



Duodenogastric Reflux after Esophagectomy and Gastric Pull-up: The Effect of the Route of Reconstruction

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Abstract. Duodenogastric reflux (DGR) is a common sequel of subtotal esophagectomy and gastric pull-up, and it may contribute to mucosal changes of both the gastric conduit and the esophageal remnant. This study investigated the effect of the route of reconstruction on the DGR. 24-hour ambulatory bilirubin monitoring was performed on patients who underwent transhiatal subtotal esophagectomy and a gastric tube interposition either in the posterior mediastinum (PM group, $n = 11$), or in the retrosternal space (RS group, $n = 8$): A Control group of 8 healthy volunteers was also studied. The median percentage of reflux time, the median number of reflux episodes, and the median number of reflux episodes longer than 5 minutes, in PM versus RS groups, were 29.1% versus 0.15% ($p < 0.001$), 185 versus 8 ($p = 0.002$) and 10 versus 0 ($p = 0.001$), respectively. The values of the above variables in PM versus control groups were 29.1% versus 3.95% ($p = 0.007$), 185 versus 21 ($p = 0.02$), and 10 versus 2 ($p = 0.009$), respectively, whereas in RS versus control groups they were 0.15% versus 3.95% ($p = 0.01$), 8 versus 21 ($p = 0.04$), and 0 versus 2 ($p = 0.05$), respectively. Posterior mediastinal gastric interposition is associated with high reflux of duodenal contents, whereas retrosternal interposition minimizes the reflux at levels even lower than those of the healthy individuals. The latter type of reconstruction may be a good alternative from that perspective, especially in patients with long life expectancy.

Stomach is considered the “gold standard” as an esophageal substitute after esophagectomy [1]. Although the whole organ can be used, the most suitable approach for reconstruction is the formation of a gastric tube by resection of the lesser curvature [1]. The substitute can be placed in the posterior mediastinum or in an extra-anatomical—most commonly retrosternal—position [2]. Extra-anatomical esophageal reconstruction offers the advantage that a recurrent intrathoracic locoregional tumor mass will not invade the neo-esophagus [3, 4]. In addition, an extra-anatomical gastric interposition may also be used to bypass a corrosive esophageal injury.

Duodenogastric reflux (DGR) is a common pathophysiological sequel of gastric pull-up and reflux symptoms adversely affect the quality of life of these patients [4–10]. Furthermore, there is

evidence that the duodenal contents are noxious and may, in the long term, cause mucosal changes both to the gastric conduit and the esophageal remnant [10–12].

Especially when longer survival is expected, it is of great significance to take into account the functional results of the substitute and the route of transposition. The aim of the present study was to investigate the effect of the route of esophageal reconstruction on (DGR).

Patients and Methods

We carried out bilirubin monitoring with the ambulatory fiber-optic spectrophotometer *Bilitec 2000* (Synectics Medical, Stockholm, Sweden) in two groups of patients and one control group of healthy volunteers matched in age and sex. This method has historically been considered the most reliable for detection of duodenal reflux in the clinical setting [13–15]. In fact, the test detects the presence of bilirubin that is the major pigment of bile, and this provides indirect information for the presence of duodenal refluxate. The posterior mediastinal (PM) group consisted of 11 patients with esophageal carcinoma who underwent transhiatal subtotal esophagectomy and gastric tube interposition in the posterior mediastinum. The retrosternal (RS) group consisted of eight patients with esophageal carcinoma who underwent transhiatal subtotal esophagectomy and gastric tube interposition in the retrosternal space. The decision on the selection of the route of reconstruction was made during the procedure and was based on the extent of the esophageal resection. After complete resections (R0), the gastric conduit was placed in the posterior mediastinum, whereas after incomplete resections (R1 and R2), it was placed retrosternally.

The transhiatal subtotal esophagectomy was performed in a standard manner. The patient was placed in the supine position with the neck extended and the head turned toward the right. After a midline abdominal incision, the greater omentum was mobilized from the transverse colon and the lesser sac was entered. The greater curve of the stomach was dissected, and the right gastroepiploic artery was carefully preserved. The short gastric vessels were divided. Dissection of the celiac axis was

Table 1. Characteristics of subtotal esophagectomy groups

	PM group	RS group	PM vs. RS*
Age	63 (42–77)	63.5 (54–74)	NS
Male:female	8:3	6:2	–
Units of blood transfused	0.0 (0–3)	0.5 (0–3)	NS
Operative time (min)	125 (95–155)	140 (100–175)	NS

*Mann–Whitney *U*-test.

NS: not statistically significant difference.

PM: posterior mediastinum; RS: retrosternal space;

subsequently performed, with division of left and right gastric vessels and meticulous lymph node clearance. The stomach was then divided with linear stapler devices and a gastric tube was fashioned. The stapling line was oversewn. No pyloric drainage procedure was performed. A cervical incision followed, across the medial border of the left sternocleidomastoid muscle. The cervical esophagus was dissected and divided. Subsequently, blunt bimanual dissection and mobilization of the esophagus from the adjacent thoracic structures was performed. After removal of the specimen, the gastric conduit was pulled up to the neck, usually through the posterior mediastinum. Alternatively, if the esophageal resection was not considered radical, a retrosternal tunnel was created for placement of the conduit. The esophagogastric anastomosis in the neck was always hand sewn in one layer. In the case of the retrosternal conduit, the mastoid origin of the sternocleidomastoid muscle was divided, and the muscle was mobilized and placed behind the anastomosis in order to obliterate the entrance of the posterior mediastinum. Drains were inserted in both the cervical and the abdominal sites. A feeding jejunostomy was always performed. Enteral feeding was started on the second postoperative day. On the eighth postoperative day a gastrografin swallow was performed, and if this was normal, oral intake was allowed.

The characteristics of each esophagectomy group are demonstrated in Table 1. The control group consisted of eight healthy volunteers (six men and two women, median age 60 years) without reflux symptoms and with normal findings on upper gastrointestinal endoscopy and on esophageal manometry.

Individuals with a history of cholecystectomy were excluded from the study, as it remains controversial whether cholecystectomy is associated with increased bile reflux into the stomach [16, 17].

Only patients who had an uneventful postoperative recovery were recruited, and all measurements were carried out within 3–6 months from the operation when the patients had returned to normal activities. Informed consent was always obtained.

The *Bilitec 2000* (Synectics Medical, Stockholm, Sweden): is an optoelectronic instrument including a fiberoptic probe and a portable unit capable of monitoring the presence of bilirubin in the foregut lumen over a 24-hour period. The distal tip of the probe contains a 2-mm space through which fluids can flow. The portable unit contains two light-emitting diodes, one having a wavelength of 470 nm (i.e., close to the absorbance peak of bilirubin at 453 nm) and the other of 565 nm (reference signal). Optical signals reflected back by the probe are converted into electrical impulses by a photodiode, and a microcomputer calculates the difference between the absorbance at 470 nm and that at 565 nm. This difference is commonly called the *absorbance*

value, and it may range from 0 (plain water) to 1 (total screen), but the working range of the instrument has been shown to extend from 0.14 to 0.60 only [13].

In the present study, after calibration of the instrument, the probe was inserted transnasally under local anaesthesia and guided with fluoroscopy. The tip of the probe in the control group was placed 5 cm above the esophagogastric junction, and in the patient groups it was placed accordingly. All medications that might alter motility and gastrointestinal secretion were suspended (i.e., histamine antagonists and prokinetic agents at least 48 hours and proton pump inhibitors one week prior to the test). All participants were advised to eat three standardized meals per day, which were composed of nutrients that could not significantly interfere with bilirubin detection (water, milk, white cheese, boiled chicken breast, boiled potatoes, white bread, banana, and apple). Alcohol and smoking were also prohibited. Participants were asked to record the time and duration of meals as well as the duration of time spent in the supine position. They were also asked to note occurrence of reflux symptoms.

A mean sampling time of 8 seconds was selected in all cases. At the end of the 24-hour study, the probe was removed and data were downloaded and analyzed with the *EsopHogram* software (Gastro soft Inc, Dallas, TX). In all cases in the present study an absorbance value of 0.14 was used as the threshold for reflux episodes. The software calculates the percentage of time that absorption of bilirubin is >0.14 units during the total monitoring time as well as during the subset periods of monitoring-i.e., upright, supine, meal, and postprandial. The software also calculates, for the same periods, the total number of episodes and the number of episodes longer than 5 minutes. To eliminate any possible false-positive results from food interference, the fasting period was calculated and included in the analysis. This period equals the total period of monitoring minus the meal and the postprandial periods [18, 19].

Statistical analysis was performed by software SPSS 11.0.1 for Windows (Chicago, IL, USA). For statistical comparisons of the data, the Mann-Whitney *U*-test was used as appropriate, and a *p* value of <0.05 was considered significant.

Results

Median, minimum, and maximum values were calculated for every variable in all groups. The median percentage of reflux time, the median number of reflux episodes, and the median number of reflux episodes longer than 5 minutes, in PM and RS groups, were 29.1% versus 0.15% ($p < 0.001$), 185 versus 8 ($p = 0.002$), and 10 versus 0 ($p = 0.001$), respectively. Likewise, the differences between the two groups of patients were statistically significant through all the subset periods of monitoring (upright, supine, meals, postprandial, and fasting).

Each group of patients was also compared to the control group. The median percentage of reflux time, the median number of reflux episodes, and the median number of reflux episodes longer than 5 minutes, in the PM and control groups were 29.1% versus 3.95% ($p = 0.007$), 185 versus 21 ($p = 0.02$), and 10 versus 2 ($p = 0.009$), respectively. The median percentage of reflux time, the median number of reflux episodes, and the median number of reflux episodes longer than 5 minutes in the RS and control groups were 0.15% versus 3.95% ($p = 0.01$), 8 versus 21

Table 2. Percentage time that absorption of bilirubin >0.14 units

	PM group	RS group	Control group	PM vs. RS*	PM vs. control*	RS vs. control*
Total	29.1 (0.1–76.2)	0.15 (0–2.3)	3.95 (0.5–9.9)	$p < 0.001$	$p = 0.007$	$p = 0.01$
Upright	8.6 (0.2–65.0)	0.1 (0–4.6)	4.85 (0–21.1)	$p < 0.001$	NS	$p = 0.03$
Supine	28.2 (0–89.7)	0 (0–1.3)	0.4 (0–4.7)	$p = 0.002$	$p = 0.009$	NS
Meal	16.8 (0–59.9)	0 (0–16.9)	3.25 (0–39.8)	$p = 0.004$	NS	NS
Postprandial	20.9 (0–86.3)	0 (0–2.9)	1.4 (0–42.10)	$p = 0.001$	NS	NS
Fasting	30.6 (0.23–73.10)	0.05 (0–1.1)	3.35 (0–8.95)	$p < 0.001$	$p = 0.003$	$p = 0.03$

*Mann-Whitney *U*-test.

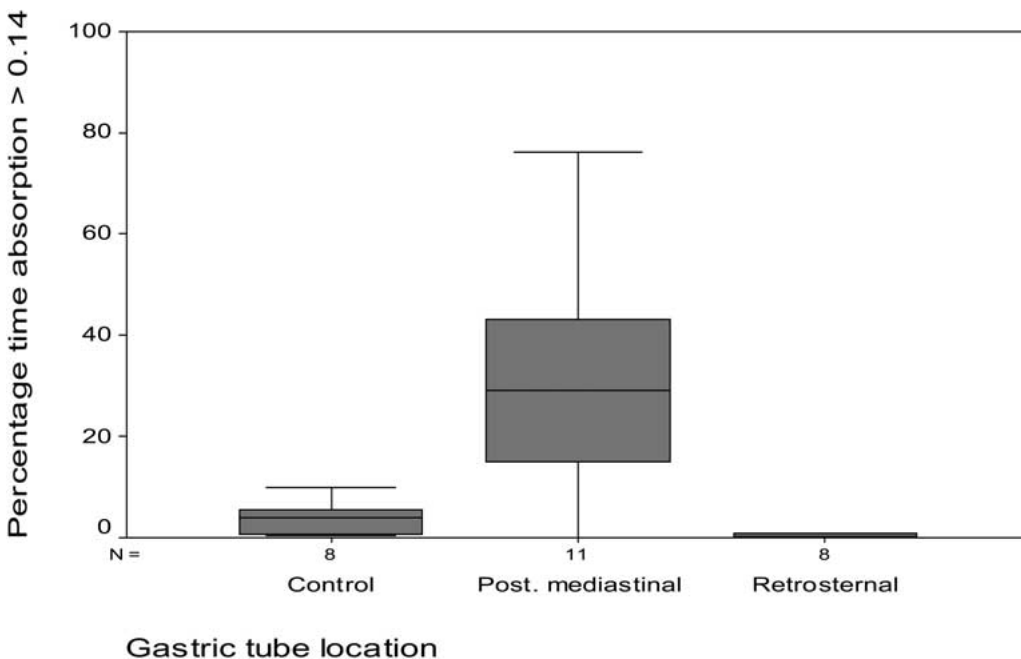


Fig. 1. Box plot of the percentage time that bilirubin absorption was >0.14 units. The retrosternal group had significantly lower time of exposure to bile compared to the posterior mediastinal group ($p < 0.001$) and the control group ($p = 0.01$). Horizontal bars denote median and range.

($p = 0.04$), and 0 versus 2 ($p = 0.05$), respectively (Tables 2 and 3).

Figures 1–3 show the plotted values of the above variables in all three groups. The 24-hour ambulatory bilirubin monitoring showed that exposure of the esophageal substitute to bile was significantly higher after posterior mediastinal gastric tube interposition than after retrosternal interposition. This referred both to the duration and to the number of reflux episodes. Comparison of both groups of patients to the control group of healthy volunteers showed that anatomical interposition is associated with very high exposure of the gastric conduit to bile, whereas retrosternal interposition minimizes the exposure to bile at levels even lower than in the healthy individuals.

No differences were found between the PM and RS groups with regard to perioperative blood transfusions and operating time (Table 1).

Seven patients from the PM group (63.6%) and two from the RS group (25%) noted occurrence of reflux symptoms. In patients with reflux symptoms, the percentage of reflux time, the number of reflux episodes, and the number of reflux episodes longer than 5 minutes were found to be significantly higher during all the periods of monitoring (Tables 5–7). Figures 4–6 show the plotted

values of the above variables in symptomatic and asymptomatic patients.

Discussion

Duodenogastric reflux is a common pathophysiological sequel after esophagectomy with gastric conduit reconstruction [4–10]. Postprandial discomfort, bilious eructations, cervical burning, and regurgitation, especially when in the supine position, are typical complaints these patients [6, 9]. Reflux occurs principally because the normal antireflux mechanisms have been resected or disrupted. Furthermore, the pressure gradient between the intra-abdominal duodenum (positive pressure) and the intra-thoracic stomach (negative pressure), promotes reflux [21]. Bilateral truncal vagotomy, on the other hand, disturbs the balance between the propulsive action of the gastric antrum and the resistance of the pylorus to the flow of contents from and to the duodenum [20, 22]. Other pathophysiological and surgical factors also contribute to reflux after surgery [9].

After an esophagectomy the substitute can be placed in the posterior mediastinum or in an extra-anatomical, most commonly retrosternal, position [2]. This sometimes becomes nec-

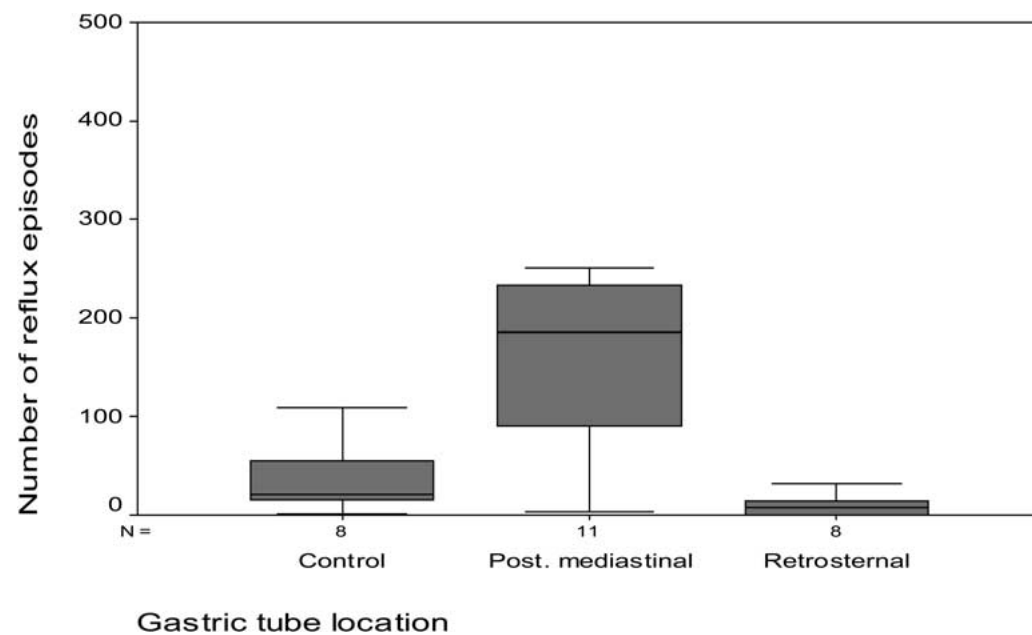


Fig. 2. Box plot of the total number of reflux episodes. The retrosternal group had significantly lower numbers of reflux episodes compared to the posterior mediastinal group ($p = 0.002$) and the control group ($p = 0.04$). Horizontal bars denote median and range.

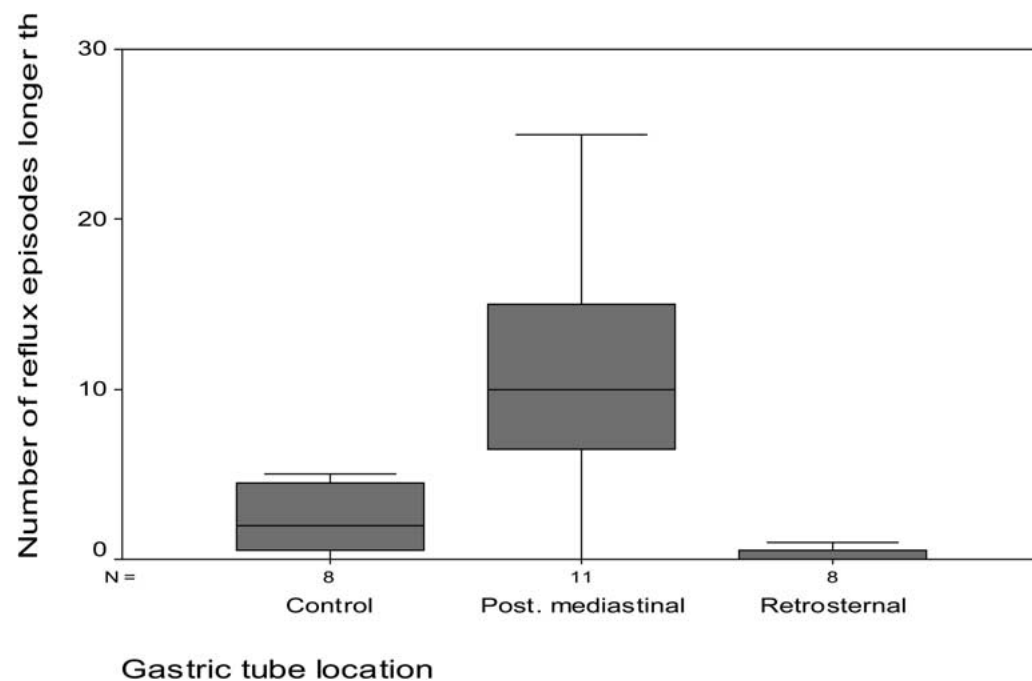


Fig. 3. Box plot of the total number of reflux episodes longer than 5 minutes. Long reflux episodes were significantly more in the retrosternal group compared to the posterior mediastinal group ($p = 0.001$) and the control group ($p = 0.05$). Horizontal bars denote median and range.

essary during intended curative esophagectomy, when complete excision cannot be achieved and extra-anatomical gastric tube interposition offers the advantage that a recurrent intrathoracic locoregional tumor mass will not invade the neo-esophagus. Retrosternal reconstruction may well be the procedure of first choice after subtotal esophagectomy for cancer in patients at high risk for developing secondary malignant dysphagia [3, 4]. Another indication for an extra-anatomical interposition is corrosive esophageal injury. Although the retrosternal route is considered superior, subcutaneous interposition of a gastric

tube may be an alternative in cases of former sternotomy or in cases of severe comorbidity, as it involves less traumatic dissection.

There have been some studies comparing the alternative routes of gastric interposition [3, 4, 7, 23–25]. Overall these studies have not shown superiority of one technique over the other with regard to morbidity. On the other hand, the functional results and the impact on quality of life have not been adequately studied. In cases of esophageal substitution, especially when longer survival is expected, it is of great significance to take into account the

Table 3. Number of reflux episodes

	PM group	RS group	Control group	PM vs. RS*	PM vs. control*	RS vs. control*
Total	185 (3–2930)	8 (0–32)	21 (1–109)	$p = 0.002$	$p = 0.02$	$p = 0.04$
Upright	45 (1–355)	3 (0–18)	18 (0–57)	$p = 0.005$	NS	$p = 0.03$
Supine	81 (0–2578)	1 (0–14)	6 (0–53)	$p = 0.003$	$p = 0.009$	NS
Meal	20 (0–61)	0 (0–8)	2 (0–21)	$p = 0.002$	$p = 0.03$	NS
Postprandial	38 (0–634)	0 (0–7)	2 (0–9)	$p = 0.001$	$p = 0.005$	NS
Fasting	113 (1–2238)	2 (0–32)	14 (1–97)	$p = 0.002$	$p = 0.03$	$p = 0.05$

*Mann-Whitney *U*-test.**Table 4.** Number of reflux episodes longer than 5 minutes

	PM group	RS group	Control group	PM vs. RS*	PM vs. control*	RS vs. control*
Total	10 (0–25)	0 (0–3)	2 (0–5)	$p = 0.001$	$p = 0.009$	$p = 0.05$
Upright	1 (0–15)	0 (0–3)	2 (0–5)	$p = 0.003$	NS	NS
Supine	7 (0–12)	0 (0–1)	0 (0–2)	$p = 0.003$	$p = 0.004$	NS
Meal	1 (0–4)	0 (0–1)	0 (0–1)	NS	NS	NS
Postprandial	2 (0–14)	0 (0–1)	0	$p = 0.01$	$p = 0.007$	NS
Fasting	8 (0–15)	0 (0–1)	2 (0–5)	$p = 0.001$	$p = 0.02$	NS

*Mann-Whitney *U*-test.**Table 5.** Percentage time that absorption of bilirubin >0.14 units in symptomatic versus asymptomatic patients

	Symptomatic	Asymptomatic	Symptomatic vs. asymptomatic*
Total	30.8 (0.8–76.2)	0.15 (0–29.10)	$p = 0.004$
Upright	37.4 (1.6–65.0)	0.2 (0–8.6)	$p = 0.001$
Supine	28.2 (0–89.7)	0 (0–2.7)	$p = 0.017$
Meal	16.9 (0–59.9)	0 (0–26.6)	$p = 0.01$
Postprandial	20.9 (0–86.3)	0 (0–30.0)	$p = 0.006$
Fasting	30.6 (0–73.10)	0.42 (0–38.2)	$p = 0.01$

*Mann-Whitney *U*-test.**Table 6.** Number of reflux episodes in symptomatic versus asymptomatic patients

	Symptomatic	Asymptomatic	Symptomatic vs. asymptomatic*
Total	192 (13–2930)	5 (0–124)	$p = 0.001$
Upright	125 (13–355)	3 (0–45)	$p < 0.001$
Supine	76 (0–2578)	2 (0–93)	$p = 0.022$
Meal	20 (0–61)	0 (0–32)	$p = 0.008$
Postprandial	40 (0–634)	0 (0–21)	$p = 0.002$
Fasting	117 (0–2238)	3 (0–83)	$p = 0.008$

*Mann-Whitney *U*-test.

functional results of the substitute and the effect of possible reflux symptoms on the quality of life of these patients.

In the present study simultaneous pH monitoring was deemed impractical and unnecessary as gastric secretion is diminished in the vagotomized stomach and recovers after 1–3 years in the majority of patients [26]. As all measurements were carried out within 3–6 months after the operation, we concentrated on the study of duodenal reflux. Besides, the classical suggestion that bilirubin monitoring underestimates duodenal reflux in an acid environment and therefore has always to be combined with pH monitoring has been brought into question [27].

Although bile exposure of the gastric transplant at the posterior mediastinum has been previously studied with the *Bilitec 2000*,

Table 7. Number of reflux episodes longer than 5 minutes in symptomatic versus asymptomatic patients

	Symptomatic	Asymptomatic	Symptomatic vs. asymptomatic*
Total	10 (0–25)	0 (0–10)	$p = 0.008$
Upright	3 (0–15)	0 (0–4)	$p = 0.008$
Supine	1 (0–12)	0 (0–9)	$p = 0.028$
Meal	1 (0–4)	0 (0–2)	$p = 0.043$
Postprandial	2 (0–14)	0 (0–4)	$p = 0.022$
Fasting	8 (0–15)	0 (0–9)	$p = 0.01$

*Mann-Whitney *U*-test.

this has never been done for extra-anatomical gastric tubes [8]. In the present study we found that exposure of the gastric tube to bile was significantly higher after anatomical interposition than after extra-anatomical interposition. This difference referred both to the duration and to the number of the reflux episodes. The exposure of the extra-anatomical gastric conduit to bile was minimal. The lack of a pressure gradient between the duodenum and the gastric body and the crooked route of the gastric transplant are the most likely causes of this difference. In fact, anatomical studies have shown that the retrosternal route can be up to 5.3 cm longer than the posterior mediastinal route [28].

Another interesting finding of this study is the significantly higher bile exposure of the conduit in patients who reported occurrence of reflux symptoms compared to the asymptomatic patients. This difference suggests that reflux of duodenal contents may cause symptoms in the absence of acid.

No pyloric drainage procedure was used in either surgical group in the present study. The presence of a pyloric drainage procedure has an uncertain effect on reflux, and evidence from the literature is conflicting [3, 8, 9, 29]. Pyloric drainage has not been universally adopted and debate continues [3]. We do not routinely perform pyloric drainage procedures after esophagectomy and gastric tube reconstruction, and we hardly ever had problems with gastric emptying. Gastric emptying can be aided by the use of prokinetic agents, including erythromycin [9]. A recent

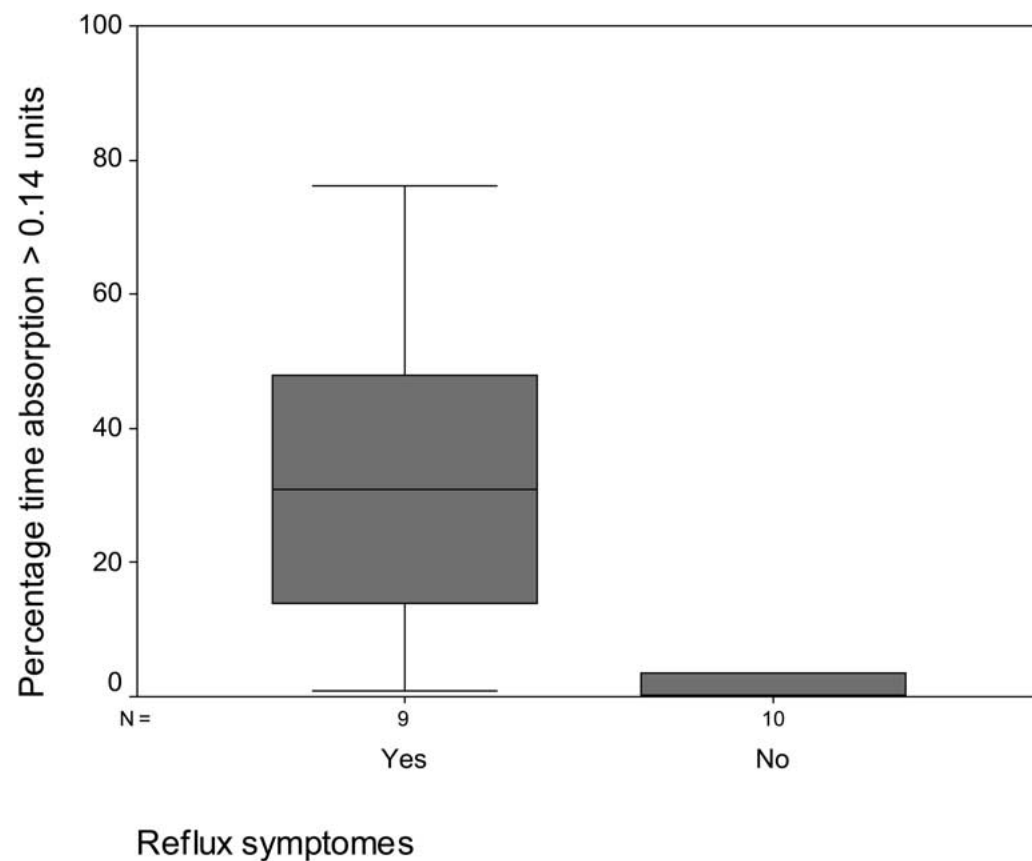


Fig. 4. Box plot of the percentage time that bilirubin absorption was >0.14 units. The symptomatic patients had significantly higher time of exposure to bile compared to the asymptomatic patients ($p = 0.004$). Horizontal bars denote median and range.

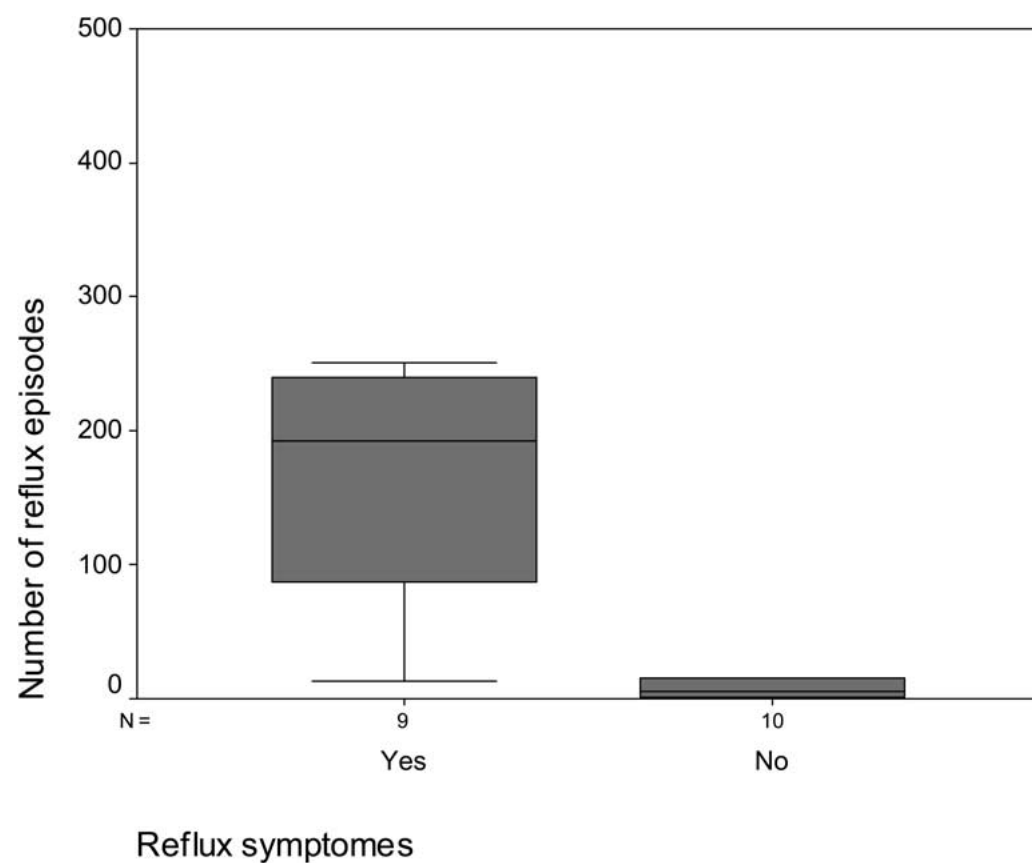


Fig. 5. Box plot of the total number of reflux episodes. The symptomatic patients had significantly higher number of reflux episodes compared to the asymptomatic ones ($p = 0.001$). Horizontal bars denote median and range.

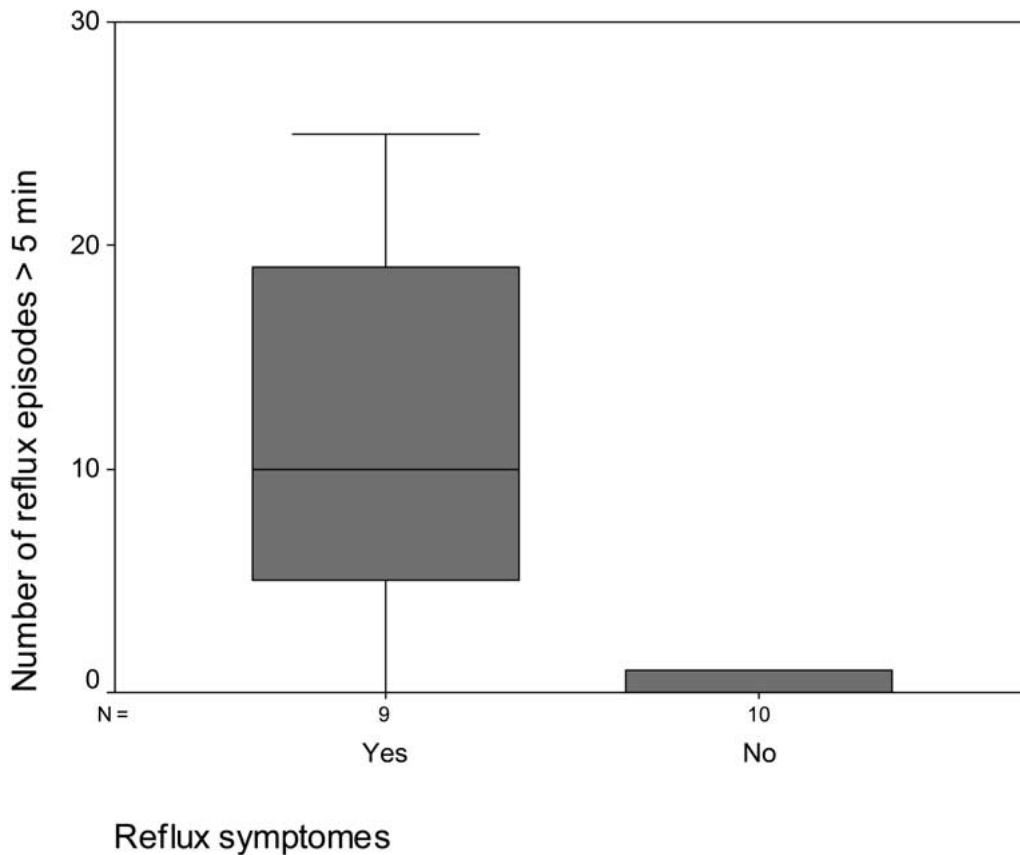


Fig. 6. Box plot of the total number of reflux episodes longer than 5 minutes. Long reflux episodes were significantly more in the symptomatic patients compared to the asymptomatic ones ($p = 0.008$). Horizontal bars denote median and range.

meta-analysis of randomized controlled trials showed that pyloric drainage procedures reduce the occurrence of early postoperative gastric outlet obstruction after esophagectomy with gastric reconstruction, but they have no effect on other early and late patient outcomes [30].

The role of duodenogastro-esophageal (DGER) reflux in the development of columnar lined esophagus has been well demonstrated, and DGOR has also been associated with the development of gastro-esophageal cancer [10–12]. After subtotal esophagectomy and gastric pull-up, reflux of duodenal contents, apart from causing symptoms that adversely affect the quality of life, may also in the long term contribute to metaplastic changes, and potentially adenocarcinoma, both in the mucosa of the gastric transplant and in the esophageal remnant.

The results of the present study clearly demonstrate that gastric interposition is associated with very high exposure of the gastric conduit to bile. On the contrary, retrosternal gastric interposition is associated with minimal exposure to bile and, from that point of view, may be a good alternative, especially in patients with long life expectancy. However, further studies are needed to verify these results and to evaluate the impact of this type of esophageal reconstruction on quality of life and pathological sequelae.

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