

ORIGINAL ARTICLE

# Staging laparoscopy to detect occult metastases in localized pancreatic cancer: global survey among nine international societies

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## Abstract

**Background:** Staging laparoscopy (SL) is performed to detect occult metastases in patients with localized pancreatic cancer. However, current guideline recommendations vary widely on routinely performing SL. This global survey investigated use and indications of SL.

**Methods:** An online survey was sent to members of nine international societies and working groups. Information was obtained about SL use, indications SL and adjunct diagnostic modalities across four clinical scenarios.

**Results:** Among 617 responding surgeons (76 countries, six continents), 82% used SL which varied between regions (Americas 90%, Asia 85%, Oceania 81%, Europe 76%, Africa 59%;  $P < 0.050$ ). Most perform SL during the same session as the scheduled laparotomy (63–79%). A SL was mainly performed at the time of upfront surgery (71%), after (60%) or before (37%) neoadjuvant/induction therapy, and before radiotherapy (31%). SL was mainly performed in selected patients, either based on indeterminate/suspicious lesions on cross-sectional imaging (78–87%), resectability status (54–64%), and/or elevated CA19-9 level (60–69%). Most common used adjuncts were cytological lavage (37–55%) and intra-abdominal liver ultrasonography (36–50%).

**Conclusion:** Despite considerable global variability, SL is widely used to detect occult metastases in pancreatic cancer, mainly in high-risk patients and often during the scheduled laparotomy. The

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observed variability highlights the need for more evidence leading to stronger guideline recommendations.

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## Introduction

Pancreatic adenocarcinoma (hereafter: *pancreatic cancer*) is an aggressive disease with a poor prognosis,<sup>1,2</sup> illustrated by the ~57 % rate of metastases rate at diagnosis.<sup>3,4</sup> Advances in cross-sectional imaging over recent decades have enhanced the detection of small metastases.<sup>5,6</sup> However, millimetric metastases are often missed, leading to inaccurate staging and treatment decision-making. Consequently, at least 6–10 % of patients are diagnosed with radiologically occult metastases during surgery intended for resection.<sup>7–9</sup>

Staging laparoscopy (SL) may detect occult metastases, thereby guiding the treatment decision-making, such as the intent of chemotherapy (i.e., palliative vs. neoadjuvant/induction therapy), optimizing patient selection for radiotherapy, and avoiding non-therapeutic laparotomy. The National Comprehensive Cancer Network (NCCN) guidelines currently mention that SL can be considered, particularly when the risk for radiologically occult metastases is high (e.g., larger tumors, pancreatic body/tail tumors, elevated tumor markers).<sup>10,11</sup> This conditional recommendation reflects the limited evidence,<sup>12–14</sup> likely contributing to global variation in SL use and indications. However, comprehensive data on the global SL practices are currently lacking.

Therefore, this international survey study aimed to investigate the use and indications of SL among pancreatic surgeons, facilitating the design of future prospective studies and support future guidelines.

## Methods

### Study population and design

An online survey was created through Survey Monkey (Survey-Monkey Inc., San Mateo, California, USA)<sup>15</sup> and sent in March 2024 to the members from the following associations and study groups related to pancreatic surgery: International Hepato-Pancreato-Biliary Association (IHPBA), European-African Hepato-Pancreato-Biliary Association (E-AHPBA), Asian

Pacific Hepato-Pancreato-Biliary Association (A-PHPBA), Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHPBS), European Pancreas Club (EPC), Pancreas Club, European Consortium on Minimally Invasive Pancreatic Surgery (E-MIPS), European Society of Surgical Oncology (ESSO), and the International Collaboration on Advanced Pancreatic Cancer. Eligibility was restricted to surgeons who had performed pancreatic cancer surgery within the preceding 12 months. Only respondents who answered the question whether they performed SL (i.e., always, in selected patients, never) were included.

### Questionnaire

The survey consists of seven sections. First, the diagnostic work-up excluding metastatic disease based on cross-sectional imaging was questioned, including the use of different imaging modalities, tumor markers, and the use of SL. In addition, information was collected about the minimal required yield of SL that would justify its use, protocolized use of SL in their center, and the optimal timing of SL. Second, if respondents performed SL in all or in selected patients with localized pancreatic adenocarcinoma at any moment in time, procedural information was collected (e.g., procedure time, assessed abdominal areas). Third, the use and indications of SL for the following four clinical scenarios were investigated:

- (1) SL prior to upfront surgery
- (2) SL after neoadjuvant/induction therapy, but prior to surgery
- (3) SL before neoadjuvant/induction chemotherapy
- (4) SL after neoadjuvant/induction chemotherapy, but prior to radiotherapy

For each of these four scenarios, it was queried whether SL is performed in all patients, selected patients, or never. Fourth, in case SL was performed in selected patients, further information was requested about the specific indications, which can be divided into **anatomical** (i.e., tumor size, tumor location, resectability status, indeterminate findings on cross-sectional

imaging), **biological** (i.e., serum tumor markers carbohydrate antigen 19-9 [CA19-9], carcinoembryonic antigen [CEA], cancer antigen 125 [CA-125], DUPAN-2, circulating tumor DNA, and other[s]), and **conditional** (i.e., patient's performance status) parameters. Fifth, information about the use and indications of additional diagnostic modalities used during SL were investigated, including cytological lavage, indocyanine green fluorescence, and intra-abdominal ultrasonography of the liver and to assess vascular involvement from the primary tumor. Sixth, respondents who never performed an SL were asked to specify their reason(s). Seventh, all respondents were asked if and how SL should be incorporated in clinical trials. The data from all questions from the survey are presented.

### Definitions

The respondents were instructed that the survey applied to their current clinical practice and focused on patients diagnosed with localized pancreatic ductal adenocarcinoma, defined as the suspicion of pancreatic cancer on cross-sectional radiological imaging (eventually pathology-proven) without any signs of extra-regional lymphadenopathy or distant metastases on imaging. The term 'localized pancreatic cancer' used in this survey refers to primary resectable, borderline resectable, and locally advanced pancreatic cancer. SL was defined as a laparoscopic procedure primarily aimed at detecting occult metastases. This may include a diagnostic intraoperative ultrasound. Some synonyms have been used in the literature (e.g., diagnostic laparoscopy), but here the term 'staging laparoscopy' was used for its simplicity and consistency. SL prior to surgical exploration can be performed either in the same procedure of the exploratory laparotomy with intent to resect (i.e., at the start), but also earlier as a standalone procedure in the diagnostic work-up. To prevent confusion and issues with terminology, laparoscopy with intention for minimally invasive resection were not considered as 'staging laparoscopy'.

### Statistical analyses

The percentage of respondents using SL per clinical scenario 1–3 is calculated with the assumption that each respondent has patients in their current clinical practice undergoing upfront surgery (**scenario 1**), starting with neoadjuvant or induction chemotherapy (**scenario 2**), and surgery following neoadjuvant or induction chemotherapy (**scenario 3**). Data analyses were performed with IBM SPSS for Windows, version 28 (IBM Corp., Orchard Road Armonk, NY). Continuous variables are presented as medians with interquartile ranges (IQR). Categorical variables are presented as frequencies with percentages and analysed using the Pearson's chi-square test. Statistical significance was considered as a two-tailed *P* value of <0.050.

## Results

Overall, 617 surgeons from 76 countries on six continents responded to the online survey and met the eligibility criteria.

Most of the respondents originated from Europe (37 %), followed by Asia (32 %) and North America (20 %). The total number of invited surgeons is unknown due to membership confidentiality and overlapping memberships among societies and working groups. See Fig. 1 and Appendix 1 for an overview of the respondents per country. Among the respondents, hepato-pancreato-biliary surgery was the most common current field of expertise (65 %). Most surgeons worked in an academic center (65 %). See Table 1 for further details about the respondents' expertise and clinical practice.

### Staging strategies to exclude metastatic disease

Multiphase contrast enhanced computed tomography (CT) was the most common routinely used imaging modality to exclude metastases in patients with suspected localized pancreatic adenocarcinoma (96 %), followed by liver-specific magnetic resonance imaging (MRI) (40 %) and positron emission tomography (PET) (32 %). Multiple imaging modalities were routinely used by 49 % of respondents. Some 19 % of respondents used MRI-liver in >95 % of their patients. Serum tumor markers were routinely used to assess the risk of metastatic disease by 98 % of respondents, predominantly serum CA19-9 (98 %), CEA (65 %) and/or DUPAN-2 (16 %). Two-thirds (67 %) of respondents used multiple serum tumor markers. See Appendix 2 for the staging modalities.

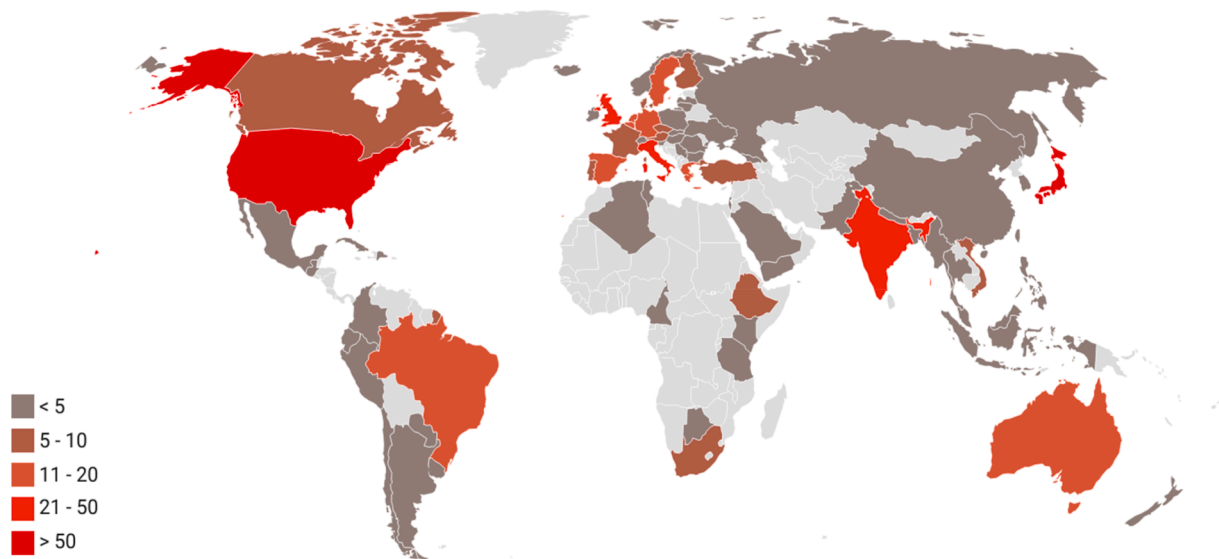
### Staging laparoscopy

An SL was used by 506 respondents (82 %), either in all or in selected patients, whereas 111 respondents (18 %) never performed an SL. See Appendix 3 for further information about the SL duration and inspected areas.

### Timing

In the setting of surgical exploration with intention for resection of pancreatic cancer, SL was performed by 436 respondents (71 %; missing *n* = 14) in case of upfront surgery (**scenario 1**) and 369 respondents (60 %; missing *n* = 64) in case of surgery following neoadjuvant/induction chemotherapy with or without radiotherapy (**scenario 2**). In the setting of upfront surgery (**scenario 1**), SL was performed as a separate procedure from the scheduled laparotomy in 21 % (*n* = 23) and in the same surgical session as the intended laparotomy in 79 % (*n* = 88) of respondents (missing *n* = 1). In the setting of surgery following neoadjuvant/induction therapy (**scenario 2**), SL was performed as a separate procedure from scheduled laparotomy in 34 % (*n* = 110) and in the same surgical session as the intended laparotomy in 63 % (*n* = 205) of respondents (missing *n* = 9).

In patients scheduled for neoadjuvant or induction therapy, 229 respondents (37 %; missing *n* = 110) performed SL before the start of chemotherapy (**scenario 3**). Among the 300 respondents performing SL and having patients in their clinical practice treated with neoadjuvant or induction chemotherapy combined with radiotherapy, a minority of 94 respondents



**Figure 1** Global distribution of respondents. Absolute number of respondents per country. See [Appendix 1](#) for further details on the respondents per country

(31 %) conducted SL after chemotherapy but before radiotherapy (**scenario 4**).

### Indications

See [Table 2](#) for the use, timing, and A-B-C indications of SL per scenario. For each of the four clinical scenarios in which SL could be performed, SL was mostly conducted in selected patients only (**scenario 1**:  $n = 324/436$  [74 %]; **scenario 2**:  $n = 248/369$  [67 %]; **scenario 3**:  $n = 154/229$  [67 %]; **scenario 4**:  $n = 72/94$  [77 %]). Indications for SL were consistent for each clinical scenario. Intra-abdominal indeterminate or suspicious findings on cross-sectional imaging (ranging from 78 % to 87 %) and resectability status (ranging from 54 % to 64 %) were the main anatomy-based indications to perform SL. The levels of serum CA19-9 were the leading biology-based indicator to selectively perform SL, ranging from 61 % to 69 %).

### Additional modalities during SL

[Table 3](#) summarizes the use of additional modalities during SL, which ranged from 68 % to 77 % among the four clinical scenarios. The most used modalities were cytological lavage (ranging from 37 % to 55 %) and intra-abdominal ultrasonography of the liver (ranging from 36 % to 50 %).

### Perspectives on SL

Some 39 % of responding surgeons considered a minimum yield of 10–20 % necessary to justify routine use of SL, whereas 29 % regarded a yield below 10 % as sufficient. About 41 % of respondents felt that future clinical guidelines should advise routine use of staging laparoscopy in all patients with localized pancreatic cancer. Further details on perspectives and

experiences with SL are presented in [Table 4](#). The main reasons to never perform SL were the perceived low yield (79 % of non-performers), limited availability of operation room resources (41 % of non-performers), and additional costs of laparoscopic instruments (22 % of non-performers).

### Geographical differences

The use of SL varies between the continents with 90 % in the Americas, 85 % in Asia, 81 % in Oceania, 71 % in Europe, and 59 % in Africa ( $P < 0.05$ ). [Appendix 4](#) provides sub-group analyses of SL use and timing, stratified by continent, center type, and case volume. Furthermore, it seems that cytological lavage was less frequently used by European surgeons (ranging from 26 % to 44 %) compared to surgeons from the Americas (ranging from 35 % to 61 %) and Asia (ranging from 40 % to 60 %). See [Appendix 5](#) for the use of additional modalities during SL, stratified per region.

Among the 114 respondents from the United States, SL was used by 104 (91 %). In the setting of surgical exploration with intention for resection, SL was performed by 94 respondents (85 %; missing  $n = 4$ ) in case of upfront surgery (**scenario 1**) and 80 respondents (81 %; missing  $n = 15$ ) in case of surgery following neoadjuvant/induction chemotherapy with or without radiotherapy (**scenario 2**). In patients scheduled for neoadjuvant or induction therapy, 62 respondents (70 %; missing  $n = 25$ ) performed SL before the start of chemotherapy (**scenario 3**). Among the 62 respondents performing SL and having patients in their clinical practice treated with neoadjuvant or induction chemotherapy combined with radiotherapy, a minority of 22 respondents (35 %) conducted SL after chemotherapy but before radiotherapy (**scenario 4**). The use of

**Table 1** Baseline characteristics of respondents

<b>Age (years) (median, IQR)</b>	<b>47 (40–55)</b>
<b>What describes the scope of your current expertise best? (n, %)</b>	
Hepato-pancreato-biliary surgery	402 (65)
Pancreatic surgery	80 (13)
Liver surgery	5 (<1)
Surgical oncology	80 (13)
Gastrointestinal surgery	24 (4)
General surgery	26 (4)
<b>What (kind of) fellowship training have you followed during your training (multiple options possible)? (n, %)</b>	
Surgical oncology	268 (43)
Hepato-pancreato-biliary surgery	453 (73)
Transplantation surgery	153 (25)
None	36 (6)
<b>How many years have you been in practice since the completion of your surgical training? (years) (median, IQR)</b>	<b>12 (6–20)</b>
<b>Geographic region</b>	
Americas	157 (25)
Europe	228 (37)
Asia	198 (32)
Africa	17 (3)
Oceania	16 (3)
Unknown	1 (<1)
<b>In what type of medical center do you work? (n, %)</b>	
Academic center	400 (65)
Teaching center	112 (18)
Community center	51 (8)
Private practice	47 (7)
Other	7 (1)
<b>What is the annual number of pancreatic resections performed in your center, in average over the last 5 years? (n, %)</b>	
<20	83 (13)
20–40	160 (26)
41–80	175 (28)
81–120	108 (18)
>120	91 (15)
<b>What is the annual number of pancreatic resections performed by yourself personally, in average over the last 5 years? (n, %)</b>	
<10	141 (23)
11–20	196 (32)
21–40	171 (28)
41–80	80 (13)
>80	29 (5)

additional modalities ranged from 58 % to 74 % among the four clinical scenarios, mainly cytological lavage (ranging from 38 % to 61 %)

Among the 121 respondents from Japan, SL was used by 102 (84 %). In the setting of surgical exploration with intention for resection, SL was performed by 82 respondents (69 %; missing  $n = 2$ ) in case of upfront surgery (**scenario 1**) and 66 respondents (60 %; missing  $n = 11$ ) in case of surgery following neoadjuvant/induction chemotherapy with or without radiotherapy (**scenario 2**). In patients scheduled for neoadjuvant or induction therapy, 56 respondents (53 %; missing  $n = 15$ ) performed SL before the start of chemotherapy (**scenario 3**). Among the 76 respondents performing SL and having patients in their clinical practice treated with neoadjuvant or induction chemotherapy combined with radiotherapy, a minority of 27 respondents (36 %) conducted SL after chemotherapy but before radiotherapy (**scenario 4**). The use of additional modalities ranged from 84 % to 96 % among the four clinical scenarios, mainly cytological lavage (ranging from 72 % to 78 %)

## Discussion

This first international survey study on SL in patients with localized pancreatic cancer among 617 surgeons from 76 countries on six continents, found that 82 % of respondents uses SL. The most common timing to use SL is at time of upfront surgery (71 %) and prior to surgery after neoadjuvant/induction therapy (60 %), both mostly at the same surgical session as the intended laparotomy. Most surgeons only considered SL indicated in high-risk patients, based on either indeterminate or suspicious lesions on cross-sectional imaging (78–87 %), local resectability stage (54–64 %), and high serum CA19-9 (60–69 %) as main indications. Most respondents used additional diagnostic modalities during SL regardless of the clinical timing of SL, mostly cytological lavage (37–55 %) and intra-abdominal liver ultrasonography (36–50 %).

In the past, a decreasing trend in the use of SL has been reported in the United States.<sup>16</sup> Surprisingly when taking into account that the American College of Surgeons considers SL as a critical element of pancreatic cancer surgery and that the incidence of metastatic dissemination has not changed in any way.<sup>3,4</sup> The 2024 NCCN guideline stated that SL can be considered prior to (upfront) surgery or before starting neoadjuvant/induction chemotherapy, particularly in patients with a high risk for radiologically occult metastases.<sup>10,11</sup> A substantial body of evidence exists on risk factors for radiologically occult metastases, including **anatomical** (e.g., resectability,<sup>17</sup> body/tail tumors,<sup>17,18</sup> large tumor size,<sup>7,8,18–20</sup> indeterminate lesions on cross-sectional imaging,<sup>7,8,18,21</sup> lymphadenopathy<sup>21,22</sup>), **biological** (e.g., serum CA19-9,<sup>8,17–22</sup> serum CEA,<sup>23</sup> serum CA125,<sup>22</sup> ALAT<sup>20,22</sup>) and **conditional** (e.g., excessive pain<sup>8</sup>) factors. Accordingly, respondents of this survey mainly performed SL in selected patients using indeterminate lesions on cross-sectional imaging, higher resectability stage, and increased serum CA19-9 levels. In contrast with the literature, tumor size was the least commonly used

**Table 2** Staging laparoscopy - Use, timing, and indications

(n, %)	Scenario 1 SL prior to upfront surgery			Scenario 2 SL after neoadjuvant / induction therapy prior to surgery			Scenario 3 SL prior to neoadjuvant / induction therapy			Scenario 4 SL after neoadjuvant / induction chemotherapy, prior to radiotherapy *		
<b>X. I never use SL</b>	111 (18)			111 (20)			111 (22)			N/E		
<b>A. I use SL, but not for this scenario</b>	56 (9)			73 (13)			167 (33)			206		
<b>B. SL in all patients</b>	112 (19)			121 (22)			75 (15)			22		
<b>C. SL in selected patients</b>	324 (54)			248 (45)			154 (30)			72		
<b>Missing</b>	14			64			110			N/E		
<b>Criteria for selected use of SL</b>	Yes	No	Missing	Yes	No	Missing	Yes	No	Missing	Yes	No	Missing
<b>Anatomy</b>												
Tumor size	104 (32)	218 (67)	2 (<1)	42 (17)	197 (79)	9 (4)	42 (27)	112 (73)	0 (0)	15 (21)	56 (78)	1 (1)
Tumor location	103 (32)	216 (67)	5 (2)	61 (25)	176 (71)	11 (4)	39 (25)	114 (74)	1 (<1)	17 (24)	53 (74)	2 (3)
Resectability status	204 (63)	113 (35)	7 (2)	135 (54)	100 (40)	13 (5)	85 (55)	67 (44)	2 (1)	46 (64)	23 (32)	3 (4)
Intra-abdominal indeterminate / suspicious findings on cross-sectional imaging	279 (86)	27 (8)	18 (6)	196 (79)	29 (12)	23 (9)	134 (87)	16 (10)	4 (3)	56 (78)	12 (17)	4 (6)
<b>Biology</b>												
Serum CA19-9	224 (69)	92 (28)	8 (2)	162 (65)	71 (29)	15 (6)	100 (65)	51 (33)	3 (2)	44 (61)	25 (35)	3 (3)
Serum CEA	30 (9)	279 (86)	15 (5)	16 (6)	214 (86)	18 (7)	9 (6)	142 (92)	3 (2)	8 (11)	60 (83)	4 (6)
Serum CA-125	18 (6)	290 (90)	16 (5)	13 (5)	215 (87)	20 (8)	4 (3)	147 (95)	3 (2)	2 (3)	66 (92)	4 (6)
Serum DUPAN-2	16 (5)	292 (90)	16 (5)	13 (5)	215 (87)	20 (8)	9 (6)	142 (92)	3 (2)	5 (7)	63 (88)	4 (6)
Serum circulating tumor DNA	6 (2)	302 (93)	16 (5)	3 (1)	225 (91)	20 (8)	4 (3)	147 (95)	3 (2)	2 (3)	66 (92)	4 (6)
Other tumor marker(s)	1 (<1)	307 (95)	16 (5)	1 (<1)	227 (92)	20 (8)	0 (0)	151 (98)	3 (2)	0 (0)	68 (94)	4 (6)
<b>Condition</b>												
Patient's physical / conditional status	92 (28)	214 (66)	18 (6)	55 (22)	170 (69)	23 (9)	38 (25)	112 (73)	4 (3)	17 (24)	51 (71)	4 (6)

\* Not applicable since none of my patients are treated with radiotherapy as part of neoadjuvant/induction therapy [n= 84]. Since it is not possible to identify the number of respondents using radiotherapy, no percentages are calculated for the clinical scenario 4 regarding its use.

nb. n=14 do perform a staging laparoscopy but any information about usage, timing and indication per scenario is unknown

anatomical indicator for SL among the respondents, ranging from 17 % after neoadjuvant/induction therapy before surgery to 32 % before upfront surgery.

In this survey, most respondents (68 %) answered that an SL yield up to 20 % justifies the routine use of SL in their opinion: a yield of <10 % according to 29 % of respondents and a yield of 10–20 % according to 39 % of respondents. An unpublished systematic review including 5037 patients from 39 studies, reported a 15 % (95 % CI, 12 to 19) overall yield of SL for the detection of occult metastases in patients with localized pancreatic cancer. The yield was particularly high before neoadjuvant/induction chemotherapy (18 % [95 % CI, 14 to 23] and in patients with locally advanced pancreatic cancer (19 % [95 % CI, 14 to 26]). This translates in a 'number needed to treat' of 7 patients undergoing SL to detect one patient with occult metastases. This explains why resectability status was one of the main indications among the respondents to perform SL. Various composite scores are developed to estimate the probability of having occult metastases; all include 'tumor size' and 'elevated tumor markers' which includes mainly serum CA19-9.<sup>24–26</sup> These composite scores can facilitate the choice to selectively perform SL.

Nevertheless, various arguments are still used against the use of SL, including the low yield (79 % of non-performers), additional costs (22 % of non-performers), and limited capacity on

operation room facilities (41 % of non-performers). Arguments for SL, however, suggest that risks are low for these procedures and if done at a separate setting would avoid having loss of operation room utilization of metastases are found at time of the planned resection. SL is performed at different settings. It can be done at the beginning of an exploratory laparotomy, as a standalone procedure, or even combined with port-a-cath placement, wherefore SL does not have to be a waste of operation room resources.<sup>18</sup> The majority of respondents from this survey performing SL in the setting of upfront surgery or after neoadjuvant/induction therapy performed SL during the same session as the scheduled laparotomy (63–79 %). Several studies which investigated the cost effectiveness of SL in different clinical scenarios, reported similar or even lower costs when using SL because of non-therapeutic laparotomies prevented as well as reducing overtreatment with chemo- and radiotherapy.<sup>27–29</sup> Non-therapeutic laparotomies are associated with impaired outcome including mortality, although this may depend on the clinical setting.<sup>30–32</sup> However, data on the clinical benefits of SL versus primary laparotomy are limited, concerning solely unadjusted analyses suggesting shorter hospital stay, shorter time to palliative chemotherapy and prolonged survival after SL.<sup>26,32,33</sup> Only Sell *et al.* adjusted for confounders, showing an association between SL and prolonged overall survival.<sup>32</sup>

**Table 3** Staging laparoscopy - Additional modalities

	Scenario 1 SL prior to upfront surgery			Scenario 2 SL after neoadjuvant/induction therapy prior to surgery			Scenario 3 SL prior to neoadjuvant/induction therapy			Scenario 4 SL after neoadjuvant/induction chemotherapy, prior to radiotherapy		
(n, %)	n = 436			n = 369			n = 229			n = 94		
	Yes	No	Missing	Yes	No	Missing	Yes	No	Missing	Yes	No	Missing
<b>Use of any additional modality</b>	289 (66)	126 (29)	21 (5)	225 (61)	117 (32)	27 (7)	167 (73)	56 (24)	6 (3)	68 (72)	22 (23)	4 (0)
<b>Use of cytological lavage</b>	179 (41)	236 (54)	21 (5)	137 (37)	205 (56)	27 (7)	126 (55)	97 (42)	6 (3)	48 (51)	42 (45)	4 (4)
Additional analyses	139 (78)	–	–	100 (73)	–	–	84 (67)	–	–	31 (65)	–	–
CA19-9	92 (51)	–	–	59 (43)	–	–	51 (40)	–	–	24 (50)	–	–
CEA	42 (23)	–	–	31 (23)	–	–	24 (19)	–	–	12 (25)	–	–
ctDNA	27 (15)	–	–	23 (17)	–	–	13 (10)	–	–	6 (13)	–	–
Other(s)	1 (<1)	–	–	1 (<1)	–	–	2 (2)	–	–	1 (2)	–	–
<b>Use of intra-abdominal ultrasonography of the liver</b>	185 (42)	221 (51)	30 (7)	147 (40)	188 (51)	34 (9)	99 (43)	123 (54)	7 (3)	47 (50)	43 (46)	4 (4)
<b>Use of indocyanine green fluorescence</b>	28 (6)	366 (84)	42 (10)	23 (6)	308 (83)	38 (10)	15 (7)	206 (90)	8 (3)	6 (6)	82 (87)	6 (6)
Inspected areas												
Liver	26 (93)	–	–	22 (96)	–	–	14 (93)	–	–	6 (100)	–	–
Omentum	7 (25)	–	–	7 (30)	–	–	4 (27)	–	–	1 (17)	–	–
Abdominal wall	6 (21)	–	–	5 (22)	–	–	2 (13)	–	–	1 (17)	–	–
Extra-regional lymph nodes	7 (25)	–	–	5 (22)	–	–	1 (7)	–	–	0 (0)	–	–
Vascular involvement	7 (25)	–	–	6 (26)	–	–	3 (20)	–	–	1 (17)	–	–
<b>Use of intra-abdominal ultrasonography to assess the tumor resectability</b>	97 (22)	295 (68)	44 (10)	75 (20)	254 (69)	40 (11)	55 (24)	165 (72)	9 (4)	27 (29)	60 (64)	7 (7)

For some parameters, no distinction was made between ‘no’ and ‘missing’ due to the design of the survey.

Regional differences in the use of SL are possibly explained by differences in guideline recommendations. The 2024 NCCN guideline stated that SL can be considered, particularly in patients at high risk for occult metastases, which explains the high rate of SL users in the Americas (90 %).<sup>11</sup> The same applies to the Asian respondents, of whom 61 % derived from Japan, having a high rate of SL use as well (85 %). The 2022 Japanese guideline recommended the use of SL to exclude metastatic disease, although the recommendation is graded as ‘weak’.<sup>34</sup> In contrast, the lower rate of SL use in Europe (71 %) can be explained by the 2023 European Society for Medical Oncology (ESMO) guideline which only mentions that some guideline authors advocate the use of SL, but is not routinely performed.<sup>35</sup> This possibly influences local protocols and thereby variety in the use of SL between regions. It is unlikely that regional differences are driven by factors related to reimbursement and surgical training programs, as this surgical procedure is not

complex and often performed during the same surgical procedure as the intended resection.

The 2024 NCCN guideline stated that additional modalities including intraoperative ultrasonography and cytological lavage can be used during SL,<sup>10,11</sup> which is consistent with the findings from the current survey. After all, most clinicians used adjuncts during SL, mainly cytological lavage and liver ultrasonography. Less frequently used adjuncts among respondents were intra-abdominal ultrasonography to assess the vascular involvement and the use of indocyanine green fluorescence to detect liver and peritoneal lesions, even though recent studies on indocyanine green fluorescence are promising.<sup>36</sup> The NCCN guideline stated that positive cytology is equivalent to M1 disease,<sup>10,11</sup> as shown by a large observational single-center study from the Mayo Clinic.<sup>18</sup> This requires a two-step up (‘standalone’) approach to SL as the pathological examination requires a few days, which means that SL must be performed as a standalone procedure

**Table 4** Staging laparoscopy - Perspectives and experiences

<b>In your personal view, what is the minimum yield that justifies the routine use of a staging laparoscopy (i.e., minimal clinically relevant yield)?</b>	
0–9 %	179 (29)
10–20 %	239 (39)
21–30 %	103 (17)
31–50 %	37 (6)
>50 %	59 (10)
<b>In your personal experience, what is the yield of occult metastases during surgery for localized pancreatic cancer in your center, regardless of the timing of staging laparoscopy?</b>	
<5 %	220 (36)
6–10 %	207 (34)
11–15 %	77 (12)
>15 %	48 (8)
Not applicable as we do not perform any staging laparoscopy at any stage	65 (11)
<b>Do you personally feel that future clinical practice guidelines on pancreatic cancer should advise routine staging laparoscopy in all patients?</b>	
I do not know	53 (9)
No	314 (51)
Yes	250 (41)
<i>If yes, what do you consider the best timing for a staging laparoscopy in patients who receive neoadjuvant/induction therapy?</i>	
Prior to neoadjuvant/induction therapy	110 (44)
After neoadjuvant/induction therapy, but prior to surgery	99 (40)
Both prior to neoadjuvant/induction therapy and prior to surgery	74 (30)
<b>Is there a protocol for performing staging laparoscopy in patients diagnosed with localized pancreatic cancer in your center?</b>	
No	466 (76)
Yes	151 (24)
<i>If yes, is this protocol consistently used by all surgeons performing pancreatic surgery in your unit?</i>	
Yes	123 (81)
No	44 (29)
I do not know	6 (4)
<b>If you never perform staging laparoscopy in patients with pancreatic cancer, what are the reason(s)? (n = 111 respondents)</b>	
Yield is too low <sup>a</sup>	88 (79)
Limited availability on the operation room program	45 (41)
Additional costs of the laparoscopy set	24 (22)
High body mass index/visceral adipositas among the general population	3 (3)
Need for a laparotomy regardless to perform palliative bypass	2 (2)
Other(s)	16 (14)

<sup>a</sup> This includes 12 respondents who did not selected this option, but answered that cross-sectional imaging is sufficient nowadays.

some days before the exploratory laparotomy. Data on the clinical value of positive cytology and additional markers (e.g., CA19-9, CEA microRNA, mutant KRAS, tumor DNA) is evolving.<sup>18,37–42</sup> An extensive Japanese retrospective multi-center study included 568 patients with pancreatic cancer having positive peritoneal cytology, derived from 78 high-

volume centers, compared patients with and without resection.<sup>43</sup> After propensity score matching, no survival benefit of resection was seen (89 versus 89 patients), including a median overall survival of 19 versus 19 months ( $p = 0.751$ ).<sup>43</sup> These findings suggest the clinical relevance of positive cytological lavage, questioning the value of surgery in these patients.

The findings from this study should be interpreted considering some limitations. First, a subset of respondents did not fully complete the survey, which may have influenced the outcome. Second, the high usage of SL among respondents could be influenced by response bias although evidence to support this is lacking. Third, most respondents originated from the United States (18 %) and Japan (20 %), which may have influenced the results, given the variances in the use of SL around the world. Fourth, the eligibility of all respondents could not be guaranteed as the survey was spread among all members of the participating societies and social media. Nevertheless, this is the first survey investigating the use and indications of SL for patients with localized pancreatic cancer among respondents from 76 countries and six continents. These results may guide the design of future research and guidelines. Future research should focus on the clinical outcome of SL compared to primary laparotomy (i.e., complications, functional recovery, and start of and time to chemotherapy) and the value of additional diagnostic adjuncts used during SL (e.g., yield and prognostic value). Moreover, optimization of radiological modalities including MRI, FDG-PET/CT, and FAPI PET/CT should be studied to prevent futile surgery.<sup>44–47</sup>

## Conclusion

This first international survey study shows that SL in localized pancreatic cancer is commonly used both as (re)staging modality as well as before proceeding to laparotomy, mostly in high-risk patients. Moreover, geographical variety is seen in the use of SL as well as in the use of adjunct modalities during SL. This variability highlights the need for more evidence on the yield, cost/benefit ratio, and optimal timing of SL aiming at stronger guideline recommendations.

## Collaborators

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## Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: (i) Marco Del Chiaro has been awarded with an industry grant (Haemonetics, Inc) to conduct a multicenter study to evaluate the prognostic implications of TEG in pancreatic cancer. (ii) Marco Del Chiaro is co-principal investigator of a Boston Scientific sponsored international multicenter study on the use of intraoperative pancreatoscopy of patients with IPMN.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.hpb.2025.12.001>.