Head-up tilt testing for diagnosing vasovagal syncope: a meta-analysis

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CRD summary
This review evaluated the accuracy of head-up tilt testing for diagnosing vasovagal syncope in patients with unexplained syncope. The authors concluded that tilt testing demonstrated good overall ability to discriminate between symptomatic and asymptomatic participants. Given the potential for bias in the review and uncertainties surrounding the evidence, the authors' conclusions should not be considered reliable.

Authors' objectives
To evaluate the accuracy of head-up tilt testing for diagnosing vasovagal syncope (fainting) in patients with unexplained syncope.

Searching
PubMed and EMBASE were searched up to March 2012 for publications in English. Reference lists of relevant publications were screened manually.

Study selection
Eligible studies were case control studies that included at least 10 participants in each treatment arm. Studies had to assess the diagnostic accuracy of head-up tilt testing (angles varied between 60° and 80°) in discriminating between symptomatic participants with unexplained syncope and asymptomatic control participants without previous syncope.

Where reported, the mean age of participants ranged from 11 to 73 years. Participants underwent single head-up tilt testing or two separate tilt tests for between 10 and 110 minutes. Some studies administered nitroglycerine and/or isoproterenol using varying regimens.

Two reviewers independently screened studies for inclusion; discrepancies were resolved through referral to a third reviewer.

Assessment of study quality
The authors did not state that they assessed studies for quality.

Data extraction
Positive tilt testing outcomes were extracted for all participants during unmedicated and medicated phases. Where studies included a pharmacological treatment phase (using agents other than nitroglycerine and/or isoproterenol) during tilt testing, where possible, only results before pharmacological administration were evaluated.

It appeared that two reviewers were involved in the data extraction process.

Methods of synthesis
A mixed-effects binomial regression model was used to calculate summary estimates of sensitivity (proportion of symptomatic participants with positive response to tilt testing), specificity (proportion of asymptomatic control participants with negative response to tilt testing) and diagnostic odds ratios (DOR), along with their 95% confidence intervals (CI). Summary receiver operating characteristics (SROC) curves were constructed. Statistical heterogeneity was assessed using the X² test. The effect of various study and participant characteristics on sensitivity and specificity were explored using multivariate analyses.

Results of the review
Fifty-five studies (4,361 participants with syncope and 1,791 controls) were included in the review.

An inverse relationship between sensitivity and specificity was observed: as sensitivity increased, specificity decreased (p<0.001). There was evidence of statistical heterogeneity across the studies (p<0.001).

The SROC curve suggested that the head-up tilt test has good overall ability to differentiate between symptomatic and asymptomatic participants (0.84, 95% CI 0.81 to 0.87).

Summary estimates according to tilt phases and pharmacological agents ranged between 25% and 66% for sensitivity, between 86% and 99% for specificity and between 5.94 and 14.40 for diagnostic odds ratios. Regimens using nitroglycerine showed the highest DOR (14.40, 95% CI 11.50 to 18.05) and the greatest sensitivity (66%, 95% CI 60% to 72%).
Multivariate analyses indicated that increasing age and a tilt angle of 60° reduced sensitivity and increased specificity. Other results were reported in the review.

**Authors' conclusions**

Head-up tilt testing demonstrated good overall ability to discriminate between symptomatic and asymptomatic participants.

**CRD commentary**

The review question and related inclusion criteria were stated clearly. The literature search was limited to two electronic databases, was restricted by language and did not appear to attempt to locate unpublished data so potentially relevant data may have been missed. The authors did not state that they assessed study quality and the reliability of the findings is therefore uncertain. It appeared that two reviewers were involved in study selection and data extraction, thereby reducing potential for reviewer error and bias.

The synthesis included a large number of studies but details on study and participant characteristics were limited. The limited details that were reported indicated considerable differences in tilting regimens. There was a disproportionately larger number of participants with syncope compared to control participants; this can increase uncertainty regarding the true diagnostic value of the test. The authors were relatively vague regarding the data extraction process. The forest plots did not include figures for sensitivity and specificity and 95% confidence intervals for individual study estimates but some wide confidence intervals were shown graphically. There was evidence of statistical heterogeneity and the authors attempted to identify the underlying causes.

The authors acknowledged that the absence of a gold-standard test for diagnosing syncope makes the calculation of the exact accuracy of tilt testing difficult to assess. They also acknowledged some other limitations of the evidence. Given the potential for bias in the review and the uncertainties surrounding the evidence, the authors’ conclusions should not be considered reliable.

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

**Practice:** The authors stated that findings from this review supported head-up tilt testing as a first choice investigation in the assessment of individual susceptibility to neurally mediated syncope. Tilt testing parameters could be variously considered according to the different age of patients with unexplained syncope. This could permit a move away from a single test that fits all to tilt testing protocols tailored on the diagnostic needs of each patient.

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

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