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Laparoscopic surgery in the treatment of stage I adult granulosa cells tumors of the ovary: Results from the MITO-9 study

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ABSTRACT

Objective: Surgery represents the mainstay of treatment of stage I adult type granulosa cell tumors of the ovary (AGCTs). Because of the rarity and indolent course of the disease, no prospective trials are available. Open surgery has long been considered the traditional approach; oncological safety of laparoscopy is only supported by small series or case reports. The aim of this study was to compare the oncological outcomes between laparoscopic and open surgery in stage I AGCTs treated within the MITO (Multicenter Italian Trials in Ovarian cancer) Group.

Methods: Data from patients with stage I AGCTs were retrospectively collected. Clinicopathological features were evaluated for association with relapse and death. Survival curves were calculated using the Kaplan-Meier method and compared with the log-rank test. The role of clinicopathological variables as prognostic factors for survival was evaluated using Cox's regression model.

Results: 223 patients were identified. Stage 1A, 1B and 1C were 61.5%, 1.3% and 29.6% respectively. 7.6% were apparently stage I. Surgical approach was laparoscopic for 93 patients (41.7%) and open for 130 (58.3%). 5-years DFS was 84% and 82%, 10-years DFS was 68% and 64% for the laparoscopic and open-group ($p = 0.6$).5-years OS was 100% and 99%, 10 years OS was 98% and 97% for the laparoscopic and open-surgery group ($p = 0.8$). At multivariate analyses stage IC, incomplete staging, site of primary surgery retained significant prognostic value.

Conclusion: The present study suggests that surgical route does not affect the oncological safety of patients with stage I AGCTs, with comparable outcomes between laparoscopic and open approach.

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Introduction

Granulosa cell tumors of the ovary (GCTs) arise from sex cord stromal cells and represent the most common tumor type among sex cord stromal tumors. 95% of the cases are diagnosed in perimenopausal or postmenopausal age and are defined as adult type GCTs (AGCTs). Surgery represents the mainstay of primary treatment [1–3]. Because of the rarity and indolent course of the disease, no prospective randomized trials specifically addressing surgical management are currently available; treatment has been assessed on the basis of small retrospective series which include tumors of different histotypes and with a short follow up period. Complete surgical resection with open total abdominal hysterectomy, bilateral salpingo-oophorectomy and complete surgical staging is the standard treatment of GCTs. In stage I patients desiring to preserve their fertility, conservative surgery can be an option.

Open surgery has long been considered as the traditional surgical route in AGCTs [4,5]. However, since most cases are detected at an early stage, often incidentally on a presumed benign cyst, laparoscopy has widely replaced open-surgery in the last decades. Moreover, minimally invasive approaches in gynecological oncology have become increasingly more common and convenient in terms of bleeding, morbidities, recovery and length of hospitalization; this approach has been recognized in ESMO guidelines as an option for selected patients with AGCT [6]. To the best of our knowledge, however, there are only small series or case reports supporting the oncological safety of minimally invasive approaches as compared to open-surgery in this clinical setting, and often patients included in these studies have heterogeneous histological diagnosis [7–10]. Our series represents the largest available evaluating oncological safety of laparoscopic approach, selectively considering stage I AGCTs.

Materials and methods

The aim of this retrospective analysis is to assess the role of minimally invasive surgery in patients with stage I AGCTs treated in the Italian Centers members of the MITO group.

Patients' characteristics have been retrospectively retrieved for diagnoses made from 1965 to May 30, 2017. A series of 270 patients with AGCTs were treated and followed in MITO centers, including patients primarily treated or referred after primary surgery. This study represent an updated follow-up study of the MITO experience, considering all patients with stage I AGCT treated until 30 June 2017.

Institutional review board approved the study. Patients' characteristics including age at diagnosis, clinical presentation, tumor pathological characteristics, intraoperative findings and surgical management at primary treatment and relapse, follow up data were collected.

All patients firstly received surgery, either laparoscopic or open. Fertility sparing approach was chosen for women desiring to preserve their uterus or in case of incidental diagnosis upon a presumed benign ovarian cyst, in case of disease macroscopically confined to the ovary. Surgery was considered conservative in case of unilateral salpingo-oophorectomy, oophorectomy or cystectomy. Radical surgery, consisting of bilateral salpingo-oophorectomy with or without hysterectomy was the standard of care when fertility was not an issue. Staging was considered complete when including peritoneal washing, multiple peritoneal biopsies, omental biopsy and biopsy of any suspicious area. Indication of adjuvant chemotherapy was not standardized among MITO centers and was therefore based on the single center's decision. All pathological analyses were only made by experienced gynecologic pathologists of MITO centers. In case of challenging diagnoses or for patients referred from centers outside the MITO group, a central review in the coordinating center was performed. Tumors were staged according to International Federation of Gynecology and Obstetrics (FIGO) staging system of 2014 [11]. Reclassification of cases diagnosed prior to this new staging system was applied evaluating surgical reports.

After being included in this study, patients were followed at MITO centers with a long-term schedule, comprising a periodic clinical, radiologic and serologic assessment.

Descriptive statistics were used to characterize the patient population. Clinicopathological features and treatment variables were evaluated for association with relapse and death. Follow up was assessed from the time of primary diagnosis to the time of last follow up visit. Disease free survival (DFS) was defined as the time period between first diagnosis to first observation of recurrence. Overall survival (OS) was defined as the time period from the date of initial diagnosis to the date of death.

Survival curves were calculated using the Kaplan-Meier method and were compared with the log-rank test to assess the statistical significance. Patients were censored when lost to follow up. Cox's regression model was used to analyze in univariate and multivariate analysis the role of clinicopathological factors as prognostic factors for survival.

Statistical analysis was conducted using Statistical Package version 18.0 for Windows (SPSS, Inc., Chicago, Illinois). Differences were considered statistically significant at p value < 0.05. Hazard ratios were calculated for potential risk factor for relapse.

Results

Among 270 patients included in the MITO-9 study with a diagnosis of AGCT, 223 had stage I disease. Patients clinicopathological characteristics are summarized in Table 1. Median age at diagnosis was 49.0 years (range 25–90). 137 patients were stage IA (61.5%), 3 were IB (1.3%), 66 were stage IC (29.6%), 17 (7.6%) were apparently stage I tumors, as the center did not provide further information. Surgery represented the first therapeutic approach in all patients. 147 patients (65.9%) received primary surgery in a MITO center. The remaining 76 (34.1%) were treated elsewhere and subsequently referred to MITO centers for restaging or follow-up. Surgical approach was laparoscopic for 93 patients (41.7%) and open for 130 (58.3%). A conservative approach was applied in 68 patients (30.5%) consisting in unilateral oophorectomy in 54 patients (79.4%) and cystectomy in the remaining 14 (20.6%). Radical surgery including bilateral salpingoophorectomy with or without hysterectomy was performed in 155 patients (69.5%).

Complete staging was performed in 157 patients (70.4%). Cyst rupture was documented at surgery in 42 patients (19.2%). The majority of these occurred at the time of surgery ($n = 30$, 13.4%). A concomitant endometrial carcinoma was detected in 10 patients (4.5%), 15 were diagnosed with complex atypical hyperplasia (6.7%).

Clinicopathological characteristics of patients according to surgical approach are summarized in Table 2.

No statistically significant difference between laparoscopy and open-surgery was detected in terms of recurrence sites, incidence of intraoperative cyst rupture or incomplete staging. Patients undergoing laparoscopic surgery were significantly younger and received conservative surgery more frequently when compared to the open-surgery group.

As of June 30th, 2017, median follow up was 81 months (10–450). During this period 53 patients (23.7%) experienced a relapse, and the mean time from initial surgery to recurrence was 80.0 ± 60.2 months (range 6–372 months). 8 patient died (3.6%), four of these as a consequence of the disease.

As shown in Fig. 1, no statistical significant difference was detected in terms of DFS, as 5-years DFS was 84% and 82%,

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Table 1
Clinicopathological characteristics of patients with stage I GCTs.

Characteristics	(n = 223)
Age (years)	
Median (range)	49.0 (25–90)
Symptoms	
Abdominal pain	54 (24.2%)
Abdominal Distension	38 (17.0%)
Vaginal Bleeding	57 (25.6%)
Ascites	10 (44.8%)
Pelvic mass	66 (29.6%)
None	81 (36.3%)
FIGO stage	
Ia	137 (61.5%)
Ib	3 (1.3%)
Ic	66 (29.6%)
Ix	17 (7.6%)
Tumor size (cm)	
<10	131 (58.7%)
≥10	92 (41.3%)
Cyst rupture	
Preoperative	13 (5.8%)
Intraoperative	30 (13.4%)
None	180 (80.7%)
Mitotic rate	
≤5/10 HPF	92 (41.3%)
>5/10 HPF	32 (14.3%)
n.a.	99 (44.4%)
Endometrial carcinoma or Complex atypical hyperplasia	25 (11.2%)
Site of primary surgery	
MITO center	147 (65.9%)
Elsewhere	76 (34.1%)
Surgical approach	
Laparoscopic	93 (41.7%)
Open	130 (58.3%)
Type of surgery	
Conservative	68 (30.5%)
Radical	155 (69.5%)
Complete staging	157 (70.4%)
Adjuvant chemotherapy	
Yes	25 (11.2%)
No	198 (88.8%)

10-years DFS was 68% and 64% for the laparoscopic and open-group, respectively (p = 0.6) (Fig. 1). No statistical significant difference was detected in terms of overall survival. 5-years OS was 100% and 99%, 10 years OS was 98% and 97% for the laparoscopic and open-surgery group, respectively (p = 0.8), as shown in Fig. 2.

Univariate and multivariate regression analyses were performed in order to assess the influence of different clinicopathologic characteristics and treatment approaches on survival. As shown in Table 3, among all variables, only FIGO stage IC, incomplete staging, site of primary surgery (MITO center vs elsewhere) retained significant predictive value in both analyses. Minimally invasive approach was not associated with a poorer prognosis.

Discussion

Surgery represents the mainstay of treatment of stage I AGCTs, the most common subtype of sex-cord stromal tumors [1,2]. Considering that often the diagnosis is incidentally made upon a presumed benign cyst at stage I and that laparoscopy is known to be associated with a reduced morbidity, hospitalization and greater cosmetic results, minimally invasive surgery has widely replaced the traditional open approach to such ovarian malignancies in routine clinical practice. However, only small case series evaluating the oncological safety of laparoscopic management of AGCTs are available in literature, most including different histological subtypes of non epithelial ovarian cancer within the same study [7–10]. Shim et al. reported the result of an analysis including women with non epithelial ovarian tumors, among which 18 were diagnosed with GCTs. All of them have been treated laparoscopically and none developed recurrent disease after a median follow/up time of 24.5 months [8]. To the best of our knowledge, this is the largest study reported to date, selectively including 223 patients with stage I AGCTs, 93 treated laparoscopically, with a median follow up of 81 months (10–450). The present study represents a long-term follow up of the whole MITO experience on stage I AGCT, part of which has already been published [12], providing a more detailed and reliable perspective.

Concerns regarding minimally invasive surgery includes intra-operative tumor rupture, given that a higher incidence of cyst rupture has been reported for laparoscopic adnexal surgery compared to the same procedure performed with an open approach, or a less thorough surgical staging [13]. Cyst rupture might lead to port site metastases, while incomplete surgical staging might affect the correct identification of high risk patients,

Table 2
Clinical and pathologic characteristics of patients treated with laparoscopy or open surgery.

Characteristics	Laparoscopy (n = 93)	Open surgery (n = 130)	p
Age (years)			0.01
Mean (±DS)	47.08 ± 14.35	52.95 ± 13.8	
FIGO stage			0.52
Ia	60 (64.5%)	77 (59.2%)	
Ib	1 (1.0%)	2 (1.54%)	
Ic	24 (25.8%)	42 (32.3%)	
Ix	8 (8.6%)	9 (6.9%)	
Site of primary surgery			0.08
MITO center	68 (73.1%)	79 (60.8%)	
Elsewhere	25 (26.9%)	51 (39.2%)	
Type of surgery			<0.01
Fertility-sparing	44 (47.3%)	24 (18.5%)	
Radical	49 (52.7%)	106 (81.5%)	
Complete staging	67 (72.0%)	90 (69.2%)	0.76
Intraoperative cyst rupture	24 (25.8%)	19 (14.6%)	0.08
Adjuvant chemotherapy			0.10
Yes	7 (7.5%)	18 (13.8%)	
No	86 (92.4%)	112 (86.1%)	
Relapse site			0.54
Pelvic	11 (11.8%)	22 (16.9%)	
Abdominal	2 (2.1%)	7 (5.4%)	
Distant	2 (2.1%)	9 (6.9%)	

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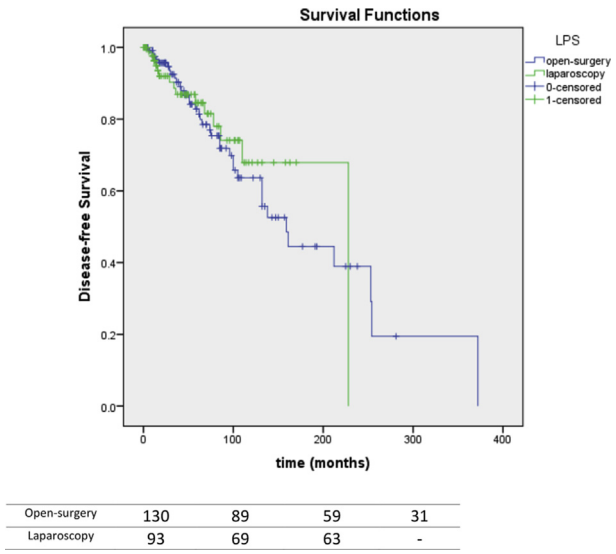

Fig. 1. Disease free survival in stage I GCT patients treated with laparoscopy or open-surgery (green line = laparoscopic approach, blue line = open surgery).

leading to worse survival rates. In our series the rate of intra-operative cystic rupture was higher in the laparoscopic group (25.8% vs 14.6%, p = 0.08), even if this difference did not reach statistical significance nor was found to affect survival: disease free survival (5 year DFS 84% vs 82%; 10 yr DFS 68% vs 64%,laparoscopic vs open surgery, p = 0.6) and overall survival (5 year OS 100% vs 99%, 10 year OS 98% vs 97%, laparoscopic versus open surgery, p = 0.8) were comparable between the two groups. No difference was found in the rate of complete staging between the two groups (72% vs 69.2%, p = 0.76) Interestingly, the distribution of site at recurrence was not related to the type of surgical approach, with no cases of port site metastases reported. At multivariate analysis, laparoscopy was not a prognostic factor for survival. FIGO stage IC, surgery performed outside a MITO center and incomplete surgical staging were the only factors retaining prognostic value. In case of laparoscopic surgery, meticulous surgical technique and the use of

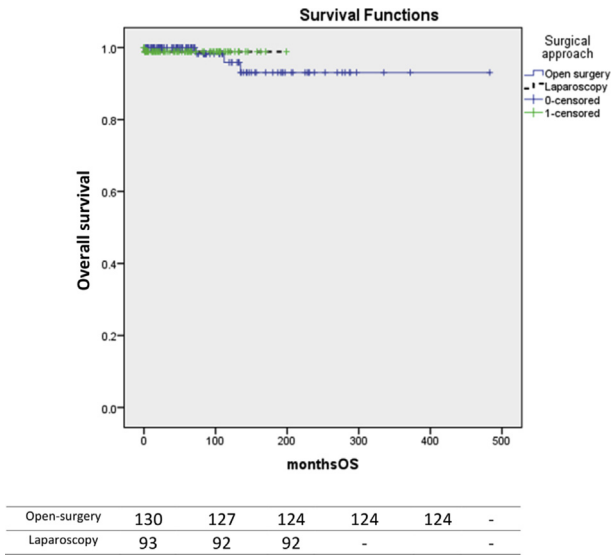

Fig. 2. Overall survival in stage I GCT patients treated with laparoscopy or open-surgery (green line = laparoscopic approach, blue line = open surgery).

Table 3
Prognostic value for disease-free survival in stage I GCTs.

Characteristics	Univariate		Multivariate	
	HR	P	HR	P
Age older than 50	0.39	<0.01	–	–
FIGO stage IC	2.72	<0.01	3.94	<0.01
Surgical Approach	0.86	0.64	–	–
Laparoscopy				
Open surgery				
Surgery outside MITO center	2.68	<0.01	2.13	0.01
Radical surgery	0.42	<0.01	–	–
Incomplete staging	1.78	0.04	2.84	0.01
Adjuvant chemotherapy	0.97	0.94	–	–

endobag are mandatory in order to prevent cyst rupture, tumor spillage and the development of port site metastases. All patients should always be appropriately staged, independently from the surgical approach chosen. Given that AGCTs diagnosis are often made incidentally, second look surgery for staging purposes is recommended in those patients who did not undergo complete staging at primary surgery. Several authors had already highlighted the role of surgical staging showing survival benefit in patients with presumed I–II stages AGCTs appropriately staged [3,13]. In this case, minimally invasive surgery is the preferred approach.

The association between AGCTs and endometrial hyperplasia or carcinoma it is well known from previous reports, with an incidence ranging from 21% to 60% for endometrial hyperplasia and from 1.3% to 12.8% for endometrial carcinoma [16–18]. Since they are estrogen-secreting tumors, the persistent hyperestrogenism might lead to excessive proliferation of endometrial glands that may undergo malignant transformation into carcinoma. In our series, 11.2% of patients had a diagnosis of endometrial cancer or complex atypical hyperplasia. To note, 40% of the patients receiving radical minimally invasive surgery underwent bilateral salpingo-oophorectomy preserving their uterus. 90% of these were older than 40 years therefore exposed to a higher risk of developing endometrial abnormalities. In a previous report from the MITO group including 150 patients with primary AGCT of the ovary, the two most important risk factors associated with endometrial pathologies were the presence of symptoms, like abnormal uterine bleeding and age over 40 years [16]. For this reason, endometrial sampling is recommended at the time of diagnosis in symptomatic or older patients. In asymptomatic women younger than 40 years, transvaginal ultrasound might help ruling out endometrial thickening.

Conclusions

The present study, the largest available in literature including only patients with stage I AGCTs, suggests that surgical route does not seem to affect the oncological safety of patients with stage I AGCTs, with comparable outcomes between laparoscopic and open approach. Its value is limited by its retrospective nature, due to the rarity and indolent course of this disease. It is already well known that randomized trials in rare ovarian tumors are difficult to be designed, thus management still remains controversial and often individualized. This limiting step might only be overcome by promoting international collaboration, as recently acknowledged during the 5th Ovarian Cancer Consensus Conference of the Gynecologic Cancer Intergroup (GCIG) in Tokyo [19].

Conflict of interest statement

The authors declares no conflicts of interest.

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References

[1] Young RH. Sex cord-stromal tumors of the ovary and testis: their similarities and differences with consideration of selected problems. Mod Pathol 2005;18(Suppl 2):S81–98.

[2] Schumer ST, Cannistra SA. Granulosa cell tumor of the ovary. J Clin Oncol 2003;21:1180.

[3] Mangili G, Ottolina J, Gadducci A, Giorda G, Breda E, Savarese A, et al. Long-term follow-up is crucial after treatment for granulosa cell tumours of the ovary. Br J Cancer 2013;109:29–34.

[4] Abu-Rustum NR, Restivo A, Ivy J, Soslow R, Sabbatini P, Sonoda Y, et al. Retroperitoneal nodal metastasis in primary and recurrent granulosa cell tumors of the ovary. Gynecol Oncol 2006;103:31.

[5] Miller K, McCluggage WG. Prognostic factors in ovarian adult granulosa cell tumour. J Clin Pathol 2008;61:881–4.

[6] Colombo N, Peiretti M, Garbi A, Carinelli S, Marini C, Sessa C. Non-epithelial ovarian cancer: ESMO Clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2012 Oct;23(Suppl.7). vii20-6.

[7] Querleu D. Laparoscopic surgical therapy and staging in a case of early malignant granulosa cell tumor of the ovary. Eur J Obstet Gynecol Reprod Biol 1994 May 18;54:215–7.

[8] Shim SH, Kim DY, Lee SW, Park JY, Kim JH, Kim YM, et al. Laparoscopic management of early-stage malignant non epithelial ovarian tumors: surgical and survival outcomes. Int J Gynecol Cancer 2013;23:249–55.

[9] Till H, Schmidt H. Juvenile granulosa cell tumour (JGCT) of the ovary in a 6-year-old girl: laparoscopic resection achieves long-term oncological success. Eur J Pediatr Surg 2005;15:292–4.

[10] Bryk S, Färkkllä A, Horlings HM, Leminem A, Tapper J, Heikinheimo M, et al. Characteristics and outcome of recurrence in molecularly defined adult-type ovarian granulosa cell tumors. Gynecol Oncol 2016;143:571–7.

[11] Prat J. FIGO Committee on gynecologic oncology. Staging classification for cancer of the ovary, fallopian tube, and peritoneum. Int J Gynaecol Obstet 2014 Jan;124(1):1–5.

[12] Mangili G, Ottolina J, Cormio G, Loizzi V, De Iaco P, Pellegrini DA, et al. Adjuvant chemotherapy does not improve disease-free survival in FIGO stage IC ovarian granulosa cell tumors: the MITO-9 study. Gynecol Oncol 2016;143:276–80.

[13] Bogani G, Borghi C, Leone Roberti Maggiore U, Ditto A, Signorelli M, Martinelli F, et al. Minimally invasive surgical staging in early-stage ovarian carcinoma: a Systematic Review and Meta-analysis. J Minim Invasive Gynecol 2017 May–Jun;24:552–62.

[16] Ottolina J, Ferrandina G, Gadducci A, Scollo P, Giorda G, Lorusso D, et al. Is the endometrial evaluation routinely required in patients with adult granulosa cell tumors of the ovary? Gynecol Oncol 2015;136:230–4.

[17] Stenwig JT, Hazekamp JT, Beecham JB. Granulosa cell tumors of the ovary. A clinicopathological study of 118 cases with long-term follow-up. Gynecol Oncol 1979;7:136–52.

[18] Ayhan A, Salman MC, Velipaasaoglu M, Sakinci M, Yuce K. Prognostic factors in adult granulosa cell tumors of the ovary: a retrospective analysis of 80 cases. J Gynecol Oncol 2009;20:158–63.

[19] Leary AF, Quinn M, Fujiwara K, Coleman RL, Kohn E, Sugiyama T, et al. Fifth ovarian cancer consensus conference of the Gynecologic Cancer InterGroup (GCIG): clinical trial design for rare ovarian tumours. Ann Oncol 2017;28:718–26.

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