Ultrasonographic detection of asymptomatic endometrial cancer in postmenopausal patients offers no prognostic advantage over symptomatic disease discovered by uterine bleeding

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of transvaginal sonography (TVS), a screening strategy to detect asymptomatic endometrial carcinoma (EC).

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised of postmenopausal patients.

Setting
The setting was a hospital. The economic study was carried out in Rostock, Germany.

Dates to which data relate
The effectiveness and resource data used were gathered between 1991 and 1997. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations to determine the sample size were not reported. Postmenopausal patients admitted at the authors’ institution from 1991 to 1997, for histological examination to detect suspicious EC, were selected. Of the 1,150 patients presenting with vaginal bleeding from the uterus, EC was confirmed histologically in 214 (19%) and 190 were considered suitable for the study. Twenty-four patients were excluded due to the lack of follow-up data. During the same period, 123 asymptomatic patients with sonographically suspicious EC presented for histological examination. Of these, the diagnosis was confirmed in 16 women (13%).

Study design
The study was a retrospective case-control study carried out in a single centre. The median follow-up time was 55
months (range: 24 - 97).

**Analysis of effectiveness**

Numerous primary health outcomes were used in the analysis. These included age, obesity (body mass index, BMI), diabetes, hypertension, frequency of gynaecological examinations before symptoms, place of residence, socio-economic status, complications due to hysteroscopy, histological findings, and correlation between bleeding times and factors such as age, disease stage, BMI, hypertension, diabetes, histological findings, and so on. Also, recurrence-free survival and overall survival rates (Kaplan-Meier analysis) were estimated with respect to tumour stage and bleeding times.

Multivariate analyses were performed to assess whether the International Federation of Gynecology and Obstetrics (FIGO) stage, age, bleeding time and sonometry were independent prognostic factors of EC.

**Effectiveness results**

The mean age (+/- standard deviation) was significantly higher in symptomatic patients (68.8 +/- 5.5 years) than in asymptomatic patients (61.1 +/- 6.7 years). The BMI (greater than 30) was also significantly higher in symptomatic patients (27%) than in asymptomatic (15%).

Significantly more patients had hypertension in the symptomatic group (52%) than in the asymptomatic group (30%).

While 68% of the symptomatic patients had not undergone a gynaecological examination, only 17% of the asymptomatic patients had not visited their gynaecologists in the last year. The difference was statistically significant.

Patients with symptomatic EC lived more frequently in rural areas (29%) than did asymptomatic patients (18%).

There were no statistically significant differences with respect to the presence of diabetes, socio-economic status and complications.

The histological findings indicated that tumour stages, as assessed through FIGO, did not differ between the patient groups.

There was evidence of significant correlation between the bleeding times and both disease stage and age. Longer bleeding times were associated with advanced tumour stages and increasing age.

With respect to bleeding times, the 5-year disease-free survival was 77% for no bleeding, 83% when bleeding lasted less than 8 weeks, 74% when bleeding lasted 8 to 16 weeks, and 62% when bleeding lasted longer than 16 weeks. The corresponding overall survival rates were 86% (no bleeding), 98% (bleeding less than 8 weeks), 90% (bleeding 8 to 16 weeks), and 69% (bleeding more than 16 weeks).

With respect to tumour stage, the disease-free survival rates were 100% for patients with stage Ia, 87% for stage Ib, 66% for stage Ic, 63% for stage II, and 36% for stages III and IV. The corresponding overall survival rates were 100% for patients with stage Ia, 95% for stage Ib, 93% for stage Ic, 78% for stage II, and 36% for stages III and IV.

Finally, the multivariate analyses indicated that age and FIGO stage were independent prognostic factors of EC, but bleeding time was not an independent early symptom.

**Clinical conclusions**

Overall, the effectiveness analysis has indicated that vaginal bleeding may be considered as an early symptom of EC in postmenopausal patients. Further, there was a significant correlation between increased bleeding time and advanced tumour stage.

**Measure of benefits used in the economic analysis**

The health outcomes were left disaggregated and no summary benefit measure was used in the study. A cost-consequences analysis was therefore carried out.
**Direct costs**
Discounting was not reported. The quantities and the costs were reported separately. The cost/resource boundary adopted was that of the hospital. The only costs included in the analysis were for hospital stay and the diagnostic procedures. These costs were estimated from actual data, on the basis of hospital charges, derived from a reimbursement system. The resources were estimated between 1991 and 1997. The price year was 2000.

**Statistical analysis of costs**
No statistical analysis of the costs was reported.

**Indirect Costs**
The indirect costs were not included.

**Currency**
Euros.

**Sensitivity analysis**
No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The cost of one hospital day was Euros 420. Overall, the additional costs of TVS screening due to unnecessary procedures amounted to Euros 116,256. This comprised Euros 30,576 for hysterectomies and Euros 85,680 for diagnostic procedures, such as chest X-ray, electrocardiogram, spirometry, and so on.

**Synthesis of costs and benefits**
Not applicable.

**Authors’ conclusions**
The analysis indicated that vaginal bleeding was an early symptom of endometrial carcinoma (EC) in postmenopausal patients. Therefore, although transvaginal sonography (TVS) was a valuable tool for the screening of EC, asymptomatic EC patients identified by screening had no prognostic advantage over patient who visited their gynaecologists immediately after bleeding. Further, TVS was associated with substantial extra costs and iatrogenic morbidity, as invasive tests were then required to confirm the development of EC.

**CRD COMMENTARY - Selection of comparators**
The rationale for the selection of the comparators was clear. They represented the routine practice in the authors’ setting. You should consider whether they represent widely used health technologies in your own setting.

**Validity of estimate of measure of effectiveness**
The internal validity of the study could have been limited by the study design (retrospective case-control study) and the lack of randomisation when allocating the patients to the groups. Although a statistical analysis was performed to show the comparability of groups with respect to demographics and clinical conditions, the role of confounding variables and
selection bias cannot be completely ruled out.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of benefit. Therefore, the study was categorised as a cost-consequences analysis.

Validity of estimate of costs
The cost estimates used in the study were quite specific to the authors' institution. Limited details relative to the resources used were reported and statistical analyses on quantities were not carried out. Discounting was not reported. However, it was relevant because the patients were followed for an average period of 55 months. The perspective of the study was not stated and some costs could have been omitted or erroneously included. Finally, hospital charges and not costs were used in the analysis. Charges may not reflect the true opportunity cost of the resource employed.

Other issues
Sensitivity analyses were not performed, thus the external validity of the analysis was fairly limited. The authors made some comparisons of their findings with those from other studies. Further comparisons would have improved the generalisability of the results obtained.

Implications of the study
The main implication of the study was that patients at high risk for EC (obese, old and suffering from hypertension) tended to avoid regular gynaecological examination, including TVS. The authors recommended that "patients who are at risk for the development of EC should be informed that vaginal bleeding is an early symptom of EC".

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