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Outcomes of patients with early stage mucinous ovarian carcinoma

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Outcomes of patients with early stage mucinous ovarian carcinoma: a Dutch population-based cohort study comparing expansile and infiltrative subtypes

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ABSTRACT

Objective This study aimed to assess the outcomes of patients with early stage mucinous ovarian carcinoma based on subtype (expansile vs infiltrative).

Methods We retrospectively analyzed all surgically treated patients with mucinous ovarian carcinoma in the Netherlands (2015–2020), using data from national registries. Subtypes were determined, with any ambiguities resolved by a dedicated gynecologic pathologist. Patients with International Federation of Gynecology and Obstetrics (FIGO) stage I were categorized into full staging, fertility-sparing, or partial stagings. Outcomes were overall survival and recurrence free survival, and recurrence rates.

Results Among 409 identified patients, 257 (63%) had expansile and 152 (37%) had infiltrative tumors. Patients with expansile tumors had FIGO stage I more frequently (n=243, 95% vs n=116, 76%, p<0.001). For FIGO stage I disease, patients with expansile and infiltrative tumors underwent similar proportions of partial (n=165, 68% vs n=78, 67%), full (n=32, 13% vs n=23, 20%), and fertility-sparing stagings (n=46, 19% vs n=15, 13%) (p=0.139). Patients with expansile FIGO stage I received less adjuvant chemotherapy (n=11, 5% vs n=24, 21%, p<0.001), exhibited better overall and recurrence free survival (p=0.006, p=0.012), and fewer recurrences (n=13, 5% vs n=16, 14%, p=0.011). Survival and recurrence rates were similar across the expansile extent of staging groups. Patients undergoing fertility-sparing staging for infiltrative tumors had more recurrences compared with full or partial stagings, while recurrence free survival was similar across these groups. Full staging correlated with better overall survival in infiltrative FIGO stage I (p=0.022).

Conclusions While most patients with FIGO stage I underwent partial staging, those with expansile had better outcomes than those with infiltrative tumors. Full staging was associated with improved overall survival in infiltrative, but not in expansile FIGO stage I. These results provide insight for tailored surgical approaches.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Mucinous ovarian carcinomas are categorized into expansile and infiltrative subtypes, with different characteristics and prognoses.
⇒ The current literature lacks sufficient clinical data supporting performing staging surgeries in both subtypes of early stage mucinous ovarian carcinoma.

WHAT THIS STUDY ADDS

⇒ This study describes the largest cohort of patients with early stage mucinous ovarian carcinoma to date, classifying them based on expansile vs infiltrative subtype and differentiating outcomes according to surgical approaches (full, fertility-sparing, or partial staging).
⇒ A minority of International Federation of Gynecology and Obstetrics (FIGO) stage I patients underwent full staging, with better outcomes observed in expansile cases.
⇒ In the infiltrative cohort, improved overall survival was observed in patients who underwent full staging compared with partial and fertility-sparing staging.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Additional staging surgeries after the initial bilateral salpingo-oophorectomy for expansile mucinous ovarian carcinoma may be omitted, while full staging is preferable for early stage infiltrative tumors.
⇒ Caution is warranted when considering fertility-sparing surgery for early stage infiltrative mucinous ovarian carcinoma.

INTRODUCTION

Mucinous ovarian carcinomas account for approximately 3% of all epithelial ovarian carcinomas.[1–6] Patients with mucinous ovarian carcinoma often present with early stage disease, presumably because these patients usually have large primary tumors that cause abdominal symptoms at an early stage.[6–17] In 2000, Lee and Scully[9] were the first to describe two subtypes of mucinous ovarian carcinoma: expansile and infiltrative subtypes. Eventually, in 2014, the WHO introduced this subdivision as the official diagnostic classification of mucinous ovarian carcinoma.[18] The expansile and infiltrative subtypes have different characteristics and prognoses.[6–17] The expansile subtype is characterized by a confluent glandular growth pattern, with minimal or no stromal invasion, and minimal normal ovarian tissue in between.[6] In

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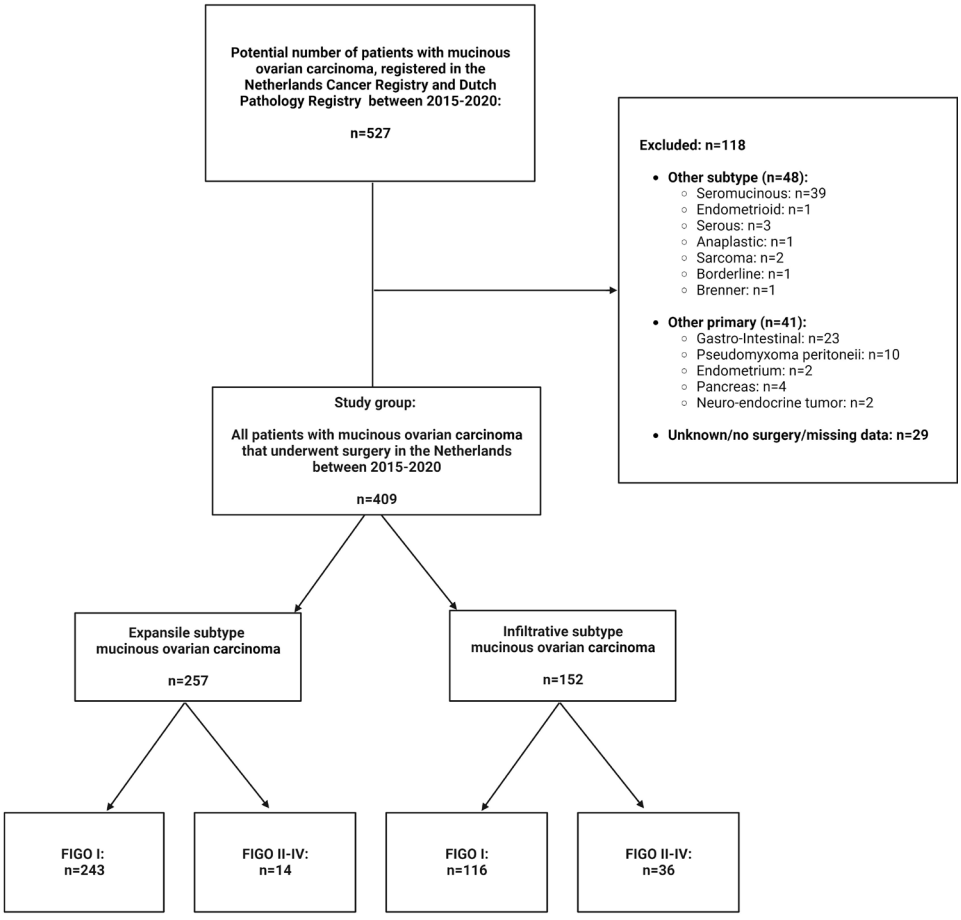

Figure 1 Patient selection flowchart. FIGO, International Federation of Gynecology and Obstetrics.

contrast, the infiltrative subtype is characterized by distinct signs of destructive invasion into the stroma caused by malignant glands, cell nests, or individual cells, and is often associated with desmoplastic stromal reaction.[6]

Patients with the infiltrative subtype, compared with the expansile subtype, more frequently present with advanced stage, have a higher occurrence of lymph node metastases, experience upstaging more frequently during staging procedures in early stage disease, and have poorer outcomes (poorer survival and higher recurrence rates).[6 7 15] Surgical treatment for early stage mucinous ovarian carcinoma includes bilateral salpingo-oophorectomy, hysterectomy, and peritoneal staging (including washings, biopsies, and omentectomy) for both subtypes. However, the occurrence of peritoneal metastases is rare, especially in patients with the expansile subtype.[6 7 19–24] The main purpose of these staging surgeries is to tailor adjuvant treatment (chemotherapy). Patients with the infiltrative subtype often undergo pelvic and para-aortic lymph node sampling, which is usually omitted in the expansile subtype.[6 7 11 15] However, the European Society of Gynaecological Oncology recommends omitting routine lymph node staging for both subtypes if lymph nodes appear normal during surgery.[20]

The literature lacks sufficient clinical data on patients with mucinous ovarian carcinoma subdivided according to the current official classification (expansile vs infiltrative). This gap in the data poses a challenge in tailoring treatment approaches for these rare tumors. To date, the literature has described only 195 patients with expansile and 158 patients with infiltrative mucinous ovarian carcinoma.[6–14 17] Therefore, we aimed to determine whether peritoneal staging is required for both subtypes of early stage mucinous ovarian carcinoma, by comparing overall and recurrence free survival, and recurrence rates.

METHODS

Study Design

This population-based, retrospective study used data from the Dutch Pathology Registry and the Netherlands Cancer Registry. The Dutch Pathology Registry is a nationwide network and registry where all histopathology and cytopathology have been registered since 1991.[25] The Netherlands Cancer Registry contains clinical data from all patients diagnosed with cancer since 1989.[26] The Dutch Pathology Registry and the Netherlands Cancer Registry provided anonymized data.

Patient Selection and Data Analysis

All patients diagnosed with mucinous ovarian carcinoma in the Netherlands between January 1, 2015, and December 31, 2020, were retrospectively included using the Netherlands Cancer Registry. Patients diagnosed from 2015 were included because the subdivision into expansile versus infiltrative subtypes became operational after 2014. Additionally, we searched the Dutch Pathology Registry for pathology records, using the terms: 'ovarium' AND 'carcinoma' AND 'mucin' and variations thereof. Via an intermediary procedure, the pathology records were matched with the clinical records.

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Table 1 Patient and tumor characteristics of all surgically treated patients with mucinous ovarian carcinoma in the Netherlands (2015–20): expansile versus infiltrative subtypes

	Expansile subtype (n=257)	Infiltrative subtype (n=152)	Total (n=409)	P value
Age (years) (median (Q1–Q3))	54 (46–65)	59 (50–70)	56 (47–67)	0.002 (Kruskal–Wallis)
FIGO (2014) stage				<0.001 (Fisher's exact, FIGO I vs II vs III vs IV)
I	243 (94.6)	116 (76.3)	359 (87.8)	
IA	152 (59.1)	72 (47.4)	224 (54.8)	
IB	3 (1.2)	2 (1.3)	5 (1.2)	
IC	88 (34.2)	42 (27.6)	130 (31.8)	
II	6 (2.3)	7 (4.6)	13 (3.2)	
IIA	0 (0)	2 (1.3)	2 (0.5)	
IIB	6 (2.3)	5 (3.3)	11 (2.7)	
III	7 (2.7)	23 (15.1)	30 (7.3)	
IIIA	1 (0.4)	4 (2.6)	5 (1.2)	
IIIB	2 (0.8)	9 (5.9)	11 (2.7)	
IIIC	4 (1.6)	10 (6.6)	14 (3.4)	
IV	1 (0.4)	6 (3.9)	7 (1.7)	
IVA	1 (0.4)	2 (1.3)	3 (0.7)	
IVB	0 (0)	4 (2.6)	4 (1.0)	

Values are number (%) unless indicated otherwise.
FIGO, International Federation of Gynecology and Obstetrics.

The following variables obtained from the Netherlands Cancer Registry were analyzed: age, International Federation of Gynecology and Obstetrics (FIGO) stage (2014), vital status, interval to death or last follow-up, type of surgery, and whether chemotherapy was administered. Data managers of the Netherlands Cancer Registry reviewed all patient records, including information from physical examination and imaging (radiology and, if performed, endoscopy) before surgery. The dataset from the Dutch Pathology Registry consisted of all pathology records (cytology, histological biopsies, and pathological surgery reports). In the event of discrepancy between FIGO stage of the Netherlands Cancer Registry and the Dutch Pathology Registry, the FIGO stage in the pathology records was used.

Based on pathology records, patients with ovarian tumors other than the mucinous type were excluded (seromucinous carcinomas, endometrioid carcinomas, serous carcinomas, anaplastic carcinomas, sarcomas, Brenner tumors, and borderline tumors). Patients with other primary tumors and those who did not undergo surgery were also excluded.

The pathology records were analyzed to stratify patients into two groups based on the subtype: expansile versus infiltrative subtypes. In the case of ambiguity concerning the subtype, records were discussed with a dedicated gynecologic pathologist. No central review of histopathology was performed because in the Netherlands all histology of patients with ovarian carcinoma are routinely reviewed by a dedicated gynecologic pathologist in a tertiary referral hospital. Patients with tumors exhibiting both expansile and infiltrative characteristics were categorized as infiltrative because these tumors demonstrate similar biological behavior to infiltrative mucinous ovarian carcinoma.

The clinical and pathology records of patients with FIGO stage I mucinous ovarian carcinoma were extensively analyzed to categorize patients into extent of staging groups: full versus fertility-sparing versus partial staging. Full staging was defined as patients undergoing bilateral salpingo-oophorectomy, hysterectomy, peritoneal sampling (≥1 biopsies), and omentectomy, with or without resection of lymph nodes. Fertility-sparing staging was defined as the preservation of the uterus and at least one ovary, without a patient history of hysterectomy or salpingo-oophorectomy, with age <40 years at diagnosis. Other surgeries were classified as partial staging surgeries.

Outcome measures were the incidence and location of recurrences, overall survival, and recurrence free survival. Also, these outcomes were analyzed within the FIGO stage I expansile and infiltrative cohorts: full versus fertility-sparing versus partial staging. Recurrences were identified through pathological records, including only cytologically or histologically confirmed cases.

Overall survival was defined as the interval between the date of diagnosis and the date of death (from any cause) or between the date of diagnosis and the date of last follow-up for patients who were alive at the data cut-off (February 1, 2021). Similarly, recurrence free survival was defined, incorporating the date of recurrence in the analysis. Kaplan–Meier curves (log-rank tests) were used for overall survival and recurrence free survival analysis.

Statistical Analysis

Data were analyzed using RStudio V.1.4.1106 (RStudio, PBC, Boston, Massachusetts, USA, 2021). Based on group sizes, categorical data were compared using the χ^2 or Fisher's exact test, and non-parametric comparisons of non-normally distributed continuous variables were performed using the Kruskal–Wallis test. A two sided p value of <0.05 was considered statistically significant. Missing data <5.0% were excluded from the analyses.

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Table 2 Patient, tumor, and treatment characteristics of patients with early stage mucinous ovarian carcinoma (International Federation of Gynecology and Obstetrics (FIGO 2014) stage I): expansile versus infiltrative subtypes

	Expansile subtype (n=243)	Infiltrative subtype (n=116)	Total (n=359)	P value
Age (years) (median (Q1–Q3))	54 (45–64)	58 (48–69)	55 (47–65)	0.006 (Kruskal–Wallis)
FIGO (2014)				0.906 (Fisher's exact, FIGO IA vs IB vs IC)
IA	152 (62.6)	72 (61.5)	224 (62.4)	
IB	3 (1.2)	2 (1.7)	5 (1.4)	
IC (unspecified)	29 (11.9)	19 (16.4)	48 (13.3)	
IC1	35 (14.4)	14 (12.1)	49 (13.6)	
IC2	13 (5.3)	4 (3.4)	17 (4.7)	
IC3	11 (4.5%)	5 (4.3%)	16 (4.5)	
Surgical resections				Not tested
Bilateral salpingo-oophorectomy	107 (42.8)	68 (58.6)	175 (48.7)	
Unilateral salpingo-oophorectomy	130 (53.5)	47 (40.5)	177 (49.3)	
Cystectomy	6 (2.5)	1 (0.9)	7 (1.9)	
Hysterectomy	50 (20.6)	33 (28.4)	83 (23.1)	
Washings (ascites)	49 (20.2)	26 (22.4)	75 (20.9)	
Peritoneal sampling (range 1–11)	69 (28.4)	36 (31.0)	105 (29.2)	
Omentectomy	61 (25.1)	40 (34.5)	101 (28.1)	
Lymph node dissection or sampling (range 1–54)	22 (9.1)	17 (14.7)	39 (10.9)	
Type of peritoneal staging surgery				0.139 (χ^2)
Full staging with(out) lymph nodes*	32 (13.2)	23 (19.8)	55 (15.3)	
Fertility-sparing†	46 (18.9)	15 (12.9)	61 (17.0)	
Partial‡	165 (67.9)	78 (67.2)	243 (67.7)	
Adjuvant chemotherapy				<0.001 (χ^2)
No	232 (95.5)	92 (79.3)	324 (90.3)	
Yes	11 (4.5)	24 (20.7)	35 (9.7)	
Recurrent disease				0.011 (χ^2)
No	230 (94.7)	100 (86.2)	330 (91.9)	
Yes	13 (5.3)	16 (13.8)	29 (8.1)	

Values are number (%) unless indicated otherwise.
*Bilateral salpingo-oophorectomy, hysterectomy, peritoneal sampling (≥1 biopsy), and omentectomy, with or without resection of lymph nodes.
†Age <40 years at diagnosis, preservation of uterus, and at least one ovary, without a patient history of hysterectomy or salpingo-oophorectomy.
‡All other surgeries.
FIGO, International Federation of Gynecology and Obstetrics.

RESULTS

Study Group

Figure 1 shows the patient selection flowchart. A total of 527 patients from the Netherlands Cancer Registration were linked with 1354 pathology records from the Dutch Pathology Registration (diagnosis between January 1, 2015, and December 31, 2020). A total of 118 patients were excluded after a detailed examination of the pathology records (Figure 1). Ultimately, 409 surgically treated patients with mucinous ovarian carcinoma were analyzed.

Characteristics

A total of 257 patients had expansile (62.8%) and 152 had infiltrative mucinous ovarian carcinoma (37.2%) (Figure 1). Characteristics of all surgically treated patients with mucinous ovarian carcinoma are displayed in Table 1. Patients with the expansile subtype were significantly younger (median 54 vs 59 years, p=0.002) and had FIGO stage I more frequently (n=243, 94.6% vs n=116, 76.3%, p<0.001).

FIGO Stage I Mucinous Ovarian Carcinoma

Characteristics

A total of 359 patients had FIGO stage I disease (expansile n=243, 67.7% vs infiltrative n=116, 32.3%). Patient, tumor, and treatment characteristics are displayed in Table 2. Patients with expansile FIGO stage I were younger than those with infiltrative FIGO stage I (median 54 vs 58 years, p=0.006). Both groups had similar proportions of patients with FIGO stage IA, IB, and IC. A minority of patients (n=55, 15.3%) underwent full staging surgery. No significant differences were observed between expansile and infiltrative subtypes regarding the extent of surgical staging: full (n=32, 13.2% vs n=23, 19.8%), fertility-sparing (n=46, 18.9% vs n=15, 12.9%), and partial staging (n=165, 67.9% vs n=78, 67.2%) (p=0.139). Most patients

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Table 3 Patient, tumor, and treatment characteristics and outcomes of patients with early stage mucinous ovarian carcinoma (International Federation of Gynecology and Obstetrics (FIGO 2014) stage I). Full versus fertility-sparing versus partial staging, for expansile and infiltrative subtypes

	Full staging	Fertility-sparing	Partial staging	Total	P value
Expansile subtype	(n=32)	(n=46)	(n=165)	(n=243)	
Age (years) Median(Q1,Q3)	56(49–63)	30(25–33)	57(51–66)	54(45–64)	<0.001 (Kruskal-Wallis)
FIGO (2014)					0.547 (Fisher Exact)
IA	22 (68.8)	27 (58.7)	103 (62.4)	152 (62.3)	
IB	1 (3.1)	0 (0)	2 (1.2)	3 (1.2)	
IC	9 (28.1)	19 (41.3)	60 (36.4)	88 (36.5)	
Chemotherapy					0.085 (Fisher Exact)
No	28 (84.8)	45 (97.8)	159 (96.4)	232 (95.5)	
Yes	4 (12.5)	1 (2.2)	6 (3.6)	11 (4.5)	
Recurrences					0.827 (Fisher Exact)
No	31 (96.9)	43 (93.5)	156 (94.5)	230 (94.7)	
Yes	1 (3.1)	3 (6.5)	9 (5.5)	13 (5.3)	
Infiltrative subtype	(n=23)	(n=15)	(n=78)	(n=116)	
Age (years) Median(Q1,Q3)	61(56–74)	33(29–35)	60(53–70)	58(48–69)	<0.001 (Kruskal-Wallis)
FIGO (2014)					0.036 (Fisher Exact)
IA	19 (82.6)	7 (46.7)	46 (59.0)	72 (62.1)	
IB	1 (4.3)	0 (0)	1 (1.3)	2 (1.7)	
IC	3 (13.0)	8 (53.1)	31 (39.7)	42 (36.2)	
Chemotherapy					0.534 (Fisher Exact)
No	17 (73.9)	11 (73.3)	64 (82.1)	92 (79.3)	
Yes	6 (26.1)	4 (26.7)	14 (17.9)	24 (20.7)	
Recurrences					0.046 (Fisher Exact)
No	22 (95.7)	10 (66.7)	68 (87.2)	100 (85.5)	
Yes	1 (4.3)	5 (33.3)	10 (12.8)	16 (13.8)	

Values are number (%) unless indicated otherwise.
FIGO, International Federation of Gynecology and Obstetrics.

with FIGO stage I did not receive adjuvant chemotherapy (n=324, 90.3%), and patients with expansile FIGO stage I received adjuvant chemotherapy less frequently compared with those with infiltrative FIGO stage I (n=11, 4.5% vs n=24, 20.7%, p<0.001) (Table 2).

Characteristics stratified by the extent of surgical staging are displayed in Table 3 for the expansile and infiltrative subtypes. Age differed significantly across the extent of staging groups in both cohorts. FIGO stage differed significantly across the extent of staging groups in the infiltrative cohort.

Recurrences

Recurrences were seen less often after expansile FIGO stage I compared with infiltrative FIGO stage I (n=13, 5.3% vs n=16, 13.8%, p=0.011, Table 2). The characteristics and locations of the recurrences are displayed in Online Supplemental Table 1. Patients with expansile FIGO stage I had recurrences after FIGO IA (n=7 out of 152, 4.6%) and FIGO IC (n=6 out of 88, 6.8%). Patients with infiltrative FIGO stage I had recurrences after FIGO IA (n=4 out of 72, 5.6%), FIGO IC (n=12 out of 42, 28.6%).

The incidence of recurrences after the different staging surgeries are shown in Table 3 for the expansile and infiltrative subtypes. Patients with the infiltrative subtype undergoing fertility-sparing stagings experienced recurrences more often compared with patients undergoing full or partial stagings (fertility-sparing: n=5 (33.3%); full: n=1 (4.3%); partial: n=10 (12.8%); p=0.046).

Overall and Recurrence Free Survival

Patients with expansile FIGO stage I had better overall survival and recurrence free survival compared with patients with infiltrative FIGO stage I (Figure 2A, p=0.006, Figure 2B, p=0.012). Median follow-up time was 999 days.

In the expansile cohort, overall survival and recurrence free survival were similar between the extent of staging groups (Figure 2C, p=0.770, Figure 2D, p=0.950). Median follow-up time was 1020 days (expansile cohort). In the infiltrative cohort, overall survival was better for patients who underwent full surgical staging compared with fertility-sparing and partial staging (Figure 2E, p=0.022). Recurrence free survival was similar between the extent of staging groups with infiltrative FIGO stage I (Figure 2F, p=0.055). Median follow-up time was 968 days (infiltrative cohort).

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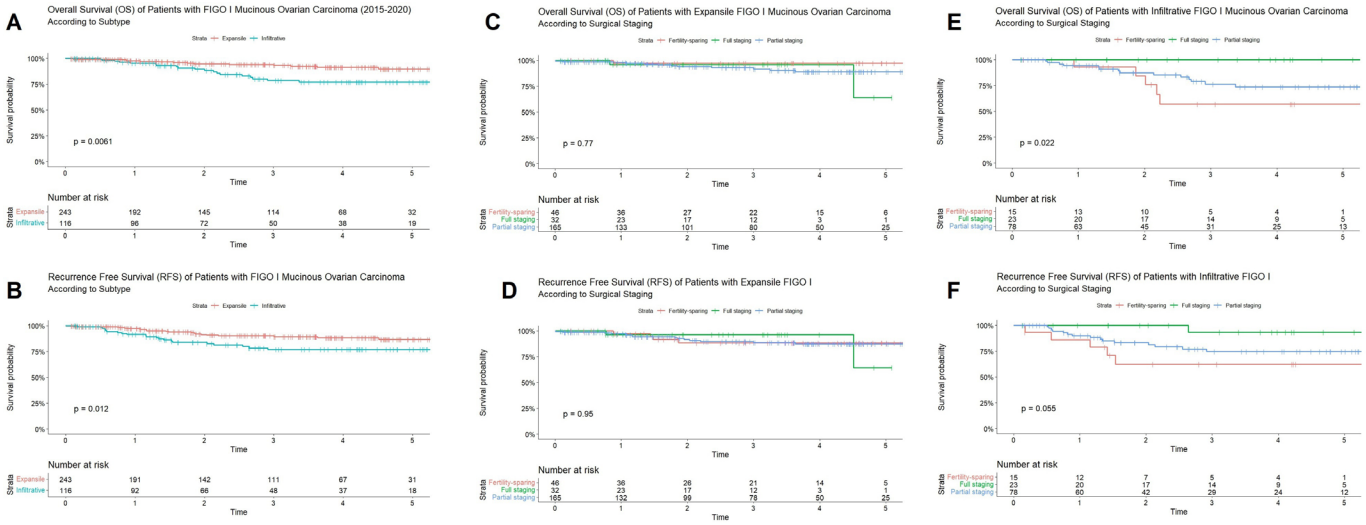

Figure 2 Kaplan–Meier estimates for overall survival (A) and recurrence free survival (B) for patients with International Federation of Gynecology and Obstetrics (FIGO) stage I mucinous ovarian carcinoma, according to subtype. Kaplan–Meier estimates for overall survival (C) and recurrence free survival (D) for patients with expansile FIGO stage I mucinous ovarian carcinoma, according to the extent of surgical staging. Kaplan–Meier estimates for overall survival (E) and recurrence free survival (F) for patients with infiltrative FIGO stage I mucinous ovarian carcinoma, according to the extent of surgical staging.

DISCUSSION

Summary of Main Results

The current data confirm the prognostic value of subdividing mucinous ovarian carcinoma into expansile and infiltrative subtypes. Only a minority of patients with FIGO stage I underwent full surgical staging. Patients with expansile FIGO stage I had better outcomes than those with infiltrative FIGO stage I. Full staging was associated with improved overall survival in infiltrative but not in expansile FIGO stage I. Moreover, patients with infiltrative tumors undergoing fertility-sparing staging experienced significantly more recurrences compared with patients undergoing full or partial staging. Outcomes were comparable across the extent of staging groups in the expansile cohort.

Results in the Context of Published Literature

Previously used classification systems, such as low-grade versus high-grade, were not specifically developed for mucinous ovarian carcinoma but have been used in other studies.[27–29] However, the grading classification system showed limited prognostic value for patients with mucinous ovarian carcinoma and was abandoned in 2014. Results from studies using the grading system cannot be combined with results comparing expansile and infiltrative subtypes, because patients with expansile tumors could have either low-grade or high-grade tumors, and patients with infiltrative tumors could also have low-grade or high-grade tumors.

Recently, Morice et al published a review of patients with mucinous ovarian carcinoma, where six studies of patients with expansile and infiltrative subtypes were analyzed.[6] Unfortunately, these six retrospective studies were limited in sample size: in total, 84 patients with expansile and 107 patients with infiltrative mucinous ovarian carcinoma were analyzed.[8 9 11–14] The results of these studies are in line with the results of our study: patients with the expansile subtype were more frequently diagnosed in the early stage and had fewer metastases and recurrences compared with patients with the infiltrative subtype.

Moreover, the abovementioned review also found that only three cases of peritoneal spread were reported in the literature in patients with expansile mucinous ovarian carcinoma, and no cases of lymph node spread or upstaging based on lymph node metastases. Our expansile data also showed a limited number of patients with peritoneal spread (expansile FIGO stages II–IV: n=13, 5%) and only one patient with expansile lymph node metastasis was observed (recurrent setting, inguinal lymph node). Furthermore, Morice et al found that 26% of patients with infiltrative mucinous ovarian carcinoma presented with an advanced stage (our study, infiltrative FIGO stages II–IV: 24%), and upstaging based on lymph node metastasis occurred in 17–30% of patients with clinical early stage infiltrative mucinous ovarian carcinoma in the Morice et al cohort. We did not calculate upstaging rates because most patients underwent incomplete stagings.

Following the review by Morice et al, two more studies have been published comparing patients with mucinous ovarian carcinoma according to subtype, with similar results.[13 17] These studies were limited by sample size and analyzed patients with early stage and advanced stage disease in one cohort. However, our results align with these studies: patients with expansile tumors had better overall and recurrence free survival compared with those with infiltrative tumors. Focusing on recurrences, Morice et al described recurrences in 7% of patients with expansile versus 34% of patients with infiltrative tumors (both early and advanced stage settings). We also found recurrences less frequently in patients with expansile FIGO stage I compared with infiltrative FIGO stage I (5% vs 13%). The proportion of patients in our study with recurrences after expansile FIGO stage IC was considerably lower compared with those with infiltrative FIGO stage IC.

Outcomes of patients undergoing fertility-sparing surgery for early stage expansile and infiltrative mucinous ovarian carcinoma were previously described by Gouy et al.[30] However, this retrospective study was limited by sample size (only 12 patients with expansile and 9 with infiltrative tumors). The authors concluded

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that the subtype did not impact the outcomes for women undergoing fertility-sparing staging. In contrast, our data do not support these results; we observed worse overall survival and more recurrences in patients with infiltrative tumors who underwent fertility-sparing staging compared with those undergoing full or partial staging. These outcomes could partially be explained by the fact that the infiltrative fertility-sparing staging group consisted of relatively more patients with FIGO stage IC. We observed no significant differences in outcomes between the extent of staging groups in the expansile cohort.

Strengths and Weaknesses

The strengths of our study include the sample size (the largest cohort of patients with mucinous ovarian carcinoma categorized by expansile and infiltrative subtypes in the literature), its population-based character, and the completeness of both the Netherlands Cancer Registration and the Dutch Pathology Registry. However, there were some limitations to the study design. First, a minority of patients underwent complete peritoneal and lymph node staging. Therefore, upstaging rates after clinical early stage could not be reported. However, this reflects real life Dutch practice. The second limitation was the retrospective design of the study. Third, recurrence rates only included pathologically confirmed recurrences; potential recurrences that were not pathologically confirmed were unknown. Fourth, there is a possibility that mucinous carcinomas of other origins could have been included, given the fact that the pathological diagnosis of mucinous ovarian carcinoma may be challenging,[31] and because endoscopy and tumor marker data were not available. However, the data managers at the Netherlands Cancer Registry thoroughly examined all patient records, including radiologic and endoscopic data (when available), classifying patients as having mucinous ovarian carcinoma.

Small gastrointestinal cancers in patients who did not undergo endoscopy could have remained undetected. However, the histology records of patients who underwent endoscopy with abnormal findings would have been documented in the Dutch Pathology Registry. Therefore, we minimized the risk of falsely including mucinous carcinoma of other origins. Lastly, no central review of histopathology was performed. However, dedicated gynecologic pathologists (in tertiary referral hospitals) routinely review all records and histopathological materials of patients with ovarian cancer in the Netherlands. Furthermore, a dedicated gynecologic pathologist reviewed the reports in the event of ambiguity concerning the subtype.

Implications for Practice and Future Research

The findings of this study could have substantial implications for clinical practice and guidelines in the surgical management of early stage mucinous ovarian carcinoma. The European Society of Gynaecological Oncology currently recommends performing peritoneal staging surgeries for both subtypes of early stage mucinous ovarian carcinoma. However, it advises against routine lymph node sampling when lymph nodes appear normal intraoperatively. Additionally, adjuvant chemotherapy is not standard practice for all early stage mucinous ovarian carcinoma.[20] Our results align with these guidelines regarding lymph node resection and adjuvant chemotherapy. Based on our results, it may be considered safe to omit an additional staging surgery after the initial bilateral salpingo-oophorectomy and hysterectomy for a tumor that is preoperatively presumed to be benign or borderline but postoperatively determined to be an expansile mucinous ovarian carcinoma. In contrast, for infiltrative tumors, we recommend performing full stagings, and a cautious approach is warranted for patients opting for fertility-sparing staging surgery.

Future studies should focus on identifying molecular markers that can reliably predict the occurrence of metastases (and recurrences) in mucinous ovarian carcinoma, in addition to the current subdivision in expansile versus infiltrative subtypes. By developing a better understanding of the underlying genetic and molecular mechanisms driving the metastatic spread, physicians could potentially more extensively tailor surgical strategies for patients with early stage mucinous ovarian carcinoma.

CONCLUSIONS

In this study, we found that patients with the expansile subtype more frequently had FIGO stage I, and those with expansile FIGO stage I had better outcomes than those with infiltrative FIGO stage I. Only a minority of patients with FIGO stage I mucinous ovarian carcinoma underwent full staging. However, in the expansile cohort, recurrences, overall survival, and recurrence free survival were similar across the different extent of surgical staging groups (full, fertility-sparing, and partial staging). In the infiltrative cohort, overall survival was better for patients undergoing full staging compared with those undergoing fertility sparing or partial staging. Patients undergoing fertility-sparing staging for infiltrative tumors experienced significantly more recurrences. These findings should contribute to the development of tailored surgical approaches for patients with mucinous ovarian carcinoma.

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