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Quality of life in patients with laryngeal cancer before and after surgery

Квалитет живота код пацијената са раком ларинкса пре и после операције

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Quality of life in patients with laryngeal cancer before and after surgery

Квалитет живота код пацијената са раком ларинкса пре и после операције

SUMMARY

Introduction/Objective Assessment of quality-of-life questionnaires filled in by patients with laryngeal cancer hospitalised in the Otolaryngology, Head and Neck Surgery Department and qualified for surgical treatment before and after surgery

Methods Fifty-four patients with laryngeal cancer in T3 and T4 stages who were qualified for total laryngectomy were asked to fill out the EORTC QLQ-30 and H&N30 modules before and a few years after surgical treatment.

Results Quality of life in patients hospitalised in the Otolaryngology Head and Neck Surgery Department increased after surgery. The level of pain after surgery decreased and was statistically significant (p = 0.025). In the study group, 90.6% of patients survived five years after surgery.

Conclusion Quality of life in patients with laryngeal cancer improved in the domain of pain. Further research should be conducted on a larger group of patients. Future results could provide useful material for analysis regarding the benefits for the patient that may be relevant to a decision to consent to the proposed treatment and the choice of its type.

Keywords: quality of life; laryngeal cancer; follow-up; laryngectomy

САЖЕТАК

Увод/Циљ Процена упитника о квалитету живота попуњавали су пацијенти са раком ларинкса хоспитализовани на Отоларингологији, Одељењу за главу и врат и квалификовани су за хируршки третман пре и после операције

Методологија Педесет четири пацијента са раком ларинкса у Т3 и Т4 стадијумима који су квалификовани за потпуну ларингектомију замољена су да попуне *EORTC KLK*-30 и *H&N*30 модуле пре и неколико година после хируршког третмана.

Резултати Квалитет живота код пацијената хоспитализованих на Отоларингологији, на Одељењу за хирургију главе и врата, порастао је после операције. Ниво бола после хируршке интервенције се смањио и био је статистички значајан (p = 0,025). У студијској групи, 90,6% пацијената је преживело пет година после операције.

Закључци Квалитет живота код пацијената са раком ларинкса побољшан је у домену бола. Даље истраживање треба спровести на већој групи пацијената. Будући резултати могу пружити корисни материјал за анализу у вези са користима за пацијента који могу бити релевантни за одлуку да се пристане на предложени третман и избор његовог типа.

Кључне речи: квалитет живота; рак грла; праћење; ларингектомија

INTRODUCTION

According to the World Cancer Research Fund International, 1.1% of all cancers are laryngeal cancer. Laryngeal cancer is the most common cancer out of head and neck neoplasms [1]. Males are affected more often than females. Primary risk factors are tobacco smoking, alcohol consumption, and human papilloma virus (HPV) infection.

Laryngeal cancer is generally squamous cell carcinoma. Symptoms mostly begin with hoarseness in the voice but also may include a lump sore, sore throat, and swallowing difficulties. Treatment methods include surgery, radiotherapy, and chemotherapy. Infiltration of the laryngeal cartilages is an indication for a procedure called laryngectomy, consisting of

total excision of the larynx [2]. Larynx plays critical role in physiologic functions such as voice production, respiration, airway protection and swallowing that is why total laryngectomy may significantly affect patients quality of life (QoL). Lately, the medical community puts great emphasis on quality of life, which is why more and more studies on QoL are conducted.

The World Health Organization (WHO) defines QoL as the person's perception of his or her individual daily life and position. It takes into consideration the context of culture, the personal relation to the goals, the situation in which the person lives, expectations, and concerns. In healthcare, QoL is an assessment of how aspects of an individual's life can be affected by disease or disability [3]. Measuring QoL gives an enormous amount of information that should be considered in the selection of a treatment method. For example, organ preservation is not necessarily needed to have better QoL. Measuring QoL also determines how important survival is after treatment [4].

Two types of QoL assessment tools exist: general and specific. QoL recorded with the impact of disease in particular is called general. Specific scales assess the QoL by taking into account a specific group of diseases, a single disease, or a single symptom [5].

In our earlier studies, all PUBMED articles about QoL in patients with laryngeal cancer were reviewed, and different measuring tools were identified. The European Organization for Research and Treatment of Cancer (EORTC) questionnaire general module (QLQ C-30) and head and neck module (QLQ-H&N35) turned out to be the most commonly used tools to assess QoL in patients with different stages of laryngeal cancer or to compare treatment methods. Therefore, we decided to use this questionnaire in the current study.

The aim of this study was to assess the QoL of patients diagnosed with laryngeal cancer and qualified for surgical treatment before and after surgery with the use of EORTC QLQ-C30 and QLQ-H&N35 modules and to compare the results.

METHODS

In this study, 54 patients hospitalised in the Otolaryngology, Head and Neck Surgery Department of the Medical University of Wroclaw who were diagnosed with laryngeal cancer in T3-T4 stages and all laryngeal locations qualified for surgical treatment were asked to fill in paper version of the EORTC questionnaire translated and validated in polish language one day before surgery. Sample of this questionnaire has been enclosed as appendix. It consists of a general module for patients diagnosed with cancer and a specific one for patients with head and neck cancer. The EORTC questionnaire was developed by Bjordal et al. in 1994. The questionnaire consists of 37 items concerning many aspects like disease-related symptoms, social function, and sexuality [6]. After a few years, a 3.0 version of the EORTC QLQ C-30 questionnaire was developed. The validity and reliability of both the QLQ-C30 and H&N35 modules was confirmed on a large group of patients from many different countries [7, 8]. Version 3.0 of the EORTC QLQ-C30 module contains 30 questions, and the H&N35 module contains 35 questions. Raw data collected from the questionnaire are calculated into the global, functional, and symptomatic scales according to the instructions provided in the scoring manual [9]. The questionnaire was well accepted and sensitive to changes during a study year. Many symptoms, such as problems with taste, swallowing difficulty, hoarse voice, and sore mouth, showed great variability [10].

From one to five years after surgery, correspondence with blank questionnaires was sent to all patients with a request to fill in the questionnaires again or to send information about the possible death of the patients. All data were collected and calculated with the instructions provided in the scoring manual for EORTC questionnaires. The calculated data create three types of scales. Data from the QLQ-C30 module are calculated into the global health status scale (QL2), five functional scales, and symptomatic scales. Functional scales are physical functioning (PF2), role functioning (RF2), emotional functioning (EF), cognitive

functioning (CF), and social functioning (SF). Symptomatic scales are fatigue (FA), nausea and vomiting (NV), pain (PA), dyspnoea (DY), insomnia (SL), appetite loss (AP), constipation (CO), diarrhoea (DY), and financial difficulties (FI). Further QLQ-H&N35 module data are calculated only into symptomatic scales like pain (HNPA), swallowing (HNSW), sensory problems (HNSE), speech problems (HNSP), trouble with social eating (HNSO), trouble with social contact (HNSC), less sexuality (HNSX), teeth (HNTE), opening mouth (HNOM), dry mouth (HNDR), sticky saliva (HNSS), coughing (HNCO), ill feeling (HNFI), pain killers (HNPK), and nutritional supplements (HNNO). All data calculated into scales create a score of 0 to 100. For global health status, a higher score represents high QoL; in functional scales, a higher score represents a high and healthy level of functioning, whereas a higher score in symptomatic scales represents a high level of symptomatology and problems. The approval of ethical review board were obtained before the beginning of study.

A statistical analysis of the obtained results was then performed using STATISTICA v. 12 (StatSoft, Tulsa, OK, USA). Statistical characteristics of variables are presented as arithmetical mean (*M*) ± standard deviation (*SD*), median (*Me*), and interquartile range (*IQR*). Statistical characteristics of discrete variables are presented as number (n) and frequency distribution (%). In the statistical analysis, the Wilcoxon matched pairs test was used for quantitative variables. Survival time was estimated using the Kaplan–Meier method.

The study was done in accord with standards of the institutional Committee on Ethics.

RESULTS

The study sample characteristics are summarised in Table 1. Fifty-four patients from 46 to 88 years of age, including 50 males and 4 females, filled in the questionnaire before surgery. From one to five years after surgery, information from 31 patients was received.

Twenty-one patients were reported dead. Ten patients filled in the questionnaire and sent it back to the clinic. Twenty-three patients did not answer the request.

Scores for all scales compared before and after treatment are presented in Table 4 After surgery, the global QoL in patients with laryngeal cancer improved, but the difference was not statistically significant (54.2 vs. 50.0, $p > 0.05$) (Figure 1). The only statistically significant difference occurred in the symptomatic scale for pain (HNPA). Pain created more problems before surgery than after surgery (16.7 vs. 8.3; $p < 0.05$) Swallowing created more problems before surgery than after surgery. The P value in this variable was on the border of statistical significance (16.7 vs 0; p=0.091).

The level of functioning mostly decreased after surgery beside emotional functioning and role functioning, but the changes were not statistically significant. The PF score was 80.0 before surgery and decreased to 73.3 after surgery. A similar situation was observed in CF, where the score decreased from 83.3 to 75.0, and SF, where the score also decreased from 83.3 to 75.0. The EF score increased from 66.7 to 70.8. RF kept the same level before and after surgery (83.3). All results above are presented in Figure 2.

Length of survival after surgery is presented in Figure 3. In this study group, 90.6% of patients survived five years after surgery. The survival function was 8.01 for the 25^{th} percentile, 9.63 for the 50^{th} percentile, and 10.81 for the 75^{th} percentile.

DISCUSSION

Because of its location and functional importance, the larynx plays a critical role in the maintenance of such cardinal physiological functions as phonation, regulation of respiratory airflow, and airway protection. Laryngeal cancer can have effects on laryngeal function, and the impact of treatment on function has to be carefully weighed against its oncological benefit. Still, in some cases the only treatment is a total laryngectomy. Lately, QoL reported

by patients regardless of correlation with clinical parameters of health has paramount importance in treatment management. Comparison of QoL in these patients might give better insight into patients' expectations and benefits from choosing the treatment method [11].

In this study, we compared QoL in patients with laryngeal cancer qualified for surgical treatment before and a few years after surgery. The results of our analysis show that the pain level after surgery is lower than before. Also, swallowing improved after surgery, but this change is on the border of statistical significance. Singer et al.'s study was the only one found in the PubMed database that covers the same topic and uses the same questionnaire as a method of QoL assessment. The results of a multicentre prospective cohort study show that the QoL domains that improved were global QoL, coughing, and weight.

In our study, changes in functional scales before and after surgery were statistically insignificant, but they found confirmation in the literature where the level of the same scales changed almost in the same way, and some of these changes were statistically significant.

A comparison is presented in Table 5 [12].

CONCLUSION

1. As it has been explained in study limitation chapter due to smaller amount of the obtained follow up questionnaires than the initial number of participants our results are not valid to be generalized however taking into consideration our statistical analysis and discussed literature it can therefore be assumed with a certain degree of probability that QoL in patients after surgery improved in the domain of pain.

2. For all domains, the result in the swallowing scale improved after surgery, and dry mouth remained on the same level. Changes in these scales were on the border of statistical significance.

3. In this study group, 90.6% of respondents survived five years after surgery.

4. Further research should be conducted on a larger group of patients. There are many studies about QoL reported by patients with laryngeal cancer researching the relationship with the type of treatment method of surgery and other variables. All of these studies present statistically significant results. Because of different study protocols, it is hard to construct a global laryngeal cancer treatment algorithm that takes into account not only oncological benefit and treatment results but also patients' reported QoL. There is a need to conduct a bigger multicentre study based on the same examination and data sampling protocol. The obtained results could become a standard for care and proposed treatment choice.

Study limitations

Assessment of QoL in patients with laryngeal cancer is prospective study which has been continued after surgery to follow up the potential change of QoL. In the present study, we show the results of 54 patients who agreed to fill in the QoL questionnaire. Because of the character of the study group and the method of sampling, the amount of follow-up questionnaires we obtained was smaller than the initial number of participants. Although the questionnaire was sent to all participants of this study after surgery, due to the death of some participants or the lack of willingness to re-fill the questionnaire, the response level in this study was low.

Conflict of interest: None declared.

REFERENCES

1. World Cancer Research Fund International [Internet]. [cited 2017 Jan 25]. Available from: http://www.wcrf.org/
2. Marur S, Forastiere AA. Head and Neck Cancer: Changing Epidemiology, Diagnosis, and Treatment. Mayo Clin Proc. 2008;83(4):489–501. DOI:10.4065/83.4.489 PMID: 18380996
3. WHO. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. Psychol Med. 1998;28(3):551–8. DOI:10.5.129626712 PMID: 9626712
4. Morton RP, Izzard ME. Quality-of-life outcomes in head and neck cancer patients. World J Surg. 2003 Jul;27(7):884–9. DOI:10.1007/s00268-003-7117-214509523 PMID: 14509523
5. Heutte N, Plisson L, Lange M, Prevost V, Babin E. Quality of life tools in head and neck oncology. Eur Ann Otorhinolaryngol Head Neck Dis. 2014 Feb;131(1):33–47. DOI:10.1016/j.anorl.2013.05.00224291153 PMID: 24291153
6. Bjordal K, Ahlner-Elmqvist M, Tollesson E, Jensen AB, Razavi D, Maher EJ, et al. Development of a European Organization for Research and Treatment of Cancer (EORTC) questionnaire module to be used in quality of life assessments in head and neck cancer patients. EORTC Quality of Life Study Group. Acta Oncol. 1994;33(8):879–85. DOI:10.3109/02841869409098450781891 9 PMID: 7818919
7. Sherman AC, Simonton S, Adams DC, Vural E, Owens B, Hanna E. Assessing Quality of Life in Patients With Head and Neck Cancer. Arch Otolaryngol Neck Surg. 2000 Apr 1;126(4):459. DOI:10.1001/archotol.126.4.459 PMID: 10772298
8. Bjordal K, de Graeff A, Fayers P, Hammerlid E, van Pottelsberghe C, Curran D, et al. A 12 country field study of the EORTC QLQ-C30 (version 3.0) and the head and neck cancer specific module (EORTC QLQ-H&N35) in head and neck patients. Eur J Cancer. 2000 Sep 9 ;36(14):1796–807. DOI:10.1016/S0959-8049(00)00186-6 PMID: 10974628
9. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A Quality-of-Life Instrument for Use in International Clinical Trials in Oncology. JNCI J Natl Cancer Inst. 1993 Mar 3;85(5):365–76. DOI:10.1093/jnci/85.5.3658433390 PMID: 8433390
10. Hammerlid E, Bjordal K, Ahlnerelmqvist M, Jannert M, Kaasa S, Sullivan M, et al. Prospective, longitudinal quality-of-life study of patients with head and neck cancer: A feasibility study including the EORTC QLQ-C30. Otolaryngol - Head Neck Surg. 1997 Jun [cited 2015 Dec 10];116(6):666–73. DOI:10.1016/S0194-5998(97)70246-8 PMID: 29389273
11. Sadoughi B. Quality of Life After Conservation Surgery for Laryngeal Cancer. Otolaryngol Clin N Am. 2015;48:655–65. DOI:10.1016/j.otc.2015.04.010 PMID: 26092764
12. Singer S, Danker H, Guntinas-Lichius O, Oeken J, Pabst F, Schock J, et al. Quality of life before and after total laryngectomy: Results of a multicenter prospective cohort study. Head Neck. 2014 Mar 36(3):359–68. DOI:10.1002/hed.2330523728844 PMID: 23728844

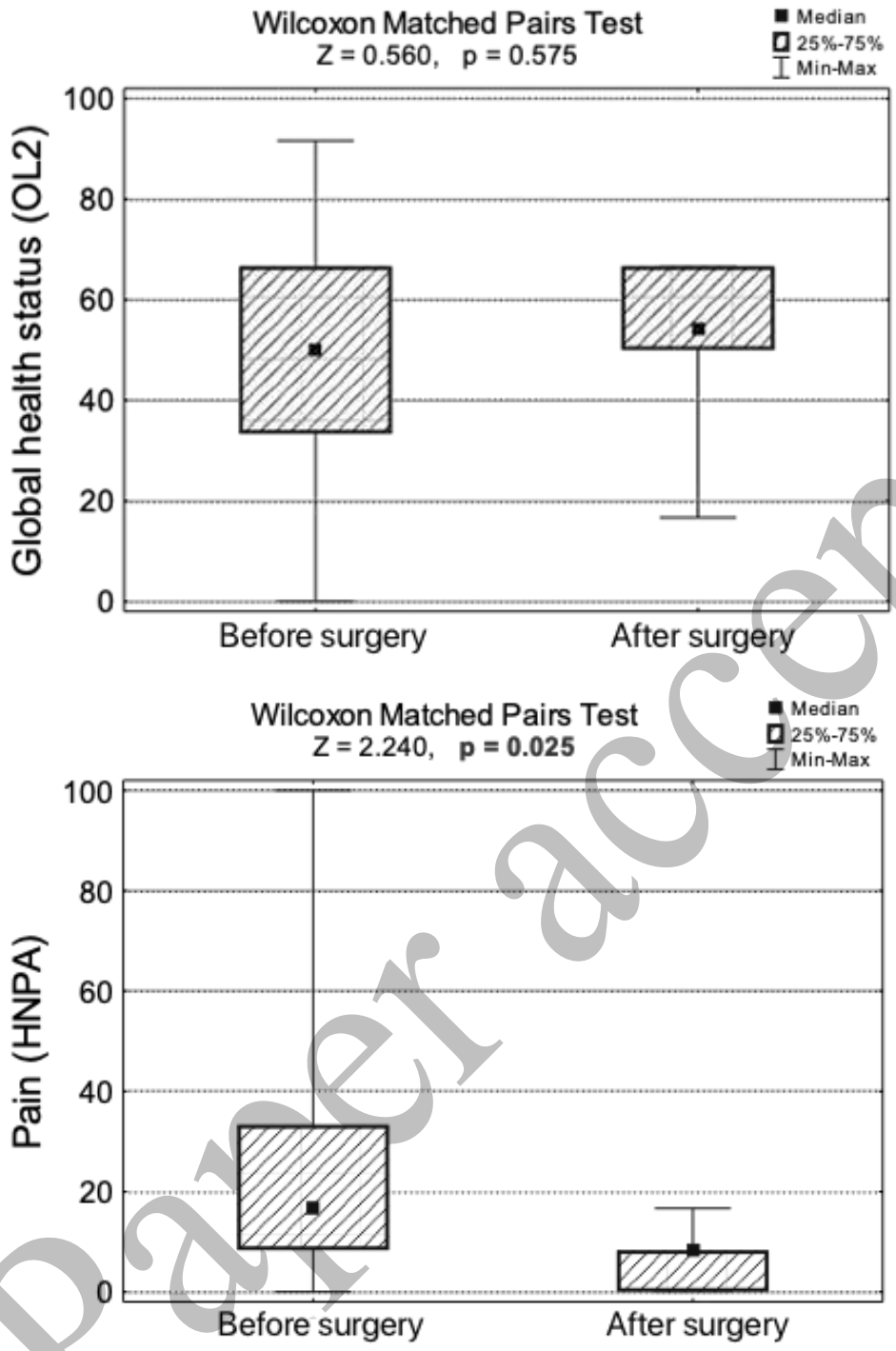

Figure 1. Comparison of the global health status before and after surgery and the result of the Wilcoxon matched pairs test

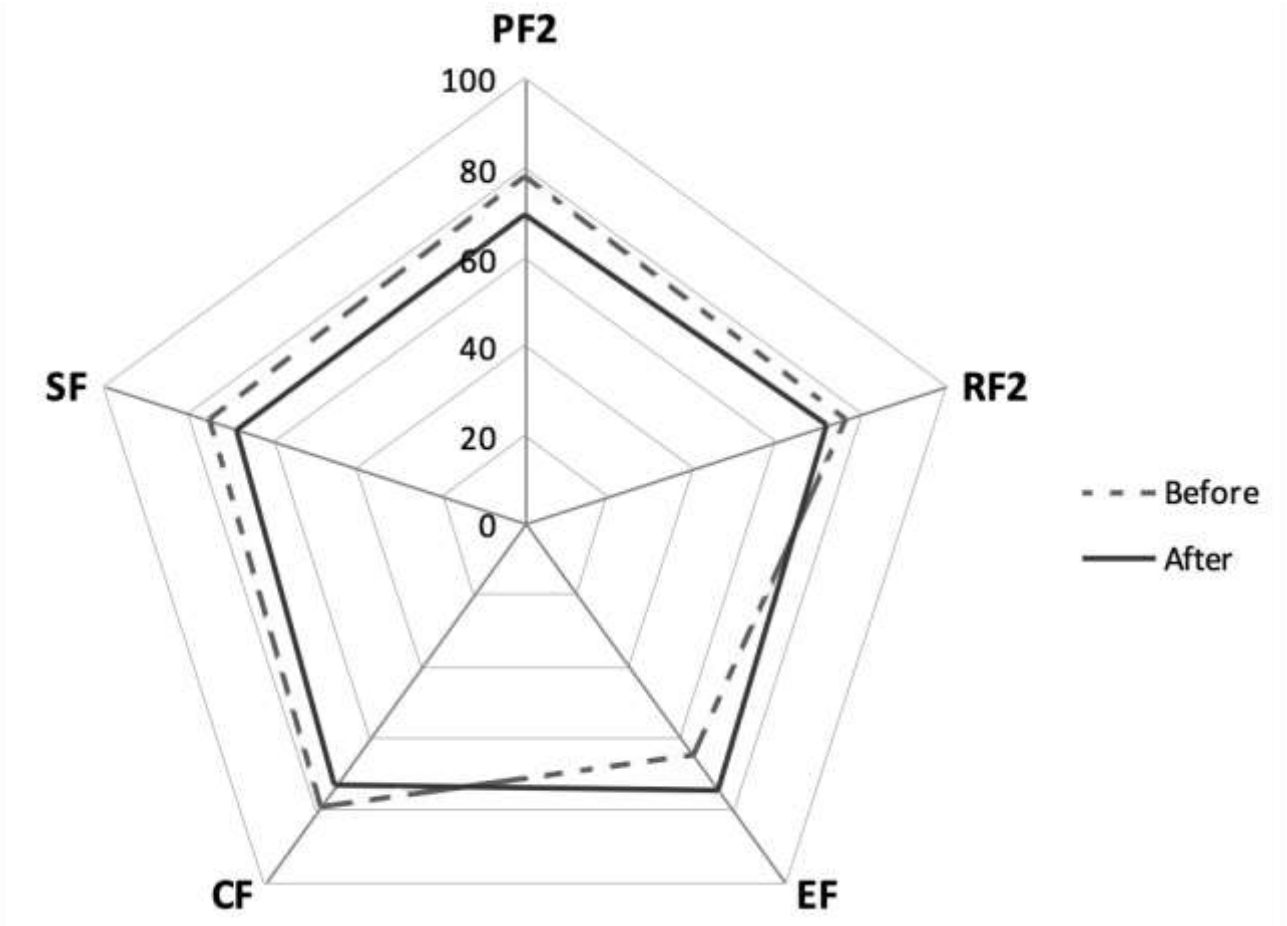

Figure 2. Comparison of the functional scales before and after surgery

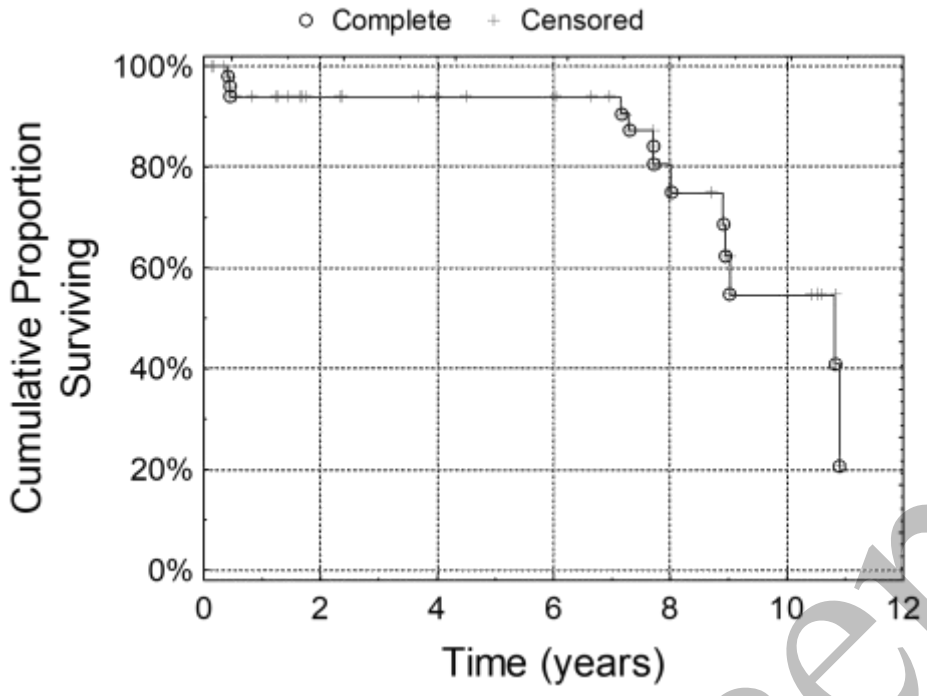

Figure 3. Kaplan–Meier's survival curve in the sample group

Table 1. Age

Age (years)	
Mean (SD)	60.5 (8.3)
Median [IQR]	59.0 [55.2–65.7]
Min–Max	46 to 88

Table 2. Gender

Male	50 (92.6%)
Female	4 (7.4%)
Replies to the questionnaire	10 (18.5%)
Death	21 (38.9%)
No answer	23 (42.6%)

Table 3. Comparison of QoL before and after surgery

Parameter	Before treatment		After treatment		p-value
	Median	[IQR]	Median	[IQR]	
Global health status/QoL	50.0	[33.3–66.7]	54.2	[50.0–66.7]	0.575
Physical functioning	80.0	[66.7–93.3]	73.3	[66.7–86.7]	0.161
Role functioning	83.3	[66.7–100.0]	83.3	[66.7–100.0]	0.345
Emotional functioning	66.7	[50.0–75.0]	70.8	[58.3–91.7]	0.308
Cognitive functioning	83.3	[66.7–100.0]	75.0	[66.7–100.0]	1.000
Social functioning	83.3	[66.7–100.0]	75.0	[66.7–100.0]	0.441
Fatigue	33.3	[22.2–50.0]	38.9	[33.3–44.4]	0.484
Nausea and vomiting	0.0	[0.0–16.7]	0.0	[0.0–0.0]	0.787
Pain	33.3	[0.0–50.0]	33.3	[33.3–50.0]	0.123
Dyspnoea	33.3	[0.0–33.3]	33.3	[33.3–33.3]	0.753
Insomnia	33.3	[33.3–66.7]	33.3	[33.3–66.7]	0.123
Appetite loss	0.0	[0.0–33.3]	0.0	[0.0–33.3]	0.345
Constipation	0.0	[0.0–33.3]	33.3	[33.3–33.3]	0.715
Diarrhoea	0.0	[0.0–0.0]	0.0	[0.0–33.3]	-
Financial difficulties	33.3	[0.0–66.7]	33.3	[0.0–100.0]	0.787
Pain	16.7	[8.3–33.3]	8.3	[0.0–8.3]	**0.025**
Swallowing	16.7	[0.0–33.3]	0.0	[0.0–0.0]	0.091
Senses problems	33.3	[0.0–50.0]	0.0	[0.0–100.0]	0.500
Speech problems	44.4	[22.2–55.6]	44.4	[22.2–66.7]	0.834
Trouble with social eating	8.3	[0.0–33.3]	0.0	[0.0–0.0]	0.176
Trouble with social contact	13.3	[0.0–33.3]	3.3	[0.0–40.0]	0.779
Less sexuality	33.3	[16.7–50.0]	33.3	[0.0–50.0]	0.343
Teeth	33.3	[0.0–66.7]	33.3	[0.0–33.3]	0.273
Opening mouth	0.0	[0.0–0.0]	0.0	[0.0–0.0]	-
Dry mouth	33.3	[0.0–33.3]	33.3	[0.0–33.3]	0.068
Sticky saliva	33.3	[0.0–66.7]	33.3	[33.3–66.7]	0.893
Coughing	33.3	[33.3–66.7]	33.3	[33.3–66.7]	0.295
Felt ill	33.3	[0.0–66.7]	33.3	[0.0–66.7]	0.447
Pain killers	0.0	[0.0–100.0]	50.0	[0.0–100.0]	1.000
Nutritional supplements	100.0	[0.0–100.0]	100.0	[100–100.0]	1.000
Feeding tube	100.0	[0.0–100.0]	100.0	[0.0–100.0]	1.000
Weight loss	0.0	[0.0–100.0]	100.0	[0.0–100.0]	-
Weight gain	100.0	[100–100.0]	100.0	[0.0–100.0]	0.593

Table 4. Comparison of changes in functional scales after surgery in the literature and in our study

Scale	Singer et al. [12]		Zatoński and Kolator	
	Changes after surgery	p-value	Changes after surgery	p-value
PF2	deterioration	< 0.01	deterioration	0.16
RF2	deterioration	< 0.01	same level	0.34
SF	deterioration	0.02	deterioration	0.30
CF	deterioration	0.59	deterioration	1.0
EF	improvement	0.37	improvement	0.44

