Health Technology Assessment 1998; Vol. 2: No. 2 (Executive summary)

Review

Executive summary

Screening for ovarian cancer: a systematic review

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Health Technology Assessment
NHS R&D HTA Programme

Executive summary

Background

Ovarian cancer is the seventh most common cancer in women. The overall 5-year survival rate is only 30%. For women whose disease at diagnosis is localised to the ovaries, survival is about 75% at 5 years, but only a quarter of cases in the UK are currently diagnosed at such an early stage. This has led to interest in screening methods that might result in earlier diagnosis and reduce both mortality and morbidity.

Screening methods include ultrasound scanning and the measurement of the tumour marker cancer antigen 125 (CA 125) in serum. When used for screening, CA 125 measurement is followed by ultrasound scanning in women with abnormal CA 125 levels ('CA 125-based screening'). Women with persistently abnormal findings are referred for diagnostic abdominal surgery for removal of ovarian tissue.

Objectives

- To evaluate the performance of current screening tests for ovarian cancer.
- To assess the adverse effects of screening, including morbidity associated with surgical intervention and psychological morbidity associated with false-positive diagnosis.
- To report on the stage of development of newer methods of screening.
- To investigate the potential cost-effectiveness of screening in different risk groups.

Methods

The review was carried out using structured guidelines for systematic reviews. These are described in detail in the full report.

Results

The effectiveness of screening

Although three large RCTs are in progress, no RCTs of screening for ovarian cancer have been completed. In the absence of evidence of effectiveness, it would be premature to establish any kind of screening programme.

Screening test performance

The evidence suggests that both CA 125-based screening and ultrasound screening can detect a higher proportion of ovarian cancers at Stage I than that currently observed in the UK. About 50% (95% CI; 23–77) are diagnosed at Stage I in CA 125-based screening studies, and about 75% (95% CI; 35–97) in ultrasound screening studies. These data should be interpreted cautiously, however, as they are based on small numbers of cancers detected in diverse studies carried out mainly on self-selected women.

From the limited data available, annual screening with ultrasound appears to have a sensitivity or detection rate close to 100%. The reported sensitivity of annual CA 125-based screening is about 80%. The precision of these estimates is low, however, as they are based on small numbers of cancers.

The false-positive result rate is about 1.2–2.5% for women screened by ultrasound scanning and 0.1–0.6%. for CA 125-based screening.

About 0.5–1% of women will suffer a significant complication due to surgery and most of those who do not have ovarian cancer will have a benign gynaecological condition. There is a risk that detection of benign and borderline tumours may become a target of ovarian screening, even though they would not have been associated with any morbidity during a patient's lifetime.

Intervals for ultrasound scanning of between 1 year and 3 years are under investigation in the RCTs. CA 125-based screening has been carried out annually. The effect of different screening intervals on the detection rate and false-positive rate has not been formally investigated.

About 3–12% of screened women are recalled for further testing and assessment, resulting in potential distress and anxiety to otherwise healthy women.

The potential impact of screening for ovarian cancer

The low positive predictive value of ovarian screening (3% for surgery and 0.6% for initial

recall for annual ultrasound screening; 15% for surgery and 1% for initial recall for annual CA 125-based screening) is due mainly to the relatively low prevalence of ovarian cancer, which limits the potential cost-effectiveness of general population screening.

Evidence suggests that ultrasound screening is more sensitive than CA 125-based screening but that the latter may result in fewer false-positives and, hence, a higher positive predictive value. However, a less sensitive test must to be repeated more frequently to achieve the same overall detection rate of ovarian cancers, which may reduce the apparent advantages of CA 125-based screening. The most efficient screening method and interval is unknown, but modelling studies suggest that annual CA 125-based screening may provide lower overall benefits but be more cost-effective at detecting early stage cancers than annual ultrasound screening.

It is suggested that the addition of colour Doppler® imaging (CDI) to ultrasound screening may reduce the false-positive rate but reported results are mixed.

Screening a higher-risk population

A family history of ovarian cancer is one of the strongest risk factors for developing the disease and some UK centres currently offer screening to women with a strong family history. Until RCTs have been completed, there is no evidence as to whether, or by how much, screening women at higher risk reduces mortality.

For some women with an extensive family history of ovarian and/or certain other cancers, the increased risk is associated with an inherited genetic mutation. Carriers of some specific mutations may have a lifetime risk of developing ovarian cancer as high as 50–60%. The identification of some of these mutations raises the possibility of testing individuals in these families to determine whether they are carriers, potentially enabling more accurate assessment of risk.

Conclusions

Implications for policy

- Further evidence is required before a decision can be made about the potential benefits, harms and costs of screening for ovarian cancer. While awaiting the results of the current trials, demand for screening is likely to increase, and a strong national lead will be required.
- The relatively low prevalence of ovarian cancer means that the positive predictive value of screening tests is low. Since the consequence of a false-positive result is a surgical procedure, consideration of the overall impact of ovarian cancer screening is important. The low prevalence also limits the potential cost-effectiveness of population screening.
- Screening women who are at risk because of a strong family history may be more cost-effective but this has not been established. No RCTs are planned in this group, but a screening study has been established. This will provide some evaluation using intermediate outcomes of screening but may also increase demand for screening services.

Implications for research

- In a few years, RCTs should provide an estimate of the impact of screening on mortality. Assessment of the adverse effects of screening and the relative cost-effectiveness of different screening strategies would enhance information from the trials.
- New or modified screening tests should be compared with those being evaluated in current trials. Test developments which require further evaluation include: the marginal impact of adding CDI to ultrasound screening; the use of CA 125 levels in multivariate algorithms to determine thresholds for ultrasound and surgical intervention, and the marginal value of adding CA 125 measurement to ultrasound screening. The screening modalities will require continuous re-evaluation in line with technical developments.
- Research efforts should be directed towards evaluating both the clinical and cost-effectiveness of screening strategies for patients at high risk. This includes: investigation of any differences in the natural history; performance of screening tests compared with the strategies used in RCTs; investigation of age-specific risks of developing ovarian cancer, and psychological impact and value of risk assessment.
- Research is also needed into the impact of genetic testing on health outcomes and the level of demand for such services.

Publication

Bell R, Petticrew M, Luengo S, Sheldon TA. Screening for ovarian cancer: a systematic review. *Health Technol Assessment* 1998; **2**(2).

NHS R&D HTA Programme

The overall aim of the NHS R&D Health Technology Assessment (HTA) programme is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and work in the NHS. Research is undertaken in those areas where the evidence will lead to the greatest benefits to patients, either through improved patient outcomes or the most efficient use of NHS resources.

The Standing Group on Health Technology advises on national priorities for health technology assessment. Six advisory panels assist the Standing Group in identifying and prioritising projects. These priorities are then considered by the HTA Commissioning Board supported by the National Coordinating Centre for HTA (NCCHTA).

This report is one of a series covering acute care, diagnostics and imaging, methodology, pharmaceuticals, population screening, and primary and community care. It was identified as a priority by the Population Screening Panel.

The views expressed in this publication are those of the authors and not necessarily those of the Standing Group, the Commissioning Board, the Panel members or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for the recommendations for policy contained herein. In England, policy options in this area are to be considered by the National Screening Committee, chaired by the Chief Medical Officer, who will take into account the views expressed here, further available evidence and other relevant considerations.

Copies of this report can be obtained from:

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ISSN 1366-5278