



Survey article

Borderline tumours of the ovary: Common practice in the Netherlands

Koen De Decker^{a,b,*}, Henk G. ter Brugge^a, Joost Bart^c, Roy F.P.M. Kruitwagen^{d,e},
Hans W. Nijman^b, Arnold-Jan Kruse^{a,c,d}

^a Isala Hospital, Department of Obstetrics and Gynaecology, Zwolle, the Netherlands

^b University Medical Center Groningen, Department of Obstetrics and Gynaecology, Groningen, the Netherlands

^c Isala Hospital, Department of Pathology, Zwolle, the Netherlands

^d Maastricht University Medical Centre, Department of Obstetrics and Gynaecology, Maastricht, the Netherlands

^e GROW, School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, the Netherlands



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ABSTRACT

Objectives: Discordance between frozen section diagnosis and the definite histopathological diagnosis and the fact that the frozen section result is not always unambiguous, may contribute to differences in clinical practice regarding perioperative treatment and follow-up of borderline ovarian tumours (BOTs) patients amongst gynaecologic oncologists, which may lead to over- and undertreatment. The aim of the study was to map the Dutch gynaecologists' preferred treatment and follow-up strategy in case of BOTs.

Methods: A questionnaire was sent to all Dutch gynaecologists involved in ovarian surgery with perioperative frozen section analysis, and the outcomes were assessed using descriptive statistics.

Results: Nearly half of the respondents (41.0%) would not perform a staging procedure in case of a BOT. In case of an ambiguous frozen section diagnosis, tending towards invasive carcinoma, a considerable number (sBOT 56.4%; mBOT 30.8%) would perform a lymph node sampling as part of the staging procedure. A relaparotomy/relaparoscopy, to perform a lymph node sampling in case of a serous or mucinous carcinoma after a BOT frozen section diagnosis, would be performed by 97.4% and 48.7% of the respondents, respectively.

Conclusions: A considerable number of gynaecologists would perform a staging procedure that is recommended for ovarian cancer in case of an ambiguous BOT frozen section diagnosis, especially for serous tumours. In addition, nearly all gynaecologists would perform a second procedure including a lymph node sampling in case of a serous invasive carcinoma after a BOT frozen section diagnosis, which applies to half of the gynaecologists in case of a mucinous carcinoma.

1. Introduction

In contrast to most other organs, the classification of surface epithelial tumours of the ovary (including serous and mucinous tumours) does not only include benign and malignant tumours, but also an intermediate category of so-called borderline tumours. From a pathological and etiological point of view, serous and mucinous borderline tumours are completely different, resulting in major differences in their biological behaviour (Kurman and International Agency for Research on Cancer, 2014). From a clinical point of view, intraoperative decision making is mainly dependent on the pathologists' judgment regarding the frozen section analysis: benign, borderline, or malignant, considering the histological appearance of the tumour as less important at that timepoint. For this reason, some gynaecologists pragmatically group mucinous and serous borderline tumours together. Since the

biological behaviour of borderline ovarian tumours is difficult to predict, optimal intraoperative management, with respect to frozen section analysis, followed by abdominal staging, remains a matter of debate.

According to Dutch guidelines, a surgical staging procedure is recommended when a Borderline Ovarian Tumour (BOT) is diagnosed during an exploratory laparotomy with frozen section analysis (Werkgroep Oncologische Gynaecologie (WOG), n.d.). Such a staging procedure includes, in addition to taking abdominal (rinsing) fluid for cytology and resection of at least the pathological adnex, a thorough inspection and palpation of the abdominal cavity, intestines and mesentery, omentum, and assessment of the contralateral ovary. Evident deviant areas must be excised. An infracolic omentectomy and collection of standardized peritoneal biopsies (from both paracolic gutters, the right diaphragmatic dome, the bladder dome and pouch of Douglas) is considered useful for finding peritoneal implants and determining the

* Corresponding author at: Isala Clinics, Department of Obstetrics and Gynaecology, PO Box 10400, 8000 GK Zwolle, the Netherlands.

E-mail address: k.de.decker@outlook.com (K. De Decker).

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definite stage and related prognosis, but has no consequences for the treatment (Morice et al., 2003; Trope et al., 1993; Akesson et al., 2008; De Decker et al., 2017). Furthermore, an appendectomy is advised in case of a mucinous BOT (mBOT) (Hart, 2005; Sherman et al., 2004). When a BOT diagnosis is established postoperatively, a relaparotomy is not indicated (Fauvet et al., 2004; Camatte et al., 2004). Follow-up in case of BOTs is advised only for patients with a remaining ovary and patients with a serous BOT (sBOT) with invasive peritoneal implants, which are also designated as extra-ovarian low-grade serous carcinoma (LGSC) (Kurman and International Agency for Research on Cancer, 2014; Yokoyama et al., 2006; Morice et al., 2012).

There are differences in clinical practice regarding perioperative treatment and follow-up of BOT patients amongst gynaecologic oncologists. Besides some optional parts of the staging procedure, another important difference in the treatment of BOTs amongst gynaecologic oncologists may be related to a discordance between the BOT frozen section diagnosis and a definite histopathological diagnosis of invasive ovarian cancer (10–17% of the patients) (Pongsuvareeyakul et al., 2012; Bozdogan et al., 2016; Ayhan et al., 2016). Some gynaecologists advocate a staging procedure as is recommended in case of invasive ovarian carcinoma, with the risk of overtreatment, whereas others will await the definitive pathological diagnosis, which may necessitate a second surgical procedure to complete the staging procedure. Finally, the perioperative histopathological BOT diagnoses based on frozen section analyses may be not unambiguous (e.g., “borderline tumour of the ovary, but cannot exclude invasive cancer”, “minimum borderline tumour of the ovary” or “borderline ovarian tumour and strong suspicion of invasive disease”), which is partly due to the common and well-known problem of sampling error in BOTs. It is interesting to know whether a gynaecologic oncologist will perform a second procedure in cases of invasive cancer as the final pathological result to complete staging irrespective of histological subtype. Recently, it has been shown that the chance of positive lymph nodes in case of mucinous ovarian carcinomas is rare, making it questionable whether lymph node staging is really necessary (Kleppe et al., 2011; Moroney et al., 2018; Nasioudis et al., 2017).

The aforementioned aspects may lead to different treatment and follow-up policies, which may ultimately lead to overtreatment because of unnecessary lymph node sampling and temporary undertreatment because of lack of lymph node sampling, necessitating a second procedure. To improve this, it is important to have more detailed information about current clinical practice regarding treatment and follow-up strategies of gynaecologic oncologists dealing with BOTs. The aim of the present study was to map the gynaecologists' preferred treatment and follow-up strategy in The Netherlands, with a special interest in the preferred staging procedure in case of both ambiguous and unambiguous BOT frozen section diagnoses, how they deal with patients with a definitive diagnosis of invasive carcinoma and initial staging according to the BOT frozen section diagnosis and whether there are differences between serous and mucinous tumours regarding these situations.

2. Methods

An anonymous electronic web-based questionnaire was developed according to the Checklist for Reporting Results of Internet *E*-Surveys (CHERRIES) guidelines (see supplementary material 1 for a completed checklist) (Eysenbach, 2004). Approval of the Ethics Review Committee was unnecessary because all items of the questionnaire were based on fictitious cases and because this was a study amongst physicians.

The questionnaire was intended for gynaecologists who perform debulking surgery and/or staging procedures with respect to ovarian tumours. Dutch hospitals are classified according to their level of specialization as general, semi-specialized, or specialized hospitals (including all University hospitals). Since 2012, surgical care for ovarian cancer is centralized in the Netherlands, and staging and debulking

surgery is solely executed in hospitals that perform a minimum of 20 debulking surgeries annually. These are semi-specialized or specialized hospitals, and the distinction between the two types of hospitals is defined by the employment of gynaecological oncologists. Following a two-year fellowship in gynaecologic oncology, the Dutch Society of Gynaecologic Oncology can certify members as gynaecological oncologists. In semi-specialized hospitals, gynaecological oncologists participate in each debulking surgery together with semi-specialized gynaecologists. In order to reach out to gynaecologists who perform staging procedures, the questionnaire was sent by email to all gynaecologists who are a member of the Working Party on Oncologic Gynaecology, which is part of the Dutch Association of Obstetrics and Gynaecology (<http://www.nvog.nl>) ($n = 251$).

Of these 251 gynaecologists, 59 are a gynaecologic oncologist and 10 are gynaecologic oncologist in training. The remainder are semi-specialized or general gynaecologists, the latter being gynaecologists with an interest in gynaecological oncology, but who do not fit in any of the foregoing professional profiles.

All authors were involved in compiling and testing the questionnaire, which consisted of a maximum of 27 items (see supplementary material 2) concerning staging procedures in case of BOTs. It was taken into account that a considerable number of possible respondents do not perform ovarian surgery with frozen section analysis, but might have done so in the past. In those cases, the questionnaire was completed after the 4th question. The first part consisted of general questions (e.g., the gynaecologist's gender, professional function), the second and third part were aimed at the surgical strategy in case of sBOTs or mBOTs, respectively. The last two parts of the survey involved questions with respect to the follow-up of sBOTs and mBOTs, respectively. All questions were multiple choice, and it was possible to specify the answer for some questions.

Invitation emails with a personal link to start the survey were sent in July of 2017. Reminders were sent after 4 and 8 weeks (only to gynaecologists who had not responded) and the system was closed after 12 weeks. Once the questionnaire was completed, it was closed and could not be accessed again. All answers were stored in the survey system automatically, and after exporting, the data were analysed with SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.).

3. Results

The survey was started by 48 gynaecologists and completed by 45. Only the completed questionnaires were included. Of these 45 responders, 22 were a gynaecologic oncologist (48.9%), 22 were a semi-specialized or general gynaecologist (48.9%) and one was a fellow in gynaecologic oncology (2.2%). So, over one third (37.7.3%) of the gynaecologic oncologists responded to the questionnaire. Table 1 shows the respondents' baseline characteristics. Six respondents did not perform surgical procedures (anymore). Their questionnaire was completed after the fourth question (because further questions were not applicable to them), and only the remaining respondents ($n = 39$) were included in further analyses.

In cases of unambiguous sBOT and mBOT frozen section diagnoses, about half of the respondents ($n = 16$, 41.0%) would not collect abdominal (rinsing) fluid for cytology, neither perform an infracolic omentectomy or omental biopsy, nor collect multiple peritoneal biopsies (no staging procedure). Two gynaecologists (5.1%) would only collect abdominal (rinsing) fluid for cytology with respect to both histological types, and one collects abdominal (rinsing) fluid for cytology and collects a biopsy of the omentum in case of an unambiguous sBOT frozen section diagnosis. In case of mBOTs, an appendectomy was considered a standard procedure within the staging procedure by two thirds of the respondents, and the remaining respondents would only remove the appendix when the macroscopic appearance is abnormal.

In case of ambiguous sBOT frozen section diagnoses, the number of

Table 1
Respondents' baseline characteristics.

What is your gender?	n (%)
• Male	24 (53.3)
• Female	21 (46.7)
How long are you working as a gynaecologist?	Mean ± SD
• Overall	16.2 ± 8.8
• Male	19.9 ± 8.8
• Female	12.1 ± 6.9
What is your professional function?	n (%)
• Gynaecologist with semi-specialization in gynaecologic oncology.	22 (48.9)
• Gynaecologic oncologist.	22 (48.9)
• Fellow gynaecologic oncology.	1 (2.2)
How many hours do you spend on gynaecologic oncologic surgery, including surgery with frozen section analysis, each week?	n (%)
• I do not participate in surgical procedures anymore, or it only concerns surgical procedures other than ovarian surgery (with frozen section analysis).	6 (13.3)
• 0–5	13 (28.9)
• 5–10	13 (28.9)
• 10–15	9 (20.0)
• 15–20	3 (6.7)
• ≥20	1 (2.2)
How many patients do you diagnose with a BOT each year (n = 39)?	n (%)
• 0–5	12 (30.8)
• 5–10	19 (48.7)
• 10–15	5 (12.8)
• 15–20	2 (5.1)
• ≥20	1 (2.6)

respondents who would perform a staging procedure substantially increased (from 51.3% to 87.2%), and the majority (56.4%) also would include a lymph node sampling as part of the staging procedure. In addition, in case of an ambiguous mBOT frozen section diagnosis the majority of respondents would perform a staging procedure (87.2%), but a minority (30.8%) would include lymph node sampling as part of the staging procedure (see Table 2). A relaparotomy or relaparoscopy to complete the staging procedure with a lymph node sampling, in case of a definite diagnosis of an assumed FIGO stage I invasive carcinoma (e.g., discordant frozen section diagnosis), would be performed by all but one respondent in case of a serous tumour (97.4%) and by almost half of the respondents in case of a mucinous tumour (48.7%). With respect to lymph node sampling in case of both serous and mucinous tumours, the majority of respondents would perform a bilateral pelvic and high para-aortic/paracaval lymph node sampling and prefers removal of at least 10 lymph nodes (see Table 3).

Follow-up visitations of patients with a FIGO stage I BOT are considered unnecessary by more than half of the respondents with respect to both serous and mucinous tumours. Some gynaecologists would only offer follow-up according to patient preference, and a small number would offer follow-up at their own initiative (see Table 4). With respect to extra-ovarian disease, all gynaecologists offer follow-up visitations in case of invasive implants/extra-ovarian LGCS and almost half of them would already offer follow-up in case of non-invasive implants. Regarding follow-up of FIGO stage I sBOTs (n = 14), almost half of the respondents would offer follow-up visitations according to a schedule that is common in case of epithelial ovarian carcinoma. The remaining respondents apply a different follow-up scheme, for instance follow-up visitations every six months (n = 5) or yearly (n = 2), where some indicate that this usually is not as long as is common for ovarian carcinoma (e.g., 2 years). The applied follow-up schedules in case of mBOTs (n = 12) are comparable to those in case of sBOTs (see Table 4). The majority of respondents consider anamnesis, transvaginal/–abdominal ultrasound and gynaecologic examination (vaginal examination with or without speculum) as standard procedures during follow-up visitations of patients with a BOT. Approximately half of the respondents routinely checks serum Ca-125 levels.

Table 2
Extent of the staging procedures performed by the respondents with respect to unambiguous and ambiguous frozen section diagnoses in case of a serous or mucinous ovarian tumour (n = 39).

	Serous tumour		Mucinous tumour	
	Unambiguous BOT frozen section diagnosis	Ambiguous BOT frozen section diagnosis	Unambiguous BOT frozen section diagnosis	Ambiguous BOT frozen section diagnosis
What kind of staging procedure do you perform during an exploratory laparotomy in case of an ovarian tumour, when no further abnormalities are seen during inspection of the abdominal cavity?	n (%)	n (%)	n (%)	n (%)
• No staging procedure.	16 (41.0)	5 (12.8)	16 (41.0)	5 (12.8)
• Infracolic omentectomy (or collection omental biopsies) and collection of ascitic fluid and peritoneal biopsies (standard BOT staging procedure).	20 (51.3)	12 (30.8)	21 (53.8)	22 (56.4)
• Ovarian carcinoma staging procedure (infracolic omentectomy, peritoneal biopsies, lymph node sampling).	0 (0.0)	22 (56.4)	0 (0.0)	12 (30.8)
• Otherwise, ...	3 (7.7%)	0 (0.0)	2 (5.1)	0 (0.0)

Table 3

Anatomical sites of lymph node sampling and the preferred number of removed lymph nodes in case of a serous or mucinous ovarian tumour with a questionable perioperative BOT frozen section diagnosis or in case of a relaparotomy or relaparoscopy after diagnosis of invasive carcinoma with a standard BOT staging procedure during initial surgery.

	Serous tumour		Mucinous tumour	
	Questionable BOT frozen section diagnosis (n = 22)	Second surgery after diagnosis of invasive carcinoma (n = 38)	Questionable BOT frozen section diagnosis (n = 12)	Second surgery after diagnosis of invasive carcinoma (n = 19)
At which locations do you perform the lymph node sampling?	n (%)	n (%)	n (%)	n (%)
• Ipsilateral in the pelvic region.	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)
• Bilateral in the pelvic region.	1 (4.5)	1 (2.6)	1 (8.3)	2 (10.5)
• Ipsilateral in the pelvic region and high para-aortic/paracaval.	3 (13.6)	5 (13.2)	2 (16.7)	1 (5.3)
• Bilateral in the pelvic region and high para-aortic/paracaval.	18 (81.8)	32 (84.2)	8 (66.7)	16 (84.2)
• Only high para-aortic/paracaval.	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
What is the preferred number of removed lymph nodes?	n (%)	n (%)	n (%)	n (%)
• No minimum number.	4 (18.2)	4 (10.5)	2 (16.7)	2 (10.5)
• 10	16 (72.7)	28 (73.7)	9 (75.0)	16 (84.2)
• 20	2 (9.1)	6 (15.8)	1 (8.3)	1 (5.3)

Table 4

Respondents' follow-up strategies in case of BOTs.

	Serous	Mucinous
Follow-up of a FIGO stage I BOT is considered unnecessary by the Dutch guideline. Do you agree (n = 39)?	n (%)	n (%)
• Yes, I will not offer follow-up visits (except one postoperative check).	25 (64.1)	27 (69.2)
• Yes, I will not offer follow-up unless the patient prefers this.	9 (23.1)	8 (20.5)
• No, I will offer follow-up on my own initiative.	5 (12.8)	4 (10.3)
Which follow-up schedule would you apply in case you would offer follow-up in patients with a FIGO stage I sBOT (n = 14) or mBOT (n = 12)?	n (%)	n (%)
• A follow-up schedule as is common for epithelial ovarian carcinoma.	6 (42.9)	4 (33.3)
• Otherwise, ...	8 (57.1)	8 (66.7)
In case you would not offer follow-up visitation in case of a FIGO stage I BOT, would you do this in case of extra-ovarian disease in the omentum or other peritoneal surfaces (n = 39)?	n (%)	n (%)
• Not applicable, I would offer follow-up visitations anyway.	4 (10.3)	Not applicable
• Yes, in that case I would offer follow-up visitations.	17 (43.6)	
• Yes, but only but only if it concerns invasive implants.	18 (46.2)	
• No, I would still not offer follow-up visitations.	0 (0)	
During a follow-up visitation of an sBOT (n = 14) or mBOT (n = 12) I consider the following procedures as standard:	n (%)	n (%)
• Anamnesis	14 (100)	12 (100)
• Transvaginal/– abdominal ultrasound	13 (92.9)	11 (91.7)
• Gynaecologic examination (vaginal examination with or without speculum)	10 (71.4)	9 (75)
• Serum Ca-125 levels	8 (57.1)	5 (41.7)
• Additional imaging studies	1 (7.1)	0 (0)
• Cytological examination of the vaginal vault	0 (0)	0 (0)

4. Discussion

In daily practice, several factors, such as the limited consequences of staging procedures in BOTs, differences in clinicopathological behaviour between the histological types, the possibility of discordance between frozen section and definite diagnosis and an ambiguous perioperative frozen section diagnosis may lead to differences between gynaecologists' treatment and follow-up strategies, which may ultimately lead to over- and undertreatment. To be able to minimize this possible over- and undertreatment, it was considered useful to gain more knowledge about current practice and opinions regarding treatment and follow-up strategies pertaining to BOTs. The current questionnaire-based study is the first to provide insight into the Dutch gynaecologists' surgical strategy related to BOTs based on frozen section diagnoses. Furthermore, the questionnaire mapped whether the respondents offer follow-up visits to their patients and if so, what diagnostic tools are used to screen for a recurrence.

In case of a straightforward sBOT and mBOT frozen section diagnosis, approximately half of the respondents would perform a staging procedure, which is significantly less than the 97% reported by Menzin et al. (2000). This may be explained by the fact that later research has

shown that upstaging may predict a worse prognosis, but does not have any influence on further treatment strategies and survival rates (Morice et al., 2003; Trope et al., 1993; Fauvet et al., 2004; Camatte et al., 2004; Menzin et al., 2000; Kristensen et al., 2014; Vasconcelos et al., 2015a; Vasconcelos et al., 2015b). When the results of frozen section analyses are not straightforward and might tend towards the diagnosis of serous invasive carcinoma, the number of respondents that would perform a complete staging procedure substantially increased, and more than half of the respondents would even perform a staging procedure as recommended in case of invasive ovarian carcinoma, which includes a lymph node sampling. Apparently, those respondents assume that the risk for an invasive carcinoma and the subsequent need for a second procedure (no lymph node sampling during initial surgery) outweighs the chance for overtreatment (unnecessary lymph node sampling during the first procedure) in cases where BOT is the definite diagnosis. A contributing factor to this strategy may be the aforementioned probability of discordance between the frozen section analysis (BOT) and definite diagnosis (invasive carcinoma) in 10–17% of the patients (Pongsuwareeyakul et al., 2012; Bozdog et al., 2016; Ayhan et al., 2016). In addition, in case of an ambiguous frozen section diagnosis, tending towards the diagnosis of mucinous invasive carcinoma, the

number of respondents that would perform a complete BOT staging procedure substantially increases. However, in contrast to serous tumours, only a minority would include a lymph node sampling as part of the staging procedure (30.8% versus 56.4%). The same is true for the number of respondents that would perform a relaparotomy or laparoscopy to complete the surgical staging with a lymph node sampling in case of patients in whom a BOT frozen section result was changed to an invasive carcinoma (48.7% and 97.4% in mucinous and serous tumours, respectively). The more aggressive strategy in case of serous ovarian tumours is most likely because of the fact that serous ovarian carcinomas have a significantly higher chance of occult lymph node metastases and because adjuvant chemotherapy is more beneficial when compared to mucinous ovarian carcinomas (Kleppe et al., 2011; Ayhan et al., 2005; Schmeler et al., 2010; Prat, 2012a; Prat, 2012b; Ricci et al., 2018).

Despite the fact that bilateral pelvic, and high para-aortic/paracaval lymph node sampling is recommended, some respondents (+/– 20%) indicated that they would perform a less extensive sampling [only (ipsilateral) pelvic lymph node sampling or ipsilateral pelvic with high para-aortic/paracaval sampling], without major differences with respect to both histological subtypes (Pereira et al., 2007; Cass et al., 2001; *UpToDate: Cancer of the ovary, fallopian tube, and peritoneum: Staging and initial surgical management*, n.d.). Concerning the minimum number of removed lymph nodes, the majority of respondents prefer removal of at least 10 lymph nodes, which is also recommended by the Dutch guideline and some previous reports (Chan et al., 2007; Carnino et al., 1997). However, some of the respondents advocate removal of at least 20 lymph nodes, probably because the 5-year survival rate seems to improve in those cases (Kleppe et al., 2016).

With regard to follow-up of BOTs in case of a bilateral salpingo-oophorectomy (BSO), approximately two thirds of the respondents report that follow-up visits in those cases (without extra-ovarian disease) are irrational because of the high disease free and overall survival rates of BOTs (Trimble et al., 2002; Karlsen et al., 2016). In contrast, all of the respondents offer follow-up visits in case of invasive extra-ovarian disease. However, the respondents offering follow-up apply different schedules with respect to the frequency and duration of follow-up. Some respondents advocate applying ovarian cancer post-treatment surveillance guidelines to patients with BOTs (with or without extra-ovarian disease), which is not in agreement with the Dutch guideline but which is recommended by others (*UpToDate: Borderline ovarian tumors*, n.d.; Cadron et al., 2007; Zanetta et al., 2001a). With respect to the procedures performed during follow-up visits regarding BOTs after a BSO, the majority of respondents would perform a clinical examination and vaginal ultrasound examination (Zanetta et al., 2001b; Testa et al., 2012; Fischerova, 2011). Furthermore, approximately half of the respondents determines serum Ca-125 levels, which is recommended by some authors. However, serum Ca-125 are less often elevated in case of sBOTs, when compared to serous carcinomas, and they are rarely elevated in mBOTs (Cadron et al., 2007; Zanetta et al., 2001b; Fischerova et al., 2012; Messalli et al., 2013).

Our study has several limitations. First of all, the questionnaire was designed and tested only by the author panel. There was no validation of the survey by a pilot study because of the small size of the target population, which made it impossible to adjust and improve the content of the questionnaire after initial testing. However, it is questionable whether these limitations affected the outcomes. Another limitation of this study was the moderate response rate. To reach out to gynaecologists involved in ovarian surgery with perioperative frozen section analysis, the questionnaire was sent to a large group of potential respondents (all gynaecologist members of the Dutch Working Party on Oncologic Gynaecology). It is known that invitations to such questionnaires are frequently declined because of a lack of time, interest or knowledge. Nevertheless, over one third of the gynaecologic oncologists who should perform or supervise all ovarian surgery with frozen section analysis completed the survey, which is sufficient to gain insight

into the current daily practice with respect to BOTs. On the other hand, gynaecologic oncologists, who are involved in all procedures, might have biased the answers of the remaining respondents (semi-specialized gynaecologists or fellow gynaecologic oncology).

In conclusion, it can be stated that different treatment strategies are applied by the Dutch gynaecologists involved in ovarian surgery with perioperative frozen section analysis. It should be noted that approximately half of the gynaecologists do not perform a staging procedure in case of BOTs, while the number decreases in case of an ambiguous frozen section result. Furthermore, a considerable number of gynaecologists would perform a staging procedure including a lymph node sampling in case of an ambiguous BOT frozen section diagnosis, especially in case of serous tumours. In addition, nearly all gynaecologists would perform a relaparotomy or laparoscopy to perform a lymph node sampling in case of a presumed FIGO stage I serous invasive carcinoma after a BOT frozen section diagnosis, which applies to only half of the gynaecologists in case of a mucinous carcinoma. Lymph node sampling is performed in the recommended regions by the majority of gynaecologists, but some prefer a less extensive sampling, which is also true for the minimum number of removed lymph nodes. Last but not least, the follow-up strategy varies considerably amongst gynaecologists, especially with respect to the duration and frequency of follow-up and also with regard to what diagnostic tools are used. Future studies should focus on whether the aforementioned differences with respect to treatment and follow-up policies regarding BOTs have any consequences for patient outcomes.

Conflict of interest statement

All of the authors of this manuscript certify that there are no conflicts of interest.

Author contribution section

All authors were involved in compiling the questionnaire. Data was collected and analysed by Koen De Decker. The manuscript was also compiled with the help of all authors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.gore.2018.12.004>.

References

- Akeson, M., Zetterqvist, B.M., Dahllof, K., Jakobsen, A.M., Brannstrom, M., Horvath, G., 2008. Population-based cohort follow-up study of all patients operated for borderline ovarian tumor in western Sweden during an 11-year period. *Int. J. Gynecol. Cancer* 18, 453–459.
- Ayhan, A., Gultekin, M., Taskiran, C., Celik, N.Y., Usubutun, A., Kucukali, T., et al., 2005 May. Lymphatic metastasis in epithelial ovarian carcinoma with respect to clinicopathological variables. *Gynecol. Oncol.* 97, 400–404.
- Ayhan, A., Ozler, A., Dursun, P., Haberal, A.N., 2016 Nov. Potential role of increasing number of sections in frozen section diagnosis of ovarian tumors. *J. Exp. Ther. Oncol.* 11, 245–250.
- Bozdog, H., Guzin, K., Gocmen, A., Kabaca, S., Usta, A., Akdeniz Duran, E., 2016 Jul. The diagnostic value of frozen section for borderline ovarian tumours. *J. Obstet. Gynaecol.* 36, 626–630.
- Cadron, I., Leunen, K., Gorp, T.V., Amant, F., Neven, P., Vergote, I., 2007. Management of borderline ovarian neoplasms. *Curr. Opin. Oncol.* 25, 2928–2937.
- Camatte, S., Morice, P., Thoury, A., Fourchette, V., Pautier, P., Lhomme, C., et al., 2004. Impact of surgical staging in patients with macroscopic stage I ovarian borderline tumours: analysis of a continuous series of 101 cases. *Eur. J. Cancer* 40, 1842–1849 Oxford, England: 1990.
- Carnino, F., Fuda, G., Ciccone, G., Iskra, L., Guercio, E., Dadone, D., et al., 1997 Jun. Significance of lymph node sampling in epithelial carcinoma of the ovary. *Gynecol. Oncol.* 65, 467–472.
- Cass, I., Li, A.J., Runowicz, C.D., Fields, A.L., Goldberg, G.L., Leuchter, R.S., et al., 2001 Jan. Pattern of lymph node metastases in clinically unilateral stage I invasive epithelial ovarian carcinomas. *Gynecol. Oncol.* 80, 56–61.
- Chan, J.K., Munro, E.G., Cheung, M.K., Husain, A., Teng, N.N., Berek, J.S., et al., 2007 Jan. Association of lymphadenectomy and survival in stage I ovarian cancer patients.

- Obstet. Gynecol. 109, 12–19.
- De Decker, K., Speth, S., Ter Brugge, H.G., Bart, J., Massuger, L.F.A.G., Kleppe, M., et al., 2017 Feb. Staging procedures in patients with mucinous borderline tumors of the ovary do not reveal peritoneal or omental disease. *Gynecol. Oncol.* 144, 285–289.
- Eysenbach, G., 2004 Sep 29. Improving the quality of Web surveys: the checklist for reporting results of internet E-surveys (CHERRIES). *J. Med. Internet Res.* 6, e34.
- Fauvet, R., Boccara, J., Dufournet, C., David-Montefiore, E., Poncelet, C., Darai, E., 2004. Restaging surgery for women with borderline ovarian tumors: results of a French multicenter study. *Cancer* 100, 1145–1151.
- Fischerova, D., 2011 Sep. Ultrasound scanning of the pelvis and abdomen for staging of gynecological tumors: a review. *Ultrasound Obstet. Gynecol.* 38, 246–266.
- Fischerova, D., Zikan, M., Dunder, P., Cibula, D., 2012. Diagnosis, treatment, and follow-up of borderline ovarian tumors. *Oncologist* 17, 1515–1533.
- Hart, W.R., 2005. Mucinous tumors of the ovary: a review. *Int. J. Gynecol. Pathol.* 24, 4–25.
- Karlsen, N.M., Karlsen, M.A., Hogdall, E., Nedergaard, L., Christensen, I.J., Hogdall, C., 2016 Jul. Relapse and disease specific survival in 1143 Danish women diagnosed with borderline ovarian tumours (BOT). *Gynecol. Oncol.* 142, 50–53.
- Kleppe, M., Wang, T., Van Gorp, T., Slangen, B.F., Kruse, A.J., Kruitwagen, R.F., 2011 Dec. Lymph node metastasis in stages I and II ovarian cancer: a review. *Gynecol. Oncol.* 123, 610–614.
- Kleppe, M., van der Aa, M.A., Van Gorp, T., Slangen, B.F., Kruitwagen, R.F., 2016 Oct. The impact of lymph node dissection and adjuvant chemotherapy on survival: a nationwide cohort study of patients with clinical early-stage ovarian cancer. *Eur. J. Cancer* 66, 83–90.
- Kristensen, G.S., Schledermann, D., Mogensen, O., Jochumsen, K.M., 2014. The value of random biopsies, omentectomy, and hysterectomy in operations for borderline ovarian tumors. *Int. J. Gynecol. Cancer* 24, 874–879.
- Kurman, Robert J., International Agency for Research on Cancer, 2014. WHO classification of tumours of female reproductive organs. IARC, Lyon.
- Menzin, A.W., Gal, D., Lovecchio, J.L., 2000. Contemporary surgical management of borderline ovarian tumors: a survey of the Society of Gynecologic Oncologists. *Gynecol. Oncol.* 78, 7–9.
- Messalli, E.M., Grauso, F., Balbi, G., Napolitano, A., Seguino, E., Torella, M., 2013 Mar. Borderline ovarian tumors: features and controversial aspects. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 167, 86–89.
- Morice, P., Camatte, S., Rey, A., Atallah, D., Lhomme, C., Pautier, P., et al., 2003 Apr. Prognostic factors for patients with advanced stage serous borderline tumours of the ovary. *Ann. Oncol.* 14, 592–598.
- Morice, P., Uzan, C., Fauvet, R., Gouy, S., Duvillard, P., Darai, E., 2012. Borderline ovarian tumour: pathological diagnostic dilemma and risk factors for invasive or lethal recurrence. *Lancet. Oncol.* 13, 103.
- Moroney, M.R., Post, M.D., Berning, A.A., Sheeder, J., Corr, B.R., 2018 Jan. An Evaluation of Frozen Section and Lymph Node Dissection results for Mucinous Ovarian Tumors. *Int. J. Gynecol. Cancer* 28, 92–98.
- Nasioudis, D., Chapman-Davis, E., Witkin, S.S., Holcomb, K., 2017 Feb. Prognostic significance of lymphadenectomy and prevalence of lymph node metastasis in clinically apparent stage I endometrioid and mucinous ovarian carcinoma. *Gynecol. Oncol.* 144, 414–419.
- Pereira, A., Magrina, J.F., Rey, V., Cortes, M., Magtibay, P.M., 2007 Jun. Pelvic and aortic lymph node metastasis in epithelial ovarian cancer. *Gynecol. Oncol.* 105, 604–608.
- Pongsuwareeyakul, T., Khunamornpong, S., Settakorn, J., Sukpan, K., Suprasert, P., Siriaunkgul, S., 2012. Accuracy of frozen-section diagnosis of ovarian mucinous tumors. *Int. J. Gynecol. Cancer* 22, 400–406.
- Prat, J., 2012 Mar. Ovarian carcinomas: five distinct diseases with different origins, genetic alterations, and clinicopathological features. *Virchows Arch.* 460, 237–249.
- Prat, J., 2012 Sepb. New insights into ovarian cancer pathology. *Ann. Oncol.* 23 (Suppl. 10), x111–x117.
- Ricci, F., Affatato, R., Carrassa, L., Damia, G., 2018 May 24. Recent insights into mucinous ovarian carcinoma. *Int. J. Mol. Sci.* 19. <https://doi.org/10.3390/ijms19061569>.
- Schmeler, K.M., Tao, X., Frumovitz, M., Deavers, M.T., Sun, C.C., Sood, A.K., et al., 2010 Aug. Prevalence of lymph node metastasis in primary mucinous carcinoma of the ovary. *Obstet. Gynecol.* 116, 269–273.
- Sherman, M.E., Mink, P.J., Curtis, R., Cote, T.R., Brooks, S., Hartge, P., et al., 2004 Mar 1. Survival among women with borderline ovarian tumors and ovarian carcinoma: a population-based analysis. *Cancer* 100, 1045–1052.
- Testa, A.C., Ludovisi, M., Mascilini, F., Di Legge, A., Malaggesse, M., Fagotti, A., et al., 2012 Jan. Ultrasound evaluation of intra-abdominal sites of disease to predict likelihood of suboptimal cytoreduction in advanced ovarian cancer: a prospective study. *Ultrasound Obstet. Gynecol.* 39, 99–105.
- Trimble, C.L., Kosary, C., Trimble, E.L., 2002 Jul. Long-term survival and patterns of care in women with ovarian tumors of low malignant potential. *Gynecol. Oncol.* 86, 34–37.
- Trope, C., Kaern, J., Vergote, I.B., Kristensen, G., Abeler, V., 1993. Are borderline tumors of the ovary overtreated both surgically and systemically? A review of four prospective randomized trials including 253 patients with borderline tumors. *Gynecol. Oncol.* 51, 236–243.
- UpToDate: Borderline ovarian tumors. (https://www.uptodate.com/contents/borderline-ovarian-tumors?search=Borderline+ovarian+tumors&source=search_result&selectedTitle=1~17).
- UpToDate: Cancer of the ovary, fallopian tube, and peritoneum: Staging and initial surgical management. (https://www.uptodate.com/contents/cancer-of-the-ovary-fallopian-tube-and-peritoneum-staging-and-initial-surgical-management?search=Cancer+of+the+ovary%2C+fallopian+tube%2C+and+peritoneum%3A+Staging+and+initial+surgical+management&source=search_result&selectedTitle=1%7E150).
- Vasconcelos, I., Olschewski, J., Braicu, I., Sehouli, J., 2015 Feba. A meta-analysis on the impact of platinum-based adjuvant treatment on the outcome of borderline ovarian tumors with invasive implants. *Oncologist* 20, 151–158.
- Vasconcelos, I., Olschewski, J., Braicu, I., Sehouli, J., 2015 Marb. Limited efficacy of platinum-based adjuvant treatment on the outcome of borderline ovarian tumors. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 186, 26–33.
- Werkgroep Oncologische Gynaecologie (WOG). Borderline ovariumtumoren, <http://www.oncoline.nl/borderline-ovariumtumoren>; (2010-03-22 [accessed 2015-12-15]).
- Yokoyama, Y., Moriya, T., Takano, T., Shoji, T., Takahashi, O., Nakahara, K., et al., 2006. Clinical outcome and risk factors for recurrence in borderline ovarian tumours. *Br. J. Cancer* 94, 1586–1591.
- Zanetta, G., Rota, S., Chiari, S., Bonazzi, C., Bratina, G., Mangioni, C., 2001a. Behavior of borderline tumors with particular interest to persistence, recurrence, and progression to invasive carcinoma: a prospective study. *J. Clin. Oncol.* 19, 2658–2664.
- Zanetta, G., Rota, S., Lissoni, A., Meni, A., Brancatelli, G., Buda, A., 2001 Aprb. Ultrasound, physical examination, and CA 125 measurement for the detection of recurrence after conservative surgery for early borderline ovarian tumors. *Gynecol. Oncol.* 81, 63–66.