

The role of perioperative oral nutrition in upper gastrointestinal surgeries

Doctoral (PhD) dissertation thesis

Dora Lili Sindler, M.D.

Doctoral School of Clinical Medicine

Head of Doctoral School: Prof. Lajos Bogár, M.D.

Supervisor: András Papp, M.D., PhD, Med. Habil



University of Pécs

Faculty of General Medicine

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1. Introduction

Gastric and esophageal tumors, which belong to cancers of the upper gastrointestinal tract, are conditions with high mortality, the early recognition and diagnosis of which is crucial for successful treatment. Application of the ERAS (Enhanced Recovery After Surgery) protocol, based on the lessons learned from both meta-analysis and practical clinical trials, is beneficial for better treatment of upper gastrointestinal cancers and speeding up patients' recovery and improving their quality of life.

Surgery is still the basis of treatment options for cancers of the upper gastrointestinal tract today. Given the high rate of anastomosis failure, several procedures have been developed to achieve the correct surgical technique to reduce the postoperative complications, of which a very important milestone was the appearance of the minimally invasive

approach during the operations of tumors of the upper alimentary canal. Minimally Invasive Esophagectomy (MIE) has become popular in upper gastrointestinal surgical practice due to the reduction of postoperative complications and its beneficial effects on promoting healing. The quality of life of patients who have undergone MIE returns to baseline more quickly than in patients who have undergone classic open surgery. The less surgical trauma and reduced postoperative pain, as well as earlier mobilization after MIE, promote earlier recovery.

2. ERAS protocol

For several decades, the initiation of oral feeding in the postoperative period after upper gastrointestinal resection surgeries was delayed until approximately the seventh day, for fear of anastomosis failure. The ERAS (Early Recovery After Surgery) complex care protocol, published in 1990, has recently become more and more accepted, recommending starting early oral feeding as soon as possible.

ERAS is an evidence-based approach that aims to improve outcomes by optimizing patient care for various aspects of the perioperative period, including postoperative nutrition.

The ERAS protocol applies important elements at all stages of treatment:

1. During the preoperative period, a lot of emphasis is placed on patient preparation and prehabilitation.

These include ensuring adequate nutritional intake, smoking cessation, and improving physical status.

2. Elements used during the intraoperative period include the use of minimally invasive surgical techniques, appropriate administration of analgesia, and appropriate dosing of intravenous fluid therapy and antibiotics.
3. In the postoperative period, the main element of ERAS is early rehabilitation, an essential part of which is the start of early oral feeding, early mobilization, or early removal of drain tubes.

The use of these interventions helps to reduce the risk of complications after surgery, for example the occurrence of pneumonia and deep vein thrombosis, and results in significantly shorter hospital stays, speeding up rehabilitation and returning to normal organ functions.

3. Meta-analysis

Goal and hypothesis

Based on numerous studies and meta-analyses investigating the effectiveness of the ERAS protocol, it's apparent that its application reduces the incidence of postoperative complications, shortens the length of hospital stay, and improves the quality of life of patients. To further provide proof, we've created a meta-analysis based on studies on the operative cases of malignant upper gastrointestinal tract's conditions, and also analyzed the effects of early and late postoperative oral feeding within the framework of a clinical study in the field of surgeries of the upper gastrointestinal tract.

Methodology

We've conducted a meta-analysis following the PRISMA protocol, collecting 6 studies examining a

total of 703 patients. All studies analyzed the effects of early and late postoperative oral feeding (EOF and LOF, respectively) among patients of surgeries of the upper gastrointestinal tract and compared the two groups' results.

We've examined 6 relevant RCTs with full text, involving a total of 703 patients. (From an initial 3147 articles from the Embase, Cochrane, and PubMed databases, we've eliminated all but 77 during multiplication, title, and abstract filtering, and further eliminated 71 studies during the full text filtering that were not RCTs or that weren't studying patients undergone surgeries of the upper gastrointestinal tract.)

Results

In our study we found no significant difference between the EOF (early oral feeding) and LOF (late oral feeding) groups regarding the occurrence of

anastomosis failure in any of the studies. (OR=0.95; p=0.88). We can state that early oral feeding does not increase the risk of anastomosis failure.

We reached significant results in 3 outcome factors: the time of the first colic, the time of the first stool, and the length of stay in the hospital. All of which showed significant improvement to be achieved with early oral feeding (EOF).

During the analysis of the onset of bowel function, we examined the data of a total of 604 patients from 5 studies. We found that start of wind was earlier in the EOF group (p=0,009). The difference between studies were significant (p <0,001).

We were able to include 3 studies to analyze first bowel movement, involving a total of 442 patients. We found that first bowel movement occurred significantly earlier in the EOF group (p<0,001).

With regards to hospital stay, we analyzed 5 studies involving 605 patients in total. We found that the average length of hospital stay was significantly shorter in the EOF group ($p=0,008$). The heterogeneity between studies was significant ($p<0,001$).

The incidences of pneumonia ($p=0.88$) and wound infection ($p=0.48$) do not show a correlation with the feeding method, as we did not find any significant differences between the results of the two groups in these outcomes.

We obtained similar results when examining the incidence of bleeding complications ($p=0.52$) and gastrointestinal paresis ($p=0.43$). We can say that the use of early oral feeding does not increase the incidence of these complications compared to the use of the late feeding method.

In summary, we can say that the ERAS protocol and early oral feeding (EOF) are not only safe to use but at the same time offer more benefits for patients, as they result in either no significant difference compared to the application of LOF, or showing objective, measurable parameter improvements in certain outcomes (start of wind, time to first bowel movement, length of hospital stay) while not increasing the incident rate of post-operative complications (anastomosis failure).

4. Propensity-score matching test

Goal, hypothesis

Based on the results of our meta-analysis, we prepared a clinical study between July 2020 and 2022 at the Department of Surgery of the University of Pécs. Our aim was to study the safety of early oral feeding (EOF) through a clinical study, using our own patient body gone through esophageal and gastric resection for malignant disease of the upper gastrointestinal tract..

Methodology

The results from patients treated by the early feeding protocol were compared with the data from the late oral (LOF) feeding method. Both groups were treated at our Clinical Center with upper alimentary canal tumors during the same period. The vast majority of patients belonging to the EOF group received both

physical and dietary prehabilitation, and immediately before surgery we performed carbohydrate loading using preop supplements (Nutricia).

We've included in our study data from 25 patients in the early oral feeding group, compared to 25 patients of similar age, gender distribution, and similar surgical treatment, who belonged to the traditional oral feeding group.

Results

In the EOF group, the median age was 61.52 years (ranging 32 to 75 years), 20% of whom were women. The start of oral feeding in the EOF group was, on average, 2.09 days after surgery, while in the LOF group it was, on average, 5.52 days after.

The median postoperative hospital stay was 8.875 days in the EOF group and 12.06 days in the control group. A statistically significant decrease was

observed in the postoperative hospital stay in the EOF group ($p < 0.05$).

There was a statistically significant reduction in the time to the first bowel movement (3.88 days in the EOF group versus 5.56 days in the LOF group, $p < 0.05$), and in the duration of postoperative intravenous fluid therapy (4.8 days in the EOF group versus a 8.83 days in the LOF group, $p < 0.05$).

The use of early oral feeding does not increase the incidence of the examined morbidity factors. No significant difference was detected in the death rate ($P > 0.05$), in the anastomosis failure rate ($p > 0.05$), in the occurrence of anastomotic inflammation ($p > 0.05$), regarding anastomotic stenosis ($p > 0.05$), or regarding the presence of seroma ($p > 0.05$).

5. Results

Our results confirmed the recommendations of the ERAS protocol, which promotes the introduction of early oral feeding after upper gastrointestinal surgeries. Both our meta-analysis and clinical study concluded that the use of EOF has many advantages, while not increasing the incident rate of complications. It significantly shortens the time until the return of bowel function and reduces the length of hospital stay, which by itself lessens the incident rate of postoperative complications and promotes early mobilization and faster recovery time.

6. Discussion

In summary, it can be said that the risks of using EOF are negligible, and at the same time it brings significant benefits to the rehabilitation process.

Shorter hospital stays not only benefit patients but can also result in significant cost savings for healthcare systems. Due to a lack of data, we did not analyze this further in our studies, however several publications clearly confirm this.

The quality of life and the patient's subjective well-being are both very important aspects. Early oral feeding, the possibility of early mobilization, and the early emission time are all factors influencing quality of life which can be significantly improved by starting early oral feeding.

Based on our results, we recommend the practical use of EOF after upper gastrointestinal surgeries,

especially within the framework of the ERAS protocol. This method can help patients recover faster, shorten the length of hospital stay, and reduce costs.

Our results and recommendations can help improve care and more effectively rehabilitate patients. Further research and studies may contribute to further, even more in-depth understanding of the topic, and aid in the future development of the ERAS protocol and the application of early postoperative nutrition.

7. New findings

1. Within our meta-analysis we proved, for the first time in Hungary, that early oral feeding can be used safely even after upper gastrointestinal surgeries, as it doesn't increase the rate of anastomosis failure and other morbidity factors, while at the same time significantly decreases the time to first bowel movement and length of hospital stay.
2. We've conducted, for the first time in Hungary, a clinical study examining the impact of early oral feeding after upper gastrointestinal surgeries.
3. Through this, we were the first in Hungary to verify, in a clinical study, the findings of the meta-analysis, and with this we hope to succeed in changing the outdated feeding

practices still used nationally during upper
alimentary canal surgeries.

8. The author's publications related to the thesis

1. **Sindler, D. L.**, Mátrai, P., Szakó, L., Berki, D., Berke, G., Csontos, A., Papp, C., Hegyi, P., & Papp, A. (2023). Faster recovery and bowel movement after early oral feeding compared to late oral feeding after upper GI tumor resections: a meta-analysis. *Frontiers in surgery*, *10*, 1092303. <https://doi.org/10.3389/fsurg.2023.1092303>
Q2, Impact factor: 1,8

2. **Sindler, D. L.**, Papp, C., Csontos, A., Szakó, L., Vereczkei, A., Halvax, P., Palkovics, A., & Papp, A. (2024). Early oral feeding does not pose a risk after upper gastrointestinal surgeries. *Medical Weekly*, *165*(1), 24–29. <https://doi.org/10.1556/650.2024.32936>
Q4, Impact factor: 0,6

The impact factor for the quotable abstracts at the basis of the thesis: 2,4

The author's publications related to the thesis

1. **Dora Lili Sindler**, András Papp: Application of the ERAS protocol in UGI surgery
Joint Congress of Surgical Endoscopy and Coloproctology Section, Tapolca, Hungary May 26-28, 2022.
2. **Dora Lili Sindler**, Csenge Papp, András Vereczkei, András Papp: Early oral feeding after upper gastrointestinal surgeries - *3rd Congress of the Surgical Oncology Section of the Hungarian Society of Surgeons* October 14-15, 2022, Szeged, Hungary
3. **Dora Lili Sindler**, András Papp: Early oral feeding after upper gastrointestinal surgeries - *ERAS Roundtable, Foundation for Young Surgeons, ERAS*

protocols use and introduction possibilities in terms of perioperative nutrition June 2022. 1. Pécs, Hungary

4. **Dora Lili Sindler, András Papp:** ERAS: one skillful surgeon is not enough? How it works for us: UGI surgeon - *66th Congress of the Hungarian Society of Surgeons*, October 5-7, 2023 Siófok, Hungary

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