CHYLOTHORAX COMPLICATING ESOPHAGECTOMY FOR CANCER: A PLEA FOR EARLY THORACIC DUCT LIGATION

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Objective: Postoperative chylothorax remains an uncommon but potentially life-threatening complication of esophagectomy for cancer, and the ideal management is still controversial. The aim of the study was to compare the outcomes of patients treated nonoperatively with those of patients promptly undergoing reoperation. **Methods:** From 1980 to 1998, 1787 esophagectomies for esophageal or cardia cancer were performed, and 19 (1.1%) patients had postoperative chylothorax. We analyzed type of operation, surgical approach, delay of diagnosis of chylothorax, daily chest tube output, type of management, major complications, death, hospital stay, and final outcome. **Results:** Of the 19 patients with chylothorax, 11 were initially managed nonoperatively (group A): 4 (36%) patients had spontaneous resolution of chylothorax, and the other 7 required reoperation for the persistence of a high-volume output. There were three infectious complications and one postoperative death in this group. No reliable predictive criteria of successful versus unsuccessful nonoperative management could be found. The 8 most recent patients underwent early reoperation (group B). All patients recovered, and no major complications possibly related to chylothorax or hospital deaths were observed. They were discharged after a median of 22 days (range, 12-85 days) compared with a median of 36 days (range, 21-64 days) for patients of group A. **Conclusions:** Early thoracic duct ligation is the treatment of choice for chylothorax occurring after esophagectomy. Reoperation should be performed immediately after the diagnosis is made to avoid the complications related to nutritional and immunologic depletion caused by prolonged nonoperative treatment. (J Thorac Cardiovasc Surg 2000;119:453-7)

Postoperative chylothorax represents an uncommon complication of esophagectomy for cancer that is responsible for respiratory, metabolic, and immunologic consequences that may threaten a patient's life.^{1,2} Significant progress has recently been made in the nonoperative management of this condition.³⁻⁵ However, morbidity and mortality are still elevated,⁶⁻⁹ especially

in patients with chylothorax complicating the results of an esophageal operation,¹⁰ because of the extension of the operation, involving exposure of the chest, abdomen, and sometimes also the neck, in patients who very often are elderly, malnourished, and have respiratory and cardiologic concomitant problems. For these reasons, the debate about the ideal treatment of this complication remains open between nonoperative and operative management.⁹⁻¹² Nonoperative management with intrapleural drainage and total parenteral nutrition usually requires several weeks for the chylothorax to resolve and is frequently unsuccessful; therefore when reoperation is eventually required, it has to be performed in a compromised patient. Different criteria for the indication and timing of reoperation have been proposed, including the persistence of the chylous leak for more than 2 weeks^{3,9,12-14} or a pleural drainage greater than 1 L per day for more than 5 days,^{8,12,15} but there are no controlled studies to define the best timing for an

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operation. Certainly an aggressive treatment is preferable before the patient is severely weakened.

This study reviews our 18-year experience and retrospectively compares the outcomes of patients initially treated nonoperatively with those of patients promptly undergoing reoperation.

Patients and methods

Since 1980, clinical data from patients with esophageal or cardia cancer were collected prospectively and electronically stored according to a standardized protocol. From 1980 to 1998, 1787 patients underwent esophagectomy for esophageal or cardia cancer. The standard operation consisted of subtotal esophagectomy with two-field lymph node dissection through a right thoracotomy and midline laparotomy. A cervicotomy with total esophagectomy or total pharyngo-laryngo-esophagectomy was also performed when indicated by the proximal location of the esophageal tumor. A transhiatal esophagectomy was performed in selected patients when thoracotomy was contraindicated. A chest drain was routinely left in place for at least 4 days in patients undergoing a transthoracic operation, and a mediastinal drain was left in place for the same period in patients undergoing a transhiatal operation. The infrahepatic drain was removed 4 days after the operation. Transthoracic esophagectomy was performed on 1273 patients, and transhiatal resection was performed on 464 patients with compromised cardiopulmonary function. In 50 patients other procedures were used.

Chylothorax was suspected in the presence of excessive (>1000 mL per day) chest or mediastinal output continuing for more than 2 days and was confirmed by physical and biochemical analysis of the fluid. A computer search in our database was undertaken to identify patients with postoperative chylothorax.

Duration of the chylous leak was defined as the period between the operation and the removal of the pleural drain, which occurred when a constant reduction of pleural output less than 100 mL per day was obtained. The delay of reoperation was defined as the period between the diagnosis of chylothorax and transthoracic ligation of the thoracic duct.

Nonoperative management consisted of intrapleural drainage, taking the thoracic drain off of suction in an attempt to allow the leak to seal, and total parenteral nutrition. Operative management consisted of right thoracotomy and ligation of the thoracic duct en bloc, with the azygos vein and adjacent soft tissue immediately above the diaphragm.¹⁵

The χ^2 or Fisher exact test was used, as appropriate, for univariate comparisons, and continuous variables were analyzed by using the unpaired Student *t* test. Medians are presented with the 25th and 75th percentiles.

Results

Postoperative chylothorax developed in 19 (1.1%) of 1787 patients who underwent esophagectomy for carcinoma of the esophagus or the cardia. There were 15

men and 4 women, with an age range of 27 to 70 years (median, 57 years). The prevalence of chylothorax in the 1273 patients operated on through a transthoracic approach was 1% (*n* = 13), whereas in the 464 patients who had a transhiatal esophagectomy, the prevalence was 1.3% (*n* = 6; *P* = .8).

All 13 patients who underwent a transthoracic procedure had excessive output of serous fluid through the chest drain placed at the time of the operation. Patients who underwent a transhiatal operation had excessive drainage through the mediastinal drain in 1 patient, through cervical and abdominal drains in 4 patients, and unilateral pleural effusion in 1 patient.

Considering all patients, diagnosis was made after a median of 4 days (range, 2-15 days) from the operation. However, the chylous leakage was diagnosed later in patients undergoing a transhiatal approach and without a thoracic drain because it is more difficult to control thoracic fluid output. In this group the diagnosis was made after a median of 7.5 days as opposed to 3 days for patients with a transthoracic approach (*P* = .006).

In 11 patients (group A) the initial management consisted of drainage of the chylous leakage and total parenteral nutrition without oral intake, balanced salt solution intravenously to maintain hydration, and supplement of albumin. Four (36%) of the 11 patients had spontaneous resolution of chylothorax with this nonoperative management after a median of 21 days (25th-75th percentile, 20-28.5 days). There were no hospital morbidities or mortalities among these patients, all of whom recovered and were subsequently discharged after a median of 38 days (25th-75th percentile, 27-49.7 days) from the operation. The other 7 patients underwent reoperation because of the persistence of a high-volume output. The median delay of reoperation was 12 days (25th-75th percentile, 9-13.5 days) after diagnosis of chylothorax, and the pleural drain was removed after a median of 6 days (25th-75th percentile, 4.5-6.7 days) after reoperation. Infectious complications were recorded in 3 (43%) of these 7 patients who underwent reoperation 10, 14, and 18 days after diagnosis of chylothorax. These included pneumonia in 2 patients, both with sepsis and severe respiratory failure (1 patient died on postoperative day 38), and urinary tract infection in 1 patient. Furthermore, another patient had a cervical anastomotic leak 11 days after the first operation.

The 4 patients in group A who underwent successful nonoperative management and the 7 patients who underwent reoperation after failure of nonoperative treatment were comparable in terms of median age (50

vs 54 years, $P = .5$), chyle peak flow (34.3 vs 35.5 mL $\cdot$ kg⁻¹ $\cdot$ d⁻¹, $P = 1.08$), chylous output per body weight on postoperative day 1 (13.3 vs 9.5 mL/kg, $P = .7$) and postoperative day 7 (15.6 vs 30 mL/kg, $P = .3$), and median postoperative hospital stay (38 vs 36 days, $P = 1.07$). However, the range for reoperation (6-18 days) of patients ($n = 7$) was uniformly shorter than the range for patients ($n = 4$) attempting spontaneous resolution of the chylothorax (20-48 days). Because this is a retrospective study, and we did not find any reliable criteria predictive of successful versus unsuccessful nonoperative management, it is possible that this may reflect the more or less aggressive surgical attitude of the different surgeons involved.

The 8 most recent patients (group B) underwent early reoperation after a median of 2 days (range, 1-3 days) from the diagnosis of chylothorax. Early thoracic duct ligation was successful in all patients, and the pleural drain was removed after a median of 5 days (25th-75th percentile, 5-7.5 days) from reoperation. No hospital deaths were observed; however, 2 patients had a prolonged hospital stay because of postoperative complications not related to chylothorax: 1 patient who underwent pharyngo-laryngo-esophagectomy and total thyroidectomy plus parathyroidectomy had a severe and persistent hypocalcemia, and the other had ischemic partial necrosis of the pulled-up stomach. All patients were discharged after a median of 22 days (25th-75th percentile, 18.5-33.7 days) from the first operation.

The 11 patients in group A who initially received nonoperative management and the 8 patients in group B who underwent early reoperation were comparable in terms of median age (54 vs 60 years; $P = .1$), chyle peak flow (35.5 vs 32.6 mL $\cdot$ kg⁻¹ $\cdot$ d⁻¹, $P = .8$), postoperative infectious complications (27% vs 0% , $P = .2$), and hospital mortality rates (9% vs 0% , $P = 1.0$). On the other hand, a significantly greater number of units of albumin (10 g/U) and fresh frozen plasma (250 mL/U) were infused in patients of group A (29 units; 25th-75th percentile, 22.5-38.5 units) than in patients of group B (8 units; 25th-75th percentile, 7.5-18.7 units; $P = .005$). After the first operation, the thoracic drain was removed significantly earlier in patients of group B (median, 14 days; 25th-75th percentile, 12-15 days) than in patients of group A (median, 20.5 days; 25th-75th percentile, 19.2-27.2 days; $P = .0007$). Furthermore, although the overall median hospital stay was not significantly shorter in patients of group B (22 days; 25th-75th percentile, 18.5-33.7 days) than in patients of group A (36 days; 25th-75th percentile, 26-51.5 days; $P = .1$), excluding the 2 patients of group B with a prolonged hospital stay because of postoperative

complications not related to chylothorax, the median hospital stay (20.5 days; 25th-75th percentile, 15.5-22.5 days) was significantly shorter than in patients of group A ($P = .007$).

Findings at the time of reoperation for chylothorax included injury to the main thoracic duct in 6 patients, injury to collateral lymphatic vessels in 2 patients, and no detectable sites of leakage in 7 patients. All patients underwent ligation of the thoracic duct en bloc, with the azygos vein and adjacent soft tissue immediately above the hiatus of the diaphragm and chylothorax resolved in all the cases.

Discussion

Postoperative chylothorax is a rare but potentially life-threatening complication of esophagectomy for cancer. A chylous leak results in important fluid loss and continued decrease of serum levels of albumin and total proteins and leads to a significant reduction in peripheral lymphocytes with subsequent impairment of both cell-mediated immunity and humoral responses.^{1,16}

In our experience the incidence of this complication has been 1.1%, which is in agreement with results from other series (Table I).^{6,8,13,17-19} Differently from Bolger and associates,⁶ we found no significant difference in the prevalence of chylothorax after transthoracic and transhiatal esophagectomy (1% vs 1.3%).

The diagnosis of chylothorax may be difficult in a fasting patient because the characteristic milky appearance of the chyle may be absent in the pleural fluid. Different techniques have been proposed for an early diagnosis, such as administration of butter or cream⁸ or methylene blue²⁰ through the nasogastric tube or jejunostomy and physical and chemical analysis of the pleural fluid. At times, lipoprotein analyses that assess the presence of chylomicrons may be required for the diagnosis.²¹

There is considerable controversy concerning the management of chylothorax. Some authors defend a nonoperative approach,²² and others advocate early reoperation.^{8,10,11,23,24} The reported mortality rate for chylothorax after an esophageal cancer operation may be as high as 50% with nonoperative management^{6,7} because these patients are unable to tolerate a depletion of nutritional reserves because their conditions are often severely compromised even before operation. The surgical treatment was first proposed by Lampson²⁵ in 1948 and then supported by Goorwitch²⁶ in 1955, and now it has gained greater support, especially in the treatment of refractory chylothorax. The first aim of surgical therapy is to relieve respiratory embarrassment, draining the chyle from the pleural

Table I. Chylothorax after esophageal resection: Prevalence, treatment (nonoperative vs reoperation), and outcome

Reference	No. of patients	Chylothorax	Nonoperative treatment			Reoperation		
			Total	Mortality rate	Cure rate	Total	Mortality rate	Cure rate
Orringer et al ⁸	320	11 (3%)	—	—	—	11	0	11 (100%)
Tam et al ¹⁷	316	4 (1.3%)	2	1 (50%)	1 (50%)	2	1 (50%)	1 (50%)
Bolger et al ⁶	537	11 (2%)	8	4 (50%)	4 (50%)	3	1 (33%)	2 (67%)
Dougenis et al ¹³	255	10 (3.9%)	3	1 (33%)	1 (33%)	1* + 7	1 (12.5%)	7 (87.5%)
Dugue et al ¹⁸	850	23 (2.7%)	14	0	14 (100%)	9	2 (22.2%)	7 (77.8%)
Bonavina et al ¹⁹	271	3 (1.1%)	3	0	0	3*	0	3 (100%)
Merigliano et al	1787	19 (1.1%)	11	0	4 (36.4%)	7* + 8	1*	14 (93.3%)
Total	4336	81 (1.9%)	41	6 (14.6%)	26 (58.5%)	11* + 40	1* + 5 (11.8%)	45 (88.2%)

*Patients who were reoperated on after failed nonoperative management.

space, and to heal the fistula, but the correct timing for reoperation is not well defined. Recently, Dugue and associates¹⁸ proposed the ratio of chylous output to body weight on the 5th day after the onset of chylothorax as a parameter of success of nonoperative treatment. In our experience this parameter was not predictive of the evolution of chylothorax, not even after 7 days from the onset of chylothorax. Because it is very difficult to predict whether a chylous leak would spontaneously heal, we think that the treatment must be prompt and aggressive to prevent the progressive weakening of the patient, which may decrease the chance of surviving this complication. This aggressive attitude has the advantages that we reoperate in a pleural space that is still free from adhesions, which makes it easier to identify the site of the chylous leak, and that the patient is not severely impaired by prolonged fluid, proteins, albumin, and lymphocyte loss. An aggressive approach was successful in our patients, and the chest drain could be removed within a few days. Reoperation took less than 1 hour to complete, and therefore it was well tolerated also by patients who had undergone a transhiatal esophagectomy because of limited respiratory reserve. The only infectious complications and the only death that we observed occurred in those patients who underwent reoperation after a prolonged period of nonoperative therapy. A recent study from the Mayo Clinic supports our attitude, strongly recommending early reoperation.¹⁰ In fact, 24 (89%) of the 27 patients who had chylothorax after an esophageal operation and who initially underwent nonoperative therapy eventually required reoperation.

Recently it has been reported^{19,22,27-29} that video-assisted thoracoscopic surgical techniques may represent a good alternative to thoracotomy in the treatment of chylothorax. This technique offers the advantage of an easier access to the entire pleural cavity without the potential morbidity of thoracotomy.

To prevent postoperative chylothorax, since 1998 we have routinely ligated the thoracic duct en bloc, with the azygos vein immediately above the diaphragm during transthoracic esophagectomy, and no chylothorax has developed in the last 106 consecutive patients.

In conclusion, early reoperation with thoracic duct ligation is the treatment of choice for chylothorax occurring after esophagectomy. Early reoperation should be performed just after the diagnosis of chylothorax is made because at this time the procedure is better tolerated by the patient without the risk of complications that may be related to nutritional and immunologic depletion.

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