Evaluation of the laparoscopic Whipple procedure

Increasing the safety of operative methods of four pioneering surgical teams in the Netherlands by a HFMEA analysis

Jolien van der Meché

Supervisors:

Prof. dr. J. Dankelman[1]

Dr. E.G.G. Verdaasdonk[2]

Drs. F.C. Meeuwsen[1]

[1]TU Delft

[2]Jeroen Bosch Ziekenhuis

21-7-2017

- This page is intentionally left blank -

Evaluation of the laparoscopic Whipple procedure

Increasing the safety of operative methods of four pioneering surgical teams in the Netherlands by a HFMEA analysis

Author

Bsc. J. van der Meché[1]

Supervisors:

Prof. dr. J. Dankelman[1]

Dr. E.G.G. Verdaasdonk[2]

Drs. F.C. Meeuwsen[1]

[1]Technical University Delft

[2]Jeroen Bosch Ziekenhuis, 's Hertogen Bosch

Delft, 2017

This thesis was presented to the Dutch Pancreatic Cancer Group (DPCG), Utrecht, 10 July 2017

- This page is intentionally left blank -

Preface

I hereby proudly present to you my master thesis. I wanted to perform a research project in which I would improve the safety in a hospital in some way. I am extremely proud of the fact that I could work together with four hospitals on a very exciting subject, pancreatic surgery. For me, my research has already been a success as two months ago, I could share valuable information between the four hospitals about a specific operation technique, hopefully improving the outcome of the patients.

This thesis is written for HPB surgeons (liver, pancreas and gall bladder), specialized in the pancreas. It is especially written for the four included hospitals to learn from each other and as a start for further research to the laparoscopic pancreaticoduodenectomy (LPD) procedure. I am proud to announce that one of the hospitals, Catharina Ziekenhuis, uses this thesis as starting point for a PhD trajectory to the learning curve of a surgeon (in residence) for the LPD procedure. In addition, research topics are suggested in response to my presentation during the meeting with the Dutch Pancreatic Cancer Group (DPCG) on July 10, 2017.

However, this thesis would have never been possible without the help of some people. First of all, I would like to thank Sander Schutte, who has introduced me to Emiel Verdaasdonk. Emiel is the brain behind the assignment and my supervisor. My special thanks to Emiel, with who I could discuss, philosophize and brainstorm about the project, but also call around midnight, eat at MacDonald's, visit each included hospital for at least one time and always bringing me back to Delft by car. Thank you for giving me the opportunity to perform a research on such an amazing subject, for your detailed commenting on written work and your supportive attitude. I want to thank Frédérique Meeuwsen. I am grateful that we could meet every week. You have supported me during the whole process as a supervisor and as a friend.

Secondly, I would like to thank each surgeon and scrub nurse participating in this study. They made it possible that I could gather this amount of valuable information on this subject. Especially to Daan, surgeon of Jeroen Bosch Ziekenhuis (JBZ), where I could visit three LPD procedure and who took the time to meet several times to improve the analysis. Next, for Misha, surgeon of Catharina Ziekenhuis, Marc Besselink, surgeon at Amsterdam Medisch Centrum (AMC) and Sebastiaan Festen, surgeon at Onze Lieve Vrouwe Gasthuis. Each took the time and improved the research with critical questions.

Off course, I want to thank my family and friends, who have supported me through the graduation process. As for my family, the love, boundless trust and support of my parents, Maeike and Rosan have made it possible for me to acquire so much knowledge, both academic and about life, happiness and energy to be able to be myself and for today, to graduate. I am forever grateful to have you in my life. As well as for Abel and Flora, my little nephew and newborn niece, who made me smile every day. A special thanks to Jeffrey, who supported and encouraged me during the process. I could not have done it without you.

Finally, I want to thank the MISIT lab for a place to work, but most of all the supportive talks, help with scientific rules and the coffee.

I hope you will enjoy reading my thesis and remember the take-home message:

"Learn from the mistakes of others. You can never live long enough to make them all yourself"

Jolien van der Meché
Delft, July 21, 2017

- This page is intentionally left blank -

Abstract

Background

In the Netherlands, approximately 1.750 people are diagnosed with pancreatic cancer each year. Approximately 20% of these new patients are operated with curative intent. This surgical treatment, called pancreaticoduodenectomy leads to a five-year survival rate of 5-10%. Laparoscopic pancreaticoduodenectomy (LPD) is a complex surgical procedure that pancreas surgeons have only started to adopt. In the Netherlands, the four pioneering hospitals in laparoscopic pancreatic surgery (Catharina Ziekenhuis (CTZ), Jeroen Bosch Ziekenhuis (JBZ), Amsterdam Medisch Centrum (AMC) and Onze Lieve Vrouwe Gasthuis (OLVG)) are still in the beginning of their learning curve. An early assessment of their operative technique could provide deep insight in the differences of the operative method between the hospitals. This is an experimental study to evaluate the LPD procedure with the aim to improve the operative techniques of the four pioneering hospitals in the Netherlands.

Method

In each of the four hospitals, the steps of the LPD procedure were defined based on the operation report. For each step of the procedure the risks and risk scores were identified. This was done with a multidisciplinary team per hospital according to the hazard analysis of the Health Failure Mode and Effect Analysis (HFMEA). In consultation with one surgeon of each of the four hospitals, the risks were converged to relevant risks s according to the adapted decision tree of the HFMEA method. The similar steps of the four hospitals were linked to each other to create an overview of the differences and similarities in process and risks. Finally, risk types and the corresponding causes were identified based on the relevant risks.

Results

In all included hospitals, relevant risks were found (CTZ: n = 10, JBZ: n = 16, AMC: n = 3 and OLVG: n = 13). The process steps which contained relevant risks by more than one surgical teams were (1) performing Kocher maneuver and exposing ligament of Treitz, (2) cholecystectomy, (3) mobilising portal vein, superior mesenteric vein and artery, (4) transection gastroduodenal artery, (5) pancreatojejunostomy (PJ), (6) hepaticojejunostomy (HJ) and (7) gastrojejunostomy (GJ). Eight out of 41 relevant risks were accepted by the surgeon of the corresponding hospital (no further action is warranted to diminish the risk). The remaining relevant risks were bleeding (n = 23), HJ failure (n = 4), PJ failure (n = 3) and GJ failure (n = 3). The prevalent reason for bleeding was unable to view or identify anatomical structures of the patient (33%). HJ and PJ failure originated from patient's habitus and iatrogenic/operative technique. GJ failure originated from iatrogenic/operative technique solely.

Conclusion

The HFMEA method provided an overview of the practiced operative methods during the LPD procedure for each of the included hospitals with detailed information of the surgical steps. There are clear differences in the order of several surgical steps between the four hospitals. This information could be used by the surgeons to learn from each other by sharing their considerations and knowledge about specific process steps.

- This page is intentionally left blank -

Table of contents

List of figures

List of tables

Abbreviation list

AMC	Amsterdam Medisch Centrum
CTZ	Catharina Ziekenhuis
DoF	Degrees of Freedom
DPCG	Dutch Pancreatic Cancer Group
FDA	Food and Drugs Administration
GJ	Gastrojejunostomy
HFMEA	Health Failure Mode and Effect Analysis
HJ	Hepaticojejunostomy
HTA	Health Technology Assessment
ISGPS	International Study Group of Pancreatic Surgery
JBZ	Jeroen Bosch Ziekenhuis
LPD	Laparoscopic pancreaticoduodenectomy / Laparoscopic Whipple procedure
OLVG	Onze Lieve Vrouwe Gasthuis
OPD	Open pancreaticoduodenectomy / Open Whipple procedure
PD	Pancreaticoduodenectomy / Whipple procedure
PJ	Pancreatojejunostomy
POPF	Post-Operative Pancreatic Fistula
RA	Robotic-assisted
WHO	World Health Organization

Glossary

Anastomosis	Connection between two organs
Antrectomy	Resection of the antrum of the stomach, whereby the pylorus is removed as well
Bolus	Food going from the mouth to the stomach
Cholecystectomy	The resection of the gallbladder
Chyme	Semifluid paste of food particles and gastric juice formed by mixing and churning of stomach
Ductal adenocarcinoma	Exocrine tumour, located in the head of the pancreas
Fistula	An abnormal connection between two body parts
Gastrojejunostomy	Anastomosis between the stomach and the jejunum
Hazard	An act or phenomenon potentially causing harm, also called an undesired event
Hepaticojejunostomy	Anastomosis between the biliary duct and the jejunum
Incidence	Occurrence of new cases during a time period
ISGPS	Classification system for pancreatic surgery
Laparotomy	A large transverse incision in the abdominal wall during surgery
Pancreas	A glandular organ, which secretes pancreatic juice containing digestive enzymes to the duodenum and which produces hormones for blood glucose control
Pancreaticogastrostomy	Anastomosis between the pancreas and the stomach
Pancreatojejunostomy	Anastomosis between the pancreas and the jejunum
Pneumoperitoneum	Gas (CO_2) in the abdominal cavity
Prevalence	The amount of people with a condition at a specific point in time
Pylorus-preserving surgery	Resection of the duodenum, and thereby sparing the pylorus
Reverse Trendelenburg position	Patient lays in one line with the upperpart higher than the lowerpart
Supine position	Patient lays in one line on their back

Anatomy peripancreatic

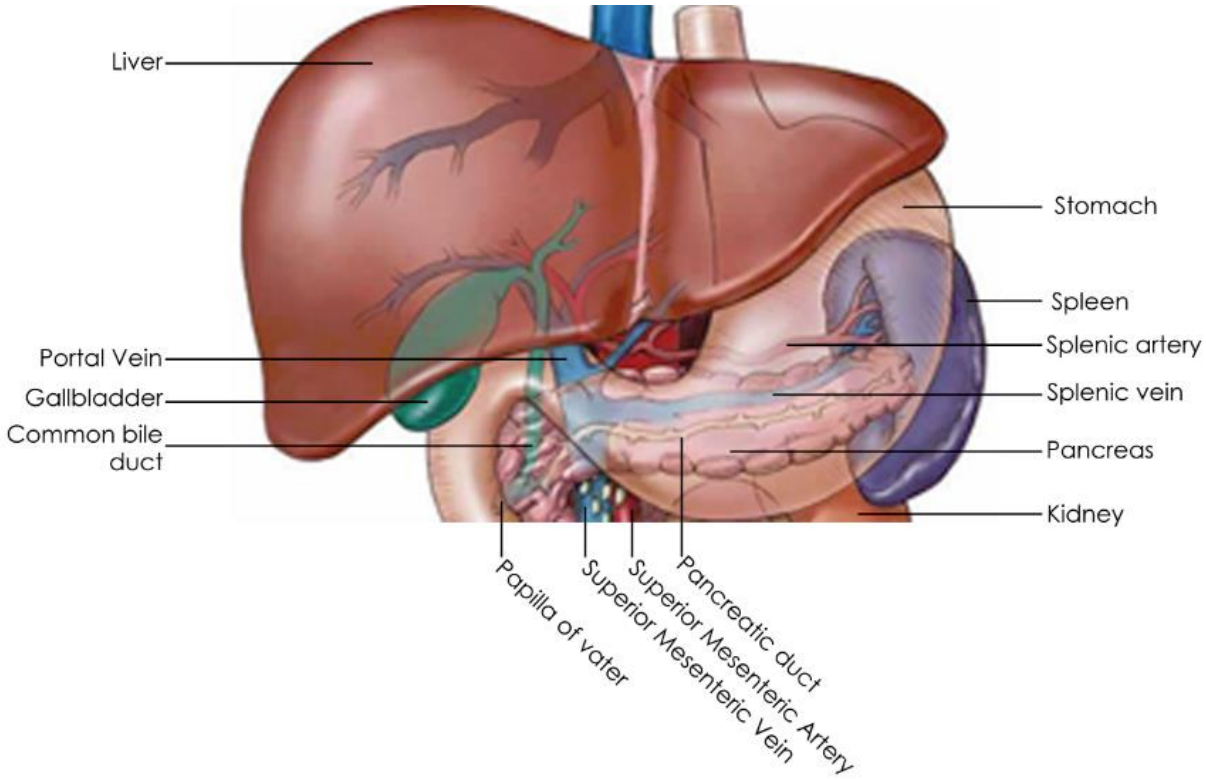

Figure 1 Human anatomy peripancreatic [1]

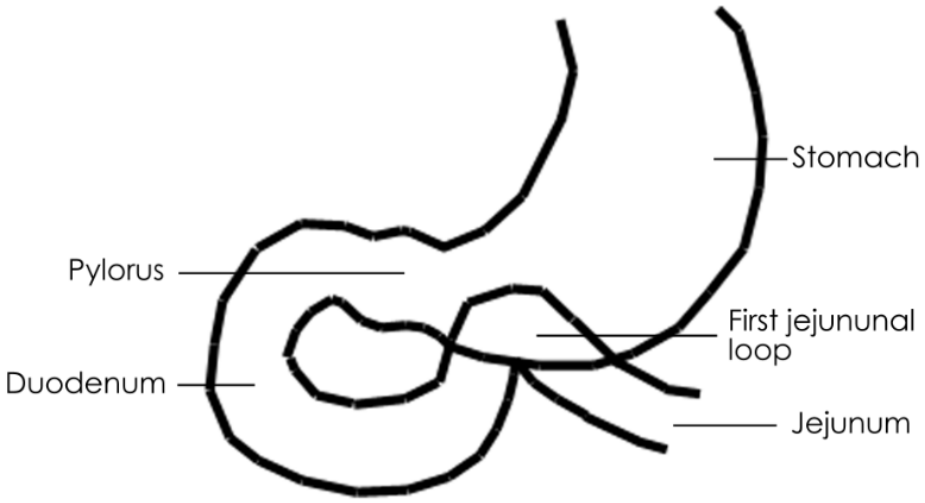

Figure 2 The anatomy of the gastrointestinal tract

Basics of the laparoscopic pancreaticoduodenectomy procedure

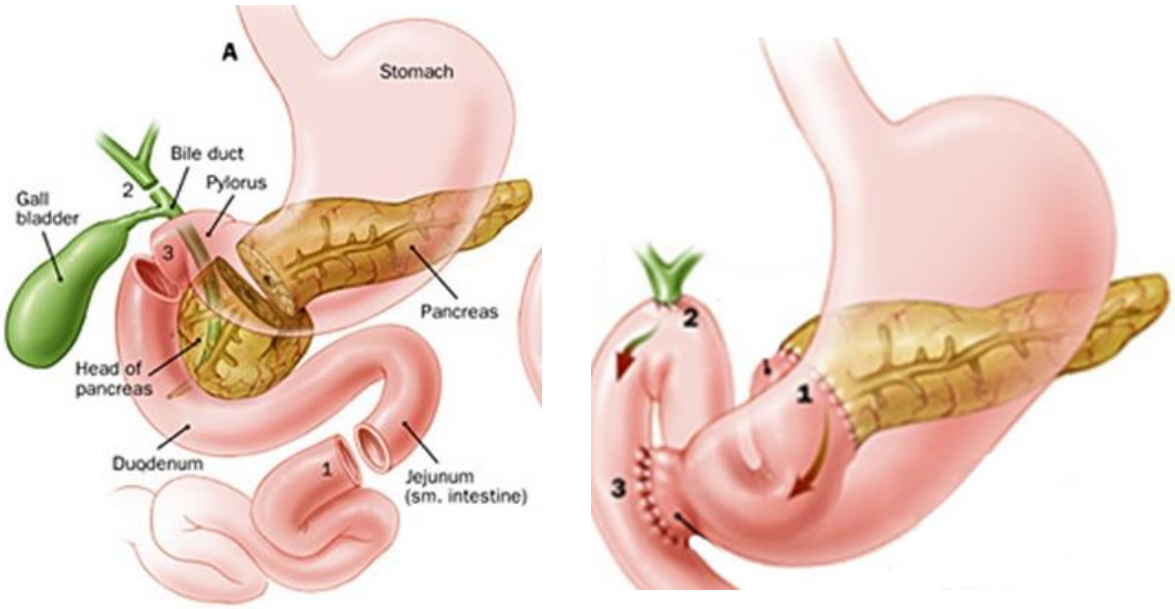

Figure 3 The basic steps of the LPD procedure. First, divide the duodenum from the stomach and from the jejunum and divide the pancreas and the common bile duct. Secondly, reconstruct the pancreatic remnant, biliary duct and stomach [55]

Directional references

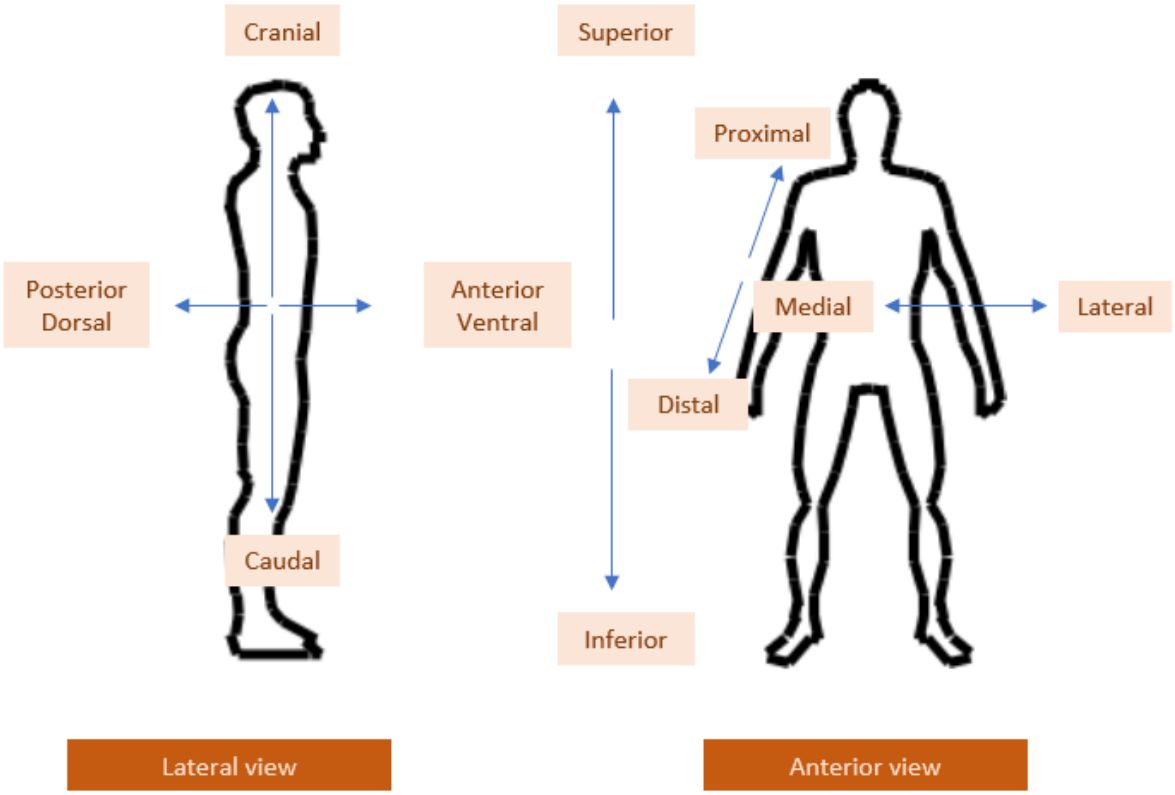

Figure 4 Directional references in medical jargon

1 Introduction

In 1935, the American surgeon Allen Oldfather Whipple published the results of a series of three operations on cancer of the pancreas [2]. Only one of the patients had the duodenum totally removed. This patient survived for two years before dying of metastasis to the liver. Whipple's success showed the way for the future, but the operation remains a difficult and dangerous one. Today, pancreatic cancer is the fourth leading cause of cancer deaths, being responsible for 7% of all cancer-related deaths in both men and women [3]. In 2015, pancreatic cancers of all types resulting in 411,600 deaths globally and 2,694 deaths in the Netherlands [4]. Pancreatic cancer is the fifth most common cause of death from cancer in the United Kingdom,[15] and the third most common in the United States [5]. In the Netherlands, approximately 1,750 patients are diagnosed with pancreatic cancer each year [6]. The only chance on curative treatment is surgery. However, approximately 20% of all new diagnosed pancreas cancer patients can be operated with curative intent. Pancreatic adenocarcinoma typically has still a very poor prognosis: after diagnosis, 25% of people survive one year and 5-10% live for five years [6].

Currently, the standard surgical treatment of pancreatic carcinoma of the head of the pancreas is still the Whipple, or pancreaticoduodenectomy (PD), procedure or modifications of this procedure. For decades, this technically challenging procedure is being performed trough a large transverse incision of the upper abdomen. However, with the increasing application of minimally invasive surgical techniques for all types of abdominal located cancers, some surgical teams in the world have started to perform the laparoscopic pancreaticoduodenectomy (LPD) procedure [7]–[11]. In 1994, Gagner and Pomp were the first to describe the LPD procedure [12]. However, long operative times, technical difficulties and the need to develop advanced laparoscopic skills were important reasons for initial reluctance for worldwide adoption of this technique. Recently, LPD procedure has started to gain wider acceptance as surgeons become more comfortable with laparoscopic technology. As a result, LPD procedures have been reported with an increased frequency from institutions internationally [13]–[19].

In the Netherlands, four hospitals, Jeroen Bosch Ziekenhuis (JBZ), Onze Lieve Vrouwe Gasthuis (OLVG), Amsterdam Medical Center (AMC) and the Catharina Ziekenhuis (CTZ), are the pioneers in performing LPD surgery. Each hospital has one dedicated surgical team which has introduced the new technique. Their operative method was based on their laparoscopic experience and their experience with open pancreaticoduodenectomy (OPD), combined with proctoring and literature about LPD. Through gaining experience in the LPD procedure and cooperation between the surgeons performing LPD, the operative technique per hospital is still developing.

Sharing experience and discussion of results is facilitated by the Dutch Pancreatic Cancer Group (DPCG). The Dutch Pancreatic Cancer Group (DPCG) is a multidisciplinary team in the Netherlands [20], which aims to improve treatment of (pre-)malignant pancreatic and periampullary tumours through multidisciplinary scientific research, prospective audit and continuing training. The DPCG has initiated an RCT on open pancreaticoduodenectomy (OPD) versus LPD in the Netherlands (LEOPARD-II). The study aims to identify the advantages of LPD in comparison with OPD and has currently (April 17, 2017) 57/136 cases performed. However, the surgical teams of participating centres in this trial are still at the beginning of their learning curve (none have performed more than 80 cases). Although they work closely together on the results as a part of the LEOPARD-II trial there is a need for further deep insight in the differences and variations of the surgical technique between the centres. Communication and sharing surgical experience with the LPD on a detailed level can enhance the learning curve and eventually improve outcome. This was the starting point of this research project.

1.1 Implementation and assessment of new surgical techniques

Safe implementation of new surgical techniques and procedures is challenging. The Food and Drugs Administration (FDA) regulates new techniques, however omits new procedures. There is no FDA template which prescribes the process of implementing a new procedure[1]. Currently the evaluation and implementation of a new procedure is commonly done on a local level [21].

In the Netherlands, the Health Care Inspectorate is an independent supervisor for Dutch healthcare. They have investigated the implementation of laparoscopic surgery in the Netherlands, where they established essential measures at national and individual level. Basically, agreements with regard to training and skills assessment need to be established at national level as well as methods and regulations to assure quality. At hospital level, policies should be formulated and thereby establishing a formal quality system. This includes assessment of laparoscopic surgery, evaluation of outcomes, incidents and complications and formal evaluation of the skills of staff using laparoscopic technique [22].

While several organisations have attempted to provide guidelines to implement new surgical procedures, there are no uniformly agreed criteria [21]. These guidelines provide global steps for the implementation of a new surgical technique. The first step is to determine if the technique has already been assessed. This can be done by literature search. Systematic reviews, assessments and RCTs of the procedure should be searched for [23]. One of a commonly used assessment method is the health

[1] The definition of 'new procedure' is a newly employed operative procedure in a hospital. So a new procedure for hospital A, can have been employed already in hospital B [23].

technology assessments (HTAs) [23], [24]. Health technology assessment is the systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences, and aimed mainly at informing decision making regarding health technologies. This method is especially useful for political strategy and decisionmakers. Another advice in the steps towards introducing new surgical techniques for surgeons is to practice device or procedure-specific training whenever possible. A commonly used method is proctoring [23], [24]. A surgical procter has expertise on specific procedure and supervises and advices surgeons or trainees during implementation of this new procedure [25]. Thirdly, the outcome of the new surgical procedure should be recorded and analysed for reporting [21],[23].

Currently, surgical procedures are usually assessed by analysing outcome data [26]. Outcome data includes mortality, morbidity[2], blood loss, operative time, length of hospital stay, conversion and procedure specific variables. Complications can be classified, where uniformity is important to be able to compare the results between institutions [27]. In pancreas surgery the classification International Study Group of Pancreatic Surgery (ISGPS) is used, which is mainly based on the provided treatment after surgery [28]. This system eliminates the subjectivity of documenting hazards, as the provided treatment is usually well-documented and available data. Whereas, by grading hazards instead of the treatment, a surgeon can down-grade serious adverse events using their interpretation.

In literature, several reports compare the outcome data of the LPD with the OPD procedure [7], [13], [29]. In the Netherlands, the Dutch Pancreatic Cancer Audit (DPCA), an audit program of DICA, registers the outcome data after a pancreas tumour procedure has been performed. Per July 1, 2013 data is accumulated [20].

However, to our knowlegde there are no reports providing a detailed assessment during implementation of the LDP with respect to possible hazards or difficulties of the surgical technique. Authors of case studies describe the practiced operative techniques and the outcomes, but not how they are implemented [18]–[21]. In one study, concerning the learning curve for the LPD procedure, the use of the hybrid approach for the first ten cases was advised as a preparation for safe implementation of a total laparoscopic PD [33]. The DPCG has the project LAELAPS-2, to organise the implementation of the LPD procedure in the Netherlands [34]. The project is subdivided in three parts. First training in the LPD procedure, then an analysis of the training and finally a randomised research to LPD versus OPD.

In conclusion, in literature the feasibility of the LPD is well described and outcome data is international and national accumulated. However, for a new surgical procedure, there is not enough outcome data for a retrospective review. Therefore, surgical teams could benefit from a prospective review on the operative technique in an early stage of their learning curve. To our knowledge, there is currently not a recommended prospective study to assess the operative techniques in an early stage.

1.2 Assessment methods

An example of an assessment of an operative method is from the Haute Autorité de Santé (HAS). HAS is an organisation which focusses on the assessment of health technologies and procedures amongst other things. They use a Health Technology Assessment (HTA) where first a literature review is conducted. This in-depth literature search has as aim to find and consult relevant literature and websites about the scope of the subject. Then, the relevant data is summarised in a report. This report and a questionnaire asking about their opinion is send to a group of health professionals from several disciplines. The results and the opinions are discussed with the aim to reach consensus on the procedure's clinical benefit. So through a systematic literature search and by gathering expert and/or stakeholders opinion, the clinical benefit can either be approved, not approved or defined as still in clinical research phase [35].

Generally speaking, with a HTA the knowledge and experience of experts is used to improve a procedure after a literature review about the procedure is done. Using the knowledge and experience of experts is called sensemaking, which is described as ´the active process of assigning meaning to ambiguous data´, which is done by human reflection [36]. Combining analytical tools, like a literature review, and sensemaking allows an organization to clarify risks and hazards and uses it as learning opportunities. Nonetheless, there is currently no emphasis on sensemaking during conversations with the physicians. The purpose of meetings for solving patient safety-problems is to gather accurate information whereby the physicians are seen as informants, instead of informants who are capable of making sense of the data [36].

During a sensemaking conversation an interactive map is displayed for the whole team to enable participants to come to a deep understanding of the risks and hazards of the procedure. The ownership of the results of the participants grows simultaneously. The advantage is that knowledge and experience are used to interpret information and involved participants will more likely work toward the identified solution. The disadvantage of this approach is the ambiguous interpretations, which is increased by the complexity of the subject [36].

[2] Morbidity is the level of health and well-being of a person. Postoperative morbidity is the measure to express the complications that occur within 30 days after the surgical procedure [52], also called postsurgical complications [53].

To conclude, a conversation based on sensemaking could provide a deep understanding in the risks and hazards of a new procedure based on the assessment method of HAS. Before it can be applied for the LPD procedure, an analysis has to be performed to enable an in-depth conversation about the operative methods. The operative method of the LPD procedure of four pioneering surgical teams in the Netherland are known and therefore an analysis based on the operative methods and the direct complications is an opportunity to gain deep insight in the risks and hazard intra-operatively. The risks and hazards cannot be directly linked to the outcome of the patient. Yet, the surgical teams perform varying operative techniques and a varying sequence of process steps. These differences can be compared with each other. A great understanding in each other's differences can lead to an improved operative method per surgical team.

A method should be chosen to assess these complications during the LPD procedure. The information that results from this kind of analysis will provide subjects to discuss with the surgeons of the hospitals in the Netherlands. A risk analysis identifies the risks of a component of system. Risk-assessment answers three basic questions. 1) What can go wrong? 2) What is the likelihood that it will go wrong? 3) What are the consequences if it does go wrong? Hazards are identified by answering question one. A hazard is an act or phenomenon potentially causing harm, also called an undesired event. It has a magnitude, which illustrates the potential amount of harm. A hazard can occur voluntarily or involuntarily. The failure probability is determined per hazard by question two. The reliability of a system or a component is defined, as the reliability is one minus failure probability. Reliability is the ability of a system or a component to fulfil '*its design functions under designated operating or environmental conditions for a specific time-period*' [37]. The consequence of an event, answered by question three, is the degree of damage or loss due to a failure. Eq. 1 describes risk as a consequence per amount of time. It is calculated by multiplying likelihood, or probability, with impact.

$$Risk\left(\frac{Consequence}{Time}\right) = Likelihood\left(\frac{Event}{Time}\right) * Impact\left(\frac{Consequence}{Event}\right) \quad (1)$$

A risk is the chance of a bad consequence due to an undesired event. A risk is the result of an event or a scenario; a sequence of events. When the undesired event or scenario occurs, it results in consequences with various severities. A risk is neither a characteristic of the present nor the past. It is a characteristic of an uncertain future [37].

An assessment can be retrospective or prospective. Retrospective record reviews are relatively standard and provide a good overview of the nature, incidence and economic impact of adverse events [38]. Adverse events which are not found during retrospective research, can be found by a prospective method. Discussion between the physicians themselves is a good source of data to prevent adverse events [39]. World Health Organisation (WHO) describes a conducted study by a French institution which found a prospective method whereby doctors and nurses gathered the data [38]. They found this method much more effective to identify preventable adverse events. This kind of study is expensive and time-consuming, but the data is richer and more valid. An advantage is the better understanding of the causes of the undesired events. The WHO concluded that a *'prospective study is warranted if they provided details on the particular types of adverse events, their causes and economic impact, over and above national incidence rates'* [38].

A qualitative assessment is used during conceptual phases. The LPD procedure is still in the conceptual phase, as there is no consensus on the best practice of the operative method [40]. In other sectors such as the engineering community, prospective risk analysis is applied to determine risks before injury occurred. To prevent harm, the executor learns before the hazards take place.

1.3 Health Failure Mode and Effect Analysis

The engineering community has used the prospective risk analysis system 'Failure Mode and Effect Analysis (FMEA)' to learn about future hazards in high risk environments. The department of Veterans Affairs National Center for Patient Safety has adjusted this risk analysis method for healthcare; Healthcare Failure Mode and Effect Analysis (HFMEA). This risk analysis method is a combination of FMEA, Hazard Analysis and Critical Control Point (HACCP) and root cause analysis [41]. The aim of the HFMEA analysis is to provide detailed insight into the hazards and risks during healthcare related processes. However, this method is not yet used to assess surgical procedures [26]. We choose the HFMEA method for analysis of the LDP for several reasons. First, in order to find a structured method to enhance safe implementation in the Netherlands. Secondly, the LDP is a technical difficult surgical procedure with numerous hazards. Thirdly, the surgical teams are at the beginning of their learning curve and therefore a prospective risk analysis will be most beneficial to the participating teams. And last, this analysis has not been used to our knowledge for surgical procedures before. If the HFMEA method is considered useful for the LPD this may be used for future new surgical procedures as well.

Health Failure Mode and Effect Analysis (HFMEA) is a 5-step process, whereby process flow diagramming, a Hazard Scoring Matrix™, and the HFMEA Decision tree™ are used to evaluate and improve health care processes proactively. This method is practiced by a multidisciplinary team in order to gather various view point. The five steps of HFMEA are as follows:

Step 1: Define the HFMEA™ topic
Exact description of the scope and the high-risk area is provided. A specified scope results in a high-quality analysis.

Step 2: Assemble the multidisciplinary team.
This team should include subject matter experts, people who do not know the process, a team leader, and an advisor. The subject matter expert(s) will give insight into how the process is carried out, while the people who do not know the process encourage critical review and identify the potential vulnerabilities that others might miss. The team leader is responsible for a smooth process and an effective team. The advisor helps the team leader during discussion with the multidisciplinary team [41].

Step 3: Graphically describe the process
A process flow diagram can help to visualize the process. The scope can be further specified to preserve the quality of the analysis, when it appears to be a complex process.

Step 4: Conduct a Hazard Analysis
First describing the possible failure modes per process step, which are 'the different ways that a particular process or sub process step can fail to accomplish its intended purpose [41]'. Then determine the severity and probability per failure mode and look up the hazard score, defined from the Hazard Scoring Matrix™ (Figure 5). Next, identify through the HFMEA Decision Tree™ with which failure mode to proceed, by answering three questions about criticality, controllability, and detectability of the failure mode (Figure 6). Assess the causes for each maintained failure mode and identify through the HFMEA Decision Tree™ with which failure mode-cause combinations to proceed.

Step 5: Actions and Outcome Measures
Define the actions that must be taken to improve the process. Define outcome measures to ensure that the system works functionally after the action(s) [41].

HFMEA™Hazard Scoring Matrix™

Probability	Severity of Effect			
	Catastrophic	Major	Moderate	Minor
Frequent	16	12	8	4
Occasional	12	9	6	3
Uncommon	8	6	4	2
Remote	4	3	2	1

Figure 5 HFMEA Hazard Scoring Matrix [41]

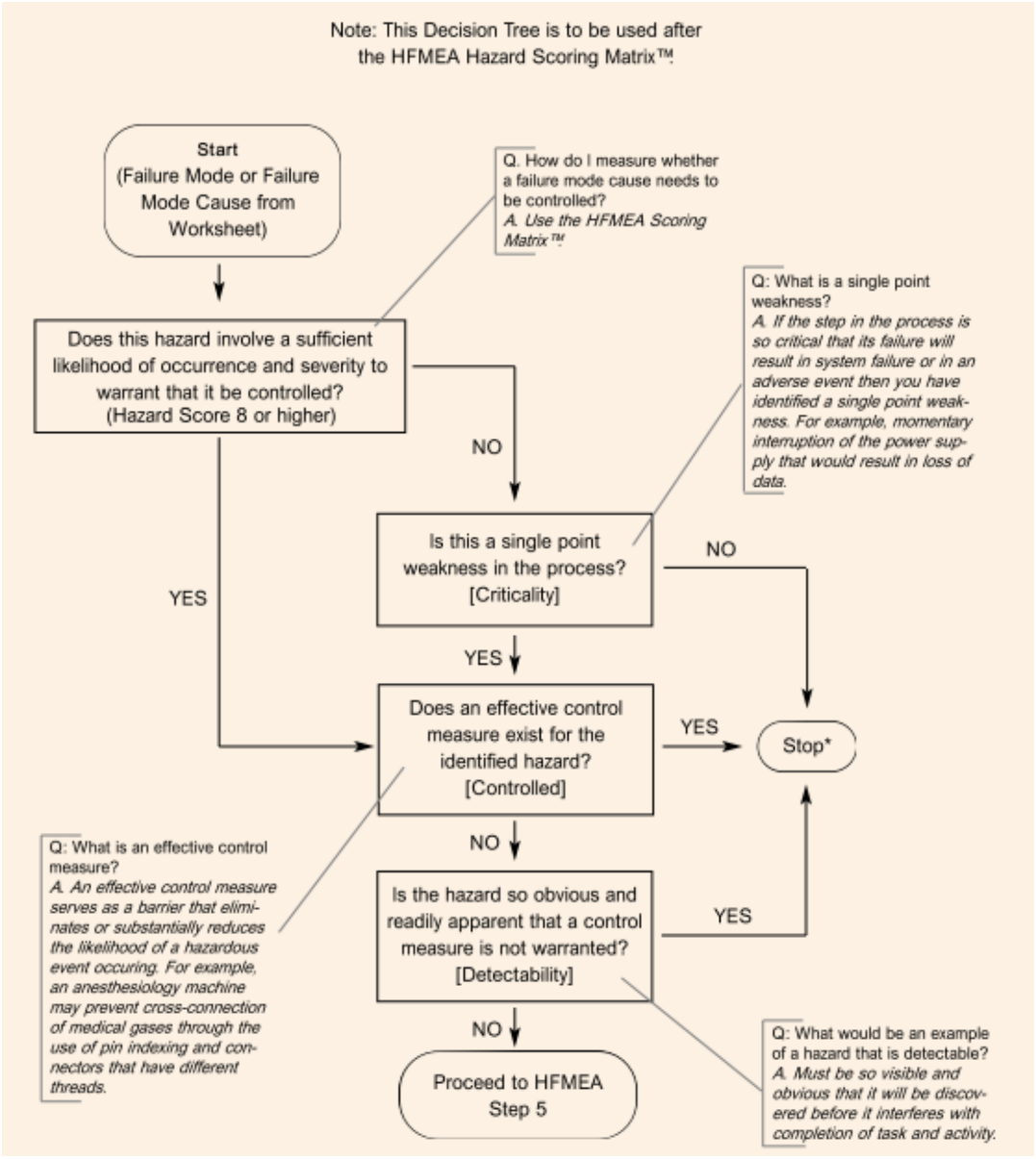

Figure 6 HFMEA Decision Tree [41]

1.4 Research aim

The study goal is to evaluate the laparoscopic Whipple procedure to increase the safety of four pioneering surgical teams in the Netherlands. For this reason, the surgical procedure of the four pioneering surgical teams in the Netherlands will be analysed with the HFMEA method. The main question to answer is: How can the operative techniques of the Whipple procedure be improved from the four hospitals in the Netherlands? Three sub-questions are drawn to answer the main question, which are:

1. What are the current operative techniques of the four hospitals?
2. Which process steps are comparable between the four hospitals?
3. Which process steps contain risks which should be reduced?

Through this research the risks will be identified where the surgeons can learn from each other and the risks where further research is needed. Altogether, the risks are reduced by enabling surgeons to learn from each other and become known with other solutions to increase the safety for the four pioneering surgical teams in the Netherland.

2 Method

The HFMEA was performed in four Dutch hospitals which are leading in the implementation of the laparoscopic Whipple procedure in the Netherlands. In order to improve the LPD procedure, the risks during surgery need to be identified of the four hospitals. The HFMEA method identifies the relevant risks of the LPD procedure which need to be prevented. Since it is a prospective research, the risks can be eliminated in an early stage of the learning curve of the four surgical teams. The analysis performed in this study follows the guidance of a safety programme for Dutch hospitals [42] and the HFMEA explained by Derosier [41], which consists of five steps. The method has been adapted firstly to be able to perform the analysis for a surgical procedure and secondly to be able to compare the results between the four hospitals. Figure 7 shows the employed HFMEA method schematically.

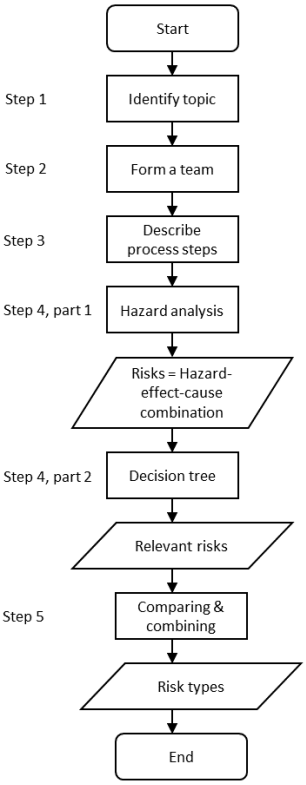

Figure 7 In short, the employed HFMEA method in this study

It is a multicentre experimental design where the first four HFMEA steps were done per hospital. The initial steps were identifying the topic (step 1), forming a team with field experts (step 2) and describing the process steps of the LPD procedure (step 3). Next, risks were identified per process step and converged to the relevant risks (step 4). Finally, the remaining risks per hospital were compared between the hospitals (step 5). In the following paragraphs, the method is explained per step.

2.1 HFMEA step 1: Define the HFMEA™ topic

In step 1 the topic of the analysis was defined. The relevant parts of the LPD procedure were taken into account in this study. The relevant parts are primarily the core steps of the LPD procedure. A process step is a core step when the surgeon could not stop the surgical procedure anymore after executing one or more of these steps without having to perform additional interventions. The preceding steps which could influence the core steps of the LPD procedure were taken into account as well.

2.2 HFMEA step 2: Assemble the multidisciplinary team

In step 2 the teams to identify the risks (first part of step 4) were formed per hospital. Per hospital, one surgeon who performs LPD procedures was the contact person for this research. To perform the hazard analysis, the first part of step four, a multidisciplinary team was formed per hospital. The team members were chosen such that all parties relevant for the Whipple procedure were represented. The researcher established that at least one surgeon who performs LPD procedure, one scrub nurse who assists LPD procedures and one HFMEA facilitator was needed. In collaboration with the contact person, the team was assembled per hospital.

2.3 HFMEA step 3: Graphically describe the process

In step 3 the LPD procedure was divided in process steps per hospital. The written standard operation report from the LPD procedure was divided in process steps in an Excel sheet of each hospital. The process steps were validated by the contact person of the related hospital. Information about the positioning of the patient and the port positions was taken from the written standard operation report, by visiting an LPD procedure, and email contact with the contact person of each hospital. This information is placed into a picture to illustrate the positions.

2.4 HFMEA step 4: Conduct a hazard analysis

In step 4 the relevant risks per hospital were defined. This step consisted of two parts. The first part was the hazard analysis, where the risks and the corresponding risk score were determined per process step of the LPD procedure (Table 1, Table 2, Table 3). The hazard analysis was performed with the multidisciplinary team (formed in step 2) per hospital in one session on an MS Excel sheet displayed on a beamer or screen visible for the participants of the analysis. An example of the Excel sheet can be found in appendix A. The risks[3] and grades were identified as follows:

1. The hazards for the specific process step were identified.
2. The potential effects per hazard were described.
3. The severity per hazard-effect combination was determined for this process step, resulting in a severity score (S).
4. The (potential) causes of the hazard-effect combination were described for this process step.
5. The probability that this hazard-effect-cause combination occurred during this process step is determined, resulting in a probability score (P).

[3] A risk is also called a failure mode, which is a combination of three factors: a hazard, the effect of the hazard and the cause of the hazard-effect combination. One hazard or a hazard-effect combination can obtain multiple failure modes.

The severity rating from the safety programme for Dutch hospitals [42] was used, which were classified from high to low as catastrophic, high, moderate and minor. A modified probability rating from the safety programme for Dutch hospitals [42] was used and an extra interval was included. Both adaptations were done in collaboration with two surgeons from the JBZ. Table 1 shows the severity and probability rating. By multiplying the severity with probability (S x P) rating for a hazard-effect-cause combination a risk score was obtained. The risk scores are shown in Table 2. The risk scores were classified in five ordinal scale categories; Extreme, Very high, High, Medium, and Low. The ordinal scale categories were communicated to the participants. To distinguish the five categories during the hazard analysis, a colour code was given. The intervals and colour code per category are shown in Table 3.

The second part was the decision tree, where the risks were converged to relevant risks and determined whether a relevant risk warranted further action (Figure 8). The decision tree was walked through per hazard-effect combination by the contact person per hospital, while having contact with the researcher via the telephone, who explained each question separately. The decision tree was slightly adapted from the decision tree of Derosier [41]. Appendix B elaborates on the adjustments of the questions. Appendix C illustrates an example of the decision tree.

The risks were converged to the relevant risks through the decision tree, which is based on the risk score and three questions about the criticality, control measurement and the detectability of the hazard-effect combinations. To explain the decision tree (Figure 8), when a risk is led to the box 'stop', it implied that this risk is not found relevant and did not need further action. When a hazard had a risk score >6, the question about criticality was automatically answered with 'yes'. When the question about controllability was answered with yes, the surgeon was asked to explain what the precautionary measurement contained. When the question about detectability was answered with 'no', this risk was defined as a relevant risk. Then the surgeon indicated if he wanted to accept, control or eliminate this risk. The questions asked in the decision tree 'Critical?', 'Controllable?' and 'Detectable?' were asked as follows:

Critical?
A risk is critical when caused by an operative technique, which can result in

- Conversion,
- Death of the patient,
- An accumulation of injuries which can cause termination of LPD and/or
- An intra-operative action which could like results in a consequence for the outcome?

Controllable?
Do you employ an effective precautionary measure through which this risk almost never occurs?
A precautionary measure reduces or eliminates the probability that the risk occurs. This could be preceding actions, choice of instruments, extensive execution of process steps, operative techniques, and more.

Detectable?
Is the hazard so obvious and readily apparent before it interferes with completion of task and activity that a control measure is not warranted?

The definitions 'accept, control and eliminate' were:

Accept:	No further action is warranted to diminish the risk
Control:	A precaution measurement need to be thought of to reduce the chance of the risk prevalence
Eliminate:	This risk is not allowed to occur

2.5 HFMEA step 5: Actions and Outcome Measures

In step 5, the relevant risks established during step 4 were compared and combined between the four hospitals. This step consisted of four parts. In the first part, the process steps were written in a way to enable comparison between the process steps of the four hospitals. To make this possible, the LPD procedure was divided in phases and sub-phases based on literature and on discussion with the participating surgeons. The phases and sub-phases were chosen to be logical for the division of the process steps. Every process step of each of the hospitals was assigned to a sub-phase. The determination of the sub-phases and the allocation of the process steps was an iterative process and validated by the contact persons of the participating hospitals. Finally, within the sub-phase the similar process steps between the hospitals were coupled to each other.

In the second part, the relevant risks were compared for every similar process step of the four hospitals. The risks were identified for a process step during step 4 of the HFMEA method. In this part, the identified relevant risks were shown for every sub-phase to be able to compare the hazardous process steps between the hospitals. The hazard-effect combination, including the risk score and if the surgeon has determined to accept, control or eliminate the risk was shown per sub-phase.

In the third part, the relevant risks were combined to identify risk types. The relevant risks which the contact person wanted to be controlled or eliminated were counted and the effect in short described. The effects of the risks or the results of the effects could be comparable. Therefore, the risk types were determined as an effect or the result of an effect.

In the final part, for each risk type the causes were indicated, which were identified by the multidisciplinary team during the hazard analysis of part 1 of step 4 of the HFMEA method. First, all hazards were extracted out of the hazard analysis of part 1 of step 4 of the HFMEA method, including the amount of time that they were mentioned. Each hazard was assigned to a risk type, determined in part 3 of step 5 of the HFMEA method. A hazard was assigned to a risk type when the effect or the result of the effect from the hazard agreed with the risk type. When a hazard did not match with a determined risk type, it was appointed to the risk type 'other'.

Next, for each risk type, except for the risk type 'other', the causes were extracted out of the hazard analysis of part 1 of step 4 of the HFMEA method. The amount of times a cause was mentioned was extracted as well. Cause-types were determined, by examining the causes and identifying the overarching reason of a group of causes. Each cause-type was explained by a definition, to know if a cause fits with this cause-type. Determining the cause-types was an iterative process, whereby several cause-types were tried until each cause could be assigned to an appropriate cause-type.

Exclusion criteria

When a contact person had determined that a relevant risk needed to be controlled or eliminated, but indicated that the risk was theoretical, the risk was excluded in step 5 of the HFMEA method.

Table 1 HFMEA™ severity and probability rating

Rating	Severity	Probability
1	Minor: No injury	0-5%
2	Moderate: Not permanent injury	5-10%
3	High: Not serious, permanent injury	10-25%
4	Catastrophic: Death/serious, permanent injury	25-50%
5	-	50-100%

Table 2 Hazard Scoring Matrix™

Probability	**Severity**			
	Catastrophic	**Severe**	**Moderate**	**Mild**
50-100%	20	15	10	5
25-50%	16	12	8	4
10-25%	12	9	6	3
5-10%	8	6	4	2
0-5%	4	3	2	1

Table 3 Classification of risk score with colour code

Extreme	> 12
Very high	10 < x ≤ 12
High	6 < x ≤ 9
Medium	3 < x ≤ 6
Low	x ≤ 3

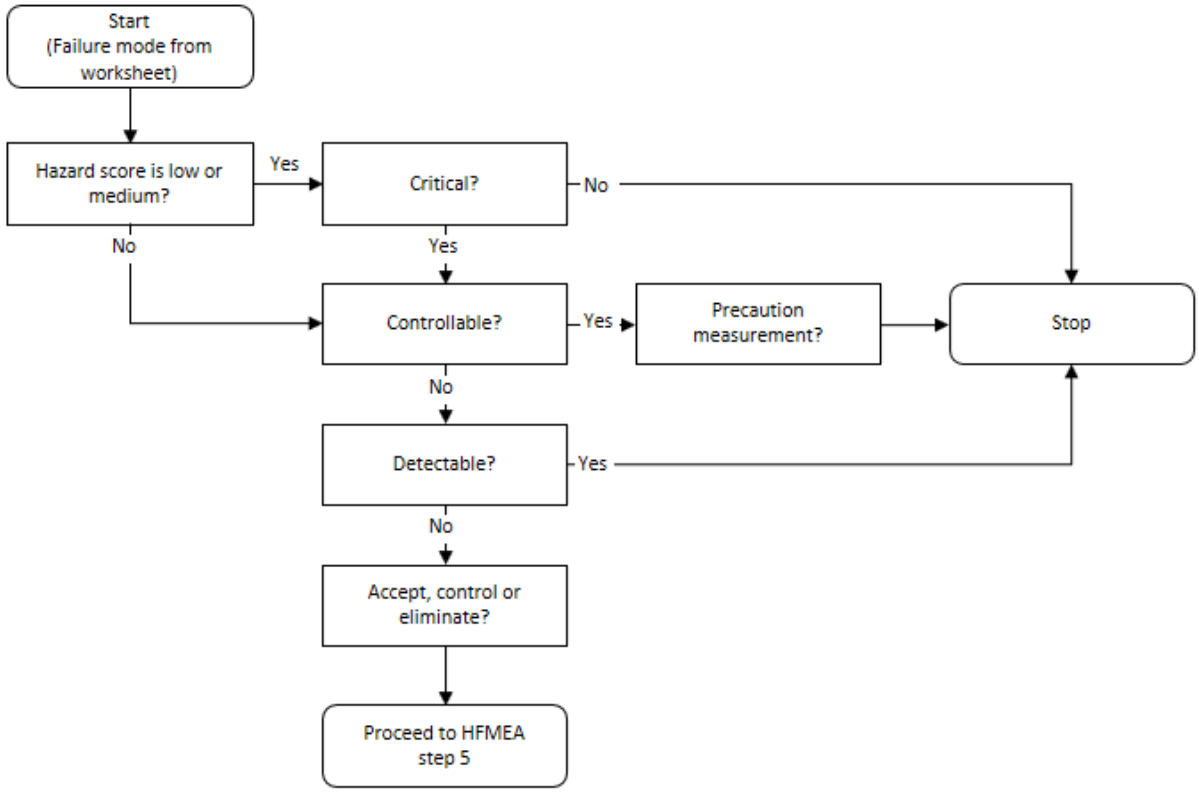

Figure 8 The decision tree after the hazard analysis to determine whether a risk warrants further action [42]

3 Results

3.1 Step 1: Define the HFMEA™ topic

In step 1 the topic of the analysis was defined. After opening of the abdomen, all surgical techniques were important as the technique could influence the core steps of the LPD procedure and/or were core steps of the procedure. The analysis ended by the closure of the abdomen.

3.2 Step 2: Assemble the multidisciplinary team

In step 2 the teams to identify the risks (first part of step 4) were formed per hospital. Table 4 describes the participants of the teams per hospital.

Table 4 Multidisciplinary team for the hazard analysis per hospital

Hospital	LPD surgeons	Scrub-nurses	Researchers	HFMEA facilitators
CTZ	2	2	1	1
JBZ	2	3	0	2
AMC	2	3	2	2
OLVG	5	5	1	1

3.3 Step 3: Graphically describe the process

In step 3 the LPD procedure was divided in process steps per hospital. Table 5 shows the process steps per hospital in chronological order. The process steps are comparable with each other, but the sequence of the process steps differ. The process steps were defined in Dutch and can be found in Appendix D. The specifics of how the process was described can be found in Appendix E. Before the surgical procedure started, the patient was positioned and the ports placed.

Three of the four hospitals operated the patient in the same position; the French position (Figure 11). The right arm is positioned alongside the patient, while the left arm is positioned to the left. The legs are bent and spread. CTZ practiced this position with one adaptation; the left arm was positioned alongside the patient. The position of the surgeon around the patient is visible in Figure 9.

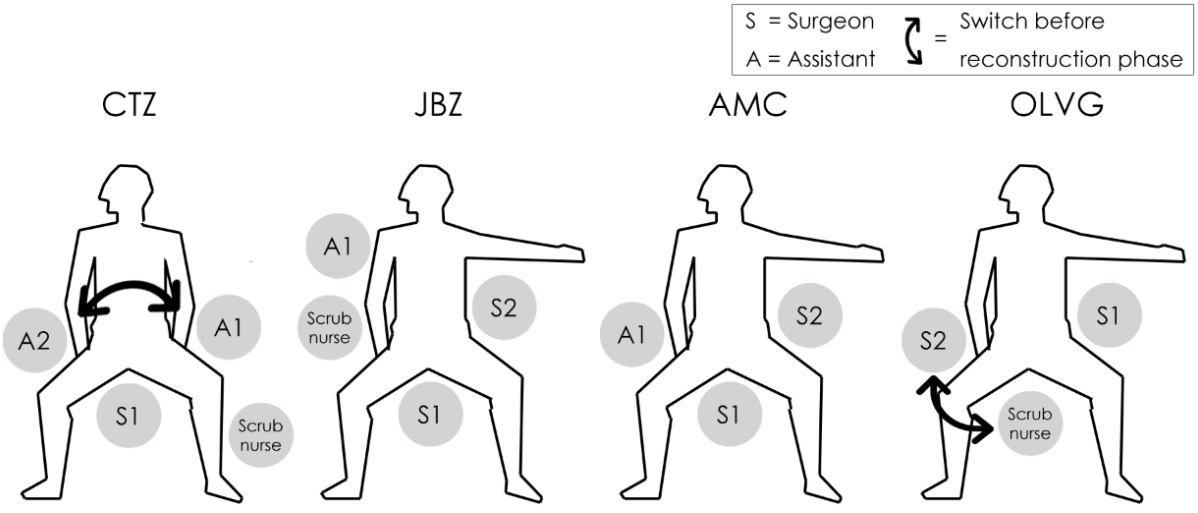

Figure 9 Position of surgical team around the patient during the LPD procedure

Figure 11 French position of a patient during a procedure

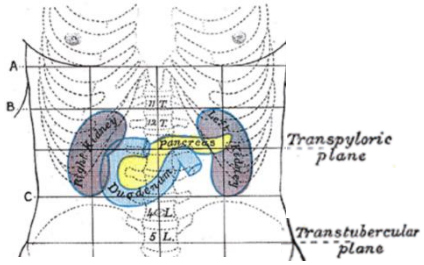

Figure 10 The upper body of the human. The planes are visible relative to the organs [54]

Port placement

Figure 12 shows the location of the ports during the LPD procedure per hospital. The upper horizontal line is the transpyloric plane. The lower horizontal line is the transtubercular plane. Figure 10 shows the planes relative to the pancreas and duodenum. The endoscope is located umbilical at CTZ and JBZ, while sub-umbilical at AMC and OLVG. During the operation, the surgeon of the AMC repositions the endoscope from subumbilical to the one port to the right.

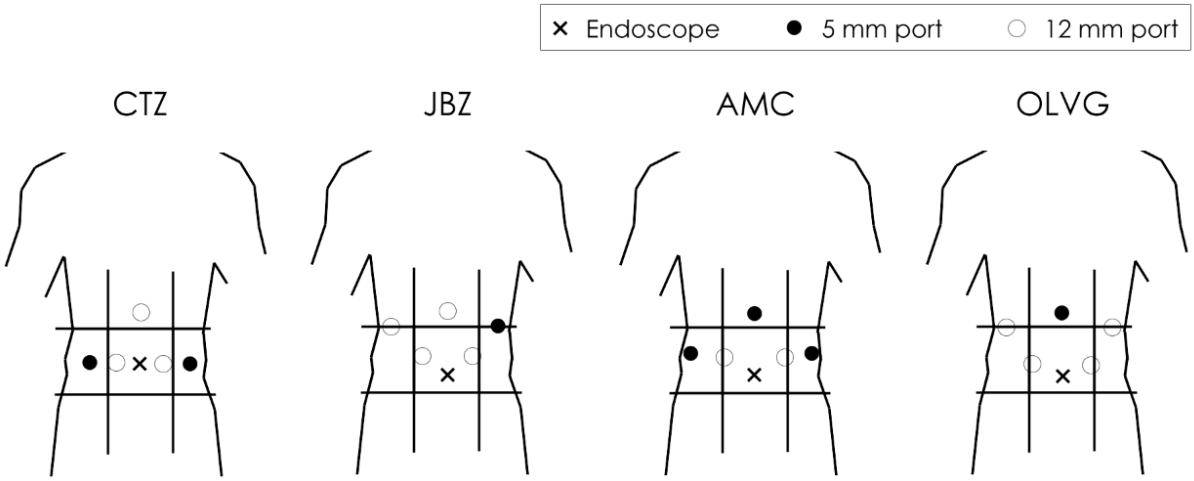

Figure 12 Port placement per hospital

Table 5 The process steps per hospitcal (CTZ, JBZ, AMC and OLVG) in chronological order of the LPD procedure

	CTZ		JBZ		AMC		OLVG
C1	Mobilising curvatura major with the LigaSure	**J1**	Attach the gall bladder to the abdominal wall	**A1**	Hanging ligamentum teres with a stitch	**O1**	Placement of endopaddle via most right trocar
C2	Mobilising flexura hepatica	**J2**	Open the bursa omentalis and mobilise the stomach	**A2**	Metal clip on and transection of a. cystica	**O2**	Lymphadenectomy node 8a and possibly 9
C3	Begin of creating a tunnel posterior of the pancreas; Mobilising the VMS and vena porta from caudal of the pancreas and transection of a/v gastroepiploica dextra	**J3**	Inciting peritoneum across duodenum towards lateral and mobilisation of flexura hepatica	**A3**	Fixating gallbladder fundus to the ventral abdominal wall	**O3**	Mobilisation and briddle of a. hepatica communis
C4	Kocher manoeuvre till over the left kidney vein and opening of Treitz	**J4**	Investigation and possibly dissection of ligamentum hepatoduodenale, open the peritoneum across the ligament and anterior lymphadenectomy (node 12a)	**A4**	Cholecystectomy: Gallbladder remains connected with the liver	**O4**	Mobilisation and transection between clips of a. gastroduodenalis
C5	Lymphadenectomy in ligamentum hepatoduodenale; including lymph nodes 12 and 8. Identification of a. hepatico communis and a. gastroduodenalis; transection of a.	**J5**	Mobilisation and transection of a. cystica and d. cysticus	**A5**	Open bursa omentalis, pass through gastrocolic ligament from 2 cm distal of a/v gastroepiploic to flexura hepatica	**O5**	Mobilisation of a. hepatica propria until over the bifurcation

	gastroduodenalis between 3 hemolocks						
C6	Finish of the tunnel dorsal of the pancreas and ventral of the vena portae	**J6**	Mobilising with lahey and bridle the d. choledochus	**A6**	Identification VMS	**O6**	Identification and transection between clips of a. gastrica dextra
C7	Transection of duodenum one cm next to the pylorus (pylorus-preserving procedure)	**J7**	Mobilising the a. hepatica communis	**A7**	Identification of a./v. gastroepiploica	**O7**	Mobilisation of vena portae anterior
C8	Mobilisation and transection of the first jejunumlis	**J8**	Lymfadenectomy node 8	**A8**	Transection of v. gastroepiploica	**O8**	Open bursa omentalis through ligamentum gastro-colic
C9	Mobilising mesenterium till contact is made with previous dissected area under Treitz with the LigaSure	**J9**	Mobilising and transection of the a. gastroduodenalis	**A9**	Kocher manoeuvre	**O9**	Mobilisation of upper edge of pancreas untill gastroepiploica dextra
C10	Stitching both intestine remnants	**J10**	Transection of d. choledochus with Echelon 60 mm white stapler	**A10**	Mobilisation lymph node 8a	**O10**	Clip on the distal side of the a. gastroepiploic and transection proximal of the pylorus
C11	Bringing the jejunumlis to the right	**J11**	Mobilisation of the vena portae crania	**A11**	Identification of a.hepatica, v.porta and a.gastroduodenalis cranial to the pancreas	**O11**	Follow bursa omentalis to the right, mobilisation of the flexura hepatica and as much as possible of the colon ascendens
C12	Transection of the pancreas with diathermy. Vriescoupe is not usual	**J12**	Lymfadenectomy node 12p	**A12**	Finish tunnel dorsal of the pancreas	**O12**	(Kocher manoeuvre and open treitz from suphepatic space) Move proximal jejunum cranial and transect it
C13	Identification of the d. pancreaticus	**J13**	Transection of a. gastroepiploica and mobilisation of proximal duodenum	**A13**	Remove nasogastric tube	**O13**	Transection of stomach with endo-stapler
C14	Separation of the pancreas from the vena portae (cranial and caudal) and the AMS (lateral on the right)	**J14**	Transection of proximal duodenum with Echelon 60 mm blue stapler	**A14**	Mobilisation stomach	**O14**	Mobilisation of lower edge of the pancreas and identification of VMS
C15	Antegrade dissection of the gallbladder	**J15**	Isolation of the a. confluence and mobilisation of the vena porta caudal	**A15**	Place a metal clip on the a. gastrica dextra	**O15**	Tunnel pancreas dorsal of the pancreatic neck and briddle
C16	Transection of the d. hepaticus, cranial to the d. cysticus after placement of bulldog	**J16**	Transection of the pancreas with Echelon 60 mm white stapler	**A16**	Transection of stomach one cm proximal to the pylorus with an endostapler	**O16**	Transection of pancreas with diathermy or harmonic ace. Transection of d. pancreaticus with scissor
C17	Extraction of the specimen in an endobag. Gallbladder en-bloc	**J17**	Kocher manoeuvre and mobilisation of the specimen at the level of the VMS/vena portae	**A17**	Move the stomach to the left	**O17**	Free processus uncinatus and head of the pancreas from the AMS and VMS
C18	Rinse, suction and extraction via a Pfannenstiel incision	**J18**	Transection of distal duodenum with stapler	**A18**	Stretch the colon to cranial and stretch the jejunumlis to caudal and to the right. Mobilisation of jejunumlis to lateral	**O18**	Lymphadenectomy nodes 12P and B dorsal in ligamentum hepatoduodenale

C19	Insufflation
C20	Pancreaticojejunostomy
C21	Choledochojejunostomy
C22	Pass the stomach probe through the pylorus
C23	Gastrojejunostomy
C24	Postion two drains

J19	Mobilisation of the specimen at the level of the AMS
J20	Extraction of the specimen in an endobag and removal via a suprapubische incision
	Break
J21	Mobilisation and transection of proximal jejunum. Stitch with PDS 3.0
J22	Choledochojejunostomy
J23	Pancreaticojejunostomy
J24	Retrograde cholecystectomy
J25	Enterotomy 40 cm distal of the CJ
J26	Gastrojejunostomy
J27	Position drains

A19	Transection first jejunumlis with endostapler
A20	Remove flush of duodenum till over the radix mesenterii
A21	Stitching both jejunum remnants
A22	Move the duodenum to the right
A23	Transection of pancreas with monopolar diathermy and the d. pancreaticus with a scissor.
A24	Transection of a. gastroduodenalis between Hem-o-lok clips
A25	Repositioning of the endoscope to the right
A26	Stretch the duodenum
A27	Start mobilisation from the processus uncinatus. Mobilisation of first the vena portae and then the AMS in layers from ventral to dorsal
A28	Open foramen of Winslow
A29	Follow a. hepatica communis to a. hepatica dextra
A30	Tunnel bile duct
A31	Extraction of retro-portal lymph node en-bloc
A32	Placement of bulldogclamp and hem-o-lok clip on biliary duct. Specimen in endobag
	Break
A33	Pancreaticojejunostomy
A34	Choledochojejunostomy
A35	Finish cholecystectomy
A36	Extraction specimen
A37	Drain placement through foramen of Winslow till cranial of the pancreas
A38	Gastrojejunostomy
A39	Placement of second drain caudal to PJ, cranial to CJ

O19	Antergrade cholecystectomy
O20	Transection of a.cystica with clips
O21	Transection of d. choledochus with scissor between a bulldog clamp and a hem-o-lok
O22	Extraction specimen in endo-catch via pfannenstiel incision
	Break
O23	Pancreaticojejunostomy
O24	Choledochojejunostomy
O25	Gastrojejunostomy
O26	Position of two silicondrains

3.4 Step 4: Conduct a hazard analysis

In step 4 the relevant risks per hospital were defined. This step consisted of two parts. The first part, the hazard analysis, took place with the four hospitals between January and April 2017. Per process step the risks were identified. The risks got a risk score with a colour code, by using the hazard scoring matrix (Table 2). The colours in next figures are similar to the colours of the hazard scoring matrix (Table 3). Table 6 gives information about the risk analysis per hospital. The number of process steps varied between 39 (AMC) and 23 (CTZ). JBZ and OLVG had 27 and 26 steps respectively.

Table 6 Information about the performed risk analyses per hospital

Hospital	Date	Duration (min)	# process steps	# hazards (% of process steps)	# risks (% of process steps)
CTZ	March, 9	120	23	20 (87)	52 (226)
JBZ	January, 18	150	27	53 (196)	110 (407)
AMC	April, 4	90	39	58 (149)	91 (233)
OLVG	April, 20	120	26	45 (173)	88 (338)

Figure 13 illustrates the highest risk per process step of the procedure per hospital after the hazard analysis. The sequence as well as the content of each process step, differed per hospital, so the process steps did not correspond with each other by number. The hazardous steps per hospital were visible. CTZ had a long period at the beginning with medium risk scores, while during the middle part there were no risks or low risk scores. JBZ and AMC were confronted with risks on and off, while OLVG had four hazardous moments. All four have two steps at the end with a higher risk, which indicate the pancreatojejunostomy and the hepaticojejunostomy (C20-21, J22-23, A33-34 and O23-24).

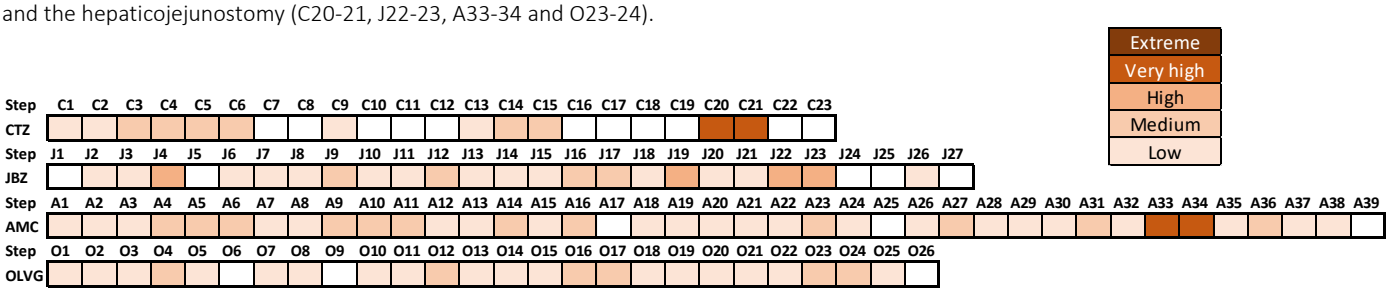

Figure 13 Highest risk per process step for four hospitals)

The datasheets of the four hazard analyses can be found in Appendix F (CTZ), Appendix G (JBZ), Appendix H (AMC and Appendix I (OLVG). The hazards, effects, causes, probability, severity and risk grade are included. Extra information per process step that was gathered during the hazard analysis for each hospital can be found in Appendix J.

The second part was the decision tree (Figure 8), where the risks were converged to relevant risks and determined whether a relevant risk warranted further action. Table 7 shows the quantitative results of the decision tree.

Table 7 Amount of remaining hazard-event combinations after each question of the HFMEA Decision TreeTM per hospital

Hospital	Date	Duration (min)	Hazard-event combinations after				Accept, control or eliminate	
			Hazard analysis	Decision tree Q1	Decision tree Q2	Decision tree Q3		
CTZ	May 15	20	28	20	11	10	Accept:	1
							Control:	9
							Eliminate:	0
JBZ	May 19	60	67	27	19	16	Accept:	3
	May 22	30					Control:	7
							Eliminate:	6
AMC	May 23	30	69	21	3	3	Accept:	1
							Control:	2
							Eliminate:	0
OLVG	May 17	30	57	22	13	13	Accept:	3
	May 19	20					Control:	10
							Eliminate:	0

The datasheets of the hazard-effect combinations for which the surgeon precaution measure has, can be found in Appendix K (CTZ), Appendix L (JBZ), Appendix M (AMC) and Appendix N (OLVG). The datasheets of the hazard-effect combinations with which the surgeons want to proceed, can be found in in Appendix O (CTZ), Appendix P (JBZ), Appendix Q (AMC) and Appendix R (OLVG).

Figure 14 illustrates the process steps with one or more risks after the decision tree.

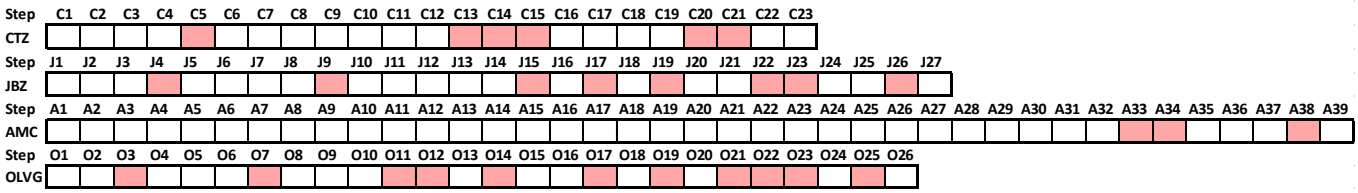

Figure 14 Process steps with risks after decision tree per hospital

3.5 Step 5: Actions and Outcome Measures

In step 5, the relevant risks established during step 4 of the HFMEA method were compared between the four hospitals. This step consisted of four parts, enabling comparison of the relevant risks, comparing the relevant risks, combining the risks into risk types and identifying the causes of the risk types.

3.5.1 Enabling comparison of the relevant risks between the four hospitals

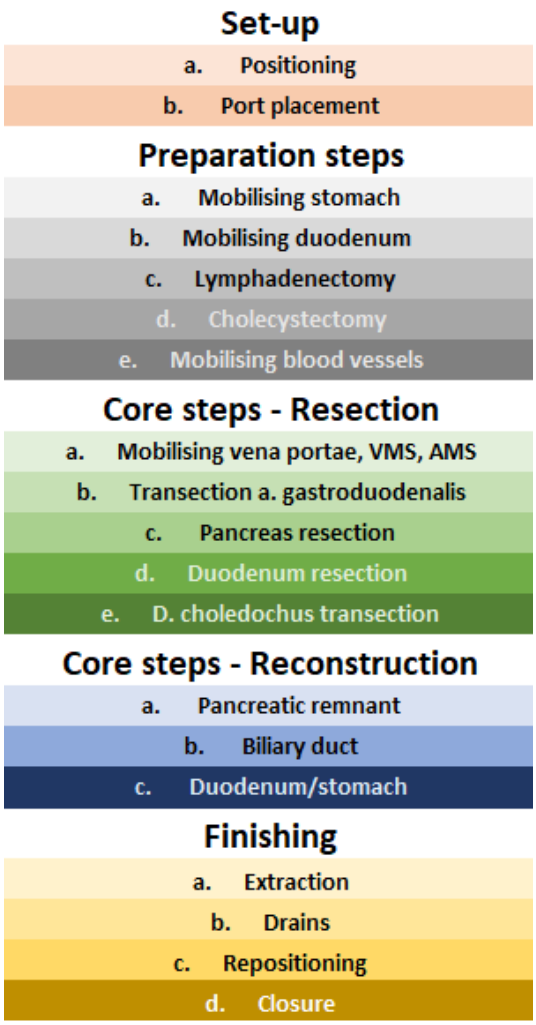

Figure 15 Phases and subphases of the LPD procedure

In the first part, the operative procedure of the Whipple procedure was divided in five phases, with in total nineteen sub phases (Figure 15). Appendix S explains the division of the phases and sub-phases elaborately. Each process step of each of the hospitals was divided over these phases and coupled to each other. Table 8 shows the phases and sub-phases. Each column shows the process steps of one hospital, whereby C = CTZ, J = JBZ, A = AMC, and O = OLVG. The similar process steps of the four hospitals were written in the same row. To give an example, process step C0 is comparable with process step J1, a combination of A1, A2 and A3, and O1. This example illustrates as well that in some cases one process step for a hospital is comparable with multiple or none process steps of another hospital. In Appendix T the process steps of the four hospital are found in chronological order and coloured with the colours of the sub phases. In Appendix U the process steps were fully written per hospital, divided over the phases. As established during step 1 of the HFMEA method, the first phase, the set-up, and the sub-phases 'Repositioning' and 'Closure', of the phase 'Finishing', were not considered during the analysis.

3.5.2 Comparison of the relevant risks between the four hospitals

In the second part, the relevant risks were compared for every similar process step of the four hospitals. In Table 8 the red-coloured process steps contain one or more relevant risks. A white-coloured process step indicates that it does not contain relevant risks. An explanation of each process step or a sequence of process steps is given. In appendix V the process steps were explained per hospital instead of a summary for each hospital. In Appendix W the process steps where the hospitals have a precaution measurement for are coloured green.

Phase 1: As established in step 1 of the HFMEA method, this phase was not taken into account.

Phase 2: The phase 'preparation steps' consisted of five sub-phases. The first sub-phase 'mobilising stomach' contained three separate process steps. There were no relevant risks identified during the three process steps by a hospital. The second sub-phase 'mobilising duodenum' contained three separate process steps. There were relevant risks identified during the second and third process step by OLVG and during the third process step by JBZ. The third sub-phase 'lymphadenectomy' contained three separate process steps. There were relevant risks identified during the first process step by JBZ. The fourth sub-phase 'cholecystectomy' contained three separate process steps. There were relevant risks identified during the third process step by CTZ and OLVG. The fifth sub-phase 'Mobilising blood vessels' contained three separate process steps. There were relevant risks identified during the first process step by OLVG.

Table 8 The process steps divided over the sub-phases and coupled between the four hospitals. The red-coulered process steps contain relevant risks. C = Catharina ziekenhuis, J = Jeroen bosch Ziekenhuis, A = Amsterdam Medisch Centrum, and O = Onze Lieve Vrouwe Gasthuis

Set-up				
a. Positioning				
b. Port placement				
Preparation steps				
a. Mobilising stomach				
C0	J1	A1 A2 A3	O1	Retracting liver
C1	J2	A5 A13 A14	O8	Exposing lesser sac and mobilising stomach
		A15		Clipping right gastric artery
b. Mobilising duodenum				
	J13	A7 A8	O9 O10	Identifying and dividing gastroepiploic artery
C2	J3	A9	O11	Mobilising hepatic flexure of the colon
C4	J17		O12	Performing Kocher maneuver and exposing ligament of Treitz
c. Lymphadenectomy				
C5	J4			Exploring hepatoduodenal ligament
	J8	A10	O2	Performing a lymphadenectomy station 8
	J12		O18	Performing a lymphadenectomy station 12
d. Cholecystectomy				
	J5		O20	Mobilising and dividing cystic artery
	J6			Dissecting biliary duct
C15	J24	A4	O19	Performing cholecystectomy
e. Mobilising blood vessels				
C5	J7	A11	O3	Mobilising common hepatic artery
			O5	Mobilising proper hepatic artery
			O6	Mobilising right gastric artery
Core steps - Resection				
a. Mobilising vena portae, VMS, AMS				
C3		A6	O14	Mobilising VMS
C6		A12	O15	Dissecting tunnel posterior to the pancreatic neck and anterior to the VMS and portal vein
		A25		Moving camera to another port
		A26		Retracting duodenum
C14	J11 J15 J19	A27	O7 O17	Dissecting portal vein, confluence, AMS and VMS
b. Transection gastroduodenal artery				
C5	J9	A24	O4	Mobilising and dividing gastroduodenal artery
c. Pancreas resection				
C12	J16	A23	O16	Dividing pancreatic neck
C13				Identifying pancreatic duct

d. Duodenum resection				
C7	J14	A16	O13	Transecting first portion of the duodenum
		A17		Moving stomach away
C8	J18	A18		Transecting fourth portion of duodenum
	J21	A19	O12	
C9		A20		Dissecting duodenum
C10		A21		Closing jejunum remnants with stitches
C11		A22		Passing jejunal stump
e. Biliary duct transection				
		A28		Dissecting tunnel posterior of the bile duct
		A29		
		A30		
C16		A32	O21	Dividing bile duct
	J10	A35		
Core steps - Reconstruction				
a. Pancreatic remnant				
C20	J23	A33	O23	Performing pancreatojejunostomy
b. Biliary duct				
C21	J22	A34	O24	Performing hepaticojejunostomy
c. Duodenum/stomach				
C22				Passing stomach probe
C23	J25	A38	O25	Performing duodenojejunostomy
	J26			
Finishing				
a. Extraction				
		A31		Removing lymphatic tissue
C17	J20	A36	O22	Removing specimen
C18				
C19				
b. Drains				
C24	J27	A37	O26	Locating operative drains
		A39		
c. Repositioning				
d. Closure				

Phase 3: The phase 'core steps – resection' consisted of five sub-phases. The first sub-phase 'mobilising vena portae, VMS, AMS' contained five separate process steps. There were relevant risks identified during the first process step by OLVG. There were relevant risks identified during the fifth process step by CTZ, JBZ and OLVG. The second sub-phase 'transection gastroduodenal artery' contained one process step. There were relevant risks identified during this process step by CTZ and JBZ. The third sub-phase 'pancreas resection' contained two process steps. There were relevant risks identified during the second process step by CTZ. The fourth sub-phase 'duodenum resection' contained six process steps. There were no relevant risks identified during the six process steps by a hospital. The fifth sub-phase 'biliary duct transection' contained two process steps. There were relevant risks identified during the second process step by OLVG.

Phase 4: The phase 'core-steps – reconstruction' consisted of three sub-phases. The first sub-phase 'pancreatic remnant' contained one process step. There were relevant risks identified during this process step by CTZ, JBZ, AMC and OLVG. The second sub-phase 'biliary duct' contained one process step. There were relevant risks identified during this process step by CTZ, JBZ and AMC. The third sub-phase 'duodenum/stomach' contained two process steps. There were relevant risks identified during the second process step by JBZ, AMC and OLVG.

Phase 5: The phase 'Finishing' consisted of four sub-phases. The first sub-phase 'extraction' contained two process steps. There were no relevant risks identified during the two process steps by a hospital. The second sub-phase 'drains' contained one process step. There were no relevant risks identified during this process step. The third and fourth sub-phase 'repositioning' and 'closure' contained no process steps.

The relevant risks per sub-phase

During the sub-phase 'mobilising duodenum the second process step, OLVG had one hazard-effect combination with a low risk score, which was decided to be accepted. During the third process step, OLVG had one hazard-effect combination with a low risk score, which were decided to be controlled. JBZ had three hazard-effect combinations with a low, medium and medium risk score, which were decided to be accepted, controlled and controlled (Table 9).

Table 9 Hazards, effects and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Mobilising duodenum'

Phase 2 Preparation steps - b. Mobilising duodenum				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
O11	Colon injury	Not identified injury; Spill colon content	Low	Accept
O12	VMS branches injury	Major intra-operative bleeding; Injury to the radiix mesenterica	Low	Control
J17	Dividing lymph nodes	Postoperative chylus leakage	Low	Accept
	VMS/portal vein branches injury	Conversion	Medium	Control
	Jejunal veins injury	Intra-operative bleeding	Medium	Control

During the sub-phase 'lymphadenectomy' the first process step, JBZ had one hazard-effect combination with a high-risk score, which was decided to be eliminated (Table 10).

Table 10 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Lymphadenectomy'

Phase 2 Preparation steps - c. Lymphadenectomy				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
J4	Common hepatic artery/gastroduodenal artery injury	Postoperative bleeding	High	Eliminate

During the sub-phase 'cholecystectomy' the third process step, CTZ had one hazard-effect combination with a medium risk score, which was decided to be controlled. OLVG had one hazard-effect combination with a low risk score, which was decided to be controlled.

Table 11 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Cholecystectomy'

Phase 2 Preparation steps - d. Cholecystectomy				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
C15	Aberrant common hepatic artery injury	Septic bleeding after bile/amylase leakage	Medium	Control
O19	Biliary duct injury	Bile leakage	Low	Control

During the sub-phase 'mobilising blood vessels' the first process step, OLVG had one hazard-effect combination with a low risk score, which was decided to be accepted.

Table 12 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Mobilising blood vessels'

Phase 2 Preparation steps - e. Mobilising blood vessels				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
O3	Common hepatic artery injury	Bleeding	Low	Accept

During the sub-phase 'mobilising vena portae, VMS, AMS' the first process step, OLVG had two hazard-effect combinations with both a low risk score, which were decided to be controlled. During the fifth process step, CTZ had three hazard-effect combinations with a medium, low, low and medium risk score, which were decided to be controlled. JBZ had six hazard-effect combinations with a low, low, low, low, high and medium risk score, which were decided to be controlled, controlled, eliminated, controlled, eliminated and eliminated. OLVG had two hazard-effect combinations with a low and medium risk score, which were decided to be controlled.

Table 13 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Mobilising vena portae, VMS, AMS'

Phase 3 Resection - a. Mobilising vena portae, VMS, AMS				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
O14	branches VMS / portal vein injury	Major intra-operative bleeding	Low	Control
		Conversion	Low	Control
C14	VMS branches (jejunal veins) / portal vein injury	Minor intra-operative bleeding	Medium	Control
		Uncontrolled intra-operative bleeding	Low	Control
	AMS injury	Major bleeding; Reconstruction of AMS	Low	Control
		AMS closure	Medium	Control
J15	Confluence vein injury	Conversion	Low	Control
	Portal vein/AMS injury	Intra-operative bleeding	Low	Control
		Conversion	Low	Eliminate
	Splenic vein injury	Conversion	Low	Control
J19	Superior Mesenteric Artery injury	Major intra-operative bleeding	High	Eliminate
		AMS injury	Medium	Eliminate
O7	Portal vein injury	Uncontrolled intra-operative bleeding	Low	Control
O17	branches VMS (jejunal veins) / portal vein injury	Uncontrolled intra-operative bleeding	Medium	Control

During the sub-phase 'transection gastroduodenal artery' the first process step, CTZ had one hazard-effect combination with a low risk score, which was decided to be controlled. JBZ had two hazard-effect combinations with both a medium risk score, which were decided to be eliminated.

Table 14 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Transection gastroduodenal artery'

Phase 3 Resection - b. Transection gastroduodenal artery				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
C5	Gastroduodenal artery injury	Major intra-operative bleeding; Extra surgery time, actions, frustration and bad view	Low	Control
J9	Gastroduodenal artery injury	Major intra-operative bleeding	Medium	Eliminate
		Common hepatic artery injury	Medium	Eliminate

During the sub-phase 'pancreas resection' the second process step, CTZ had one hazard-effect combination with a low risk score, which was decided to be accepted.

Table 15 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Pancreas resection'

Phase 3 Resection - c. Pancreas resection				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
C13	Insufficient view	Prolonged surgery	Low	Accept

During the sub-phase 'biliary duct transection' the second process step, OLVG had one hazard-effect combination with a low risk score, which was decided to be controlled.

Table 16 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Biliary duct transection'

Phase 3 Resection - e. Biliary duct transection				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
O21	Portal vein injury	Intra-operative bleeding	Low	Control

During the sub-phase 'pancreatic remnant' the first process step, CTZ had two hazard-effect combinations with a low and very high-risk score, which were decided to be controlled. JBZ had two hazard-effect combinations with a medium and high-risk score, which were decided to be accepted and controlled. AMC had one hazard-effect combination with a very high-risk score, which was decided to be accepted. OLVG had one hazard-effect combination with a low risk score, which was decided to be accepted.

Table 17 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Pancreatic remnant'

Phase 4 Reconstruction - a. Pancreatic remnant				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
C20	Difficult to identify the pancreatic duct	Prolonged surgery and frustration	Low	Control
	Pancreas fistula	POPF ISPGS Grade B and C	Very high	Control
J23	Pancreas rupture	Pancreas rupture	Medium	Accept
	Pancreas fistula	POPF ISPGS Grade B and C	High	Control
A33	Pancreas fistula	POPF ISPGS grade B and C	Very high	Accept
O23	Difficult to identify the pancreatic duct	Anastomosis is performed without the pancreatic duct; Pancreatitis	Low	Accept

During the sub-phase 'biliary duct' the first process step, CTZ had one hazard-effect combination with a very high-risk score, which was decided to be controlled. JBZ had one hazard-effect combination with a high-risk score, which was decided to be controlled. AMC had one hazard-effect combination with a very high-risk score, which was decided to be controlled.

Table 18 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Biliary duct'

Phase 4 Reconstruction - b. Biliary duct				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
C21	Bile leakage	Bile leakage ISGPS Grade B and C	Very high	Control
J22	Bile leakage	Bile leakage ISGPS Grade B and C	High	Control
A34	Bile leakage	Bile leakage ISGPS grade B and C	Very high	Control

During the sub-phase 'duodenum/stomach' the second process step, JBZ had one hazard-effect combination with a low risk score, which was decided to be accepted. AMC had one hazard-effect combination with a low risk score, which was decided to be controlled. OLVG had two hazard-effect combinations with both a low risk score, which were decided to be controlled.

Table 19 Hazards, effects, risk scores and what to do with the hazard-effect combinations (accept, control or eliminate) for sub-phase 'Duodenum/stomach'

Phase 4 Reconstruction - c. Duodenum/stomach				
	Hazard	**Effect**	**Risk score**	**Accept, control or eliminate**
J26	Incomplete anastomosis	Postoperative anastomotic leakage	Low	Accept
A38	Incomplete anastomosis	Postoperative anastomotic leakage	Low	Control
O25	Torsion	Delayed gastric emptying	Low	Control
	Too tight anastomosis	Stenosis	Low	Control

3.5.3 Combining the relevant risks of the four hospitals to identify risk types

In the third part, the relevant risks were combined to identify risk types. Table 20 shows the effects of the relevant risks and the amount of times the contact person determined to accept, control or eliminate the risk. Four risk types can be identified, shown in Table 21. The risk types were bleeding, pancreatojejunostomy failure, hepaticojejunostomy failure and gastrojejunostomy failure.

Table 20 The effects of the relevant risks which were determined to be controlled or eliminated

Phase Sub phase	A	C	Effect	E	Effect	Total ACE	Total ACE /phase	Total CE	Total CE /phase
Phase 2 Preparation steps b. Mobilising duodenum	2	3	Bleeding	0	0	**5**	**9**	**3**	**6**
Phase 2 Preparation steps c. Lymphadenectomy	0	0	0	1	Bleeding	**1**		**1**	
Phase 2 Preparation steps d. Cholecystectomy	0	2	Bleeding (1) Bile leakage (1)	0	0	**2**		**2**	
Phase 2 Preparation steps e. Mobilising blood vessels	1	0	0	0	0	**1**		**0**	
Phase 3 Resection a. Mobilising vena portae, VMS, AMS	0	11	Bleeding	3	Bleeding	**14**	**19**	**14**	**18**
Phase 3 Resection b. Transection gastroduodenal artery	0	1	Bleeding	2	Bleeding	**3**		**3**	
Phase 3 Resection c. Pancreas resection	1	0	0	0	0	**1**		**0**	
Phase 3 Resection e. Biliary duct transection	0	1	Bleeding	0	0	**1**		**1**	
Phase 4 Reconstruction a. Pancreatic remnant	3	3	Prolonged surgery and frustration (1) POPF ISPGS Grade B and C (2)	0	0	**6**	**13**	**3**	**9**
Phase 4 Reconstruction b. Biliary duct	0	3	Bile leakage ISGPS Grade B and C	0	0	**3**		**3**	
Phase 4 Reconstruction c. Duodenum/stomach	1	3	Postoperative anastomotic leakage (1) Delayed gastric emptying (1) Stenosis (1)	0	0	**4**		**3**	
Total	**8**	**27**		**6**		**41**		**33**	

A = Accept; C = Control, E = Eliminate

Table 21 The risk types identified out of the relevant risks. Risk types result in the same kind of effect.

Risk type	Effect	C	E	Total
Bleeding	Bleeding	17	6	**23**
Pancreatojejunostomy failure	Prolonged surgery and frustration	1	0	**3**
	POPF ISPGS Grade B and C	2	0	
Hepaticojejunostomy failure	Bile leakage ISGPS Grade B and C	4	0	**4**
Gastrojejunostomy failure	Postoperative anastomotic leakage	1	0	**3**
	Delayed gastric emptying	1	0	
	Stenosis	1	0	
Total		**27**	**6**	**33**

3.5.4 Causes of risks

In the final part, for each risk type the causes were indicated. Figure 17 shows the percentage that the risk types were mentioned during the hazard analysis by the four multidisciplinary teams. Bleeding was the prevalent mentioned hazard-effect combination (n = 76; 43%), then PJ (n = 20; 11%), GJ (n = 13,5; 8%) and HJ (n = 12; 7%) failure. The other hazard-effect combinations were in total 31% of the times mentioned. Figure 16 shows the five prevalent hazards which do not fall under one of the risk types, which were intestine (n = 16; 29%) and colon (n = 5,5; 10%) injury, incomplete staple (n = 5; 9%), mesocolon injury (n = 4; 7%) and dividing lymphatic pathways (n = 4; 7%). Appendix X shows all the hazards for each risk type that have been mentioned by the multidisciplinary teams with more details.

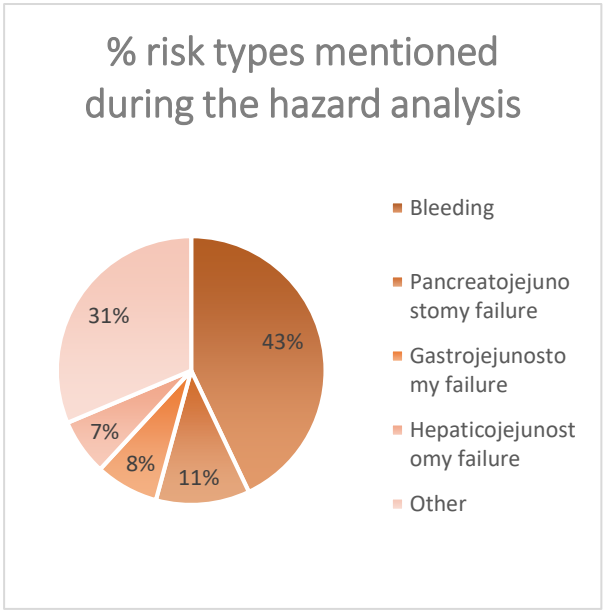

Figure 17 The amount of times a risk type has been mentioned during the hazard analyses with the four hospitals

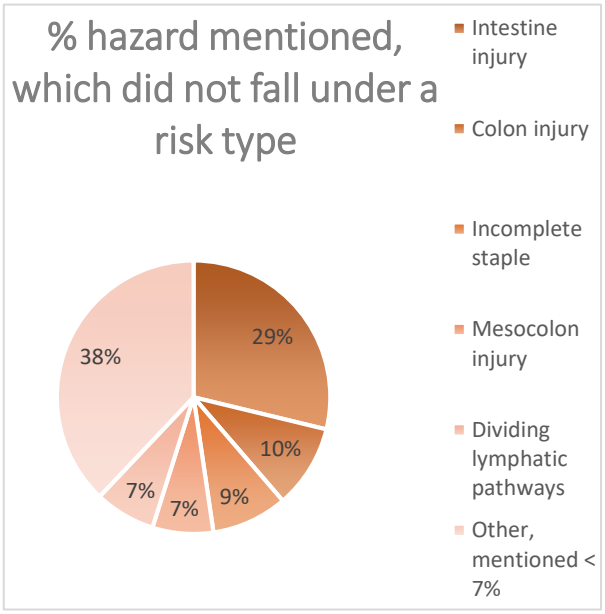

Figure 16 The amount of times a hazard has been mentioned which do not fall under one of the four risk types

Exclusion criteria

In process step O22 of OLVG a relevant risk was established after the decision tree. Nevertheless, the surgeon determined that the risk was theoretical. Therefore, this risk was excluded in step 5 of the HFMEA method.

Cause-types

The cause types with their definitions were determined as:

Patients pathology:	The cause is a disease
Patients habitus:	The cause is an aspect of the body, including anatomy, body weight and an effect of a previous disease cause by human interference and excluding a disease.
Iatrogenic/operative technique:	The cause is an act of a human
Instrument/material:	The cause is a defect instrument or rupture of material

Risk type: bleeding

The risk type 'bleeding' included three hazards (Figure 18), which were blood vessel injury (n = 70; 92%), clip loosening (n = 3; 4%) and forget clip placement (n = 3; 4%). Appendix Y shows the causes that have been mentioned by the surgical teams for each of the three hazards for the risk type 'Bleeding'. Appendix Z shows the causes for the risk type 'bleeding' combined. Figure 19 shows the six prevalent causes for the risk type 'bleeding'. Two of the six causes were pathological rooted, which were pancreatitis (n = 39; 18%) and tumour invasion (n = 23; 11%). One of six causes was patients habitus rooted, which was congenital and acquired anatomical abnormalities (n = 30; 14%). Three of the six causes were iatrogenic /operative technique rooted, which were, not recognizing the anatomy (n = 24; 11%), iatrogenic injury (n = 19; 9%) and insufficient view on anatomy (n = 18; 8%).

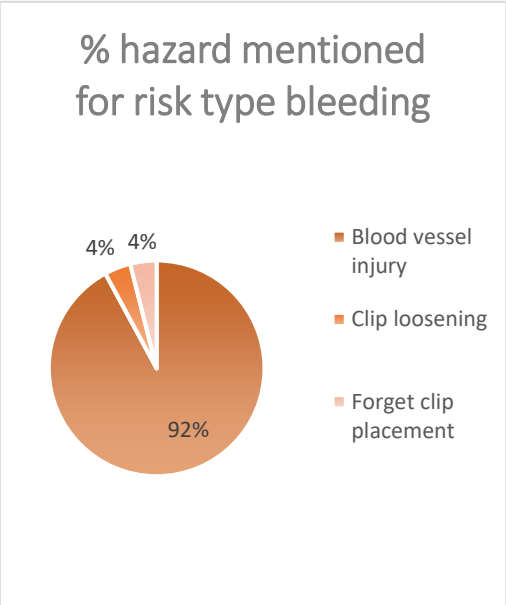

Figure 18 The amount of times a hazard has been mentioned which fall under the risk type bleeding

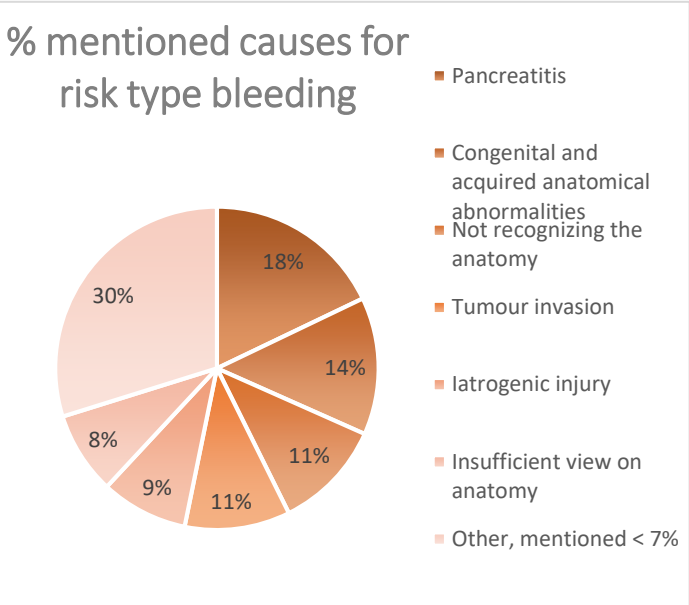

Figure 19 The amount of times a cause has been mentioned which fall under the risk type bleeding

Risk type: pancreatojejunostomy failure

The risk type 'Pancreatojejunostomy failure' included seven hazards (Figure 21), which were difficult to find pancreatic duct (n = 5; 25%), pancreas tears (n = 4; 20%), suture breaks (n = 3; 15%), pancreas fistula (n = 3; 15%), suture through the pancreatic duct (n = 2; 10%), irradical resection (n = 2; 10%) and parenchym pancreas injury (n = 1; 5%). Appendix AA shows the causes that have been mentioned by the surgical teams for each of the seven hazards for the risk type 'Pancreatojejunostomy failure'. Appendix AB shows the causes for the risk type 'pancreatojejunostomy failure' combined. Figure 20 shows the five prevalent causes for the risk type 'pancreatojejunostomy'. Two out of five were patient habitus rooted, which were small pancreatic duct (n = 7; 18%) and soft pancreas tissue (n = 5; 13%). Three out of five were iatrogenic/operative technique rooted, which were high traction force (n = 6; 16%), insufficient view (n = 5; 13%) and divided diathermic (n = 4; 11%).

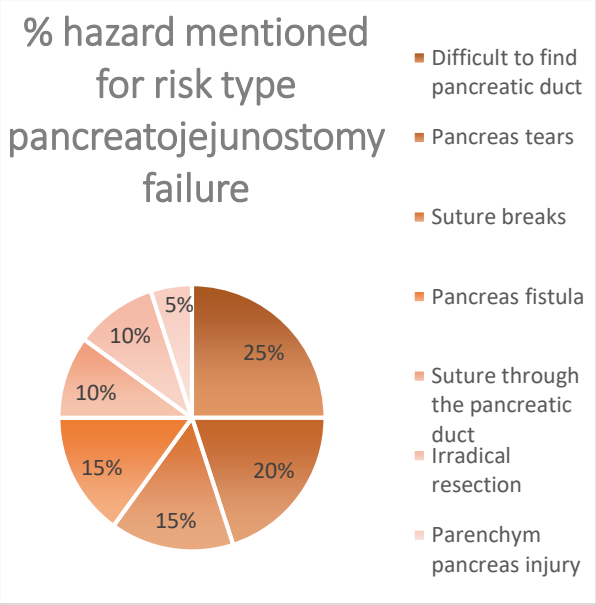

Figure 21 The amount of times a hazard has been mentioned which fall under the risk type pancreatojejunostomy failure

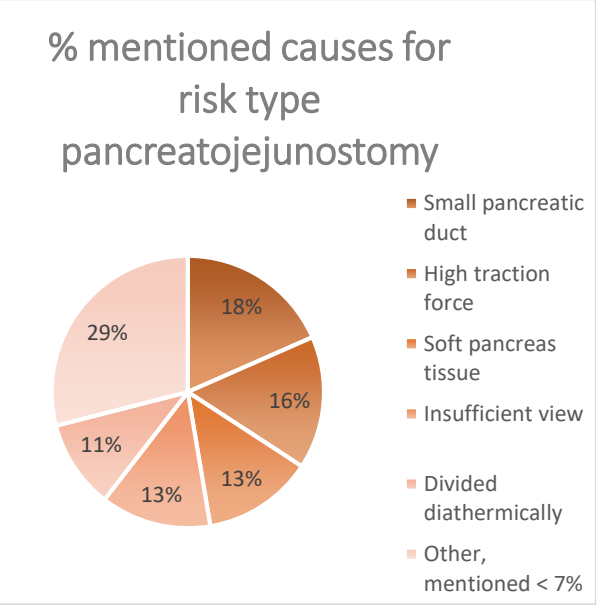

Figure 20 The amount of times a cause has been mentioned which fall under the risk type pancreatojejunostomy

Risk type: Gastrojejunostomy failure

The risk type 'Gastrojejunostomy failure' included six hazards (Figure 23), which were stomach injury (n = 4,5; 33%), insufficient GJ anastomosis (n = 3; 22%), forget probe removal (n= 2; 15%), torsion in GJ anastomosis (n = 2; 15%), Too wide (n = 1; 7%) and too narrow GJ anastomosis (n = 1; 7%). Appendix AC shows the causes that have been mentioned by the surgical teams for each of the six hazards for the risk type 'Gastrojunostomy failure'. Appendix AD shows the causes for the risk type 'gastrojejunostomy failure' combined. Figure 22 shows the four prevalent causes for the risk type 'gastrojejunostomy'. Each were iatrogenic/operative technique rooted, which were stomach injury (n = 4; 16%), insufficient view (n = 4; 16%), iatrogenic injury (n = 3; 12%) and wrong stapler (n = 3; 12%).

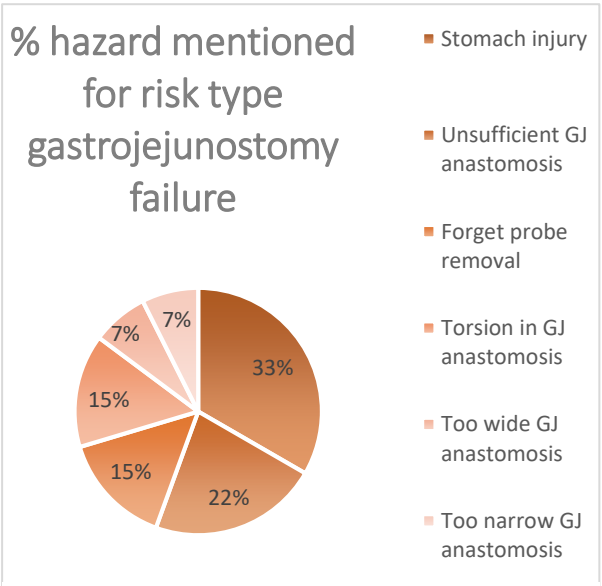

Figure 23 The amount of times a hazard has been mentioned which fall under the risk type gastrojejunostomy failure

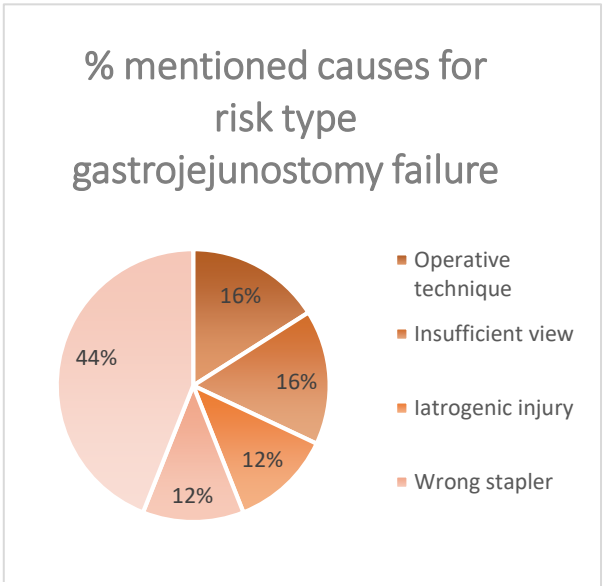

Figure 22 The amount of times a cause has been mentioned which fall under the risk type gastrojejunostomy

Risk type: Hepaticojejunostomy failure

The risk type 'Hepaticojejunostomy failure' included five hazards (Figure 25), which were biliary duct injury (n = 4; 33%), dividing biliary duct on the wrong level (n = 3; 25%), bile leakage (n = 3; 25%), torsion in HJ anastomosis (n = 1; 8%) and enterotomy > biliary duct diameter (n = 1; 8%). Appendix AE shows the causes that have been mentioned by the surgical teams for each of the seven hazards for the risk type 'hepaticojejunostomy failure'. Appendix AF shows the causes for the risk type 'hepaticojejunostomy failure' combined. Figure 24 shows the four prevalent causes for the risk type 'hepaticojejunostomy'. Two out of four were patient's habitus rooted, which were small biliary duct (n = 4; 14%) and quality of the biliary duct (n = 3; 10%). The other two out of four were iatrogenic/operative technique rooted, which were iatrogenic injury (n = 3; 10%) and quality of the anastomosis (n = 3; 10%).

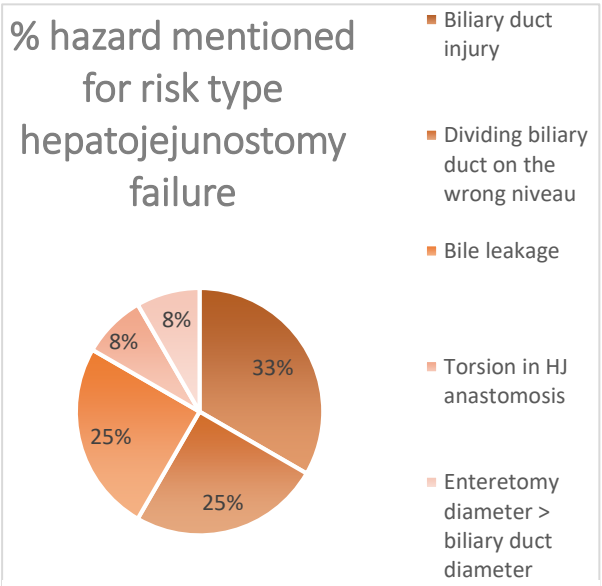

Figure 25 The amount of times a hazard has been mentioned which fall under the risk type hepaticojejunostomy failure

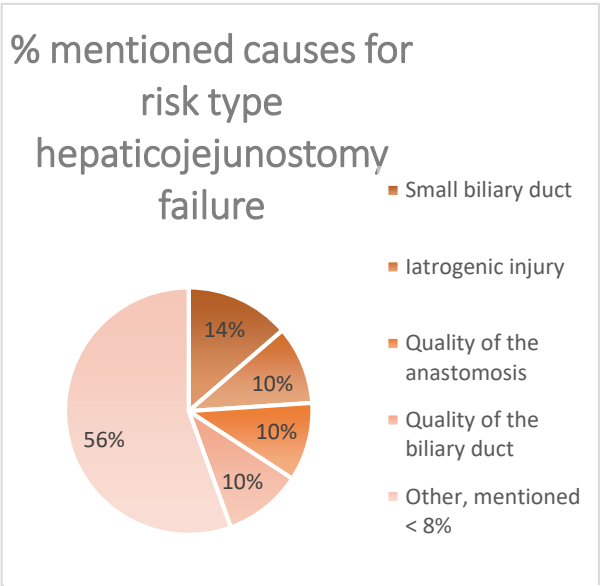

Figure 24 The amount of times a cause has been mentioned which fall under the risk type hepaticojejunostomy

In appendix AG additional findings can be found.

4 Discussion

In this study, an HFMEA study has been conducted for the LPD procedure with four pioneering surgical teams in the Netherlands. The goal of this study was to assess the operative techniques of these surgical teams for the LPD procedure currently used in the Netherlands. The approach of this study was firstly to define the current operative techniques and identify the risks for each of the hospitals, secondly to link the comparable process steps between the hospitals and finally to determine which risks should be reduced. This study identified the relevant risks of the LPD procedure by using the HFMEA hazard analysis and a modified decision tree. The hazard analysis identified the risks per step of the process and per hospital. The identified risks were then analysed and reduced to the most relevant risks by using a modified decision tree. These risks were categorised into four relevant risk types.

4.1 Most relevant results

In this study, it was noted that the four hospitals cooperated with each other to implement the LPD procedure, but identified two main differences in the process steps of the surgical procedure. The first difference noted is the number of process steps described in the standard operation report of the four hospitals. Overall the four hospitals identified similar process steps, however it was observed that there are differences in the detailed description of the process steps. The second result of this study was that the order of the process steps, mobilisation in the abdomen, resection of the specimen and reconstruction of the biliary duct and pancreatic remnant, were performed in a different order in the different hospitals.

Several surgical teams identified a relevant risk during the hazard analysis in the following process steps: (1) performing Kocher maneuver and exposing ligament of Treitz, (2) cholecystectomy, (3) mobilising portal vein, superior mesenteric vein and artery, (4) transection gastroduodenal artery, (5) PJ, (6) HJ and (7) GJ. In total 33 relevant risks were identified, which could be divided in main intra-operative risk and post-operative risks. The main intra-operative risk was bleeding which could result in conversion, major or uncontrollable bleeding, and minor bleeding. Two third of the bleeding occurs during the mobilisation of the portal vein and superior mesenteric vein and artery. The other one third was spread between five phases. The most important causes resulting in bleeding were firstly anatomical related reasons and secondly pancreatitis or tumour invasion.

Relevant risks which resulted in postoperative consequences were identified for the three anastomoses PJ, GJ and HJ. The prevalent and only consequence for the PJ and HJ anastomosis were postoperative leakage. Leakage of pancreatic fluid is mainly caused by a soft pancreas, small pancreatic duct, and the quality of the anastomosis. Similar, bile leakage is mainly caused by a small biliary duct and the quality of the anastomosis. For GJ, three different relevant risks were identified, each resulting in different postoperative consequences, which were postoperative leakage, delayed gastric emptying and stenosis. The prevalent causes were iatrogenic injury and the operative technique. In contrary to the PJ and HJ, the patient habitus was hardly mentioned as a cause.

4.2 Evaluation of the laparoscopic pancreaticoduodenectomy procedure

This study compared the process steps of the LPD procedure between the four surgical teams in four different hospitals. The process steps were based on the standard surgical operation report of each participating hospital. However, there is a bias by using the standard operation report as this does not always reflect all the surgical actions. In the comparison of the surgical reports, it was noted that the level of detail of the reports differed per hospital. While some noted every ligated blood vessel, others only provided a high-level description of certain process steps. Furthermore, the operation report is a combination of personal phrasing and individual practiced operative techniques. A second bias is that the surgical teams are still in their learning curve such that the operative methods and the order of process steps are still in development and have changed over the months. Nevertheless, to investigate the most important differences between the four surgical teams/hospitals, and as a first step with the HFMEA method, the use of standard operation report provided important insights in the differences and similarities between the hospitals. The analysis during this part of the study showed clear differences between the order of several surgical steps. Differences were identified in the order of mobilisation, resection and reconstruction. In addition, it is expected that there are differences in the exact execution of the operative techniques, which could all influence the outcome of the procedure. This study provided detailed information of the surgical process steps for the four surgical teams. This information could be used by the surgeons to learn from each other more and improve their processes. The employment of a different order and different techniques by the different surgical teams could be an advantage as it enables comparison between different methods for the same purpose. It gives the surgeons a choice between four techniques for a specific part of the procedure.

The prevalent relevant risk of this procedure is bleeding, which was 33% of the instances the result of the surgeon being unable to view or identify anatomical structures of the patient[4] by the surgeon. This could be subdivided in two causes being firstly, the misinterpretation of the exact location or the course of structures during the procedure which can be caused by changes during the procedure and anatomical abnormalities in combination with a lengthy procedure. The surgeons meticulously

[4] A combination of the causes 'congenital and acquired anatomical abnormalities', 'not recognizing the anatomy' and 'insufficient view on anatomy'.

analyse the CT-scan preceding the procedure and analyse the anatomical abnormalities which they need to remember during the long LPD procedure. In addition, the location and the course of the structures change during the procedure, when the surgeon mobilises and resects the organs. This increases the difficulty to remember the exact location of a structure. Secondly, the small working area and a non-optimal view may complicate the procedure for the surgeon. When the surgeon does not have an overview of the working area, it is difficult to view and work around the blood vessels. The risk of bleeding were identified during multiple process steps of the procedure.

Whereas bleeding is a clear result of blood vessel injury, the effects of the risks during the anastomoses are not a clear result of the hazards of the risks. The effects occur postoperative and could be caused by other reasons than those identified during this analysis.

4.3 Evaluation of the HFMEA method

In this study, the surgeons had to provide their standard surgical operation report. During this process, most surgeons revised their operation report. Consequently, the surgeons seemed to become more aware of their surgical methods.

During the hazard analysis, the surgeons were the experts on the subject. Counterweight was necessary to start discussions about the techniques and risks to create an accurate overview of the possible hazards, effects and causes. Scrub nurses and several surgeons were included in the discussions as counterweights. In addition, the accurate overview was established by using the hazard-effect-cause combinations from the preceding hospital(s) in the discussions with the following hospitals. This way the multidisciplinary team could focus on identifying other risks, instead of thinking about already identified risks.

It was challenging for the multidisciplinary team to identify the relevant effects of the hazards. During grading the severity and probability of risks, it was identified that the severity grades were multiple interpretable and the probability grades were not based on data[5], resulting in an arbitrary risk score. Therefore, comparing the identified risk scores between the four hospitals was not insightful. When Figure 13 is compared with Figure 14, it is visible that the process steps with the highest hazards after the hazard analysis do not correspond with the process steps with the relevant risks after the decision tree. It seems that the decision tree filters the risks which are relevant. Nonetheless, the decision tree was discussed with one of the surgeons of each of the hospitals.

The standard HFMEA is executed for one instance. To enable comparison between the four hospitals the LPD procedure was categorised in phases and sub-phases. Insightful information was obtained by comparing the relevant risks on the basis of the phases. Determining the phases was an important and iterative process. It was helpful in the identification of the phases to start with defining the core steps, then the global phases and filling those in.

4.4 Recommendation for the LPD procedure

At least two analyses indicated that the LPD is challenging due to the difficult access and exposure of the pancreas, haemorrhage control from major vasculature and a technically demanding PJ and HJ [9], [43], which is in line with half of the critical process steps identified in this study. The most difficult part of the LPD procedure is the reconstruction of the biliary duct and pancreatic remnant [44], [45], [46]. With help from the HFMEA method, it is found that the risks during the PJ, HJ and GJ were mainly caused by iatrogenic injury and the operative technique. The surgeons could benefit from the precision and dexterity of robotic surgery during the reconstruction phase. However, the causes for bleeding identified during this study, are unable to view or identify anatomical structures, which will not be improved by robotic surgery. In literature, robotic surgery is proposed as an option to attenuate the difficulties of the reconstruction, but high cost and time to learn this type of surgery are important disadvantages [43], [46]–[48]. In conversations with the surgeons during the hazard analysis it became apparent that the suture angle and the view on the reconstruction working area make the anastomoses difficult. This should be investigated by a questionnaire or a film analysis. If these are the main challenges, another solution could be an instrument with two extra Degrees of Freedom (DoF) for the tip of the instrument, pitch and yaw. The two extra DoF enable the surgeon to get beyond the biliary duct or pancreatic remnant, which might make suturing less challenging for the surgeon, without needing robotic surgery. However, as the extra DoF will not improve the vision or identification of anatomical structures of the patient, it will probably not reduce the risk for bleeding. In other studies, the importance of anatomical knowledge was mentioned in line with this study [9], [49]. A solution to reduce the misinterpretation of anatomical structures is intra-operative anatomical feedback. The surgeons will be able to see a real-life image of the anatomical structures of a patient, while performing surgery. The changes that the surgeon makes to the working area during the surgical procedure are immediately visible. Currently, research is done to this kind of technique for liver surgery, called a real-time 3D image reconstruction guidance [50]. During laparoscopic surgery the virtual information, a 3D model of the patient, is displayed with the real view of the patient through Augmented Reality (AR). As a result, the structures which are not directly visible are made virtually transparent and therefore visible for the surgeon [50]. In one case, it has been used for an LPD procedure. They specifically found it advantageous for mobilising the superior mesenteric artery [51]. Although it remains ongoing research, it is very interesting for the future of the LPD procedure.

[5] The probability score was most times rated on 0-5%

4.5 Recommendation for the HFMEA method

The HFMEA method in this study proved to be valuable as a systematic approach to gather and discuss a complex relatively new surgical procedure. The HFMEA protocol helped to uniformly describe the process steps and identify general risks and hazards. This analysis method could be adapted and validated to use it for other new surgical techniques or the LPD procedure in other countries. During the validation, it is recommended to adapt the severity and probability scoring from the hazard analysis and for example only discuss the risks and causes during this step. The severity and probability rating were found less valuable, because they were rated so arbitrarily. Severity and probability scores on objective data from procedures, for example from video analyses or auditing, could be useful in the future. Furthermore, the questions of the decision tree should be evaluated if the questions and the phrasing of the questions results in the converging of the risks to the relevant risks. A study has been performed concerning HFMEA studies in Dutch health care where the participants did not find the decision tree helpful [26]. In this study, the decision tree was valuable to distinguish relevant from irrelevant hazards.

When using the HFMEA method for analysing surgical procedures, surgeons and researchers should be aware to define and describe the correct process steps. Without the correct process steps the hazard analysis will take much more effort and revisions. To define the effects of hazards during a surgical procedure, the division of controllable and uncontrollable bleeding and noticed and unnoticed organ injuries were found useful. It could be considered to walk through the decision tree with the multidisciplinary team. Finally, the division of the phases is very important for the comparison. It is recommended to discuss this division of phases with the multidisciplinary teams.

5 Conclusion

The HFMEA method provided an overview of the practiced operative method of the LPD procedure from each of the hospitals. Differences in order of the procedure and executed process steps were made clear. Through the hazard analysis and the decision tree, bleedings and the reconstruction of the pancreatic remnant, biliary duct and stomach were found to be relevant risks. The process steps which contain relevant risks for more than one hospital were Kocher maneuver and exposing ligament of Treitz, cholecystectomy, mobilising portal vein, superior mesenteric vein and artery, transection gastroduodenal artery, PJ, HJ and GJ. The surgical teams can learn from each other by sharing their considerations and knowledge about specific process steps. Future research should aim on investigating solutions to diminish bleeding causes and different reconstruction techniques in order to improve the outcome.

Through the HFMEA method a surgical procedure can be compared between multiple hospitals, by systematically identifying the surgical steps and relevant risks. It is a structured method to enable discussions about procedure dependent risks, the order, process steps and operative techniques of the surgical procedure.

Bibliography

[1] Baroda Gastro Clinic, “Welcome to Baroda Gastro Clinic.” [Online]. Available: http://www.barodagastroclinic.com/. [Accessed: 01-Jan-2016].

[2] A. O. Whipple, W. B. Parsons, and C. R. Mullins, “Treatment of carcinoma of the ampulla of Vater,” *Ann. Surg.*, vol. 102, no. 4, pp. 763–79, 1935.

[3] National Cancer Institute, *Pancreatic Cancer Statistics | Did you know?* USA: National Cancer Institue, 2015.

[4] Cijfers over kanker, “Kerncijfers over kanker,” 2015. [Online]. Available: http://www.cijfersoverkanker.nl/selecties/Dataset_1/img593a84a78c621. [Accessed: 09-Jun-2017].

[5] Pancreatic Cancer Action Network, “PANCREATIC CANCER FACTS 2016,” 2016, p. 2.

[6] Landelijke werkgroep Gastro-intestinale tumoren, “Pancreascarcinoom,” 2011. [Online]. Available: http://www.oncoline.nl/pancreascarcinoom. [Accessed: 11-Jan-2017].

[7] A. H. Zureikat, J. A. Breaux, J. L. Steel, and S. J. Hughes, “Can Laparoscopic Pancreaticoduodenectomy Be Safely Implemented?,” *J. Gastrointest. Surg.*, vol. 15, no. 7, pp. 1151–1157, 2011.

[8] O. Suzuki, S. Kondo, S. Hirano, E. Tanaka, K. Kato, T. Tsuchikawa, T. Yano, K. Okamura, and T. Shichinohe, “Laparoscopic pancreaticoduodenectomy combined with minilaparotomy,” *Surg. Today*, vol. 42, no. 5, pp. 509–513, 2012.

[9] H. J. Asbun and J. A. Stauffer, “Laparoscopic vs open pancreaticoduodenectomy: Overall outcomes and severity of complications using the accordion severity grading system,” *J. Am. Coll. Surg.*, vol. 215, no. 6, pp. 810–819, 2012.

[10] M. J. Jacobs and A. Kamyab, “Total laparoscopic pancreaticoduodenectomy,” *JSLS J. Soc. Laparoendosc. Surg. / Soc. Laparoendosc. Surg.*, vol. 17, no. 2, pp. 188–193, 2013.

[11] F. Corcione, F. Pirozzi, D. Cuccurullo, D. Piccolboni, V. Caracino, F. Galante, D. Cusano, and A. Sciuto, “Laparoscopic pancreaticoduodenectomy: Experience of 22 cases,” *Surg. Endosc. Other Interv. Tech.*, vol. 27, no. 6, pp. 2131–2136, 2013.

[12] M. Gagner and A. Pomp, “Laparoscopic pylorus-preserving pancreatoduodenectomy,” *Surg. Endosc.*, vol. 8, no. 5, pp. 408–410, 1994.

[13] U. Boggi, G. Amorese, F. Vistoli, F. Caniglia, N. De Lio, V. Perrone, L. Barbarello, M. Belluomini, S. Signori, and F. Mosca, “Laparoscopic pancreaticoduodenectomy: A systematic literature review,” *Surg. Endosc. Other Interv. Tech.*, vol. 29, no. 1, pp. 9–23, 2014.

[14] Pugliese, “Laparoscopic Pancreaticoduodenectomy A Retrospective Review of 19 Cases,” *Surg. Cancers Gastrointest. Tract*, vol. 49, no. 1, pp. 119–129, 2015.

[15] C. L. Tan, H. Zhang, B. Peng, and K. Z. Li, “Outcome and costs of laparoscopic pancreaticoduodenectomy during the initial learning curve vs laparotomy,” *World J. Gastroenterol.*, vol. 21, no. 17, pp. 5311–5319, 2015.

[16] M. Matsuda, S. Haruta, H. Shinohara, K. Sasaki, and G. Watanabe, “Pancreaticogastrostomy in pure laparoscopic pancreaticoduodenectomy—A novel pancreatic-gastric anastomosis technique -,” *BMC Surg.*, vol. 15, no. 1, p. 80, 2015.

[17] Z. Liu, M. C. Yu, R. Zhao, Y. F. Liu, J. P. Zeng, X. Q. Wang, and J. W. Tan, “Laparoscopic pancreaticoduodenectomy via a reverse-‘V’ approach with four ports: Initial experience and

perioperative outcomes," *World J. Gastroenterol.*, vol. 21, no. 5, pp. 1588–1594, 2015.

[18] S. Chen, J.-Z. Chen, Q. Zhan, X.-X. Deng, B.-Y. Shen, C.-H. Peng, and H.-W. Li, "Robot-assisted laparoscopic versus open pancreaticoduodenectomy: a prospective, matched, mid-term follow-up study," *Surg. Endosc.*, vol. 29, no. 12, pp. 3698–3711, 2015.

[19] Y. Wang, S. Bergman, S. Piedimonte, and T. Vanounou, "Bridging the gap between open and minimally invasive pancreaticoduodenectomy: The hybrid approach," *Can. J. Surg.*, vol. 57, no. 4, pp. 263–270, 2014.

[20] DPCG, "Dutch Pancreatic Cancer Group." [Online]. Available: http://www.dpcg.nl/. [Accessed: 17-Apr-2017].

[21] V. E. Strong, K. a Forde, B. V MacFadyen, J. D. Mellinger, P. F. Crookes, L. F. Sillin, and P. P. Shadduck, "Ethical considerations regarding the implementation of new technologies and techniques in surgery," *Surg. Endosc.*, vol. 28, no. 8, pp. 2272–6, 2014.

[22] Dutch Health Care Inspectorate, "Risico's minimaal invasieve chirurgie onderschat," no. november, 2007.

[23] The Royal Australiasian College of Surgeons, "General Guidelines for Assessing , Approving & Introducing New Surgical Procedures into a Hospital or Health Service," p. 21.

[24] S. Dimitrios, R. D. Fanelli, R. Price, W. Richardson, and SAGES Guidelines, "Guidelines for the introduction of new technology and techniques," *Surg. Endosc. Other Interv. Tech.*, vol. 28, no. 8, pp. 2255–2256, 2014.

[25] American Academy of Family Physicians, "Clinical Proctoring," 2017. [Online]. Available: http://www.aafp.org/about/policies/all/clinical-proctoring.html. [Accessed: 01-May-2017].

[26] M. M. P. Habraken, T. W. Van der Schaaf, I. P. Leistikow, and P. M. J. Reijnders-Thijssen, "Prospective risk analysis of health care processes: a systematic evaluation of the use of HFMEA in Dutch health care," *Ergonomics*, vol. 52, no. 7, pp. 809–819, 2009.

[27] M. R. Veen, J. W. Lardenoye, G. W. Kastelein, and P. J. Breslau, "Recording and classification of complications in a surgical practice.," *Eur. J. Surg.*, vol. 165, no. 5, p. 421–4; discussion 425, 1999.

[28] Dutch Pancreatic Cancer Group, "ISPGS definities uitgebreid," 2016.

[29] S. M. Sharpe, M. S. Talamonti, C. E. Wang, R. A. Prinz, K. K. Roggin, D. J. Bentrem, D. J. Winchester, R. D. W. Marsh, S. J. Stocker, and M. S. Baker, "Early national experience with laparoscopic pancreaticoduodenectomy for ductal adenocarcinoma: A comparison of laparoscopic pancreaticoduodenectomy and open pancreaticoduodenectomy from the National Cancer Data Base," *J. Am. Coll. Surg.*, vol. 221, no. 1, pp. 175–184, 2015.

[30] S. Chalikonda, J. R. Aguilar-Saavedra, and R. M. Walsh, "Laparoscopic robotic-assisted pancreaticoduodenectomy: A case-matched comparison with open resection," *Surg. Endosc. Other Interv. Tech.*, vol. 26, no. 9, pp. 2397–2402, 2012.

[31] S. J. Hughes, B. Neichoy, and K. E. Behrns, "Laparoscopic Intussuscepting Pancreaticojejunostomy," *J. Gastrointest. Surg.*, vol. 18, no. 1, pp. 208–212, 2014.

[32] Z. Lei, W. Zhifei, X. Jun, L. Chang, X. Lishan, G. Yinghui, and Z. Bo, "Pancreaticojejunostomy sleeve reconstruction after pancreaticoduodenectomy in laparoscopic and open surgery.," *JSLS*, vol. 17, no. 1, pp. 68–73, 2013.

[33] P. J. Speicher, D. P. Nussbaum, R. R. White, S. Zani, P. J. Mosca, D. G. Blazer, B. M. Clary, T. N.

Pappas, D. S. Tyler, and A. Perez, “Defining the learning curve for team-based laparoscopic pancreaticoduodenectomy.,” *Ann. Surg. Oncol.*, vol. 21, no. 12, pp. 4014–9, 2014.

[34] Dutch Pancreatic Cancer Group, “DPCG LAELAPS 2,” 2015. [Online]. Available: http://www.dpcg.nl/projecten/laelaps-2.html. [Accessed: 19-Jul-2017].

[35] Haute Autorité de Santé, “Rapid assessment method for assessing medical and surgical procedures,” no. June, pp. 1–2, 2007.

[36] J. B. Battles, N. M. Dixon, R. J. Borotkanics, B. Rabin-Fastmen, and H. S. Kaplan, “Sensemaking of patient safety risks and hazards,” *Health Serv. Res.*, vol. 41, no. 4 II, pp. 1555–1575, 2006.

[37] B. M. Ayyub, *Risk Analysis in Engineering and Economics*. Boca Raton: Chapman & Hall/CRC, 2003.

[38] World Health Organisation, “Patient Safety : Rapid Assessment Methods for Estimating Hazards Report of the WHO Working Group meeting,” 2003.

[39] L. B. Andrews, C. Stocking, T. Krizek, L. Gottlieb, C. Krizek, T. Vargish, and M. Siegler, “An alternative strategy for studying adverse events in medical care,” *Lancet*, vol. 349, no. 9048, pp. 309–313, 1997.

[40] J. D. Andrews and T. R. Moss, *Reliability and Risk Assessment*, Second. Chippenham: Professional Engineering Publishing Limited, 2002.

[41] J. DeRosier, E. Stalhandske, J. P. Bagian, and T. Nudell, “Using health care Failure Mode and Effect Analysis: the VA National Center for Patient Safety’s prospective risk analysis system.,” *Jt. Comm. J. Qual. Improv.*, vol. 28, no. 5, pp. 248–267, 209, 2002.

[42] Veiligheids Management Systeem, “Guide for risk analysis (Praktijkgids Prospectieve Risico Inventarisatie),” 2012.

[43] H. Qin, J. Qiu, Y. Zhao, G. Pan, and Y. Zeng, “Does minimally-invasive pancreaticoduodenectomy have advantages over its open method? A meta-analysis of retrospective studies,” *PLoS One*, vol. 9, no. 8, 2014.

[44] P. Sperlongano, E. Esposito, A. Esposito, G. Clarizia, G. Moccia, F. A. Malinconico, F. Foroni, C. Manfredi, S. Sperlongano, and A. Gubitosi, “Laparoscopic pancreatectomy: Did the indications change? A review from literature,” *Int. J. Surg.*, vol. 21, no. S1, pp. S22–S25, 2015.

[45] J. S. Lee, J. H. Han, G. H. Na, H. J. Choi, T. H. Hong, Y. K. You, and D. G. Kim, “Laparoscopic pancreaticoduodenectomy assisted by mini-laparotomy.,” *Surg. Laparosc. Endosc. Percutan. Tech.*, vol. 23, no. 3, pp. e98-102, 2013.

[46] H. J. Zeh, A. H. Zureikat, A. Secrest, M. Dauoudi, D. Bartlett, and a J. Moser, “Outcomes After Robot-Assisted Pancreaticoduodenectomy for Periampullary Lesions,” *Ann. Surg. Oncol.*, vol. 19, no. 3, pp. 864–870, 2012.

[47] D. Joyce, G. Morris-Stiff, G. A. Falk, K. El-Hayek, S. Chalikonda, and R. M. Walsh, “Robotic surgery of the pancreas,” *World J. Gastroenterol.*, vol. 20, no. 40, pp. 14726–14732, 2014.

[48] V. K. Narula, D. J. Mikami, and W. S. Melvin, “Robotic and laparoscopic pancreaticoduodenectomy: a hybrid approach.,” *Pancreas*, vol. 39, no. 2, pp. 160–164, 2010.

[49] S. C. Kim, K. B. Song, Y. S. Jung, Y. H. Kim, D. H. Park, S. S. Lee, D. W. Seo, S. K. Lee, M. H. Kim, K. M. Park, and Y. J. Lee, “Short-term clinical outcomes for 100 consecutive cases of laparoscopic pylorus-preserving pancreatoduodenectomy: Improvement with surgical experience,” *Surg. Endosc. Other Interv. Tech.*, vol. 27, no. 1, pp. 95–103, 2012.

[50] L. Soler, S. Nicolau, P. Pessaux, D. Mutter, and J. Marescaux, “Real-time 3D image reconstruction guidance in liver resection surgery,” vol. 3, no. 2, pp. 73–81, 2014.

[51] E. Marzano, T. Piardi, L. Soler, M. Diana, D. Mutter, J. Marescaux, and P. Pessaux, “Augmented Reality-Guided Artery-First Pancreatico-Duodenectomy,” *J. Gastrointest. Surg.*, vol. 17, no. 11, pp. 1980–1983, 2013.

[52] C. G. Gerestein, “Postoperatieve morbiditeit en mortaliteit na cytoreductieve chirurgie voor hoogstadium ovariumcarcinoom,” no. 4, pp. 149–153, 2011.

[53] S. F. Khuri, J. Daley, W. Henderson, K. Hur, J. Demakis, J. B. Aust, V. Chong, P. J. Fabri, J. O. Gibbs, F. Grover, K. Hammermeister, G. Irvin, G. McDonald, E. Passaro, L. Phillips, F. Scamman, J. Spencer, and J. F. Stremple, “The Department of Veterans Affairs’ NSQIP: the first national, validated, outcome-based, risk-adjusted, and peer-controlled program for the measurement and enhancement of the quality of surgical care. National VA Surgical Quality Improvement Program.,” *Ann. Surg.*, vol. 228, no. 4, pp. 491–507, 1998.

[54] “Human Body > XII. Surface Anatomy and Surface Markings > Surface Markings of the Abdomen.” [Online]. Available: http://www.theodora.com/anatomy/surface_markings_of_the_abdomen.html. [Accessed: 15-Apr-2017].

[55] Geeky medics, “Pancreatic cancer,” 2016. [Online]. Available: http://geekymedics.com/pancreatic-cancer/. [Accessed: 01-Jan-2016].