Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis
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CRD summary
The review concluded that compared with central venous catheters, peripherally inserted catheters were associated with a raised risk of deep vein thrombosis, especially in critically ill patients or those with a malignancy. The conclusions of the review reflect the evidence presented and are likely to be reliable despite quality issues associated with the design of the included studies.

Authors' objectives
To compare the risk of venous thromboembolism between peripherally inserted catheters and central venous catheters and evaluate the frequency of peripherally inserted catheter-related venous thromboembolism in specific populations.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), BIOSIS and EBM were searched up to the end of 2012 with no language or date restrictions. ClinicalTrials.gov and databases of conference abstracts and papers were searched. Additional studies were identified through internet searches and handsearches of bibliographies. Search terms were reported.

Study selection
Studies that included patients aged 18 years or over with peripherally inserted catheters placed in the arm were eligible for inclusion. Studies had to report occurrences of venous thromboembolism (deep vein thrombosis or pulmonary embolism) after catheter insertion. Outcome definitions were provided. Studies that compared different types of peripherally inserted catheters and case reports of unusual complications were excluded.

Patients had a wide range of conditions. Nearly half of the studies evaluated patients with cancer and a quarter included patients treated in intensive care. The most frequent method of deep vein thrombosis diagnosis was symptomatic testing with compression ultrasound. The most common comparator was triple lumen catheters. One third of the studies reported using deep vein thrombosis prophylaxis and most reported verifying the position of the peripherally inserted catheter's tip.

Studies were selected by three reviewers. Disagreements were resolved by consensus.

Assessment of study quality
Study quality was assessed by two reviewers independently using the Newcastle-Ottawa scale of selection of study groups, comparability of groups and ascertainment of outcomes. Studies with a low risk of bias in each domain were classed as being of high quality.

Data extraction
Outcomes data (number of deep vein thromboses, pulmonary embolism or both) were extracted by two reviewers independently to calculate odds ratios (OR) for comparative studies and frequency rates for non-comparative studies. Study authors were contacted for missing data.

Methods of synthesis
Studies were combined in meta-analyses to calculate frequency of venous thromboembolism in non-comparative studies and pooled odds ratios in comparative studies. A random-effects model was used. The unit of analysis was per patient (rather than per event). Heterogeneity was assessed using $I^2$ and Cochran's Q tests. Subgroups analyses were used to evaluate the effect of several variables (patient population, approach to venous thromboembolism diagnosis, peripherally inserted catheter tip position ascertainment, use of pharmacological prophylaxis and year of publication) on the main conclusions. Several sensitivity analyses were performed to test the robustness of the findings. Publication bias was assessed with Harbord's test.
Results of the review
Twelve comparative studies were included (4,643 patients, range 28 to 1,260): 11 cohort studies (five prospective, four retrospective and two mixed) and one case series. Four studies had gaps in reporting follow-up, exposure and ascertainment of diagnosis and were classed as low quality. Eight studies were considered to be high quality. Fifty-two non comparative studies (25,587 patients) were also included: 20 were classed as high quality and 32 were low quality.

Peripherally inserted catheters were associated with a statistically significant increase in the odds of deep vein thrombosis compared with central venous catheters (OR 2.55, 95% CI 1.54 to 4.23; 11 studies). There was no evidence of significant heterogeneity (I²=27%). No significant differences were found between subgroups, although odds of deep vein thrombosis were highest in patients treated in intensive care units (OR 4.08, 95% CI 2.17 to 7.70). Results of the sensitivity analyses confirmed the robustness of the findings. With an estimated baseline rate of 2.7% for peripherally inserted catheter-related deep vein thrombosis, the number needed to harm relative to central venous catheters was 26 (95% CI 13 to 71).

One of the 12 studies reported evidence of pulmonary embolism (numbers of patients and events not reported). The pooled frequency of venous thromboembolism with peripherally inserted catheters was 4.86% (95% CI 4.08 to 5.64).

Authors’ conclusions
Compared with central venous catheters, peripherally inserted catheters were associated with a raised risk of deep vein thrombosis, especially in patients who were critically ill or those with a malignancy.

CRD commentary
The review question and selection criteria were stated clearly. Several databases were searched and attempts were made to identify unpublished data using multiple sources. Attempts were made to minimise reviewer error and bias throughout the review stages. Quality assessment results were reported. Two thirds of the comparative studies were considered to be of high quality. However, no studies were randomised and this suggested a risk of selection bias. Although all cohorts were considered to be comparable, the risk of confounding from unknown variables could not be ruled out. A wide variety of patients were included. Methods of analysis appeared appropriate and there was no evidence of substantial heterogeneity. The magnitude of the pooled estimate for the primary analysis appeared relatively large. Additional analyses confirmed the robustness of the findings.

The conclusions of the review reflect the evidence presented and appear likely to be reliable despite the risk of bias associated with the design of the included studies.

Implications of the review for practice and research
Practice: The authors stated that a thoughtful consideration of the risk of deep vein thrombosis weighed against the benefits of a peripherally inserted catheter was important, especially when peripherally inserted catheters were placed in patients with critical illness or cancer. They stated that non-pharmacological methods (such as early catheter removal and guidance to appropriately place peripherally inserted catheters) might be relevant to prevent peripherally inserted catheter related deep vein thrombosis.

Research: The authors stated that only a randomised controlled trial of the risk of benefits associated with pharmacological deep vein thrombosis prophylaxis could resolve the issue of the clinical relevance of asymptomatic thrombosis and the best approach to manage it.

Funding
None.

Bibliographic details

PubMedID
23697825
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.