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## Surgery for advanced epithelial ovarian cancer

5 Neville F. Hacker, Professor <sup>a, b, \*</sup>, Archana Rao, Dr <sup>a</sup>

<sup>a</sup> Gynaecological Cancer Centre, Royal Hospital for Women, Randwick NSW 2031, Australia

Keywords: advanced epithelial ovarian cancer cytoreductive surgery neoadjuvant chemotherapy Cytoreductive surgery for patients with advanced epithelial ovarian cancer has been practised since the pioneering work of Tom Griffiths in 1975. Further research has demonstrated the prognostic significance of the extent of metastatic disease preoperatively, and of complete cytoreduction post-operatively. Patients with advanced epithelial ovarian cancer should be referred to high volume cancer units, and managed by multidisciplinary teams. The role of thoracoscopy and resection of intrathoracic disease is presently investigational. In recent years, there has been increasing use of neoadjuvant chemotherapy and interval cytoreductive surgery. In patients with poor performance status, which is usually due to large volume ascites and/or large pleural effusions. Neoadjuvant chemotherapy reduces the post-operative morbidity, but if the tumour responds well to the chemotherapy, the inflammatory response makes the surgery more difficult. Postoperative morbidity is generally tolerable, but increases in older patients, and in those having multiple, aggressive surgical procedures, such as bowel resection or diaphragmatic stripping. Primary cytoreductive surgery should be regarded as the gold standard for most patients until a test is developed which would allow the prediction of platinum resistance pre-operatively.

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Ovarian cancer is the seventh most common cancer in women worldwide, with 239,000 new cases estimated to have been diagnosed in 2012. About 65,000 cases occurred in Europe. The incidence rate for the United Kingdom is 11.7 per 100,000 women per year.(www.cancerresearchuk.org).

About 70% of patients with epithelial ovarian cancer present with advanced disease, because of the lack of any satisfactory screening test and the lack of early symptoms. These patients will require a

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<sup>&</sup>lt;sup>b</sup> School of Women's and Children's Health, University of New South Wales, Kensington NSW 2052, Australia

<sup>\*</sup> Corresponding author.

E-mail addresses: n.hacker@unsw.edu.au (N.F. Hacker), Archana.Rao@health.nsw.gov.au (A. Rao).

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combination of cytoreductive surgery and chemotherapy to give them their best chance of long term survival. Cytoreductive or debulking surgery entails bilateral salpingo-oophorectomy, typically along with hysterectomy, gastrocolic omentectomy, and resection of as much other gross metastatic disease as possible.

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With advancements in ovarian cancer surgery and modern chemotherapy, median and overall survivals for patients with even advanced ovarian cancer have improved over the last 15 years. Using data on 40,692 patients from the Surveillance, Epidemiology and End Results (SEER) database taken from 1995 to 2007, Baldwin et al reported that patients with FIGO stages III and IV epithelial ovarian cancer had relative 5-year survivals of 36% and 17% respectively, and relative 10-year survivals of 23% and 8% respectively (Figure 1) [1]. Most of these patients are not disease-free, but some of them are, and it is not possible to predict which patients will apparently be cured of advanced disease with currently available prognostic factors. This will require genetic profiling of all patients in the future.

International differences in ovarian cancer survival are wide, even between high-income countries with similar health systems. The International Cancer Benchmarking Partnership obtained data from population-based cancer registries in Australia, Canada, Denmark, Norway and the United Kingdom, and analysed 20,073 women who were diagnosed between 2004 and 2007 [2]. For patients with FIGO stages III and IV, women in the UK had lower one-year survival than women in the other four countries (61.4% vs 65.8-74.8%). This was particularly so for older women, and the authors suggested that the management of these women should be investigated.

#### Historical perspective

Although earlier surgeons had recommended "maximal surgical effort" when operating on patients with advanced ovarian cancer [3,4], the first to quantify the benefits of aggressive surgery was Griffiths in 1975 [5]. In a retrospective series of 102 patients treated at the Boston Hospital for Women and the Sidney Farber Cancer Institute, Griffiths reported improved survival if what he termed "optimal" cytoreduction could be performed, meaning no residual disease >1.5 cm in diameter. He confirmed these results in a subsequent prospective study of 26 consecutive patients [6]. Griffith claimed that patients who started with large metastatic disease fared as well as those whose largest metastatic lesions were below 1.5 cm at the outset.

The next contribution to the discussion was from Hacker et al, at the University of California at Los Angeles (UCLA) [6]. They confirmed the importance of small residual disease, but showed that patients who were cytoreduced to individual nodules not greater than 5 mm in diameter had an even better prognosis. However, their data refuted the concept that patients who started with large metastatic

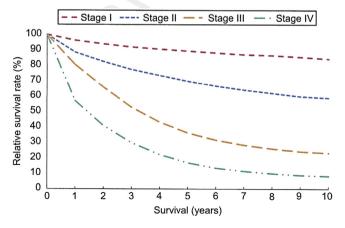


Figure 1. Ten-year relative survival for epithelial ovarian cancer by stage of disease. Information from the Surveillance, Epidemiology and End Results (SEER) database (N = 40,692) (Reproduced with permission) [1].

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