Physical activity in patients with deep venous thrombosis: a systematic review

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CRD summary
The authors concluded that walking exercise was safe in acute deep venous thrombosis (DVT) and may improve acute symptoms. Exercise training did not acutely increase leg symptoms of previous DVT and may prevent or improve post-thrombotic syndrome. Much of the review was well-conducted, but diversity among studies and predominantly non-significant findings suggest that the conclusions be interpreted with caution.

Authors' objectives
To evaluate the benefits and risks of physical activity in patients with an acute or previous deep venous thrombosis (DVT) of the leg.

Searching
PubMed, EMBASE and Science Citation Index were searched up to July 2007 for studies published in English. Search terms were reported. Reference lists of retrieved studies and the authors’ personal files were handsearched.

Study selection
Randomised controlled trials (RCTs) and prospective studies that evaluated the effects of exercise interventions or exercise exposure on clinical outcomes in patients with objectively diagnosed DVT were eligible for inclusion.

The included studies evaluated a variety of different interventions, including walking, early ambulation, treadmill exercise, wearing elastic compression stockings during exercise, self-reported physical activity levels and structured exercise programmes.

Cointerventions included early compression therapy (provided to all patients in some studies and only to patients in the early walking group in other studies) and leg elevation in the intervention group. Control interventions, where these existed, included bed rest and no exercise. Studies assessed a variety of different outcomes, including pulmonary embolism, leg pain, limb symptoms, limb function, joint flexibility, post-thrombotic syndrome, venous recanalisation, leg circumference and quality of life. Where reported, mean age of patients ranged from 51 to 70 years. Percentage of males ranged from 0% to 50%. Duration of follow-up ranged from 30 minutes to two years.

Two reviewers selected potentially relevant studies then both agreed on which studies to include.

Assessment of study quality
The validity of RCTs was assessed using validity of randomisation methods, concealment of randomisation, intention-to-treat (ITT) analysis, baseline similarity of treatment groups, blinding of outcome assessors and follow-up of at least 90%. The validity of observational studies was assessed using enrolment of unselected patients with thromboembolism, a clearly defined cohort at baseline and follow-up at least 90%.

Two reviewers independently assessed validity.

Data extraction
Proportions of patients with outcomes of interest were presented in tables for each study.

Two reviewers independently extracted data onto a standardised form.

Methods of synthesis
Where more than one comparable study reported similar outcomes, pooled relative risks (RR) and 95% confidence intervals (CI) were calculated using a random-effects model. Heterogeneity was assessed using the $I^2$ statistic (taking
I² > 50% as indication of substantial heterogeneity). Otherwise, studies were combined in a narrative synthesis.

Results of the review
Seven RCTS (n=554) and two observational studies (n=342) were included. Participants in one observational study were the same as participants in one of the RCTs. Sample size ranged from 30 to 126 for RCTs and from 41 to 301 for observational studies.

The authors stated that overall study quality was moderate to good. Most RCTs met at least four of the six validity criteria; both observational studies met all three validity criteria.

Acute DVT: There were no statistically significant differences between early walking and bed rest in the risk of pulmonary embolism at 10 days (four RCTs) or risk of thrombus progression (two RCTs). One follow-up study reported a reduced risk of post-thrombotic syndrome in the early walking group, but the difference was not statistically significant.

Two of three RCTs reported no significant difference between early walking and bed rest in speed of improvement in leg pain; one RCT reported that early walking was associated with a significant improvement in acute pain (p<0.01) and quality of life (p<0.05).

Previous DVT, short-term exercise: One observational study reported that 30 minutes of treadmill exercise did not worsen venous symptoms. One cross-over RCT in the same patients reported no significant effect of wearing elastic compression stocking during exercise on acute symptoms, leg swelling or joint flexibility.

Previous DVT, longer-term exercise: There were no statistically significant differences between daily walking and no exercise (one RCT) and with exercise training versus no training (one RCT) in venous recanalisation, leg circumference, quality of life, valvular reflux or venous clinical severity scores. One of the RCTs reported that exercise training was associated with significantly improved calf muscle strength (p=0.03) and pump function (p<0.03).

One cohort study reported a trend towards less severe post-thrombotic syndrome in patients who reported higher levels of physical activity, but the association was not statistically significant.

Authors' conclusions
Early walking exercise was safe in patients with a DVT and may have improved acute symptoms. Exercise training did not acutely increase leg symptoms in patients with a previous DVT and may prevent or improve post-thrombotic syndrome.

CRD commentary
The review question was clearly stated. Inclusion criteria were defined for intervention, participants and study design. Inclusion criteria were not specified for outcomes and this could have led to selective reporting of results. Several relevant sources were searched, but no attempts were made to minimise publication and language biases. Appropriate methods were used to minimise reviewer error and bias during the review process. Study validity was assessed and results were reported. The wide variety of outcome measures made it difficult to interpret review findings. Given the diversity among studies, a predominantly narrative synthesis was appropriate. Some limitations of the evidence were discussed. Much of the review was well-conducted, but the diversity among studies with respect to intervention and outcomes and the predominantly non-significant findings suggest that a more cautious conclusion may have been more appropriate.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further larger, adequately powered studies were required to evaluate the safety and benefits of more vigorous exercise training started soon after DVT and the effects of early exercise on the prevention and treatment of post-thrombotic syndrome.
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