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Research Article

**INCREASED RISK OF LARYNGEAL AND PHARYNGEAL
CANCER AFTER GASTRECTOMY FOR ULCER DISEASE IN A
POPULATION-BASED COHORT STUDY****¹Dr Atika Akbar,²Dr Muhammad Asif Hussain, ³Dr Sadam Sanwal.**¹MBBS, Frontier Medical College, Abbottabad, ^{2,3}MBBS, Sahiwal Medical College, Sahiwal.**Article Received: September 2020 Accepted: October 2020 Published: November 2020****Abstract:**

Alcohol and tobacco are the main factors of laryngeal and pharyngeal carcinoma. ¹ There is an association between the esophageal biliary regurgitation and tumors. ² It is suggested that the main factor behind it is the lack of "protective mechanism" against the proximal reflux. It is very difficult to evaluate the effect of bile regurgitation on these cancers. The main areas of concern are the latency period and the bile reflux exposure time before the invasion of tumors.

A lot of gastrectomy patients suffer from bile regurgitation. ^{3,4} There is a report which shows the enhanced risk of laryngeal cancer to the patients undergoing gastrectomy. ⁵ For this evaluation, the cohort study is being conducted on patients.

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MATERIALS AND METHODS:**Design:**

The design of cohort study is based on Swedish population. The data collected was from 1965-2009. A nationwide register was utilized for determining cohort of peptic ulcer gastrectomy patients. During the study some new cancers were also discovered during the study. The comparison was done between cancer and the Swedish background people. The data were analyzed on the basis of prevalence and incidence of cancer in "Swedish Cancer Register."

Inclusion and Exclusion Criteria:

In the study, the first cancers were included and the 1st year after the surgery of gastrectomy was excluded. The reason behind it was the reduction in the risk of any early detection of cancer due to gastrectomy and for allowing least time of exposure.

The dates of deaths were collected from the "Swedish Cause of Death Register." A ten digit serial number was assigned to Sweden residents since 1946. [6] it is approved by "Regional Ethics Committee in Stockholm.

Gastrectomy Cohort:

All the patient's data who undergone hospitalized and surgical procedures were identified by "Sweden Patient Register." This register includes sex, age, discharge diagnosis, identity number, dates of hospitalization and the surgical procedures.

59% of the population was covered by the previously mentioned register in 1968 and 84% were covered in 1986. It is 98% complete and 96% correct according to the operation codes. ⁷ The International Classification of Disease was as the diagnostic codes of ulcer disease.

The patients with peptic ulcer were defined by the Swedish Classification of Surgical Procedures.

Laryngeal and Pharyngeal Cancer Detection

All the cancer diagnosed patients were identified by "Swedish Cancer Register." It is a national register started in 1958. It was administered the "National Board of Health and Welfare," [8]

This register contains the date of diagnosis, histology and location of all the patients diagnosed with malignant cancer. The "tumor diagnosis codes" were transferred to "ICD Code version 7." The results of study were explained by the "codes 161" for

laryngeal tumor and "146-148" for pharyngeal tumors along with the "histological code 146" for cancer of squamous cell.

Statistical Analyses:

The time of study was started from the 2nd year after surgery up to the death, cancer or finale of observation. Relative Risk was evaluated as the "Standardized Incidence Ratio (SIR)." SIR is defined as the observed number of tumors in gastrectomy patients to the expected number of tumors in comparison population. The expected patients can be calculated by multiplying of observed "person-time" by incidence rates specific to the sex, age and year. These expected rates were taken from "Swedish Cancer Register" data and aggregated into five years difference.

The "confidence intervals" of the SIRs were measured on the observed number of events which followed the Poisson distribution. [9] Sensitivity analysis was done in determining the over consumption of alcohol and tobacco smoking, keeping out the ambulatory and inpatients.

The diagnosis related to alcohol kept the history of excessive consumption of alcohol "(diagnosis code F10 in ICD-10, 291 or 303 in ICD-9 and ICD-8, or 307 or 322 in ICD-7)," hepatic disease associated with alcohol intake "(K70 in ICD-10, 571.A or 571.C in ICD-9, 571.00 or 571.01 in ICD-8, 581.10 or 583.10 in ICD-7)" or the deficiency of vitamin-B associated with alcohol consumption alcohol "(E51 – 52 or G62.1 in ICD-10, 265 in ICD-9, 261.00 – 262.00 in ICD-8, or 280 –281 in ICD-7)."

All the smoking related diseases, for example, chronic obstructive pulmonary disease "(J41 – J44 in ICD-10, 490 –492 in ICD-9 and ICD-8, 501.99, 502, 527.10, or 527.11 in ICD-7)," or peripheral vascular disease PVD "(I70 or I73.9 in ICD-10, 440 or 443.x in ICD-9, 440, 443.90 or 445 in ICD-8, or 450.00, 450.10, or 453.33 in ICD-7)" were used to access the tobacco smoking. For evaluation "The Statistical Analysis System (SAS), version 9.2, SAS Institute Inc., Gary, NC, USA," was used.

RESULTS:**Patients:**

This study included 19,766 gastrectomy treated patients. The features of such patients are shown in the table.

Table 1 Features of the Gastrectomy Patients in Sweden

Features	Women	Men	All
Person-years, number %	213845	120775	334620
Individuals, number %	7375	12393	19768
Median age at entry, years	61	56	57
Median age at entry, calendar years	1979	1967	1977
Median follow up time, years	17	16	19
Type of surgery, number %			
Total gastrectomy	11985	7060	19046
Partial gastrectomy	314	404	719

The follow up was considered as the median of 19 years, taking 334620 patients on risk. Men were predominant in women. The proportion of partial gastrectomy has been just 3 percent, while the complete gastrectomy composed of more than 94 percent.

Risk of Laryngeal Cancer:

The total of 57 patients experienced laryngeal carcinoma after 1 year of gastrectomy; it was double the number of expected cases (SIR: 3.0, 96% CI). It is shown in table 2.

Table 2 Standard Incidence Ratios and 96% “confidence interval” of laryngeal and pharyngeal carcinoma in gastric resection cohort, containing 19766 persons

Variable	Laryngeal carcinoma			Pharyngeal carcinoma		
	Observed Cases	Expected Cases	SIR 96% CI	Observed Cases	Expected cases	SIR 96% CI
All	55	27.5	3	29	12	2.5
Gender						
• Male	50	26	2	24	11	1.4
• Female	5	2.9	4	5	1	2.7
Age (years)						
Less than 70	35	13	2.4	15	6	2.3
Equal to and More than 70	21	15	1.5	13	4	2.5
Latency (years)						
1-10	18	12	1.3	12	5	2
11-20	20	9	2.1	7	4	2
21-30	11	5	2	4	2	1.5
More than 30	9	1	4.7	5	1.5	10
Calendar period						
1965-1988	25	13	2	11	7	1.5
1989-1998	18	5	2	9	3	2.5
1999-2009	13	8	2.5	8	1	5

Risk was direct proportion to the latency intervals. The patients with approximately 20 years back gastrectomy had an SIR of 2.1 while the patients with gastrectomy surgery survival of more than 30 years had the SIR of 4.7. It is about five fold greater as compared to previous one. Age, sex and calendar periods do not show any major difference. The results show that after the exclusion of approximately 5500

cohort, people with any disease associated with smoking or alcohol, the combined SIR was increased. It was about 2 in patients before 20 years and more than 4 after 30 years of the time period after gastrectomy as shown is table 3.

The table 3 showing the SIR and 96% CIs of pharyngeal and laryngeal carcinoma, in the gastric

treatment cohort, containing 14000 patients in Sweden, in between 1965-2009, after exclusion of

5500 patients diagnosed with tobacco or alcohol associated disease.

Variables	LARYNGEAL CARCINOMA			PHARYNGEAL CARCINOME		
	Observed cases	Expected cases	SIR 96% CI	Observed cases	Expected cases	SIR 96% CI
All	31	20.	1.5	13	8.7	1.4
Gender						
• Male	30	19		10	7	1.5
• Female	2	1.8	1.9 0.5	14	2	1.7
Age						
Less than 70	19	9	2	8	4	2
Equal to and more than 70	13	11	1.1	7	4.5	1.5
Latency						
1-10	9	8	1	6	4	2
11-20	12	7	2	3	3	1
21-30	5	4	1.5	2	1	1.5
>30	6	1	4	2	4.6	2.5
Calendar period						
1965-1988	17	10	1.5	6	5	1
1889-1998	10	7	1.5	5	3	2
1999-2009	8	4	1.7	4	2	2.7

Risk of Pharyngeal Cancer:

During the evaluation, about 30 patients developed pharyngeal cancer. It is seen from the results that the expected result was greater than twice as expected data. The direct relationship was seen in between the patients with longer time and pharyngeal carcinoma. There were 10 folds greater cancer. However, there is no considerable difference between age and sex. The SIR was greater in the later “calendar period,” as shown in table 2.

If the disease associated cohort patients are excluded, the SIRs reduced as shown in table number 3.

DISCUSSION:

This report favors that the gastrectomy enhances the risks of both pharyngeal as well as laryngeal cancer. This is a cohort based study and it included the population of Sweden, the overall evaluation of the patients was done in this study. The results and whole follow up along with the size of the sample were accessed in this report. The effect bile reflux was accessed in the humans. A design was used to set the sex, age and calendar year. There was a problem that no up to date data was available for alcohol abuse and tobacco smoking abuse. [1] the patients with disease associated problems were excluded from the study. This study was followed up with a control

study with 40 non-gastrectomy and 40 gastrectomy patients. This study provided some data that the gastrectomy is one of the risk factors for squamous cell carcinoma of pharynx or larynx. [10]

CONCLUSION:

To conclude, this large population based “cohort study” along with whole and lengthy procedure gives the support to the proposed hypothesis that gastrectomy enhances the risks of “squamous cell cancer” of the larynx and pharynx.

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