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Chyle Leak after Pancreas Surgery: A Review

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Abstract

Background: Chyle leak is a rare complication after pancreatic surgeries. In 2017, the ISGPS accepted a new consensus of its' classification. However, this is yet to be accepted universally. The diagnosis of this complication is evident since it is characterized by a milky white color fluid.

Etiology and Management: Several risk factors have been suggested by different authors in previous literatures. The understanding of precise mechanisms of chyle leak after pancreatic surgeries is vital for appropriate management. Damage to cisterna chyli, early enteral nutrition, chronic pancreatitis and neoplastic diseases have shown to be associated with high risk occurrence of chyle leak. Conservative management has been the mainstay so far.

Conclusion: Chyle leakage can be potentially life-threatening complication after pancreatic surgeries due to reported increase mortality and morbidity in literatures. Surgery is specifically for refractory chyle leak cases.

Keywords: Chyle Leakage After Pancreatic Surgeries; Cisterna Chyli; Early Enteral Nutrition; Surgery

Introduction

Chyle leak after pancreas surgery is best defined as the appearance of milky, non-purulent fluid from a drain, drain site or wound on or after postoperative day 3, with a triglyceride level greater or equal to 110mg/dL (greater or equal to 1.2mmol/L) [1-11]. Chyle is lymphatic fluid in the wall of the bowel consisting of an emulsion of lymph and triglyceride fat (chylomicrons); chyle is transported from the lymphatic vessels in the wall of the intestine to the lymphatic vessels in the mesentery, where they coalesce into the cisterna chyli, which joins the thoracic duct to drain into the venous circulation. The cisterna chyli is a roughly 5-cm sac-like dilatation of the lymphatic system located deep within the retroperitoneum at the level of first and second lumbar vertebrae. The structure is located to the right of the aorta, deep within the interval of the aorta and the inferior vena cava. Chyle leak is a general term that includes two distinct entities each with a unique natural history. These include a contained chyle leak and a chylous ascites. These two types of chyle leaks are very different in regard to management and outcome. A contained chyle leak is a walled-off collection that communicates with disrupted visceral lymphatics, whereas chylous ascites is a diffuse free-flowing chyle leak. The latter has a much higher impact on survival since it results in more significant immunosuppression, malnutrition, a prolonged hospital stay and fluid/electrolyte imbalances [7]. The increased mortality with chylous ascites following pancreatectomy has been reported [8,12]. A recent large series demonstrated the presence of a chyle leak in 12.5% of patients after pancreaticoduodenectomy. This article focuses on the concise review of chyle leak after pancreatic surgeries and the treatment strategies.

Historical background

In 2008, Van der Graag, et al. [1] developed the first grading system for isolated chyle leak based on the clinical condition of the patient, duration of chyle leak, management and hospital stay. Chylous ascites were graded into grade A, B and C. Grade A chylous ascites was described as chylous leakage persistent for less than 7 days. Grade B chylous ascites requires the therapeutic measures and resolves within 7 to 14 days. Any duration of chylous ascites longer than 14 days despite therapy and the requirement of surgical intervention or readmission to hospital was defined as Grade C [1]. However, this grading system has never been validated and the relevance of chyle leak remained poorly defined. The weakness of this grading system is that it is based on hospital

stay and parameters that vary with the clinical management of chyle leak rather than objective parameters characterizing the chyle leak itself [1,12]. In 2017, Besselink, et al. [13] came up with a classification of chyle leak, after pancreatic surgery, which was a consensus accepted by the International Study Group on Pancreatic Surgery (ISGPS) (Table 1).

	Grade A	Grade B	Grade C
Therapeutic consequence	None or oral dietary restrictions	Nasoenteral nutrition with dietary restriction and /or TPN, percutaneous drainage by IR, maintenance of surgical drains, or drug (e.g. octreotide) treatment	Other invasive in-hospital treatment, admission to ICU and/ or mortality.
Discharge with (surgical) drain or readmission	No	Possibly	Possibly
Prolonged hospital stays	No	Yes	Yes
TPN, Total parenteral Nutrition; IR, Interventional Radiology			

Table 1: ISGPS consensus definition and grading system for isolated chyle leak after pancreatic resection.

According to the clinical scenario, management and duration of hospital stay, three different grades (A, B and C) were defined. The grading system applies to isolated chyle leak. A clinically irrelevant chyle leak is described as grade A. There is no prolonged hospital stay. Restrictions in oral diet, as a conservative approach, is adopted. If one of the following criteria is met then it is grade B; nasoenteral nutrition with dietary restriction and/or TPN, percutaneous catheter drainage by interventional radiology or maintenance of the surgical drains, or drug treatments (e.g. octreotide) to control chyle leak. Prolonged hospital stay is caused by grade B, and is related directly to chyle leak. A patient might be discharged with the surgical drain in situ or be readmitted for chyle leak. The requirement of more invasive treatment such as interventional radiology involving lymphatic embolization/ sclerosis, admission to an intensive care unit, operative exploration and peritoneovenous shunt, or implies mortality directly due to chyle leak, is described a grade C. Patients readmitted for management of chyle leak for these more invasive approaches change from a grade B to a grade C chyle leak.

Epidemiology

The true incidence of chyle leak after pancreatic surgery is unknown [1,8,12]. This is because chyle leak has rarely been reported after pancreatic surgery. The incidence is reported to occur in 1.3% to 12.0% [1,8,14,15]. At the other end of the reported range, Hilal, et al. [16] published a 16.3% rate of chyle leak in 245 patients undergoing pancreatectomy.

Diagnosis

Chyle leak is a rare clinical entity characterized by a milky white color. The most common presenting symptom is abdominal distention [17-19]. A pure chyle leak is most often homogenous and pure white. The drain fluid should be analyzed for triglycerides and a level of 110mg/dL is necessary to make the diagnosis. Once the diagnosis is confirmed, the next step is to classify the leak as either a contained leak or as free-flowing ascites. If this is not apparent based on physical examination demonstrating ascites, an imaging study may be required [20].

Etiology and Pathogenesis

Chyle leak results in compromise of quality of life of a patient after pancreas surgery. Several authors suggest lymph node dissection, neoplastic diseases, and chronic pancreatitis as risk factors for the development of chyle leak [1,7,8]. Therefore, understanding the precise mechanisms for the development of chyle leak is crucial for early diagnosis and appropriate treatment. The direct operative trauma to the main chyle ducts, is branches, or lymph nodes is believed to be the major cause of chyle leak [21]. The risk increases in extended resections, because it correlates with the number of lymph nodes harvested [2,8,10,22]. The origin of the thoracic duct, known as cisterna chyli, is located just posterior to the pancreas, hence, it is vulnerable to extensive lymph node dissection [8,23]. Major pancreatic surgery results in interruption of the mesenteric lymphatic plexus. Lymphadenectomy was graded as standard or extended as described by Pedrazzoli, et al. [24] Standard lymphadenectomy included the anterior and posterior panceatoduodenum, the pylorus, the bile duct, superior and inferior pancreatic head, and body lymph node stations. Extended lymphadenectomy required the additional removal of lymph nodes from the hepatic hilum and along the aorta, including the inter-aoro-caval nodes, along with the neurolymphatic tissue on the inferior aspect of the celiac trunk and the right side of the superior mesenteric artery. Current studies have questioned the anatomic vulnerability of the cisterna chyli during pancreatic surgery. The existence and location of the cisterna chyli has been variable and poorly understood. In two studies, cisterna chyli was identified 20% at the time of autopsy and 50% at the time with lymphangiography [25,26]. Besides, a Japanese cadaver anatomic study suggested the

paraortic node pathways rather than the cisterna chyli as the origin of the thoracic duct [27]. The cisterna chyli is located anterior to the first and second lumbar vertebrae at the same level as the pancreas head and neck [18,28]. Therefore, surgical disruption of the cisterna chyli or its major tributaries, induced by extended lymphadenectomy or dissection of the retroperitoneum seems to be an etiology [1,8,18,29]. However, there are studies which still show controversy about this etiology: Assumpcao, et al. [8] reported that extensive lymph node harvesting during pancreatic surgery marginally increased the relative risk of chyle leakge (OR 1.07, p=0.007) and on the other hand, Van der Graag, et al. [1] reported similar numbers of harvested lymph nodes between chyle leakage and non-chyle-leakage groups. Hence, more studies are required to confirm this etiology.

Furthermore, increased incidence of chyle leakage after pancreatic surgery has been reported due to early enteral nutrition [1,8,30]. Early enteral feeding is traditionally thought to minimize septic complications, attenuate catabolic stress response, and maintain gut structure and function [31-35]. However, early enteral feeding has been recognized in literatures as a cause of higher incidence of chyle leak [7,14]. The effects of early enteral feeding via a feeding jejunostomy in upper gastrointestinal surgery have been controversially discussed [36-39]. Watters, et al. [40] argued that early enteral feeding may impair postoperative vital capacity, Forced Expiratory Volume (FEV1), and mobility. Noji, et al. [6] showed that early oral feeding with liquid diet and 15g fat from postoperative day 3 also increased the rate of chyle leak. Therefore, routine use of a feeding jejunostomy cannot be recommended and a fat-containing diet before the 4th postoperative day should be avoided.

In addition, the association between chylous ascites and chronic pancreatitis is of growing interest. It is an uncommon entity and has been reported both with acute and chronic pancreatitis [30,41]. Chronic pancreatitis has been shown as an etiology of atraumatic chylous ascites in a few case reports and the exact mechanism is uncertain [41,42]. It has been hypothesized that surrounding infiltration or inflammation in patients, with chronic pancreatitis, require more extensive surgery risking leakage [1]. Another hypothesis, found in literatures, states that the longstanding inflammatory process causes congestion of lymph with subsequent lymph duct enlargement, due to enzyme rich fluid and extra-pancreatic necrosis, more likely to be interrupted during surgeries [43-45]. Besides, there is a possible interaction between chylous ascites development and anastomotic leakage. When leakage occurs, aggressive pancreatic enzymes and bilirubin damage surrounding soft tissue. This in turn could interfere with the triglyceride content of drain output. Hence, it is very hard, if not impossible, to diagnose chylous ascites based on triglyceride level and milky appearance. Multivariate analysis for chyle leakage showed that diagnosis of pancreatic fistula formation was inversely correlated. There has been no evidence presented that a pancreatic fistula prevents chyle leakage because the fistula causes delayed gastric emptying, and there would be less chyle formation. This correlation has not been fully understood. However, the increased lymphatic volume induced the decreased peritoneal amylase concentration, which partially explains this inverse relation.

Moreover, early malignancy of less that stage T2 was a marginally significant risk factor for chyle leakage. This maintained inflow from the distal lymphatic duct is well-established pathophysiology of chyle leakage from damaged proximal collecting ducts [1,46]. The flow into the cisterna chyli and its tributaries is preserved in patients with early stage cancer, which could explain why early-stage malignancy was a risk factor for chyle leakage. Alternatively, it was found in a pig model of pancreatic duct obstruction to be caused by reflux of lymphatic flow due to inflammation around the pancreas [47]. However, this finding seems questionable because chyle leakage possibly develops because of compromised lymphatic drainage due to lymph node fibrosis in patients with advanced malignancy [48]. There continues to be a lack of studies regarding how the relation between periampullary cancer and lymphatic flow changes with different stages of malignancy in humans. Assumpcao, et al. [8] did not report that advanced tumors were a risk factor for chyle leakage. Van der Gaag et al. [1] reported that the presence of an advanced tumor (2.6cm) reduced the risk of developing chyle leakage, even though the finding was not statistically significant.

Treatment

The majority of chyle leaks will resolve spontaneously with conservative treatment which includes management of fluid, electrolytes, nutrition, and chyle drainage. The general aim in management of chyle leak is to control the output and optimize the fluid and nutrition until the leak closes. Conservative management has proven to be the mainstay in treatment [17]. It consists of a dietary control with a Medium-Chain Triglycerides (MCT) containing diet or Total Parenteral Nutrition (TPN) with or without octreotide, intended to decrease the flow of lymph [17, 49-52]. The administration of somatostatin has also been reported to be beneficial [53-55]. The low-fat elemental formula, ELENTAL (Ajimonoto Pharmaceuticals CO., LTD., Tokyo, Japan) was recently recommended for the management of postoperative chyle leak. ELENTAL consists of 15% protein, 83.5% carbohydrate, and 1.5% as caloric distribution, and can provide nearly fat-free enteral nutrition. The formula of ELENTAL is almost identical to that of VIVONEX T.E.N (Nestle Health Science), marketed in many western countries, and also was recommended for conservative treatment of postoperative chyle leak to achieve complete recovery [56-59]. The fruitful resolution of chylous ascites was described in 77% to 100% of the cases with TPN alone, 75% in cases with MCT diet and 100% in cases with addition of octreotide to MCT diet

or TPN. TPN alone was successful in suspending chylous ascites within 5 to 19 days in pancreatic surgery [6,10,14,18,60]. MCT alone showed success within 6 days in 75% of patients in a study by Kaas, et al. [60] Therefore, we can conclude that conservative treatment is sufficient in resolving chylous ascites in up to 100% of the cases especially when patients are treated with TPN. MCT diet provides the advantage of continuous enteral feeding but proved to have relatively lower success rates than TPN, in suspending chylous ascites (Figure 1).

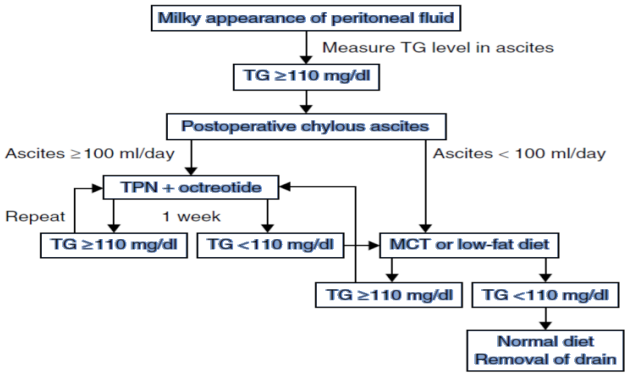

Figure 1: Algorithm for the treatment of postoperative chylous ascites. TG: triglyceride level; TPN; Total parenteral nutrition; MCT; medium-chain triglyceride).

Moreover, understanding the timing for the start of enteral intake plays a strategic role in managing chyle leak as it may be related to the development of chyle leakage. TPN does carry its own disadvantages and hence, enteral feeding is encouraged after surgery. TPN is expensive. The dedicated central venous catheter harbors a risk of infection. Enteral feeding maintains the intestinal mucosa integrity, in contrast to TPN. A recent systematic review found that routine postoperative TPN was associated with a higher incidence of complications compared with enteral nutrition, specifically in patients undergoing a pancreaticoduodenectomy [61]. However, when it comes to chyle leakage, the surgical team must be careful on when to begin oral diet. It has been found that the volume of drainage significantly increases after enteral intake in the chyle-leakage group. Chyle is a lymphatic fluid containing emulsified fat [62]. 50% to 90% of lymph from the intestine and liver flows into cisterna chyli. During fasting the flow is at a rate of 1mL/min. After absorption of a fatty diet, the flow can increase to as high as 200mL/min [7,63]. Several randomized controlled trials demonstrated that immediate post-operative enteral feeding through a jejunostomy tube is not beneficial in patients undergoing pancreaticoduodenectomy and is even associated with impaired respiratory mechanics and postoperative mobility [38]. Chyle leakage decreases as the broken lymphatic integrity is restored after pancreatic surgery. Hence, timing for the start of enteral intake may be related to the development of chyle leakage.

Furthermore, an intraoperative milk test which is the insertion of 100mL milk via a nasogastric tube reduces the incidence of postoperative chylous ascites. In a study carried out by Aoki, et al. [7] the incidence of postoperative chylous ascites after pancreatic surgery was decreased from 7.7% to 2.9% via milk test. Such a test may be used in cases of increased risk for chylous ascites, although this is not a standard procedure. In addition, the placement of one or more percutaneous drains or intermittent therapeutic paracentesis maybe required to alleviate the increased abdominal pressure, pain and respiratory compromise caused by chylous ascites. Chylous ascites can interfere with wound healing can cause a fascial dehiscence as chyle flows through the path of least resistance. The poor wound healing is exacerbating by malnutrition resulting from deranged fat metabolism. In most cases of chyle leak following pancreatic surgeries, drains are already in place form the surgery or percutaneous drains are replaced to divert flow from healing wound. The disadvantage of paracentesis is the need for frequent procedures and the abrupt shifts in the third space fluid. Therefore, optimal placement of drainage tubes is a prerequisite for postoperative detection of chylous ascites.

Besides, surgical and interventional approaches are used for intractable cases of repeated chylous ascites. Bipedal lymphangiography with lipiodol has proven to be a promising tool with occlusion rates of chylous leakage reaching up to70% [64]. Usually cases of chyle leakage requiring surgical approach are scarce. Open surgical ligation of the leaking vessels or the implantation of a peritoneovenous shunt are last-resort options [17,58]. However, they carry a higher rate of morbidity [8,19].

Conclusion

Finally, it can be concluded that chyle leak after pancreatic surgeries is an uncommon but potentially life-threatening complication. Chylous ascites are more likely to be associated with higher morbidity, rather than a continued chyle leak. ISGPS accepted a new grading system for isolated chyle leak after pancreatic surgeries. The etiology for a chyle leak after pancreatic surgery include extended lymphadenectomy and early enteral feeding. The therapeutic management comprises of conservative treatment mainly, and surgical approaches to refractory chyle leak cases.

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