Lower ovarian cancer tumour volume at diagnosis on screening symptomatic women – how much of this is a ‘healthy volunteer effect’?

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Comment on

In their recent study, Gilbert et al\textsuperscript{1} were able to detect high grade serous ovarian cancer (HGSC) by screening symptomatic women. While they were not able to diagnose early stage disease, there was a suggestion of lower (not clearly defined) tumour burden. This was accompanied by a trend to higher complete resection rates in study women (73\%) diagnosed with ovarian cancer (OC) compared to patients (44\%) diagnosed outside the study during the same period (standard care). The data is encouraging and echoes our experience of large OC screening trials\textsuperscript{2,3} in the general population. Complete resection with no gross residual disease has been shown to be associated with superior survival outcomes in patients with advanced-stage epithelial OC.\textsuperscript{4} We believe low volume Stage III disease may have contributed to the significant difference in 5-year survival observed in our first OC screening randomised controlled trial (RCT).\textsuperscript{2}

We commend the team on the huge effort invested in performing this study but would like to point out a key issue related to study design. The findings of a trend in nine patients diagnosed with OC in their single arm prospective pilot study, however encouraging, may to a large extent be due to a 'healthy volunteer effect' (HVE). The DOvE cohort have all the hallmarks (younger, more educated, more English speaking) of one which would be associated with a marked HVE. In the control (no intervention) arm of our United Kingdom Collaborative Trial of Ovarian Cancer Screening, the overall standardised mortality rate was 37.3\% compared to the age matched UK population. The HVE in cancer was more pronounced with regard to mortality (standardised cancer specific mortality rate 55.9\%) compared to incidence (standardised cancer incidence rate 88.1\%).\textsuperscript{5} This was also observed in the control
arm of the PLCO trial. In addition the inference is limited by inability to control for preferential selection of patients to DoVE rather than standard care.

In a recent UK multicentre study, we have found that in two thirds of symptomatic patients, it may be possible to bring the OC diagnosis forward by 3 months or more. While this is a significant proportion of patients, the window of opportunity for a symptom based algorithm to impact on optimal resection is small. The resulting improved survival may be a worthwhile end point even in the absence of a mortality benefit in symptomatic women presenting to clinicians as opposed to asymptomatic women. However it needs to be balanced by the risks to the women who do not have OC and the resource implications of such a strategy.

The authors plan to expand the single arm study by setting up satellite clinics and introducing widespread symptom awareness measures. Given the inherent issues of this study design, we would strongly urge them to consider validating their preliminary findings in a prospective multicentre RCT to ensure the trend observed is not due solely to HVE and address the balance of risk versus benefits for the whole cohort.

References:


