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## Chylothorax in cancer patients: methods of treatment

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### ХІЛОТОРАКС В ОНКОХВОРИХ: СПОСОБИ ЛІКУВАННЯ

**On the basis of domestic and foreign scientific publications considered methods of diagnosis and treatment of chylothorax in cancer patients. From clinical positions evaluated conservative treatment, duct embolization, and surgical thoracic duct ligation. It is concluded that chylothorax is life-threatening complication that postpones time of the special anticancer treatment. Therefore, when a chylothorax is occurred in cancer patients the active surgical tactics as the thoracic lymphatic duct ligation should be done.**

У статті на основі вітчизняних і зарубіжних наукових публікацій розглянуто методи діагностики та лікування хілотораксу в онкохворих. З клінічних позицій оцінено консервативне лікування, емболізацію і хірургічну перев'язку грудної лімфатичної протоки. Зроблено висновок, що хілоторакс – це життєво небезпечне ускладнення, яке віддаляє час проведення спеціального протипухлинного лікування. Тому при виникненні хілотораксу в онкохворого слід дотримуватись активної хірургічної тактики – виконувати перев'язку грудної лімфатичної протоки після правобічної торакотомії або з використанням відеоторакоскопічної техніки.

Chylothorax is a presence of lymph in pleural cavity which is accumulated in it because of damage of thoracic lymph duct. Chylothorax belongs to the complications potentially dangerous for life and is accompanied with the respiratory changes, metabolic and immunologic imbalance. Over the last 10–15 years diagnostic capabilities and therapeutic approach considerably changed, which let successfully fight with such difficult complication now [1, 20–21, 24].

*Etiology.* Thoracic lymph duct (TLD) injuries occur not so often (1.0–4.0 %) after surgeries in thorax and dilated cervical lymphadenectomies [1, 3, 20]. According to Merigliano and co-authors (2000), chylothorax occurred in 19 patients (1.1 %) of 1787 operated for cancer of oesophagus or cardia of stomach [14].

Chylothorax may be caused by traumatic and non-traumatic etiological factors. Traumatic chylothorax is a complication of surgery: most often after esophagectomy in patients with oesophagus cancer (41.3 %), pneumonectomy or lobectomy (10.3 %), chest injury (6.9 %), thymomectomy, cervical lymphodissections (Crile's operation or casing-fascial lymphadenectomy) [2, 8, 11, 16, 22, 24].

Non-traumatic chylothorax sometimes occurs at lymphoproliferative disorders with the primary localization of tumors in mediastinum (17.2 %), during

obstruction of the upper vena cava, at malignant tumors of pleura, in the process of cytostatic chemotherapy or radiation treatment of the chest in patients with lymphomas and breast cancer [1, 6, 17–18, 21].

*Diagnostics.* Clinically injuries of TLD are appeared with chylothorax, chylopericardium or cervical lymphatic fistula. Patient has dispnea, during percussion – dullness of lung sound, auscultation – weak or absence of breathing on the affected side. On an x-ray picture and CT there is an effusion in the pleural cavity with the mediastinal displacement and compression of lung. At thoracocentesis they get milk-like with chylomicrons liquid, without any smell. Chylous exudates contains high concentration triglycerides (>1.24 mmol/l) [1–3, 20].

Postoperative (traumatic) chylothorax is diagnosed with some delay (2–5 days) which is connected with the intravenous infusion therapy that is actual parenteral nutrition of the patient. If drainages are present in pleural cavity chylorrhea may be found the next day after the surgery [17, 18].

*Conservative treatment.* Treatment of chylothorax depends on its aetiology and volume of daily lymph discharge. Traditionally conservative therapy includes fatless diet, parenteral nutrition, daily monitoring of liquid and electrolytes, drainage of pleural cavity (or

repeated punctures of pleural cavity with the maximum possible evacuation of chylous liquid), replacement of lymph losses. Change to the full parenteral nutrition is the most effective for reduction of lymphopoiesis. After liquid evacuation intrapleural injection of antibiotics for prevention of infection of pleural cavity is essential [8, 10, 15, 20, 21].

Some authors recommend to carry out reinfusion of lymph 0.8–1.5 l per one procedure, 2–4 times with a break in 2–3 days [1]. “Octreotide” is used for the pharmacological blockage of lymphopoiesis. This preparation increases the resistance of microcirculatory course in abdominal cavity and reduces gastrointestinal secretion. Almost in 50 % (from 25 to 75 %) of cases conservative approach is effective and chylorrhea stops during 10–14 days [1, 21].

Conservative treatment is based on the peculiarities of lymph composition and chylopoiesis. Lipids are the main constituent component of lymph; 60–70 % of consumed fat is absorbed by the intestinal lymphatic system and through thoracic duct gets into the bloodstream. Extravascular protein returns to the blood stream through thoracic duct too; protein content in lymph is half of its concentration in blood plasma. The main cellular elements of lymph are lymphocytes, 90 % of them is T-lymphocytes. That is why prolonged chylorrhea of the thoracic duct leads to hypoproteinemia, lymphocytopenia, electrolyte imbalance, immune, metabolic, nutritional and general exhaustion [1, 20, 21]. Prolonged conservative treatment of chylothorax is associated with mortality in 50–82 % of cases. Results of surgical ligation of lymphatic duct are more encouraging with 10–16 % of mortality rate [10, 24].

Still, there is no consensus on the optimal duration of non-surgical period. It is believed that if this approach does not bring any success, operative measures (ligation of the thoracic duct) should be taken. Surgical methods are used only when there is no response to medical therapy or when lymph loss is more than 500–1000 ml/day [10, 17].

*Thoracic duct embolization.* In order to visualize the lymphatic ducts it is necessary to perform lymphangiography. First, catheterization of lymph vessels in the feet using lymphotropic dye indigocarmine or lymphazurin is performed; then contrast medium lipiodol is injected intralymphatically. Thoracic duct begins with cisterna chyli which is located in the abdomen at the level of L1–L2 (behind the right crus of diaphragm). From radiological point of view during lymphangiography cisterna chyli is seen as an oblong sack 2.0×1.0 cm. With the help of interventional radiology, percutaneous transabdominal cannulation

(catheterization) of cisterna chyli or thoracic duct is performed. In this case, spiral ring is inserted into the lumen of thoracic duct which serves as a support for polymerization material n-Butyl cyanoacrylate (n-BCA), which is actually used to embolize duct lumen. The efficiency of thoracic duct embolization ranges from 69 to 91 % [5, 12]. In one of the studies lymphangiography was not only a diagnostic but also therapeutic procedure in eight of the nine patients [13]. That is, the procedure of diagnostic lymphangiography itself can stop lymph leakage in the thoracic cavity, and, thus, surgical intervention (thoracotomy) can be avoided. Lymphangiography is recommended in cases when conservative treatment of chylothorax will not probably be effective [9, 13].

Percutaneous embolization of thoracic duct is indicated in cases when there is high risk of complications after rethoracotomy. According to Cope (2004), after thoracic duct embolization had been performed, chylorrhea completely ceased during the first week in 61.5 % of patients, and during the next two weeks in 23.0 % of patients [7]. In another report, chylothorax was eliminated in 69.0 % of patients [12]. Thoracic duct embolization has become an important therapeutic alternative due to its high efficiency level with minimal complications [5]. If percutaneous embolization is not successful, surgical ligation of thoracic duct or pleurodesis should be performed [12].

*Surgical treatment – ligation of the thoracic duct.* Timing of the operation still remains disputable. The indications for surgery are the following: chylothorax lasting for 1–3 weeks, or daily lymph loss more than 500 ml. Most surgeons believe that (re)operation should be performed immediately after diagnosing chylothorax or within 48 hours if intensive conservative treatment is not effective [15, 19, 20, 24]. The choice of the technique depends on surgeon's qualification, existing clinical equipment, and results of previous surgical interventions. The following methods are used: direct ligation of the thoracic duct, supradiaphragmatic dressing “ad masum” of the thoracic duct, video-assisted thoracoscopic ligation of the thoracic duct, pleurodesis, pleural-peritoneal bypass. As for the access, usually right-side, sometimes left-side thoracotomy is used; video-assisted thoracoscopy has also become preferable recently [17, 21, 23].

Video-assisted ligation of thoracic duct is an effective method for chylothorax elimination and has minimal complications [6, 10]. If chylorrhea is higher than 1000 ml per day, there are all indications for early thoracoscopic ligation of the thoracic duct [18, 23]. Early reoperations with thoracic duct ligations, in the

comparison with the delayed ones, do not cause fatal complications, and usually are successful [17, 19]. Early ligation is the operation of choice in cases when chylothorax occurs after esophagectomy [14]. If chyloorrhea does not stop after ligation of the thoracic duct has been performed, pleurodesis is indicated [17, 21].

The standard surgical operation involves precision dissection of tissues in the location of the thoracic duct in the lower posterior mediastinum and further ligation of the thoracic duct above and below the defect. The thoracic duct is sutured and bandaged in the typical location between the aorta and azygos vein at the level of ThX–ThXI vertebrae [1, 18, 21]. In the case of impossibility to identify the place of rupture, a continuous stitch is sutured a wound on the paraaortic tissues in the typical place on the right side at the ThX vertebra level [1, 2].

The plastic surgery of the damaged area of the thoracic duct with the application of the microsurgical anastomosis or lymphovenous anastomosis between the thoracic duct and azygos vein is performed at some clinics [2, 3].

For intraoperative identification of the damaged area of the thoracic duct location, the fat mixture, dyed by indigo carmine, is injected through the nasoenteric tube or 200.0 ml of milk with 20.0 grams of margarine is given to drink to the patient immediately before the surgery. In case I, lymph is dyed in blue colour, in case II lymph gets intensive milky white colour, and it allows to identify the location of the thoracic duct defect [1, 16].

Rudimentary postoperative lymphorrhea is observed in some patients, they are exposed to the pleural cavity puncture, lymph evacuation and pleural sclerosant injections (doxycycline, hypertonic glucose solution) [1, 17].

Surgical pleurodesis is effective in some cases and it may be the method of choice for critically ill patients [17]. In severe cases, when the damaged place of the thoracic duct can not be identified, pleurodesis is the only method of chylothorax elimination [18].

*Preventive intraoperative ligation of the thoracic duct.* Comparative study of 243 patients with the cancer of oesophagus (surgical preventive ligation of the thoracic duct was performed during the surgical operation for half of them) showed that there was chylothorax in 8 (3.3 %) patients. Statistical analysis showed that there was no significant difference in the rise of this complication between these two groups. Therefore, the preventive ligation of the thoracic duct has no effect on the reduction of the frequency of the traumatic chylothorax after the esophagotomy [11].

Three clinical cases of chylothorax in cancer patients were observed in our practice – after left sided neck dissection, during radiotherapy of the mediastinal lymphoma and after diagnostic pleuracotomy in patients with lymphogranulomatosis. In the first two cases, the conservative treatment (diet, parenteral nutrition, pleural puncture, intrapleural cytostatic drug injection) was applied and it was found ineffective method. The lymphocytic exhaustion and further cachexia and death of patients came after 4–5 weeks.

The active surgical tactics was used for the patient with lymphogranulomatosis. On the fifth day after the diagnosis of chylathorax was made, the surgical operation (re-thoracotomy with the thoracic duct ligation) was performed. After the chylathorax was eliminated, the patient had a complete course of the thoracic duct treatment (6 courses of the post-thrombotic syndrome using ABVD scheme, radiotherapy of the lymph mediastinum nodes – 40.0 Gy) and the patient had been in clinical remission for four years [4].

*Conclusion.* 1. Chylothorax in cancer patients is a life-threatening complication that shows metabolic, immune and nutritional exhausting and delays the time of the special anti-tumour treatment.

2. In the case of chylothorax onset in cancer patients, one should follow active surgical tactics and perform ligation of the thoracic duct after the right sided thoracotomy or using video-assisted thoracoscopy under conditions of the absolute parenteral nutrition.

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