Medical Research Archives

ESMED
European Society of Medicine

OPEN ACCESS

Published: July 10, 2023

Citation: Rietveld SCM, Latenstein AEJ, et al., 2023. Large Variation in Diagnosis and Treatment of Chyle Leak after Pancreatic Surgery: A Nationwide Insight, Medical Research Archives, [online] 11(7). https://doi.org/10.18103/mra.v11i7.1.4008

DOI
https://doi.org/10.18103/mra.v11i7.1.4008

ISSN: 2375-1924

RESEARCH ARTICLE

Large Variation in Diagnosis and Treatment of Chyle Leak after Pancreatic Surgery: A Nationwide Insight

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ABSTRACT

Background: In the current literature different diagnosis and treatment strategies for chyle leak after pancreatic surgery are described. In 2017, the International Study Group for Pancreatic Surgery defined a consensus-based definition for diagnosis. However, consensus on the optimal treatment strategy is lacking.

Aim: The aim of this multicenter study is to investigate the current treatment and diagnosis of chyle leak after pancreatic surgery in clinical practice in the Netherlands to gain insight into practical applications of chyle leak.

Methods: A nationwide survey about the diagnosis and treatment of chyle leak was sent to specialized dieticians and pancreatic surgeons from all 16 pancreatic centers collaborating in the Dutch Pancreatic Cancer Group. Data was quantitative processed according to thematic content analysis and by using descriptive analysis.

Results: In total, 16 dieticians from 16 centers and 20 surgeons from 12 centers completed the questionnaire. Analysis showed that the International Study Group for Pancreatic Surgery-definition for chyle leak was used in clinical practice by 31% (n=11) of the respondents. The results show also large nationwide variation in treatment of chyle leak after pancreatic surgery, as well between as within centers. The most common treatment was a step-up approach of nutritional therapies (44% (n=16)), which starts with an enteral fat restricted diet enriched with medium chain fatty acids followed by total parenteral nutrition.

Conclusion This study shows that the current diagnosis and treatment strategies for chyle leak after pancreatic surgery in clinical practice on a nationwide scale are different. More comparable studies are needed to define the optimal treatment strategy for chyle leak. There is need for an international multidisciplinary (sub)working group to reach consensus on the treatment strategy of chyle leak and to discuss implementation strategies for clinical practice.

Keywords: Chyle, chyle leak, lymphatic leak, chylous ascites, pancreatic cancer, pancreatic surgery, nutrition, nutrition therapy

Introduction

Pancreatic resections for pancreatic cancer are complex operations with a relatively high risk on complications such as chyle leak (CL). [1-3] Up to 22% of patients after a pancreatic resection develops CL and in literature associations with longer hospital stay, decreased survival, increased healthcare costs, dehydration, malnutrition and immunologic dysfunction are described. [1,2,4-15] Numbers about incidence are, however, reaching from 0.6% to 22% [2,5,8,9,14,16] due to different methods of diagnosing CL. A uniform way of diagnosing is important to assess the real burden of CL in the pancreatic surgery population and to be able to compare studies on this subject. Therefore, the International Study Group for Pancreatic Surgery (ISGPS) defined a consensus based definition for CL after pancreatic surgery. [5] It is not known how this definition is integrated in clinical practice. Besides the diagnosis, also different treatment strategies for CL are described. Consensus on the optimal treatment strategy is lacking. [2,4,5,8,17-19] Due to an increasing number of patients with pancreatic cancer, the incidence of CL might also increase and therefore gains more interest in the research field. [19,20] The aim of this multicenter study is to investigate the current treatment and diagnosis of chyle leak after pancreatic surgery in clinical practice in the Netherlands to gain insight into practical applications of chyle leak. This could be used to uniform future treatment guidelines for CL.

Methods

We developed a cross-sectional nationwide survey which was sent to specialized dieticians and pancreatic surgeons from all 16 pancreatic centers collaborating in the Dutch Pancreatic Cancer Group (DPCG). At least one dietician and surgeon from each center were asked to participate. There was no need for approval of the Medical Ethic Review Committee since no patient data was used. The questionnaires were composed by the authors and consisted of 20 general questions (diagnosis of CL, and type, duration and (possible changes in) treatment of CL) and four or five specific questions for surgeons or dieticians, respectively. The questionnaires were sent on paper by post or digitally using Google Forms. In case of no response after a few weeks, a reminder was sent until the questionnaire was completed. Non-responders were asked for the reason for not responding. The CL definition as stated by the ISGPS was stated as the standard method of diagnosing CL in the questionnaire. This definition describes CL as: output of milky-colored fluid from a drain, drain site, or wound on or after postoperative day 3, with a triglyceride content ≥110 mg/dL (≥1.2 mmol/L. [5] The responses were manually coded and quantitative processed according to thematic content analysis. In addition, data were analyzed by descriptive analysis using IBM SPSS Statistics for Windows version 26 (IBM Corp., Armonk, N.Y., USA).

Results

In total, 16 dieticians from 16 centers and 20 surgeons from 12 centers completed the questionnaire between April, 2018 and December, 2019. Four surgeons did not completed the questionnaire because the questionnaire was too extensive or unclear in their opinion or by unknown reason. The methods used for diagnosing CL are shown in table 1. The ISGPS definition for CL was used in clinical practice by 31% (n=11) of the respondents whereas 78% (n=28) of the respondents was familiar with this definition.

The most common treatment was a step-up approach of nutritional therapies (44% (n=16), Table 2), which starts with an enteral fat restricted diet enriched with medium chain fatty acids (MCT diet: by mouth or by means of (semi-)elemental tube feeding) followed by total parenteral nutrition (TPN). An extremely high or low drain output volume influenced the (first) type of therapy in 17%. Several respondents indicated TPN was started immediately if the drain output was more than 500 or 1000 ml. An extremely high or low level of triglyceride did not affect the type of therapy. Usually, therapy was changed based on non-specific reasons (63% (n=23)). One of the reasons mentioned in the answers of the questionnaire was an insufficient effect or decrease of (chyle) drain production. Octreotide was used according to 36% (n=13) of respondents.

Table 1. Diagnosis for chyle leak after pancreatic surgery in the Netherlands (n=36)

ISGPS	31%
Inconsistent determination of TG, other cut-off values, TG in combination with chylomicrons and/or TG serum	36%
Visual assessment, eventual additional TG determination	28%
Unknown diagnostics	3%
No diagnostics	3%

ISGPS: International Study group on Pancreatic Surgery; TG: Triglycerides

Table 2. Strategies for treatment for chyle leak after pancreatic surgery in the Netherlands (n=36)

Enteral fat restricted/MCT enriched diet, if no effect; TPN	44%
Oral fat restricted/MCT enriched diet, if no effect tube feeding	3%
Oral fat restricted/MCT enriched diet, if no effect; tube feeding, if no effect; TPN	36%
Only oral MCT diet	17%

MCT: Medium Chain Triglyceride; TPN: Total Parenteral Nutrition

The majority (72% (n=26)) reported that a surgical intervention as treatment for CL was (almost) never considered or necessary. Duration of treatment varied from a certain period, up to nine weeks to discontinuation of treatment if CL was no longer present.
The mean agreement regarding the main questions between dieticians and surgeons in 12 DPCG centers was 57% (± 17%, range 15%-80%). The mean agreement between surgeons within one center was 66% (± 6%, range 60%-74%, measured in 4 centers).

Discussion

The results from our survey provide insight into the nationwide diagnosis and treatment strategies in clinical practice for CL after pancreatic surgery in the Netherlands. This survey shows that treatment strategies are very different within and between centers. In addition, the CL definition, as published by the ISGPS in 2017 [5], is not even used in two thirds of the respondents.

A recent review of Muzzolini et al.[8] also describes a large heterogeneity in practical used definitions for the diagnosis of CL after pancreatic surgery. Two important points of discussion regarding the ISGPS definition are mentioned. First, the need of triglyceride quantification, as used in the definition, might be irrelevant because of the debatable cut-off value and questionable added value compared to milky appearance of the drain outflow. Second, the daily volume output of the drain, which is not taken into account in the definition, might be of clinical relevance. This was also reported by some of our respondents and both points might be a (partial) explanation for not using the ISGPS definition in clinical practice. Besides, it is suggested to redefine the current definition because grade C CL is extremely rare. [4,18,21] In addition, in our opinion, only a distinction within invasive or non-invasive treatment would be preferable because the optimal treatment for CL after pancreatic surgery is still unknown. However, in all ISGPS definitions the grades are based on the degree of intensity of a treatment and therefore redefining would not be recommended. [4] Using the current ISGPS definition should be encouraged to enhance data for incidence comparisons, research and quality measures.

The most commonly used treatment for CL in the Netherlands is the so-called step-up approach. [5,6,22] This approach starts with an enteral MCT diet and is followed by TPN if the drain output does not significantly decrease. The effect of an enteral MCT diet has been described in multiple studies [23,24] The other methods that were used by our respondents were comparable with methods presented in other studies.[3,10,25,26] These treatments include 'mixing and matching' the MCT diet and TPN, and/or addition of somatosatin. In contrast to the results of our study, some studies suggest TPN and clear liquids/nil per mouth as main therapy for CL after pancreatic surgery.[7,9,13,27-29] A review suggests that after major abdominal surgery success rates of TPN as treatment for CL may be higher compared to a MCT diet.[2] Although no adverse outcomes of TPN are described in these studies, historically TPN has shown to have adverse effects such as cholestasis, fatty liver, and fungal infections. [17] In addition, TPN is expensive, a risk for infection and associated with postoperative morbidity. [30] This makes TPN more invasive compared to treatment with an enteral diet [17] and therefore TPN should not be recommended as first step. One study shows that none of the nutritional therapies were associated with reduction in morbidity or duration until drain removal.[18] A direct comparison of TPN, MCT diet and/or other therapies is not described in current literature. It could be advised to set up a trial comparing different treatment strategies with clear definitions for effectiveness which will ease the future translation into clinical practice.

Early enteral feeding is found as risk factor for CL in several recent studies, which can be explained by the fact that the lymphatic flow increases by fat absorption from early enteral intake and consequently the drain output volume will earlier increase in patients with CL.[5] This would make early postoperative enteral feeding a possible contra-indication in patients with the risk on CL. In contrast, Chen et al. shows in a recent study that early oral intake is not associated with CL.[6] Over the last years fast-track perioperative care programs, which

propagate early postoperative enteral feeding, became increasingly important and show improved patient outcomes.[6,31] There is no clear evidence that withholding enteral intake postoperatively will decrease the development of CL and therefore, early enteral feeding should be part of the postoperative track.

The present survey showed that use of somatostatin analogs is low in the treatment of CL in the Netherlands. Some countries/hospitals frequently use these analogs in the treatment of CL.[2,3,10,17,23,26,27] It is suggested that somatostatins safely shorten the time to resolution of CL. [2,3,29,32] However, there is not sufficient evidence for using somatostatin analogs in the treatment of CL after pancreatic surgery and therefore further research is required. [8,18]

The duration of treatment of CL after pancreatic surgery varies in the current survey and is in line with other studies. In general, a median of 7-15 days is described in literature, but large ranges (5-27 days) were seen. [10,13,18,23,29] A description of 'recovery of CL' has not been defined and is necessary to compare treatment duration and different treatment strategies. [4,18] Vailas et al suggested removal of the surgical drain once drain output volume is <50 ml/24h. [19] A clear definition might even decrease hospital length of stay as patients can be discharged safely after a certain treatment time.

Some limitations were present in our study. First, the number of participating hospitals might be small, but since these include all pancreatic centers, the surgeons and dieticians are specialized within this area. Second, dieticians completed the questionnaire almost one year earlier compared to the surgeons. To our knowledge, no relevant new treatments were implemented in the meantime. Moreover, after the surgeons completed the questionnaire, all dieticians were approached to update their answers changed during that past year. In majority, no changes were necessary. Third, surgeons from some centers did not complete the questionnaire whereas from other centers more than one surgeon completed the questionnaire. This could have influenced our results, but this effect is probably limited because also in-hospital differences are large. Lastly, a limitation of this study could be that it is only conducted in the Netherlands. However, given the similarities between our results and the literature and the described diversity of definitions and treatment for CL in the literature, it could be expected that the generalizability for the results of this study are broader than only the Netherlands.

Conclusion

The results of this study showed that the ISGPS definition for CL after pancreatic surgery has not yet been integrated into clinical practice. In addition, this study showed large nationwide variation in treatment of CL after pancreatic surgery in clinical practice, as well between as within centers. It should be worldwide encouraged to use the ISGPS definition for CL. Comparative studies among therapies are needed to define the optimal management strategy. It is recommendable to create an international multidisciplinary (sub)working group to discuss implementation strategies for clinical practice and to reach consensus for the treatment strategy of CL which makes further research, evaluation and further optimization of treatment and outcomes unambiguously.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Note: Results of this research were presented at the (online) ESPEN congress, September 2020

Acknowledgments

Surgeons: K Bosscha (Jeroen Bosch Hospital Den Bosch), B. Bonsing (University Medical Center Leiden), O. Busch (Amsterdam University Medical Center, location AMC), C. Buis (University Medical Center Groningen), M. den Dulk (Maastricht University Medical Center), J. Erdmann (Amsterdam University Medical Center, location AMC), S. Festen (OLVG Hospital Amsteram), J. Klaasse (University Medical Center Groningen), B. Groot Koerkamp (Erasmus University Medical Center Rotterdam), I. de Hingh (Catharina Hospital Eindhoven), M. Liem (MST Hospital Enschede), D. Lips (MST Hospital Enschede), M. Meerdink (University Medical Center Groningen), V. de Meijer (University Medical Center Groningen), K. Nielsen (Amsterdam University Medical Center, location VUmc), J. Schreinemakers (Amphia Hospital Breda), G. van der Schelling (Amphia Hospital Breda), M. Stommel (Radboud University Medical Center), J. Wijsman (Amphia Hospital Breda).

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der Steen (St. Antonius Ziekenhuis Nieuwegein), E. Steenhagen (University Medical Center Utrecht), M. Tjalsma- de Vries (University Medical Center Groningen), R. Vehof (Radboud University Medical Center Nijmegen), M. Vogels (Catharina Hospital Eindhoven), J. Witvliet (Amsterdam University Medical Center, location VUmc), M. van Zandvoort (University Medical Center Leiden) and the "Dutch Surgical Dietitian Group University Medical Centers".

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