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Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)
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Early mobilization versus bed rest for deep vein thrombosis

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Abstract

Aiming to prevent thromboembolic events, bed rest has been historically considered in the management of patient with deep vein thrombosis. Nevertheless early ambulation could have beneficial effects. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified seven systematic reviews including 10 randomized trials answering this question. We combined the evidence using meta-analysis and generated a summary of findings table following the GRADE approach. We concluded early ambulation is probably effective in reducing deep vein thrombosis progression and improving limb pain, and might not increase the risk of thromboembolism.

Problem

Bed rest has been considered standard treatment of patients with deep venous thrombosis based on the assumption that rest decreases the risk of deep venous thrombus detachment and subsequent pulmonary embolism [1]. However, bed rest may have negative consequences, such as work absenteeism or morbidity associated with immobilization. In this context, it has been proposed that early mobilization might be a better alternative for these patients.

Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages
- Early ambulation probably results in improvement of pain associated with deep vein thrombosis.
- Early ambulation probably reduces the risk of progression of deep vein thrombosis.
- Early ambulation may not increase the risk of pulmonary thromboembolism or death in comparison to mandatory bed rest.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found seven systematic reviews [2],[3],[4],[5],[6],[7],[8] considering 13 primary studies [9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19],[20],[21],[22],[23] including 10 randomized controlled trials [9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19],[20] and three observational studies [21],[22],[23]. This table and the analysis as a whole is based on the randomized controlled trials.
What types of patients were included	Patients with a diagnosis of acute deep vein thrombosis.
What types of interventions were included	Early ambulation compared with forced bed rest. Both strategies were associated with anticoagulation.
What types of outcomes were measured	Pulmonary thromboembolism, death due to thromboembolic event, deep vein thrombosis progression and pain associated with deep vein thrombosis.

Summary of findings

The information about the effects of early ambulation on deep vein thrombosis is based on 10 randomized controlled trials including 927 patients. Eight randomized controlled trials reported incidence of pulmonary embolism (including 863 patients), three trials reported death due to thromboembolic event (including 231 patients), three trials reported deep vein thrombosis progression (including 171 patients) and five trials reported pain associated with deep vein thrombosis (including 287 patients). The summary of findings is the following:

- Early ambulation probably results in improvement of pain associated with deep vein thrombosis. The certainty of the evidence is moderate.
- Early ambulation probably reduces the likelihood of progression of deep vein thrombosis. The certainty in the evidence is moderate.
- Early ambulation may not significantly increase the risk of pulmonary embolism in relation to the strategy of forced bed rest. The certainty of the evidence is low.
- Early ambulation may not significantly increase the risk of death due to a thromboembolic event in relation to the strategy of forced bed rest. The certainty of the evidence is low.

Early ambulation for acute deep vein thrombosis				
Patients	Acute deep vein thrombosis			
Intervention	Early ambulation			
Comparison	Bed rest			
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITH bed rest	**WITH early ambulation**		
	Difference: patients per 1000			
Pulmonary embolism	64 per 1000	77 per 1000	RR 1.20 (0.68 a 2.13)	⨁⨁◯◯[1,2] Low
	Difference: 13 patients more per 1000 (Margin of error: 20 less to 72 more)			
Death due to thromboembolic event	9 per 1000	8 per 1000	RR 0.87 (0.06 to 13.60)	⨁⨁◯◯[1,2] Low
	Difference: 1 patient more per 1000 (Margin of error: 8 less to 106 more)			
Deep vein thrombosis progression	257 per 1000	129 per 1000	RR 0.5 (0.27 to 0.92)	⨁⨁⨁◯[2] Moderate
	Difference: 128 patients less per 1000 (Margin of error: 20 less to 188 less)			
Deep vein thrombosis pain associated improvement # **	740 per 1000	913 per 1000	OR 3,68 (1.1 to 12.27)	⨁⨁⨁◯[2] Moderate
	Difference: 173 patients more per 1000 (Margin of error: 18 more to 232 more)			

RR: Risk ratio.
OR: Odds ratio.
Margin of error = 95% confidence interval (CI).
GRADE: evidence grades of the GRADE Working Group (see later in this article).

* The risks **WITH BED REST** are based on the risk in the control group of the trials. The risk **WITH EARLY AMBULATION** (and its margin of error) is calculated with the relative effect (and its margin of error).
** The relative effect for this outcome was calculated dichotomizing the outcome "amelioration of pain associated to deep vein thrombosis using a visual analogue scale" assuming a 20 mm change as minimal important difference [24], [25], [26].
# Studies in which the average pain associated with deep vein thrombosis was judged as important at the beginning of the study were included. Important pain was defined as greater than 40 mm in pain visual analog scale (range 0 - 100 mm).

[1] Risk of bias due to unclear allocation concealment of the randomization and lost to follow-up
[2] Imprecision due to low number of events/patients not reaching optimal information size, and confidence intervals including possible benefits and harm.

About the certainty of the evidence (GRADE)*

⨁⨁⨁⨁
High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⨁⨁⨁◯
Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⨁⨁◯◯
Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⨁◯◯◯
Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.
† Substantially different = a large enough difference that it might affect a decision.

Other considerations for decision-making

To whom this evidence does and does not apply

- This evidence applies to every patient with deep vein thrombosis.

About the outcomes included in this summary

- Most studies assessed the incidence of pulmonary embolism as the main outcome. It is important to note that in many of them a screening tomography mas performed to identify pulmonary embolism even in the absence of symptoms. This could overestimate the risk of events and show differences of dubious clinical value (at the expense of incidental pulmonary embolism).
- Some studies also performed systematic Doppler screening to all patients regardless of deep vein thrombosis symptoms. The same considerations regarding the outcome pulmonary embolism could be applied to this case.
- Studies that evaluated pain used visual analogue scale as a continuous outcome. In order to improve its interpretability, we dichotomized the results (proportion of patients with significant improvement in pain) as recommended by the GRADE [27]. The outcome was converted using a minimal important difference of 20 mm in the visual analogue scale. To determine minimum important difference publications in which threshold was determined for the same scale under similar conditions were used [24],[25],[26]. It is worth mentioning that only studies with average pain associated with deep vein thrombosis at the beginning of the study (baseline pain) greater than 40 mm in the visual analog scale in (range 0 - 100 mm) were included.

Balance between benefits and risks, and certainty of the evidence

- Early ambulation is undoubtedly related to the benefits of patients retaining their usual mobility (e.g. less work absence). Therefore the indication should only be questioned if there were negative aspects overweighting these benefits.
- Existing evidence suggests there may be a subtle increase in the risk of pulmonary embolism associated with early ambulation. Certainty of this evidence is low because it is based on studies with moderate risk of bias (unclear allocation concealment, loss to follow-up and imprecision). The risk of death may not be increased although the certainty is also low (based on the same reasons).
- Evidence suggests early ambulation probably leads to additional benefits as deep vein thrombosis progression or pain improvement. The certainty on these outcomes is moderate due to imprecision.

What would patients and their doctors think about this intervention

- We consider all patients would prefer the strategy of early ambulation to gain functionality and autonomy if this were not harmful or dangerous.

Resource considerations

- The intervention does not imply direct increase in costs. Indirect costs associated with thromboembolic events or absenteeism could be considered but this aspect would probably not be relevant when making the decision.

Differences between this summary and other sources

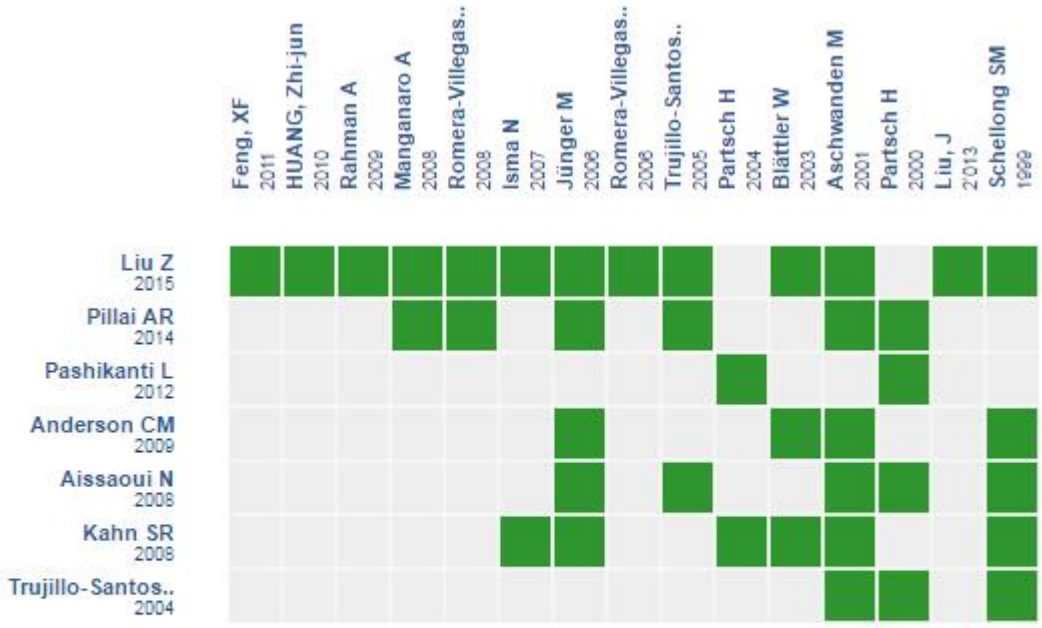
- The findings of systematic reviews included in the analysis are consistent with each other. The key messages of our summary are consistent with some of them, which concluded that existing evidence suggests no significant risks associated with this intervention.
- This analysis adds information regarding improvement in progression of thrombosis and deep vein thrombosis associated pain.

Could this evidence change in the future?

- The probability that the conclusions reached in this analysis change substantially in the future is moderate for pulmonary embolism or mortality due to thromboembolic events and low or very low for the progression of deep vein thrombosis and associated pain.
- At least one randomized controlled trial evaluating the effectiveness of strategies involving early exercise in the context of deep vein thrombosis is ongoing [28].

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.
The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.
The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.
The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version:** Early mobilization versus bed rest for deep vein thrombosis

Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here http://dx.doi.org/10.5867/medwave.2014.06.5997.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).
These summaries follow a rigorous process of internal peer review.

Conflicts of interest
The authors do not have relevant interests to declare.

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