Supplementary file

3. Data collection and analysis

We considered participants with the previous history of hospitalisation, VTE, or any other outcome of interest for inclusion in this review.

Anticoagulation in this context means anticoagulation therapy (heparin or oral anticoagulation or both) in any dose for more than two days. If we found studies with mixed populations, that is, submitted to stenting or angioplasty and not, or submitted to stenting or angioplasty with or without thrombectomy, and only a subset of the participants met our inclusion criteria, we attempted to obtain data for the subgroup of interest from the study authors in order to include the study. For studies with mixed populations for which we could not get the subgroup of interest's data but at least 50% of the study population are of interest, we included all participants in our analysis. Moreover, we explored the effect of this decision in a sensitivity analysis. Studies in which less than 50% of the population were of interest and the subgroup of interest data were not available were excluded.

We considered as primary outcomes 1) PTS; diagnosed by objective clinical examination (signs and symptoms) with or without the support of any classification of severity such as Villalta scores, CEAP (clinical, aetiological, anatomical, and pathological elements) or VCSS (Venous Clinical Severity Score), 2) VTE; including recurrent DVT and PE, fatal or non-fatal, diagnosed by clinical examination and diagnostic assessment including ultrasonography or angiography (CTA, MRA or DSA), and 3) mortality: all-cause, procedure-related, and VTE-related. The secondary outcomes were: 1) major bleeding: defined by a decreased haemoglobin concentration of 2 g/dL or more, a retroperitoneal or intracranial bleed, a transfusion of two or more units of blood, or fatal haemorrhagic events, as defined by the International Society on Thrombosis and Haemostasis[1], 2) secondary patency after revascularisation; for patency and all other definitions that are not specified, we used the guidelines by Vedantham 2009, 3) duration of hospitalisation (days), 4) QoL or patient's subjective perception of improvement (yes or no). We considered any valid score or scale (e.g. Short Form-36 Health Survey (SF-36)[2]. If we were unable to pool data on QoL due to use of different measurements we attempted to extract data on improvement[3], 5) adverse events (e.g. haematoma, pain, allergic reactions, vein rupture, contrast-induced nephropathy, etc.).

After merging the search results and removing duplicate records, we examined titles and abstracts to select the relevant reports. Two review authors (RLGF and LCUN) independently screened the trials identified by the literature search. We retrieved and examined the full text of the selected trials for compliance with eligibility criteria. We documented the reason for the exclusion of individual trials. We consulted the authors' team (LLA, VTC, CDQF, JEA, RDL and JCCBS) in the case of any disagreements and used the Covidence tool[4] for study selection.

Two review authors (RLGF and CDQF) extracted data independently and collected data on a paper data extraction form. We resolved discrepancies in the results by discussion. We consulted the authors' team (LLA, VTC, LCUN, JEA, RDL and JCCBS) in the case of any disagreements. We collected the following information: 1) study features: publication details (e.g. year, country, authors); study design; population data (e.g. age, comorbidities, severity, duration, history concerning treatments, and responses); details of intervention (e.g. manufacture, material, site of insertion, additional procedures or treatments); number of participants randomised into each treatment group; the number of participants in each group who failed treatment; the numbers of participants lost to follow-up; the duration of follow-up, and 2) outcomes: types of outcomes measured; timing of outcomes; adverse events.

In order to assess the risk of bias, two review authors (RLGF and VTC) independently assessed the included trials according to the domains and criteria of the Cochrane Risk of Bias tool, version 1 (RoB1) described by Higgins et al.[5] They resolved discrepancies by discussion and consulted the other authors (LLA, CDQF, LCUN, JEA, RDL and JCCBS) in the case of any disagreements. We assessed the following domains and rated them as being at low, unclear, or high risk of bias:

1. Random sequence generation;
2. Adequate concealment of allocation;
3. Blinding of participants, personnel, and outcome assessment;
4. Incomplete outcome data;
5. Selective outcome reporting; and
6. Other potential threat to validity.

We reported these assessments for each individual study. We contacted the study author(s) to seek clarification in cases of uncertainty over data. We followed the guidance in the *Cochrane Handbook of systematic Reviews of Interventions* on summary 'Risk of bias' assessments.[5]

- Low risk of bias: low risk of bias for all key domains
- Unclear risk of bias: unclear risk of bias for one or more key domains
- High risk of bias: high risk of bias for one or more key domains

Concealment of allocation and blinding are difficult for this kind of intervention. We took this into consideration when assessing for risk of bias in these domains.

We calculated risk ratios (RR) and 95% confidence intervals (CIs) for dichotomous variables. We calculated the mean difference (MD) and 95% CIs for continuous outcomes that have used similar scales. We calculated the standardised mean difference (SMD) and 95% CIs for continuous outcomes where different scales have been used. In the event that study authors do not have the necessary information available, we presented any data from primary studies that are not parametric (e.g. effects reported as medians, quartiles, etc.) or without sufficient statistical information (e.g. standard deviations, numbers of participants, etc.) in an 'Additional table'.

We considered each participant as a unit of analysis. For trials that considered multiple interventions in the same group, we analysed only the partial data of interest. We planned for trials that considered each limb as a unit of randomisation, we would report it explicitly.

For missing or unavailable data, we contacted the study authors for additional information. In cases of non-response, irrespective of the type of data, we reported dropout rates, and used intention-to-treat analysis.

We qualified inconsistency among the pooled estimates using the I^2 test.[6,7] As strict thresholds for interpretation of I^2 are not recommended, we followed the rough guide to interpretation in the *Cochrane Handbook for Systematic Reviews of Interventions.*[7].

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity

We planned to assess reporting biases or small study effects by drawing a funnel plot (trial effect versus trial size) if we had included a sufficient number of studies (more than 10) in the review, but it was not possible because seven trials were included.[8]

We synthesised qualitative information relative to methods, risk of bias, description of participants, and outcomes measures, and described this information. We did not include qualitative (non-randomised) studies in the review.

We would have used a fixed-effect model in meta-analysis with very homogenous included studies, considering population, interventions, comparators and outcome characteristics. However, we used a random-effects model as the included trials were heterogeneous.[7] For a better comprehension of the results, we reported the results of different time points of follow-up in different comparisons separately.

Where possible - for different score/scales for PTS and QoL and different type of adverse events - we performed a subgroup analysis for the trials examining the effect of stenting or angioplasty. Also, we intended to perform subgroup analyses to consider the following, but it was not possible with the available data:

- Age;
- Gender;
- Intervention material (e.g. self-expanding versus balloon-expanding stent; bare-metal stent versus drug-eluting stent);

If we found substantial heterogeneity, and there were sufficient data, we planned to investigate the possible causes by further exploring the impact of the condition of the individuals and interventions (i.e. participant characteristics, adjuvant drugs) using subgroup analysis. We planned to test for subgroup differences using interaction tests.

If there were an adequate number of studies, we planned to perform a sensitivity analysis based on separation of studies according to allocation concealment quality (high, low, or unclear) and blinding of outcome assessment (high, low, or unclear). We planned to carry out a sensitivity analysis by excluding trials of low and moderate methodological quality, as defined by the 'risk of bias' table. We explored the decision to include all participants when at least 50% are of interest in a trial with a mixed population. We presented these results and compared them with the overall findings where it was possible with the available data.

We prepared one 'Summary of findings' table for each comparison to provide the key information presented in the review comparing treatments in participants with acute and chronic DVT. For each comparison summarised and for each time point (early, intermediate and long-term), we included the outcomes described in the Types of outcome measures:

- PTS
- VTE
- Mortality
- Major bleeding
- Secondary patency after revascularisation
- Duration of hospitalisation
- QoL
- Adverse events

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