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THE POTENTIAL VALUE OF PROPHYLACTIC LIGATION OF THE THORACIC DUCT IN PREVENTING CHYLOUS LEAKAGE AFTER OESOPHAGECTOMY

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Abstract:

Introduction: *Chylothorax is an uncommon but serious complication after esophageal resection which have a reported incidence of 0.6–4.0%. It is caused by the injury of the thoracic duct or its tributaries. Chylothorax may lead to dehydration as it may cause loss of about several liters per day, it can cause also malnutrition and immunosuppression. Unfortunately, Therapeutic approach has not been standardized yet. During primary resection of cancer esophagus, prophylactic thoracic duct ligation can decrease the incidence of chylothorax.*

Method: *All the potentially relevant studies were chosen by a literature search in PUBMED from the year 2009 to 2019. We chose articles using PUBMED for the terms [prophylactic thoracic duct ligation].*

Results: *The electronic search initially resulted in 14 eligible articles. All the studies were screened by title and abstract for relevance, and subsequently, 9 irrelevant manuscripts were excluded. Next, we reviewed 5 articles which met the inclusion criteria. The sample sizes in the studies ranged between 58 and 653 patients. A total of 906 subjects were included in the 5 studies examined into the current study.*

Conclusion: *prophylactic thoracic duct ligation after esophageal resection could be considered as an effective preventative measure to reduce the incidence of postoperative chylothorax.*

Key words: *chylothorax – esophagectomy - prophylactic thoracic duct ligation.*

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INTRODUCTION AND BACKGROUND

Chylothorax is defined as accumulation of chyle in the pleural cavity. Chyle is a Greek word and is originally derived from "Chylos," which means juice. The lacteal system of the intestine is the site where Chyle is formed [1]. The small intestine enzymes are responsible for digestion and breaking down the small and medium chain triglycerides taken in the diet and convert them into free fatty acids and then it is absorbed into the portal circulation [2]. Although, the intestinal lipases cannot break the large molecules of triglycerides; being complex long-chain. So, long chain triglycerides combine with cholesterol, phospholipids and cholesterol esters to form chylomicrons in the jejunum. Then these large molecules can be absorbed into the lymphatic system in the small intestine to form the chyle. The thoracic duct system is formed when the lymphatic drainage of intestine joins the lymphatic drainage from the lower extremities which in term drains in the system circulation. If any shortage happened in the integrity of thoracic duct function, the milky lipid-rich chyle will be leaking into the surrounding structures [3]. Chylothorax happens when there is chyle leak into the pleural cavity caused by any destruction of the thoracic duct structure or function. A Considerable amount of chyle could be accumulate in the pleural cavity in a very short period because the normal daily chyle production is around 2.4 liters. Chylothorax was originally mentioned by Dr. Bartloet in the 17th century and in the it has a particular importance as there are new management techniques and strategies which have favorable outcomes [4].

Chylothorax can be caused by different mechanisms. The most common cause of non-traumatic chylothorax is the neoplastic chylothorax . Various types of cancers can cause chylothorax such as esophageal cancer, chronic lymphoid leukemia, lymphoma, lung cancer and metastatic carcinoma [5]. There is a relative decrease in the incidence of chylothorax in cancer patients recently. This is may be due to early diagnosis and treatment of cancer patient and early and prophylactic management of complicating chylothorax [6].

Chylothorax is a potentially serious postoperative complication although it is uncommon. During routine esophagectomy in cancer patient, this complication has been reported in 0.6–4.0% of all cases [7].Complication of chylothorax after an esophagectomy are serious such as hypovolemia, infection, metabolic and nutritional depletion and the mortality rate exceeds 50% if left untreated [8]. The certain management of post esophagectomy chylothorax remains controversial [9]. The trial to undertook conservative management with thoracic drainage and total parenteral nutrition can be successful in some cases, although it requires long hospital stay with severe discomfort to the patient from pleural drainages and parenteral nutrition, it also has a high risk of infection. However, conservative management have a little chance of success in case of accumulation of the pleural effusion in a rate exceeding 1,000 ml per day [10]. Surgical ligation of the thoracic duct after esophagectomy is probably more appropriate treatment for chylothorax as it is claimed to have excellent outcomes [11]. Video-assisted thoracoscopic esophagectomy technique was developed to reduce the severe stress accompanying surgical treatment for esophageal cancer in cases of minimally invasive esophageal cancer surgery [12]. Video-assisted thoracoscopic esophagectomy has many advantages such as minimizing the reduction in vital capacity which occurs due to injury of the chest wall and reducing surgical trauma which result from a decreased production of cytokines and polymorphonuclear leukocyte elastase [11]. However, in literature it was claimed that patients underwent video-assisted thoracoscopic esophagectomy, the incidence of postoperative chylothorax is higher than for those patients who underwent open esophagectomy [11].

METHODS AND DATABASES USED:

All potentially relevant studies were chosen by a literature search in PUBMED through the last 10 years from the year 2009 to the year 2019. We chose articles using PUBMED for the terms [prophylactic thoracic duct ligation].

Inclusion criteria:

(1) only the papers that directly compared the incidence of chylothorax in patients who underwent prophylactic ligation with those who had conservative treatment were selected.

(2) the article must present original data and supply sufficient information on the chylothorax rate after esophagectomy.

The exclusion criteria in this review were as follows:

(1) articles that did not satisfy the current inclusion criteria.

(2) some publication types, such as letters and proceedings.

(3) unpublished sources of data.

(4)Systemic reviews and meta-analysis

RESULTS:

The electronic search initially resulted in 20 eligible articles. All the studies were screened by title and abstract for relevance, and subsequently, 14 irrelevant manuscripts were excluded. Next, we reviewed 6 articles which met the inclusion criteria. The sample sizes in the studies ranged between 58 and 653 patients. A total of 1229 subjects were included in the 6 studies examined into the current study.

Jínek et al.,[11] presented a retrospective study of patients who underwent transthoracic esophagectomy for cancer esophagus. In the study 58 patients underwent transthoracic esophagectomy. 31 patients (53%) underwent prophylactic ligation of the thoracic duct. The incidence of chylothorax and analysis of the amount of harvested lymph nodes was done in the group with thoracic duct ligation (A 31 patients) and in the non-ligation group (B 27 patients).

The overall incidence of chylothorax after esophagectomy was 3.4%. Incidence of chylothorax was (6.5%) in the prophylactic group, it occurred in two men and it was not observed in the non-ligation group. Chylous leakage was successfully treated by thoracotomy and thoracoscopically in which repeat ligation of the thoracic duct was done. More lymph nodes were harvested in the prophylactic group, but it was non-significant.

Glatz et al., [13] provided an overview of the existing literature on the prevention and surgical therapy of chylothorax after esophagectomy and found that either prophylactic primary or therapeutic secondary ligature of the thoracic duct is an effective surgical preventive procedure of postoperative chyle leakage as well as an effective therapy.

Yang et al., [14] undertook randomized control trial in which 60 patients were recruited, the study results showed that Ligation of thoracic duct during esophagectomy is effective in prevention of Chylothorax and could decreased percentage of T lymphocyte. The lymphocyte percentage through ligation group was lower than that of in non-ligation group after operation ($P < 0.05$), especially after transection of the arch of azygos vein. And the study recommended that thoracic duct should be selectively ligated during esophagectomy.

Guo et al., [15] assessed 70 video-assisted thoracoscopic esophagectomies was done for esophageal carcinoma (group A) were performed without prophylactic thoracic duct ligation and 65 patients with esophageal cancer (group B) underwent video-assisted thoracoscopic esophagectomy in which routine ligation of the thoracic duct during the operation was done. Postoperative chylothorax occurred in seven patients in group A (7/70) with incidence of (10%) and one patient in group B (1/65) with incidence of (1.5%). From all subjects, there were one woman and seven men with chylothorax with a mean age of 56.7 (range, 47–72) years. All of these patients have daily accumulation of pleural effusion exceeding 1,000 ml per day and lasted more than 5 days so, they required surgical intervention as they were unresponsive to conservative management. The conservative management was in the form of pleural drainages, fasting diet and parenteral nutritional support using medium-chain triglycerides and continuous albumin infusions. 87.5% of the chyle leak (7/8) was near the arch of azygos vein and happened immediately after thoracic duct ligation. In the one remaining patient the location of chyle leak was 8 cm above the diaphragm. For correction of the resulting chylothorax , the first six cases were managed by open thoracotomies. In which , patients were placed in left-lateral position and a lateral incision was made from the mini thoracotomy in the fifth ICS to the port in seventh ICS between the posterior AL and subscapular angle line. The study chose the fifth ICS as the approach for thoracic duct ligation. And for the other two patients, thoracic duct ligation by VATS was performed. If we compare patient in group A with patients in group B there is significantly lower incidence of chylothorax ($P = 0.0375$), proving that preventive thoracic duct ligation can effectively reduce the incidence of chylothorax which result after video-assisted thoracoscopic esophagectomy for esophageal carcinoma.

Lai et al., [16] studied 653 patients undergoing transthoracic esophagectomy for esophageal cancer. In which patients were randomly assigned to two groups: 328 patients underwent esophagectomy (preservation group) and 325 patients underwent thoracic duct mass ligation during esophagectomy (prevention group). The patients who had chylothorax as a complication were identified and comparison between the occurrence rates between the two groups was done. The study recorded also the management and outcome of postoperative chylothorax.

The results showed that demographic details of all patients were similar between the two groups. There were No minor or major intraoperative or postoperative complications occurred due to prophylactic mass thoracic duct ligation. Chylothorax occurred in 8 patients, with incidence of 1.2%. There

were 2 female and 6 male patients, the mean age was 65.4 years. In the 93 patients who were excluded from the study, No Chylothorax occurred. 7 patients representing (2.1%) had Chylothorax as a complication in the preservation group. In the other hand 1 patient (0.3%) in the prevention group had chylothorax as a complication. The result of Fisher's exact test between the two groups was $p = 0.046$.
Four patients were treated through conservative treatment by intrapleural drainage, talc pleurodesis and total parenteral nutrition. Only one patient had a severe complication experiencing high-output chylous fistula and early onset of acute respiratory distress syndrome. The patient was managed by mechanical ventilation and showed recovery after 31 postoperative days. Three patients had recoveries without mechanical ventilation after 19 to 27 days (mean, 23.5 days).

Four patients underwent surgical treatment. In all cases, a repeated thoracotomy was performed. In 2 patients, chylothorax occurred which was managed by direct ligature on either side of the leak. In the other 2 patients, the sites of leakage were not identifiable, in these cases thoracic duct mass ligations were done. Two patients were discharged from hospital after 8 and 12 days after reoperation, respectively, making recoveries without mechanical ventilation. The other 2 patients died of complications of multiple organ system failure (mortality rate 25%).

Cagol et al., [17] studied 323 patients underwent transthoracic esophagectomy for cancer with routine duct ligation during the operation was performed.

From 2001 to 2006, 323 patients underwent transthoracic esophagectomy for esophageal and cardiac cancer; of these patients 146 (45%) received preoperative chemo-therpy and radiotherapy for advanced cancer. The operation consisted of subtotal esophagectomy through a midline laparotomy and right thoracotomy for infra-carinal tumors; cervicectomy was added for supra-carinal tumors requiring a nearly total esophagectomy. All the patients underwent prophylactic thoracic duct mass ligation. 304 patients underwent digestive tract reconstruction surgery done with gastric pull-up (intrathoracic anastomosis, n = 250; cervical anastomosis, n = 54) and 19 patients had jejunum or colon interposition. No major or minor intraoperative or postoperative complications related to prophylactic thoracic duct mass ligation were recorded. In 323 consecutives transthoracic esophagectomies there was no postoperative chylothorax observed. The study claimed that, there is no difference in the ability to perform thoracic duct mass ligation in patients who had preoperative chemotherapy or radiotherapy. The study concluded that Prophylactic thoracic duct mass ligation was performed in 323 consecutive patients who underwent transthoracic esophagectomy for cancer with no procedure-related complications and no postoperative chylothorax. It is an easy and safe procedure, even in patients underwent preoperative chemoradiotherapy. The study proved that prophylactic thoracic duct mass ligation could minimize the risk of chylothorax in patients with transthoracic esophagectomy for cancer.

DISCUSSION:

Chylothorax is a serious complication after esophagectomy with an incidence ranging from 0.4 to 4% [18]. Chyle deficiency leads to immunological depletion and malnutrition and therefore poses a significant clinical problem especially in cases of persistent chyle leaks [19]. The management is significantly controversy as some advocating conservative management, while others claim that surgical management is more effective [20].

In accordance with surgical ligation, Orringer et al. [21] expressed a non-comparative study, which showed that operative intervention for patients with chylothorax resulted in a 100% resolution rate.

Merigliano et al. [22] examined 19 patients who developed postoperative chylothorax and found no complications or deaths related to thoracic duct ligation in the surgical group whencomparedwitha9% mortality rate in the conservative group. Also, Schumacher et al.[23] published a comparative study between conservative treatment and prophylactic ligation and found that patient who underwent surgical prophylactic ligation showed a higher resolution rate from chylothorax and a shorter hospital stay, and the study strongly recommended an aggressive treatment for chylothorax with early thoracic duct ligation after esophagectomy.

Dougenis et al.[24] published a retrospective analysis of 255 patients who had undergone elective thoracic duct ligation (n= 189) compared with the patients who had their thoracic ducts preserved (n=66). This study demonstrated a statistically significant reduction in chylothorax rates in patients who had undergone prophylactic ligation. Similarly, Cagol et al.[17] showed a reduction in incidence of chylothorax rates in the ligation group, albeit their overall incidence of postoperative chylothorax was very low (0.9%) and no statistical analysis was performed. To date, the only large-scale

In contrast, Rao et al.[25] showed no difference between the two groups in terms of resolution of chylothorax.

In complete contrast to the above-mentioned studies, the series by Fu et al. [26] on 389 patients showed a statistically significant increase in postoperative chylothorax following ligation (1.17 vs 0.46%), suggesting that prophylactic thoracic ligation was not only unnecessary but also harmful. Later, Hou et al. [12] published a retrospective cohort study concluding that prophylactic thoracic ligation had an adverse impact on the overall survival (42.9 months for patients of the ligation group vs 54.4 months for patients of the preservation group). However, they did not notice a reduction in the occurrence of chylothorax of resectable esophageal cancer patients; indeed, only a rather small difference between the two groups (0.9% for the ligation group vs 1.0% for the preservation group) was described.

CONCLUSIONS:

The prophylactic primary or therapeutic secondary ligature of the thoracic duct is an effective surgical preventive measure and therapy of postoperative chyle leakage.

There is some evidence that early surgical reoperation may reduce hospital stay in patients with postoperative chylothorax following esophagectomy when compared with conservative treatment. However, it is dependent on the clinical condition of the patient, volume of chylous output, and needs to be assessed on an individual case basis.

thoracic duct ligation during video-assisted thoracoscopic esophagectomy for cancer is an effective and safe method for the prevention of postoperative chylothorax. The long-term effect of thoracic duct ligation on patients' survival requires further investigation.

RECOMMENDATIONS:

ligature of the thoracic is recommended after surgical esophagostomy

further investigation on the long-term effect of thoracic duct ligation on patients' survival is needed.

Early surgical reoperation in patients with postoperative chylothorax following esophagectomy

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