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Original Research Article

Optimizing care for low-grade serous ovarian carcinoma: insights from a tertiary care centre

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ABSTRACT

Background: Low-grade serous ovarian carcinoma (LGSC) is an uncommon epithelial ovarian malignancy with distinct tumour biology, relatively indolent behaviour, frequent advanced-stage presentation and limited sensitivity to conventional chemotherapy. This study evaluated the clinicopathological profile, treatment pattern, perioperative outcomes and survival of patients with LGSC managed at a tertiary cancer centre.
Methods: A retrospective review was conducted of 23 patients with histologically confirmed LGSC treated between 2014 and 2025. Demographic characteristics, clinical presentation, tumour markers, FIGO stage, disease distribution, chemotherapy response, surgical approach, completeness of cytoreduction, postoperative morbidity, recurrence and survival outcomes were analyzed descriptively.
Results: The median age was 47 years. Abdominal pain was the most common presenting symptom, reported in 17 patients (73.91%). Serum CA-125 was elevated in 19 patients (82.6%), with a median value of 89 U/ml. FIGO stage III disease was present in 18 patients (78.26%). Nine patients received neoadjuvant chemotherapy; objective response was observed in only 2 patients (22.2%), while 5 had stable disease and 2 progressed. Primary cytoreductive surgery was performed in 12 patients, interval cytoreduction in 9 and staging laparotomy in 2. Complete cytoreduction was achieved in 19 patients (82.6%). Grade III morbidity occurred in 21.7%, with no Grade IV/V complications or 30-day mortality. At 36-month median follow-up, recurrence occurred in 6 patients; 3 years overall survival was 75% and disease-free survival was 66%.
Conclusions: LGSC commonly presents with advanced peritoneal disease and poor chemotherapy response. Complete cytoreduction remains the key therapeutic goal.

Keywords: Cytoreductive surgery, Chemotherapy resistance, Low-grade serous ovarian carcinoma, Neoadjuvant chemotherapy, Ovarian cancer, Overall survival

INTRODUCTION

LGSC is an uncommon epithelial ovarian malignancy, accounting for less than 10% of epithelial ovarian cancers and is now recognized as a disease entity biologically distinct from high-grade serous ovarian carcinoma (HGSC).[1,2] Unlike HGSC, LGSC generally affects younger women, shows low-grade cytologic atypia and relatively low proliferative activity and often follows a protracted clinical course.[1,5] Its slower tempo, however, should not be equated with low clinical risk: many patients present with advanced peritoneal disease and may experience repeated recurrences over many years.[1] One of the central therapeutic problems in LGSC is relative resistance to conventional platinum-taxane chemotherapy.[6,8,9] This feature changes the balance between surgery and systemic therapy: when complete gross resection is technically achievable and the patient is fit, surgery assumes greater importance, whereas routine reliance on neoadjuvant chemotherapy (NACT) may delay definitive cytoreduction in a tumour with modest expected radiological response.[1,6] The clinical decision is therefore

not simply whether chemotherapy can be administered, but whether it is likely to improve resectability without sacrificing the opportunity for maximal cytoreduction.

Molecularly, LGSC is enriched for alterations in the mitogen-activated protein kinase (MAPK) pathway, including KRAS, BRAF and NRAS, while TP53 mutation and BRCA-associated homologous-recombination deficiency are far less characteristic than in HGSC.[3,4,7] These differences are therapeutically relevant. Endocrine strategies have shown clinical utility in selected patients and MAPK-directed therapy has moved from biological rationale to randomized evidence, with trametinib improving outcomes in recurrent disease.[15,16] More recently, the RAF/MEK-clamp avutometinib combined with the focal adhesion kinase inhibitor defactinib demonstrated clinically meaningful activity in recurrent LGSC, further supporting a disease-specific, molecularly informed treatment paradigm.[17]

Despite these advances, several practical questions remain unsettled, particularly in the upfront setting: who should undergo primary cytoreduction rather than NACT, how aggressively multivisceral disease should be pursued, how endocrine therapy should be integrated and how molecular results should alter treatment sequencing.[1] Because LGSC is rare, prospective datasets remain relatively small; therefore, real-world surgical series are valuable, particularly from high-volume centres where completeness of cytoreduction can be evaluated together with perioperative morbidity and longer-term outcome.

The present retrospective study examines patients with histologically confirmed LGSC managed over 12 years at a tertiary cancer centre. We evaluated clinical presentation, disease distribution, chemotherapy response, surgical strategy, completeness of cytoreduction, perioperative outcomes, recurrence and survival. Our objective was to identify clinically useful patterns that may help optimize treatment selection in a tumour for which surgical judgment and disease-specific systemic therapy are increasingly important.

METHODS

This retrospective observational study included all patients with histologically confirmed low-grade serous ovarian carcinoma (LGSC) treated in the Department of Surgical Oncology, Dr. B. R. Ambedkar Institute Rotary Cancer Hospital (Dr. BRA-IRCH), All India Institute of Medical Sciences (AIIMS), New Delhi, India, between January 2014 and December 2025. Eligible patients were identified from institutional medical records and pathology databases. Patients with incomplete diagnostic confirmation or non-serous/high-grade serous histology were excluded.

Data were collected retrospectively using a predefined data extraction format. Variables recorded included age at diagnosis, presenting symptoms, performance status, serum tumour markers including CA-125 and carcinoembryonic antigen, radiological findings, operative details, histopathological characteristics, FIGO 2014 stage, anatomical distribution of disease, treatment sequence, chemotherapy details, surgical procedures, postoperative outcomes, recurrence and survival status.

Radiological assessment was performed using contrast-enhanced computed tomography and/or other imaging modalities as clinically indicated. Disease distribution was documented according to site-specific involvement, including lower abdomen, upper abdomen, bowel, hepatosplenic region, omentum, lymph nodes and extra-abdominal disease where applicable.

Treatment strategy was individualized through multidisciplinary tumour board discussion. Patients underwent either primary cytoreductive surgery, interval cytoreductive surgery following neoadjuvant chemotherapy or staging laparotomy, depending on disease extent, resectability, performance status and institutional practice. Neoadjuvant chemotherapy, when administered, generally consisted of platinum-based combination regimens according to institutional protocols. Response to neoadjuvant chemotherapy was assessed using RECIST 1.1 criteria wherever measurable disease was available and was categorized as complete response, partial response, stable disease or progressive disease. Tumour marker response and clinical assessment were also reviewed as supportive parameters.

Surgical adequacy was evaluated according to residual disease status at the completion of surgery. Complete cytoreduction was defined as no macroscopic residual disease (CC-0), while visible residual disease was documented according to the extent of residual tumour. Postoperative morbidity was graded using the Clavien-Dindo classification. Intensive care unit stay, total hospital stay, major complications, reintervention, readmission, 30-day mortality, recurrence, disease-free survival and overall survival were analyzed.

Descriptive statistics were used for data analysis. Continuous variables were expressed as median or mean, as appropriate and categorical variables were reported as frequencies and percentages. The study was conducted in accordance with institutional ethical standards and patient confidentiality was maintained throughout data collection and analysis.

Statistical analysis

Data were analyzed using descriptive statistical methods appropriate for a retrospective cohort with a limited sample size. Continuous variables were summarized as median with range, while categorical variables were expressed as frequencies and percentages. Treatment response, surgical outcomes, postoperative morbidity, recurrence and survival status were tabulated and analyzed descriptively. Survival outcomes were assessed in terms of

overall survival (OS) and disease-free survival (DFS). Overall survival was defined as the interval from the date of diagnosis or initiation of treatment to death from any cause or last follow-up. Disease-free survival was defined as the interval from completion of definitive treatment to documented recurrence, progression, death or last follow-up, as applicable. Three-year OS and DFS were reported as outcome measures. Given the small cohort size, no formal comparative or multivariable statistical analysis was performed.

RESULTS

Baseline characteristics

A total of 23 patients with histologically confirmed low-grade serous ovarian carcinoma were included in the study. The median age at diagnosis was 47 years, with an age range of 28–52 years. Most patients had preserved functional status at presentation; ECOG performance status was 0 in 5 patients (21.7%), 1 in 16 patients (69.6%) and 2 in 2 patients (8.7%).

Abdominal pain was the most frequent presenting symptom, reported in 17 patients (73.91%). Other common symptoms included abdominal distension in 12 patients (52.17%), loss of appetite in 10 patients (43.47%), abdominal lump in 7 patients (30.43%), weight loss in 6 patients (26.08%) and abnormal vaginal bleeding in 4 patients (17.39%). The baseline demographic and clinical characteristics of the study cohort are summarized in Table 1.

Disease characteristics

Baseline tumour marker assessment showed elevated serum CA-125 levels in 19 patients (82.6%), with a median value of 89 U/mL. In contrast, carcinoembryonic antigen was elevated in only 2 patients (8.69%), suggesting that CA-125 was the more frequently abnormal marker in this cohort. At diagnosis, most patients had advanced-stage disease. FIGO stage III was the most common stage, observed in 18 patients (78.26%). Early-stage disease was uncommon, with stage I in 2 patients (8.69%) and stage II in 1 patient (4.34%). Stage IV disease was present in 2 patients (8.69%). The predominance of stage III disease indicates that LGSC, despite its relatively indolent tumour biology, frequently presents after substantial peritoneal dissemination. The disease characteristics are summarized in Table 2.

Chemotherapy characteristics

Nine patients received neoadjuvant chemotherapy before definitive surgical intervention. The median number of chemotherapy cycles administered was 3, with a range of 3–6 cycles. The most commonly used regimen was three-weekly carboplatin plus paclitaxel, administered to 8 patients (88.9%). One patient (11.1%) received weekly carboplatin. The radiological and clinical response to neoadjuvant chemotherapy was modest. Objective response, defined as complete or partial response, was observed in only 2 patients (22.2%). Stable disease was the most frequent outcome, documented in 5 patients (55.5%). Two patients (22.2%) showed disease progression during chemotherapy. These findings support the relatively chemoresistant nature of low-grade serous ovarian carcinoma and reinforce the importance of surgical cytoreduction as a major component of treatment. Chemotherapy-related characteristics are summarized in Table 3.

Surgery characteristics

Surgical management was planned according to disease extent, resectability, performance status and multidisciplinary clinical assessment. Of the 23 patients, 2 patients (8.69%) underwent staging laparotomy, 12 patients (52.17%) underwent primary cytoreductive surgery and 9 patients (39.13%) underwent interval cytoreductive surgery following neoadjuvant chemotherapy. Cytoreductive surgery with HIPEC was performed in 16 patients, representing 69.57% of the total cohort.

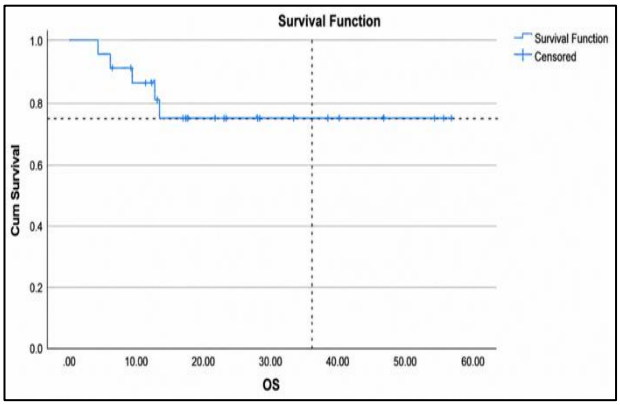

Figure 1: Overall survival.

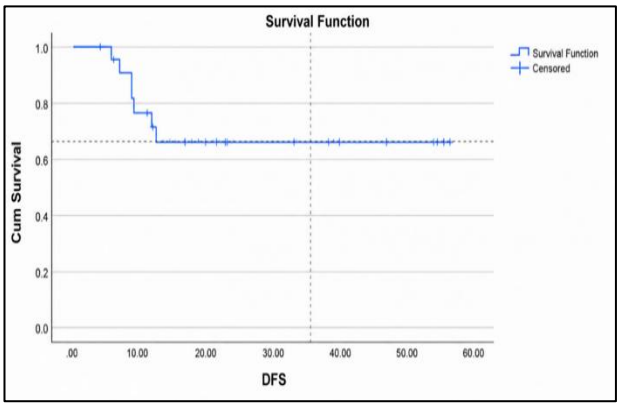

Figure 2: Disease free survival.

Disease distribution demonstrated a predominantly disseminated peritoneal pattern. Lower abdominal involvement was observed in 11 patients (47.82%), upper

abdominal involvement in 9 patients (39.13%) and disease confined to the pelvis in 1 patient (4.34%). Hepatic or splenic surface involvement was documented in 7 patients (30.43%), while bowel and lymph node involvement were each present in 6 patients (26.08%). Bladder involvement and pleural/lung involvement were each recorded in 2 patients (8.69%). The median peritoneal cancer index was 9, with a range of 3–21. The median operative duration was 320 minutes, ranging from 180 to 520 minutes. Mean intraoperative blood loss was 400 ml. Complete macroscopic cytoreduction was achieved in 19 patients (82.6%), while 4 patients (17.39%) had CC-1 residual disease. No patient had CC-2 residual disease. Bowel resection was required in 6 patients (26.08%) and stoma formation was performed in 3 patients (13.04%). The median surgical complexity score was 4, with a range of 3–7. These findings suggest that optimal cytoreduction was feasible in the majority of patients despite multifocal intra-abdominal disease. Results are shown in Table 4.

Postoperative course and major morbidity profile

The postoperative recovery profile is summarized in Table 5. The median intensive care unit stay was 1 day, with a range of 0–3 days and the median hospital stay was 5 days, ranging from 4 to 10 days. For clinically meaningful morbidity assessment, only major postoperative complications were analyzed. Major morbidity was defined as Clavien-Dindo Grade III or higher. Grade III complications occurred in 5 patients (21.7%) and were managed with appropriate surgical, endoscopic or radiological intervention. No Grade IV life-threatening complications and no Grade V mortality were observed. There was no 30 days postoperative mortality. These findings indicate that comprehensive cytoreductive surgery was associated with acceptable major morbidity and no early postoperative mortality in this cohort.

Survival outcomes

At a median follow-up of 36 months, disease recurrence was documented in 6 patients (26%). The estimated 3 years overall survival for the cohort was 75%, while the 3 years disease-free survival was 66% as shown in Fig 1, 2 and Table 6. These findings provide clinically relevant survival benchmarks for low-grade serous ovarian carcinoma in a tertiary care setting. Despite the limited objective response to neoadjuvant chemotherapy observed in this cohort, favourable survival outcomes were achieved in selected patients, likely reflecting the importance of optimal cytoreduction as a central component of multimodal management. The results further support the need for individualized treatment planning in LGSC, with emphasis on maximal safe cytoreductive surgery, careful assessment of chemotherapy benefit and structured long-term surveillance because of the recurrent nature of this disease.

Table 1: Baseline characteristics of patients with low-grade serous ovarian carcinoma (n=23).

Characteristics	Value
Median age, years	47
Age range, years	28–52
ECOG performance status, n (%)	
0	5 (21.7)
1	16 (69.6)
2	2 (8.7)
Presenting symptoms, n (%)	
Abdominal pain	17 (73.91)
Abdominal distension	12 (52.17)
Loss of appetite	10 (43.47)
Abdominal lump	7 (30.43)
Weight loss	6 (26.08)
Abnormal vaginal bleeding	4 (17.39)

Table 2: Disease characteristics of patients with low-grade serous ovarian carcinoma (n=23).

Parameters	Value
Elevated CA-125, N (%)	19 (82.6)
Median CA-125, U/ml	89
Elevated CEA, N (%)	2 (8.69)
FIGO stage, N (%)	
Stage I	2 (8.69)
Stage II	1 (4.34)
Stage III	18 (78.26)
Stage IV	2 (8.69)

Table 3: Chemotherapy characteristics among patients receiving neoadjuvant chemotherapy (n=9).

Parameters	Value
Median number of chemotherapy cycles, range	3 (3–6)
Three-weekly carboplatin+paclitaxel, n (%)	8 (88.9)
Weekly carboplatin, n (%)	1 (11.1%)
Response to NACT	**N (%)**
Complete/partial response	2 (22.2)
Stable disease	5 (55.5)
Progressive disease	2 (22.2)

Table 4: Surgical characteristics of patients with low-grade serous ovarian carcinoma (n=23).

Parameters	Number (%)
Surgical approach	
Staging laparotomy	2 (8.69)
Primary cytoreductive surgery	12 (52.17)
Interval cytoreductive surgery	9 (39.13)
CRS+HIPEC	16 (69.57)
Disease sites involved	
Lower abdomen	11 (47.82)
Upper abdomen	9 (39.13)
Pelvis only	1 (4.34)
Liver/spleen	7 (30.43)
Bowel involvement	6 (26.08)
Lymph nodes	6 (26.08)
Bladder involvement	2 (8.69)
Lung/pleura	2 (8.69)
Median PCI, range	9 (3–21)
Median operative duration, minutes, range	320 (180–520)
Mean blood loss, ml	400
Completeness of cytoreduction	
CC-0	19 (82.6)
CC-1	4 (17.39)
CC-2	0 (0)
Bowel resection required	6 (26.08)
Stoma formation	3 (13.04)
Median surgical complexity score, range	4 (3–7)

Table 5: Postoperative course and major morbidity profile (n=23).

Events	Value
Median ICU stay, days, range	1 (0–3)
Median hospital stay, days, range	5 (4–10)
Major postoperative complications	**N (%)**
Clavien-dindo grade III	5 (21.7)
Clavien-dindo grade IV	0 (0)
Clavien-dindo grade V	0 (0)
30-day mortality	0 (0)

Table 6: Survival outcomes of patients with low-grade serous ovarian carcinoma (n=23).

Outcomes	Value
Median follow-up	36 months
Recurrence	6 (26%)
3-year overall survival	75%
3-year disease-free survival	66%

DISCUSSION

This institutional series highlights a clinically important contradiction in LGSC: indolent histology does not necessarily imply limited disease burden. Most patients presented with advanced-stage disease, objective response to NACT was low, yet complete macroscopic cytoreduction was achieved in 82.6% of the cohort. The practical implication is that LGSC often behaves as a surgically demanding but relatively chemotherapy-insensitive malignancy and treatment planning should reflect this biology rather than default to algorithms developed primarily for HGSC.[1,6]

The median age at presentation was 47 years, consistent with the recognized tendency of LGSC to affect women at a younger age than HGSC.[5] Stage III disease was present in 78.26% and stage IV disease in 8.69%, confirming that slow tumour kinetics do not prevent extensive peritoneal dissemination. For surgeons, this distinction is important: a long natural history may coexist with substantial anatomical disease and resectability should therefore be judged by disease distribution and the feasibility of complete gross resection rather than by the apparently indolent label alone. Presenting symptoms were predominantly non-specific, with abdominal pain and distension being most common. Serum CA-125 was elevated in 82.6% of patients and can be useful for baseline assessment and longitudinal monitoring, but it should not be used as a surrogate for resectability or treatment response in isolation. In LGSC, clinical examination, cross-sectional imaging, operative assessment, pathology and tumour-marker trends are complementary rather than interchangeable sources of information.

The limited response to NACT is one of the most clinically relevant findings of this study. Among nine patients receiving NACT, only two (22.2%) achieved an objective response, while five (55.5%) had stable disease and two (22.2%) progressed. This pattern is consistent with the well-described relative chemoresistance of LGSC.[6,8,9] Stable disease should not automatically be interpreted as a meaningful therapeutic gain if the anatomical conditions for surgery are unchanged. In a potentially resectable patient, prolonged NACT without clear benefit may consume time without materially improving the probability of complete cytoreduction. These findings support selective, rather than routine, use of NACT in LGSC, with early reassessment of resectability when chemotherapy is chosen.[1,6]

Complete macroscopic cytoreduction was achieved in 19 of 23 patients (82.6%), with only four patients having CC-1 residual disease. The prognostic importance of residual disease in LGSC has been demonstrated in larger datasets, in which complete resection is associated with superior progression-free and overall survival.[6] The high CC-0 rate suggests that careful patient selection, experienced upper-abdominal and bowel surgery and multidisciplinary perioperative support can make extensive disease surgically manageable. However, because this is a retrospective series without an internal comparator, the observed survival cannot be attributed to cytoreduction alone.

The anatomical distribution of disease further illustrates the technical demands of LGSC surgery. Upper-abdominal disease was present in 39.13%, liver or splenic surface involvement in 30.43% and bowel involvement in 26.08%; bowel resection was required in six patients and stoma formation in three. These data support an operative strategy in which the goal is maximal safe clearance of disease rather than avoidance of multivisceral procedures when complete resection is realistically achievable. At recurrence, secondary cytoreduction also remains a rational option for carefully selected patients when complete gross resection appears feasible.[12]

A distinctive feature of this cohort is that 16 patients (69.57%) underwent cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC). This observation should be interpreted cautiously. The study was not designed to evaluate the efficacy of HIPEC, there is no non-HIPEC comparator, treatment selection was non-randomized and LGSC-specific evidence for HIPEC remains limited. Consequently, no independent survival benefit from HIPEC can be inferred from these data; in this manuscript it is more appropriately regarded as an institutional component of multimodal treatment rather than an explanation for the observed outcomes.

The perioperative results show that extensive cytoreduction was achievable without 30 days mortality or Clavien-Dindo Grade IV/V complications. Nevertheless, Grade III morbidity occurred in 21.7% of patients and should not be minimized. The absence of mortality is reassuring, but a major-complication rate of approximately one in five patients underlines the need for realistic preoperative counselling, careful patient selection, experienced anaesthesia and critical-care support and active postoperative complication management.

At a median follow-up of 36 months, the estimated 3 years overall survival was 75% and disease-free survival was 66%. These outcomes are encouraging in a cohort dominated by advanced-stage disease, but they require cautious interpretation because of the small sample, heterogeneous treatment pathways, limited number of events and absence of comparative or multivariable analysis. The survival estimates should therefore be regarded as institutional benchmarks rather than evidence of superiority of any specific treatment component. The contemporary systemic-treatment landscape also changes how these results should be interpreted. Retrospective data support a role for hormonal maintenance therapy in selected patients, while the randomized GOG 281/LOGS trial established trametinib as an active option in recurrent LGSC.[15,16] In 2025, the phase II ENGOT-OV60/GOG-3052/RAMP 201 study further demonstrated clinically meaningful activity with avutometinib plus defactinib in

recurrent disease.[17] These advances strengthen the case for routine capture of hormone-receptor status and MAPK-pathway alterations, including KRAS, BRAF and NRAS, whenever feasible. For tertiary centres, a pragmatic disease-specific pathway is therefore to prioritize complete primary cytoreduction when achievable, use NACT selectively with early reassessment, integrate endocrine and targeted therapies according to clinical context and molecular findings and maintain prolonged surveillance because late recurrence is characteristic of LGSC.[1]

This study has several limitations. It is retrospective, single-centre and includes only 23 patients treated over a long period during which systemic options evolved. Selection bias is unavoidable, particularly for primary surgery, NACT and HIPEC. Molecular profiling, hormone-receptor status, endocrine-treatment exposure and detailed treatment at recurrence were not uniformly available, limiting correlation between tumour biology and outcome. The median follow-up of 36 months may also underestimate late recurrence in a disease with a prolonged natural history. Future multicentre prospective studies should integrate standardized resectability assessment, surgical complexity and residual-disease reporting, molecular characterization, endocrine therapy and contemporary MAPK-directed strategies to define the optimal sequence of treatment.[1,15-17]

CONCLUSION

Low-grade serous ovarian carcinoma is a rare and biologically distinct ovarian malignancy that requires an individualized treatment strategy rather than direct extrapolation from high-grade serous ovarian cancer. In this tertiary cancer centre experience, most patients presented with advanced-stage disease and response to neoadjuvant chemotherapy was limited, reinforcing the relatively chemo resistant nature of LGSC. Maximal safe cytoreductive surgery remains a principal therapeutic objective and appears central to achieving favourable outcomes in appropriately selected patients. The high rate of complete cytoreduction, acceptable major postoperative morbidity, absence of 30 days mortality and 3 years overall survival of 75% with disease-free survival of 66% provide useful real-world benchmarks for LGSC management in a specialized setting.

Optimal care for LGSC should be delivered through a multidisciplinary approach involving careful preoperative assessment, appropriate surgical planning, selective use of systemic therapy, structured follow-up and long-term surveillance. Future multicentre prospective studies incorporating molecular profiling, endocrine therapy evaluation and targeted treatment strategies are required to refine treatment sequencing and improve both survival and quality of life in patients with LGSC.

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