Management of Borderline Ovarian Tumours

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Borderline ovarian tumours are known to occur in younger women than invasive cancers and to also have a better prognosis. However, there is also much disagreement about the best approaches to management. At the Queensland Centre for Gynaecological Cancer we have had a particular interest in this disease for some years. Regular reviews of our management have indicated many important guides to management.

In our most recent review of 606 cases we have concluded that:

- *Early stage disease can and should be treated conservatively if the patient desires to retain her reproductive function,*
- *Treatment should be aimed at leaving no visible disease,*
- *Adjuvant therapy does not improve survival,*
- *Re-staging laparotomy in clinical Stage 1A patients is not justified as the pick-up is too small,*
- *The best prognosis is to be expected in the youngest patients.*

We will continue to track the progress of these patients in the hope that better management can be offered in the future.

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Borderline ovarian tumours are a group of ovarian neoplasms which are confusing as much by their confusing terminology as by their difficult pathology. They are a group of tumours that lie in an intermediate position between benign and malignant ovarian neoplasms and their terminology has been confused from early last century. In 1929 Taylor coined the term "semimalignant" to describe a group of serous ovarian tumours associated with peritoneal implants but which did not have the typical malignant course associated with serous ovarian cancers. Since then they have variously been referred to as:

- tumours of intermediate malignancy,
- cystadenocarcinomas of low malignant potential,
- ovarian carcinoma-in-situ,
- ovarian intraepithelial neoplasia,
- non-invasive ovarian carcinoma, and
- and probably now most widely as borderline ovarian cancers.

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From a linguistic point of view the name per se is not that important as long as its meaning is understood. The major draw back with the term "borderline" is that it often conveys the belief that the pathologist cannot decide whether or not the tumour is benign or malignant. However, the distinction is a very real one in that borderline ovarian tumours are a distinct entity that I terms of their prognosis lie between benign and malignant tumours but if anything closer to the benign end of the spectrum.

The recognition of borderline ovarian tumours can at times be difficult. These are tumours which manifest some of the cytological and structural changes associated with ovarian cancers but who do not show stromal invasion. The WHO classification defines borderline ovarian tumours as follows:

Tumours that have some, but not all, of the morphological features of malignancy; those present include, in varying combinations: stratification of the epithelial cells, apparent detachment of cellular clusters from their sites of origin and mitotic figures and nuclear abnormalities intermediate between those of clearly benign and unquestionably malignant

tumours of a similar cell type; on the other hand obvious invasion of the stroma is lacking".

This final point is one of the most difficult aspects to assess as the complex structure of some of these tumours can make it appear that there is glandular invasion of stroma when one is only looking at tangential cutting through profuse papillary structures.

In 1997 The Queensland Centre for Gynaecological Cancer published a review of 175 consecutive cases of borderline or low malignant potential tumours of the ovary. A recent up-date shows that we have 606 cases between 1982 and 2003 and we now have up to 15 year survival figures for these patients. Of our 606 patients, 536 (88.7%) had Stage 1 disease, 34 (5.6%) had Stage 2 disease and 34 (5.6%) had Stage 3 disease. Only two patients had Stage 4 disease and they will be excluded from further analysis because of the small numbers.

It is well recognised that borderline ovarian tumours occur in younger women than do invasive ovarian cancers. In our patients the majority were aged 40-49 years, followed by 30-39 years then 50-59 years. Eleven patients were aged between 10-19 years.

The most common surgical procedure (359 cases) was an omentectomy which was combined with variably a bilateral salpingo-oophorectmy (343) a unilateral salpingo-oophorectmy (221) and/or an extra-fascial hysterectomy (333). However, 26 patients had radical hysterectomies, 67 had a pelvic lymphadenectomy, 55 had pelvic node sampling and 30 had a para-aortic lymphadenectomy. An appendicectomy was performed on 181 occasions and there were 8 small bowel resections and 7 large bowel resections. As a result of our 1997 study we were of the opinion that the most important aspect was to leave the patient with no visible evidence of disease. Accordingly the use of radical hysterectomies and lymph node dissections has decreased with time.

Analysis of survival figures showed that when looking at deaths from any cause, Stage 1 patients had a 78% 15 year survival, Stage 2 had a 62% 15 years survival and Stage 3 a 59% 15 year survival. However when one corrects for the differences in surgery between these three stages there is no significant differences in outcome between stages 1,2 and 3 disease. Further more, when analysis was done of individual sub-stages there were no significant differences in survival.

Univariate analysis showed that the addition of chemotherapy was not associated with any survival improvement. This would be in line with overseas findings. Those patients treated by unilateral salpingo-oophorectomy did better than those treated by extra fascial hysterectomy and bilateral salpingo-oophorectomy, 96% v 70% 15 year survival ($p = 0.03$). One of the strongest determinants of survival was the patients age at initial presentation. Pre-menopausal patients (<50 years) did much better that post-menopausal patients (> 50 years), 93% v 57% ($p < 0.001$). However, a more detailed analysis showed that this trend was not based just on menopausal status as it was present throughout age decades with deteriorating survival relating to increasing age.

A Cox Multivariate analysis showed only one significant determinant of survival and that was age at presentation.

These results confirm our earlier findings:

- Early stage disease can and should be treated conservatively if the patient desires to retain her reproductive function,
- Treatment should be aimed at leaving no visible disease,
- Adjuvant therapy does not improve survival,
- Re-staging laparotomy in clinical Stage 1A patients is not justified as the pick-up is too small,
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