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Colon Interposition for Esophageal Reconstruction in Cancer Patients

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Objective: The aim of this study was to report our experience with colon interposition (COI) and to compare the results with an extensive review of the COI literature.

Summary of Background Data: The stomach is the first choice as an esophageal substitute following esophagectomy in cancer patients, while COI is reserved for patients where the stomach is not available or must be included in the resection due to cancer.

Methods: We retrospectively reviewed the records of cancer patients undergoing colon interposition from 2006 to 2017. Outcomes were compared with an extensive review of the literature published between 2000 and 2017.

Results: A total of 13 patients underwent planned COI. Mortality was zero and overall morbidity was 53%; 4 patients suffered from leakage and 2 patients from strictures. None of the patients suffered from necrosis of the interponat and there was no need for subsequent redundancy operations.

The extensive review identified 23 publications. Overall study grading was low (grade C). Only 3 studies were prospective, no randomized studies were found, and many outcomes were poorly defined. The rates for 30-day and in-hospital mortality were 1% and 2%, respectively. Overall morbidity was 43%. The reported number of leakages, strictures, necrosis of the interponat, and redundancy operations varied between 0% and 50%, 0% and 21%, 0% and 9%, and 0% and 2%, respectively.

Conclusions: COI is a complex technique that is necessary in a relatively small group of selected patients after esophagectomy for cancer. Prospective and comparative studies with strict outcome definitions, long-term follow up, and patient reported outcome measures are lacking.

Key words: Colon-interposition – Review – Esophagectomy – Postoperative complications – Choice of conduit – 30 days mortality – In-hospital mortality

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The stomach is widely used as an esophageal substitute following esophagectomy in both benign and malignant esophageal diseases. However, this reconstruction technique may be compromised in patients where the stomach is not available or in cases where the stomach is involved in the disease. Colon interposition (COI) as replacement of the thoracic esophagus dates back to 1911 and is used for reconstruction in both benign and malignant diseases.\(^1\) The length, acid resistance, and excellent blood supply makes the colon a great interponat,\(^2,3\) but the COI operation is technically demanding with a long operating time and a significant risk of complications.\(^1,4–7\) The preferred use of the stomach as conduit and the complexity of the COI have made the latter a somewhat rare operation, and this is reflected in the lack of prospective studies and COI reviews.

The aim of this study was to report our experience with COI and to compare the results with an extensive review of the COI literature.

**Material and Methods**

**Clinical study**

All patients having a COI at the Upper GI Section, Department of Surgery, Odense University Hospital, between 2006 and 2017 were included in the study. Patients were identified in the institution’s electronic patient databases and reviewed individually in terms of indication, preoperative performance status, comorbidity, cancer type and location, pTNM stage, adjuvant therapy, as well as peri- and postoperative details including morbidity, and 30-day- and in-hospital mortality. Postoperative complications were ranked by the Dindo-Clavien Classification. Observation time ended May 2017.

**Literature review**

A literature search in PubMed (MEDLINE) and EMBASE was conducted using the following Medical Subject Heading terms: Colon interposition, conduit, colon interposition esophagus, esophagectomy colon interposition, esophago-colonic anastomosis and esophageal cancer. The search was limited to studies on cancer published in the English language and not before 2000. The latest search was conducted May 2017. Each of the included studies were evaluated in detail regarding number of included patients, case load, cancer type/location, adjuvant treatment, preferred colon segment and route, operation time, blood loss, complications (leakage, stricture, necrosis, redundancy operation), and overall procedure-related morbidity and mortality (30 day/in-hospital).

The literature’s quality of evidence was assessed by the GRADE system.\(^8\)

**Ethical approval**

Since this is a registry-based study, there were no need for approval from either the Danish The National Committee on Health Research Ethics or the Danish Data Protection Agency.

**Results**

**Clinical experience**

During the inclusion period, a total of 13 patients (10 men, 3 female) underwent esophageal resection followed by COI. Five of the patients were initially treated with Ivor Lewis esophagectomy; but due to anastomotic leakage or relapse of the cancer, the patients subsequently underwent total esophagectomy followed by COI. Patient characteristics and outcomes are shown in Table 1. All patients were diagnosed with esophageal carcinoma and the tumors were all located in the lower third of the esophagus. All COIs were planned and preoperative bowel preparation was performed in all patients. Patient operative and postoperative outcomes are shown in Table 2. Eight out of the 13 patients had either intra-abdominal or intrathoracic adherences due to prior surgery. The right colon was used as the interponat for all operations. Before dividing the colon, artery supplies to the right colon (except the right branch of the middle colic artery) were clamped with a bulldog to ensure that there were no signs of ischemia (Figs. 1 and 2). The retrosternal route was used in all patients, and an end-to-side, one-layer, continuous anastomosis between the colon and the oral esophagus were performed. A Penrose drain was placed at the neck wound. Seven patients had a feeding jejunostomy placed since a longer recovery was expected. The median operating time was 345 minutes (range: 285–420) with a median blood loss of 1200 mL (range: 275–2500). Five of the patients needed blood transfusion. The median postoperative length of stay in the intensive care unit was 2 days (range: 1–13) and the median hospital stay was 21 days (range: 11–40). Six patients (46%) suffered major complications: Anastomotic leakage was found in 4 patients (grade IIIb), 1 of these patients also developed sepsis (grade II), and 2 patients suffered from stricture (grade IIIb). Six
patients (86%) suffered from minor complications: 1 pneumothorax (grade IIIa), 2 fascia ruptures (grade IIIb and IIIa), 2 cases of atrial fibrillation (grade II), 2 cases of pneumonia (grade II), and 1 case of a short delirium (grade II). Thus, the overall morbidity was 53%, whereas the 30-day and in-hospital mortality was 0. The median overall survival for the 13 patients was 668 days (range: 63–1619 days). None of the deaths were related to the COI procedure.

**Literature review**

The literature search yielded 23 publications, which met the inclusion criteria (Table 3). Twenty studies were retrospective and 3 were prospective.\(^{7,9,10}\) There were no randomized studies, but 7 studies compared COI results with those following the use of stomach as conduit. The overall study grading was low (grade C). The studies included between 3 and 347 patients, and although some studies included both benign and malignant diseases, the majority of patients were resected due to malignancy. The largest COI experience in cancer patients included 95 patients.\(^{11}\) We calculated the caseload of COI procedures on cancer patients in the reported studies and found a median caseload of 4 per year (range: 0.4–17). The majority of the cancers were either adenocarcinomas or squamous cell carcino-

![Fig. 1](image1) The ileocolic artery is clamped with a bulldog while checking sufficient blood supply for the right colon from the middle colic artery.

![Fig. 2](image2) The anastomosis between the remaining stomach and the mobilized right colon has been performed and the colon is ready for the upper anastomosis.
ma. One study\textsuperscript{12} reported surgical outcome in tumors located in the upper part of the esophagus only, whereas the majority of tumors were located in the middle or lower part of the esophagus. Between 0% and 89% (median 33%) of the patients received either neoadjuvant or adjuvant therapy.

The right colon was the preferred segment of choice and—when reported, the colon graft was most often positioned in the posterior mediastinum. The median operation time was 540 minutes (range: 270–881), and the median blood loss was 1065 mL (range: 687–2000; Table 3). The reported number of leakages, strictures, and necrosis varied between 0% and 50%, 0% and 21%, and 0% and 9%, respectively. Six of the 22 studies described the need for redundancy operations and this ranged from 0% to 2%. The median 30-day and in-hospital mortality were 1% (range: 0%–17%) and 3% (range: 0%–17%), respectively. The median morbidity was 43% (range: 21%–90%).

**Discussion**

Reviews on postoperative outcome assessment, measurement, and comparison between studies are traditionally difficult to perform for several, well known reasons. This becomes especially true during a literature review of the published data on colon interposition (COI). The majority of data are retrospective, and the key outcome parameters (e.g., leakage, strictures, morbidity, and mortality), included patients (both benign and malignant) and the surgical procedures are often poorly defined. The complications related to esophageal reconstruction may also be subdivided according to time frame\textsuperscript{13} and severity, and this will also contribute to inhomogeneous data for comparison.

**Cancer type, location, and adjuvant treatment**

Despite the inhomogeneous data regarding cancer type, location, and use of adjuvant treatment, there are no obvious differences in the outcome that may be attributed to these factors. One would assume that the relatively small number of tumors high in the esophagus (Table 3) is merely reflecting the nature of the disease and the thus possibility of resection rather than a deliberate choice of not doing reconstruction with COI. Neoadjuvant therapy and comorbid conditions have been identified as risk factors for anastomotic leaks following colon and stomach interposition,\textsuperscript{14} but more specific information and classification are seldom available in retrospective studies.

**Conduit route**

The anterior (retrosternal) and the posterior mediastinal conduit routes were preferred in the majority of COI patients.\textsuperscript{1,5,15} Older non-randomized data suggest that the posterior mediastinal route provided a better function than the anterior approach, but data are limited and extrapolating the results from gastric interponat reconstruction may not be rele-

---

**Table 2** Patient operative and postoperative outcomes

<table>
<thead>
<tr>
<th>Patient*</th>
<th>Adhesion</th>
<th>Operation length, min</th>
<th>Blood loss, mL</th>
<th>Transfusion</th>
<th>Jejunostomy</th>
<th>Postoperative complications</th>
<th>ICU length of stay, d</th>
<th>Hospital stay, d</th>
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<td>335</td>
<td>2500</td>
<td>Yes</td>
<td>No</td>
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<td>40</td>
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<td>375</td>
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<td>No</td>
<td>No</td>
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<tr>
<td>#3</td>
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<td>300</td>
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<td>Yes</td>
<td>Yes</td>
<td>Pneumothorax</td>
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<tr>
<td>#4</td>
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<td>1200</td>
<td>Yes</td>
<td>Yes</td>
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<td>21</td>
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<tr>
<td>#5</td>
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<td>275</td>
<td>No</td>
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AF, atrial fibrillation.

*COI due to leakage (L) or relapse (R).
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<th>Article, year</th>
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<th>Case load</th>
<th>Neoadjuvant/adjuvant therapy</th>
<th>Pref. segment</th>
<th>Pref. route</th>
<th>Op. time (min.)</th>
<th>Blood loss (mL)</th>
<th>Leakage*</th>
<th>Stricture*</th>
<th>Necrosis*</th>
<th>Redundancy operations*</th>
<th>Mortality 30 days*</th>
<th>Mortality in hospital*</th>
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<td>Overall</td>
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*aPercentage + any kind of stricture regardless of time.

bThe figures are given in either median or mean.
vant in COI patients. However, the shorter distance with less tension (or torsion) of the interponat and thus potential lower risk of anastomotic leaks could provide arguments in favor of the posterior route.5,13 According to Urschel,13 the advantages of the retrosternal route with gastric interponat reconstruction include: ease of drainage for anastomotic leaks and reoperation for anastomotic strictures, avoidance of conduit irradiation if postoperative radiation therapy is needed and, maybe the most compelling argument, prevention of tumor bed recurrence affecting the interponat. The latter view was supported by others regarding COI patients,11 but again more solid evidence is lacking. A subcutaneous route provides easy access and treatment in cases of leakage or conduit necrosis, but the higher risk of graft ischemia and the unsightly look makes it a rare choice among surgeons.11,13

Choice of conduit

The choice of colon graft may depend on local tradition and preferences.5,16 We use the right colon and this was also the most frequent choice of conduit in studies published after 1999 (Table 3). The left colon was a more common choice in the past,5,5,17 and its mobility, better vascular anatomy, and smaller diameter (i.e., lesser risk of dilation) were some of the arguments for this approach.16–18 The argument of an isoperistaltic reconstruction would apply for both types of conduits,16–18 but the decision to use the right, left or transverse part of the colon should probably be based on intraoperative findings in order to have the optimal conduit. Thus, the surgeon should be able to perform the COI with different parts of the colon, but this may be a problem related to experience (see caseload below).

New techniques have been described to secure adequate blood supply for the right colon and a better adjustment of the graft to fit the patient.17 In addition, the right colon requires less dissection16; and should the graft fail, there is still the possibility to use the left colon. Another option when using the right colon is the incorporation of 15 to 20 cm of the terminal ileum. The advantage of this approach is that the ileum and the esophagus have a similar diameter, which makes for a better fit, the ileum is less bulky and finally, the ileocecal valve may prevent regurgitation.5,5,11,16 In addition, retrospective data suggest that the use of an ileocolon graft may lead to a reduced rate of anastomotic leakages.11

Some surgeons prefer colon preparation prior to COI in order to avoid contamination when performing the anastomoses or to avoid dealing with a filled colon during dividing and mobilization of the interponat. Based on experience, COI in children mechanical bowel preparation should probably be avoided.

Another choice for an interponat is the jejunum, which has received a more widespread use over the years.15 The proponents of the jejunum graft highlight its inherent peristalsis superior to the colon interponat. As opposed to the colon interponat, it does not stretch over time, which reduces the likelihood of redundancy operations.15 Compared to COI, the jejunal interposition has significantly lower blood loss, fewer anastomotic leakages, shorter hospital stay, and the patients’ postoperative body weight loss is less.15,19,20 However, sufficient prospective data to support a general use of jejunal interposition are still lacking.20

Supercharging

Postoperative ischemia, leakage, and necrosis remain a problem with all kinds of conduits. According to the data presented in this review, the necrosis rate following COI was below 10%, but clinical leakages were observed more often, and perhaps at a higher rate than after gastric pull-up reconstruction. The use of preoperative angiography did not seem to influence ischemic complications,21 but securing adequate arterial supply and venous drainage (“supercharging”) by microvascular surgery may reduce the risk of conduit necrosis in selected cases.15,16,18,22 Probably due to the numbers needed, no prospective and randomized studies have compared the outcome after supercharged versus standard COI.

If a long-segment supercharged jejunal conduit is used for esophageal replacement, some institutions prefer to have an indicator flap created using the most proximal 2 to 3 cm of the jejunum. After externalization at the end of the procedure, this flap will allow continuous monitoring of conduit viability until patient discharge. One of the largest reported experiences with the use of long-segment supercharged jejunal conduits in cancer patients found a leak rate of 32%, graft loss in 8%, and a 90-day mortality rate of 10%.23 Again, there are no comparative data, but the surgical complexity of microvascular augmentation and the relative high leak rate and postoperative mortality after this kind
of jejunal interposition compared to COI data has limited this technique to selected patients.\textsuperscript{23,24}

**Operating time and blood loss**

Long operating time and a substantial blood loss may be a surrogate marker of both advanced cancer disease and a difficult surgical procedure—or a mixture of both. Operation time was not reported in half of the studies and intraoperative blood loss was only reported in 7 studies. Thus, even with a reported median operating time of 9 hours and a blood loss of 1100 mL, both parameters may be underestimated. This suggests that both the underlying disease as well as the complexity of the surgical procedure would apply to an esophageal resection followed by COI. No pattern was recognizable in terms of the number of patients operated, cancer type, location, choice of colon segment, or conduit route. The addition of a supercharging procedure may explain a longer operating time in some cases, but the rate and extent of such procedures were not recorded.

**Surgical complications**

As mentioned above, short-term complications linked to the COI procedure include graft ischemia and anastomotic leakage, while long-term complications include graft redundancy and anastomotic stricture. A review on data published before 2000, including both benign and malignant diseases, revealed leakage in 3\% to 10\% of the patients, strictures in 2\% to 46\%, and redundancy in up to 25\% of the cases.\textsuperscript{1} Briel \textit{et al}\textsuperscript{14} assessed the prevalence and risk factors for ischemia, leakage, and stricture and found that 7 out of 19 in-hospital-deaths were caused by short-term complications. One-third of patients with graft ischemia developed stricture and one-third anastomotic leakage. Half of the patients with leakage subsequently developed stricture. Patients with diabetes, chronic obstructive lung disease (COLD), or cardiovascular disease were more likely to develop graft ischemia.

Redundancy operations are scarcely mentioned, and only 7 of the 23 studies provided specific data on this topic (Table 3). DeMeester\textsuperscript{1} found that a long-term re-operation rate between 15\% and 38\% was mostly due to redundancy of the graft. However, the majority of patients with a redundancy problem had benign disease, thus indirectly suggesting that patients with a malignant indication for COI seldom live long enough to experience a late complication like redundancy. A very limited motility of the colon after interposition, and the ability to stretch over time may be part of the redundancy problem following COI.\textsuperscript{15} The redundant colon may be treated by resection and re-anastomosis, coloplasty, or side-to-side bypass. If severely dilated, the colonic graft may also be treated by a longitudinal anti-mesenteric stapled resection. The use of long-segment jejunal interposition seems to require fewer reoperations for redundancy\textsuperscript{23}; but as mentioned above, the majority of cancer patients will not live to experience this problem.

**Hospital and surgeon caseloads**

Although not addressed in national cohort studies, the present data (including our own data) raise the issue of sufficient COI caseload in hospitals and among gastroesophageal surgeons. A German survey revealed that less than 40\% of the centers performing esophagectomies did COI as well, and that reconstruction with COI was performed in 12\% of the recorded esophagectomies.\textsuperscript{25} A review of studies published before 2000 revealed COI hospital caseloads between 1 and 19 patients per year, but the median caseload was less than 4 patients per year.\textsuperscript{4} The figures are difficult to compare, but the present review of studies published between 1999 and 2017 did not show any increase in the annual hospital COI caseloads (median of 4 patients per year). It should be noted Briel \textit{et al}\textsuperscript{14} included 163 patients, but since the number of patients with malignant disease was not reported, we chose not to include this study in our analysis. Since a positive outcome of esophagectomy is related to a high surgeon volume\textsuperscript{26}, as well as for research reasons, COI surgery should probably be better organized and probably more centralized within the individual national settings. According to the published data, the caseload problem seems to be the same when a jejunal conduit is used for reconstruction.\textsuperscript{15}

**Quality of life (QoL) after COI**

QoL is reduced after esophageal resection.\textsuperscript{27} Long-term outcome after COI is important, but the data are limited. A recent retrospective study focusing on QoL in a group of long-term survivors (median follow-up of 13 years) found that the majority of these patients had no dysphagia, regurgitation, or heartburn, whereas early satiety was more prominent (40\%). Despite the potential bias when looking at a selected group of long-term survivors, it was
interesting to note that the QoL scores were at least at the level of the normal population. These observations suggest that COI should not be avoided on arguments of poor long-term outcome in patients who are expected to survive long-term after esophagectomy (e.g., benign or early stage malignant disease).

Numerous techniques and variations of COI have been suggested in order to provide a better short and long-term patient outcome, but few have been tested in relevant trials. Gastrocolic reflux is one of several postoperative problems that may influence QoL. A simple modification of the cologastric anastomosis creating a cologastric angle may reduce gastrocolic reflux to a minimum, and thereby reduce the negative impact of repeated reflux episodes on the QoL. Alternatively, the terminal ileum (i.e., ileocecal valve) may be included as mentioned above.

Data on the short- and long-term outcome after long-segment jejunal interposition is limited, and although the esophageal clearance may be higher following jejunal interposition, the rate of dysphagia, regurgitation, and reflux is probably similar to patients with COI reconstruction.

Overall morbidity and mortality after COI

The previous mentioned review of older and mixed studies published before 2000 reported an overall procedure related morbidity and mortality of 15% to 67% and 4% to 9%, respectively. In the present review covering data published after 1999, we found a morbidity of 22% to 90%, and both a 30 days and an in-hospital mortality of 0% to 17%. Again, comparison is difficult and should be avoided especially regarding morbidity, but the general improvement in surgical techniques and perioperative patient care over the past decades, seems to have had little impact on the reported outcome after COI. Some studies have tried to compare COI with traditional gastric pull-up, but the patients are probably not always comparable (e.g., the former patients may have more aggressive/extensive tumors) and there are no randomized studies.

COIs are accompanied with high postoperative morbidity rates, and most often occurring is postoperative respiratory complications (PRCs), dominated by pneumonia (20%–60%). Although being elicited by gastrointestinal surgery, PRC is associated with a high mortality as well as increased hospital length of stay. In our small study and in some of the reviewed studies (Table 3), PRCs were seen in about one-third to half of all patients. Risk factors for the development of pneumonia were age, male gender, active smoking, COLD, diabetes mellitus and transthoracic operative approach (as opposed to transhiatal). Operation time, BMI, and neoadjuvant therapy on the other hand were not identified as risk factors.

If given the opportunity to choose between the stomach and the colon for esophageal reconstruction, some papers argue that the colon is a better choice than the stomach, both regarding immediate complications and long-term functional outcome. However, it is important to emphasize that COI is most often used when there is no stomach available or when the stomach is involved in the cancer disease. Large-volume institutions (Table 3) seem able to provide excellent results even in complex COI surgery, and it would seem fair to conclude that COI may be performed with no significant additional morbidity or mortality provided the necessary surgical routine and relevant perioperative setup are present.

Limitations

This study was a retrospective single-center study with a small number of patients and a low annual caseload hospital COI caseload. The conclusions based on a review of the present literature should be cautioned by the lack of prospective and homogeneous data. The literature review was not “systematic” according to the general rule; however, both authors performed the extensive literature search and subsequent study evaluation.

Conclusion

COI is a complex technique that is necessary in a relative small group of selected patients after esophagectomy for cancer. The low caseload in the majority of centers suggests that centralization is warranted. Prospective and comparative studies with clear outcome definitions, long-term follow-up and patient reported outcome measures are lacking.

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