Optimal Debulking Targets in Women With Advanced Stage Ovarian Cancer: A Retrospective Study of Immediate Versus Interval Debulking Surgery

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Abstract

Objective: The objective of this study was to examine both overall and disease-free survival of patients with advanced stage ovarian cancer after immediate or interval debulking surgery based on residual disease.

Methods: We performed a retrospective chart review at the Tom Baker Cancer Centre in Calgary, Alberta of patients with pathologically confirmed stage III or IV ovarian cancer, fallopian tube cancer, or primary peritoneal cancer between 2003 and 2007. We collected data on the dates of diagnosis, recurrence, and death; cancer stage and grade, patients' age, surgery performed, and residual disease.

Results: One hundred ninety-two patients were included in the final analysis. The optimal debulking rate with immediate surgery was 64.8%, and with interval surgery it was 85.9%. There were improved overall and disease-free survival rates for optimally debulked disease (< 1 cm) with both immediate and interval surgery ($P < 0.001$) compared to suboptimally debulked disease. Overall survival rates for optimally debulked disease were not significantly different in patients having immediate and interval surgery ($P = 0.25$). In the immediate surgery group, patients with microscopic residual disease had better disease-free survival ($P = 0.015$) and overall survival ($P = 0.005$) than patients with < 1 cm residual disease. In patients who had interval surgery, those who had microscopic residual disease had more improved disease-free survival than those with < 1 cm disease ($P = 0.05$), but they did not have more improved overall survival ($P = 0.42$). Patients with microscopic residual disease who had immediate surgery had a significantly better overall survival rate than those who had interval surgery ($P = 0.034$).

Conclusion: In women with advanced stage ovarian cancer, the goal of surgery should be resection of disease to microscopic residual at the initial procedure. This results in improved overall survival than lesser degrees of resection. Further studies are required to determine optimal surgical management.

Key Words: Ovarian cancer, neoadjuvant treatment, gynaecologic surgery, residual tumour

Competing Interests: None declared.

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Résumé

Objectif : Cette étude avait pour objectif d'examiner les taux de survie globale et sans récidive des patientes présentant un cancer de l'ovaire de stade avancé, à la suite de la tenue d'une chirurgie de réduction tumorale immédiate ou d'intervalle en fonction de la malignité résiduelle.

Méthodes : Nous avons mené, au *Tom Baker Cancer Centre* de Calgary, en Alberta, une analyse rétrospective des dossiers des patientes qui présentaient un cancer de l'ovaire, de la trompe de Fallope ou péritonéal primitif de stade III ou IV (confirmé par analyse pathologique) entre 2003 et 2007. Nous avons recueilli des données sur les dates de diagnostic, de récurrence et de décès, le stade et le grade du cancer en question, l'âge de la patiente, la chirurgie effectuée et la malignité résiduelle.

Résultats : Cent quatre-vingt-douze patientes ont été incluses aux fins de l'analyse finale. Le taux de réduction tumorale optimale de la chirurgie immédiate était de 64,8 %; dans le cas de la chirurgie d'intervalle, il était de 85,9 %. Une amélioration des taux de survie globale et sans récidive a été constatée pour ce qui est des pathologies ayant fait l'objet d'une réduction tumorale optimale (< 1 cm), tant à la suite d'une chirurgie immédiate que d'une chirurgie d'intervalle (P < 0,001), par comparaison avec les cas de pathologie ayant fait l'objet d'une réduction tumorale sous-optimale. Dans les cas de pathologie ayant fait l'objet d'une réduction tumorale optimale, les taux de survie globale n'étaient pas considérablement différents chez les patientes qui ont subi une chirurgie immédiate et chez celles qui ont subi une chirurgie d'intervalle (P = 0,25). Au sein du groupe « chirurgie immédiate »,

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les patientes présentant une malignité résiduelle microscopique ont connu de meilleurs taux de survie sans récidive (P = 0,015) et de survie globale (P = 0,005) que les patientes présentant une malignité résiduelle < 1 cm. Au sein du groupe « chirurgie d'intervalle », les patientes présentant une malignité résiduelle microscopique ont connu une meilleure amélioration du taux de survie sans récidive que les patientes présentant une malignité résiduelle < 1 cm (P = 0,05); toutefois, leur taux de survie globale ne présentait pas une telle amélioration (P = 0,42). Les patientes présentant une malignité résiduelle microscopique qui ont subi une chirurgie immédiate ont connu un taux de survie globale considérablement plus élevé que celui des patientes ayant subi une chirurgie d'intervalle (P = 0,034).

Conclusion : Chez les femmes qui présentent un cancer de l'ovaire de stade avancé, l'objectif de la chirurgie devrait être, dans le cadre de l'intervention initiale, la résection de la pathologie jusqu'à l'obtention de résidus microscopiques. Une telle façon de faire entraîne une amélioration du taux de survie globale, par comparaison avec les degrés moindres de résection. La tenue d'autres études s'avère requise pour déterminer les paramètres de la prise en charge chirurgicale optimale.

INTRODUCTION

In Canada, ovarian cancer affects approximately 2500 new patients per year and is responsible for approximately 1750 deaths per year.[1,2] Seventy-five percent of ovarian cancers are diagnosed as stage III or stage IV disease.[3] Surgical debulking is a mainstay of ovarian cancer treatment.[4] Debulking surgery allows for removal of large quantities of potentially chemotherapy-resistant disease, improves the immune response to chemotherapy, and improves drug delivery.[5,6]

Ovarian cancer debulking has traditionally been considered optimal when there is residual disease of < 1 cm.[3,4,6,7] The size of residual tumour after surgery is one of the most important prognostic factors for survival.[6] Bristow et al., in a review of 6885 patients, found a 5.5% increase in median survival for every 10% increase in optimal cytoreduction.[8] Multiple studies in recent years have suggested that complete surgical resection of the tumour improves survival in patients who have immediate surgery,[4,8–11] interval surgeries,[4,12–14] and secondary cytoreduction.[5] A meta-analysis of three randomized controlled trials showed a survival advantage for patients with complete surgical resection.[15] This has led various cancer societies to redefine optimal debulking as leaving residual microscopic disease only.[5,13,16,17]

ABBREVIATIONS

EORTC	European Organization for Research and Treatment of Cancer
IDS	interval debulking surgery
PDS	primary debulking surgery

It is still unclear whether surgical debulking should be performed before or after chemotherapy. Randomized studies have shown both a benefit[18,19] and a lack of benefit[20] from interval debulking surgery. A recent international randomized trial showed lower complication rates and higher optimal debulking rates in patients who received initial neoadjuvant chemotherapy followed by debulking surgery.[13] This trial has been criticized on the basis of its low rate of optimal debulking with primary surgery.[10] Some argue that suboptimal debulking is due to a lack of surgical effort.[3,4,6,7] Currently there is no good preoperative testing or imaging that can determine whether or not patients will have suboptimal debulking.[3,10]

Many trials have attempted to compare survival outcomes between patients who have primary debulking surgery and those who have IDS. Heterogeneity in these trials, including variations in optimal debulking rates, chemotherapy regimens, and period of observation, has made reported differences in survival difficult to interpret.

The purpose of our study was to clarify whether immediate or interval debulking surgery results in improved survival.

MATERIALS AND METHODS

We performed a retrospective chart review of all patients with serous ovarian, fallopian tube, or peritoneal cancer receiving treatment at the Tom Baker Cancer Centre in Calgary, Alberta between 2003 and 2007. Inclusion criteria included all adult women (> 18 years old) with stage III or IV serous epithelial ovarian, fallopian tube, or primary peritoneal cancer and three years of survival data. The starting date was chosen because it was the earliest year with available computerized data. Women with a diagnosis of germ cell, metastatic, sex-cord stromal, and non-serous epithelial tumours of the ovaries were excluded. If the primary site of disease was unknown, or if the woman had a second primary neoplasm, the corresponding data were excluded from the study. The primary outcome of the study was the overall mean survival interval and the secondary outcome was the recurrence-free mean survival interval, both based on the amount of residual disease and the type of surgery. We also examined the rate of optimal debulking in primary versus interval debulking surgical cases. All patients received IDS within four to six weeks after chemotherapy, except in exceptional circumstances.

Residual disease status was determined from operative reports and physician notes. Overall survival was defined as the interval from the date of initial diagnosis to the date of death or date of last known contact. Disease-free survival was defined as the interval from date of initial diagnosis