Systematic review and meta-analysis of duplex ultrasonography, contrast-enhanced ultrasonography or computed tomography for surveillance after endovascular aneurysm repair

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CRD summary
This review concluded that both contrast-enhanced and duplex ultrasound were specific for detection of types 1 and 3 endoleak and there was no evidence of a clinically important difference in sensitivity. A number of limitations with both the review and the available evidence may limit the reliability of the authors’ conclusions.

Authors’ objectives
To assess the diagnostic accuracy of contrast-enhanced and duplex ultrasound for detection of clinically relevant types 1 and 3 endoleak after endovascular aneurysm repair (EVAR).

Searching
MEDLINE and EMBASE were searched from 1996 until 2012 for studies in English; search terms were reported. Conference abstracts from five relevant societies, Current Controlled Trials, Cochrane Central Register of Controlled Trials (CENTRAL), DARE and reference lists of retrieved articles were searched.

Study selection
Studies that evaluated the accuracy of duplex and/or contrast-enhanced ultrasound for detection of endoleak after EVAR in at least 10 unselected patients who had undergone EVAR (using computed tomography as the reference standard) were eligible for inclusion. Studies had to provide sufficient data to construct 2x2 tables of test performance.

Technical specification of computed tomography varied across studies; where reported, slice thickness varied from 0.3mm to 10mm. Where reported, most endografts were modular. Many studies did not report a definition of a positive ultrasound and definitions varied considerably across those that did. Contrast agents used for contrast-enhanced ultrasound included SonoVue, Optison and Levovist. No population characteristics were reported.

The authors did not state how many reviewers selected studies for the review.

Assessment of study quality
Study quality was assessed by two independent reviewers using the 14-point QUADAS tool. Disagreements were resolved by a third reviewer.

Data extraction
Data were extracted to construct 2x2 tables of test performance; sensitivity and specificity were calculated.

The authors did not state how many reviewers extracted data.

Methods of synthesis
Summary estimates of sensitivity and specificity with 95% confidence regions were calculated using a bivariate model and a hierarchical summary receiver operating characteristic (HSROC) curve was produced. Estimates were presented in the text with 95% confidence intervals (CI). The area under the curve with standard error (SE) was calculated. Heterogeneity was assessed using the I² statistic. Normal approximations on the logit scale were used to compare sensitivity of contrast-enhanced and duplex ultrasound. Subgroup analyses were conducted for different subtypes of endoleak.

Results of the review
Thirty-one studies were included in the review: 25 studies evaluated duplex ultrasound (3,975 paired scans) and 11 evaluated contrast-enhanced ultrasound (961 paired scans). Sixteen studies passed all 14 criteria on QUADAS; 10 studies did not report blinding of interpreters of the index and/or reference standard tests, six studies may have been
subject to progression bias and three subject to differential verification bias.

**Duplex ultrasound**: Pooled sensitivity for all endoleaks was 74% (95% CI 62 to 83; $I^2=88\%$), specificity was 94% (95% CI 90 to 97; $I^2=92\%$) and the area under the curve was 0.93 (SE 0.02). Pooled sensitivity for types 1 and 3 endoleaks (13 studies; 2,650 paired scans) was 83% (95% CI 40 to 97; $I^2=83\%$), specificity was 100% (95% CI 97 to 100; $I^2=86\%$) and the area under the curve was 0.998 (SE 0.004).

**Contrast-enhanced ultrasound**: Pooled sensitivity for all endoleaks was 96% (95% CI 85 to 99; $I^2=64\%$), specificity was 85% (95% CI 76 to 92; $I^2=85\%$) and the area under the curve was 0.97 (SE 0.02). Pooled sensitivity for types 1 and 3 endoleaks (eight studies; 887 paired scans) was 99% (95% CI 25 to 100; $I^2=28\%$), specificity was 100% (95% CI 98 to 100; $I^2=32\%$) and the area under the curve was 0.999 (SE 0.002).

When comparing duplex ultrasound with contrast-enhanced ultrasound there was no statistically significant difference in sensitivity for type 1 or 3 endoleak; the lack of a significant difference was attributed to wide confidence intervals for the estimates for each technology.

Additional results were reported for computed tomography using contrast-enhanced ultrasound as the reference standard and incidence of re-interventions; each was reported in a subset of studies.

**Authors' conclusions**

Both contrast-enhanced ultrasound and duplex ultrasound were specific for detection of types 1 and 3 endoleak; estimates of sensitivity were uncertain but there was no evidence of a clinically important difference. Duplex ultrasound detected types 1 and 3 endoleak with sufficient accuracy for surveillance after EVAR.

**CRD commentary**

The review addressed a clear objective supported by reproducible inclusion criteria. Various sources were searched for published and unpublished studies; the restriction to studies in English meant that some relevant studies may have been missed. Measures to minimise error and/or bias were applied to the quality assessment of included studies; it was unclear whether similar methods were used during study selection and data extraction. Authors were not contacted for 2x2 data from some otherwise eligible studies. Appropriate criteria were used to assess study quality and the results were published in full in an online appendix. There was a discrepancy between the paper and online appendix; the authors stated that the minimum score on QUADAS was 11 but studies met as few as six QUADAS criteria.

Appropriate methods of analysis were used but heterogeneity was not fully explored; it seemed that covariates were not incorporated into the bivariate/HSROC analyses despite substantial differences between studies. There was no investigation of the impact on the pooled estimates of studies prone to bias. The authors stated that a prior analysis showed no impact of blinding of interpreters of computed tomography but this did not necessarily transfer to interpretation of ultrasound scans or apply when the additional studies were included. Cost-effectiveness was not assessed in the review yet the cost of the technologies was used to inform the authors' recommendations for clinical practice.

A number of limitations with both the review and the available evidence may limit the reliability of the authors' conclusions.

**Implications of the review for practice and research**

**Practice**: The authors stated that contrast-enhanced ultrasound cannot be recommended to replace duplex ultrasound for primary surveillance as contrast-enhanced ultrasound would have greater cost implications and it was uncertain whether it could improve the accuracy of detection of types 1 and 3 endoleak.

**Research**: The authors did not state any implications for research.

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