



Staging laparoscopy in gastric cancer patients: From a Dutch nationwide Delphi consensus towards a standardized protocol

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ABSTRACT

Background: Staging laparoscopy is a common diagnostic tool in gastric cancer, but its performance varies widely. The aim of this study was to gain Dutch nationwide consensus regarding the indications for and execution of staging laparoscopy in patients with gastric cancer.

Methods: All surgeons in the Netherlands specialized in gastric cancer surgery (n = 52) were asked to participate in a Delphi consensus study. The study involved an initial questionnaire with a 3-point Likert scale, an online consensus meeting, and a second questionnaire using a 2-point Likert scale (agree/disagree). Consensus was defined as 70% or more agreement among participants.

Results: In total, 45 experts completed both questionnaires (87% response rate). Consensus was reached on the indication to perform staging laparoscopy in cT3-4 or cN + or diffuse-type gastric cancer, including Siewert type III oesophagogastric junctional cancer. The experts agreed that if preoperative scans suggest infiltration of surrounding organs (cT4), the tumour's resectability should explicitly be investigated. Consensus was also reached for a systematic peritoneal cavity inspection according to Sugarbaker's Peritoneal Cancer Index (PCI) score. All regions should be inspected routinely, although the omental bursa may be inspected on indication. Aspiration of ascites or peritoneal washing should be performed for cytology. The experts agreed that restaging laparoscopy should be performed before resection in case of progressive disease on preoperative imaging. Without progression, global inspection was considered sufficient.

Conclusions: The results of this Dutch nationwide Delphi consensus study exposed the variability of performing staging laparoscopy in patients with gastric cancer and provided the concept for a standardized protocol.

1. Introduction

Gastric cancer is the fifth most common cancer and the third leading cause of cancer-related deaths worldwide [1]. Standard curative treatment consists of D2-gastrectomy in combination with perioperative chemotherapy in most Western countries [2–5]. However, metastatic disease, especially peritoneal dissemination, is common in gastric cancer and limits potentially curative treatment. Recent population-based studies estimate the incidence of peritoneal metastasis at diagnosis from 10 to 27% [6,7]. Peritoneal dissemination including tumour positive peritoneal cytology is associated with a poor prognosis. Therefore,

early and accurate detection of peritoneal disease is critical for improving patient outcomes [8].

Conventional imaging modalities, such as a CT or PET-scan, have a low sensitivity to detect peritoneal disease in gastric cancer patients [9–11]. Consequently, peritoneal metastases and/or irresectability are often detected during surgical exploration [12]. Staging laparoscopy detects non-resectable or peritoneal disease in 19% of patients before potentially curative treatment [11]. Staging laparoscopy, introduced in the early 1980s, has been implemented as a diagnostic tool in the work-up of gastric cancer patients. The optimal execution, however, has been the subject of ongoing debate, since its inception [13–15]. Despite

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its decades-long history, there is still no consensus on its indications and the optimal technique. The National Comprehensive Cancer Network (NCCN) guidelines recommend performing a staging laparoscopy with cytology in all patients with clinical stage T1b or higher gastric cancer [16]. In addition, the European Society of Surgical Oncology advises performing a staging laparoscopy in clinically stage IB-III gastric cancer considered potentially resectable [17]. The Japanese Gastric Cancer Association, on the other hand, restricts the use of a staging laparoscopy to patients with bulky nodal involvement [18]. Moreover, all guidelines lack clear instructions on how to perform an adequate staging laparoscopy.

The aim of this study was to unravel the variability in performing staging laparoscopy in gastric cancer patients and to develop consensus among regarding its indications and performance. For this, all experts in the field were asked to participate in a Dutch nationwide Delphi consensus study.

2. Methods

2.1. Delphi method

This Delphi consensus study was conducted between December 2022 and April 2023. The Delphi method is a well-recognized method for gathering opinions to determine consensus within a group of experts in a structured manner [19]. Several rounds, consisting of anonymous questionnaires and an online consensus meeting, are designed to create an internal reassessment of the process in general, without overpowering opinions of dominant participants. The anonymity of questionnaires ensures voting without external pressure and the ability to reconsider previously given answers. At the start, designated criteria ensure quality control during the process [20]. This study has been carried out in accordance with the Declaration of Helsinki. Ethical approval of the medical ethical committee was waived.

2.2. Development of the questionnaire

Before the start of this Delphi study, a systematic review was conducted to determine relevant parameters and to unravel the variability in performing staging laparoscopy in gastric cancer patients. The search included the following MeSH terms: “gastric cancer”, “gastroesophageal cancer”, “cancer staging”, “laparoscopy”, “peritoneal lavage fluid”, “ascites”, “assessment” and “cytology”. The results of this systematic review have been submitted for publication. The retrieved parameters were grouped in the following four domains [1]: indications to perform a staging laparoscopy [2], determining resectability of the primary tumour [3], inspection of the peritoneum for metastases and [4] indications to perform a re-laparoscopy. Furthermore, to gain a better understanding of the variability of the definition of peritoneal metastases a fifth domain was added to the initial questionnaire. The elicited was not to gain consensus, but solely to inform the researchers about the variability in the definition. Within these five domains, multiple topics were drafted by the study team containing statements regarding a standardized staging laparoscopy and reviewed by experts consisting of experienced gastroenterological/oncological upper gastrointestinal (GI)-surgeons in the Netherlands.

2.3. Expert panel recruitment

All Dutch Upper GI surgeons were asked to join the expert panel (n = 59). Criteria to be eligible to join the expert panel were: surgeon (or in training) practicing Upper GI surgery and/or performing staging laparoscopies for gastric cancer. Recruitment was performed by promoting the study during the Dutch Upper GI Cancer Group meeting and by inviting all Upper GI surgeons in the Netherlands by email.

2.4. Definition of consensus

Consensus was defined as 70% or more agreement among participants on a specific topic. Experts could comment on every statement. Topics on which no consensus was obtained during the first Delphi round, were discussed during an online consensus meeting and rephrased in the second questionnaire.

2.5. Description of the consensus method

This Delphi study consisted of three rounds. The first round consisted of a digital questionnaire sent by using Castor EDC software [21]. A 3-point Likert scale (agree/neutral/disagree) was proposed per statement in the first four domains. The fifth domain (definition of peritoneal metastases) contained eight additional questions with a dichotomous answer modality (non-metastatic or metastatic peritoneal disease). After completing the first questionnaire, all answers and comments were analysed by the study team (KvdS, NADG, LT) and checked for consensus as defined above. Statements for which no consensus or consensus between 70 and 80% was obtained, were discussed during the online consensus meeting. This meeting was video-recorded. Discussed questions were rephrased if necessary. The second questionnaire was only sent out to the participants of the expert panel who had completed the first questionnaire. The experts were asked to reconsider their responses based on the results of the first round, and they were allowed to provide additional comments or suggestions. The statements were presented as a dichotomous answer modality (agree/disagree). The responses were compiled and analysed again. The goal was to reach a consensus on the elements of a standardized staging laparoscopy in gastric cancer patients. Finally, a standardized staging laparoscopy protocol was proposed based on the outcomes.

3. Results

3.1. Course of the Delphi rounds

A total of 52 experts joined the panel, consisting of 47 surgeons and 5 surgeons in training. The experts were from different geographic regions in the Netherlands and represented both academic and general hospitals. Of these experts, 47 fully fulfilled the questionnaire and one participant nearly (74%) completed the questionnaire. One surgeon who fulfilled only 8% of the questionnaire was excluded. A total response rate of 92% (n = 48) was reached. The first questionnaire contained 66 questions. The online consensus meeting was attended by 26 members (54%) of the 48 respondents. The second questionnaire contained 56 questions and was sent to the 48 participants, who completed the first questionnaire. This round yielded a response rate of 94% (n = 45). A flowchart is presented in Fig. 1. All statements used in the second questionnaire and corresponding results are visualised in Fig. 2.

3.2. Indications for staging laparoscopy

Statements to determine the indications for a staging laparoscopy were subdivided into statements regarding indications based on tumour characteristics and indications based on the location of the primary tumour. Consensus was reached that not all gastric cancer patients should undergo staging laparoscopy. Staging laparoscopy should only be performed in patients with an increased risk for peritoneal dissemination (cT3-4, nodal involvement/N+, and diffuse-type tumours). No consensus was reached regarding the statement that all patients undergoing neoadjuvant chemotherapy should undergo staging laparoscopy.

The first questionnaire failed to reach consensus on the indication to perform a staging laparoscopy concerning tumour location (except in Siewert type I tumours, where consensus was reached that staging laparoscopy is not needed). During the expert panel meeting, voting was

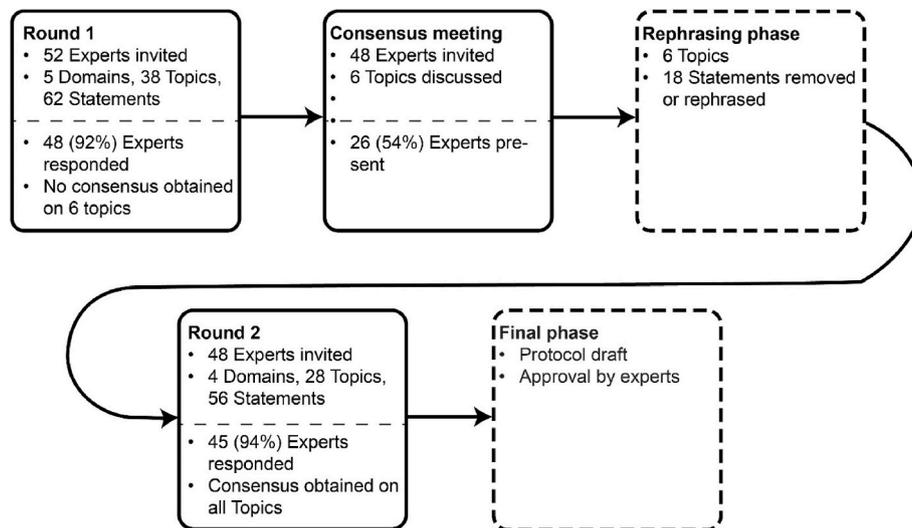


Fig. 1. Flowchart of this Delphi study.

conducted, in which 91% of the present experts voted against primary tumour location being an indicator for performing a staging laparoscopy, when the bulk of the tumour is in the stomach. After the discussion, consensus was reached to perform staging laparoscopy in Siewert type III tumours and not in Siewert type I tumours. No consensus was reached for Siewert type II tumours.

3.3. Assessment of resectability of the tumour

Consensus was reached that infiltration of surrounding structures or organs (diaphragm, oesophagus, spleen, pancreas and posterior vascular structures, mesentery of the colon) should only be inspected during a staging laparoscopy when preoperative radiological imaging suggests ingrowth. Regardless of prior suspicion of ingrowth, the left lobe of the liver should always be inspected as no additional dissection needs to be performed to judge this.

3.4. Inspection of the peritoneum

Consensus was reached to assess the peritoneum according to the Peritoneum Cancer Index (PCI) of Sugarbaker et al. and to document the corresponding PCI score in the operation report [22]. Peritoneal metastases should be proven in at least one of the regions suspected of peritoneal metastases. It was felt that the omental bursa does not require routine inspection, but only in patients in whom there is a preoperative suspicion of tumour on imaging studies. Consensus was reached to perform peritoneal lavage and/or aspirate ascites during staging laparoscopy for cytology. The expert panel agreed that the protocol suggested by the AJCC (left and right subphrenic space and Douglas cavity) with a minimum total volume of 200 cc should be followed [23].

3.5. Re-staging laparoscopy

Agreement was reached to perform systematic re-staging, by using the PCI score, if there is progressive disease on preoperative imaging. Otherwise, global re-inspection of the peritoneal cavity is sufficient. Re-staging laparoscopy does not necessarily take place separately from gastric resection unless logistical arguments warrant this.

3.6. Definition of peritoneal metastases

The expert team agreed on the following criteria to be classified as peritoneal metastases from gastric cancer: lesions on the greater and lesser omentum and gastrohepatic ligament separate from the primary

tumour, lesions in the omental bursa and the presence of tumour positive ascites or lavage. The presence of peritoneal lesions on the stomach, independent of the presence of serosal involvement was subject to discussion. In the end, it was agreed that these are not classified as peritoneal metastases.

3.7. Standardized protocol for staging laparoscopy in gastric cancer

Based on the results of the different statements on each domain in this Delphi study, a standardized protocol for performing and reporting staging laparoscopy in gastric cancer was conceptualised (Appendix A, Supplementary Data).

4. Discussion

This study provides a tool for performing a staging laparoscopy in the work-up of patients with gastric cancer, based on consensus among a panel of experts using the Delphi method. This study exposes the variability of performing staging laparoscopy among experts and provides input for a protocol that can be used for standardizing staging laparoscopy.

Heterogeneity concerning the indications for staging laparoscopy in gastric cancer patients is reflected by differences between international guidelines. Although, these indications are based on limited evidence. The criteria in the current Dutch guideline are based on the clinical T-category of the primary tumour [24]. A recent study demonstrated understaging in about 40% of early gastric cancer patients, particularly in the case of diffuse-type tumours [25]. However, no differentiation is made between Lauren's intestinal and diffuse-type tumours within the international guidelines [26]. The experts in our panel agreed to include diffuse-type tumours as a criterion to perform a staging laparoscopy [25]. No consensus was reached to perform a staging laparoscopy in all patients scheduled for neoadjuvant chemotherapy. Reflecting the limited existing knowledge regarding the a priori likelihood of peritoneal metastases in patients with cT1-2N0 gastric cancer, although a recent retrospective study revealed a 17.6% incidence of peritoneal disease [27]. Considering the association between peritoneal metastases and diffuse-type tumours, performing staging laparoscopy in diffuse-type tumours may potentially allow accurate patient selection.

The location of the primary tumour as an indication for a staging laparoscopy was only relevant for oesophagogastric junction tumours with high-risk characteristics. The expert panel agreed that patients with Siewert type III tumours should undergo a staging laparoscopy, which is in line with international guidelines that Siewert type III should

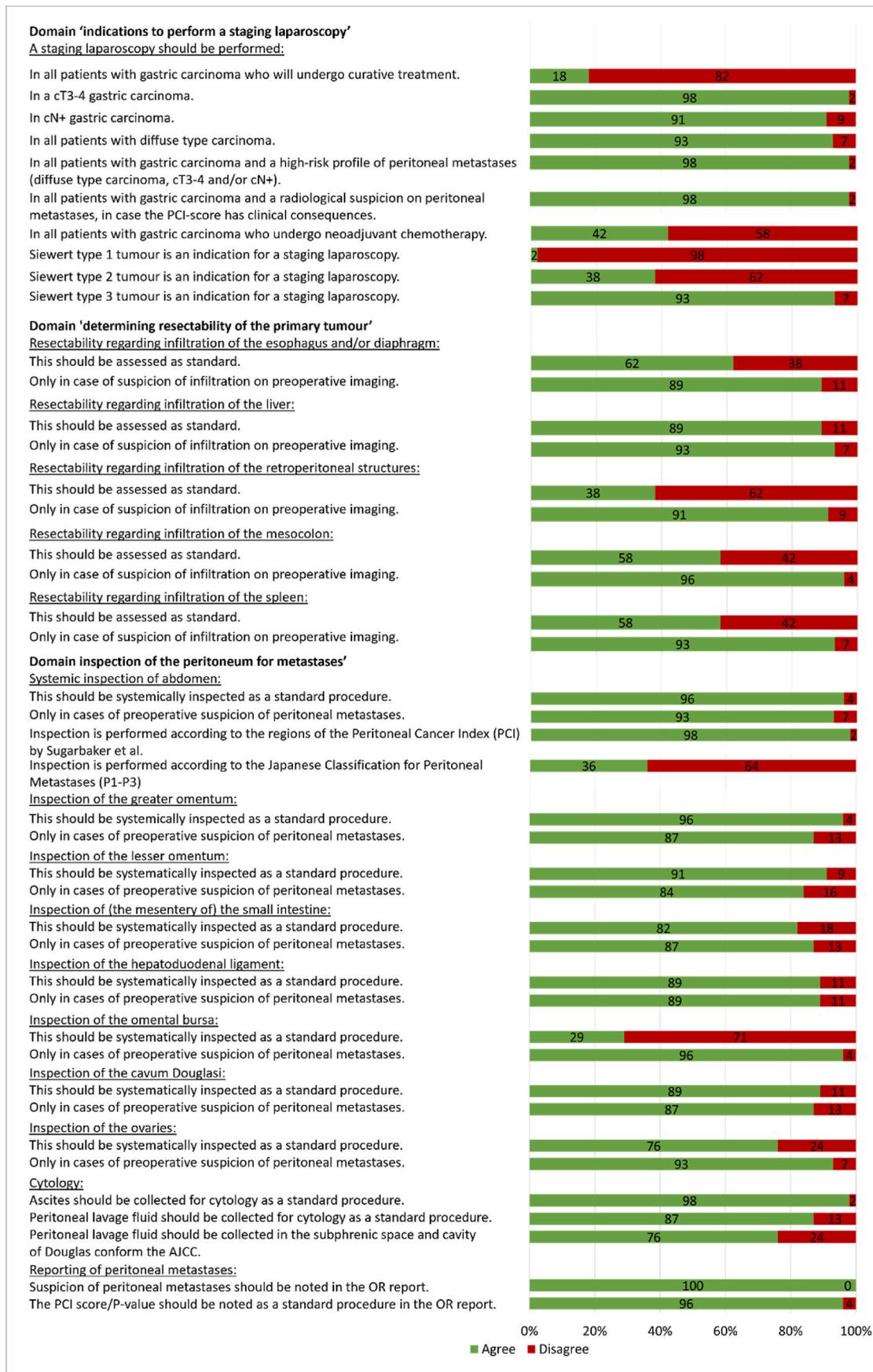


Fig. 2. Overview of all statements in the second questionnaire with percentage agree/disagree (n = 45).

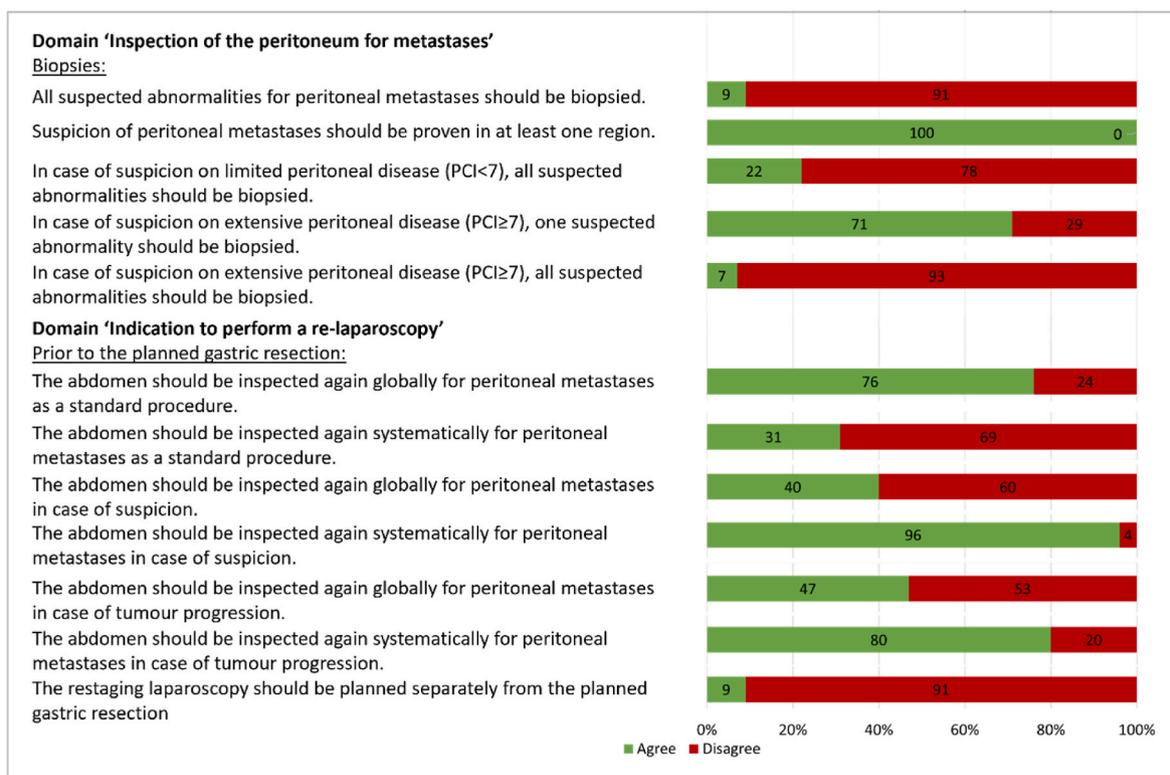


Fig. 2. (continued).

predominantly be regarded as gastric cancer. Siewert type I is usually considered an oesophageal tumour, and therefore not an indication for a staging laparoscopy [28]. As synchronous peritoneal metastases are rare in oesophageal tumours, the addition of a standard staging laparoscopy was not considered useful [29]. Siewert type II tumours remain a topic of debate and the decision to perform a staging laparoscopy should be made according to tumour characteristics, such as the clinical T-stage or the histological subtype, and to determine the technical possibilities for the type of reconstruction.

Assessment of the resectability of the primary tumour by staging laparoscopy has been proven successful, as 4% of the patients are diagnosed with an unresectable primary tumour [11]. Assessment of organs that need dissection to be inspected raises the risk of complications, whereas staging laparoscopy serves a non-therapeutic purpose. As inspection of the omental bursa requires some dissection, this is only indicated in patients in whom there is suspicion of peritoneal metastases or infiltration. Unfortunately, this increase in risk is not thoroughly described in the literature.

The ability to detect peritoneal metastases during staging laparoscopy has been well-established [30]. Consensus was reached that standard inspection of the abdominal cavity should include all abdominal regions, except for the omental bursa. The participants stated that balancing the risks and implications of an inspection is important. Inspection of the omental bursa should be limited to patients with pre-operative suspicion. During the consensus meeting, discussions were held regarding the assessment of the ovaries. Although there is a low a priori chance of ovarian involvement in gastric cancer [31], the ease of inspecting the ovaries outweighs the potential risks according to the expert panel, especially taking into account the negative influence of ovarian metastases on the patient's prognosis [32]. The quantity of lavage fluid used during staging laparoscopy and the optimal location for sampling showed no consensus among the participants. Agreement was reached to adopt the protocol proposed by the AJCC to facilitate standardization and to allow for the systematic collection of data on the incidence of gastric cancer with tumour-positive cytology only [23].

Despite a favourable staging laparoscopy, non-curable disease (ingrowth in the adjacent organs and/or peritoneal metastases) is detected during surgery in 8% of the patients resulting in open-closure procedures [12,33]. Therefore, global re-inspection of the abdominal cavity should be performed before resection according to the expert panel. The experts advise a systematic inspection of the abdominal cavity before resection after systemic chemotherapy in two situations: either in the event of primary tumour progression or in the event of progression to peritoneal disease on preoperative imaging. The re-staging laparoscopy may be planned separately or in the same session as the resection as long as the frozen section can be performed. The logistical planning differs per hospital and is therefore not restricted.

The staging laparoscopy is preferred over traditional imaging modalities such as CT scans and PET scans in detecting peritoneal metastases, given its superior sensitivity. However, it is crucial to acknowledge the evolving landscape of diagnostic tools. Emerging molecular-based imaging techniques, particularly fibroblast activation protein inhibitor (FAPI) PET/CT, are undergoing investigation and were shown to have a high sensitivity for detecting peritoneal metastases in patients with colorectal cancer [34–36]. Prospective studies are required to investigate the use of the FAPI-PET/CT in the diagnostic work-up for gastric cancer, with the potential to serve as a non-invasive alternative to staging laparoscopy.

Based on the results of this Delphi study, a standardized protocol for staging laparoscopy was formulated that can be used in daily clinical practice (Supplementary Materials). In the Netherlands, this protocol will be discussed within the Dutch Upper GI Cancer Group to be evaluated prospectively.

One limitation of the current study is that the consensus statements reached in this study are not supported by scientific evidence and require prospective validation. While the Delphi method served as a starting point to standardize the staging laparoscopy, it is important to recognize that the method relies on expert opinions, which can be influenced by individual experiences, beliefs and dogmas, and varying levels of experience. Additionally, the panel of experts was entirely

Dutch primarily treating Western patients. Therefore, these results cannot be extrapolated to the Eastern population, since differences exist regarding tumour biology, screening programs/disease stage, and multimodality treatment strategies [37]. The higher incidence of gastric cancer in Asian countries has led to the implementation of screening programmes, leading to a lower ratio of advanced/early stage gastric cancer [38]. Consequently, staging laparoscopy in Asian countries is weakly recommended to establish the therapeutic strategy and is more commonly used only for conforming eligibility criteria in clinical trials [39–41]. As a result, the current study findings may have limited applicability to Asian countries. However, this could also be seen as a strength of the current study as this consensus statement corresponds to a homogeneous group of patients. Other strengths include the pre-defined definitions of consensus and the establishment of a standardized protocol for performing staging laparoscopy in gastric cancer that can enhance the reproducibility of findings in future research and clinical settings.

To conclude, this Dutch Delphi study represents an initial effort towards establishing a broad consensus on standardizing the staging laparoscopy in patients with gastric cancer. This standardization would enable prospectively recording patient outcomes and facilitate comparisons across healthcare institutions and countries.

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Data availability statement

The data that support the findings of this study are available from the corresponding author, NADG, upon reasonable request.

CRediT authorship contribution statement

Karen van der Sluis: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Project administration, Funding acquisition. **Niels A.D. Guchelaar:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Project administration. **Lianne Triemstra:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Project administration. **Ron H.J. Mathijssen:** Investigation, Writing – review & editing, Supervision. **Jelle P. Ruurda:** Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision, Project administration. **Bas P.L. Wijnhoven:** Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision, Project administration. **Johanna W. van Sandick:** Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision, Project administration.

Declaration of competing interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2024.108278>.

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