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Krukenberg tumours revisited: A regional review of their hidden origins and clinical journey

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Abstract
Background: Krukenberg tumours (KTs) are rare metastatic ovarian tumours characterized by mucin-producing signet-ring cells, most commonly originating from the gastrointestinal tract. Their clinical presentation is often nonspecific, and prognosis remains poor. We aimed to assess the clinical profile, primary tumour origins, treatment modalities, and outcomes in patients diagnosed with Krukenberg tumours at a tertiary care centre in Central India.
Materials and Methods: A retrospective record-based study was conducted on 18 female patients with histopathologically confirmed KTs, from 2023 to 2025. Data on demographics, clinical features, tumour characteristics, treatment received, and survival outcomes were extracted.
Results: The median age was 49 years, with 77.8% presenting with abdominal distension and pain. The most common primary site was colorectal cancer (33.3%), followed by stomach (27.8%). Bilateral ovarian involvement was observed in 83.3%, and 88.9% had synchronous metastases. Cytoreductive surgery was performed in 27.8%, with R0 resection achieved in 22.2%. FOLFOX was the most common chemotherapy regimen. Partial response was observed in 38.9%, complete response in 5.6%, and disease progression in 22.2%. The median progression-free survival was 4 months (IQR: 3-6), and overall survival was 6 months (IQR: 4-11.5).
Conclusions: Krukenberg tumours most often arise from gastrointestinal primaries with a typically delayed presentation. Despite chemotherapy, outcomes remain dismal without complete surgical resection. A strategic combination of timely diagnosis, aggressive multimodal therapy, and meticulous surgical management offers the best hope for improving survival in these challenging cases.

Keywords: Krukenberg tumour, metastatic ovarian cancer, colorectal carcinoma, chemotherapy, survival analysis, cytoreductive surgery, signet-ring cell carcinoma

Introduction
Krukenberg tumours (KTs) are uncommon metastatic ovarian cancers characterized by mucin-secreting signet-ring cells found within the ovarian stroma. [1] Originally identified by the German pathologist Friedrich Ernst Krukenberg in 1896, these tumours are now understood to be secondary cancers, predominantly arising from the gastrointestinal tract, especially the stomach. While the stomach is the most common primary site for Krukenberg tumours, they can also develop secondary to cancers from the appendix, breast, colon, small intestine, gallbladder, pancreas, and genitourinary tract.[1] Nevertheless, recent research suggests a changing pattern, with colorectal cancers increasingly recognized as a common primary origin of KTs. [2, 3]
Metastatic tumours account for about 10% of all ovarian tumours, with nearly half of these cases being Krukenberg tumours. The spread of these tumours typically occurs through lymphatic channels but can also occur via the bloodstream or direct extension, influenced by the location of the original tumour relative to the ovaries and lymph nodes. In some cases, the primary tumour remains unidentified. [4, 5] The clinical presentation of Krukenberg tumours is nonspecific, leading to diagnostic challenges. Patients may present with abdominal distension, pain, weight loss, or ascites, and in some cases, the ovarian tumours are discovered incidentally during imaging or surgical procedures. Such symptoms may be the heralding sign of an underlying malignancy and can include abdominal pain, swelling, fluid accumulation (ascites), abnormal vaginal bleeding, and painful intercourse. Additionally, these tumours can stimulate the ovarian stroma to produce hormones, leading to further clinical manifestations. [6] The mean age at presentation is typically around 45-46 years, with a higher prevalence in premenopausal women, possibly due to the increased vascularity and hormonal activity of the ovaries during this period. [7]

The diagnosis of Krukenberg tumour relies on criteria established by the World Health Organization, which are based on the pathological features described by Serov and Scully. To confirm the diagnosis, the tumour must exhibit stromal involvement, contain mucin-producing signet ring cells, and demonstrate sarcomatoid proliferation within the ovarian stroma. [8] The prognosis for patients with Krukenberg tumours varies depending on the site of primary tumour. Patients with gastric cancer-related KTs have a median overall survival of approximately 11 months, while those with colorectal cancer-related KTs have a median survival of about 21.5 months. Factors influencing prognosis include the presence of ascites, peritoneal involvement, and the ability to achieve complete surgical resection. [8]

Given the rarity and diagnostic challenges associated with Krukenberg tumours, a comprehensive understanding of their primary sites, clinical presentations, and management strategies is essential for clinicians. In this study we aimed to provide an analysis of Krukenberg tumours, focusing on their origins, clinical profile and survival of these patients.

Materials and Methods

The present study was conducted as a record based retrospective study on patients diagnosed with Krukenberg tumours during 3 years period (2023 to 2025) at a tertiary care centre in Central India. All the available complete medical records of female patients diagnosed with Krukenberg tumours confirmed by histopathology were included whereas patients with primary ovarian tumours other than KTs were excluded. Data regarding sociodemographic variables, presenting complaints, comorbid conditions, and site of primary tumours, synchronicity and laterality was noted in proforma.

Apart from this, findings of relevant tumour markers, radiologic imaging, biopsy and immunohistochemistry (IHC) were documented. History regarding cytoreductive surgery, chemotherapy (date of initiation of chemotherapy, regimen, lines of chemotherapy), progression of disease, response to treatment and outcome was documented.

Statistical analysis

Data was compiled using Microsoft Excel and analysed using IBM SPSS software version 20 (IBM Corp., Statistical Package for Social Sciences, Illinois Chicago). Categorical data was expressed as frequency and proportions whereas continuous data was expressed as median and IQR. Survival analysis was done using Kaplan-Meier analysis.

Results

In this study, we could retrieve data of 18 patients and median age of patients was 49 (41.25-56) years. The majority of patients fell within 41 to 50 years age group. The Eastern Cooperative Oncology Group performance status (ECOG PS) was reflective of a real world scenario where 72.2% presented with an ECOG PS 2. Abdominal distension and pain were the most common symptoms, each reported by 77.8% of patients. Ascites was present in 61.1% whereas indigestion (50.0%) and weight loss (44.4%) were also frequent (Table 1).

Table 1: Baseline variables of patients with Krukenberg Tumours

Variable	n	Percentage (%)
Age		
≤40 years	4	22.2
41-50 years	7	38.9
51-60 years	4	22.2
>60 years	3	16.7
ECOG PS		
PS 1	5	27.8
PS 2	13	72.2
Presenting Symptoms		
Abdominal distension	14	77.8
Abdominal pain	14	77.8
Ascites	11	61.1
Indigestion	9	50.0
Weight loss	8	44.4

Legend: ECOG - Eastern Cooperative Oncology Group Performance Status.

The most common site of the primary tumour was colorectal carcinoma (33.3%), followed by the stomach in 27.8%, and less frequently the appendix, breast, and gall bladder, each in 11.1%. The majority of patients (88.9%, n=16) presented with synchronous tumours, while 11.1% (n=2) had metachronous presentations. Regarding laterality, bilateral tumour involvement was observed in 83.3% of cases, suggesting widespread or aggressive disease, while only 16.7% were unilateral. (Table 2)

On histopathological evaluation, the most frequent tumour type was adenocarcinoma, seen in 50.0% (n=9), with mucinous adenocarcinoma observed in 38.9% (n=7) and signet ring cell adenocarcinoma in 11.1% (n=2).

These variations are typically associated with a more aggressive biology. (Table 2)

Table 2: Pathologic Characteristics of primary and metastatic tumours

Variable	n	Percentage (%)
Primary Site		
Colorectal	6	33.3
Stomach	5	27.8
Appendix	2	11.1
Breast	2	11.1
Gall bladder	2	11.1
Pancreas	1	5.6
Synchronicity and Laterality		
Synchronous metastases	16	88.9
Bilateral ovarian involvement	15	83.3
Unilateral ovarian involvement	3	16.7
Histology		
Adenocarcinoma	9	50
Adenocarcinoma with Mucinous/Signet Cell Morphology	9	50
Immunohistochemistry		
CK7+	11/18	61.11
CK20+	7/18	38.88
SATB2+	7/8	87.5
CDX2+	12/16	75
CK19+	3/8	37.5

Immunohistochemistry profiling was done for all cases. CK7 positivity was seen in 61.11% cases which were of Breast, Stomach, and Hepatobiliary origin. CK20 highlighted 38.88% of tumours suggesting Colorectal and Appendiceal origin. Among these, 87.5% were also SATB2 positive. Three-fourths of patients (75%) showed CDX2 staining. Among the 8 tumours of Upper gastrointestinal and hepatobiliary origin, 37.5% showed CK19 staining pattern. Both cases of primary breast origin were ER and/or PR positive and Her2neu negative (Table 2).

In the present study, 27.8% cases underwent cytoreductive surgery, of them, 22.2% achieved R0 resection, while 5.6% had R2 resection. Regarding systemic therapy, a wide range of chemotherapy regimens was utilized, based upon the site of primary tumour and clinical scenario. The most commonly administered regimen was FOLFOX (5-Fluorouracil, Leucovorin, and Oxaliplatin) 27.8%. CAPOX (Capecitabine + Oxaliplatin) was used in 22.22%, and Gemcitabine-based therapies were used in a combined 16.7% of patients. Half of the patients (50%) received only one line of chemotherapy, while 33.3% progressed to a second line, and 16.7% underwent three lines of chemotherapy, indicating that the delayed presentation and poor presenting performance status precludes multiple lines of therapy administration leading to poorer outcomes (Table 3)

Table 3: Treatment details and outcomes

Treatment parameter	n	Percentage (%)
Cytoreductive surgery performed	5	27.8
R0 resection	4	22.2
R2 resection	1	5.6
Chemotherapy regimens used		
FOLFOX regimen	5	27.8
CAPOX regimen	4	22.2
Gemcitabine-based therapy	3	16.7
Paclitaxel-Carboplatin	2	11.1
Capecitabine	2	11.1
Lines of chemotherapy		
One line	9	50.0
Two or more	9	50.0
Radiologic response (RECIST 1.1)		
Complete response	1	5.6
Partial response	11	61.1
Stable Disease	2	11.1
Progressive disease	4	22.2

Legend: RECIST - Response Evaluation Criteria in Solid Tumors

In our study, we observed a singular complete response while most patients (61.11%) had partial response (Figure 1). In 4 cases (22.22%), there was disease progression. Notably, 3 of these 4 cases were of Gastric primary.

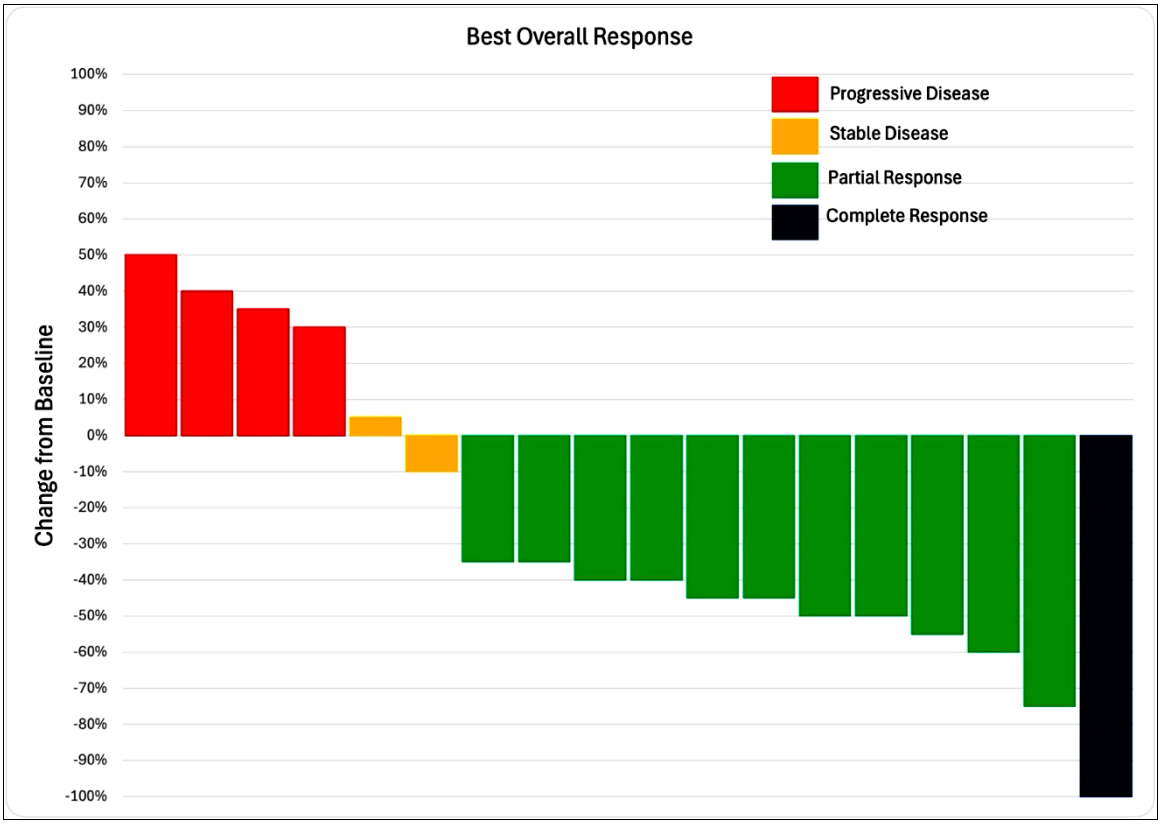

Fig 1: Waterfall Plot showing best overall response (based on RECIST 1.1 criteria).

Median progression free survival duration was 4 (IQR-3 to 6) months and overall survival was 6 months (IQR-4-11.5). Overall, mortality was documented in 10 (55.6%) cases. In the progression-free survival (PFS) analysis of 18 patients, the highest number of progression events occurred in the first 6 months (n=8), with an additional 3 events between 6-12 months. No further events were recorded beyond 12 months, although withdrawals continued through to 24 months, indicating possible censoring or loss to follow-up. In contrast, overall survival (OS) showed a more gradual pattern of events. Only 2 deaths occurred in the first 6 months, followed by 6 between 6-12 months and 2 more between 12-18 months. No deaths were observed beyond 18 months. These findings suggest that while disease progression was most common early in treatment, overall survival extended further, reflecting the potential benefit of subsequent therapies or supportive care beyond initial progression (Figure 2 and Figure 3).

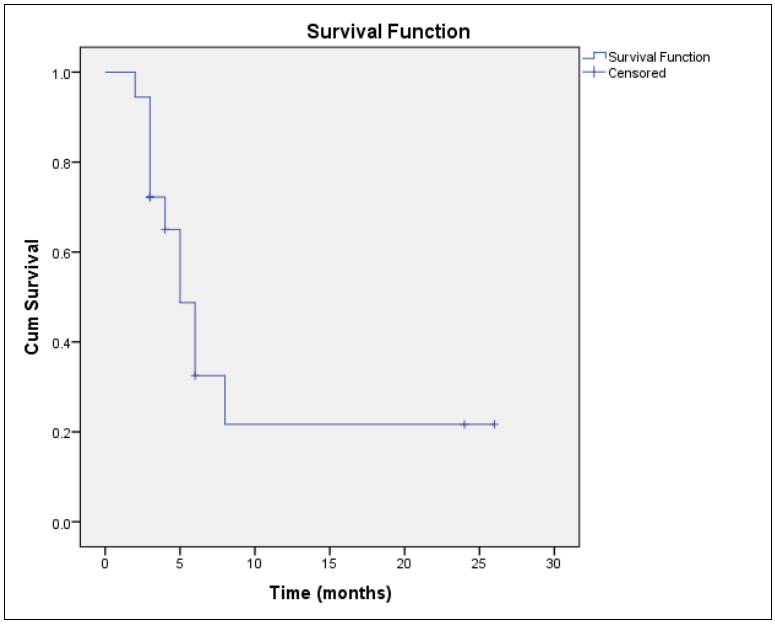

Fig 2: Kaplan-Meier curve showing progression-free survival (PFS)

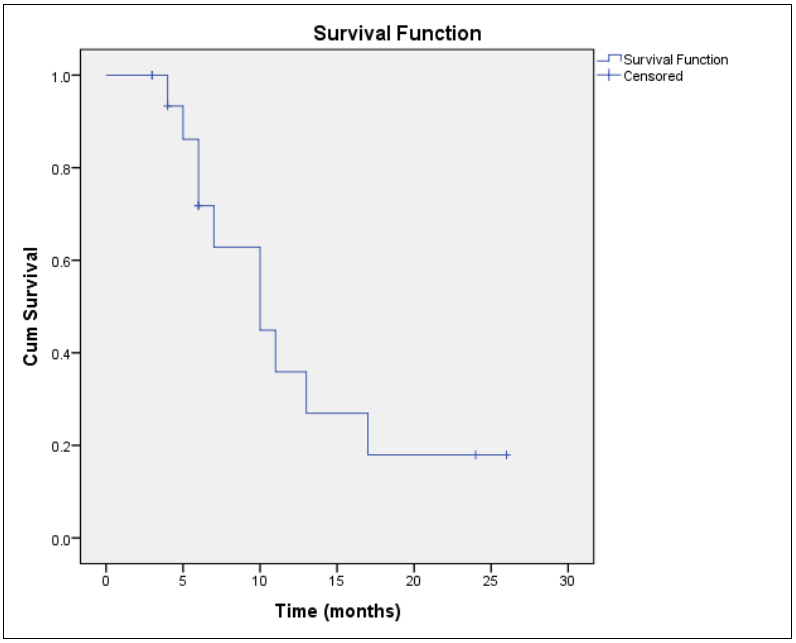

Fig 3: Kaplan-Meier curve showing overall survival (OS)

Discussion

The present study was conducted at a tertiary care cancer centre in Central India as a retrospective record based study on 18 cases of Krukenbergs' tumour. We aimed to explore the origin, clinical presentation and outcome of these patients. The median age of patients was 49 (IQR 41.25-56 and range- 34 to 65) years and the majority of them presented in fourth decade of life. Our study findings were supported by the findings of Wu *et al*, in which the median age of patients at the time of diagnosis was 48 years (range, 27-65 years). [9] Similar findings were documented by Zulfiqar *et al*, in which the median age of patients was 48 years.[6] Literature suggests that women with gastrointestinal primary tumours tend to be older, while those with breast cancer-associated Krukenberg tumours are generally younger. Notably, ovarian metastases are more commonly observed in younger women compared to primary ovarian cancers. This may be due to the increased vascular supply to the ovaries during younger reproductive years, potentially facilitating hematogenous spread. Furthermore, younger women with gastric adenocarcinoma often present with the signet-ring cell subtype, which has a particular tendency to metastasize to the ovaries. [10]

The most common primary site of tumour was colorectal carcinoma (33.3%), followed by stomach cancer (27.8%). Similarly, Wu *et al* documented colorectal carcinoma as the most common primary site (45.3%), followed by stomach cancer (32.03%). [9] In contrast, Lionetti *et al* documented stomach as the most common site of primary tumour (42.5%), followed by colon-rectum (26.1%).[7] Recent studies have indicated a shift toward a higher prevalence of colorectal origin for Krukenberg tumours, particularly arising more often from the colon than the rectum.[11]

In the present cohort, the most commonly reported clinical manifestations among patients with Krukenberg tumours were abdominal distension and pain, each observed in 77.8% of cases. These findings are consistent with the typical presentation of advanced intra-abdominal malignancies, particularly those involving the peritoneal surface or causing significant ascites.[1] Ascites, documented in 61.1% of patients, is a hallmark feature of peritoneal carcinomatosis and reflects extensive disease spread, commonly seen in Krukenberg tumours arising from gastrointestinal primaries.[10] Indigestion (50.0%), weight loss (44.4%), and reflux (16.7%) further support gastrointestinal tract involvement, which aligns with the predominant tumour origins in this cohort (colorectal and gastric). Such nonspecific symptoms may delay diagnosis, emphasizing the need for heightened clinical suspicion in women presenting with persistent gastrointestinal complaints and adnexal masses. [2] Less frequent but notable symptoms included hematemesis (11.1%), breast lump (11.1%), and per rectal bleeding (5.6%), which may provide clues to the primary tumour site. The presence of breast lumps corresponds with breast-origin Krukenberg tumours, although this was relatively rare. Similarly, dysphagia, solid (16.7%) and liquid (5.6%) and jaundice (5.6%) indicate upper gastrointestinal or hepatobiliary tract involvement, likely secondary to tumour burden or metastatic obstruction. The diversity of symptoms observed underscores the metastatic and multi-organ nature of Krukenberg tumours. Importantly, these findings reaffirm the clinical challenge in early diagnosis due to the overlapping symptomatology with other gastrointestinal or gynecological disorders. [1, 2, 10]

The radiologic response to first-line chemotherapy in our cohort of patients with Krukenberg tumours showed a spectrum of outcomes. A complete response (CR) was achieved in only one case, while partial response (PR) was the most frequent outcome, seen in 61.11% of patients. Stable disease (SD) was observed in 11.1%, and progressive disease (PD) in 22.22%. These findings are in keeping with the literature, which consistently reports limited radiologic response rates in Krukenberg tumours due to their aggressive biology and late-stage presentation. The relatively higher proportion of partial responses in our study may reflect the use of platinum-based or fluoropyrimidine-containing regimens, such as FOLFOX and CAPOX, which are standard treatments for gastrointestinal malignancies and have shown some efficacy in ovarian metastases. However, 75% (3 of 4) of disease progressors had primary Gastric malignancy. This highlights the role for molecular guided therapeutic options which have improved the response rates and survival outcomes. The low rate of complete response and early progression in a substantial proportion of patients highlight the limited curative potential of chemotherapy in Krukenberg tumours.

In our study, 18 patients with Krukenberg tumours exhibited a median progression-free survival (PFS) of 4 months (IQR: 3-6) and an overall survival (OS) of 6 months (IQR: 4-11.5). These figures align with established literature indicating the generally poor prognosis associated with Krukenberg tumours. In a larger retrospective series of 128 patients, the median OS was approximately 16 months, considerably longer than our cohort, which may be attributed to broader inclusion criteria and possibly differences in treatment aggressiveness or patient selection.[9] In our cohort, molecular based target therapies were not feasible due to logistic constraints. This would limit the survival outcomes in comparison to data worldwide. Nonetheless, this study provides insight on the limitations of a chemotherapy-only approach in gastrointestinal primaries where target and immunotherapies are a frontline option. A separate meta-analysis encompassing over 1, 500 cases reported a median OS with chemotherapy only of 6.7 months, surgical resection alone achieving 12.8 months, and a combined approach yielding 16.2 months. These data underscore that multimodal treatment strategies, particularly combined cytoreduction and systemic therapy, confer superior outcomes. [12]

Our cohorts lower OS also reflects a higher proportion of inoperable tumours or limited application of surgery: 72.2% patients could not be operated upon, due to disease extent and/or performance status. Of the 5 patients that underwent cytoreductive surgery, R0 was achieved in 4 patients. Studies have demonstrated that metastasectomy, particularly R0 resection, significantly improves survival. For example, a Chinese single-centre reported median OS of 19 months for R0 patients versus 10 months for R1/R2 resections. [13] Similarly, in a cohort of gastric-origin Krukenberg tumours, those undergoing both surgery and chemotherapy achieved median OS of 19-24 months compared to 11-14 months without surgery.[14]

Progression-free survival also benefits from surgical intervention. In colorectal-origin Krukenberg cases, surgical resection extended median PFS to 22.2 months, compared to 6.7 months with medical management alone.[15] These findings are especially relevant considering our own PFS data; the rapid early progression (8 events within the first 6 months) suggests that delayed or absent surgical intervention may portend a poorer early outcome. Notably, synchronous metastasis and ascites, both common in our cohort (88.9% synchronous, 61.1% ascites), are well-known adverse prognostic indicators.[9] These variables likely contributed to surgical inoperability. Our findings justify the importance of early identification of surgical candidates and favour aggressive multimodal treatment in eligible patients. Future efforts should aim to increase access to cytoreductive surgery and refine selection criteria using imaging biomarkers and IHC profiles. These interventions may offer improved survival in this high-risk patient population.

The study had certain limitations, which must be acknowledged. First, the study was conducted as a retrospective record based study that may have introduced selection and reporting bias, particularly regarding incomplete documentation of radiologic responses and immunohistochemistry results. Second, the small sample size (n=18) limits the statistical power and generalizability of the findings. As Krukenberg tumours are relatively rare, accumulating a larger cohort was challenging, potentially affecting the robustness of subgroup analyses. Third, Next Generation Sequencing to assess for personalised therapeutic approach was not possible due to logistic limitations. This also impacted the usage of target therapies, especially for Gastric and Colorectal primaries, which have shown survival benefit.

Conclusion

Krukenberg tumours are an uncommon and highly aggressive form of metastatic ovarian cancer, most often arising from primary tumours in the gastrointestinal tract particularly the colon. Colorectal cancer emerged as the most common primary source, with the majority of ovarian metastases being bilateral and synchronous in nature. Chemotherapeutic response varied among patients, with only a limited number achieving complete or partial remission. Both progression-free and overall survival times were relatively short, highlighting the poor prognosis typically associated with these tumours. Future studies with larger, prospective datasets are needed to confirm these observations and refine treatment strategies based on molecular tumour profiling.

Conflict of Interest

Not available

Financial Support

Not available

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