

Positron emission tomography/ computerised tomography imaging in detecting and managing recurrent cervical cancer: systematic review of evidence, elicitation of subjective probabilities and economic modelling

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Executive summary

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Executive summary

Background

Cancer of the uterine cervix is a common cause of mortality in women. After initial treatment women may be symptom free, but the cancer may recur within a few years. It is uncertain whether it is more clinically effective to survey asymptomatic women for signs of recurrence or to await symptoms or signs before using imaging. This project compared the diagnostic accuracy of imaging using positron emission tomography/computerised tomography (PET-CT) with that of imaging using CT or magnetic resonance imaging (MRI) alone and evaluated the cost-effectiveness of adding PET-CT as an adjunct to standard practice.

Methods

Standard systematic review methods were used to obtain and evaluate relevant test accuracy and effectiveness studies. Databases searched included MEDLINE, EMBASE, Science Citation Index and The Cochrane Library. All databases were searched from inception to May 2010. Study quality was assessed using appropriately modified Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria. Included were any studies of PET-CT, MRI or CT compared with the reference standard of histopathological findings or clinical follow-up in symptomatic women suspected of having recurrent or persistent cervical cancer and in asymptomatic women a minimum of 3 months after completion of primary treatment. Subjective elicitation of expert opinions was used to supplement diagnostic information needed for the economic evaluation. The effectiveness of treatment with chemotherapy, radiotherapy, chemoradiotherapy, radical hysterectomy and pelvic exenteration was systematically reviewed. Meta-analysis was carried out in RevMan 5.1 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark) and Stata version 11 (StataCorp LP, College Station, TX, USA). A Markov model was developed to compare the relative cost-effectiveness using TreeAge Pro software version 2011 (TreeAge Software, Inc., Evanston, IL, USA).

Results

From 7524 citations retrieved, 12 test accuracy studies were found: six studies evaluated PET-CT, two evaluated MRI, three evaluated CT and one evaluated both MRI and CT. All studies were underpowered and the majority evaluated imaging in women in whom recurrence was suspected on the basis of symptoms. The PET-CT studies evaluated local and distant recurrence and most used methods similar to current practice, whereas five of the six CT and MRI studies evaluated local recurrence only and were published between 1981 and 2000, and not all employed currently used methods.

Meta-analysis of PET-CT studies gave a sensitivity of 92.2% [95% confidence interval (CI) 85.1% to 96.0%] and a specificity of 88.1% (95% CI 77.9% to 93.9%). MRI sensitivities and specificities varied between 82% and 100% and 78% and 100%, respectively, and CT sensitivities and specificities varied between 78% and 93% and 0% and 95% respectively. One small study directly compared PET-CT with older imaging methods and showed more true-positives and fewer false-negatives with PET-CT.

The subjective elicitation from 21 clinical experts gave test accuracy results for asymptomatic and symptomatic women and the results for symptomatic women were similar to those from the published literature. Their combined opinions also suggested that the mean elicited increase in accuracy from the addition of PET-CT to MRI and/or CT was less than the elicited minimum important difference in accuracy

required to justify the routine addition of PET-CT for the investigation of women after completion of primary treatment.

From 24,943 citations, 62 effectiveness studies were included (chemotherapy, 19 randomised controlled trials; radiotherapy or chemoradiotherapy, 16 case series; radical hysterectomy and pelvic exenteration, 27 case series). None provided the effectiveness of cisplatin monotherapy, the most commonly used chemotherapeutic agent in the NHS, compared with supportive care in a background of other treatment such as radiotherapy in recurrent and persistent cervical cancer. The model results showed that adding PET-CT to the current treatment strategy of clinical examination, MRI and/or CT scan was significantly more costly with only a minimal increase in effectiveness, with incremental cost-effectiveness ratios for all models being >£1M per quality-adjusted life-year (QALY) and the additional cost per additional case of recurrence being in the region of £600,000.

Conclusion

Given the current evidence available, the addition of PET-CT to standard practice was not found to be cost-effective in the diagnosis of recurrent or persistent cervical cancer. There was considerable uncertainty in many of the parameters used because of a lack of good-quality evidence in recurrent or persistent cervical cancer. The evidence on diagnostic and therapeutic impact incorporated in the economic model was poor and there was little information on surveillance of asymptomatic women. Although probabilistic sensitivity analysis showed that the main conclusion about cost-ineffectiveness of PET-CT was firm given the range of assumptions made, should more reliable information become available on accuracy, therapeutic impact and effectiveness, and the cost of PET-CT reduce, this conclusion may need revision. Current guidelines recommending imaging for diagnosis using expensive methods such as PET-CT need to be reconsidered in the light of the above.

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