Comparison of virtual cystoscopy and ultrasonography for bladder cancer detection: a meta-analysis
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CRD summary
The review concluded that computed tomography (CT) virtual cystoscopy had higher diagnostic value for bladder cancer than magnetic resonance (MR) virtual cystoscopy or ultrasound. There were weaknesses in analyses and the conclusions were not fully supported by data; specificity estimates did not differ significantly between the three modalities and sensitivity of CT virtual cystoscopy was similar to MR virtual cystoscopy.

Authors' objectives
To compare the accuracy of computed tomography (CT) virtual cystoscopy, magnetic resonance (MR) virtual cystoscopy and ultrasonography in the diagnosis of bladder cancer.

Searching
EMBASE, PubMed, The Cochrane Library, Science Direct, SpringerLink and Scopus were searched from 1966 to December 2009. Search terms were reported and included methodological terms for test accuracy studies. The bibliographies of retrieved articles and relevant reviews were screened for additional studies. Only studies published in English were included.

Study selection
Studies using CT virtual cystoscopy, MR virtual cystoscopy or ultrasonography for the assessment of patients with suspected or previously diagnosed bladder cancer were eligible for inclusion. Eligible studies used conventional cystoscopy and/or histopathological analysis and/or close clinical follow-up for at least six months as the reference standard. Studies were required to report sufficient data to populate 2x2 contingency tables, such as numbers of true positive, false negative, false positive and true negative test results and to include at least 10 patients. Studies were excluded if tests were assessed in combination and separate accuracy data could not be calculated for the different imaging modalities, or if patients had co-existing diseases that could not be differentiated from bladder cancer.

Most included studies were conducted in Europe, with the remainder in North America, South America and Asia. The median age of the study participants was 57 years. Most studies of CT virtual cystoscopy used helical CT and contrast-enhanced techniques. All studies of MR virtual cystoscopy used 1.5T magnets. Most studies of ultrasonography described the scan location (details not reported). All studies used conventional cystoscopy as reference standard.

Two reviewers independently assessed studies for inclusion and disagreements were resolved by consultation with a third reviewer.

Assessment of study quality
The methodological quality of included studies was assessed using the 14-item QUADAS tool. The QUADAS assessment was used to calculate an overall quality score (maximum 14).

Two reviewers independently assessed study quality and disagreements were resolved by consultation with a third reviewer.

Data extraction
The numbers of true positive, false negative, false positive and true negative test results, for the detection of bladder cancer, were extracted for each study and imaging modality. These data were used to calculate sensitivity and specificity and 95% confidence intervals (CIs). Authors of abstracts and studies that did not report sufficient data were contacted for additional information.

Two reviewers independently extracted data and disagreements were resolved by consultation with a third reviewer.
Methods of synthesis
Pooled estimates of sensitivity and specificity, with 95% confidence intervals, were calculated using a random-effects model. Summary receiver operating characteristic (SROC) curves were estimated using the Moses and Littenberg model.

Between-study heterogeneity was assessed using $\chi^2$ and $I^2$. Linear regression was used to evaluate the potential relationship between log diagnostic odds ratio (DOR) and the percentage of lesions that were less than 5mm. Subgroup analyses were performed for CT (un-enhanced CT versus enhanced or contrast-enhanced CT, prospective versus retrospective or un-specified, test interpreter blinded versus test interpreter not blinded) and for ultrasonography (prospectively versus retrospective or un-specified, test interpreter blinded versus test interpreter not blinded).

Publication bias was assessed with funnel plots.

Results of the review
Twenty-six studies (3,084 patients, range 10 to 1,007) were included in the review. Thirteen studies only included data on CT virtual cystoscopy, nine only included data on ultrasonography, two only included data on MR virtual cystoscopy, one included data on both CT virtual cystoscopy and MR virtual cystoscopy, and one included data on both CT virtual cystoscopy and ultrasonography. All studies had QUADAS scores above 9, which indicated that they were of good quality. Twelve studies were prospective, three were retrospective and the remainder did not specify study design; recruitment was consecutive in 14 studies and un-defined in 12. Most studies did not describe the reference standard in sufficient detail to permit replication and did not apply the same reference standard in all participants.

Pooled estimates of sensitivity for CT virtual cystoscopy were 93.9% (95% CI 91.9 to 95.6) and specificity estimates were 98.1% (95% CI 97.3 to 98.8). MR virtual cystoscopy sensitivity estimates were 90.8% (95% CI 82.7 to 95.9) and specificity estimates were 94.8% (95% CI 88.4 to 98.3). Ultrasonography sensitivity estimates were 77.9% (95% CI 74.4 to 81.2) and specificity estimates were 96.2% (95% CI 95.3 to 96.9). The sensitivity estimates for CT virtual cystoscopy and MR virtual cystoscopy were significantly higher than for ultrasonography, and the specificity estimates did not differ significantly across the three imaging modalities.

There was evidence of significant heterogeneity in specificity estimates for CT virtual cystoscopy and in both sensitivity and specificity for ultrasonography. The pooled DOR estimate for CT virtual cystoscopy, 604.22 (95% CI 292.11 to 1249.8), was significantly higher than that for MR virtual cystoscopy, 144.35 (95% CI 43.833 to 475.36), or ultrasonography, 72.472 (95% CI 30.534 to 172.01). Areas under the SROC curves (AUC) were similar across imaging modalities, 0.9854 for CT virtual cystoscopy, 0.9620 for MR virtual cystoscopy and 0.9458 for ultrasonography.

Regression analysis indicated no relationship between the proportion of lesions less than 5 mm and CT virtual cystoscopy sensitivity.

Subgroup analyses indicated that the sensitivity for un-enhanced CT scans was higher than for enhanced or contrast-enhanced CT scans and there was no difference in specificity. The results of further subgroup analyses, based on study design characteristics, were reported in the article.

There was some evidence of possible publication bias.

Authors' conclusions
Both CT virtual cystoscopy and MR virtual cystoscopy performed better for diagnosing bladder cancer than ultrasonography. CT virtual cystoscopy had higher diagnostic value (sensitivity, specificity and DOR) for the detection of bladder cancer than either MR virtual cystoscopy or ultrasonography.

CRD commentary
The review addressed a clearly stated research objective and defined appropriate inclusion criteria. Several sources were searched for relevant studies, but the restriction to English language studies raised the possibility of language bias and this, combined with the use of methodological search terms for test accuracy studies (known to reduce search sensitivity) may have resulted in relevant studies being missed. Measures to minimise error and bias were applied throughout the review process.

The methodological quality of included studies was assessed and, though summary scores (not recommended for
QUADAS) were used, individual components of study quality were reported and their effects on test performance were investigated in the meta-analyses. The use of a simple random-effects model to generate pooled estimates of sensitivity and specificity, in the presence of significant between-study heterogeneity, had questionable validity; a bivariate or hierarchical SROC model may have been more appropriate. Comparisons between the performance of different imaging modalities were largely based on data from different studies; few studies reported direct comparisons of more than one imaging modality and direct comparison data were not reported separately.

The authors' conclusion that CT virtual cystoscopy had higher diagnostic value (sensitivity, specificity and DOR) for the detection of bladder cancer than either MR virtual cystoscopy or ultrasonography was not supported by the data. Specificity estimates did not differ significantly between the three modalities and the sensitivity of CT virtual cystoscopy was not significantly different to MR virtual cystoscopy.

Implications of the review for practice and research

Practice: The authors stated that choice of imaging modality might currently depend on factors other than test accuracy; ultrasonography might be considered the most appropriate choice in patients with a serious risk of reaction to contrast media. The authors also noted that when ultrasonography was negative and the source of haematuria remained uncertain, examination with other imaging modalities such as CT virtual cystoscopy, MR virtual cystoscopy or conventional cystoscopy should be performed.

Research: The authors did not specify any recommendations for future research.

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