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Intraoperative pancreatoscopy can improve the detection of skip lesions during surgery for intraductal papillary mucinous neoplasia: A pilot study

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ABSTRACT

Objectives: Intraoperative pancreatoscopy is a promising procedure that might guide surgical resection for suspected main duct (MD) and mixed type (MT) intraductal papillary mucinous neoplasms (IPMNs). The aim of the present study was to assess the diagnostic yield and clinical impact of intraoperative pancreatoscopy in patients operated on for MD and MT-IPMNs.

Methods: This is a retrospective cohort study. Patients undergoing surgery for suspected MD or MT-IPMN underwent intraoperative pancreatoscopy and frozen section analysis. In all patients who required extended resection due to pancreatoscopic findings, we compared the final histology with the results of the intraoperative frozen section analysis.

Results: In total, 46 patients, 48% females, mean age (range) 67 years (45–82 years) underwent intraoperative pancreatoscopy. No mortality or procedure related complications were observed. Pancreatoscopy changed the operative course in 30 patients (65%), leading to extended resections in 20 patients (43%) and to parenchyma sparing procedures in 10 patients (22%). Analyzing the group of patients who underwent extended resections, 7 (35%) displayed lesions that needed further surgical treatment (six high grade dysplasia and one with G1 pancreatic neuroendocrine tumor) and among those 7, just 1 (14%) would have been detected exclusively with histological frozen section analysis of the transection margin. The combination of both pancreatoscopy and frozen section analysis lead to 86% sensitivity and 92% specificity for the detection of pathological tissue in the remnant pancreas.

Conclusion: Intraoperative pancreatoscopy is a safe and feasible procedure and might allow the detection of skip lesions during surgery for suspect MD-involving IPMNs.

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1. Introduction

Pancreatic Cystic Neoplasms (PCNs) are common diseases, with a prevalence up to 49% in the general population. Half of them are represented by intraductal papillary mucinous neoplasms (IPMNs)

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that can harbor a wide spectrum of cellular alterations through the known sequence of adenoma with low grade dysplasia, high grade dysplasia, and cancer [1,2]. Considering their malignant potentiality and their easy detection, IPMNs can be considered the best precursor lesions of pancreatic cancer suitable for early diagnosis and potentially preemptive and curative treatment. Since the dilation of the main pancreatic duct (MPD) is associated with a higher risk of harboring high-grade dysplasia (HGD) or cancer [3–5], the European Evidence Based Guidelines on the Management of Cystic Tumors recommends surgery in every fit patient with main duct IPMN (MD- IPMN) or mixed-type IPMN (MT-IPMN), defined by MPD dilation ≥5 mm [1].

In cases of focal pathological dilation of the MPD, a segmental resection (pancreaticoduodenectomy or distal pancreatectomy) including the affected area is recommended. When the whole MPD is dilated the options are to perform, either a partial pancreatectomy with frozen section analysis of the resection margin or a total pancreatectomy [6]. If the former alternative is chosen, histological analysis is done to exclude the presence of remnant disease and to assess the radicality of surgery [1]. However, this approach assumes that the transection margin is representative of the remnant unresected parenchyma. A meta-analysis of 1488 patients showed no clear relation between the status of the margin at frozen section and the rates of recurrence in the remnant pancreas [7]. In addition, it is known that IPMNs recur in up to 15–22% of operated patients during follow-up [8–10] and that this could be due to the epiphenomenon of undetected skip lesions along the unresected part of the MPD [11–13].

Therefore, many experts prefer to perform a total pancreatectomy, when the whole MPD is dilated but this strategy bears the possible risk for overtreatment [6] and the value of such approach has recently been questioned.

During the past few years, single operator peroral cholangiopancreatoscopy (SOCP) has been described as an accurate method to preoperatively explore the MPD, to map the possible presence of IPMN lesions in its entire length [14]. The main disadvantage is that SOCP is highly technically demanding and it is associated with a significant risk of complications [14–19]. Moreover, it cannot exactly define the limit of surgical resection preoperatively [14]. More recently, the use of intra-operative pancreatoscopy has been proposed as a useful method to “personalize” the resection margins during pancreatic resections for IPMNs in small series of patients [20,21]. However, no data is available about its feasibility and diagnostic yield. The aim of this study is to assess the safety, diagnostic yield and clinical impact of intraoperative pancreatoscopy in patients with MD and MT-IPMN.

2. Methods

2.1. Study design

This is a retrospective, pilot, cohort study of patients referred to Karolinska University Hospital from October 2015 to April 2018. Due to the retrospective nature of the manuscript informed consent was not applicable. The local ethical committee in Stockholm approved the study (EPN 2015/1544–31/4). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

2.2. Patient population

Consecutive patients undergoing surgery for suspect main duct involving IPMN defined according to the European Guidelines, were included [22]. A main pancreatic duct (MPD) ≥ 6 mm and age ≥18 years were considered necessary prerequisites for intraoperative pancreatoscopy.

All patients were discussed in a multidisciplinary conference before surgery. Radiology images were reviewed by an expert radiologist who specifically evaluated the preoperative extent of MPD dilatation. This information has been compared with the length of the inspected MPD during pancreatoscopy, to assess the complete or incomplete evaluation of the MPD in the remnant pancreas.

2.3. Technical description of intraoperative pancreatoscopy

A pancreas surgeon divided the pancreas and sent the analysis of the frozen section at the level of transection margin. Intraoperative pancreatoscopy was prepared and before inserting the pancreatoscope through the open main pancreatic duct, the pancreatoscope was tested for functioning. Both endoscopist and a surgeon were surgically dressed to keep the instrument sterile during the entire procedure. To enable a clear view during the inspection we irrigated the main pancreatic duct with sterile saline, that was delivered by a standard endoscopic irrigation pump. We set the pump to a minimum injection-pressure to avoid potential barotrauma on the secondary branch ducts. The entire pancreatoscopy prolonged the surgical time by 5–10 min. Inspection was performed using a 4 handed technique with one operator advancing or retracting the pancreatoscope, and the other focusing in keeping an optimal view, and inspecting the duct for possible lesions.

2.4. Surgical management strategy

Fig. 1 and its legend explain the intraoperative strategy in standard Whipple operations (Panel A), and in intraoperative pancreatoscopy-guided surgery (Panel B and C).

In case of suspected skip lesions, surgeons and the endoscopist discussed the possibility of performing an extended resection, taken into consideration the pancreatoscopic findings, result of frozen section analysis and patient characteristics such as life expectancy and comorbidities. The length of the extended resection margin was always guided by pancreatoscopy and the final histology of the extended resection specimen was compared with the intraoperative frozen section analysis (Fig. 1 Panel B and C).

Postoperative outcome and histology were prospectively recorded in our institutional database. Complications were recorded according to the Clavien-Dindo classification [23] and the postoperative pancreatic fistula was classified according to the International Study Group in Pancreatic Surgery (ISGPS) classification [24].

Pancreatoscopic findings were standardly described by endoscopists as follow (Fig. 2):

- Length of inspected MPD
- Presence/absence of intraductal mucus
- Dilated duct with normal or pathological appearance

In case of pathological appearance, the operator specifically assessed the following features:

- Presence/absence of finger-like lesions
- Pathological vessels (curly vessels, signs of neovascularization)
- Aspecific nodular-inflammatory pattern

2.5. Statistics

Descriptive statistics were used to summarize patients’

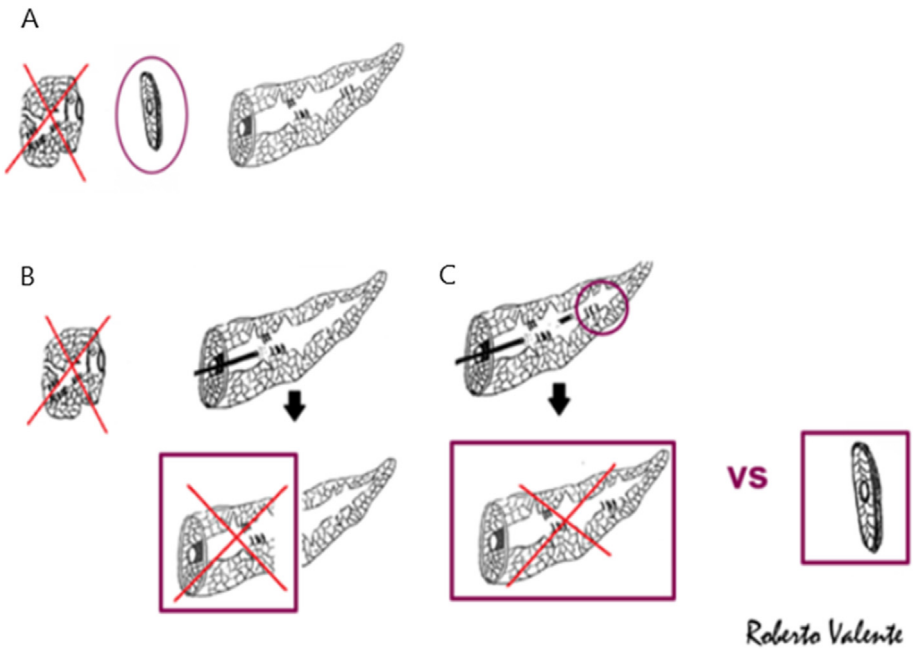

Fig. 1. Panel A shows the standard intraoperative strategy, which is based on the analysis of the frozen section. The red cross outlines the resected specimen. Panel B and C show the possible impact of the intraoperative pancreatoscopy in the detection of skip lesions. In Panel B skip lesions are close to the resection line, therefore operators decided to further extend the resection a few centimeters. In Panel C skip lesions are detected throughout the entire length of the remnant main pancreatic duct, leading to total pancreatectomy. The specimen from extended resection (B and C) was then analyzed and compared to intraoperative frozen section analysis to assess the diagnostic yield. Intraoperative pancreatoscopy was performed using a 4 handed technique by an endoscopist and a surgeon.

characteristics. In the sub-class analysis of operated patients, we present sensitivity, specificity, negative predictive value, and positive predictive value with 95% Confidence intervals of each evaluated endoscopic feature as well as for frozen section analysis and operator assessment. Dedicated software (Medcalc 12.1, Belgium) was used.

3. Results

Overall, 46 patients, 22 females (47.8%), were included in the study. The mean age was 67.3 years (range 45–82 years). Pancreaticoduodenectomy was performed in 28 patients (60.8%), total pancreatectomy in 14 (30.4%) and distal pancreatectomy in 4 (8.6%). The mean hospital stay was 18 days (14–21 95% CI). Pancreatoscopy was able to explore the entire dilated duct in 43 cases (93.4%) and the mean length of inspected duct was 7.5 cm (6.7–8.4, 95% CI). Fifteen patients (32.6%) developed post-operative complications but none of those were related to pancreatoscopy. We observed no perioperative mortality (0%) and no cases of fistula grade B and C (0%). One patient (2.1%) was re-operated on because of an incisional hernia, and 3 (6.3%) experienced postoperative bleeding. Among them 1 (2.6%) was managed with re-operation, 1 (2.6%) was managed endoscopically and another (2.6%) was conservatively managed. Overall, 5 patients (10.8%) experienced post-operative complications $\geq$ grade 3 in the Clavien-Dindo Classification, Table 1.

During intraoperative pancreatoscopy, mucus was found in 12 patients (26.0%), pathological vessels in 11 (23.9%), exophytic growth in 19 (41.3%) and finger like projections in 12 (26.0%). The operator final assessment regarding the presence/absence of suspect IPMN in the remnant pancreas led to a positive answer in 16 (34.7%) of patients, Table 1. Thirty patients (65.2%) experienced a change in the operating plan, either because 20 patients underwent an extended resection (43.4%) or because the operating plan was turned into a more conservative approach in 10 patients (21.7%). The latter group, were preoperatively planned for a total pancreatectomy, but were intraoperatively converted into a segmental resection. In fact, these patients displayed no signs of IPMN in the remnant pancreas. The diagnostic yield of different pancreatoscopic findings is described in Table 2.

Among the 20 patients (43.4%) who had undergone extended resections, the specimen of extended resection displayed LGD in 11 (55%), HGD in 6 (30%), chronic pancreatitis in 2 (10%), G1 pancreatic neuroendocrine tumor (PNET) in 1 (5%) and cancer in 0 (0%). Therefore, analyzing the group of patients who have undergone extended resections, 7 (35%) displayed lesions that needed further surgical treatment (six high grade dysplasia and one G1 PNET) and among those 7, only 1 (14.2%) would have been detected exclusively with histological frozen section analysis of the transection margin. In 4 patients (25%), it significantly impacted the oncological radicality, allowing the removal of undetected HGD/NET skip lesions in patients that otherwise displayed no cancer on the main resected specimen (Table 3).

The combination of operator assessment during intraoperative pancreatoscopy and frozen section provided the highest score in sensitivity and specificity, 85.7%, 95% CI (42.1–99.6) and 92.3%, 95% CI (63.9–99.8), respectively with overall best diagnostic precision.

After a mean 34.7 (range 32.3–37.0) months of follow-up, 10 out of 46 patients (21.7%) died because of cancer recurrence. Three patients (6.5%) with verified pancreatic cancer displayed peritoneal carcinomatosis during follow-up. Among them, 1 displayed local recurrence and peritoneal carcinomatosis and died 13 months after the operation, 1 displayed mesenteric carcinomatosis and was still alive at 36 months follow-up, and one who had confirmed M1 disease at final histology developed liver and mesenteric metastasis and died 7 months after surgery. Two further patients developed peritoneal carcinomatosis from other cancers (histologically verified metastasis from cardias and uterine cancer).

Evaluating the yield of intraoperative pancreatoscopy, histology of the extended resection specimen confirmed the presence of IPMN lesions in 15 patients (93.7%), Fig. 4.

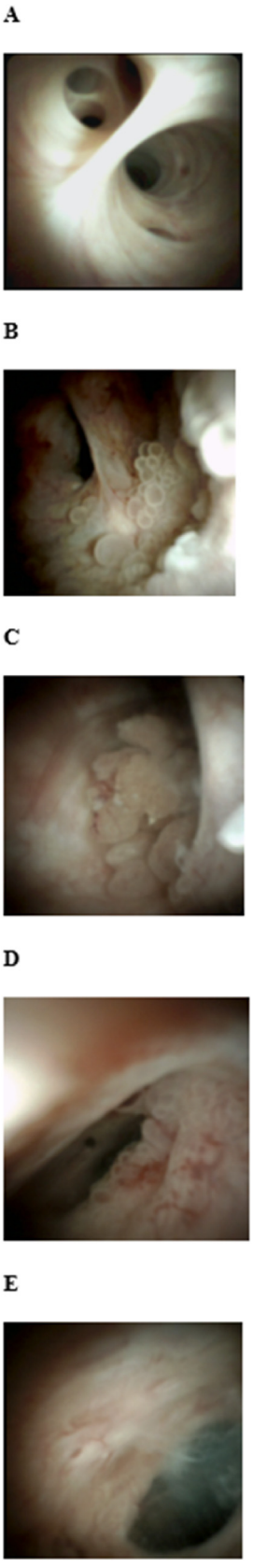

Fig. 2. Overview of the different pancreatoscopic findings (A = normal duct; B = "finger like" pattern; C = aspecific nodular changes; D = neovascularization; E = intraductal mucus).

Table 1
Summary of patient characteristics. Categorical variables are presented as counts and relative percentages, n (%) and continuous variables as mean and range, mean (range).

Categorical variables	N (%)
Total patients	46 (100%)
Sex (female)	22 (47.8%)
ASA1	4 (8.6%)
ASA2	18 (39.1%)
ASA3	21 (45.6%)
ASA4	3 (6.5%)
Pancreaticoduodenectomy	28 (60.8%)
Total pancreatectomy	14 (30.4%)
Distal pancreatectomy plus splenectomy	4 (8.6%)
Continuous variables	**Mean (Range)**
Age (years)	67.3 (45–82)
Hospital stay (days)	18 [14–21]
Length of dilated duct (cm)	7.5 (6.7–8.4)

4. Discussion

In the last two decades, the incidence of patients affected by IPMNs has increased. Considering the high prevalence of this disease, further knowledge is demanded to achieve a better diagnostic yield and to improve overall management.

If on preoperative imaging there is no suspicion for IPMN extension throughout the entire length of the MPD, guidelines recommend a partial pancreatic resection with intra-operative frozen section analysis [1,23]. However, this approach relies on the assumption of the transection margin being representative of the entire remnant parenchyma.

The preoperative work-up has a low diagnostic yield in assessing the extent of MPD involvement [24] and intraoperative assessment of the exact extent of IPMN extension into the MPD can be extremely challenging. Therefore, to avoid possible undertreatment many centers prefer to perform total pancreatectomy, with potential risk of overtreatment.

Scholten et al. performed a survey involving 97 experts in IPMNs from all over the world and asked whether in cases of dilation of the entire MPD >5 mm would they have chosen a conservative or an interventional approach. Overall, 41% of participants advised nonoperative surveillance, whereas the majority (59%) favored intervention. Of those who advised surgery, 46% chose to perform a total pancreatectomy while 31% would have advised a partial resection and continued follow-up of the remnant pancreas [6]. The reason of such debate is related to two main issues; first, the low preoperative accuracy of radiology in the preoperative assessment of pancreatic cystic neoplasms [24], and secondly, the possibility that MPD dilatation might be related to an upstream extension of the disease or to upstream chronic pancreatitis due to mucus or stricture [1,24,25].

The value of the intraoperative frozen section analysis to define the limit of the pancreas transection and to avoid recurrence in the remnant is highly debated. Bhardwaj et al. reported in a meta-analysis on 1488 patients who underwent resection for IPMN, with 263 recurrences (18%), of which 198 (75%) had a negative resection margin. No statistically significant relationship was shown between the status of the resection margin and risk for recurrence [7]. In our opinion, at least part of such a discrepancy might be explained by an inadequate visualization of skip-lesions in the remnant MPD.

Single operator cholangiopancreatoscopy (SOCP) has developed as a tool to investigate both the biliary and the pancreatic duct in pre-malignant lesions and chronic inflammatory conditions harboring risk for cancer [26–28]. Optical digital resolution has allowed better visualization of intraductal lesions and improved

Table 2
Intraoperative pancreatoscopy findings, diagnostic yield of the different pancreatoscopic findings, and operative outcomes.

Pancreatoscopy findings	Prevalence of macroscopic lesions %
- Finger like projections	12 (26%)
- Exophytic growth	19 (41.3%)
- Pathological vessels	11 (23.9%)
- Mucus	12 (26%)
Final assessment of possible remnant IPMNs	17 (36.9%)
Pancreatoscopy findings	**Diagnostic yield % (95% CI)**
Finger like projections	Sensitivity 42.8% (9.8–81.5)
	Specificity 46.1% (19.2–74.8)
	PPV 30.0% (13.7–53.6)
	NPV 60.0% (38.5–78.1)
Intraductal Exophytic growth	Sensitivity 57.1% (18.4–90.1)
	Specificity 30.7% (9.0–61.4)
	PPV 30.7% (17.5–48.1)
	NPV 57.1% (29.0–81.2)
Pathological vessels	Sensitivity 42.9% (9.8–81.5)
	Specificity 53.8% (25.1–80.7)
	PPV 33.3% (15.0–58.5)
	NPV 63.6% (43.6–79.8)
Mucus	Sensitivity 57.1% (18.4–90.1)
	Specificity 69.2% (38.5–90.9)
	PPV 50.0% (26.1–73.8)
	NPV 75.0% (54.2–88.3)
Operator assessment	Sensitivity 85.7% (42.1–99.6)
	Specificity 23.0% (5.0–53.8)
	PPV 37.5% (28.1–47.8)
	NPV 75.0% (27.4–95.9)
Frozen Section	Sensitivity 28.5% (3.6–70.9)
	Specificity 92.3% (63.9–99.8)
	PPV 66.6% (17.8–94.8)
	NPV 70.6% (59.4–79.7)
Pancreatoscopy related complications	0 (0%)
Peroperative mortality	0 (0%)
Reoperation (incisional hernia)	1 (2.1%)
Fistula B or C	0 (%)
Bleeding (1 reoperation, 1 endoscopic managed,1 conservative managed)	3 (6.3%)
Clavien Dindo≥3	5 (10.8%)
Technical success	43 (93.4%)
Adverse events:	21 (45.6%)
Ascites	2 (4.3%)
Lung embolism	6 (13.0%)
Cardiovascular	3 (6.5%)
Cerebrovascular	2 (4.3%)
Infections	10 (21.7)
Others	6 (13.0%)
Changing of operating course	30 (65.2%)
Extended resection	20 (43.4%)
Spared parenchyma	10 (21.7%)
Extension of PD margins	7 (15.2%)
Completing total pancreatectomy	12 (26%)
Completing distal pancreatectomy	1 (2.1%)
Pancreatoscopic biopsies	19 (41.3%)

biopsy targeting, possibly changing the operative strategy [29]. To date, most of the studies on SOCP have been performed in the biliary duct. The main reason is that single operator peroral pancreatoscopy still suffers from a relative high risk for postoperative complications, and is technically demanding as shown in Fig. 3 [14–19].

To overcome the technical demands and the risk of complications, some authors have suggested the application of intraoperative pancreatoscopy. Such approach is easier to perform (direct visual guidance from the operator during surgery). It is also probably associated with a lower risk of post procedural pancreatitis. In fact, a dilated and transected MPD is subjected to less barotrauma during pancreatoscopy. Finally, an intraoperative approach might avoid the risk of post-ERCP acute pancreatitis related to difficult cannulation and sphincterotomy of intact native papilla [30,31]. The current study confirms the safety and feasibility of intra-operative pancreatoscopy that has been previously suggested in smaller series [20,21].

In this study, overall, 65.2% of patients had a change in operative strategy due to the application of intraoperative pancreatoscopy. In our series, the advantage of such a strategy was not only confined to the detection of suspected skip lesions (43.4%). Additionally, 21.7% of patients that had been scheduled for a total pancreatectomy based on preoperative evaluation instead received an organ sparing surgery due to the absence of skip lesions in the remnant pancreatic parenchyma on intraoperative pancreatoscopy. Overall, the operator assessment of the remnant duct by intraoperative pancreatoscopy was found to have a higher sensitivity than frozen section analysis in defining the resection margins, with lower specificity.

Noteworthy, we have performed a total of 14 pancreatectomies; however, we excluded one patient from the diagnostic yield analysis due to incomplete data on the histology, and the absence of any disease found during intraoperative pancreatoscopy. We have included this patient in the general description (Table 1) because

Table 3
Comparison between the results of frozen section analysis and the final histology. Variables are expressed as absolute numbers and relative percentages, n (%). Clinically relevant changes is defined as the detection and treatment of HGD/cancer through extended resection only in those patients who displayed a negative frozen section (which would have missed the skip lesion) and did not have cancer in the main resected specimen (which could have had a significant impact on prognosis).

Patients with extended resection	20
Frozen section	LGD 17 (85%) HGD 2 (10%) Cancer 0 (0%) Benign 1 (5%)
Final histology on extended resection	LGD 11 (55%) HGD 6 (30%) pNET 1 (5%) Cancer 0 (0%) Benign 2 (10%)
Final histology on the main resected specimen	LGD 6 (30%) NET 1 (5%) HGD 4 (20%) Cancer 9 (45%)
Undetected HGD by frozen section	6 (30%)
Clinically relevant changes (no cancer in the main resected specimen and no detection at the frozen section)	4 (20%)

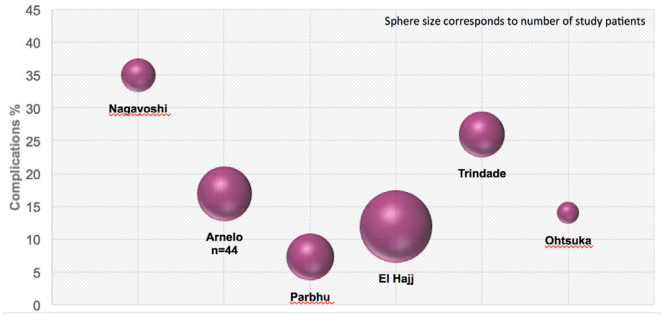

Fig. 3. Summarizes sample sizes and complication rates reported in the main series published to date on single operator peroral pancreatoscopy [14–19].

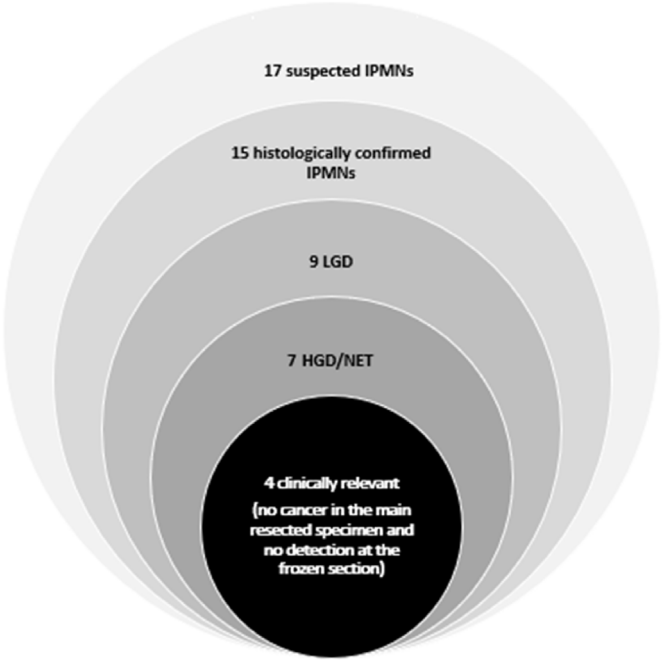

Fig. 4. Summarizes the diagnostic yield of on single operator peroral pancreatoscopy.

the total pancreatectomy following intraoperative pancreatoscopy could provide additional information for the primary endpoint analysis (feasibility and safety of intraoperative pancreatoscopy), but not for the secondary endpoint (assessment of diagnostic yield).

Although the endoscopist did not have any direct suspicion of intraductal papillary mucinous neoplasm (IPMN) in three patients, we discovered other findings that could indicate pathology. One patient had pathological vessels, another had nodular lesions, and the third had a combination of both.

During a mean 34.7 months follow-up, we reported 3 patients (6.5%) with peritoneal carcinomatosis from metastatic spread of pancreatic cancer. The risk of seeding the peritoneum during intraoperative pancreatoscopy has never been investigated. Two out of the 3 patients displayed peritoneal carcinomatosis in the setting of additional metastatic disease, with either local recurrence or liver metastasis. Additionally, 1 of these patients had a non-radical resection (M1 disease) on final surgical pathology. There was just 1 patient (2.1%) who displayed peritoneal carcinomatosis as an exclusive site of recurrence. This rate is close to what is reported for other endoscopic procedures, such as endoscopic ultrasound with fine needle aspiration (2.3%), which has been shown to have no statistically significant increased risk when compared to non-invasive endoscopy [32]. We did not identify pancreatic cancer in any of the remnant tissue that was explored endoscopically and thus it is very unlikely that the carcinomatosis could have been caused by seeding during the main pancreatic duct exploration. Therefore, although we cannot completely exclude the possibility of an intraoperative seeding during our procedure and further studies are needed to assess and quantify such risk, it is more likely peritoneal metastasis in our series was the epiphenomenon of disease spread rather than the result of an intraoperative seeding.

The current study displays some limitations. First, this is a retrospective study, has no control group, and includes a relatively small sample size. Another limitation is that the assessment of macroscopic findings in MPD during pancreatoscopy still deserves further evidence and standardization. It is particularly challenging to assess the degree of dysplasia, which remains matter of debate. The utility of endoscopic MPD biopsies and eventually their evaluation at intraoperative frozen section analysis was beyond the scope of the study.

We were unable to perform frozen section analysis on the pancreatoscopy guided biopsies due to their small size, and

therefore we did not consider the diagnostic yield of the pancreatoscopy guided biopsies itself as one of the endpoints of the study. Instead, our aim was to identify features that could alter the surgical management during the operation. Since we could not obtain quick frozen section results for the pancreatoscopy guided biopsies, we decided not to analyze such data.

Moreover, the current study has not evaluated the use of intra operative pancreatoscopy as part of a multimodal endoscopic work-up. In fact, in selected cases, EUS and CH-EUS with or without through the needle biopsy can increase the diagnostic accuracy of mural nodules, at the cost of a low rate of possible adverse events [33,34].

While we acknowledge that the finding of cancer in the resected specimen may drive the prognosis more than HGD, we want to emphasize that our focus was on identifying potential clinically relevant changes in the detection of HGD and cancer during intraoperative pancreatoscopy. Furthermore, we were uncertain about the final diagnosis of cancer in the intraoperative setting. Therefore, we decided to prioritize the detection of HGD and cancer during intraoperative pancreatoscopy as these findings could lead to a change in surgical management and improve patient outcomes.

Cancer was found in a higher proportion of resected specimens, with 23 patients (50%) displaying IPMN cancer. Due to the nature of our small series, we focused more on sensitivity than specificity. Specifically, we aimed to evaluate how many undiagnosed lesions were eventually detected through the application of intraoperative pancreatoscopy. While we acknowledge that some cases of cancer may have developed from undiagnosed HGD or cancer in the spared parenchyma, the fact that we observed a lower rate of cancer recurrence compared to the rate of cancer found in the primary resected specimen is somewhat encouraging in terms of achieving better radicality through the use of intraoperative pancreatoscopy. However, further evidence is needed to confirm these findings.

On the other hand, the present study also has several strengths. This is the largest series of intra-operative pancreatoscopy examinations performed during pancreatic surgery for IPMN. The current study is focused on safety and reproducibility of the method. It is also the first series analyzing the diagnostic yield of macroscopic findings on pancreatoscopy with histological confirmed specimens. The reporting of endoscopic findings was standardized in all procedures. Such consistency has allowed easy comparison of results for the assessment of the diagnostic yield, despite the retrospective setting. A final strength, is the innovative character of the proposed technique, that can be summarized as follows:

1) It allows precise localization of skip lesions and makes the extent of resection personalized.
2) It requires less endoscopic technical skills and after short training, can be employed by the surgeons on-site.
3) It allows for a clinically relevant operative change in planned surgery.
4) It possibly avoids endoscopic related complications (i.e. acute pancreatitis, duodenal perforation, bleeding) since it does not require either cannulation nor sphincterotomy of the papilla of Vater [14].

Of course, with the current study we cannot suggest a replacement of frozen section analysis, with intraoperative pancreatoscopy. On the contrary, we do think that frozen section analysis still represents the standard of care. Intraoperative pancreatoscopy represents an additional and complementary tool that might improve the diagnostic precision and guide surgeons towards a more tailored resection. In fact, pancreatoscopy suffers from a low specificity, that is compensated by the higher specificity of frozen section analysis. On the other hand, frozen section analysis suffers from low sensitivity, that might be increased using intraoperative pancreatoscopy. Further, larger and hopefully multicenter studies, are needed to confirm our results and to drive personalization and accurate pancreatic surgery for IPMNs.

Intra operative pancreatoscopy seems to be a feasible, safe and effective tool to personalize transection margins during surgery for MT/MD IPMNs. In addition to intra-operative frozen section analysis intraoperative pancreatoscopy increases the diagnostic precision of detecting skip lesions in the MPD. Intraoperative pancreatoscopy might also allow the sparing of unaffected parenchyma in cases of secondary dilatation of the MPD. Prospective studies, including a larger number of patients, are recommended to validate this method, to confirm its safety and to better understand the relevance and histological correlation of the visual findings with grade of dysplasia.

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Authors contributions

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Declaration of competing interest

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