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Research Article

Comparing Total Parenteral Nutrition with Other Methods in Treating Chylotorax

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ABSTRACT

Objectives: This study aimed to examine the role of total parenteral nutrition in the treatment of chilotorax.

Methods: A total of 1149 patients who were operated for esophagus cancer were screened between 2010 and 2021. Of these patients, 49 were identified with chilorotax. Patients were divided into three groups. Some of these were treated surgically (first group) and through conventional approaches such as plorodesis, and somatostatin (second group). The only method of treatment used for the remaining patients was total parenteral feeding (third group). These three groups were statistically compared using clinical data to demonstrate that total parenteral nutrition is as effective as other treatments for chilotorax.

Results: A total of 1144 patients who received surgical treatment for esophageal cancer were analyzed. Chilotorax was used to diagnose 49 of these patients. Fewer deaths and complications occurred in the third group who were treated with just total parenteral nutrition. When the groups were compared using post hoc multiple comparison tests, based on the length of stay in the hospital after diagnosis and treatment initiation, it was discovered that; the average length of stay in the hospital in group 3 was less than the other two groups.

Conclusion: The use of total parenteral nutrition alone or in conjunction with surgical and another interventional processes in the treatment of chylothorax importantly reduces the risk of difficulties as well as the death rate. In all patients with chylothorax, parenteral nutrition should be included to the treatment protocol.

Keywords: Chylotoraks, esophagus cancer, parenteral nutrition

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Introduction

Chylothorax is a condition defined by the accumulation of lymphatic fluid in the intrathoracic area as a result of ductus thoracic integrity disruption. Its treatment is a significant clinical table because it raises therapy costs due to its possibility to cause morbidity and mortality and prolong hospital stays.[1] Malnutrition can result from the loss of chylous fluid, which is high in protein, fat, electrolytes, bicarbonate, lymphocytes, and fat-soluble vitamins in chylothorax. As a result, it is necessary to clarify the etiology and rapidly plan the treatment (Table 1). Treatment of the malnutrition clinic, in addition to removing the etiological cause, is critical for rapid and successful treatment. Because of the frequent complications of surgical treatment in a chylothorax and the requirement for optimal parenteral nutritional therapy, the significance of total parenteral nutrition (TPN) in the treatment of chylothorax is becoming clearer day by day. The purpose of this study was to evaluate the efficacy of TPN therapy in comparison to other chylotorax treatment options.

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Table 1. Etiology of the Clinical Course of Chylothorax

Etiology of Chylothorax
Congenital Causes
Ductus anomaly
Acquired Causes
Traumatic
Blunt trauma
Penetrating trauma
Surgical procedures
Nontraumatic
Malignancy
Infection
Idiopathic

Methods

Upper gastrointestinal system cancers are most common between 40. and 50. degrees east meridians and between 120. and 150. degrees east meridians worldwide.[2] In particular, esophageal cancers occur significantly more frequently in Persian regions than elsewhere in the world. Our research was carried out in the east of Türkiye, where upper gastrointestinal system cancers are the most common. As a result, surgical treatment of cancers, particularly esophageal cancers, is common, and surgical treatment complications are common. One of the most critical complications among these is chylothorax.[2] Patients who had undergone esophageal surgery and then developed chylothorax and applied to two centers in Van where surgical treatment of esophageal cancers is commonly performed were reviewed retrospectively and included in our study. In this research; 1144 patients who underwent surgical treatment for esophageal cancer, between January 2010 and June 2021, were evaluated. Patients with metastatic illness, liver and kidney failure, patients with extra metabolic illness, and patients undergoing surgical therapy for the second time, were removed from our research patient population. Among the remaining patients, 49 patients who developed chylothorax were included in the research and were split into three groups. Group 1; is the patients who had just surgical treatment, group 2; is the patients who had other treatment methods in addition to surgical treatment, and group 3; is the patients who receive just TPN treatment.

TPN was planned and overseen by the nutritional support unit of Van Education and Research Hospital, and all clinical information was recorded. A clinician, a pharmacist, a dietitian, two nurses, and a secretary make up the nutritional support team at our hospital, which is overseen by a doctor. The NRS 2002 (Nutritional risk screening) scale, which is advised by ESPEN, was used to determine and calculate the patients' nutritional needs (The European Society for Clinical Nutrition and Metabolism). The Harris–Benedict or Schofield equations were used to determine the patients' energy requirements. Patients have been found to have an average energy need of 50 kcal/kg/day. We employed solutions developed to provide 30% of total energy from lipids and 65%–70% from carbohydrates. It is aimed at providing 1.5 g/kg/day protein to the patients. Blood sugar, fluid, electrolyte, and mineral requirements of the patients were frequently monitored, and any deficiencies were treated with additional treatments as required. None of the patients was provided human albumin support.

Results

A total of 49 of 1144 esophageal cancer patients treated at the Ministry of Health Sciences University Van Education and Research Hospital and Yüzüncü Yıl University Faculty of Medicine Dursun Odabaş Medical Center experienced chylothorax due to ductus thoracic injury. The ethics committee of the Republic of Türkiye Ministry of Health Van Education and Research Hospital evaluated these patients retrospectively according to the ethics committee accepted dated 03.02.2022 and numbered 2022/78-11. Eight (3♂ 5♀) of the 49 patients, had only surgical treatment. While 21 patients (8♂ 13♀) had surgical treatment and extra treatment methods (TPN, somatostatin, talc, and pleurodesis, etc.), and 20 (7♂ 13♀) patients had only TPN and medical support. The patients were grouped demographically dependent on their age and gender (Table 2). Before the patients were diagnosed with chylothorax, the average amount of drainage fluid entering the thoracal tube was 850 cc/day, 770 cc/day, and 650 cc/day, respectively (Table 2). The mean daily drainage amounts in these patients were as follows after the drainage fluid turned chylous, the diagnosis of chylothorax was made as a result of the necessary laboratory tests, and the necessary treatment was initiated: 190 cc/day in group 1, 110 cc/day in group 2, and 260 cc/day in group 3 (Table 2). In patients who underwent only surgery, the following complications were noted: empyema in 2 (25%) patients, hemothorax in 4 (50%), bilateral pneumothorax in 5 (62%), atelectasis in 3 (37%), pneumonia in 7 (88%), thrombophlebitis in 1 (12%), hypoproteinemia in 9 (92%), and hyperglycemia in 1 (12%). Complications included empyema in 4 patients (19%), hemothorax in 7 (33%), pneumothorax in 15 (71%), atelectasis in 5 (23%), pneumonia in 12 (57%), thrombophlebitis in 1 (9%), hypoproteinemia in 3 (23%), hyperglycemia in 5 (19%). In the patients who had just TPN, the following complications were noted: empyema in 2 (5%), atelectasis in 2 (10%), pneumonia in 12 (35%), hypoproteinemia in 3 (18%), and hyperglycemia in 5 (25%) (Table 3, Figs. 1–2). Following

Table 2. Results

	Surgery	Surgery & Other Treatments	TPN
Sex	3♂ 5♀	8♂ 13♀	7♂ 13♀
Mean Age, years	66	73	71
Mean drainage in patients diagnosed but not receiving treatment, cc/day	850	770	650
Mean drainage in patients diagnosed and receiving treatment, cc/day	190	110	260
Number of complications	32	52	22
TPN, kcal/day	0	1400	2850
Mean blood albumin amount during the treatment, gr/day	2.4	2.9	3.1
Hospitalization after the treatment, day	22	25	19
Mortality (1 month) (in hospital)	2	7	1
Mortality (3 months)	1	4	2
Total Mortality	3	11	3

Table 3. Numerical Distribution of Complications

	Surgery	Surgery & Other	TPN
Empyema	2	4	2
Hemothorax	4	7	0
Pneumothorax	5	15	0
Atelectasis	3	5	2
Pneumonia	7	12	12
Thrombophlebitis	1	1	0
Hypoproteinemia	9	3	3
Hyperglycemia	1	5	5

chylothorax treatment, the hospitalization duration of the patients whose thoracostomy tubes were excluded and challenges were treated for group 1, group 2, and group 3 were recorded as 22, 25, and 19, respectively, while they were in the hospital (Table 2). These values were 1, 4, and 2 months after discharge, respectively (Table 2, Fig. 3).

Statistical Analysis

Cohen's T-test was used to determine the minimum number of samples, that is, for power analysis, following the hypothesis of our study research. The minimum number of samples required to achieve an 80% power value was determined to be 51. Our sample number was 49; therefore, it was very close to this value. The Chi-square test was employed in our research to compare the expected values with the discovered values. In this research, the Chi-square distribution table was research to calculate the approximate importance level (p-value) after calculating the degrees of freedom and Chi-square values. The p-value was calculated as an important value between 0.01 and 0.05 (i.e., 5%–1%). The analysis was performed using the one-way ANOVA test. Post hoc multiple comparison tests were added to find out which groups had important p-values.

Discussion

The ductus thoracicus is an extension of the cisterna chile that runs between the aorta and the azygos vein, in the chest and opens into the left jugular-subclavian venous junction (Fig. 4). Several more lymphaticovenous anastomoses are created by the ductus thoracicus with the vena

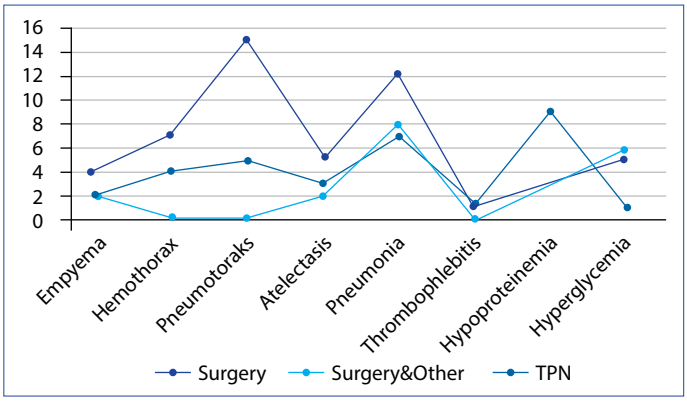

Figure 1. Numerical Distribution of Complications by Groups.

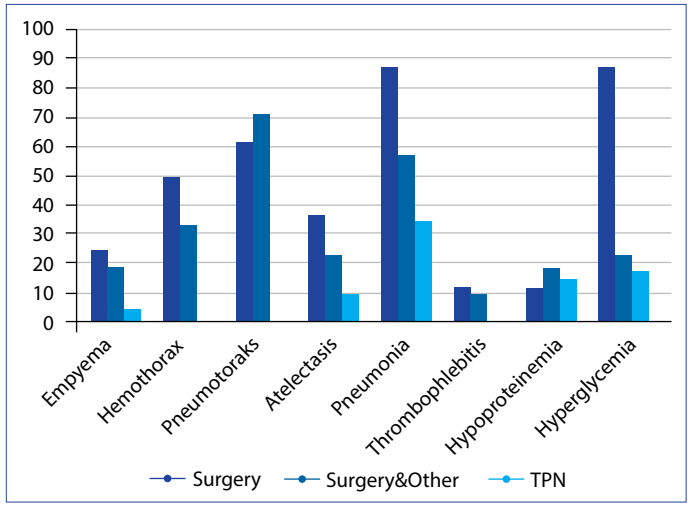

Figure 2. Percentage Distribution of Complications by Groups.

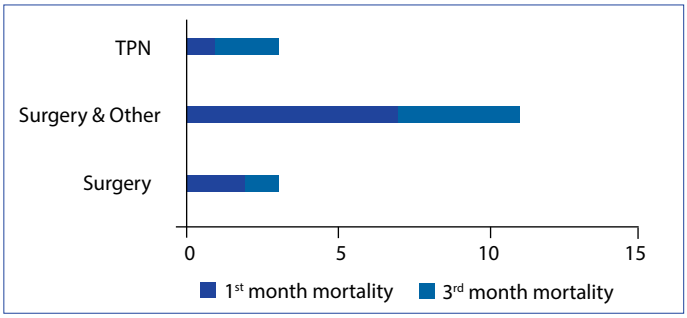

Figure 3. First month, third month, and total mortality numbers by groups.

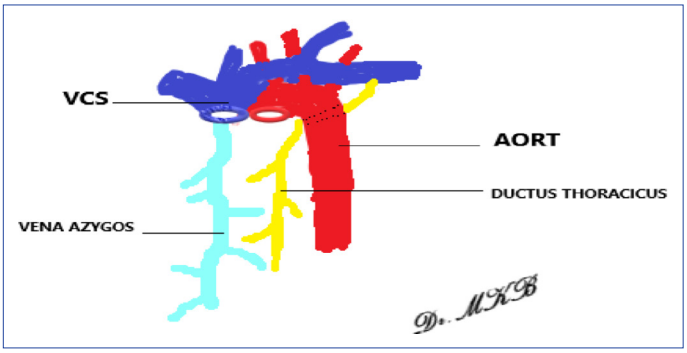

Figure 4. Anatomy of the ductus thoracicus.

azygos, intercostal, and lumbar veins. It also communicates with the right lymphatic duct on multiple occasions.[1]

The ductus thoracicus' primary function is to transport fats and return extravascular proteins to the blood. The lymphocyte is the most common cell type in lymphatic fluid, and the basal flow rate is 0.82–0.27 ml/kg/hour, depending on the meal and its fat content.[1,2] Approximately 60%–70% of digested lipids are absorbed by intestinal lymphatics and transmitted by the ductus thoracicus. Fatty acids with fewer than ten carbons are directly absorbed by the portal system, whereas fatty acids with more carbons are transported after being changed to chylomicrons in the lymphatics.[2]

While esophageal surgery, cardiovascular surgery, thoracic surgery, and mediastinal dissections for lung cancer may all play a role in the etiology of chylothorax. The etiology of the condition may also be influenced by nonsurgical factors such as certain infections or penetrating neck and thoracic trauma. Congenital causes, such as duct anomaly or idiopathic chylothorax, may also contribute to the ethiology.

Because chylothorax does not cause much pleural irritation, the clinical manifestation is dyspnea rather than pain and fever. This liquid is bacteriostatic because it contains lecithin and fatty acids.[3] The amount of effusion is also proportional to the clinical severity of breathlessness. On auscultation, there is a clear reduction in lung sounds on the side with effusion. Other clinical symptoms caused by immunodeficiency and malnutrition include weakness, dehydration, metabolic acidosis, and other clinical symptoms. Malnutrition caused by chylothorax can be discovered in 25%–50% of thoracic surgery patients.[3,4] Due to pleural effusion or mediastinal chyloma, a mediastinal radiopaque shadow appears on the chest X-ray. The ductus thoracicus can be imaged by lymphangiography and nuclear scintigraphy methods. These imaging methods, while showing the anatomy of the duct as well as the location of the leak, are rarely used as diagnostic methods. The examination of pleural fluid obtained via thoracentesis or tube thoracostomy supports the diagnosis. Pleural fluid with the appearance of milk is present in ~50% of chylothorax cases. This situation could be caused by poor nutritional habits and foods with variable lipid content. As a result, the appearance of effusional fluid may not always result in the correct diagnosis. This milk-like off-white liquid is also identified as chylous. In the chemical evaluation of this chylous fluid, the number of triglycerides was discovered to be greater than in other effusions, but the amounts of LDH, protein, and cholesterol were reported to be similar.[4] The triglyceride cholesterol ratio is >1, this ratio is <1 in nonchylous pleural effusions. If the triglyceride level is <50 mg/dl, the likelihood of chylothorax is 4%, whereas 98% of effusions with a triglyceride level > 110 mg/dl are chylous.[5] The total protein content of chylous effusion was pH 7.3–7.8, albumin 1.2–3.9 g/dl, globulin 1.1–3.6 g/dl, and total lipid 0.5–6 g/dl. The electrolyte values of chylous fluid were discovered to be about equal to those of plasma.[4,5] However, not every aspirate obtained via thoracentesis or tube thoracostomy that has a chylous consistency and appearance is a chylothorax. Pseudochylothoraxis a clinical condition caused by long-term pleural effusions that can be distinguished from chylothorax through chemical analysis. The following are the most significant diagnostic criteria: Microscopic examination revealed a higher cholesterol-triglyceride ratio, a higher lymphocyte ratio, and fat lobules stained with Sudan III.[5] Pseudochylothoraces are also high in lipids, but the main attribute of the effusion's lipid content is cholesterol rather than triglycerides. In chylothorax, the number of triglycerides is high.[6] Chylothorax was diagnosed in our study using clinical features, imaging, and laboratory tests. In the postoperative period, lymphatic fluid leakage from the thoracic duct occurs at a rate of 1%–4% after esophageal surgeries and 0.5%–2.5% after cardiac and thoracic surgeries.[7,8]

Chylothorax treatment can be performed medically, i.e., conservatively, interventionally, or surgically.[9] Because this procedure also provides a definitive diagnosis, the first step

in treatment is to drain the fluid that has accumulated in the pleural space. While thoracentesis is sometimes essential for this process, tube thoracostomy is frequently needed for chylous fluid drainage.[9] Only the patient group that received surgical treatment (group 1) was comprised of patients diagnosed at an early stage and treated using relatively more traditional treatment methods. Some reports state that drainage in the spontaneous closure of the duct is effective.[9] However, because the loss of lipid, fluid, electrolyte, and metabolite can harm the patient's clinic table until this effect occurs, it is recommended to be used in the early stages of chylothorax when protein and fat loss are not excessive.[10] Daily drainage can range from 2500 to 3000 cc, according to studies, but conservative treatment methods are generally considered successful if the drainage is ≤500 cc.[11] Some clinical studies reveal that somatostatin analogs can decrease or even completely stop chylous pleural effusion. These drugs are thought to work by decreasing intestinal blood flow and preventing lipid absorption.[1] As a result, the belief that somatostatin therapy must be supplemented with parenteral nutrition predominates.[1] In our study, group 2 patients received treatment in addition to surgery, while group 3 patients did not have surgery and received only TPN treatment. If there is an important decrease in drainage, that is, the daily drainage does not fall below 500 cc, or full lung expansion is not able due to inadequate drainage, a switch from conservative treatment to treatment with interventional procedures is needed.[12] The most commonly used interventional treatment methods are pleurodesis with povidone-iodine, fibrin glue or talc, tetracycline sclerotherapy, and fluoroscopic embolization to the duct using platinum micro coils.[13-15] Interventional treatment methods include pleuroperitoneal shunting and pleurectomy.[13] The surgical treatment aims to ligate the thoracic duct. This procedure can be performed using either thoracoscopic or open surgery.[13] It is suggested that the patient drink olive oil or employ dyes such as methylene blue or solvent black to help identify the duct before surgery.[13]

Parenteral nutrition in chylothorax can take the form of peripheral or central parenteral nutrition. Because the nutritional risk index in these patients is usually >84 due to hypercatabolism, parenteral nutrition can be started quickly. Another indication for TPN is the presence of severe lymphatic leakage in these patients. If nutrition is to be conducted peripherally, the osmolality of the provided product should not exceed 600 mOsm/L, and the calcium content should be applied with care.[16] The number of calories needed, the total amount of fluid to be provided to the patient, and the predicted duration of the parenteral nutrition support all affect whether the parenteral nutrition will be prescribed centrally or peripherally.[17] If parenteral nutrition is to be conducted via the central vein, the catheter entry site should be as far away from wounds, previous catheter entry sites, tracheostomy, or fistulas as possible from wounds, previous catheter entry sites, tracheostomy, or fistulas. The use of simultaneous ultrasonography during central venous catheterization can make the procedure easier and safer.[18] A treatment plan based on all of these recommendations was developed for the patients in our study who received only TPN.

When our research was examined demographically, no statistical difference was discovered between the groups in terms of gender and age. The intergroup p-value for gender and age were respectively calculated to be 0.08 ($p>0.05$) and 0.11 ($p>0.05$).

When the daily drainages from the thoracic cavity of all three groups were followed and recorded before starting treatment after the chylothorax diagnosis, there was no statistical difference between the three groups, and the p-value was calculated as 0.15 ($p>0.05$). When the thoracic tube drainages were compared between the start of treatment and the removal of the chest tube after diagnosis, group 2 drained approximately 190 cc per day, which was significantly less than the other groups. The p-value was reported to be 0.045 when the drainages were equated following treatment ($p<0.05$). The low number of drained chylous has been attributed to the aggressive use of surgical and nonsurgical treatment methods. However, it was found that aggressive treatment methods were employed, the risk of problems increased in this group, the length of hospital stay was prolonged, and the number and rate of death in the hospital were greater than in the other groups. Two had 52 complications, which was found to have significantly more complications than the other groups ($p=0.03$). Some of the complications were caused by surgical and interventional procedures, while others were caused by medical treatment methods used. No difference was discovered in terms of the risk and number of problems between the surgical treatment group and the only TPN-given group ($p=0.095$). In terms of early mortality, group 2 patients were found to be at a higher risk than the other groups ($p=0.015$). This is thought to be because infections cause patients to rapidly enter multi-organ failure, the catabolic process cannot recover quickly, and the complications of aggressive treatment methods are severe.

Following treatment initiation, patients' blood albumin levels were continuously monitored for nutritional monitoring. It was recorded that albumin values had similar rates. In this comparison, the significance value was discovered as $p=0.068$ ($p>0.05$). Because of the heavy catabolic pro-

cess and the long half-life and synthesis of albumin, it is thought that this result is not statistically significant.

When the total number of deaths during and after hospitalization was examined, group 3, which included 20 patients, had three deaths, which was discovered to be significantly different from the other groups. When the groups were equated in this way, the p-value was 0.009 ($p<0.05$), which was regarded as highly statistically important ($p<0.01$).

When the groups were examined based on the length of stay in the hospital following diagnosis and treatment initiation, it was discovered that group 3 had a 19-day average length of stay in the hospital. This was 22 days for group 1 and 25 days for group 2. The length of stay in the hospital was statistically importantly shorter in the group that got only TPN ($p=0.036$). In group 3, we believe that, in addition to the absence of invasive interventions and a lesser postsurgical recovery period following the discharge, full nutritional support allows patients to recover more quickly. This is because nutritional support promotes not only the rapid replacement of necessary metabolites but also the immune system. Therefore, we found that our study's primary hypothesis and goal were achieved and supported.

In conclusion, the use of TPN alone or in combination with surgical and other interventional procedures in the treatment of chylothorax significantly decreases the risk of complications as well as the death rate. The length of stay in the hospital of these patients was found to be statistically significantly lower in patients with chylothorax treated with only TPN, which was the primary goal of the study. It was determined that all patients with chylothorax should receive parenteral nutrition as part of their treatment plan.

Disclosures

Ethics Committee Approval: The ethics committee of the Republic of Türkiye Ministry of Health Van Education and Research Hospital evaluated these patients retrospectively according to the ethics committee accepted dated 03.02.2022 and numbered 2022/78-11.

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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