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Review

Frequency of Polyps and Adenocarcinoma in Colon Interposition After Esophagectomy in Adulthood – A Systematic Review

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Abstract. *Background/Aim: Colon interposition counts among the most common techniques for reconstruction after esophagectomy. Availability of data on metachronous mucosal pathologies is weak. The aim of this review was to identify all reports on the development of metachronous adenoma and adenocarcinoma in colon interposition after esophagectomy in adulthood. Materials and Methods: A comprehensive search was conducted in MEDLINE/PubMed, Science Direct, Cochrane Library, Bayerische Staatsbibliothek München. All studies reporting on patients who received colon interposition as substitute after esophagectomy in adulthood for benign and malignant reasons were included. Results: Five retrospective studies were included, reporting on 1016 patients. Therein, no interval lesion was identified. One further study, which formally must be excluded for a misfit to inclusion criteria reports on three interval carcinomas within 365 patients. Because these lesions were the only ones found within a cohort analysis, results were supplementary reported in this review. Additionally, 31 case reports including 32 patients with benign (n=7) or malignant (n=25) findings were analyzed. Median age was 63.5 years (interval carcinoma) and 69 years (benign lesion). Benign and malignant lesions were diagnosed after a median of 8.5 years. Conclusion: Due to the rareness of respective cohort studies, the frequency of metachronous lesions cannot be calculated accurately. The estimated rate of interval carcinoma is 0-0.22%. Life-long endoscopic surveillance of patients with colon interposition is recommended.*

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Esophagectomy with replacement by colon interposition was first described by Kelling and Vuillet in 1911 (1, 2). Since then, the colon developed into the most commonly used esophageal substitute if the stomach is not available for reconstruction (3). The majority of patients undergoing esophagectomy with colon interposition for malignant disease are older than 55 years and thereby at risk for the development of colonic polyps. Further, patients with adenocarcinoma of the esophagus showed a significantly higher risk for the occurrence of colonic polyps (4). Patients, who receive the interposition procedure for benign pathologies are relevantly younger in common, therefore their lifetime risk for the development of mucosal changes in the substitute is relatively higher. To date, no systematic review focuses on the rate of mucosal changes such as adenoma and adenocarcinoma in colon interposition in adulthood.

This review was performed to identify available evidence on the development of metachronous adenoma and adenocarcinoma in colon interposition after esophagectomy for benign (*e.g.* Boerhaave-Syndrom, trauma, corrosive injury) and malignant reasons (esophageal cancer) in adulthood.

Materials and Methods

Protocol and registration. The systematic review is based on a review protocol, designed in accordance to the PRISMA-P-Statement (5-7).

The protocol is registered with the PROSPERO International Prospective Register of Systematic Reviews as CRD42017082144.

Eligibility criteria. All studies (randomized, non-randomized, case series, case reports), reporting on patients who received colon interposition after esophagectomy for benign (*e.g.* Boerhaave-Syndrom, trauma, caustic injury) and malignant reasons (adenocarcinoma or squamous cell carcinoma of the esophagus) were eligible for data analysis. The search was not limited to a certain time frame. Studies had to be fully published, available as full text and written in English or German language.

Exclusion criteria. Exclusion from the analysis: colon interposition in children, abstract/full-text was not available, not in English or German language, review articles.

Information sources and search strategy. A bibliographic search was conducted in Medline/PubMed, Science Direct, Cochrane database and Bayerische Staatsbibliothek from 12-1-2017 to 4-1-2018. In two cases, authors were contacted for full text transfer. In 13 cases of older full-text articles, not available in one of the abovementioned databases, full-text articles were directly requested from editorial offices of the publishing journals. Combinations of the following terms were used: “polyp”, “interposition”, “colon” ("polyps"[MeSH Terms] OR "polyps"[All Fields] OR "polyp"[All Fields]) AND “interposition”[All Fields] AND ("colon"[MeSH Terms] OR "colon"[All Fields]). The PubMed similar articles function was used to extend potential hits. References of all eligible reports were screened for further information.

Study selection. Selection process. Three authors (SM, GF, PR) independently assessed titles and/or abstracts of all identified reports and excluded those considered irrelevant. Afterwards, full-text papers were screened on their accordance to inclusion criteria. One author (SM) extracted data from the included studies and a second (GF) checked extracted data. Disagreements were discussed and solved.

Data items. Data were extracted using the PICO-System (8, 9). The PICO tool focuses on the Population, Intervention, Comparison and Outcomes of scientific publications. It is used to identify components of clinical evidence within the literature. Additionally, the following items were extracted: first author, year of publication, study type, patient age, patient gender, underlying disease, intervention, main outcome measures, evidence of polyps and/or adenocarcinoma, interval between colon interposition and diagnosis of polyps/adenocarcinoma, evidence of colonic polyps/adenocarcinoma within preoperative colonoscopy, metastatic disease in case of carcinoma, therapy of polyps/adenocarcinoma prior to interposition, therapy of polyps/adenocarcinoma in interposition.

Risk of bias in individual studies. Risk of bias of non-randomized studies was assessed using the Newcastle-Ottawa Scale (NOS). NOS was designed as a quality assessment tool to evaluate both non-randomized cohort and case control studies. The quality of assessed studies was evaluated, using a star rating system. The overall maximum score was nine stars. The following domains were included: selection of study groups (maximum score: four stars), comparability of study groups (maximum score: two stars), ascertainment of exposures (for case control studies) or outcome of interest (for cohort studies) (maximum score: 3 stars) (10) (Table I).

Synthesis of results. A narrative synthesis of the results was performed since the number of cohort studies was too low for meta-analysis. Further, inclusion criteria as well as follow-up workflow and follow-up examinations were inhomogeneous.

Results

Study selection. Overall, 157 studies were screened for eligibility. Thereof, 72 records remained after exclusion of duplicates. After screening and full-text assessment, 37 records remained (case reports: n=31; non-randomized cohort studies: n=6). No randomized trials were identified according to the inclusion criteria. Six studies were excluded within the screening process and 29 more after full-text assessment (Figure 1, Table II).

Characteristics of cohort studies. Detailed study characteristics are depicted in Tables III and IV.

Study 1. In 1982, Akiyama and coworkers published data from a questionnaire-based national survey (9). Therein, 223 members of the Japanese society for Esophageal Diseases were asked to report on interval carcinoma within the substitute after esophagectomy. In 9.5% (n=617), colonic interposition was applied for intestinal reconstruction. In these cases, no carcinoma occurred. The authors did not indicate the time frame in which the abovementioned operations were performed. Moreover, it is not clearly described whether all patients were followed up consequently or if only symptomatic patients received further diagnostic work up (11).

Study 2. Eleftheriadis reported on a series of 13 patients who received colonic interposition after esophagectomy for benign disease from 1967 to 1983. Eight of them were available for endoscopic follow up, applied within an average time of 7.2 years after initial surgery. While endoscopic examination did not render relevant evidence of colitis, histologic samples of all but one patient showed microscopic changes: inflammation (n=6) and fibrosis (n=1). No cases of malignancy or pre-malignant adenoma were found (12).

Studies 3+4. Two studies by Isolauri *et al*. focused on both an isolated cohort of patients who received colon interposition for benign disease (Timeframe: 1964-1985) and a mixed cohort of patients with underlying malignant and benign pathologies (Timeframe: 1964-1985). According to the period of patient inclusion, the benign cohorts in both

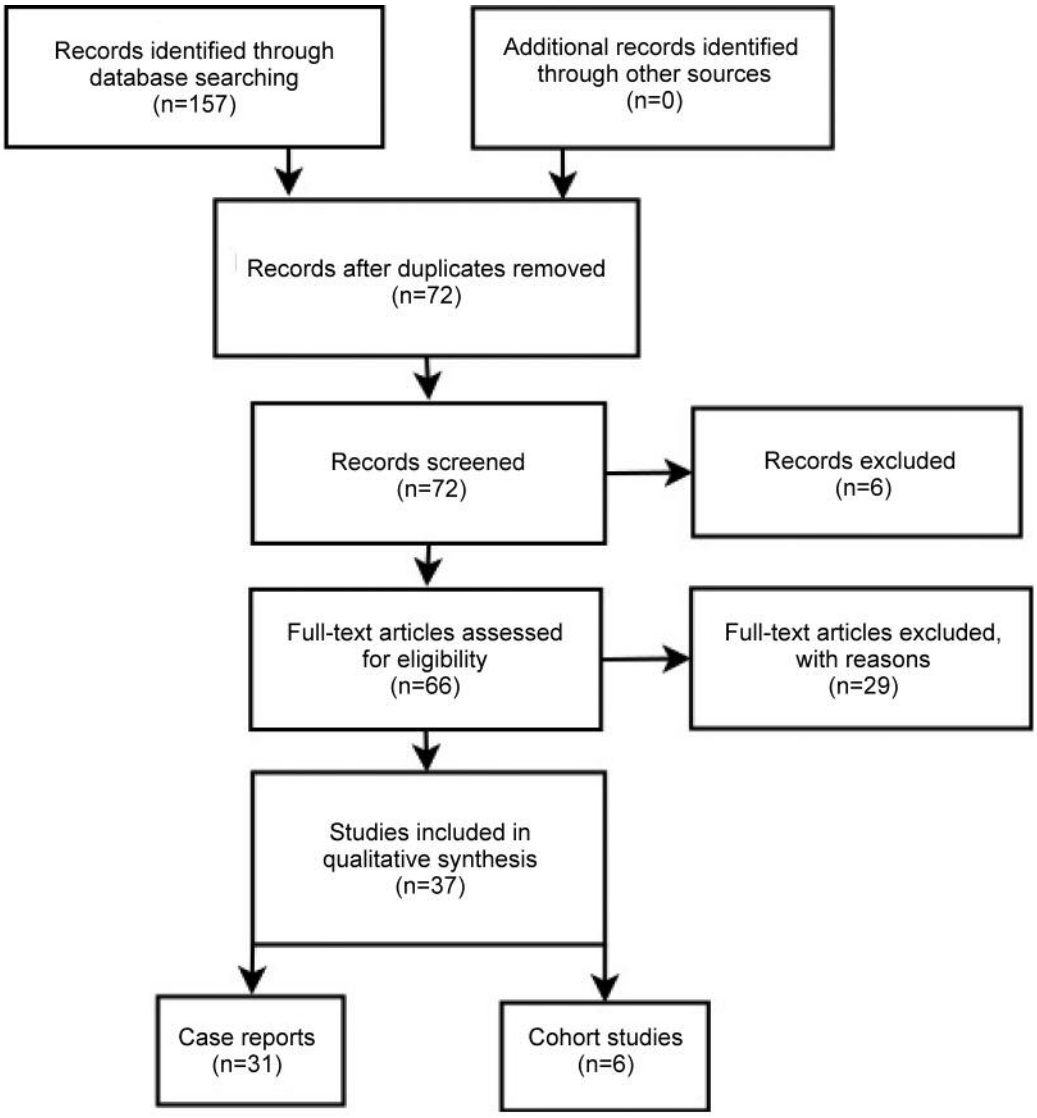

Figure 1. *PRISMA flow sheet*.

studies seem to be the same. Therefore, a certain overlap must be assumed within the results. Retrospectively, it is not possible to explain slight differences between both cohorts. All patients available for follow up underwent endoscopic examination of the interposition. Therein, the mucosa was evaluated macroscopically. Moreover, bacterial and fungal specimens were obtained. Overall, no graft-malignancies were found after a median follow up of 57 months, respectively 67 months in both studies. However, within the 1991 analysis, one carcinoma was found, classified as "recurrent carcinoma" and not as malignancy, originating from the interposition. Since no histopathologic analysis was available, this carcinoma could not be clearly assigned to the organ it originated from (13, 14).

Study 5. In 1996, Pompeo *et al*. published data on 100 consecutive patients having received esophagocoloplasty (13). Patients were divided into three groups: group A: congenital disease (n=22), group B: acquired benign lesions (n=36), group C: malignant disease (n=42). Out of the 42 patients belonging to group C only 5 survived more than 5 years. These patients were excluded from the analysis by the authors. Moreover, all patients with follow-up examinations of less than one year and two cases of late deaths were excluded (n=7). Thus, data from the 51 remaining patients were reviewed. A subdivision into pediatric (n=25) and adult (n=26) patients was made. The follow up rate was 100%. Due to inclusion criteria of the presented study, only information on adult patients was included into the analysis. Within the

Table I. *Newcastle-Ottawa Scale for assessing the quality of nonrandomized studies.*

		Selection				Comparability	Outcome assessment			
Author	Year	1	2	3	4	5	6	7	8	Score (max 9 Stars)
Akiyama	1982	*	*	*	*	**	-	-	-	6
Eleftheriadis E	1987	*	-	*	*	-	*	-	*	5
Isolauri	1988	*	-	*	*	-	*	*	*	6
Isolauri	1991	*	-	*	*	-	*	*	*	6
Pompeo	1996	*	-	*	*	-	*	*	*	6
Jeysingham	1999	*	-	*	*	-	*	*	*	6

Table II. *Excluded studies with reasons for exclusion.*

Author	Year	Reason for exclusion
Jayes P	1957	Carcinoma in a skin tube reconstruction
Hanna EA	1967	Analysis of postoperative function, no endoscopic follow-up, no information on primary or secondary outcome parameters
Mullen DC	1970	No structured follow-up, no endoscopic follow-up, no information on primary or secondary outcome
Stephens H	1971	No endoscopic follow-up
Harvey JG	1979	Report on postoperative fibrosis of the interposition, no information on primary or secondary outcome parameters
Wilkins EW	1980	No endoscopic follow-up, no information on primary or secondary outcome parameters
Hankins JR	1984	Analysis of postoperative function, no endoscopic follow-up, no information on primary or secondary outcome parameters inclusion of adults and children
Larson TC 3rd	1985	No endoscopic follow-up, no information on primary or secondary outcome parameters
Wetstein L	1988	Letter to the editor, no original case report
Paris F	1991	No structured endoscopic follow-up, no information on primary or secondary outcome parameters, follow-up on postoperative function
Theile	1991	Double publication of one single case
Lindahl H	1992	Follow-up of interposition in children
Cerfolio RJ	1995	No structured endoscopic follow-up, no information on primary or secondary outcome parameters
Mansour KA	1997	No endoscopic follow-up, no information on primary or secondary outcome parameters
Del Rosario MA	1998	Colon interposition in children
Jung	1999	Esophageal Cancer
Fürst H	2001	No follow-up, no information on primary or secondary outcome parameters
Kotsis L	2002	No structured endoscopic follow-up, no information on mucosal changes within the cohort
Popovici Z	2003	No structured endoscopic follow-up, no information on primary or secondary outcome parameters, follow-up postoperative function
Novotny AR	2005	Adenocarcinoma in a skin tube reconstruction
Martín MA	2005	Not written in English
Hwang HJ	2007	Double publication of a single case in two journals
Knezevic JD	2007	No structured endoscopic follow-up, no information on primary or secondary outcome parameters, long term follow-up focusing pattern of swallowing an eating, weight gain, presence of aspiration, quality of life
Beaton MD	2008	Rectal cancer in FAP, no carcinoma in colonic interposition
Dhir	2008	Report on patients with colonic interposition in the neonate period
Chirica M	2010	No mucosal changes within the cohort, endoscopic follow-up on a symptom-based indication
Klink	2010	No structured endoscopic follow-up, no information on primary or secondary outcome parameters
Elshafei H	2012	Colon interposition in children
Yeo MS	2016	Letter to the Editor, no original data on the disease

endoscopic follow up, no cases of interval carcinoma in the interposition were found. Since a differentiation between group A and B was not given in regard to benign interval lesions, those were not included in the review (15).

Jeyasingham *et al.* (14) reported on two cases (0.6%) of adenocarcinoma at the cologastric junction and one case of adenocarcinoma of the interposed colon (0.3%) within a cohort of 365 patients who survived hospital stay after

Table III. *PICOS question for cohort studies*.

Author	PICOS					
	Patient/ Population	Intervention	Comparison	Outcomes	Study design	Median Follow-up (month)
Akiyama (1982)	Adult patients after esophagectomy for benign and malignant disease	Esophageal replacement by colon	Esophageal replacement by stomach, skin or other	Interval carcinoma in the esophageal replacement	Retrospective, questionnaire-based survey	Not mentioned
Eleftheriadis (1987)	Adult patients after esophagectomy for benign disease	Replacement Replacement by colon	None	Mucosal changes in interposed colon by endoscopy	Retrospective (Follow-up: prospective)	86.4 (12-156)
Isolauri J (1988)	Adult patients after esophagectomy for benign disease	Esophageal replacement by colon	None	Mucosal changes in interposed colon by endoscopy	Retrospective (Follow-up: prospective)	67 (5-180)
Isolauri J (1991)	Adult patients after esophagectomy for benign and malignant disease	Esophageal replacement by colon	None	Mucosal changes in interposed colon by endoscopy	Retrospective (Follow-up: prospective)	57 (5-180)
Pompeo (1996)	Consecutive patients after esophagectomy	Esophageal replacement by colon	None	Results after esophagocoloplasty	Retrospective	6.6 (1-12)
Jeyasingham (1999)	Adult patients and children who survived immediate postoperative hospital stay after esophagectomy for benign disease	Esophageal replacement by colon	None	Functional and mechanical problems after esophageal replacement by colon interposition	Retrospective	(84-456) (median not mentioned)

esophagectomy with colon interposition for benign reasons. The cohort consisted of pediatric and adult patients and was therefore formally excluded from the analysis, because allocation of respective cases to the adult or pediatric cohort was not completely comprehensible. Because the described interval carcinomas are the only ones reported in the context of a cohort study and not as single case reports or case series, we decided to report on the analysis even though it did not accurately fit our inclusion criteria (16).

Overall, five retrospective cohort studies by four authors were included in the analysis, reporting on 1016 patients. Therein, no case of an interval carcinoma or premalignant adenoma was diagnosed in the interposed colon. Adding results of Jeyasingham to the analysis, interval carcinoma would have been detected in 0.22% of analyzed patients.

Risk of bias within studies. Per protocol, the risk of bias within retrospective studies was assessed, using the Newcastle-Ottawa scale (10). No study was rated with the highest possible score of 9 stars (Table I).

Characteristics of case reports. Overall, 31 case reports including 32 patients who developed benign or malignant interval pathologies within their colon interposition were identified (17-47). Baseline characteristics and findings of the specific lesions are depicted in Table V. Therein, reports on benign (n=7) and malignant (n=25) findings are presented separately. Median age was 63.5 years (range=18-80 years) in patients with interval carcinoma and 69 years (range=60-73 years) in cases of benign lesions of the interposition. Carcinomas as well as benign lesions of the interposition were diagnosed after a median of 8.5 years (7 months to 55 years in cases of malignant findings, 1 to 16 years in cases of benign findings). Information on endoscopic findings of the colon before being used as interposition were only available in one report, showing an adenomatous polyp. Underlying disease leading to esophagectomy was malignant in 42.9% of cases with benign interval lesion and in 52% of reports on interval carcinoma.

Discussion

Esophageal replacement using the colon is one of the most common techniques of reconstruction after esophagectomy for both benign and malignant diseases. In general, the colon is proven to be a long lasting and well fit substitute, showing excellent postoperative function as well as alimentary satisfaction and quality of life (3, 48). However,

Table IV. *Characteristics of cohort studies.*

Author	Benignant (n)	Malignant (n)	Finding at follow-up examination	Interval carcinoma (n)	Follow-up, n (%)	Time to interval adenoma/ carcinoma	Results after therapy of interval pathology
Akiyama (1982)	35	582	-	0	Not indicated	-	-
Eleftheriadis (1987)	13	0	Microscopic inflammation (n=6); fibrosis (n=1)	0	8 (61.5)	-	-
Isolauri (1988)	60	0	Macroscopic colitis (n=6); inflammatory polyp (n=1), evidence of candida (n=23)	0	41 (68.3)	-	-
Isolauri (1991)	60	248	Macroscopic inflammation (n=5); hyperanemia and friability (n=2)	0	36 (11.7)	Not mentioned	Not mentioned
Pompeo (1996)	Acquired: n=36; congenital: n=22	42	Proximal anastomosis stenosis (n=18), Distal anastomosis stenosis (n=1), Esophagitis (n=1), Stasis due to redundancy (n=5), Stasis due to pylorospasm (n=1), Peptic colitis (n=2), Anastomotic ulcus (n=1)	0	51%	-	-
Jeyasingham (1999)	365	-	Colo-bronchial fistula (n=2), Colo-cutaneous fistula (n=2), Diaphragmatic herniation (n=3), Pseudodiverticulosis (n=2), Redundancy of the colonic segment (n=17), Adenocarcinoma of the cologastric junction (n=2); Adenocarcinoma of the interposed colon (n=1)	3	100%	Carcinoma of the cologastric junction: 14 and 17 years No information on the case of adenocarcinoma of the interposition	Not mentioned

apart from functional issues, mucosal pathologies of the interposition have been described but are yet to be systematically assessed. Therefore, we performed the presented systematic review.

According to data extracted from the included cohort studies, the risk of interval lesions was found to be extremely low. With inclusion criteria applied strictly, a rate of 0% can be calculated from a cohort of 1016 patients. Beyond this, 7 case reports present data on benign interval lesions and 25 report on interval carcinoma in the esophageal substitute. In this context, a certain risk of mucosal changes must be estimated. Characteristics given by the analyzed case reports are all limited to the index case. Information on the total cohort of esophagectomies with consecutive interposition of the colon from the respective institution is lacking. Since the overall number of operations is not known, calculation of the occurrence risk of metachronous lesions is not possible. According to the presented data, the development of mucosal changes takes several years, showing a median of 8.5 years after index operation. A potential rearrangement of the mucosal microbiota following the positional change of the colon, with respective alteration of mucosal resistance may be assumed. Yet, no experimental studies report on this thesis. However, the interposed colon is exposed to an altered dietary composition as well as to potential gastric and biliary reflux in the distal part of the substitute. These aspects potentially facilitate the additional development of mucosal changes (14, 49). Improved diagnostic techniques as well as the improvement of perioperative (neoadjuvant and adjuvant) therapies lead to earlier detection and a significantly higher rate of long-term survival in patients suffering from esophageal cancer (37). Moreover, patients operated for benign disease have no relevant limitations of their life expectancy in case of survival of the acute postoperative phase and adequate anastomotic healing. Consecutively, a theoretical risk of mucosal interval pathologies exists in both groups. Moreover, evidence was found, that patients, suffering from esophageal cancer are at

Table V. *Case reports*.

Author	Year	Age	Gender	Underlying disease	Initial operation	Findings at follow-up endoscopy within the interposition	Histology	Time between initial operation and interval-lesion (years)	Eendoscopic therapy	Surgical therapy
Benign interval lesion										
Szántó (17)	1981	65	M	Mechanic esophageal stenosis after tube insertion	PE	5 mm polyp (6 cm aboral of the anastomosis)	Adenoma	1	EMR	No
Kovacs (18)	1997	66	M	Inflammatory Recurrent esophageal stricture	PE	Two sessil polyps	TA without dysplasia	13	EMR	No
Altomare (19)	2006	64	M	ACE	PE	6 mm polyp 3 cm proximal to the colonic-gastric anastomosis	TA	2	EMR/ Polypectomy	No
Tanno (20)	2010	73	M	Carcinoma of the esophagus (no information on histopathology)	TE	Laterally spreading tumors	TA, HGIN	16	EMR	No
Ramage (21)	2012	63	F	Iatrogenic perforation after Fundoplicatio	TE	2 polyps	TA, LGIN	UK	EMR	No
Ramage (21)	2012	65	M	Carcinoma of the esophagus (no information on histopathology)	TE	1 cm polyp	Tubovillous adenoma, LGIN	UK	EMR	No
Ng (22)	2016	60	M	Extrahepatic portal hypertension	TE	1 polyp and a mass	TA, LGIN	13	No	No
Malignant interval lesion										
Goldsmith (23)	1968	51	F	Epidermoid carcinoma	TE	Esophagram: 5×3 cm filling polypoid defect	AC	2	No	Segmental resection of the interposition
Licata (24)	1978	40	M	CI	TE	Friable mass	Colonic AC	11	No	No
Haerr (25)	1987	72	M	SCC	TE	Primary adenocarcinoma of the interposed colon	AC	9	No	No surgical therapy due to infiltration of the sternum
Houghton (26)	1989	64	M	Benign esophageal stricture	PE	Polypoid “neo-esophageal“ growth	AC	20	No	Resection of the interposition with gastric interposition
Theile (27)	1991	55	M	Adenocarcinoma of the gastro-esophageal junction	TE	Colonic adeno-carcinoma in the interposition	AC	13	No	Segmental resection of the interposition, colo-jejuno-stomy
Lee (28)	1994	75	F	SCC	Pharyngola-rygectomy	Tight structure at the upper part of the colonic graft with a luminal diameter of 1 mm	AC	20	No	Colonic graft resection

Table V. *Continued*

Table V. *Continued*

Author	Year	Age	Gender	Underlying disease	Initial operation	Findings at follow-up endoscopy within the interposition	Histology	Time between initial operation and interval-lesion (years)	Eendoscopic therapy	Surgical therapy
Altorjay (29)	1995	65	M	Grave esophagitis	Distal esophagectomy, esophago-colo-gastrostomy	Carcinoma of the interposed colon	AC	7	No	*En bloc* resection of the interposition with stomach and spleen, restoration by Roux-en-y esophago-jejunostomy
Fritscher-Ravens (30)	1999	62	F	SCC	Transhiatal esophagectomy	3-cm sized proliferative tumor with induration and infiltration at the base	AC	0.58	EMR	Segmental resection with end-to-end anastomosis 6 weeks after endoscopy
Goyal (31)	2000	78	M	AC	Distal esophagectomy and total gastrectomy	3.5-cm diameter, non-obstructing infiltrative growth in the interposed colon approximately 5 cm distal to the esophago-colic anastomosis	Colonic AC	10	No	Segmental resection of the interposition
Liau (32)	2004	49	M	Carcinoma of the esophagus (no information on histo-pathology)	TE	Ulcerative mass in the colonic conduit	Colonic AC	30	No	No
Hsieh (33)	2005	18	M	CI	PE	Large erosional lesion 20 cm from the incisor	Colonic AC	37	No	Resection of the interposition with cervical esophagostomy
Hwang (34)	2007	60	F	CI	TE	Six polyps within the colon interposition (3-5 mm)	Intramucosal AC	40	EMR	no
Kuwabara (35)	2008	68	F	Adenocarcinoma of the stomach	TE	Mass arising at the upper end of the colonic graft	Colonic AC	9	No	Segmental resection of the interposition
Lin (36)	2008	74	F	Carcinoma of the esophagus (no information on histopathology)	TE	Irregular, ulcerative, circumferential mass located in the lower part of reconstruction colon	AC	33	No	Segmental resection of the interposition
Bando (37)	2010	80	M	SCC	TE	Laterally spreading tumor of granular type, 20 mm diameter	Intramucosal AC	14	ESD	No

Table V. *Continued*

Table V. *Continued*

Author	Year	Age	Gender	Underlying disease	Initial operation	Findings at follow-up endoscopy within the interposition	Histology	Time between initial operation and interval-lesion (years)	Eendoscopic therapy	Surgical therapy
Kia (38)	2012	76	M	ACE	TE	2 small polyps just proximal to the colo-gastric anastomosis+ a larger 4-cm sessile polyp 10-cm distal to the upper esophageal sphincter	AC	15	EMR	No
Shersher (39)	2011	60	M	Benign esophageal stricture	TE	Adenocarcinoma obstructing 40% of the graft lumen, 25 from the incisor teeth	AC	40	No	Resection of the interposition, Ivor-Lewis esophago-gastric anastomosis
Kim (40)	2012	70	F	CI	TE	3-cm ulcerative, extruding mass with friable mucosa, no obstruction in the mid portion of the interposition	AC	47	No	No
Spitali (41)	2012	66	M	ACE	Total esopha-gectomy	Circumferential mass arising from the colon	Colonic AC	2	No	Resection of the ileocecal part of the interposition
Sikorszki (42)	2012	75	F	CI	Bypass of the stenotic eso-phagus in two sessions using the ileocolon presternally a ugmented by a skin tube	No endoscopic finding; exulcerating lesion in the collar region	Colonic AC	44	No	Segmental resection of the interposition
Aryal (43)	2013	60	M	CI	PE	4×3-cm ulcerated mass in the colonic esophagus	Colonic AC	30	No	No
Grunner (44)	2013	59	F	Anastomotic stricture after proximal gastre-ctomy for ulcer	PE	Ulcerated lesion obstructing the distal interposed colon	Colonic AC	55	No	Segmental resection of the interposition
Tranchart (45)	2014	66	M	CI	TE	3-cm non-obstructive tumor in the colon interposition	Colonic AC	19	No	No
Cheng (46)	2015	40	F	CI	PE	Esophageal tumor in the colonic interposition 27 cm from the incisors	Colonic AC	15	No	No
Kröner (47)	2015	67	M	ACE	TE	8×5-cm mass at the colonic interposition with partial occlusion	No information on histological findings, macroscopical characteristics of malignancy	10	2×SEMS	No

SCC: Squamous cell carcinoma; ACE: adenocarcinoma of the esophagus; AEG: adenocarcinoma of the esophago-gastric junction; CI: caustic injury; TE: total esophagectomy; PE: partial esophagectomy; UK: unknown; HGIN: high grade intraepithelial neoplasia; LGIN: low grade intraepithelial neoplasia; TA: tubular adenoma; AC: adenocarcinoma; EMR: endoscopic mucosa resection; ESD: endoscopic submucosal dissection; SEMS: self-expanding metal stent.

higher risk for colonic lesions such as adenoma and carcinoma (4, 50). In this context, the need for a structured endoscopic follow up must be highlighted. According to current international guidelines, follow-up colonoscopy for colorectal cancer screening is recommended 10 years after the first screening colonoscopy without pathologic findings (51). The risk of interval pathologies after colonic interposition, derived from included cohort studies, is extremely low. However, following the authors' personal opinion, follow up endoscopy should be applied within a closer interval, such as five years, even if preoperative colonoscopy was without pathologic findings and no risk factors were identified, as suggested by Imperiale and coworkers (52). Moreover, it has been previously shown before, that patients with adenocarcinoma of the esophagus have a significantly higher risk for the occurrence of colonic polyps (4). Because interval lesions are typical late complications and the risk increases over a longer time after index surgery, a life-long endoscopic follow-up must be postulated. In addition, the individual risk can be assessed by anamnestic factors such as colitis, history of colonic polyps, positive family history for colonic carcinoma (43). Positive information should lead to a closer follow-up interval. In addition, it is of significant importance to perform preoperative colonoscopy before using the colon as esophageal substitute.

Limitations

The presented systematic review is biased by the lack of randomized and structured prospective observational trials. None of the included cohort studies was rated with the full score of nine stars according to the Newcastle-Ottawa scale. This study is thereby at risk of being biased by the relatively low quality of these studies (*e.g.* lack of controls, short period of structured follow up, symptom-based follow-up). Data, extracted from case reports are all limited to the index case and give no information on the whole cohort. In this context, no risk calculation was possible.

Authors' Recommendations

The risk for pre-malignant and malignant interval pathologies within the colon interposition is extremely low. Therefore, the authors of the present review recommend:

- Preoperative assessment of the risk of development of colonic neoplasia;
- Standard preoperative colonoscopy;
- Lifelong endoscopic assessment of the interposed colon within an interval of five years;
- Adjustment of follow-up endoscopy to the individual's risk, preoperative endoscopic findings within the colon and potential interval pathologies.

Conclusion

In conclusion, esophageal substitute by parts of the colon is associated with a low but important risk of mucosal interval pathologies such as adenoma and carcinoma. This may be caused by the positional change of the colon as well as by individual risk factors. Therefore, preoperative endoscopic assessment of the colon must be strictly claimed, as well as a structured and life-long endoscopic follow up of the interposition. To date, no randomized trials or structured prospective observational studies are available on this topic. Overall, the available evidence is relevantly low, wherefore further investigations are of significant importance.

Conflicts of Interest

The Authors have no conflicts of interest to declare regarding this study.

Authors' Contributions

MS and PR designed the review, wrote the manuscript and analyzed results of literature research, AA revised the review and screened full text articles, ST did literature research and selected studies as well as data items, CM did literature research and selected studies as well as data items, FG did literature research and selected studies as well as data items, AH did native revision of the manuscript and designed the review together with MS and PR, JP revised the design and the manuscript, FA reviewed full text articles and selected data items. All Authors finally revised and approved the manuscript and agreed to be accountable for all aspects of the review.

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