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REVIEW ARTICLE

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Enhanced recovery after surgery protocols for outpatient operations in otolaryngology: Review of literature

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Abstract

Objective: Enhanced recovery after surgery (ERAS) protocols are patient-centered, evidence-based pathways designed to reduce complications, promote recovery, and improve outcomes following surgery. These protocols have been successfully applied for the management of head and neck cancer, but relatively few studies have investigated the applicability of these pathways for other outpatient procedures in otolaryngology. Our goal was to perform a systematic review of available evidence reporting the utility of ERAS protocols for the management of patients undergoing outpatient otolaryngology operations.

Methods: A systematic literature review was conducted using MEDLINE, EMBASE, SCOPUS, and gray literature. We identified studies that evaluated ERAS protocols among patients undergoing otologic, laryngeal, nasal/sinus, pediatric, and general otolaryngology operations. We assessed the outcomes and ERAS components across protocols as well as the study design and limitations.

Results: A total of eight studies fulfilled the inclusion criteria and were included in the analysis. Types of procedures evaluated with ERAS protocols included tonsillectomy and adenoidectomy, functional endoscopic sinus surgery, tympanoplasty and mastoidectomy, and septoplasty. A reduction in postoperative length of stay and hospital costs was reported in two and three studies, respectively. Comparative studies between ERAS and control groups showed persistent improvement in pre- and postoperative anxiety and pain levels, without an increase in postoperative complications and readmission rates.

Conclusions: A limited number of studies discuss implementation of ERAS protocols for outpatient operations in otolaryngology. These clinical pathways appear promising for these procedures as they may reduce length of stay, decrease costs, and improve pain and anxiety postoperatively.

KEYWORDS

enhanced recovery after surgery, otolaryngology, outpatient surgery, patient safety, PSQI

Highlights

- Enhanced recovery after surgery (ERAS) protocols in outpatient otolaryngology operations are effective in significantly decreasing hospital length of stay, hospital costs, and postoperative pain/anxiety.
- The most common components among ERAS protocols were postoperative analgesia regimen, postoperative nutrition, fluid management, and preoperative education/counseling.

INTRODUCTION

In recent years, there has been a paradigm shift to provide more quality-focused, cost-effective, and patient-centered care. Enhanced recovery after surgery (ERAS) protocols have evolved as strategies to meet these goals by improving surgical outcomes, reducing complications, and shortening length of stay (LOS).[1,2] There are several key tenets incorporated into these protocols, some of which include preoperative counseling, nutrition optimization, standardized anesthesia and analgesia regimens, and early mobilization.[3–5] By implementing these multimodal perioperative interventions, the hope is to reduce the patient's stress response associated with surgery, maintain preoperative organ function, and expedite recovery.[6–8] Not surprisingly, we have seen perioperative guidelines published by the ERAS society for several operations, along with numerous meta-analysis reporting favorable outcomes in terms of complication rates, hospital LOS, postoperative opioid use, and readmissions.[9–14]

Of critical relevance to otolaryngology, ERAS protocols have become increasingly important for the perioperative management of head and neck cancer. Consensus-based recommendations are available for patients undergoing major head and neck surgery and microvascular free-flap reconstruction,[15] and a meta-analysis of several institutional studies for this patient population demonstrated a reduction in hospital LOS, wound complication, and rates of readmission, without an increase in reoperation or hospital mortality.[16] In addition to ERAS protocols for head and neck cancer surgery, there is growing literature supporting the role of ERAS protocols for the perioperative management of thyroidectomy and parathyroidectomy. A recently published systematic review and meta-analysis showed that ERAS protocols for thyroid and parathyroid surgery significantly reduced hospital LOS and costs without increasing complications or readmission rates.[17] In light of the benefits seen in patients with head and neck cancer and those undergoing thyroid and parathyroid surgery, we were interested in investigating the role of ERAS protocols for other patient populations in otolaryngology. Our objective therefore was to collate, critically appraise, and analyze the published literature regarding the use and efficacy of ERAS protocols for outpatient operations in otolaryngology.

METHODS

We conducted a systematic review according to the Cochrane Handbook for Systematic Reviews of Interventions and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria.[18]

Two authors (K. C. and S. H.) systematically reviewed MEDLINE via PubMed, SCOPUS, EMBASE, and gray literature to identify studies evaluating ERAS protocols and clinical care pathways in patients undergoing outpatient otologic, laryngeal, nasal/sinus, pediatric, and general otolaryngology operations. Studies that evaluated clinical pathways for inpatient surgeries including traditional head and neck cancer operations (oral cavity, oropharynx, hypopharynx, larynx, salivary gland, thyroid) were excluded. Our search strategy included articles published from inception of the database to December 1, 2020. Retrieved articles were then reviewed manually. A set of controlled variables including ("Head and Neck" or "Head and Neck surgery" or "Otolaryngology" or "Otorhinolaryngology" or "ENT" or "Ear, nose, and throat") and ("ERAS" or "enhanced recovery after surgery" or "clinical pathway" or "clinical care pathway" or "critical pathway") was used to identify articles. No limit was set for language, location, or sample size. K. C. and S. H. each independently reviewed the titles and abstracts of all articles. This was followed by full-text review to ensure eligibility for inclusion in this study. Disagreements were settled by a third author (K. R.).

Two investigators (K. C. and S. H.) independently extracted study-specific data using a standardized collection form. We retrieved the following information: study characteristics, components of ERAS and clinical care protocols, patient demographics, perioperative details, patient characteristics, study outcomes, and study limitations. If any outcomes were reported as median and interquartile range, we converted them into mean ± standard deviation per Luo et al.[19] If details about patient population, protocol, or relevant findings were not provided in the manuscript, we emailed the corresponding authors of the studies to retrieve this information.

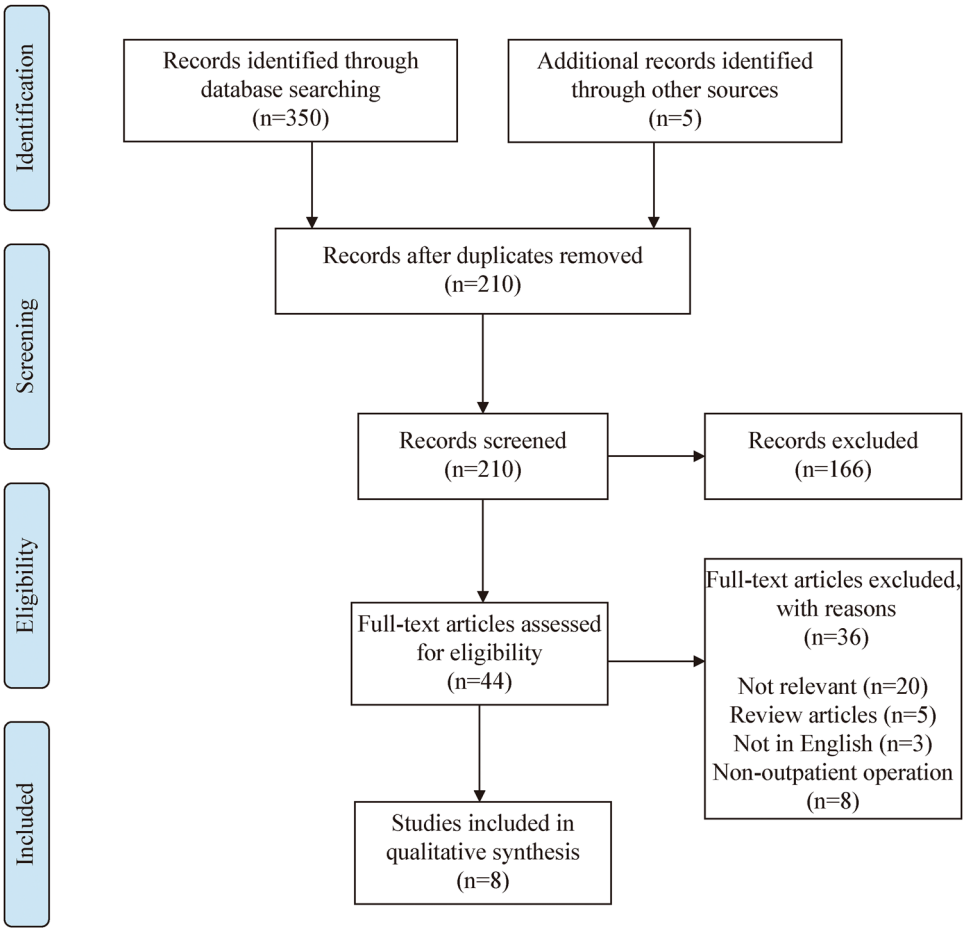

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the systematic search strategy

RESULTS

The initial search yielded 355 articles from the selected database. After excluding duplicates, 44 full-text articles were assessed in their entirety for inclusions. Finally, eight articles were deemed appropriate for inclusion for this study.[20–27] The flowchart in Figure 1 provides a summary of the article selection process.

The included studies with a description of their study type, population, and limitations are summarized in Table 1. Two of the studies were performed in the United States, while the other six were conducted in China. Seven studies each reported the age ranges and gender distributions for enrolled patients. Of the studies that report gender, the percentage of females ranged from 20% to 75%. Clinical care protocols for several operations were identified including tonsillectomy/adenoidectomy, septoplasty, functional endoscopic sinus surgery, and tympanoplasty/mastoidectomy. The studies took place from 1995 to 2018. Seven of the studies lasted less than 1 year, and the timeline for one study was not reported. All studies included 50 patients or more. It is noteworthy that the studies by Wu et al.[23] and Wu et al.[24] were unified by contributions from the same authors.

Four of the included studies used a randomized control design, and four studies were cohort studies. Of the cohort studies, three trials used a retrospective cohort before implementation of clinical pathway as a source of control.

Table 2 summarizes the elements of the enhanced recovery protocols implemented by each study. These elements included preoperative education, preoperative analgesia, preoperative nutrition, standard anesthesia protocol, temperature regulation, fluid management, mobilization, postoperative analgesia, and postoperative nutrition. The most common elements reported in these protocols included postoperative analgesia regimen (eight studies), postoperative nutrition (eight studies), fluid management (eight studies), and preoperative education (eight studies). In contrast, fewer studies included preoperative analgesia administration (four studies) as part of their ERAS protocol.

Table 3 summarizes the results commonly reported between studies. Hospital LOS was compared for the intervention versus the control group in five studies. For patients enrolled in ERAS protocols for septoplasty, tonsillectomy, and adenoidectomy, and endoscopic sinus surgery a significant reduction in postoperative LOS was noted.[21–23] Conversely, a separate ERAS protocol for pediatric patients undergoing tonsillectomy and adenoidectomy, and for adults undergoing a tympanoplasty did not demonstrate a difference in postoperative LOS.[20,26]

TABLE 1 Characteristics of studies describing enhanced recovery after surgery protocols for outpatient operations in otolaryngology

Author (year)	Journal	Study type and date	Population	Mean age	Procedure	Limitations
Lawson et al. (1997)[20]	*Journal of PeriAnesthesia Nursing*	Prospective cohort June 1995–September 1995	100 Patients	–	Tonsillectomy and adenoidectomy	Controls were conventionally managed patients before pathway implementation
Pestian et al. (1998)[21]	*American Journal of Otolaryngology*	Retrospective cohort	80 Patients, 50% male	6.3 ± 3.06	Tonsillectomy and adenoidectomy	Retrospective analysis Controls were conventionally managed patients before pathway implementation
Liao et al. (2018)[22]	*Therapeutics and Clinical Risk Management*	Randomized control trial December 2017–February 2018	50 Patients, 56% male	36.4 ± 12.1	Septoplasty	No blinding of assessors or subjects Single-institution experience
Wu et al. (2019)[23]	*Chinese Medical Journal*	Randomized control trial January 2018–April 2018	102 Patients, 75% male	39.4 ± 10.0	Functional endoscopic sinus surgery	Overlapping authors Single-institution experience Small sample size No blinding of assessors or subjects
Wu et al. (2019)[24]	*Therapeutics and Clinical Risk Management*	Randomized control trial January 2018–May 2018	74 Patients, 74% male	38.7	Functional endoscopic sinus surgery	Overlapping authors Single-institution experience SNOT-22 questionnaire scores only reflect a subjective assessment of patients Lack of objective metrics of inflammation No blinding of assessors or subjects
Gao et al. (2020)[25]	*American Journal of Otolaryngology*	Prospective cohort May 2018–October 2018	55 Patients, 80% male	42.4	Functional endoscopic sinus surgery	Small sample size Single-institution experience Nonrandomized design
Tan et al. (2020)[26]	*Ear, Nose & Throat Journal*	Randomized control trial April 2018–February 2019	84 Patients, 25% male	36.2 ± 10.7	Tympanoplasty and mastoidectomy	Small sample size Single-institution experience
Zhang et al. (2020)[27]	*Clinical Otolaryngology*	Retrospective cohort April 2016–March 2017	394 Patients, 53% males	5.4 ± 2.5	Tonsillectomy and adenoidectomy	Single-institution experience Controls were conventionally managed patients before pathway implementation

Abbreviation: SNOT-22, sinononasal outcome test.

TABLE 2 Components of enhanced recovery after surgery protocols across studies

Author (year)	Preop education	Preop analgesia	Preop nutrition	Standard anesthesia protocol	Temperature	Fluid management	Mobilization	Postop analgesia	Postop nutrition
Lawson (1997)[20]	+	+			+	+	+	+	+
Pestian (1998)[21]	+			+		+		+	+
Liao (2018)[22]	+		+	+	+	+	+	+	+
Wu (2019)[23]	+	+	+	+	+	+	+	+	+
Wu (2019)[24]	+	+	+	+	+	+	+	+	+
Gao (2020)[25]	+		+		+	+	+	+	+
Tan (2020)[26]	+	+	+	+	+	+	+	+	+
Zhang (2020)[27]	+		+	+	+	+	+	+	+

Other variables that were evaluated were unplanned readmissions to the hospital, hospital costs, and postoperative complications. However, they were not evaluated in every study. Only one study reported readmission rates and observed no difference between the control group and those patients receiving the ERAS protocol. In terms of hospital costs, four studies compared the cost of the hospitalization for patients enrolled in the ERAS pathway compared to patients in the control group. Patients in the ERAS pathway who underwent a septoplasty,[22] endoscopic sinus surgery,[23] and tonsillectomy and adenoidectomy had reduced hospital costs,[21] but ERAS pathway patients who underwent tympanoplasty/mastoidectomy did not.[28] Operative complications were investigated in five studies, and all of them defined complications (Table 3). The ERAS protocol was noted to significantly reduce postoperative complications in patients undergoing a tonsillectomy and adenoidectomy.[27] The other four studies noted no difference in complication rates.

Perioperative pain and anxiety reduction were the other important components of the ERAS protocol that were studied. Pain was assessed using the Visual Analog Scale (four studies) and institutional-specific pain metrics (one study). All of the studies demonstrated a significant reduction in postoperative pain in the ERAS protocol group compared to the control group. Anxiety was assessed using the Zung Self-Rating Anxiety Scale (four studies) and the modified Yale Preoperative Anxiety Scale (one study). Similar to the pain metric, all patients in the ERAS protocol demonstrated a significant reduction in perioperative anxiety.

DISCUSSION

As health care systems begin to shift toward value-based programs and cost containment, the focus now transitions to strategies to maximize clinical outcomes and patient satisfaction, all while minimizing hospital expenditure.[29] ERAS protocols have been shown to be effective methods at addressing these needs and are being adopted across a wide variety of surgical disciplines.[30–32] Preliminary evidence from this systematic review suggests that ERAS protocols are useful for outpatient operations in otolaryngology.

Hospital LOS was among the most commonly reported outcome among these studies, and results from this systematic review show that ERAS protocols may lead to meaningful reductions in postoperative stay. However, the improvements in LOS for some operations should be viewed with caution and need further examination. Two studies evaluating endoscopic sinus surgery and septoplasty reported a 3.6- and 1.4-day improvement in LOS, respectively. However, as these operations lead to no significant postoperative complications, these operations should be routine ambulatory operations, so it is unclear why these patients remained hospitalized for so long before ERAS initiation. Incidentally, these studies were performed at Chinese institutions, so perhaps postoperative management for these procedures differs when compared to North American and European practices. Even so, another study for tonsillectomy and adenoidectomy also demonstrated significant reductions in LOS, so it is possible that these clinical pathways are still beneficial for outpatient operations.

In this review, the studies demonstrated that clinical care pathways generally did not increase readmission rates, complications, or hospital costs. Only one study on tonsillectomy actually showed significant reductions in postoperative complication rates.[27] This could be attributed to the fact that complications and readmissions following outpatient operations are low in general,[28,33] even without ERAS protocols, and therefore larger sample sizes would be needed to discern a difference. It is noteworthy that the findings from this study are similar to the findings observed for other surgical specialties that evaluated the role of ERAS for outpatient surgeries.[31,34] Most importantly, it is reassuring to see that the upfront effort, time, and coordination required to implement an ERAS protocol does not lead to worse outcomes and hospitals costs. In other words, there is no downside in the creation and implementation of an ERAS protocol.

Traditionally, patient outcomes research has focused on specific endpoints such as patient survival, LOS, and postoperative complications because they are easily measurable and objective. However,

TABLE 3 Outcomes assessed across studies evaluating enhanced recovery after surgery (ERAS) protocols($\bar{x} \pm s$)

Author (year)	Hospital length of stay	Pain levels	Anxiety levels	Readmission (%)	Hospital costs ($)	Complications (%)	Other findings
Lawson (1997)[20]	Hospital LOS ERAS: 3 h postop (mean) Control: 4–7 h postop (mean)	–	–	–	–	–	
Pestian (1998)[21]	Hospital LOS ERAS: 14.8 ± 6.9 h postop[a] Control: 17.8 ± 5.4 h postop	–	–	Readmission rate ERAS: 2.5 Control: 2.5	Patient costs ERAS: 520 ± 136[a] Control: 590 ± 80	–	–
Liao (2018)[22]	Hospital LOS ERAS: 4.4 ± 0.5 days[a] Control: 5.8 ± 0.8 days	VAS (POD 1, 2, & 3) ERAS: 3.5 ± 1.3[a] 2.4 ± 0.9[a] 2.0 ± 0.8[a] Control: 6.5 ± 2.2 6.0 ± 2.0 3.9 ± 0.9	SAS (preop, POD 3, POD 7) ERAS: 35.4 ± 6.2[a] 31.6 ± 5.4[a] 29.2 ± 5.0 Control: 43.6 ± 8.6 38.1 ± 10.4 31.2 ± 9.3	–	Hospital costs ERAS: 1252.5 ± 21.0[a] Control: 1333.7 ± 38.1	–	EBL: ERAS: 6.2 ± 2.1 ml Control: 6.6 ± 2.3 ml VAS sleep (POD 1 & 2) ERAS: 3.1 ± 1.4[a] 2.6 ± 1.3[a] Control: 6.7 ± 2.4 6.5 ± 2.3 VAS nasal obstruction (POD 1, 2, 3) ERAS: 5.1 ± 1.2[a] 3.5 ± 1.2[a] 2.8 ± 0.9[a] Control: 9.2 ± 0.7 9.0 ± 0.8 5.5 ± 1.7
Wu (2019)[23]	Hospital LOS ERAS:	VAS (2, 24, 48 h postop) ERAS: 0.7 ± 0.8[a]	SAS (preop) ERAS: 29 ± 8.4[a]	–	Hospital costs ERAS: 2595 ± 278.3[a]	Postoperative complications[b]	Postop MOS-SS sleep quality ERAS: 44.7 ± 5.3[a]

(Continues)

TABLE 3 (Continued)

Author (year)	Hospital length of stay	Pain levels	Anxiety levels	Readmission (%)	Hospital costs ($)	Complications (%)	Other findings
	4.7 ± 0.76 days[a] Control: 8.3 ± 0.76 days	0.7 ± 0.8[a] 0.3 ± 0.8[a] Control: 1.7 ± 3.8	Control: 44 ± 3.8		Control: 3233.7 ± 259.5[a]	ERAS: 3.8 Control: 4.0	Control: 28.3 ± 9.9 Postop CRP level ERAS: 2.6 ± 1.9[a] Control: 6.5 ± 4.0
Wu (2019)[24]	–	–	–	–	–	Postoperative complications[c] ERAS: 11.1 Control: 7.9	SNOT-22 (preop, POD 1, POD 3, POD 6) ERAS: 39.89 ± 4.86 51.77 ± 5.59[a] 48.22 ± 6.22 39.39 ± 4.73 Control: 40.52 ± 3.61 62.02 ± 3.86 51.11 ± 5.14 40.13 ± 3.31
Gao (2020)[25]	–	VAS (2, 6, 24, 48 h postop) ERAS: 4 ± 1.7 2.3 ± 0.8[a] 2.0 ± 1.7[a] 1.3 ± 0.8[a] Control: 3.7 ± 2.4 4.0 ± 1.7 3.7 ± 1.7 2.7 ± 0.8	SAS (at discharge) ERAS: 28.7 ± 5.1[a] Control: 33.7 ± 4.2	–	–	Postoperative complications[d] ERAS: 27.2 Control: 0	–
Tan (2020)[26]	Hospital LOS ERAS: 4.75 ± 1.0 days Control: 5.0 ± 1.5 days	VAS (postop) ERAS: 107.9 ± 0.0[a] Control: 1.0 ± 1.5	SAS ERAS: 29.8 ± 2.7[a] Control: 36.0 ± 10.0	–	Hospital costs ERAS: 105.1 ± 12.9 Control: 107.9 ± 13.4	Postoperative complications[e] ERAS: 0 Control: 0	–
Zhang (2020)[27]	–	Pain scores (POD 1, POD 3, POD 7) ERAS: 3.3 ± 0.7[a] 2.3 ± 0.7[a]	m-YPAS (Preop) ERAS: 37.66 ± 6.68[a] Control:	–	–	Postoperative complications[f] ERAS: 1.92[a]	Dietary Intake Score (POD 1, 3, & 7) ERAS: 0.7 ± 0.7[a] 1.7 ± 0.7[a]

TABLE 3 (Continued)

Author (year)	Hospital length of stay	Pain levels	Anxiety levels	Readmission (%)	Hospital costs ($)	Complications (%)	Other findings
		1.3 ± 0.7[a] Control: 3.7 ± 07 2.7 ± 0.7 1.7 ± 0.7	47.70 ± 7.51			Control: 10.22	2.3 ± 0.7[a] Control: 0.3 ± 0.7 1.3 ± 0.7 1.3 ± 0.7

Abbreviations: CRP, C reactive protein; EBL, estimated blood loss; ICU, intensive care unit; LOS, length of stay; MOS-SS, Medical Outcomes Study Sleep Scale; m-YPAS, modified Yale Preoperative Anxiety Scale; POD, postoperative day; postop, postoperative; SAS, Self-Rating Anxiety Scale; SNOT-22, sinononasal outcome test; VAS, Visual Analog Scale.

[a]Statistically significant difference between intervention and control group ($P < 0.05$).

[b]Nausea/emesis, hemorrhage, tumble, aspiration.

[c]Nausea/emesis, hemorrhage, aspiration, dizziness.

[d]Nausea/emesis, postoperative bleeding.

[e]Nausea/emesis, dizziness, hematoma formation.

[f]Fever, hemorrhage, wound infection, pneumonia.

when patients undergo surgical operations, they often experience a multitude of intangible, subjective symptoms that are nonspecific and harder to assess.[35,36] These include pain, fatigue, anxiety, emotional distress, or cramping. It is equally important to address these nonspecific symptoms as they may lead to improved functional recovery, facilitate early discharge, and prevent postoperative opioid abuse.[37,38] Fortunately, this study reported that ERAS protocols are effective at reducing subjective pain and anxiety at various points in the perioperative phase. There are perhaps a couple of reasons for these findings. One reason is that all studies included preoperative education and psychological counseling in their protocols. These sessions provided details about the surgery, educated patients on what to expect postoperatively with regard to pain, and discussed the value of cooperation between the patient and the treatment team.[39,40] The other reason that these ERAS protocols were effective in reducing pain and anxiety is that many of the clinical pathways used a variety of opioid-sparing regimens and preemptive analgesia treatment as a method for pain control. In fact, several studies have shown that these strategies, when included as part of ERAS protocols, can reduce postoperative pain and VAS scores immediately after surgery.[32,41–43]

When designing ERAS programs, several common elements are seen across society guidelines for major operations in the preoperative, intraoperative, and postoperative setting. These include preadmission counseling, goal-directed fluid therapy, early allowance of food intake, and early mobilization. Interestingly, many of these components were discussed and incorporated across these outpatient surgeries. There are reasons to believe that the inclusion of several ERAS components leads to cumulative benefits on patient outcomes and promotes recovery. Studies have shown that the use of a standardized anesthetic protocol in many of these outpatient protocols provides superior intraoperative hemodynamic stability, expedited return of cognitive function, improved postoperative pain, and decreased incidence of postoperative nausea and vomiting.[44–47] Furthermore, deliberate hypotension intraoperatively may reduce blood loss and improve the surgical field in these procedures.[48–50] On the other hand, several other elements typically found in ERAS protocols are not well supported for these outpatient operations and must be extrapolated from other studies. These include pre-/postoperative nutrition, temperature monitoring, and mobilization. Future studies are needed to evaluate whether additional ERAS elements can be incorporated as future perioperative guidelines are fully designed and customized for these operations.

Despite the popularity and efficacy of ERAS protocols for surgical operations, implementation and compliance remain some of the greatest challenges when establishing these programs.[51,52] The adherence rate for components of ERAS protocols can be low, especially in the postoperative period, with some studies demonstrating less than 50% compliance rates.[53,54] Furthermore, several surveys and reports emphasize the apparent discordance between current intra/postoperative practices and best-available evidence.[55,56] Unfortunately, all studies included in this analysis failed to address or report these important points when designing their

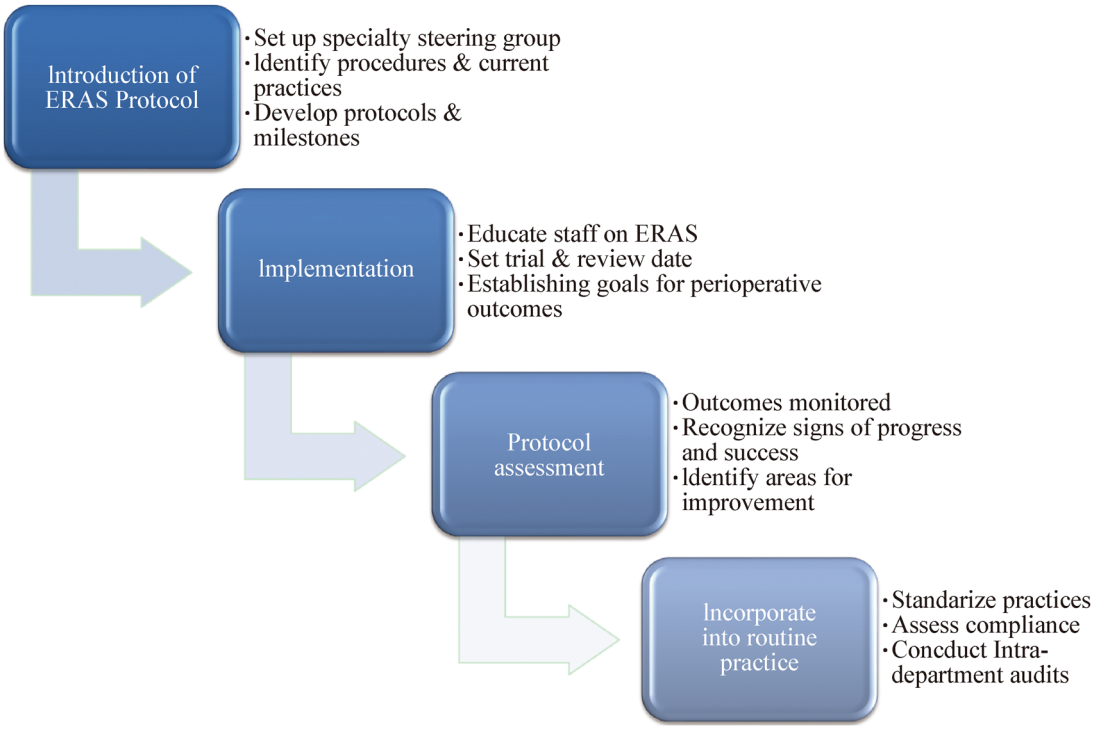

FIGURE 2 Strategies for implementation of enhanced recovery after surgery (ERAS) protocols

protocols. It is clear that development of a protocol is not enough to incorporate these clinical care pathways into routine practice. Figure 2 highlights a potential algorithm based on thorough literature reviews that features the most important steps for implementation of these programs.[57–60] Of particular importance, continuous auditing is necessary to ensure high level of compliance and helps with identification of potential deviations from the protocol. Additionally, it is imperative that all members of the treatment teams should be familiar with the principles of these programs, and any ambiguities about the protocols should be addressed and clarified early on.

There are several limitations to this systematic review. Although we performed a thorough literature review, we only discovered eight studies, of which very few were randomized control trials. The studies were performed across various geographical locations and may account for variations in practice patterns that can affect the overall outcomes. Two of the studies had overlapping authors, which may limit the generalizability of these findings. Furthermore, there was significant variability in the components of individuals ERAS programs and heterogeneity in terms of quality of reporting and relevant outcomes. However, these are expected because of differences in operations. The operations included in this analysis are generally performed for benign conditions in otherwise healthy individuals. Many times, ERAS protocols are designed and implemented for larger operations with sicker patient populations requiring inpatient hospitalization. The findings from this analysis attest to the strengths of these programs and emphasize the feasibility of these protocols for outpatient operations in otolaryngology. This study also highlights potential areas of improvements and implementation strategies for these ambulatory procedures.

CONCLUSIONS

ERAS protocols for outpatient otolaryngology operations appear to be promising and warrant further investigation. There is a need to customize these protocols for specific operations and to use consistent and quantifiable outcomes to assess the benefits of these programs. This study also guides future research efforts, as there is little published data in the literature discussing operational challenges and compliance when implementing ERAS protocols.

AUTHOR CONTRIBUTIONS

Kevin Chorath was involved in the conceptualization, methodology, validation, investigation, and data curation of this study, and writing – original draft, writing – reviewing and editing, and visualization of the manuscript. Sara Hobday was involved in the investigation and data curation of this study, and writing – original draft, writing – reviewing and editing, and visualization of the manuscript. Neeraj V. Suresh was involved in the writing – original draft, writing – reviewing and editing, and visualization of the manuscript. Beatrice Go as involved in the writing – original draft, writing – reviewing and editing, and visualization of the manuscript. Alvaro Moreira was involved in the writing – original draft, writing – reviewing and editing, and visualization of the manuscript. Karthik Rajasekaran was involved in the conceptualization, methodology, validation, investigation, and data curation of this study, and writing – original draft, writing – reviewing and editing, and visualization of the manuscript, supervision, and project administration.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data without patients' recognizable identification can be acquired by contacting the corresponding author.

ETHICS STATEMENT

This study did not involve human studies or contain any protected patient health information. As a result, there was no ethics approval applicable to this study.

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