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National consensus on a new resectability classification for perihilar cholangiocarcinoma - A modified Delphi method

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ABSTRACT

Background: Currently, no practical definition of potentially resectable, borderline or unresectable perihilar cholangiocarcinoma (pCCA) is available. Aim of this study was to define criteria to categorize patients for use in a future neoadjuvant or induction therapy study.

Method: Using the modified DELPHI method, hepatobiliary surgeons from all tertiary referral centers in the Netherlands were invited to participate in this study. During five online meetings, predefined factors determining resectability and additional factors regarding surgical resectability and operability were discussed.

Results: The five online meetings resulted in 52 statements. After two surveys, consensus was reached in 63% of the questions. The main consensus included a definition regarding potential resectability. 1) Clearly resectable: no vascular involvement (≤90°) of the future liver remnant (FLR) and expected feasibility of radical biliary resection. 2) Clearly unresectable: non-reconstructable venous and/or arterial involvement of the FLR or no feasible radical biliary resection. 3) Borderline resectable: all patients between clearly resectable and clearly unresectable disease.

Conclusion: This DELPHI study resulted in a practical and applicable resectability, or more accurate, an explorability classification, which can be used to categorize patients for use in future neoadjuvant therapy studies.

1. Introduction

Up to now, the decision whether a patient with perihilar cholangiocarcinoma (pCCA) is eligible for surgical exploration is discussed in multidisciplinary Hepato-Pancreato-Biliary (HPB) teammeetings and decided by consensus and is not based on objective or reproducible criteria. Several staging systems exist, but these systems fail to accurately predict resectability [1–6]. This leads to futile surgical explorations in up to 30% of patients [7,8]. Furthermore, these staging systems are not widely accepted nor implemented. Therefore, large (inter)national differences in the assessment of resectability still remain. A reproducible uniform resectability classification is much needed to compare results for quality purposes and to set up future clinical trials, especially focussing on preoperative (systemic) therapy.

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The main challenge in the assessment of these patients and the resectability of their tumours is the vast clinical and surgical complexity of pCCA. The ultimate goal is to select patients for exploration with a high chance of a successful resection with subsequent long-term survival.

In pCCA progressive disease is typically detrimental to performance status and disease- and drainage-related mortality is high in the first months after diagnosis [9]. Because of biliary complications and disease progression, about one-third of the initial presumed resectable patients do not make it to surgical exploration. For those who do undergo exploration, another one third turns out to be unresectable due to more advanced disease than expected [7,8,10]. A resection for pCCA carries significant morbidity and a post-operative mortality up to 15%. Recurrence after resection is frequent and overall survival is poor. Interestingly, surgical mortality is highest in those patients with poor oncological features [11]. Addition of preoperative (systemic) therapy could potentially lead to down staging and improve selection of patients which could ultimately lead to better outcomes [12–14].

As an analogy, practical resection criteria for pancreatic cancer, incorporating the superior mesenteric artery, the common hepatic artery, the superior mesenteric vein, and the portal vein, were designed during the initiation of the PREOPANC trial in the Netherlands in 2016 (15). Although these criteria were not completely in line with other criteria such as NCCN nor completely evidence based, they were a major contributor to the success of the first completed randomized controlled trial for preoperative (chemo) therapy (PREOPANC-1) [15–17]. Since these criteria were set up, the staging of pancreatic cancer became more standardized and widely implemented in different studies towards pancreatic surgery. As a result implementation of these criteria evolved and facilitated the evolvement of new studies and applications.

Based on current guidelines and previous studies, we selected several areas of interest for an optimal resectability classification. These included determination of: vascular involvement, suspected positive lymph nodes, size of the tumour, serum CA19-9 level, bilirubin level, volume/function of the future liver remnant (FLR), and WHO performance status. The aim of this study was to define practical resectability criteria to categorize patients for use in a future neoadjuvant or induction therapy study.

2. Methods

In order to find consensus, the (modified) DELPHI method was used. The (modified) DELPHI method is a widely used method to find consensus on different complicated topics [18].

Five online meetings were set up with surgeons from six tertiary referral centers in the Netherlands. All of these meetings were held online, first mainly because of restrictions due to the COVID-19 pandemic and later for practical reasons. During these meetings predetermined and additional factors determining resectability were discussed preceded by an update from current literature. These factors included remnant liver function, lymph node involvement, vascular involvement, biliary extent of the disease, and additional patient, and tumor biology factors. Statements regarding the different resectability items produced from these meetings, were presented via a 5-point Likert scale survey to the participating surgeons [19]. Consensus on this survey was defined as 80% agreement. “Agree” and “strongly agree” were both analyzed as positive, whether “disagree” and “strongly disagree” both were analyzed as negative. Moderate agreement was defined as consensus with 60–79% agreement. Statements that did not reach consensus were modified and presented again. This was continued until the majority of the statements had found consensus.

3. Results

3.1. Expert group

A total of 13 surgeons participated in this Dutch Delphi. These surgeons are all specialised hepatobiliary surgeons working in Dutch HPB expert centers. Due to centralisation of care, practically all patients who undergo explorations for pCCA in the Netherlands will be treated by one of these surgeons [20].

3.2. Online meetings

During the first meeting the DELPHI method was introduced. Consensus was met on several basic definitions. For example: there is a difference between preoperatively deemed “unresectable” tumours (based on radiological imaging during preoperative work-up) and unresectable tumours found during staging laparoscopy or explorative laparotomy, the latter could be divided in patients with occult metastasis and locally advanced disease. This led to the definition of a “potentially resectable” group and “unresectable” group. In addition, first thoughts about resectability criteria were shared. This meeting resulted in three statements. These statements can be found in Table 1.

The second meeting was dedicated to arterial involvement including several predefined questions, e.g.,: which imaging characteristics define arterial involvement? When would you perform an arterial resection/reconstruction? Is there a role for preoperative (systemic)therapy? This meeting resulted in 15 statements.

The third meeting was dedicated to the involvement of the portal vein and biliary system including several predefined questions, e.g.,: would you prefer standard *en* bloc portal resection and reconstruction? What is the indication for portal resection with reconstruction? To what extent is bile duct resection possible? This meeting resulted in four statements.

The fourth meeting was dedicated to the involvement of lymph nodes. Further attention was paid to the differences between N1 and N2 positive lymph nodes. Several predefined questions were discussed, e.g.,: when to consider an involved lymph node a distant metastasis? Which and how many lymph nodes should be (routinely) sampled? This meeting resulted in 12 statements.

The fifth meeting was dedicated to liver metastasis of the non-FLR and additional factors: Age, ECOG performance status, serum CA19-9 level, bilirubin level as well as liver function and volume. This included several predefined questions, e.g.,: which is more important, age or ECOG performance score? What is the minimum volume or function not requiring portal vein embolization? If a patient presents with cholangitis, how long would you wait to continue with resection. This meeting resulted in 18 statements.

3.3. Surveys

During these five online meetings a total of 52 statements were established and presented to the surgeons via a survey presented to the surgeons (Table 1). On 9th of November 2020, the first survey was sent out. After the first survey, consensus was reached in 21 statements (40%). In 15 statements (29%) a moderate consensus was reached. A total of 28 questions were modified after which the survey was sent again on the 22nd of January 2021, Table 2. This resulted in consensus for 12 statements (43%). In 8 statements (29%) a moderate consensus was reached. In total after the two surveys, consensus was reached in 63% (33/52) of the statements. A flow diagram of the modified Delphi is presented in Fig. 1.s

3.4. Resectability classification

Throughout the meetings it was clear that resectability was the most difficult point to define. However, we were able to define the following

Table 1
Results of survey 1. SA: strongly agree, A: agree, N: neutral, D: disagree, SD: strongly disagree, C: Consensus.

	Statements, n = 11	SA	A	N	D	SD	Total agree	C
General statements								
1	For allocating patients in studies and comparison between studies, a practical classification into three groups: resectable, borderline (un)resectable and unresectable is useful.	4	5	1			82%	X
2	Definition resectable: radical resection possible on bile duct and no vascular involvement of the Future liver remnant.	3	4	1	1		64%	
3	Definition unresectable: no radical resection of the bile duct possible and/or unreconstructable venous involvement and/or arterial involvement FLR, or function/volume (possibly after PVE) too little.	5	6				100%	X
Resectability and arterial involvement								
4	Radical resection is the general aim for performing surgery.	6	4				91%	X
5	Arterial involvement of the future liver remnant is an oncological contraindication for resection.		4	1	5		36%	
6	Arterial resection with reconstruction is only useful in the absence of (regional) lymph node metastases.	2	3	2	3		45%	
7	If an R0 resection is possible, an arterial reconstruction can be justified.	2	7				82%	X
8	An R1 resection is oncologically not useful.		2	3	5		18%	
9	An R2 resection is oncologically not useful.	5	3	2	1		73%	
10	There is limited space for palliative/irradical resections.	2	6	2	1		73%	
11	At how many degrees of arterial involvement on preoperative imaging (CT-scan) you can assume that this is very likely also the case peroperatively: 90, 180, 270°.	90°: –	180°: 4	270°: 5			270°: 45%	
12	The length of arterial involvement is more important than the degrees of arterial involvement as a predictor of intraoperative arterial involvement.		7	2			64%	
13	If so, what length: 10, 15, 20 mm.	10 mm: 2	15 mm: 3	20 mm: 1			15 mm: 27%	
14	By analogy with pancreatic cancer, a tumor on radiological imaging after preoperative (systemic) therapy may suggest more involvement than it is reality.		6	4			55%	
15	If a patient shows stable disease or partial response after preoperative (systemic)therapy, I am inclined to proceed with (arterial) resections/reconstructions.	2	7	1			82%	X
16	Response is not always easy to measure on radiological imaging, therefore a significant decrease in serum CA19-9 level after (systemic) therapy is also sufficient.	1	8	1			82%	X
17	If the future liver remnant is not involved, arterial involvement of the non FLR is usually not a contraindication for resection, but a poor prognostic oncological factor.	4	5		2		82%	X
18	Arterial resection can only be performed if the ECOG performance status is less than three.	2	6	3			73%	
Portal involvement								
19	Portal vein involvement is not a contraindication for resection from an oncological point of view.	3	8				100%	X
20	Portal vein reconstruction does not lead to much more morbidity.	1	6	1	3		64%	
21	If the portal vein is involved and seems reconstructable a resection can be performed.	4	7				100%	X
22	Routine no touch/*en* bloc porta resections are better than selective portal vein resections and reconstructions.		4	1	6		36%	
Lymph node involvement								
23	I routinely sample lymph nodes and perform intraoperative frozen sections to determine the strategy.	3	5	2	1		73%	
24	I always sample at least three lymph nodes to determine whether I continue with the resection or not.		3	3	5		27%	
25	I sample up to and including the gastroduodenal lymph node (station 8) to get a good picture of the patient's lymph node status.		7		2	1	64%	
26	I always sample the glands around the base of the coeliac trunk (station 9).	1	6	1	3		64%	
27	The extent of the lymph nodes which need to be sampled or resected is standardized in our center.	1	3	3	3	1	36%	
28	It would be good to agree on a standard national policy on lymph node dissections and sampling.	3	8				100%	X
29	An (AJCC7th) N1 positive node is a contraindication for resection.				8	2	0%	X
30	An (AJCC7th) N2 positive node (station 9/16) is a contraindication for resection.		7	3	1		64%	
31	If a patient with a positive N2 lymph node has stable disease under preoperative (systemic) therapy, I would consider to continue with the resection		7	1	2	1	64%	
32	I (almost) never sample the lymph nodes between the aortic artery and vena cava (station 16).	1	6		4		64%	
33	Endoscopic Ultrasound (EUS) with fine needle aspiration (FNA) is the test of choice if nodes appear positive on a CT scan.	1	9	1			91%	X
34	Lymph node sampling by endo-echo may be useful to detect N2 disease preoperatively.	1	8	1	1		82%	X
Additional factors								
35	Post-hepatectomy liver failure is the leading cause of postoperative (post-hepatectomy) death.	2	5	2	2		64%	
36	Infection is the main cause (besides small future liver remnant volume) of post-hepatectomy liver failure.	3	7	1			91%	X
37	Primary post-hepatectomy liver failure (without infection) is often preventable by properly estimating future liver remnant volume and/or function preoperatively.	2	7	1			82%	X
38	Volumetry is a reliable method to predict post-hepatectomy liver failure.		4	2	4		36%	
39	Volumetry including a function test (limax/ICG/Mebrofenine) makes prediction of post-hepatectomy liver failure more reliable	6	3	1			82%	X
40	If the volume of the future liver remnant is over 50%, an additional function scan is not necessary.	1	5	1	2	1	55%	
41	Regardless of the future liver remant function/volume, portal vein embolization lowers the probability of post-hepatectomy liver failure.		5	4	2		45%	
42	The above (regardless of future liver remnant function/volume, a portal vein embolization lowers the risk of post-hepatectomy liver failure) is only applicable for a right hemi-hepatectomy.	2	3	3	3		45%	
43	The above (regardless of future liver remnant function/volume, a portal vein embolization lowers the risk of post-hepatectomy liver failure) is only applicable for a left hemi-hepatectomy.			3	8		0%	
44	If possible, I always save segment one.		1		7	3	9%	X
45	I always resect segment 1.	3	6				82%	X
46	A more senior age is a predictor of mortality.	4	7				100%	X
47	Preoperative cholangitis is an important predictor of mortality.	4	6	1			91%	X
48	If a patient has had preoperative cholangitis, I will continue the antibiotics until the surgery.	2	2	1	4		36%	
49	If a patient has had preoperative cholangitis, I will wait at least <2 weeks/>2 weeks before I operate.	<2: 8	>2: 3				<2: 73%	

(*continued on next page*)

Table 1 (*continued*)

	Statements, n = 11	SA	A	N	D	SD	Total agree	C
50	General performance status plays a more important role than age in the decision to proceed with exploration/resection.	2	8		1		91%	X
51	Jaundiced patients cannot undergo palliative (systemic) therapy.	1	2	3	4	1	27%	
52	(Systemic) therapy can reduce jaundice in patients that are difficult to drain.		4	5	2		36%	

practical classification based on preoperative imaging:

1) *Clearly resectable*: no vascular involvement (≤90° abutment) of the future liver remnant (FLR) and possibility for a radical biliary and liver parenchyma resection.
2) *Borderline resectable*: all patients between clearly resectable and clearly unresectable disease.
3) *Clearly unresectable*: non-reconstructable venous involvement and/or arterial involvement of the FLR or no possibility for radical biliary resection.

4. Discussion

This national modified Delphi study, is the first of its sort to define a resectability classification for patients with pCCA. This method has been successfully used in defining consensus regarding liver surgery and drainage methods in patients with pCCA [21–24]. The obligatory online format due to the COVID-19 pandemic proved to work well for this purpose. A positive effect of the online meetings was that the attendance was quite high for each session. Sharing thoughts on the complex surgical management of patients with pCCA among experienced surgeons was generally highly appreciated by the participants. In addition, the following discussions were fruitful and gave several new insights.

The main topic proved to be the most difficult. Defining resectability, or perhaps better formulated as deciding which patients "benefit from a surgical exploration" remains subjective in many cases. The most important achievement was identification of those patients with a clear definition who did not need to be discussed: clearly resectable and clearly unresectable. What remained was the complex borderline group. This "by exclusion" approach is methodologically different from previous classifications.

To date, the most used staging system is the American Joint Committee of Cancer/Union for International Cancer control tumour-node-metastasis (TNM) system [5]. In addition, the Bismuth-Corlette classification for pCCA is used to describe the location and extent of pCCA along the biliary tree [4]. A disadvantage of these systems is that vessel involvement and for the latter possible positive lymph nodes are not taken into account. The Memorial Sloan Kettering Cancer/Blumgart staging system is a preoperative staging system based on imaging data that contains biliary tumour growth to the second-order biliary radicles, portal venous involvement and hepatic lobar atrophy [3]. Chaiteerakij et al. described a staging system based on preoperative information of pCCA to classify patients into four prognostic stages [2]. In addition, Gaspersz et al. designed a preoperative prognostic model to predict surgical success (R0 resection without 90-day mortality) and found a relationship between age, cholangitis, hepatic artery involvement, lymph node metastasis, and the Blumgart stage in combination with the success of the surgery [25]. Wiggers et al. developed a preoperative risk score to predict occult metastatic or locally advanced disease based on several factors (e.g., bilirubin level, arterial and venous involvement, bismuth classification and lymph nodes involvement) [26]. As mentioned before most of these criteria largely fail to accurately assess and predict resectability for patients with pCCA, which is reflected by the high number of explorations not leading to a resection in these patients [7,8]. Especially for a classification/staging system applicable to identify patients for potential preoperative systemic therapy (neo-adjuvant or induction), prediction of oncological outcome may not be the main goal. Instead, it is crucial to identify whether patients would normally undergo surgical exploration or not and how high the chances would be for successful (radical) resection or futile exploration. Several questions in this Delphi are therefore based on our recent experiences and the developments in pancreatic cancer.

For patients with pancreatic cancer, the NCCN criteria are widely used and implemented [27]. An important difference between pCCA and pancreatic cancer is the anatomical location of the tumor and the variety of options to perform resections, including arterial resections and reconstructions. Imaging of pCCA regarding arterial involvement is notoriously difficult and results misleading due to frequent false positive and false negative findings [28]. This is the reason why we were probably not able to find consensus on this point, neither for the length nor for the degrees of arterial involvement. Although generally considered a negative predictive factor for survival, arterial involvement on the side of the future liver remnant necessitating reconstruction was not thought to be a strict contraindication for resection [29]. In the Netherlands, CT scans are the preferred modality as it comes to arterial involvement [30,31]. Currently the addition of 3D reconstruction of the most important vascular structures to clarify involvement is investigated [32]. Consensus was found on the following statement; If a short arterial segment is involved, a tumor could also be considered resectable as long as it was reconstructable without an interposition graft. The general opinion was that the use of an interposition graft greatly increases the surgical risk in light of predicted poor oncological outcome in these patients. Therefore, we concluded that the longer the length of the arterial involvement, the greater the chance the tumor will be unresectable. These statements, however, might be more experience based practice rather than evidence based practice. This due to the fact that, current literature often only outlines the frequency of graft usage and not specific outcomes [33,34]. As an example Nagino et al., describes a patient who developed a thrombus in the used graft requiring re-anastomosis following thrombectomy [35]. Which might be a frequent issue, but is unfortunately not described as such.

Another interesting finding was the lack of consensus regarding standardized lymph node dissection. The participating surgeons did not agree on which and how many lymph nodes need to be sampled or cleared. In daily practice there remains some confusion about the AJCC 7th and 8th lymph node classifications [36–38]. The 8th edition abandoned the location of nodes and replaced this by the absolute number of positive nodes. In accordance with the 7th but in contrast to the 8th, most surgeons agreed on the statement that a positive lymph node at station 9 or 16 is a contraindication for resection in an older and moderately fit patient, for a younger and fit patient this was less clear. This finding is supported by a previous study, where younger patients more often underwent resection regardless of positive nodes [11].

The need for standardized portal vein embolization and the difference between volume and functional liver tests also resulted in some interesting discussions. Most surgeons agree on the statement that the combination of volumetry and a function test (limax/ICG/Mebrofenin) makes the prediction of post-hepatectomy liver failure more reliable. Only for right-sided hepatectomies consensus was found on the statement that portal vein embolization lowers the risk of post-hepatectomy liver failure. This thought is supported by the article of Olthof et al. They describe that because left hepatic resections leave a larger liver remnant and carry less surgical risks, portal vein embolization is more frequently unnecessary. Hence, portal vein embolization is often necessary in right

Table 2
Results of survey 2. SA: strongly agree, A: agree, N: neutral, D: disagree, SD: strongly disagree, C: Consensus.

	Statements, n = 10	SA	A	N	D	SD	Agree	C
General statements								
1	When pragmatically dividing patients into three categories (resectable, borderline (un) resectable and unresectable) on the basis of preoperative imaging, the following definitions can be used (with sufficient future liver remant): Clearly resectable: no vascular involvement (≤90°) of the future liver remnant and possibility for radical biliary resection. Borderline resectable: all patients between clearly resectable and clearly unresectable disease. Venous vascular involvement of the future liver remnant and/or small segment arterial involvement of the FLR that appears reconstructable Clearly unresectable: non-reconstructable venous involvement and/or arterial involvement of the future liver remnant or no possibility for radical biliary resection.	2	7		1		90%	X
Resectability and arterial involvement								
2	Arterial involvement is not a contraindication for resection, of a radical resection deemed possible.	1	6				70%	
3	Arterial resection with reconstruction is only useful in the absence of regional lymph node metastases and favorable concomitant factors such as ECOG performance status 1–2, residual volume and age.	2	7		1		90%	X
4	An R1 resection is not necessarily meaningless.	1	8				90%	X
5	A planned R2 resection is oncological not useful.	4	5		1		90%	X
6	In very exceptional cases there is room for palliative resections.	1	7	2			80%	X
7	At how many degrees of arterial involvement on preoperative imaging (CT-scan) you can assume that this is very likely also the case peroperatively: 0–90° is not involved and therefore resectable, 90–270°: borderline resectable, >270 is unresectable.		5	1	3		50%	
8	Arterial involvement is difficult to estimate on the basis of preoperative radiological imaging. Resectability criteria are difficult to define for unresectable arterial involvement. This should be reviewed case by case.	1	9				100%	X
9	The length of the arterial involvement does not matter if this is reconstructable.		5	1	3	1	50%	
10	The longer the length of the arterial involvement, the greater the chance of unresectability.	1	8	1			90%	X
11	Arterial resection can only be performed if the ECOG performance status is one or two.	2	4	2	1		60%	
Portal involvement								
12	Portal vein reconstruction does not lead to much more morbidity.		7	2			70%	
13	Routine no touch/*en* bloc porta resection is better than selective portal vein resections and reconstructions.		2	5	3		20%	
Lymph node involvement								
14	I routinely sample N2 (AJCC7th) nodes and perform intra operative frozen sections to determine the strategy.	2	4	2	1		60%	
15	I routinely sample N1 (AJCC7th) nodes and perform intra operative frozen sections to determine the strategy.		2	3	4		20%	
16	I always sample at least 2 lymph nodes to determine whether I continue the resection or not.		4	1	5		40%	
17	I sample up to and including the gastroduodenal lymph node (station 8), and if positive further to get a good picture of the patient's lymph node status.		4	1	3		40%	
18	An (AJCC7th) N2 positive lymph node (station 9/16) is a contraindication for resection in an old/moderately fit patient.	3	6	1			90%	X
19	An (AJCC7th) N2 positive lymph node (station 9/16) is not a contraindication for resection in a young/fit patient.	1	2	1	5		30%	
Additional factors								
20	Post-hepatectomy liver failure, along with Hepatic-jejunostomy leakage, is the leading cause of death.	2	7	1			90%	X
21	Volumetry alone is not a reliable method to predict post-hepatectomy liver failure.	3	4				70%	
22	If the volume of the future liver remnant is over 60%, an additional function scan is not necessary.	1	5	2	1		60%	
23	Regardless of future liver remnant function/volume, a portal vein embolization prior to a right hemihepatectomy lowers the likelihood of post-hepatectomy liver failure.		8	2			80%	X
24	regardless of future liver remnant function/volume, a portal vein embolization prior to a left hemihepatectomy lowers the likelihood of post-hepatectomy liver failure.		2	3	5		20%	
25	If a portal vein embolization is required, you can actually consider the patient as borderline resectable.		2	2	7		20%	
26	I prefer not to operate on a patients over 85 years old (with ECOG performance status one or two).		6	2	1		60%	
27	If a patient has had preoperative cholangitis, I optimize the drainage and continue the antibiotics until the surgery.	1	7		2		80%	X
28	If a patient has had preoperative cholangitis, I optimize drainage, start antibiotics and wait 5–10 days before surgery.	2	8				100%	X

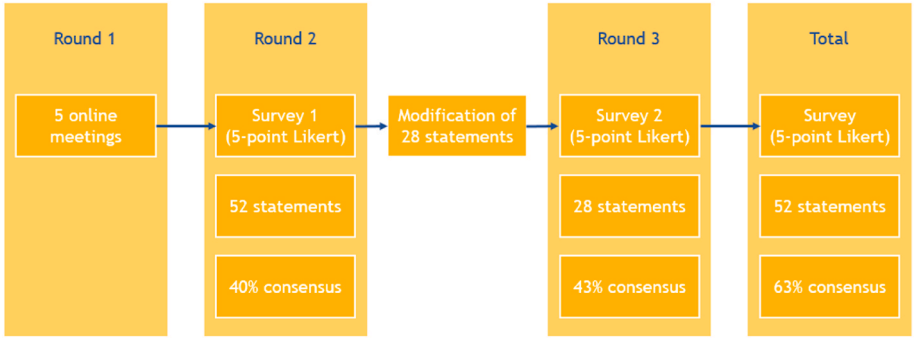

Fig. 1. Flow diagram of the modified Delphi study.

liver, and thus larger, resections [39]. A direct comparison is however not made.

This study needs to be seen in the light of some limitations. Although we included surgeons from all tertiary centers operating on patients with pCCA and these surgeons are the surgeons performing the majority of resections for pCCA in the Netherlands, only thirteen surgeons participated. In addition, the use of the 5-point Likert scale results in some difficulties of the interpretation. There is a neutral option, which give participants the option not to choose. In two statements this was the most used option. In addition, this study stated a 60–79% agreement, as moderate consensus. However, most of these statements are based on experience instead of evidence, which leaves room for future studies; e.g., studies towards standardized lymph node dissections, studies towards preoperative (systemic) therapy, the need for improved drainage procedures and studies comparing volume and function of the remnant liver.

In addition, for the analysis, agree and strongly agree were analyzed as one, although some critics may suggest that a strong opinion should have more impact. There may also be some unavoidable internal inconsistencies, for instance: Only 50% agreement was reached on the proposed criteria for arterial involvement but 90% of the surgeons agreed on pragmatically dividing patients into three categories. Interestingly in the proposed resectability classification a statement about arterial involvement of 0–90° was included and supported by a consensus. Most importantly, we found consensus on our most important statement, a subclassification of resectability. A clear secondary goal was however in mind: determining those patients that have a low or high chance of unresectability during exploration. The high risk patients have a chance of 30–50% of having a negative laparotomy. This is a strong argument for neoadjuvant treatment of this group for several reasons. First, those who do not undergo resection will have no delay in palliative treatment (chemo and drainage) and this may strongly influence outcomes in this group. (Lamarca chemo bij icterus en de paper van Olthof waar 30% dood is na 90 dagen als geen resectie plaatsvindt). Second we may induce resectability by response to therapy and or select patients with favorable biology and perhaps consider more extensive resections (i.e. arterial reconstructions) when needed. Third many (30–50%) patients will decline adjuvant therapy after surgery, so giving it before also conveys this potential benefit to the resectable patients. There is a significant role of the MDT meeting to discuss and classify these patients accordingly and perhaps consider upfront "explorable" a more appropriate term than resectable, because for most patients the latter is ultimately determined intraoperatively.

In order to widely implement this classification, this study should probably be repeated and validated internationally and should be refined during application in clinical trials. Therefore, we are currently preparing a world-wide consensus DELPHI meeting and we would like to encourage the reader to comment on this article and fill in the attached survey (https://www.surveymonkey.com/r/ZXCRGWW).

In conclusion, we were able to define the terms resectable, unresectable, and borderline resectable. This has led to a new practical and applicable resectabilty or perhaps better formulated as "explorability" classification to identify patients for use in future neoadjuvant or induction (chemo)therapy studies.

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Disclosure statement

There are no conflicts of interest to declare.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article.

Ethical approval

No ethical approval was obtained. This study does not include patient related data. Only surgeons participated in this Delphi study.

CRediT authorship contribution statement

Lynn E. Nooijen: Conceptualization, Data curation, Investigation, Formal analysis, Writing – original draft, Visualization. **Marieke T. de Boer:** Data curation, Writing – review & editing. **Andries E. Braat:** Data curation, Writing – review & editing. **Maxime Dewulf:** Data curation, Writing – review & editing. **Marcel den Dulk:** Data curation, Writing – review & editing. **Jeroen Hagendoorn:** Writing – review & editing. **Frederik J.H. Hoogwater:** Data curation, Writing – review & editing. **Hwai-Ding Lam:** Data curation, Writing – review & editing. **Quintus Molenaar:** Data curation, Writing – review & editing. **Ulf Neumann:** Data curation, Writing – review & editing. **Robert J. Porte:** Data curation, Writing – review & editing. **Rutger-Jan Swijnenburg:** Data curation, Writing – review & editing. **Babs Zonderhuis:** Data curation, Writing – review & editing. **Geert Kazemier:** Data curation, Writing – review & editing. **Heinz-josef Klumpen:** Writing – review & editing. **Thomas van Gulik:** Data curation, Writing – review & editing. **Bas Groot Koerkamp:** Data curation, Writing – review & editing. **Joris I. Erdmann:** Writing – original draft, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Lynn Nooijen reports financial support was provided by Amsterdam

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