The Role of Secondary Cytoreductive Surgery in Relapsed Ovarian Cancer: A Comprehensive Review

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Abstract: Ovarian cancer is the second most common and the most lethal gynecological malignancy worldwide, with approximately two-thirds of patients presenting with advanced-stage disease. The standard of care consists of cytoreductive surgery, either primary or following neoadjuvant chemotherapy, combined with platinum-based chemotherapy. Despite advances in surgical techniques and the development of novel chemotherapeutic agents, most women with ovarian cancer ultimately experience recurrence and succumb to the disease.

In contrast to primary disease management, the optimal treatment strategy for recurrent ovarian cancer remains a subject of ongoing debate. While platinum-based or second-line systemic chemotherapy, depending on the platinum-free interval, is the current standard, the role of secondary cytoreductive surgery has long been controversial. Any potential survival benefit must be carefully balanced against the risks of significant surgical morbidity, potential deterioration in quality of life, and economic cost.

In cases of platinum-resistant recurrence, defined as relapse occurring within six months of completing platinum-based chemotherapy, secondary cytoreduction is generally not recommended due to the aggressive tumor biology and limited efficacy of systemic treatments. This comprehensive review focuses on the current role of cytoreductive surgery in platinum-sensitive recurrent ovarian cancer, with a detailed discussion of recent randomized trials and meta-analyses. Emerging evidence supports a role for secondary cytoreductive surgery in carefully selected patients where complete resection of macroscopic disease is achievable. However, its indication must be continually reassessed in light of the evolving landscape of systemic therapies for recurrent ovarian cancer.

Keywords: Recurrent ovarian cancer, secondary cytoreductive surgery, platinum- sensitive chemotherapy, hyperthermic intraperitoneal chemotherapy.

1. INTRODUCTION

Ovarian cancer remains one of the most lethal gynecologic malignancies, accounting for approximately 4% of all cancer-related deaths in women [1]. Despite advances in surgical techniques and systemic therapies, the majority of patients with advanced-stage disease experience recurrence, with an estimated 80% of cases relapsing within five years of initial treatment [2]. The high recurrence rate underscores the critical need for effective salvage strategies, among which secondary cytoreductive surgery (SCR) has emerged as a potentially curative option for carefully selected patients. However, its role remains one of the most debated topics in contemporary oncology, balancing potential survival benefits against surgical risks, quality-of-life considerations, and the rapidly evolving landscape of targeted therapies.

The concept of SCR was first introduced in the 1980s, when Berek *et al.* [3] demonstrated that patients with recurrent ovarian cancer and no ascites could benefit from aggressive surgical resection. Since then, the role of SCR has evolved significantly, driven by improvements in preoperative imaging, surgical techniques, and a deeper understanding of tumor biology. However, the use of SCR remains controversial, with ongoing debates regarding patient selection, surgical feasibility, and survival benefits in the era of modern systemic therapies and anti-angiogenic agents.

The standard management of advanced epithelial ovarian cancer (EOC) combines primary cytoreductive surgery—either upfront or after neoadjuvant chemotherapy—with platinum-based chemotherapy [4]. While this approach has improved progression-free survival (PFS), most patients eventually relapse, with median overall survival (OS) for recurrent disease rarely exceeding 24-36 months [2]. Recurrences are broadly classified as platinum-sensitive (relapse ≥6 months after last platinum therapy) or platinum-resistant (relapse <6 months), with the former group generally having better response to salvage chemotherapy and thus being the primary candidates for SCR [5]. The most important factor to well-defined is the following, concerning the relapse disease· is this a “real” recurrence disease or a “false” due to residual disease after primary cytoreduction? (6). In this retrospective analysis, the 75% of recurrent cases are residual diseases due to CC_2 or CC_3 cytoreduction.

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The management of recurrent ovarian cancer presents unique challenges compared to primary disease. Unlike the well-established paradigm of maximal upfront cytoreduction, the role of surgery in recurrence must be carefully weighed against multiple factors such as disease biology (recurrent tumors often exhibit more aggressive behavior and may be less responsive to subsequent therapies), surgical complexity (prior surgeries and chemotherapy can lead to extensive adhesions and altered anatomy, increasing operative risks), patient factors (*e.g*. performance status, comorbidities, and cumulative toxicity from prior treatments must be considered or chemoresistance disease and **therapeutic alternatives (t**he emergence of PARP inhibitors, anti-angiogenics, and other targeted therapies has expanded non-surgical options).

2. HISTORICAL PERSPECTIVE ON SCR

As already mentioned, the concept of SCR was first introduced in the 1980s, when Berek et al. demonstrated that selected patients with recurrent disease and no ascites could benefit from aggressive surgical resection. Early experiences were characterized by heterogeneous outcomes, with retrospective series consistently showing that only patients achieving complete gross resection (R0) derived meaningful survival advantages, while those left with residual disease often fared worse than counterparts treated with chemotherapy alone [7]. These observations led to two critical developments:

1. **Refinement of Selection Criteria**: Recognizing that not all patients benefit equally from SCR, researchers developed predictive models to identify optimal candidates. The German AGO score (based on performance status, ascites volume, and completeness of primary surgery) and the Chinese iMODEL score (incorporating FIGO stage, residual disease, platinum-free interval, and CA-125 levels) emerged as valuable tools (5, 8).
2. **Advances in Surgical Technique**: The adoption of extended upper abdominal procedures, minimally invasive approaches for isolated recurrences, and the incorporation of hyperthermic intraperitoneal chemotherapy (HIPEC) expanded the possibilities for achieving R0 resection while minimizing morbidity [9, 10].

Building upon the established role of primary cytoreductive surgery (CRS) in ovarian cancer management, secondary CRS has emerged as a viable treatment option for select patients with recurrent disease [11]. This approach holds particular promise for two distinct patient populations: those experiencing platinum-sensitive recurrence (defined as disease recurrence occurring ≥6 months after completing platinum-based therapy) and patients presenting with limited-volume recurrent disease [12, 13].

The aggressive nature of platinum-resistant disease and its poor response to current systemic therapies generally preclude consideration of secondary CRS as a beneficial intervention [14, 15]. This clinical understanding is substantiated by numerous retrospective analyses and meta-analyses demonstrating that the primary benefits of secondary CRS are most evident in platinum-sensitive recurrences, particularly when complete macroscopic resection (R0) or optimal resection (typically defined as residual disease <1 cm) can be achieved [11, 13, 16].

Significant variability exists in the literature regarding the definition of "optimal" cytoreduction, with thresholds ranging from microscopic residual (<0.25 cm) to macroscopic deposits up to 2.5 cm [11]. A comprehensive meta-analysis revealed weighted mean complete and optimal secondary CRS rates of 52.2% and 70.3%, respectively [11]. Multivariate analysis identified complete CRS as the sole clinical variable significantly associated with prolonged post-recurrence survival (p=0.019), demonstrating that each 10% increase in complete CRS rates correlated with a 3.0-month improvement in median overall survival [11]. The survival advantage was less pronounced for optimal (but not complete) CRS, suggesting a biological continuum where progressively smaller residual tumor burdens correspond to better clinical outcomes.

This differential impact on survival may be explained by two potential, non-mutually exclusive mechanisms: a) residual disease may accelerate the development of chemoresistance, or b) tumors that remain unresectable despite expert surgical intervention may represent a more aggressive biological subtype with inherent resistance to multimodal therapy [11, 13].

3. ADVANCES IN SURGICAL APPROACHES

Contemporary surgical innovations have significantly expanded the technical possibilities for secondary CRS:

1. **Minimally Invasive Techniques**: Laparoscopic CRS has emerged as both feasible and safe for carefully selected patients with localized recurrent disease [17]. This approach offers the dual advantage of achieving complete tumor resection while minimizing surgical morbidity.
2. **Salvage Lymphadenectomy**: For isolated nodal recurrences, lymphadenectomy demonstrates particular efficacy, with median progression-free survival reaching 27 months in optimal candidates [18]. Favorable prognostic indicators include longer platinum-free intervals and limited nodal disease burden, with benefits appearing independent of BRCA mutational status [18].
3. **Complex Vascular Procedures**: Even challenging recurrences involving major vascular structures may be amenable to resection with meticulous preoperative planning and surgical expertise (19), underscoring the importance of centralized care at high-volume specialty centers.

The successful integration of these advanced surgical techniques necessitates rigorous patient selection and comprehensive multidisciplinary evaluation. As systemic therapies continue to evolve, the role of secondary CRS must be continually reassessed within the context of modern ovarian cancer treatment paradigms [13]. Future research priorities should focus on three key areas: (i) optimization of patient selection criteria, (ii) refinement of surgical approaches, and

(iii) investigation of synergistic combinations with novel systemic agents [13, 20].

4. THE MODERN ERA OF SCR

The past decade has witnessed three pivotal developments that have reshaped the SCR landscape:

Randomized Evidence: The publication of three major randomized trials (GOG-213, DESKTOP III, and SOC-1) provided the first high-level evidence on SCR's efficacy, though with seemingly conflicting results that reflect differences in patient selection, surgical quality, and adjuvant therapies [2, 5, 8].

Molecular Characterization: The discovery of BRCA mutations and homologous recombination deficiency (HRD) has enabled more precise prognostication and treatment selection, raising questions about how these biomarkers should inform SCR decisions [21].

Therapeutic Innovations: The introduction of PARP inhibitors and bevacizumab maintenance therapy has dramatically altered the natural history of platinum-sensitive disease, necessitating reevaluation of where SCR fits within contemporary treatment algorithms [22].

5. MATERIALS AND METHODS

This comprehensive review synthesizes evidence from 14 key studies (2020-2025) to critically evaluate SCR's evolving role in ovarian cancer management. By examining survival outcomes, recurrence patterns, selection criteria, and emerging trends, we aim to provide clinicians with an evidence-based framework for incorporating SCR into personalized treatment plans while highlighting knowledge gaps that warrant further investigation.

5.1. The GOG-0213 Trial

The Gynecological Oncology Group (GOG) performed the multicenter GOG-0213 trial to analyze the role of bevacizumab in patients with recurrent ovarian cancer and if secondary CRS would increase overall survival between patients with platinum-sensitive recurrence and who were candidates for potential operation. In a 10-year period, 240 patients went through secondary CRS plus systemic chemotherapy and 245 patients followed chemotherapy only, consisted of paclitaxel-carboplatin or gemcitabine-carboplatin. After a median follow-up period of 48, 1 months, there were no significant differences in both groups. The 3-year PFS rates were 29% in the surgery group and 20% in the other group. Even though, patients with complete CRS did not experience an improved survival compared with those who received systemic chemotherapy only, a benefit regarding PFS was observed.

Design: multicenter trial (N=485) comparing SCR plus chemo vs. chemo alone in platinum-sensitive relapse.

Resection Status: R0=67%

Survival Outcomes: 22.4 mo (SCR) *vs*. 13.1 mo (chemo alone; HR 0.51)

OS trend: 56 *vs*. 38 mo (HR 0.61)

Implications: no difference in QoL in both groups after 12 months.

5.2. SOC-1 Trial

This Chinese phase III randomized trial compared SCR plus chemotherapy versus chemotherapy alone in 357 patients with platinum-sensitive recurrent ovarian cancer (PFI ≥6 months). Using the iMODEL score and PET-CT for patient selection, complete cytoreduction was achieved in 76.7% of surgical cases (61.1% even in high iMODEL score subgroups). After median follow-up, the SCR group showed significantly longer PFS (17.4 *vs*. 11.9 months; HR 0.58, $p<0.001$) and delayed time to first subsequent therapy (18.1 *vs*. 13.6 months). While interim OS analysis showed a trend (58.1 *vs*. 53.9 months; HR 0.82), patients achieving R0 resection had markedly better treatment-free survival (median not reached *vs.* 39.5 months). The trial demonstrated that rigorous preoperative selection enables high R0 rates and meaningful clinical benefits.

Design: Phase III RCT (N=357) comparing SCR + chemo *vs*. chemo alone in platinum-sensitive recurrent OC (PFI ≥6mo).

Resection Status: R0=76.7% (61.1% in high iMODEL score subgroup).

Survival Outcomes:

- PFS: 17.4mo (SCR) vs. 11.9mo (chemo alone; HR 0.58).
- OS trend: 58.1 vs. 53.9mo (HR 0.82; NS).
- **Recurrence Rate:** Lower in R0 subgroup (TFSa 6.2 vs. 4.2mo at 60–72mo).
- **Key Findings:** iMODEL + PET-CT improved patient selection; SCR delayed TFST (18.1 vs. 13.6mo).
- **Implications:** SCR benefits carefully selected patients but requires R0 resection.

5.3. DESKTOP III Trial (2021)

This international multicenter phase III trial randomized 407 AGO score-positive patients (ECOG 0, ascites <500mL, complete primary resection) to SCR plus chemotherapy or chemotherapy alone. Complete cytoreduction was achieved in 76% of surgical cases. With 69.8 months median follow-up, the SCR group showed superior OS (53.7 *vs*. 46.0 months; HR 0.75, $p=0.02$) and PFS (18.4 *vs*. 14.0 months; HR 0.66). Strikingly, R0 patients achieved 61.9 months median OS versus 27.7 months for incomplete resections. The trial established that proper patient selection using the AGO score optimizes surgical outcomes without compromising quality of life.

Design: Phase III RCT (N=407) in AGO score-positive PSROC.

Resection Status: R0=75.5%.

Survival Outcomes:

- OS: 53.7mo (SCR) *vs*. 46.0mo (HR 0.75).

- PFS: 18.4 *vs*. 14.0mo (HR 0.66).
- **Recurrence Rate:** 27.7mo OS if incomplete *vs*. 61.9mo (R0).
- **Key Findings:** AGO score predicted R0 success; no QoL detriment.
- **Implications:** SCR improves survival in selected patients; incomplete resection harms outcomes.

5.4. MSK HIPEC Phase II (2021)

This multicenter phase II "pick-the-winner" trial evaluated SCR with carboplatin HIPEC versus standard chemotherapy in 98 platinum-sensitive recurrent ovarian cancer patients. While R0 rates were high (82% HIPEC vs 94% standard), HIPEC failed to meet efficacy endpoints with inferior PFS (12.3 vs 15.7 months; HR 1.54) and OS (52.5 vs 59.7 months; HR 1.39). Notably, BRCA-mutated patients derived no additional benefit from HIPEC. The study concluded that carboplatin HIPEC at this dose/regimen did not improve outcomes compared to standard therapy.

Design: Phase II RCT (N=98) comparing SCR + HIPEC vs. standard chemo.

Resection Status: R0=82% (HIPEC) vs. 94% (standard).

Survival Outcomes:

- OS: 52.5 *vs*. 59.7mo (HR 1.39).
- PFS: 12.3 *vs*. 15.7mo (HR 1.54).
- **Recurrence Rate:** No difference in local/distant recurrence.
- **Key Findings:** Carboplatin HIPEC did not improve outcomes.
- **Implications:** HIPEC not recommended at this regimen.

5.5. Indian HIPEC Trial (2001)

This small phase II trial (N=15) assessed SCR with cisplatin HIPEC in platinum-sensitive recurrences. Achieving optimal cytoreduction in all cases, median OS was 26 months and PFS 15 months, though 77% experienced recurrence (mostly peritoneal). High PCI scores (>20) correlated with worse outcomes. While demonstrating feasibility, the trial was limited by its non-randomized design and small sample size, highlighting the need for larger randomized studies.

Design: Phase II trial (N=15) of SCR + cisplatin HIPEC.

Resection Status: Optimal cytoreduction in all (R0 not reported).

Survival Outcomes:

- OS: 26mo; PFS: 15mo.
- **Recurrence Rate:** 76.9% (peritoneal dominant).
- **Key Findings:** High PCI (>20) predicted worse outcomes.
- **Implications:** Small sample limits conclusions; HIPEC safety shown.

5.6. Korean HIPEC RCT (2022)

This single-blind RCT of 184 patients compared interval or primary cytoreduction with/without cisplatin HIPEC. While no overall survival benefit was seen (69.5 *vs* 61.3 months; HR 0.87), subgroup analysis revealed significant PFS (17.4 *vs* 15.4 months; HR 0.60) and OS (61.8 *vs* 48.2 months; HR 0.53) advantages for HIPEC in the neoadjuvant chemotherapy subgroup. HIPEC increased electrolyte disturbances (80.4% *vs* 44.6%) but was otherwise tolerable. The findings suggest HIPEC may benefit select patients undergoing interval debulking.

Design: RCT (N=184) in primary/interval cytoreduction ± HIPEC.

Resection Status: R0=81.5% (HIPEC) vs. 87.0%.

Survival Outcomes:

- OS: 69.5 *vs*. 61.3mo (HR 0.87).
- PFS: 19.8 *vs*. 18.8mo (HR 0.88).
- **Recurrence Rate:** Benefit only in interval cytoreduction subgroup.
- **Key Findings:** HIPEC increased kidney injury (20.7%).
- **Implications:** HIPEC may benefit post-neoadjuvant patients only.

5.7. Italian IDS/PDS Study (2022)

This retrospective cohort (N=272) compared SCR outcomes between primary debulking (PDS) and interval debulking (IDS) patients. With 87.1% R0 rate, both groups showed similar PFS (21 months) and OS (81 vs 77 months; p=0.574). Non-SCR patients had significantly worse outcomes (median PRS 27 vs 77 months). The study confirmed that SCR benefits IDS patients comparably to PDS when complete resection is achieved, supporting its use regardless of primary treatment approach.

Design: Retrospective (N=272) comparing SCR in PDS *vs*. IDS.

Resection Status: R0=87.1%.

Survival Outcomes:

- PFS: 21mo (both groups).
- OS: 81mo (PDS) vs. 77mo (IDS).
- **Recurrence Rate:** Non-SCR group had worse PRS (27 vs. 77mo).
- **Key Findings:** SCR benefits IDS patients similarly to PDS.
- **Implications:** PET-CT + laparoscopy optimizes selection.

5.8. European MIS Review (2023)

This expert consensus review stratified outcomes by recurrence pattern, finding lymph node metastases had best prognosis (median OS 61.9 months) versus peritoneal (45.2 months) and parenchymal (28.4 months) recurrences. The authors emphasized that minimally invasive SCR (feasible in

20-30% of cases) reduces morbidity without compromising oncology outcomes when performed for localized disease. They advocated integrating PET-CT and laparoscopy for surgical planning in the era of PARP inhibitors.

Design: Narrative review on SCR approaches.

Resection Status: R0 critical for all techniques.

Survival Outcomes:

- Lymph node recurrences: best OS/PFS.
- Parenchymal: worst outcomes.
- **Recurrence Rate:** Lower with MIS (QoL advantage).
- **Key Findings:** MIS feasible for localized disease.
- **Implications:** Precision surgery requires multidisciplinary planning.

5.9. MSK Morbidity Analysis (2023)

This exploratory analysis of 83 SCR±HIPEC cases found that while grade ≥3 complications (40%) delayed chemotherapy by 3 days, they didn't significantly impact survival. Complete resection was paramount - R0 patients had 78.0 month median OS versus 40.1 months for residual disease (HR 4.76, p<0.001). Multi-site disease predicted poorer PFS (HR 2.65). The study reinforced that surgical morbidity is acceptable when R0 is achieved.

Design: Phase II RCT (N=83) of SCR ± HIPEC.

Resection Status: R0=88%.

Survival Outcomes:

- OS: 78mo (R0) vs. 40.1mo (residual).
- PFS: 14.3mo (entire cohort).
- **Recurrence Rate:** Multi-site disease predicted poorer PFS (HR 2.65).
- **Key Findings:** Grade ≥3 complications did not impact survival.
- **Implications:** R0 resection outweighs morbidity risks.

5.10. Turkish HIPEC Study (2024)

This retrospective analysis of 63 SCR+HIPEC cases reported 56-month median OS despite aggressive surgeries (53.9% colectomies, 26.9% splenectomies). CC-0 resection (71.1%) was critical for survival, but high-grade complications (22.2%) and 7.9% 30-day mortality underscored the procedure's complexity. The authors concluded that while feasible, such extensive cytoreduction requires specialized centers and careful patient selection.

- **Design:** Retrospective (N=63) of SCR + HIPEC.
- **Resection Status:** CC-0=71.1%.

Survival Outcomes:

- OS: 56mo.
- **Recurrence Rate:** Not reported.
- **Key Findings:** 7.9% 30-day mortality (high complexity).
- **Implications:** Aggressive SCR requires expertise.

5.11. PARPi Era Study (2024)

This U.S. retrospective cohort (N=245) compared pre- and post-PARPi/bevacizumab eras. Despite maintenance therapy use increasing from 5.3% to 39%, SCR maintained benefit (3-year PFS2 31.3% for R0 vs 12.5% for R1/R2). R0 rates remained stable (85-86%) using MSK selection criteria. The study proved SCR's enduring value alongside targeted therapies, particularly for patients with longer DFI and resectable disease.

Design: Retrospective (N=245) pre-/post-PARPi approval.

Resection Status: R0=85–86%.

Survival Outcomes:

- PFS2: 20.1mo (post-2017).
- **Recurrence Rate:** 3-year PFS2=31.3% (R0) vs. 12.5% (R1/R2).
- **Key Findings:** PARPi use ↑ from 3.8% to 27%.
- **Implications:** SCR retains value alongside targeted therapies.

5.12. Chinese PROC Trial (2024-2026)

This ongoing phase III RCT (NCT05633199) is evaluating SCR in platinum-resistant ovarian cancer (≤5 lesions, ascites <500mL) - a population lacking randomized data. Based on preliminary retrospective data (32 vs 8-month OS with SCR), the trial may expand SCR indications. Results post-2026 will clarify whether surgical cytoreduction can overcome platinum resistance in oligometastatic disease.

- **Design:** Ongoing Phase III RCT (N=140) in platinum-resistant OC.
- **Resection Status:** Target R0 (≤5 lesions, PET-CT selection).
- **Survival Outcomes:** PFS primary endpoint.
- **Recurrence Rate:** Pending results.
- **Key Findings:** First RCT in PROC.
- **Implications:** May expand SCR indications.

5.13. Indian SCR Cohort (2024)

This single-center study (N=52) achieved 93% R0/R1 rates with SCR, yielding 22-month median OS versus 7 months for suboptimal resection. However, high surgical complexity increased mortality risk (HR 8.26), and HIPEC (used in 21%) showed no benefit. The data confirmed SCR's viability in resource-limited settings when strict selection criteria (AGO score, PET-CT) are applied.

- **Design:** Retrospective (N=52).
- **Resection Status:** R0/R1=93%.

Survival Outcomes:

- OS: 22mo (R0/R1) vs. 7mo.
- PFS: 19 vs. 7mo.
- **Recurrence Rate:** 30.76% second recurrence.
- **Key Findings:** High complexity increased mortality (HR 8.26).
- **Implications:** SCR feasible in resource-limited settings.

5.14. Indian Matched Cohort (2025)

This propensity-matched study (N=58) demonstrated SCR's robust benefit in PSROC: 40.3-month OS versus 23.2 months with chemotherapy alone (p=0.002), and 26.5-month PFS versus 8.6 months (p<0.001). Remarkably, 93% achieved optimal cytoreduction without formal scoring systems, suggesting surgeon experience may complement selection criteria in high-volume centers.

- **Design:** Propensity-matched (N=58).
- **Resection Status:** R0=93.1%.
- **Survival Outcomes:**
- OS: 40.3mo (SCR) vs. 23.2mo (HR 0.59).
- PFS: 26.5 *vs*. 8.6mo.
- **Recurrence Rate:** 72.4% *vs*. 89.6% (*P*<0.001).
- **Key Findings:** Surgeon expertise achieved high R0 rates.
- **Implications:** SCR improves survival even without formal selection scores.

6. DISCUSSION

The evidence from these clinical studies presents a compelling case for secondary cytoreductive surgery (SCR) in carefully selected patients with recurrent ovarian cancer, while also highlighting important limitations and areas requiring further research. The collective findings demonstrate that SCR, when performed with complete resection (R0), can significantly improve both progression-free survival (PFS) and overall survival (OS) compared to chemotherapy alone in platinum-sensitive recurrent ovarian cancer (PSROC).

The SOC-1 trial [23] established that rigorous patient selection using the iMODEL score and PET-CT imaging could achieve complete cytoreduction in 76.7% of cases, resulting in significantly improved PFS (17.4 *vs*. 11.9 months) and a trend toward better OS (58.1 *vs*. 53.9 months). Importantly, this study showed that even patients with higher iMODEL scores could benefit if R0 resection was achieved (61.1% success rate in high iMODEL subgroups). The delayed time to first subsequent therapy (18.1 *vs*. 13.6 months) suggests SCR may prolong treatment-free intervals, potentially impacting quality of life.

The DESKTOP III trial (2021) provided even stronger evidence for SCR's survival benefit, showing superior OS (53.7 *vs*. 46.0 months) and PFS (18.4 *vs*. 14.0 months) in AGO score-positive patients. The dramatic difference in outcomes between R0 (61.9 months median OS) and incomplete resections (27.7 months) underscores the critical importance of complete cytoreduction. This trial's finding that SCR didn't compromise quality of life is particularly noteworthy, addressing a key concern about aggressive surgical approaches.

The Italian IDS/PDS study (2022) expanded our understanding by demonstrating that SCR benefits patients regardless of whether they initially underwent primary debulking (PDS) or interval debulking (IDS), with similar outcomes (81 *vs*. 77 months OS) when complete resection was achieved. This finding is clinically important as it supports considering SCR for appropriately selected patients irrespective of their primary treatment approach.

Several studies have explored technical aspects of SCR. The European MIS Review (2023) highlighted that minimally invasive approaches may be feasible for selected patients (20-30% of cases), particularly those with lymph node recurrences (best prognosis with 61.9 month median OS). The MSK Morbidity Analysis (2023) provided reassuring data that while grade ≥3 complications occurred in 40% of cases, they didn't significantly impact survival outcomes when R0 was achieved (78.0 vs. 40.1 month OS for residual disease).

The PARPi Era Study (2024) addressed an important contemporary question, demonstrating that SCR maintains its benefit even in the era of PARP inhibitors and bevacizumab. The stable R0 rates (85-86%) and maintained survival advantage (3-year PFS2 31.3% for R0 vs 12.5% for R1/R2) suggest that surgical cytoreduction provides independent value beyond these targeted therapies.

Emerging data from the Indian SCR Cohort (2024) and Indian Matched Cohort (2025) indicate that SCR can be successfully implemented in resource-limited settings, with the latter study achieving 93% optimal cytoreduction rates based primarily on surgical expertise rather than formal scoring systems. However, the former study's finding that high surgical complexity increased mortality risk (HR 8.26) serves as an important caution.

In clinical practice, these findings support the following approach:

- All patients with PSROC should be evaluated by a multidisciplinary team including surgeons experienced in radical cytoreduction
- Preoperative assessment should include PET-CT and consideration of selection criteria (AGO/iMODEL scores)
- SCR should only be undertaken when there is high confidence in achieving R0 resection
- Patients should be counseled about the risks (including significant morbidity) and potential benefits
- SCR should be followed by appropriate systemic therapy, with consideration of maintenance options like PARP inhibitors when indicated

CONCLUSION

The extensive review of these 14 contemporary studies (2020-2025) provides critical insights into the evolving role of secondary cytoreductive surgery (SCR) in recurrent

Table 1. Results of studies on secondary cytoreductive surgery for recurrent ovarian cancer

Study	Year	SCR (N)	Selection Criteria	Complete CRS (%)	PFS* (Months)	HR (*p*-value)	OS* (months)	HR (p-value)	Survival for Complete *vs*. Incomplete CRS*
GOG-0213	2019	Yes (240)	Clinical opinion	67%	18.9	HR=0.82	50.6	HR=1.29 (p=0.08)	PFS 22 vs. 13 mo OS 56 vs.38 mo.
SOC-1	2020	Yes (175)	iMODEL plus PET-CT	76.7%	17.4	HR=0.58 (p<0.001)	58.1 **	HR=0.82 (NS)	PFS 19 vs. 13 mo OS NR vs. 39.5 mo
DESKTOP III	2021	Yes (206)	AGO Score	75.5%	18.4	HR=0.66 (p<0.001)	53.7	HR=0.75 (p=0.02)	PFS 21 vs. 12 mo OS 61.9 vs. 27.7 mo
MSK HIPEC	2021	Yes (49)	PCI≤17	82% (HIPEC) 94% (Std)	12.3 (HIPEC) 15.7 (Std)	HR=1.54 (NS)	52.5 (HIPEC) 59.7 (Std)	HR=1.39 (NS)	-
Korean HIPEC	2022	Yes (92)	Residual < 1 cm	81.5%	19.8	HR=0.88 (p=0.43)	69.5	HR=0.87 (p=0.52)	PFS 17.4 vs. 15.4 mo (HR=0.6) OS 61.8 vs. 48.2 mo (HR=0.53)
Italian IDS/PDS	2022	Yes (178)	PET-CT plus laparoscopy	87.1%	21 (both groups)	-	81 (PDS) 77 (IDS)	P=0.574	Non-SCR OS 27 vs. 77 mo (p<0.001)
Indian HIPEC	2001	Yes (15)	PFI>6 mo	100% (optimal)	15	-	26	-	PCI>20: worse outcomes
Turkish HIPEC	2024	Yes (63)	PCI≤18	71.1% (CC-0)	-	-	56	-	30-day mortality 7.9%
PARPi Era	2024	Yes (114)	MSK criteria	86%	-	-	3-yr PFS2: 31.3% (R0) 12.5% (R1/R2)	P=0.001	-
Indian SCR Cohort	2024	Yes (52)	AGO Score	60% (R0) 33% (R1)	19 (R0/R1) 7 (R2)	-	22 (R0/R1) 7 (R2)	-	-
Indian Matched	2025	Yes (29)	Surgeon discretion	93.1%	26.5	HR=0.59 (p<0.001)	40.3	HR=0.59 (p<0.002)	vs. chemo alone: PFS 26.5 vs 8.6 mo OS 40.3 vs. 23.2 mo

Abbreviations: CRS: cytoreductive surgery; PFS: progression-free survival; OS: overall survival; NR: not reached; NS: not significant; PCI: peritoneal cancer index; PFI: platinum-free interval; HR: hazard ratio; QoL: quality of life
Notes: *SOC-1 OS data are interim; Korean HIPEC benefits were seen only in interval cytoreduction subgroup
Selection criteria details:
AGO score: ECOG 0, ascites ≤500mL, complete primary resection
iMODEL: Incorporates FIGO stage, residual tumor, PFI, ECOG, CA-125, ascites
MSK criteria: DFI, resectability on imaging

ovarian cancer management. Three landmark randomized controlled trials - SOC-1 (23), DESKTOP III (5), and GOG-0213 (2) - have established an evidence-based framework for SCR, while simultaneously highlighting important nuances in patient selection, surgical outcomes, and integration with modern systemic therapies.

The current evidence consistently demonstrates that successful SCR outcomes depend on two fundamental principles: rigorous patient selection and achievement of complete gross resection (R0). The AGO score (used in DESKTOP III) and iMODEL score (employed in SOC-1) have proven particularly valuable, predicting complete resection rates

exceeding 75% in qualified patients (5, 23). These selection tools emphasize:

1. **Performance status** (ECOG 0)
2. **Limited disease burden** (ascites <500mL, respectables lesions on imaging)
3. **Favorable tumor biology** (platinum-free interval ≥6 months)
4. **Prior surgical outcomes** (complete resection at primary surgery)

The survival differential between R0 and incomplete resections remains striking across all studies. In DESKTOP III, R0 patients achieved 61.9 months median overall survival (OS) versus just 27.7 months for those with residual disease (5). Similarly, the Italian IDS/PDS study (24) showed that when complete resection was achieved, outcomes were excellent regardless of whether patients had initially undergone primary (81 months OS) or interval debulking (77 months OS).

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