Surgical management and outcomes for stage 1 malignant ovarian germ cell tumours: a UK multicentre retrospective cohort study

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ABSTRACT

Objective: To describe the current surgical management of stage 1 malignant ovarian germ cell tumours and correlated oncological outcomes.

Study Design: We undertook a retrospective study of all stage 1 primary ovarian germ cell tumours treated in four major UK gynaecology oncology centres over 12 years. We assessed route of surgery, fertility-sparing approaches, ovarian cystectomy alone, and surgical staging and correlated these with clinical outcomes.

Results: Eighty-six patients were followed-up for a median of 4.4 years (IQR 4.3). The median age was 26 (range 11-47). There were 24 (27.9%) dysgerminomas, 13 (15.1%) yolk sac tumours, 10 (11.3%) mixed germ cell tumours, and 39 (45.3%) immature teratomas. Overall survival was 96.6% (OS, 95% CI 91.9-100%), with event free survival of 81.8% (EFS, 95% CI 72.5-92.3) at 5 years.

The majority had fertility-sparing surgery (93%, n=80). In a subset of patients with immature teratoma, there was no significant difference in recurrence or survival if patients underwent unilateral cystectomy only or salpingo-oophorectomy. Laparotomy was the most common approach (n=66, 76.7%), used more frequently for larger tumours >10cm. Surgical staging procedures were undertaken in 42 (48.6%) patients with no significant difference in rates of staging across histological subtypes. Peritoneal biopsies were taken in 11 (12.7%), omental assessment in 40 (46.5%) and lymphadenectomy in 10 (11.6%). There was no significant difference in EFS between patients who underwent staging procedures (83%, CI 71-98%) versus those that did not (84%, CI 72-98%). There was no significant difference in the rate of staging procedures in paediatric (42.1% 8/19) and adult (57.9% 34/67) populations.

Conclusions: Across all histologies and ages, the absence of surgical staging did not impact upon disease free or overall survival in this cohort. This study also raises the possibility of a role for ovarian cystectomy in immature teratoma. These findings warrant investigation in larger prospective studies.

Key words: Germ cell tumour, surgery, ovary

1. **INTRODUCTION**

Malignant ovarian germ cell tumours (MOGCTs) are rare with a yearly-adjusted incidence of 3.7 per million [1]. These account for 1-2% of all ovarian malignancies in Europe [2–4] and comprise the histological subtypes: dysgerminoma, yolk sac tumour, mixed germ cell tumour, immature teratoma (IT) and embryonal carcinoma [5,6]. Fertility sparing surgery is a safe and effective strategy with excellent five year survival of 95% for stage one tumours [2,7].

Recommendations regarding staging differ between paediatric and adult practice. Paediatric practice is guided by two major trials and is limited to pelvic washings, tumour removal, and biopsy of suspicious implants [8,9]. The National Comprehensive Cancer Network (NCNN) advises that in the paediatric, adolescent and young adult population, comprehensive staging may be omitted[10]. These tumours predominantly affect the adolescent and young adult population, and the European Society of Gynaecological Oncology (ESGO) and the European Society for Paediatric Oncology (SIOPE) has produced guidance for the 15-25 age group, which advocates peritoneal washings, pelvic, para-colic gutter and diaphragmatic biopsies and a large omental biopsy[11]. The European Society for Medical Oncology (ESMO) and NCNN guidance both recommend peritoneal washings and biopsies, but stipulate an omentectomy rather than omental biopsy [2,10]. Routine lymphadenectomy is not recommended in ESGO and ESMO guidance, but remains within NCNN guidance [2,10,11].

The role of adjuvant chemotherapy in stage 1 MOGCT is guided by histological subtype and disease stage [2]. Although open surgery is standard, guidance states that surgery can be performed laparoscopically or using robotics in selected cases if full exploration of the peritoneal cavity can be performed [2].

Due to their rarity, and the resultant challenges of conducting prospective trials in this field, we aimed to examine these approaches in a real-world series in patients of all ages, describing current surgical management with particular reference to fertility-sparing procedures, staging and surgical approaches and correlate these with oncological outcomes.

2. MATERIALS AND METHODS

In this retrospective cohort study we report all stage 1 primary ovarian germ cell tumours recorded across four UK sites (Barts Health NHS Trust, University College Hospital, University Hospitals Bristol and Weston NHS Foundation Trust and the Royal Marsden Hospital) between 01 January 2005 and 31 December 2016.

Local hospital ethical approval for audit was obtained and data collection was undertaken in 2016. Data sharing agreements were established to enable the dataset to be shared between partner organisations in accordance with the European General Data Protection Regulations.

Histology was reported by supra-regional specialists in each centre and verified by a single expert germ cell tumour pathologist. The follow-up duration was recorded up to the date of last follow-up or death. Event free survival (EFS) was defined as the time from date of diagnosis until the date of recurrence or progression. We defined complete, comprehensive staging as evidence of both peritoneal and omental assessment (either omentectomy or omental biopsy) as per ESMO or ESGO guidance. Overall survival was defined as the time from diagnosis to date of death from any cause. Women who were alive were censored at the date of their last follow-up.

Patient characteristics were summarized using descriptive statistics. Statistical analyses were performed using R version 3.6.0. Wilcoxon rank sum test was used as required for between group comparisons of non-normally distributed continuous data, t-tests for normally distributed continuous variables and Chi-squared test for categorical variables, with post-hoc tests using Bonferroni correction. Two sided tests were performed throughout and a P value threshold of 0.05 was considered statistically significant. Survival analyses were performed in R using the Survival/Survminer packages.

3. RESULTS

3.1 Patient characteristics and outcomes

Eighty-six patients were diagnosed with a stage one malignant ovarian germ cell tumour during the study period and were therefore eligible for inclusion in the study. No patients were excluded (Figure 1A). Histological assessment revealed 24 (27.9%) dysgerminomas, 13 (15.1%) yolk sac tumours, 10 (11.3%) mixed germ cell tumours, and 39 (45.3%) ITs (Figure 1B). Nine (90.0%) of the 10 mixed germ cell tumours contained yolk sac elements. Patients were followed-up for a median of 4.4 years (IQR 4.3, range 0.03–16.5 years) and all participants underwent surgical management (see Table 1). All surgeries were either performed at tertiary gynaecological oncology centres, or in a small minority, at a local hospital and subsequently referred for multidisciplinary team ongoing management.

There were two deaths over the follow-up period, one in a 32-year-old patient with a stage 1C yolk sac tumour and one in a 44-year-old patient with a stage 1 mixed germ cell tumour, contributing to poorer OS and EFS in these groups. Both received adjuvant chemotherapy. The resultant differences in survival estimates did not reach statistical significance. Recurrence of disease was more common in mixed germ cell (50%) and yolk sac tumours (38.5%), but infrequent in IT (15.4%) and dysgerminoma (12.5%). Kaplan Meier estimates revealed excellent 5-year overall survival of 96.6% (95% CI 91.9-100%), and event free survival of 81.8% (95% CI 72.5-92.3) across the whole patient group. (Figure 2).

3.2 Fertility sparing surgery

The majority of surgeries were fertility sparing (n=80 patients, 93.0%). Six patients (7.0%) underwent bilateral salpingo-oophorectomy. Two were undertaken in patients with chromosomal abnormalities (Swyers syndrome and Turners syndrome). Two underwent bilateral salpingo-oophorectomy for stage 1B/ 1C disease. Two patients aged 36 and 44 who had completed their families underwent a total abdominal hysterectomy and

bilateral salpingo-oophorectomy for a Stage 1A mixed germ cell tumour and stage 1A IT respectively. These were the only two patients in the cohort who underwent a hysterectomy (2.3%).

Both deaths in the study (n=2, 100%) occurred in patients who underwent fertility sparing surgery. EFS and OS were therefore reduced in patients who had fertility sparing approaches, but this was not statistically significant.

3.3 Ovarian Cystectomy

Eleven patients with a median age of 27 (range 14-35) underwent an ovarian cystectomy as their primary surgical procedure (Table 2) and comprised nine IT, one mixed and one yolk sac tumour. Seven cystectomies were performed laparoscopically and four via laparotomy. Cyst rupture occurred in four of the seven laparoscopic cases (57.1%). None of these four recurred, although two received adjuvant chemotherapy as a result of upstaging due to cyst rupture. The EFS and OS following ovarian cystectomy were both 100.0% (95% CI 100.0-100.0).

Completion unilateral salpingo-oophorectomy was performed in a patient with a yolk sac tumour who had evidence of cyst rupture at surgery. Residual disease was found in the ovary and she received adjuvant chemotherapy. Completion unilateral salpingo-oophorectomy was also undertaken for two patients with stage 1C IT, but no residual disease was found.

Although there was no recurrence of malignant disease, one patient had later evidence of benign disease recurrence. She had initially undergone a cystectomy for a Grade 2 Stage 1C IT followed by adjuvant chemotherapy. She underwent surgery to resect an anterior abdominal wall recurrence, and histology confirmed mature teratoma only. She was alive and well at censor at 47 months.

Since cystectomy was most commonly performed in IT patients, outcomes of these 9 patients was compared to patients with IT who underwent a USO (n=29). One of the 39 patients with IT underwent a bilateral

salpingo-oophorectomy and was therefore excluded from these analyses. Alpha-fetoprotein (AFP) levels were available in six patients undergoing an ovarian cystectomy and 15 patients undergoing a USO. AFP was raised in only one patient undergoing a cystectomy. Patients undergoing a USO were significantly more likely to have a larger tumour, have a higher pre-operative AFP and undergo a laparotomy. There was no significant difference found in rates of recurrence and no deaths in either group (Table 3). Paediatric patients were no more likely to undergo a cystectomy than patients aged over 18 (2/9 vs 13/29).

3.4 Surgical Staging

We assessed whether the addition of surgical staging procedures related to better patient outcomes. Eleven (12.7%) patients had peritoneal biopsies, omental assessments were performed in 40 patients (46.5%) (19 omentectomies and 21 omental biopsies) and ten patients underwent lymphadenectomy, all with negative results (0% upstaged). Cytology assessment via peritoneal washings or fluid samples was not comprehensively recorded in this study. There was no statistically significant difference in the proportion of patients undergoing staging procedures across histological subtypes.

Overall, nine (10.4%) patients had complete surgical staging with both peritoneal biopsies and omental assessment, and 33 (38.4%) were incompletely staged, with either peritoneal or omental assessment alone.

There was no significant difference in 5-year event free survival estimates in patients who underwent any form of staging procedure: EFS was was 87% in incompletely staged (CI 74-100%) and 71% in completely staged (95% CI 45-100%) versus 84% (95% CI 72-98%) in unstaged patients. There were no deaths in the group which underwent staging procedures.

We next further assessed outcomes by stratifying by whether adjuvant therapy was administered (Table 4). Staging procedures were performed in 42 patients, 15 (35.7%) of whom received adjuvant chemotherapy and none recurred. Adjuvant chemotherapy was given in 11 (26.2%) of the 42 patients who did not undergo staging. Three (27.3%) subsequently recurred.

Despite undergoing staging procedures, both patients with yolk sac tumour and three of four patients with a mixed germ cell tumour who underwent surveillance without adjuvant chemotherapy, subsequently recurred.

Only one of 18 patients with IT who did not undergo staging and did not receive adjuvant chemotherapy recurred.

We next assessed for a possible influence of age on staging decisions. Age at presentation was not a significant predictor of decision to stage on logistic regression modelling, across the group. Staging was performed in 8 (42.1%) patients aged under 18, and 11 (57.9%) were unstaged. There was no significant difference in the rate of staging in paediatric (42.1% 8/19) and adult (57.9% 34/67) populations.

3.5 Adjuvant Treatment

Adjuvant chemotherapy was given in 26 (30.2%) of patients. These comprised seven patients with Stage 1C dysgerminoma, and one patient with stage 1A dysgerminoma, seven patients with Stage 1C yolk sac tumour and two patients with Stage 1A yolk sac tumour, three patients with mixed germ cell tumours (two stage 1 unspecified, one stage 1C) and six patients with immature teratoma (four Stage 1A and two Stage 1C).

3.6 Outcomes by route of surgery

The majority (76.7%, n=66) of surgeries were performed via laparotomy, with laparoscopy in only 17 cases (19.8%). Route of surgery was not recorded in three patients (3.4%). Clinical features and patients' outcomes according to surgical route were compared (Table 5). The histopathological case mix differed significantly between the laparoscopic and open groups ($P=0.043$, $X^2=8.1$;DF=3). Surgical decision was related to tumour size, known for 80 tumours in the dataset (93.0%). Tumours managed laparoscopically were significantly smaller (median size 45mm, IQR 37.5) compared with open cases (median 160mm, IQR 82; $P<0.001$, $W=614$) and all patients undergoing laparoscopy had a tumour size of ≤100mm.

4. DISCUSSION

This study provides a comprehensive description of the surgical management and long-term outcomes in a large UK population with presumed stage I ovarian germ cell tumours.

There were excellent outcomes in the nine patients undergoing ovarian cystectomy for IT, although notably cystectomy was predominantly performed for small tumours with a low pre-operative AFP level. A retrospective study of 43 patients similarly found excellent long-term outcomes, with no cases of disease recurrence in 14 patients undergoing ovarian cystectomy[12]. However, in this group, 57% of ovarian cystectomies were followed by adjuvant therapy, whereas we found that despite only an 11% rate of adjuvant chemotherapy following cystectomy, there were no recurrences or deaths. In our cohort, the vast majority of patients were of reproductive age, so maintaining ovarian function is of real importance. This study does not aim to describe cystectomy in other histological subtypes, where it remains contra-indicated as a germ cell tumour may arise as part of a syndrome such as Swyer syndrome. Finally, the ability to perform an ovarian cystectomy rather than a USO may be limited by tumour size, and absence of normal remaining ovarian tissue. Further data are needed to draw conclusions about this approach.

Low rates of upstaging have been previously observed in a large study of 147 patients which found a 10.3% rate of positive lymph nodes [13], and even lower in a Chinese study with 0.8% (1/119) positive lymph nodes and no omental metastases in 183 patients [14]. The rate of upstaging may be affected by tumour subtype and stage. In a detailed Italian analysis in which patients were stratified into three subgroups of varying risk, in the lowest risk subgroup comprising stage 1A dysgerminoma and stage 1A Grade 1 IT, all peritoneal and omental biopsies were negative[15], whereas peritoneal upstaging occurred in patients with a 1A G3 IT and 1A mixed germ cell tumour.

We report a lower rate of recurrence of 16% (5/31), in unstaged patients undergoing surveillance than other studies have described. Previously, such good long term outcomes have been seen in unstaged patients receiving high rates of adjuvant therapy [16,17] but not in the setting of surveillance, where higher recurrence rates have been reported [18]. However, these results have not been always stratified by histological subtype as our study does. These contrary results may be therefore be explained by small cohorts in which the proportions of different histological subtypes and rates of adjuvant therapy differ. In this study, IT, comprised 45.3% of the cohort. We found that outcomes in this subgroup were excellent irrespective of whether staging procedures were performed. The role of staging in IT has been previously assessed in a study of 75 patients,

finding similarly that incomplete surgical staging with subsequent surveillance did not affect disease free or overall survival [19]. The absence of staging in a series of patients with Stage 1A dysgerminoma has been reported to not affect overall survival, due its chemosensitivity and potential for salvage of recurrence [20]. However if surveillance is considered in yolk sac tumour, complete staging has been advocated[17][21]. This study suggests that staging is not the only important parameter however, as five patients with mixed and yolk sac tumours that underwent staging procedures and subsequent surveillance nevertheless went on to recur. These results therefore support a role for adjuvant chemotherapy for all adequately staged yolk sac tumours, as has been recently advocated in a large French network study[21]. This study identified a high prevalence of yolk sac elements in the mixed germ cell tumours, which may have contributed to the high recurrence rate in this group and suggests that a similar approach is justified.

The safety of a laparoscopic approach in stage one ovarian germ cell tumours has been recently demonstrated in a large study which showed three-year survival rates of 97.9% (733 patients) in the laparotomy group and 99.4% (294 patients) in the minimal access group . It was noted however that there was a lower rate of surgical staging (omentectomy and lymph node sampling/dissection) in the laparoscopy group [22]. The safety of laparoscopic ovarian cystectomy for ovarian germ cell tumour has not been addressed, but our results suggest that this should be avoided due to the risk of rupture at laparoscopic cystectomy and potential for upstaging. In this cohort two patients received adjuvant chemotherapy as a result of upstaging due to cyst rupture. Recurrence of immature teratoma may result in potentially significant surgical morbidity as the tumour is not chemo-sensitive. Careful surveillance of immature teratoma is essential, due to the risk of growing teratoma syndrome [23].

The primary strength of this study is that it is one of only a very few large contemporary series of these rare tumours with extensive information about surgical procedures performed, and with central pathological review to confirm histological diagnoses. All cases were recorded consecutively across four major cancer centres and no cases were excluded. It therefore reflects a typical clinical population, without the limitations of restrictive inclusion and exclusion criteria which are often necessary in clinical trials settings, but which can limit applicability to unselected patient groups.

However, there are several potential limitations. As other retrospective studies in this field have found, practice varied widely [8,13], with clinicians following different guidance and management approaches both surgically and in offering adjuvant therapy. As a retrospective study, there is a risk of selection bias as patients were not assigned to pre-defined staging procedures or route of surgery. The rarity and heterogeneity of these tumours limits the ability to detect and verify significant differences and the potential to draw robust conclusions. As in any cohort study, there is missing data and loss to follow-up, although retention rates and follow-up duration were very good in this specific population. In this study, the use of an incompletely staged group as a comparator to the unstaged group may limit the ability to detect a significant difference in outcomes as a result of staging. Previous studies have identified an association between comprehensive staging and a lower rate of recurrence, but even these differ with respect to which staging procedures are considered to be necessary [24]. Palenzuela et al 2008 describes complete staging as peritoneal cytology and exploration of the peritoneal and abdominal cavity, with biopsy of any abnormal areas, whereas Mangili et al 2017 describes complete staging as peritoneal biopsies, omentectomy or omental biopsy, and peritoneal washings [17,24].

In this study we have identified low rates of complete surgical staging procedures across all ages. As this is a primarily a malignancy affecting adolescents and young adults, there is likely to be limited clinical value in offering differing approaches to individuals either side of an arbitrary age range. These findings warrant assessment in other larger prospective studies, or in a systematic review. Similarly, these would be necessary to further assess the role of cystectomy in immature teratoma. Collaborative research such as the RaNGO (Rare Neoplasms of Gynaecological Origin) study [25], are hoped to be able to improve data collection in these tumours, as the UK lags behind countries with centralised cancer registries. A national rare gynaecological tumour database to assimilate the management and outcomes of these patients prospectively is needed [26].

In conclusion, this multicentre retrospective cohort study provides added support for a fertility sparing approach, with consideration of laparoscopy if tumour size allows and if tumour rupture may be avoided. The omission of surgical staging did not affect disease free or overall survival in this particular cohort. However, in light of the limitations as described above, this study does not provide definitive evidence to refute current

guidance, recommending staging. This study also raises questions about a potential role for ovarian cystectomy in immature teratoma, though unilateral salpingo-oophorectomy remains standard of care pending validation of these results in larger cohorts.

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CREDIT AUTHOR STATEMENT

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DATA AVAILABILITY STATEMENT

Data are available upon reasonable request. In accordance with the journal's guidelines, we will provide our data for the reproducibility of this study in other centers if such is requested.

DECLARATION OF INTEREST STATEMENT

None declared.

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TABLES

a1. Clinical and demographic characteristics of the cohort

	All pathologies	Dysgerminoma	Yolk sac tumour	Mixed germ cell tumour	Immature teratoma
Total, N (%)	86 (100.0)	24 (27.9)	13 (15.1)	10 (11.3)	39 (45.3)
Age					
Median (IQR)	26 (14.0)	22 (11.0)	26 (15.5)	29 (11.0)	31 (10.0)
< 18, N (%)	19 (22)	5 (20.8)	2 (15.4)	0 (0.0)	12 (30.8)
> 18, N (%)	72 (84)	19 (79.2)	11 (84.6)	10 (100.0)	32 (82.1)
Surgical route					
Laparotomy, N (%)	66 (76.7)	13 (54.2)	12 (92.3)	9 (90.0)	32 (82.1)
Laparoscopy, N (%)	17 (19.8)	9 (37.5)	1 (7.7)	1 (10.0)	6 (15.4)
Unknown, N (%)	3 (3.4)	2 (8.3)	0 (0.0)	0 (0.0)	1 (2.6)
Surgery type					
Fertility sparing, N (%)	80 (93.0)	20 (83.3)	13 (100.0)	9 (90.0)	38 (97.4)
Non-fertility sparing, N (%)	6 (7.0)	4 (16.7)	0 (0.0)	1 (10.0)	1 (2.6)
Staging surgery, N (%)	42 (48.9)	11 (45.8)	7 (53.8)	5 (50.0)	19 (48.7)
Chemotherapy					
None, N (%)	58 (67.4)	15 (62.5)	4 (30.1)	6 (60.0)	33 (84.6)
Neoadjuvant, N (%)	2 (2.3)	1 (4.2)	0 (0.0)	1 (10.0)	0 (0.0)
Adjuvant, N (%)	26 (30.2)	8 (33.3)	9 (69.2)	3 (30.0)	6 (15.4)
Recurrence, N (%)	18 (21.0)	3 (12.5)	5 (38.5)	5 (50.0)	5 (13.0)
Time to recurrence (days)					
median (IQR)	200 (261)	363 (1398.5)	103 (462)	119 (106)	211 (208)
Censor outcome					
Dead, N (%)	2 (2.3)	0 (0.0)	1 (7.7)	1 (10.0)	0 (0.0)
Alive and disease free, N (%)	84 (97.7)	24 (100.0)	12 (92.3)	9 (90.0)	39 (100.0)
Time to censor outcome (years)					
median (IQR)	4.4 (4.3)	6.6 (4.8)	3.8 (3.5)	5.1 (4.8)	3.2 (3.6)
Survival, 5 year					
Event free survival (95% CI)	81.8 (72.5-92.3)	95.5 (87.1-1)	54.5 (31.8-93.6)	77.1 (53.5-100.0)	82 (65.1-100.0)
Overall survival (95% CI)	96.6 (91.9-100.0)	100.0 (100.0-100.0)	85.7 (63.3-100.0)	90.0 (73.2-100.0)	100.0 (100.0-100.0)

IQR, interquartile range, CI, confidence interval

Table 2. Surgical management, pathology and disease recurrence in patients undergoing ovarian cystectomy

Stage	Histology	AFP (ng/ml)	Cyst rupture	Cyst size (mm)	Route	Completion surgery	Residual ovarian disease	Chemo-therapy	Recurrence	Total follow up (days)
IC	Yolk sac	249	Cyst ruptured	75	Laparoscopy	Unilateral salpingo-oophorectomy, ovarian cystectomy	Present	BEP x4	–	4474
I	Immature teratoma G1	0.6	Cyst ruptured	28	Laparoscopy	–	–	–	–	2517
I	Immature teratoma G1	1.3	No rupture	95	Open	–	–	–	–	1336
IC	Immature teratoma G2	NA	Cyst ruptured	60	Laparoscopy	Unilateral salpingo-oophorectomy, omental biopsy	Absent	BEP x3	Recurrence of mature teratoma only at 306 days	1741
IC	Immature teratoma G3	NA	No rupture	90	Open	Unilateral salpingo-oophorectomy	Absent	Carbotaxol x6	–	921
I	Immature teratoma G3	300	No rupture	140	Open	–	–	–	–	2114
IA	Immature teratoma G2	2	No rupture	Unknown	Laparoscopy	–	–	BEP x4	–	2872
1C	Immature teratoma G2	3	Cyst ruptured	90	Laparoscopy	–	–	–	–	1817
IA	Immature teratoma G1	1	No rupture	30	Laparoscopy	–	–	–	–	357
IA	Immature teratoma G1	NA	No rupture	130	Open	–	–	–	–	1169
I	Mixed germ cell tumour	NA	No rupture	50	Laparoscopy	–	–	BEP x4	–	675

AFP= alpha-fetoprotein, BEP= Bleomycin, etoposide and platinum chemotherapy, G1, Grade 1, G2, Grade 2, G3, Grade 3, NA=not available

Table 3. Surgical management and clinical outcomes in stage one immature teratoma

	All	Ovarian cystectomy	Unilateral salpingo-oophorectomy	P
Total, N (%)	38 (100.0)	9 (23.7)	29 (76.3)	
FIGO 2014 stage				0.027
1 (undefined)	5 (13.2)	3 (33.3)	2 (6.9)	
1a	26 (68.4)	3 (33.3)	23 (79.3)	
1b	0 (0.0)	0 (0.0)	0 (0.0)	
1c	7 (18.4)	3 (33.3)	4 (13.8)	
Grade				NS
1	11 (28.9)	4 (44.4)	7 (24.1)	
2	15 (39.5)	3 (33.3)	12 (41.4)	
3	12 (31.6)	2 (22.2)	10 (34.4)	
AFP (ng/ml)				0.030
Median (IQR)	6.2 (57.4)	1.7 (1.7)	10.2 (57.4)	
Tumour size (mm)				0.008
Median (IQR)	147.5 (88.8)	90.0 (51.3)	167.5 (52.5)	
Surgical route				<0.001
Laparotomy	32 (84.2)	4 (44.0)	27 (93.1)	
Laparoscopy	5 (13.2)	5 (56.0)	1 (3.5)	
Recurrence	5 (13.1)	0 (0.0)	5 (17.2)	NS
Time to recurrence (days)				
Median (IQR)	211 (208)	NA	211 (208)	
Censor outcome				
Dead	0 (0.0)	0 (0.0)	0 (0.0)	
Alive and disease free	38 (100.0)	9 (100.0)	29 (100.0)	
Time to censor outcome (years)				
Median (IQR)	3.2 (3.5)	4.8 (2.6)	3.0 (3.0)	NS

IQR, interquartile range, NS, not significant, AFP= alpha-fetoprotein

Table 4. Outcomes following surgical staging in relation to adjuvant chemotherapy administration

	All pathologies	Dysgerminoma	Yolk sac tumour	Mixed germ cell tumour	Immature teratoma
Staging surgery performed, N (%)	42 (50.0)	11 (47.8)	7 (53.8)	5 (55.6)	19 (48.7)
Adjuvant chemotherapy, N (%)	15 (35.7)	5 (45.5)	5 (71.4)	1 (20.0)	4 (21.1)
Subsequently recurred, N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
No adjuvant chemotherapy, N (%)	27 (64.3)	6 (54.5)	2 (28.6)	4 (80.0)	15 (78.9)
Subsequently recurred, N (%)	10 (37.0)	1 (16.7)	2 (100.0)	3 (75.0)	4 (26.7)
Staging surgery not performed, N (%)	42 (50.0)	12 (52.2)	6 (46.2)	4 (44.4)	20 (51.3)
Adjuvant chemotherapy, N (%)	11 (26.2)	3 (25.0)	4 (66.7)	2 (50.0)	2 (10.0)
Subsequently recurred, N (%)	3 (27.3)	0 (0.0)	2 (50.0)	1 (50.0)	0 (0.0)
No adjuvant chemotherapy, N (%)	31 (73.8)	9 (75.0)	2 (33.3)	2 (50.0)	18 (90.0)
Subsequently recurred, N (%)	5 (16.1)	2 (22.2)	1 (50.0)	1 (50.0)	1 (5.6)

Patients undergoing neo-adjuvant chemotherapy (n=2) excluded from analysis.

Table 5. Route of surgery and clinical outcomes

	Laparoscopy	Laparotomy	P
Total, N (%)	17 (19.8)	66 (76.7)	
Histology			0.043
Dysgerminoma	9 (52.9)	13 (19.7)	
Yolk Sac Tumour	1 (5.9)	12 (18.1)	
Mixed Germ cell tumour	1 (5.9)	9 (13.6)	
Immature Teratoma	6 (35.2)	32 (48.5)	
Tumour size (mm)			
Median (IQR)	45 (37.5)	160 (82)	< 0.001
Chemotherapy			NS
None	12 (70.1)	43 (65.1)	
Neoadjuvant	0 (0.0)	2 (3.0)	
Adjuvant	5 (2.9)	21 (31.8)	
Recurrence, N (%)	1 (5.9)	16 (24.2)	NS
Censor outcome			
Dead	0 (0.0)	2 (3.0)	
Alive and disease free	17 (100.0)	64 (97.0)	
Time to censor outcome (years)			
median (IQR)	5.4 (4.2)	3.9 (4.0)	
Estimated 5 year			
Overall survival (95% CI)	100.0 (100.0-100.0)	95.3 (89.0-100.0)	NS
Event free survival (95% CI)	90.9 (75.4-100.0)	78.7% (67.6-91.5)	NS

FIGURE LEGENDS

Figure 1. Demographics, disease subtypes and outcomes

A. Age at diagnosis and outcome at time of censor. B. Histopathological tumour type in relation to outcome. Y axis denotes number of patients. Dys= dysgerminoma, IT= immature teratoma, YST= yolk sac tumour, MGCT= mixed germ cell tumour

Figure 2. Survival curve by histopathological type of tumour

Kaplan–Meier survival curve and table for n=86 patients in the cohort, stratified by tumour subtype with 95% confidence intervals shown. MGCT =Mixed germ cell tumour

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