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HEAD AND NECK

The Enhanced Recovery After Surgery (ERAS) protocol in head and neck cancer: a matched-pair analysis

Protocollo di recupero ottimizzato (ERAS) in oncologia testa-collo: un'analisi a coppie appaiate

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SUMMARY

Objective. In this study, we aimed to describe the prospective implementation of the Enhanced Recovery after Surgery (ERAS) protocol in an Italian tertiary academic centre.

Methods. Adult patients receiving surgery for primary or recurrent clinical stage III/IV squamous cell carcinoma of the oral cavity, oropharynx, larynx, or hypopharynx were enrolled. The primary objective was to evaluate the impact of the ERAS protocol on length of hospital stay (LOS). The secondary objective was to assess its impact on complications. To evaluate the results of the ERAS protocol, a matched-pair analysis was conducted, comparing ERAS patients with comparable cases treated before 2018.

Results. Forty ERAS and 40 non-ERAS patients were analysed. There were no significant differences between the cohorts regarding age, gender, stage of disease, comorbidity, ASA score, and duration of surgery. A significantly shorter LOS for the ERAS group (median, 14 days; range, 10-19) than for non-ERAS patients (median, 17.5 days; range, 13-21) was observed (p = 0.0128). The incidence of complications was not significantly different (p = 0.140).

Conclusions. Our study demonstrates that the introduction of an ERAS protocol in the daily practice is feasible, and can result in significant reduction in LOS.

KEY WORDS: head and neck cancer, enhanced recovery after surgery, length of stay, postoperative complications, patient education handout

RIASSUNTO

Obiettivo. L'obiettivo dello studio è descrivere l'attuazione del protocollo di recupero postoperatorio ottimizzato ERAS in un centro ospedaliero universitario di terzo livello italiano.

Metodi. Sono stati inclusi pazienti adulti operati per carcinoma squamoso di cavo orale, orofaringe, laringe o ipofaringe stadi III/IV. L'obiettivo primario era valutare l'impatto del protocollo sulla durata della degenza (LOS). L'obiettivo secondario era valutare l'impatto sulle complicanze. I risultati del protocollo ERAS sono stati analizzati con un confronto a coppie appaiate, confrontando pazienti ERAS con casi paragonabili trattati prima del 2018.

Risultati. Quaranta pazienti ERAS e 40 non-ERAS sono stati inclusi. Non sono state riscontrate differenze significative tra le due corti per quanto riguarda età, genere, stadio di malattia, comorbilità, punteggio ASA e durata dell'intervento. La LOS era significativamente minore per il gruppo ERAS (mediana, 14 giorni; range, 10-19) rispetto ai pazienti non-ERAS (mediana, 17,5 giorni; range, 13-21) (p = 0,0128). L'incidenza di complicanze non è risultata significativamente differente (p = 0,140).

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*Conclusion*i. Lo studio ha dimostrato che l'introduzione di un protocollo ERAS nella pratica clinica è fattibile e può portare ad una riduzione della LOS.

PAROLE CHIAVE: *tumori testa-collo, recupero ottimizzato dopo chirurgia, lunghezza della degenza, complicanze postoperatorie, opuscoli informativi per pazienti*

Introduction

The Enhanced Recovery After Surgery (ERAS) protocol is an evidence-based, multimodal, multidisciplinary, and integrated program of interventions aimed at minimising metabolic stress and postoperative organ dysfunction, reducing complications, and shortening the duration of hospitalisation. Recent experiences since 2017 have confirmed that the improvements associated with ERAS in other specialties can be transferred to the head and neck (HN) scenario [1-5]. In addition, a consensus review and recommendations for patients undergoing HN surgery with free flap reconstruction have been published [6]. However, in this field, the evidence is still limited compared to other specialties, and highly prevalent issues in HN cancer patients, such as preoperative malnutrition, should be more intensively addressed using ERAS protocols.

In this study, we aimed to describe the prospective implementation of the ERAS protocol in an Italian tertiary academic centre. To precisely evaluate its impact, a matched-pair analysis between the ERAS series and patients treated before implementation of the protocol was performed.

Materials and methods

This prospective study was conducted from August 2018 to September 2019 in the Department of Otorhinolaryngology - Head and Neck Surgery of the University of Brescia, Italy.

Patient selection

Patients older than 18 years receiving HN surgery for primary or recurrent clinical Stage III/IV squamous cell carcinoma (SCC) of the oral cavity, oropharynx, larynx, or hypopharynx were enrolled.

Exclusion criteria were: a) active psychiatric disease, including substance and/or alcohol abuse; b) Karnofsky performance status < 70; c) uncontrolled/acute comorbidities, such as recent acute cardiac ischaemic attack, or severe pulmonary, hepatic, renal, or cardiac organ failure; d) Comorbidity-Polypharmacy Score (CPS) > 22; e) language barrier.

Study objectives

The primary objective was to evaluate the impact of the ERAS protocol on both hospitalisation and dischargeability (defined as the absence of active medical or surgical problems requiring hospitalisation and preventing actual discharge). The secondary objective was to assess its impact on the incidence of complications.

ERAS protocol

The protocol was designed according to previously published recommendations from the ERAS society and taking into account previous protocols implemented for HN surgery [2,11]. A multidisciplinary team composed of otolaryngologists, nurses, speech therapists, and anaesthesiologists collaborated on the elaboration of internal procedures and guidelines to implement the protocol. Furthermore, the team drafted an informative booklet to promote pre-admission education of patients, describing in appropriate and comprehensible language what patients should do to promote their health before and after surgery (e.g., appropriate nutrition, cessation of smoking/alcohol), as well as detailing the postoperative course to promote patient engagement in early mobilisation, respiratory exercises, pain assessment/control, and tracheostomy management.

Preoperative nutritional/metabolic status was assessed by calculating the body mass index (BMI) and Nutritional Risk Assessment Score (NRS2002). Whenever the NRS2002 was ≥ 3, medical nutritional evaluation was performed by a dedicated specialist. The decision to place a percutaneous endoscopic gastrostomy (PEG) or a radiologically inserted gastrostomy (RIG) pre- or postoperatively was taken by considering the potential advantage to the patient following a previously published model [7].

Immunonutrition (Impact® Oral, Société des Produits Nestlé S.A., Vevey, Switzerland) was prescribed to all patients: 3 servings per day for 7 days before surgery if malnourished according to the nutritional evaluation, for 5 days if not.

As per normal clinical practice, patients with diabetes were hospitalised the day before surgery and treated with a continuous insulin infusion to control glycaemia.

In preparation for surgery, patients consumed a carbohydrate-rich drink (Nutricia Fantomalt, Danone, Paris, France), which consisted of 800 ml the evening before surgery and 400 ml 2-3 hours before surgery.

The risk of deep vein thrombosis was calculated using the Caprini Score [8]; prophylactic antithrombotic therapy was administered accordingly.

The intra- and postoperative procedures of the protocol are listed in Table I.

Postoperative free flap monitoring was performed at 12 hours after the end of surgery, in accordance with current evidence, which shows that more frequent monitoring does not change the rate of flap salvage [9].

Sample size

Study numerosity was calculated for the matched paired analysis between ERAS and non-ERAS patients, taking as primary endpoint the length of hospital stay (LOS). Data extrapolated from the literature indicated 14.55 days of hospitalisation for ERAS patients *vs* 18 days for non-ERAS patients, with a standard deviation of 7.48 days [6]. For an inferiority test, assuming that the difference between the two groups is at least 4 days, considering a significance level of 0.05 and planning a one-tailed comparison using Student's t test (or non-parametric equivalent), an adequate study power (77%) was deemed to require 40 cases for each group.

Statistical analysis

Descriptive statistics (Shapiro-Wilk normality test, mean, standard deviation, median, and interquartile range) were calculated, as appropriate, for each group. Qualitative variables were analysed with Student's t test, Welch's t test, and Mann-Whitney U test. Student's t test was used for paired samples or Wilcoxon test according to data pairing, normality or non-normality, and homoscedasticity or non-homoscedasticity of distributions.

In order to evaluate the results of implementation of the ERAS protocol, a matched-pair analysis was conducted. For each patient who participated in the study, a comparable case among patients treated before 2018 (2000-2017) was identified. In order to minimise the risk of bias, patients were matched based on cancer stage and extent of surgery (Tab. II). Other factors potentially influencing the LOS, which were identified through a literature review [5,10-21] and are reported in Table II, were also considered in the matched-pair analysis. Type of surgery, reconstruction, neck dissection, overall comorbidities assessed through Comorbidity-Polypharmacy Score (CPS), American Society of Anesthesiologists (ASA) status and preoperative staging were given priority in the selection of patients to be matched.

Whenever an exact match between two patients was not possible, an overall balance between the two groups (ERAS and non-ERAS) was sought, including an equal

Table I. Intra- and postoperative procedures of the protocol.

Intraoperative
Antibiotic prophylaxis prior to incision, according to the current recommendations of the Italian Association of Head and Neck Oncology (AIOCC)
Anesthesiologic premedication for anxiolysis if needed
Standard anesthesiologic protocol
Prevention of hypothermia with fluid warmers and forced air patient warming devices
Fluid balance and, if necessary, goal directed fluid therapy
Total intravenous anaesthesia (TIVA) using entropy monitoring
Slow magnesium sulphate and lidocaine infusion prior to surgical incision, followed by continuous perfusion of lidocaine
Anti-emetic prophylaxis for postoperative nausea and vomiting (PONV)
Multimodal pain management following opioid-sparing strategies
Postoperative
Intensive care unit (ICU) admission if necessary (free flap, frail patient); transfer to the general surgical ward as soon as the patient is stable.
Urinary catheter removal within 24 hours after surgery
Nutrition
Start of enteral nutrition through nasogastric or PEG tube at 12-24 hours after the end of surgery
Immunonutrition, 2 servings per day for 10 days
Tracheostomy management
Tracheostomy tube cuff deflation on postoperative day 1
Assessment of tolerance to tracheotomy closure using a capped small-caliber cannula from postoperative day 3
Tracheostomy tube removal and compressive medication of the stoma after keeping the cannula closed for 24 hours
Suture of tracheostomy under local anaesthesia at 24 hours after uneventful tracheostomy tube removal
Assisted mobilisation within 24 hours from surgery, whenever possible; implementation of a daily and incremental mobilisation program over the following days
Wound dressing changes as needed, following daily assessment
Speech and language therapist evaluation on postoperative day 1

Table II. Matched pair analysis: items and groups.

	Number of patients		Percentage of patients		P-value	Rate of Symmetry
	ERAS	NON-ERAS	ERAS	NON-ERAS		
Type of surgery on T					0.912*	95%°
	Resection of the oral cavity and oropharynx with tracheotomy	24	24	60	60	
	Pharyngolaryngectomy	4	3	10	7.5	
	Laryngectomy	12	13	30	32.5	
Neck dissection					0.230*	80%°
	Bilateral	20	17	50	42.5	
	Monolateral	19	18	47.5	45	
	Not performed	1	5	2.5	12.5	
Clinical stage of disease[1,2,7]					0.102*	75%°
	Stage 1	2	0	5	0	
	Stage 2	0	4	0	10	
	Stage 3	8	9	20	22.5	
	Stage 4	30	27	75	67.5	
Comorbidity polypharmacy score					0.758*	85%°
	Mild	26	29	65	72.5	
	Moderate	13	10	32.5	25	
	Severe	1	1	2.5	2.5	
ASA Score [8,9]					1.000*	100%
	Class 1-2	19	19	47.5	47.5	
	Class 3-4	20	20	52.5	52.5	
Chronic obstructive pulmonary disease [10,11]	6	7	15	17.5	0.761*	86%
Diabetes mellitus [10-12]	5	3	12.5	7.5	0.456*	60%°
Liver disease [11]	3	3	7.5	7.5	1.000*	100%
Weight loss (BMI < 19 or loss > 10%) [13]	12	9	30	22.5	0.445*	75%°
Preoperative haemoglobin < 11 g/dL [14]	2	5	5	12.5	0.235*	40%
Preoperative radiation therapy greater than 60 Gy [15]	3	4	7.5	10	0.692*	75%
Active smoker status [14]	14	14	35	35	1.000*	100%
Sex (male)	26	28	65	70	0.633*	93%
			ERAS	NON-ERAS		
Mean age [10]	64.4 ± 15.03	62.8 ± 13.76	0.214**	0.214**		
Operative time [8,16,17]	471.1 ± 142.2	459.92 ± 139.03	0.486**	0.486**		

** Chi-square test; ** Paired t-test; ° symmetry rate favours the NON-ERAS group.*

number of patients presenting the same characteristics in the two groups (e.g., active smoker status or ASA score). If an equal distribution of patients with similar features could not be obtained, whenever possible, a greater number of patients with favourable features that potentially play a beneficial effect on postoperative outcomes was tolerated in the non-ERAS group (e.g., fewer patients with weight loss were included in the non-ERAS group).

In addition, since the pair-matched group encompassed patients who had been treated over a long time interval (2000-2017), in order to make sure that study results were not affected by changes in medical practice over time, LOS was also compared with all patients who would have met the study inclusion criteria but who were treated in our centre during 2017 (before ERAS implementation).

Results

Protocol implementation and compliance

Compliance data are shown in Table III. Overall, protocol adherence ranged from 70 to 100% in most items. In particular, a

high rate of protocol adherence was observed for preoperative patient education, nutrition, immunonutrition, preparation for surgery, and overall postoperative management (removal of urinary catheter, early start of enteral and oral feeding, early mobilisation, management of the tracheotomy cannula).

Matched-pair analysis

A total of 80 cases were analysed, 40 ERAS and 40 non-ERAS patients. Patient features that were considered in the matched pairing of the two cohorts are summarised in Table II. There were no significant differences between the

Table III. Adherence to the protocol.

	Patients	Percentage
Preoperative education		
Intervention for smoking cessation	14/14	100%
Patients who received preoperative counselling and information booklet	40/40	100%
Preoperative risk assessment		
Patients with NRS-2002 ≥ 3 who underwent nutritional evaluation	17/21	81%
Planned preoperative/intraoperative PEG placement according to Wake Forest School of Medicine formula or medical indication	13/40	32.5%
Patient with positive Caprini score who were administered correct prophylactic anticoagulant therapy	19/19	100%
Anaesthesia		
Total intravenous anaesthesia (TIVA) using entropy monitoring	37/40	92.5%
Opioid sparing analgesia with slow magnesium sulphate and lidocaine infusion prior to surgical incision and continuous perfusion of lidocaine	39/40	97.5%
Antibiotic prophylaxis prior to incision	40/40	100%
PONV prophylaxis	32/40	80%
Nutrition and immunonutrition		
Preoperative carbohydrate-rich drink	40/40	100%
Immunonutrition		
Preoperative	39/40	97.5%
Complete	33/40	82.5%
Partial	6/40	15%
Postoperative	37/40	92.5%
Postoperative course		
Number of days spent in ICU; median (IQR)	1 (1-1)	
Removal of urinary catheter within 24 hours after the end of surgery	33/40	82.5%
Start of mobilisation		
Assisted within 24 hours after the end of surgery	39/40	97.5%
Autonomous (median postoperative day of start on 39 patients)	3 (2-6)	
Nutrition		
Enteral		
Within 12 hours after the end of surgery	8/40	20%
Within 24 hours after the end of surgery	31/40	77.5%
Number of postoperative days before oral feeding (median, 37 patients)	9 (7-12.5)	
Tracheostomy management		
Tracheostomy tube cuff deflation on postoperative day 1	39/40	97.5%
26 patients underwent temporary tracheostomy:		
Assessment of tolerance to tracheostomy closure using a capped small-calibre cannula from postoperative day 3	26/26	100%
Tracheostomy tube removal and compressive medication of the stoma after keeping the cannula closed for 24 hours consecutively	26/26	100%
Suturing of tracheostomy under local anaesthesia 24 hours after uneventful tracheostomy tube removal	6/26	23%
Speech, swallowing and language therapist evaluation on postoperative day 1	21/39	54%

cohorts regarding age, gender, stage of disease, CPS score, ASA score, rate of diabetes mellitus, chronic liver disease, preoperative weight loss, active smoker status and mean duration of surgery.

Postoperative length of stay

The dischargeability was significantly shorter (p = 0.0117) in the ERAS group (median, 12 days; range, 9-17) than in the non-ERAS group (median, 16 days; range, 13-20). The same was observed for postoperative hospitalisation (p = 0.0128), with shorter LOS (median, 14 days; range, 10-19) for the ERAS group than for non-ERAS patients (median, 17.5 days; range, 13-21).

Comparison with the 2017 cohort

Ninety-one patients treated in 2017 would have met inclusion criteria for the present study, and therefore their postoperative LOS was compared with the ERAS and non-ERAS groups. No significant difference in LOS was observed between the non-ERAS group (median, 17.5 days; range, 13-21) and the 2017 cohort (median, 17 days; range, 13-23) (p = 0.9712), while a significantly shorter LOS was seen in the ERAS group (median, 14 days; range, 10-19) compared to the 2017 cohort (median, 17 days; range, 13-23), with a median gain of 3 days (p = 0.0131).

Complications

The impact of ERAS on complications is shown in Table IV. In the ERAS group, 20 complications in 16 patients (40%) were recorded, while in the control group there were 32 complications among 20 patients (50%). The difference was not statistically significant (p = 0.140).

Discussion

The results of the present study indicate that implementation of the ERAS protocol in HN surgery has significant impact in reducing the LOS, and confirm what was observed in similar studies[1,4,5]. The absence of a significant difference between median LOS in the non-ERAS group and the 2017 cohort confirms that the former can be reasonably considered a reliable control group, without major selection bias impacting LOS. Our results are also corroborated by the high level of correspondence between the two matched-paired groups. The process used to select control cases in the non-ERAS group is probably the most complex attempted to date among HN ERAS studies with the intent of minimising potential selection biases [4]. Undoubtedly, since an ideal match is not always possible, some factors included in the pairing were hierarchically considered, in accordance with the previous literature. In particular, preoperative staging, type of surgery and reconstruction, CPS and ASA scores were considered first in the selection of patients to be matched. When it was not possible

Table IV. Incidence and type of complications.

	Number of patients		Percentage of patients	
	ERAS	NON-ERAS	ERAS	NON-ERAS
Incidence of complications				
Total complications	16	20	40	50
Medical complications only	8	11	20	27.5
Surgical complications only	6	6	15	15
Medical and surgical complications	2	3	5	7.5
More than 24 hours after surgery	12	14	30	35
Within 24 hours after surgery	3	3	7.5	7.5
Both within and after 24 hours of surgery	1	3	2.5	7.5
Patients who had no complications	24	20	60	50
Type of complication and its incidence				
Bleeding	2	3	5	7.5
Surgical site infection	2	2	5	5
Wound dehiscence	0	3	0	7.5
Salivary fistula	4	1	10	2.5
Flap failure	1	2	2.5	5
Deep vein thrombosis	1	0	2.5	0
Pneumonia	2	3	5	7.5
Other	8	13	20	37.5

to obtain a match for all factors identified for comparison, a balance between the two samples was sought by selecting and including in the non-ERAS group an equal global number of the same characteristics, forgoing equality between individual pairs. Furthermore, if this balance could not be achieved, an excess of favourable factors was tolerated for non-ERAS patients. Accordingly, a greater prevalence of factors associated with longer LOS was observed among ERAS patients (3 more patients with BMI < 19 or weight loss > 10%, 2 more patients with diabetes mellitus, and 3 more patients with moderate rather than mild CPS), further enhancing our results.

Significant reduction in mean postoperative LOS was demonstrated in the majority of studies on ERAS in HN cancer surgery published to date (Tab. V). Of note, LOS reduction was not the primary endpoint in all investigations [22,23], and preoperative patient education was not performed in some [22,23]. These discrepancies could explain why a significant difference in LOS between ERAS and non-ERAS patients was not always demonstrated. Noticeably, one of the two studies that did not demonstrate LOS reduction showed significant improvements in LOS in the intensive care unit (ICU) and costs [22].

Another relevant aspect to consider is the difficulty in drawing substantial comparisons between studies conducted in different healthcare systems with heterogeneous organisation, imbalanced availability of social services, different post-hospital care facilities and variability in the overall efficiency of public or insurance-based services. Interestingly, studies on ERAS in HN surgery in the United States (US) reported a LOS of < 10 days both before and after ERAS implementation [4,22], in contrast to European (EU) studies that have a longer average LOS [5,15] (Tab. V). The analysis of the possible causes of such differences between EU and US centres is beyond the scope of the current study, although it is possible that insurance-based systems have historically put greater emphasis on the development of strategies to shorten LOS, even before implementation of ERAS [22]. In particular, US studies mention that patients were discharged with nasogastric feeding tube [4,22] or with tracheostomy still in place [2], while in all EU studies, as well as in the present one, patients were discharged after regaining oral feeding and tracheostomy closure [2,5].

Early mobilisation and feeding are considered among the major determinants of the rapid recovery observed in the ERAS cohort [1,2]. The median postoperative day (POD) of initiation of oral feeding for our ERAS patients was POD 9 (range, POD 7-12.5), while in the study by Bater et al. it was POD 8 [2]. This could partially explain the shorter median hospital stay of patients in the UK study compared with ours, and the greater difference in terms of LOS between control and experimental samples in the two studies (4 days for the Bater study [2] *vs* 3.5 in ours). Indeed, further early initiation of oral feeding could result in greater reduction in LOS without leading to an increased incidence of complications [2].

LOS is a general indicator of the quality of care, since prolonged hospitalisation determines not only an increase in overall costs, but also a significant increase in the incidence of in-hospital/perioperative complications, especially infections and mortality [24]. However, LOS does not represent the only parameter to assess the impact of ERAS implementation: economic factors such as better allocation of resources, or reduction of length of ICU occupation, should also be taken into account. However, an economic analysis of savings related to LOS reduction in ERAS patients was not performed in the present study.

As mentioned, one of the problems in employing LOS as the main outcome measure is that this parameter is affected by other variables that are not addressed by the ERAS protocol, leading to difficulties in interpretation of the results. In an attempt to univocally identify the results of ERAS on the patients' clinical course, the dischargeability, in the absence of active medical or surgical problems requiring hospitalisation and actual discharge were distinguished. Significant discharge delay can prolong LOS and during this time the patient, although medically and surgically a candidate for discharge (i.e. dischargeable), remains hospitalised for reasons that are not related to clinical conditions.

Table V. Impact of ERAS protocols for oncological surgery of the head and neck on length of stay.

Study		Number of patients		Length of stay (days)		
Name	Study type	ERAS	Control group	ERAS	Control group	P-value
Current study	Prospective	40	40 (matched)	14 (10-19.5)*	17.50 (13-21)*	0.013
Bater 2017 [2]	Prospective	100	40	10 (8-14)*	14.00 (11-21)*	0.003
Jandali 2019 [4]	Retrospective	92	93	7.8 ± 4.8**	9.7 ± 4.7**	0.008
Coyle 2016 [5]	Prospective	31	-	14.55 ± 7.48**	18**	-
Bertelsen 2020 [22]	Prospective	61	61	10	8.5	0.346
Kiong 2021 [1]	Retrospective	200	200 (matched)	7.2 ± 2.3**	8.7 ± 4.2**	< 0.001

** median (first quartile-third quartile); ** mean ± standard deviation.*

A review on the subject identified insurance issues, need for transfer to another facility, undergoing surgery on the last days of the week, and eligibility for patient discharge early or late in the week as significant determinants of discharge delay. In our study, discharge was postponed mainly due to delays in the organisation of home care, unavailability of social services if patients were discharged over the weekend, procrastination of medical consultations from other specialists, and, above all, the long time needed to deliver health care supplies to the patient's home. The difference between median LOS until discharge and dischargeability was 2 days in the ERAS group, while dischargeability was not evaluated in the 2017 cohort.

While dischargeable ERAS patients spent on average 2 extra days in the hospital before actual discharge, non-ERAS patients spent an average of 1.5 days. A possible reason for this difference is that the collection of data for the control sample was performed retrospectively, and estimation of dischargeability was not always straightforward. It is relevant to note that optimised management of organisational aspects could significantly affect LOS in our healthcare system, with potential reductions that are similar to what can be attributed to the ERAS implementation itself.

The ERAS protocol was also associated with a positive trend in reduction of postoperative complications that was not statistically significant. This aspect is most likely related to the relatively low number of cases included, since the sample was not sufficiently powered considering this outcome measure. Secondly, it is likely that complications were more attentively reported in the prospective ERAS group, while being underestimated in the retrospective control group. Of note, a shorter LOS in the ERAS group, despite a comparable rate of complications, could indicate quicker recovery of patients, which could be attributed to the ERAS protocol. In the literature, few studies have thoroughly analysed the complication rate [1,3,22] and in some HN cancer ERAS protocols this aspect has not been satisfactorily evaluated [4]. On the other hand, a recent retrospective pair-matched study, which included 200 pairs of patients, showed a significant reduction in both LOS and medical complications [1].

The implementation of the ERAS protocol was challenging due to organisational difficulties. For example, patient recruitment was operator-dependent and the crucial step was to propose and illustrate the ERAS protocol to all potentially eligible patients at first contact in order to immediately implement the preoperative education and risk assessment representing the first gate entry for inclusion in the prospective cohort. Many patients were non-eligible because the preoperative part of the protocol could not be implemented.

Nevertheless, rates of compliance to the protocol were high overall, and compare favourably with those reported by Coyle and Jandali [4,5]. The assessment of compliance with the protocol is a fundamental aspect of the ERAS philosophy and it is surprising that, so far, it has been analysed by so few studies in the HN literature [4,5]. Reporting compliance data is fundamental in the presentation of the ERAS results, since it allows to fully understand and interpret the results. As a consequence, all studies reporting no differences in outcome measures after ERAS implementation do not mention data on protocol adherence. In addition, addressing areas of low compliance may give the opportunity to further improve patient outcomes, thus broadening the scope and opportunities offered by adopting the ERAS framework.

Conclusions

Our study demonstrated that the introduction of an ERAS protocol in the daily practice is feasible, as shown by the excellent adherence to the protocol, and can result in significant reduction in LOS. As with all ERAS protocols, due to the multimodal nature of the program, assessing the impact of each individual procedure implemented is not possible. The study also gave us the opportunity to update our practice and deliver up-to-date care, and can be a starting point for further discussion to address failures and improve outcomes.

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Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

GB designed the study, supervised and participated in data collection and analysis, wrote the main article draft. GT collaborated to data collection and analysis and to initial

manuscript drafting. MT collaborated to study design and manuscript drafting. DM supervised study design, data collection and analysis and contributed to manuscript drafting. FDB supervised study design and contributed to manuscript drafting. NM contributed to study design and data collection. MF contributed to study design and statistical analysis. MA, RM, NS and DV contributed to data collection and study design. CP, PN and AD supervised the overall work, guided the study design process and the bibliographic research, and contributed to the final version of the manuscript.

All authors contributed to manuscript drafting and approved the final version.

Ethical consideration

This prospective study was conducted according to the ethical standards established in the 1964 Declaration of Helsinki (revised in 2013), and approved by the local Ethics Committee ("Comitato Etico di Brescia", Protocol Number 3131).

Written informed consent was obtained from each participant/patient for study participation and data publication.

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