perform such surgeries) were mentioned by 54 (47.4%) surgeons (fig. 3).

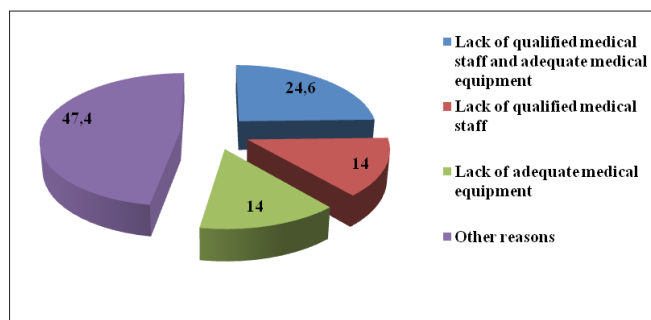
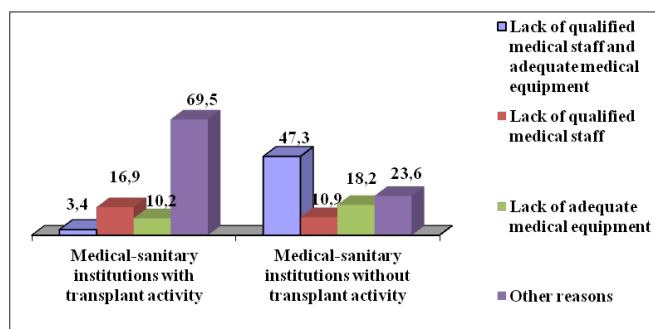


Fig. 3. The main reasons why the medical-sanitary institutions do not perform cornea transplantation (%).

According to the medical-sanitary institutions' authorization provided to perform activities in the field of tissues and cells donation and transplantation, the following results were obtained. Respondents from institutions with activities in this field mentioned that the corneal grafting is not performed due to the fact that there is no qualified medical personnel and no adequate medical equipment in 2 (3.4%) cases, no qualified medical staff – 10 (16.9%) cases, no adequate medical equipment – 6 (10.2%) cases and the institution has another transplant profile – 41 (69.5%) cases. Re-

spondents from institutions not performing activities in the field of tissues and cells donation and transplantation noted that the cornea transplantation is not performed due to the absence of qualified medical personnel and adequate medical equipment – 26 (47.3%) cases, qualified medical staff – 6 (10.9%) cases, adequate medical equipment – 10 (18.2%) cases and authorization for performing donation and transplantation – 13 (23.6%) cases (fig. 4).



**Fig. 4. The main reasons why the medical-sanitary institutions do not perform cornea transplantation (%) depending on the deployment activities in the field of tissue and cell donation and transplantation.**

The musculoskeletal tissue transplantation is performed in 6 (60.0%) medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation. The total annual number of musculoskeletal tissue grafting surgeries is in average of  $21.83 \pm 6.48$  (from 1 up to 43 musculoskeletal tissue grafting surgeries) (fig. 2). The cancellous bone or cortical bone transplantation was mentioned by 25 (32.9%) surgeons, where the bone and tendon transplantation was mentioned by 51 (67.1%) surgeons. Over 2/5 (34 – 44.7%) of surgeons would perform more musculoskeletal tissue grafting surgeries if those grafts were offered by the tissue bank. As to the republican medical-sanitary institutions this parameter is statistically more frequent (32 – 50.0%) compared to the private institutions (0 – 0%;  $p < 0.001$ ).

Moreover, over 4/5 (67 – 88.2%) of surgeons will need the provided bone grafts in other forms than the frozen ones (lyophilized, demineralized, morsel): statistically less often in the republican medical-sanitary institutions (55 – 85.9%) against private ones (7 – 100.0%;  $p < 0.01$ ) and municipal ones (5 – 100.0%;  $p < 0.01$ ).

Wang W, Yeung KW. highlight that autologous bone graft is the gold standard clinical material for bone regeneration. However, limited availability and donor site morbidity are concerned. Bone allograft becomes the second higher option for orthopaedic procedures due to the availability in various forms and large quantities [22].

Skin transplantation is performed in 2 (20.0%) medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation. Annually there are performed skin grafting surgeries  $10.0 \pm 1.0$  (from 9 up to 11 surgeries) in average (fig. 2), with  $71.5 \pm 0.5$  grafts (from 71 up to 72 grafts) on a surface of  $11005.0 \pm 358.5$  cm<sup>2</sup> (from 10647 up to 11364 cm<sup>2</sup>).

Over 1/2 (23 – 57.5%) of surgeons would perform more skin grafting surgeries if those grafts were provided by the tissue bank. All respondents are hired by the republican medical-sanitary institutions.

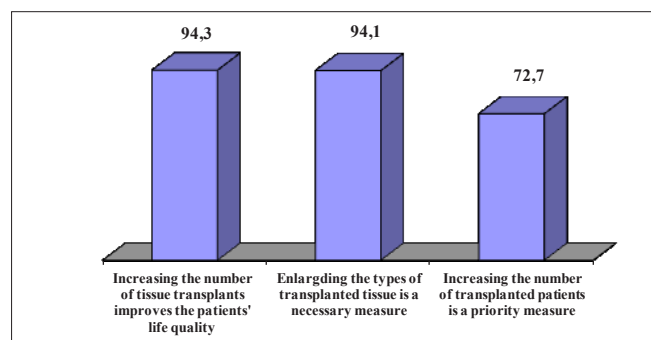
The amniotic membrane transplantation is performed in 6 (60.0%) medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation. The total annual number of amniotic membrane transplantations in average is of  $10.67 \pm 6.72$  (from 3 up to 44 amniotic membrane grafting surgeries) (fig. 2), with  $11.83 \pm 6.55$  grafts (from 3 up to 44 grafts) on a surface of  $559.0 \pm 279.16$  cm<sup>2</sup> (from 45 up to 1814 cm<sup>2</sup>).

Over 1/2 (39 – 52.7%) of surgeons would perform more amniotic membrane grafting surgeries if those grafts were provided by the tissue bank – in average  $7.75 \pm 0.75$  grafts (from 7 up to 10 grafts). In the private medical-sanitary institutions this parameter is statistically more frequent (6 – 100.0%) compared to the municipal institutions (0 – 0%;  $p < 0.001$ ) and the republican institutions (33 – 53.2%;  $p < 0.001$ ).

Our study showed that musculoskeletal grafts for transplant surgery remain the most requested in our country as in the other countries of the world [5, 9].

Generally, 100 (94.3%) surgeons from the medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation consider that the increasing in number of tissue grafting surgeries performed in their institutions would contribute to improve the patients' life quality. As to the republican medical-sanitary institutions, this opinion is statistically less often (76 – 92.7%), compared to the municipal institutions (11 – 100.0%;  $p < 0.05$ ) and private institutions (13 – 100.0%;  $p < 0.05$ ) (fig. 5).

About 64 (94.1%) surgeons from the medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation declared that enlarging the types of tissues transplanted is a very necessary measure. This opinion is also shared ( $p > 0.05$ ) by respondents from the republican (55 – 94.8%), municipal (4 – 80.0%) and private (5 – 100.0%) institutions.



**Fig. 5. Opinion of surgeons from the medical-sanitary institutions with transplant activities regarding the perspective of tissues and cells transplantation (%).**

Over 2/3 (117 – 72.7%) of surgeons from all medical-sanitary institutions participating in the survey consider

that increasing the number of transplanted patients in the next 5 years is a priority for the institution management. This opinion is also shared by surgeons from the institutions with activities in the field of tissues and cells donation and transplantation (80 - 75.5% of respondents) and from the institutions without the activities in this field (37 - 67.3% of respondents;  $p > 0.05$ ).

Despite this, only about 2/3 (68 - 64.2%) of respondents plan in the next 5 years to extend the types of tissue and cell grafting (other than those transplanted currently): 5 (45.5%) respondents from the municipal institutions, 5 (38.5%) respondents from the private institutions and 58 (70.7%) respondents from the republican institutions (fig. 6).

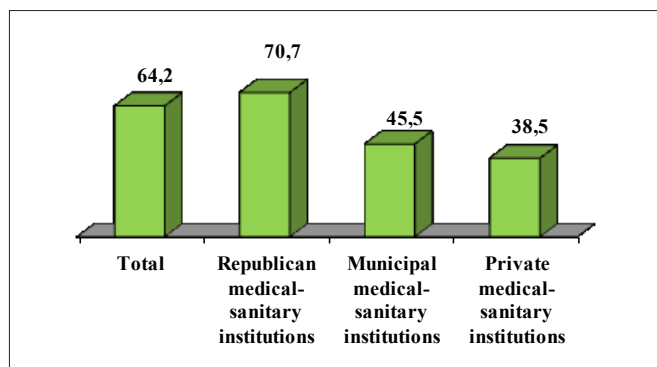


Fig. 6. Surgeons' plan to extend the types of tissues and cells transplanted over the next 5 years by institution level (%).

This expectation is statistically more frequent among surgeons from the republican medical-sanitary institutions - 58 (70.7%) respondents compared to surgeons from the private institutions - 5 (38.5%) respondents ( $p < 0.05$ ).

The assessment of opinion of surgeons regarding the dynamic of providing those institutions with tissue grafts over the past 5 years found that 81 (76.4%) respondents confirmed that situation has improved and 25 (23.6%) respondents consider that it has not changed. Depending on the level of institution, the following results were achieved: 64 (78.0%) respondents from the republican medical-sanitary institutions, 11 (100.0%) respondents from the municipal institutions and 6 (46.2%) respondents from the private institutions consider that situation in providing the institution with tissue grafts over the last 5 years has improved; 18 (22.0%) respondents from the republican institutions and other 7 (53.8%) respondents from the private institutions consider that situation with providing grafts has not changed over the past 5 years. Statistically significant differences in those opinions as to tissue grafts provided to the institutions were noted in respondents from the municipal and private institutions ( $p < 0.01$ ), in respondents from the municipal and republican institutions ( $p < 0.01$ ) and in respondents from the private and republican institutions ( $p < 0.05$ ) (fig. 7).

About 2/3 (66 - 62.3%) of surgeons from the medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation declare that the number of patients needing transplant has increased, 38 (35.8%)

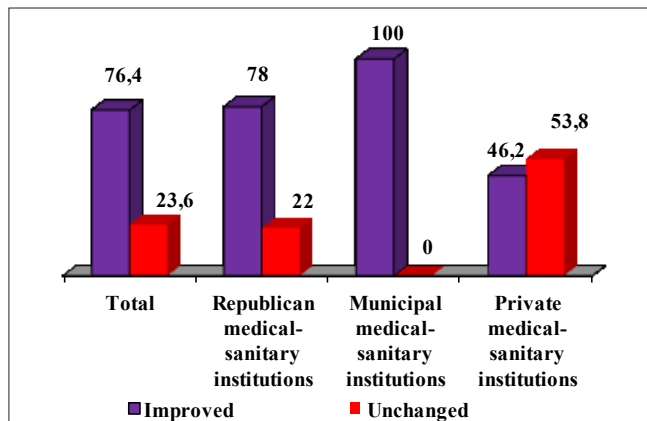


Fig. 7. The opinion of surgeons regarding the dynamic of providing with tissue grafts during the last 5 years depending on the level of the institution (%).

respondents consider that the number of patients needing transplant has unchanged and only 2 (1.9%) respondents mentioned that the number of patients needing transplant has decreased. As many as 51 (62.2%) respondents from the republican institutions, 9 (81.8%) respondents from the municipal institutions and 6 (46.2%) respondents from the private institutions revealed that number of patients who need grafting has increased, 29 (35.4%) respondents from the republican institutions, 2 (18.2%) respondents from the municipal institutions and 7 (53.8%) respondents from the private institutions declared that the number of patients in need of a transplant has remained unchanged and only 2 (2.4%) respondents from the republican institutions noted that the number of patients who need transplant has decreased. Differences in those opinions could not be set statistically significant (fig. 8).

Therefore, priority in establishing an efficient tissue and cell transplantation system should be given to: promoting the training of specialists based on the best experiences, endowing the medical-sanitary institutions with adequate medical equipment, establishing an efficient system for identifying persons that could become tissue donors post-mortem and studying how to encourage donors alive to donate [11, 16, 23, 24].

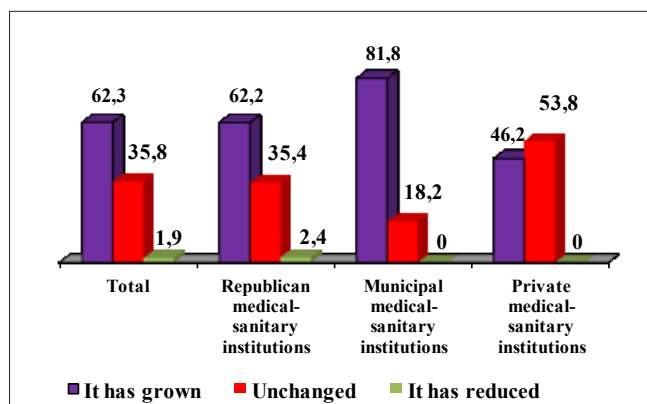


Fig. 8. Opinion of surgeons regarding the dynamics of the number of patients requiring transplantation according to the institution level (%).

## Conclusions

1. The estimation of surgeons' opinion regarding the clinical needs for tissues and cells revealed the following: 59.4% of respondents consider that their institutions are sufficiently supplied with grafts, 21.7% of respondents consider that their institutions deal with exceptional cases of lack of grafts, 13.2% respondents consider that the grafts are sufficient for urgent patients and 5.7% respondents consider that grafts are enough only for patients in emergency need.

2. About 44.7-57.5% of surgeons from the medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation would transplant more grafts if those grafts were provided by the tissue bank, and 64.2% of surgeons plan to extend the types of transplanted tissues and cells (other than those transplanted currently) over the next 5 years.

3. About 94.3% of surgeons from the medical-sanitary institutions with activities in the field of tissues and cells donation and transplantation consider that the increasing in number of tissue transplants performed will contribute to improve the patients' life quality, 94.1% of surgeons declare that enlarging the types of tissues transplanted is a necessary measure, and 72.7% of surgeons are convinced that increasing the number of transplanted patients over the next 5 years is a priority measure in the management of the institution they operate.

## References

1. WHO. Human Cell and tissue transplantation [Internet]. Geneva: WHO; c2019- [cited 2019 Jul 10]. Available from: [https://www.who.int/transplantation/cell\\_tissue/en/](https://www.who.int/transplantation/cell_tissue/en/)
2. WHO. First Global Consultation on Regulatory Requirements for Human Cells and Tissues for Transplantation. Ottawa, 29 November to 1 December 2004: report [Internet]. Geneva: WHO; 2005 [cited 2019 Jul 12]. Available from: <http://www.who.int/transplantation/ReportOttawaCTTx.pdf?ua=1>
3. WHO. Second Global Consultation on Regulatory Requirements for Human Cells and Tissues for Transplantation: Towards Global Harmonization through Graduated Standards. WHO Geneva, 7-9 June 2006: Report [Internet]. Geneva: WHO; 2006 [cited 2019 Jul 12]. Available from: <http://www.who.int/transplantation/2dHTTGHreport.pdf?ua=1>
4. American Association of Tissue Banks (AATB). Tissue Banking: the basics [Internet]. McLean, VA: AATB; 26 March 2014 [cited 2019 Apr 16]. Available from: <https://www.aatb.org>
5. American Association of Tissue Banks (AATB). Working together for life: Annual Report 2017 [Internet]. McLean, VA: AATB; 2017 [cited 2019 May 10]. Available from: <https://www.aatb.org/sites/default/files/sites/default/files/private/AATB2017AnnualReport.pdf>
6. Ministry Of Health, Social Services and Equality (Spain). Balance de actividad de la Organización Nacional de Trasplantes en 2017 [Balance of activity of the National Transplant Organization in 2017] [Internet]. Madrid: The Ministry; 2017 [cited 2019 Jul 23]. Available from: <http://www.ont.es/Documents/Datos20172018ENE11.pdf>. Spanish.
7. International Registry in Organ Donation and Transplantation 1995 [Internet]. Barcelona: © IRODaT; 2019- [cited 2019 Jun 21]. Available from: <http://www.irodat.org/?p=database&c=ES&year=1995#data>
8. Matesanz R, editor; Council of Europe. International figures on donation and transplantation - 2011. Newsletter Transplant (Spain). 2012;17(1). ISSN: 2171-4118.
9. Domínguez-Gil B, Matesanz R, editors; Council of Europe, European Directorate for the Quality of Medicines & HealthCare (EDQM). International figures on donation and transplantation – 2016. Newsletter Transplant. 2017;22. ISSN: 2171-4118.
10. International Registry in Organ Donation and Transplantation 2017 [Internet]. Barcelona: © IRODaT; 2019- [cited 2019 Oct 15]. Available from: <http://www.irodat.org/?p=database&c=HR&year=2017#data>
11. Council of Europe, European Directorate for the Quality of Medicines & HealthCare (EDQM). Guide to the quality and safety of tissues and cells for human application. 3rd ed. Strasbourg: EDQM; 2017. ISBN: 978-92-871-8443-6.
12. Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. OJEU L102, 7.4.2004:48-58 [cited 2019 Jan 15]. Available from: <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:102:0048:0058:en:PDF>
13. Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells. OJEU L38, 9.2.2006:40-52 [cited 2019 Jan 15]. Available from: <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32006L0017&from=EN>
14. Commission Directive 2006/86/EC of 24 October 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells. OJEU L294/32, 25.10.2006:32-50 [cited 2019 Jan 15]. Available from: <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:294:0032:0050:EN:PDF>
15. Directorate-General for Health and Food Safety (European Commission), Foundation of European Tissue Banks; Rathenau Institute; TRIP office for hemo- and biovigilance. Economic landscape of human tissues and cells for clinical application in the EU: Final report. Luxembourg: EU; 2016 [cited 2019 Oct 15]. Available from: <https://publications.europa.eu/en/publication-detail/-/publication/5a0fd429-4a4e-11e6-9c64-01aa75ed71a1>.
16. Nacu V. Banca de țesuturi și celule în asigurarea sănătății populației [The tissue and cellular bank role in ensuring population health]. Sănătate Publică, Economie și Management în Medicină [Pub Health Econ Manag Med] (Chisinau). 2014;2(53). ISSN: 1729-8687. Romanian.
17. Timbalari T, Lozan O, Nacu V. History of tissue and cell transplantation's development: review article. Mold J Health Sci. 2017;14(4):108-122. ISSN: 2345-1467.
18. Nacu V. Optimizarea regenerării osoase posttraumatice dereglate [Optimization of posttraumatic disturbed bone regeneration]. Chișinău: Sirius; 2010. 188 p. Romanian.
19. Nacu V, Ispas A, Rudenco E, Codreanu I, Timbalari T, Topor B, Soltan V. Sistemul informational automatizat în asigurarea managementului calității în Banca de Țesuturi Umane [Automated information system as quality management providing human tissue banks]. Curierul Medical (Chisinau). 2014;57:49-55. Romanian.
20. Riegman PH, Morente MM, Betsou F, De Blasio P, Geary P. Marble Arch International Working Group on Biobanking for Biomedical Research. Biobanking for better healthcare. Mol Oncol. 2008;2(3):213-222.

21. Timbalari T, Codreanu I, Lozan O, Nacu V. Assessment of human tissue transplantation activities in the Republic of Moldova. In: Tighianu I, Sontea V, Railean S, editors. 4th International Conference on Nanotechnologies and Biomedical Engineering; 2019 Sep 18-19; Chisinau. Cham: Springer; 2020. p. 621-625. (IFMBE Proceedings, Vol. 77). Available from: [https://doi.org/10.1007/978-3-030-31866-6\\_110](https://doi.org/10.1007/978-3-030-31866-6_110)
22. Wang W, Yeung KWK. Bone grafts and biomaterials substitutes for bone defect repair: a review. *Bioact Mater.* 2017;2(4):224-247 [cited 2019 Sept 15]. Available from: <https://doi.org/10.1016/j.bioactmat.2017.05.007>.
23. Codreanu I, Romanciuc G, Timbalari T, et al. Development of the national transplant system in the Republic of Moldova. *Organs Tissues Cells.* 2012;15(3):197-200. ISSN: 1828-0595.
24. Codreanu I, Lozan O, Timbalari T. Evaluation of the transplant system in the Republic of Moldova. *Manag Health (Bucharest).* 2014;18(4):4-10. ISSN: 1453-4541.

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#### Author's contribution

TT conceptualized the idea, conducted literature review, wrote the manuscript, revised and approved the final text.

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#### Ethics approval and consent to participate

The study was approved by the Ethic Committee of *Nicolae Testemitsanu* State University of Medicine and Pharmacy, Chisinau (protocol No 2, 27.10.2016).

#### Conflict of Interests

No competing interests were disclosed.

