Cochrane Library

Cochrane Database of Systematic Reviews

Vena caval filters for the prevention of pulmonary embolism (Review)

Young T, Tang H, Hughes R

Young T, Tang H, Hughes R.
Vena caval filters for the prevention of pulmonary embolism.
Cochrane Database of Systematic Reviews 2010, Issue 2. Art. No.: CD006212.
DOI: 10.1002/14651858.CD006212.pub4.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Vena caval filters for the prevention of pulmonary embolism

Tim Young[1], Hangwi Tang[2], Rodney Hughes[3]

[1]Department of Respiratory and Sleep Medicine, Camperdown, Australia. [2]Department of Respiratory and Sleep Medicine, Princess Alexandra Hospital, Brisbane, Australia. [3]Sheffield Pulmonary Vascular Diseases Unit, Royal Hallamshire Hospital, Sheffield, UK

Contact address: Tim Young, Department of Respiratory and Sleep Medicine, PO Box M103, Missenden Road, Camperdown, New South Wales, 2050, Australia. timyoung1@optusnet.com.au.

Editorial group: Cochrane Vascular Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 2, 2010.
Review content assessed as up-to-date: 20 October 2009.

Citation: Young T, Tang H, Hughes R. Vena caval filters for the prevention of pulmonary embolism. *Cochrane Database of Systematic Reviews* 2010, Issue 2. Art. No.: CD006212. DOI: 10.1002/14651858.CD006212.pub4.

ABSTRACT

Background

Pulmonary emboli (PE) can have potentially fatal consequences. Inferior vena caval filters (VCFs) are metal alloy devices that mechanically trap fragmented thromboemboli from the deep leg veins en route to the pulmonary circulation. Filters are designed to be introduced (and in the case of retrievable filters, removed) percutaneously. Although their deployment seems of theoretical benefit, their clinical efficacy and adverse event profile is unclear.

This is an update of a Cochrane review first published in 2007.

Objectives

To examine evidence for the effectiveness of VCFs in preventing pulmonary embolism (PE). Secondary outcomes were mortality, distal (to filter) thrombosis, and filter-related complications.

Search methods

The Cochrane Peripheral Vascular Diseases Group searched their Specialised Register (last searched October 2009) and the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* 2009, Issue 4 for randomised or controlled clinical trials of VCFs for the prevention of PE. The authors contacted filter manufacturers for information.

Selection criteria

Controlled clinical trials (CCTs) and randomised controlled trials (RCTs) that examined the efficacy of filters in preventing PE.

Data collection and analysis

Two authors independently extracted information.

Main results

Two studies were included involving a total of 529 people. One open quasi-randomised trial of 129 participants with traumatic hip fractures showed a reduction in PE but not mortality over a 34 day period in the filter group. The PREPIC (Prévention du Risque d'Embolie Pulmonaire par Interruption Cave) trial, was an open RCT of 400 participants with documented proximal deep vein thrombosis (DVT) or PE who received concurrent anticoagulation. Permanent VCFs prevented PE at eight years. No reduction in mortality was seen, but this reflected an older study population; the majority of deaths were due to cancer or cardiovascular causes. There was an increased incidence of (DVT) in the filter group. Adverse events were not reported.

Authors' conclusions

No recommendations can be drawn from the two studies. One study showed a reduction in PE rates but not mortality, but was subject to significant biases. The PREPIC study lacked statistical power to detect a reduction in PE over shorter and more clinically significant time periods. However, the trial demonstrated that permanent VCFs were associated with an increased risk of long term lower limb DVT.

There is a paucity of VCFs outcome evidence when used within currently approved indications and a lack of trials on retrievable filters. Further trials are needed to assess vena caval filter safety and effectiveness.

PLAIN LANGUAGE SUMMARY

Vena caval filters for the prevention of pulmonary embolism

Blood clots in the lungs are called pulmonary emboli. They originate in the legs, fragment and travel to the lungs via the inferior vena cava. Vena caval filters are metal alloy devices inserted within the inferior vena cava to trap blood clots and thus prevent pulmonary emboli. Further emboli are usually prevented by blood thinning medications (anticoagulants).

In some instances (approximately 4% of cases), anticoagulation alone is insufficient to prevent more emboli or it is too dangerous for anticoagulation to be given because the person has a high risk of bleeding. Blood clots are known to occur as a result of certain types of surgery or injuries, and are more likely to fragment if they extend into the thigh or pelvis.

Vena caval filters have been in use since the 1970s and were designed to be left permanently within the inferior vena cava. The latest generation of filters are temporary or 'retrievable'. They can be removed at the manufacturer's recommendation between two to 12 weeks, if their use is no longer required. However, despite being called retrievable, a number of retrievable filters cannot be removed because of complications. The long-term safety profile of these devices left inside the body remains to be seen. The authors looked for articles comparing permanent and temporary (or retrievable) filters and comparisons between the different filter designs.

Two trials were included in the review involving a total of 529 people. No recommendations can be made regarding filter efficacy in preventing pulmonary embolism. One trial which was conducted in 1972 showed a reduction in pulmonary embolism rates but not deaths in a group of people who suffered traumatic hip fractures and who had a filter inserted. No preventive DVT treatment was given as this was controversial at the time. Outcomes were given at 34 days.The trial participants were inadequately randomised, had a higher proportion of people who were not able to undergo surgical fixation in the control group, and outcome assessors were not blinded.

In the PREPIC trial, caval filters were associated with an increased risk of blood clot formation in the legs following their insertion. This study did not demonstrate any difference in the death rates between the two groups; the participants were older (average age 73 years) with co-existing medical conditions and the majority of people died from cancer-related causes or heart problems. No details were recorded of adverse events of filters, but the numbers in this trial were not of sufficient size to detect them.

There is a lack of information on the effectiveness of caval filters in other clinical scenarios, especially in the two situations where they are used most frequently and thought to be the most advantageous. These are when patients cannot be anticoagulated, or when pulmonary embolism occurs despite adequate anticoagulation. Vena caval filter use is increasing and more trials are needed to confirm their benefit and accurately assess their safety.

BACKGROUND

Description of the condition

Blood clots or deep venous thrombosis (DVT) form in the lower extremities and can occur under a number of different circumstances. Temporary circumstances are prolonged immobility, recent surgery, trauma, pregnancy, or oestrogen therapy. Longer term

situations include people who have cancer, or people who have an inherited hypercoagulable tendency.

Deep vein thromboses can fragment and travel through the venous system to the lungs causing pulmonary embolism (PE). The major conduit of venous drainage from the lower half of the body is the inferior vena cava.

Deep vein thromboses that extend into the thigh or pelvis are more likely to embolise than those that do not extend beyond the calf. Case series data indicate a rate between 27% to 60% for the risk of embolism if the clot is situated either within the inferior vena cava or the thigh or pelvic veins (Norris 1985; Radomski 1987).

The current treatment for pulmonary embolism is anticoagulation (heparin and vitamin K antagonists (warfarin, coumadin)). Infrequently, recurrent pulmonary emboli can occur despite therapeutic levels of anticoagulation; Douketis suggested a rate of 3.8% in a systematic review of the literature (Douketis 1998).

Deep vein thromboses can also occur in the upper limbs and neck, because of the increasing use of semi-permanent venous access devices and catheters. They can embolise to the lungs via the superior vena cava.

Description of the intervention

The concept of caval interruption was identified as far back as the 1700s. The first surgical vena caval ligation (complete occlusion of the vena cava with sutures or external clips) was successfully performed in 1893. It required general anaesthesia and abdominal surgery, and was associated with considerable mortality. Vena caval ligation in the 1960s carried an operative mortality risk of 14%, and pulmonary embolism still occurred at a rate of 6% (due to the development of a large collateral circulation) with fatal embolism occurring at a rate of 2% (Greenfield 1992). Anticoagulation became the mainstay of treatment in the 1950s. Filters which could be inserted percutaneously were developed in the 1970s, and are used in increasing numbers.

How the intervention might work

Vena caval filters may be placed in the inferior or superior vena cava to mechanically trap emboli, interrupting their course before reaching the heart and lungs. These devices most commonly resemble an umbrella in appearance, are made from metal alloys, and can be inserted percutaneously. Inferior vena caval filters are usually inserted below the level of the renal veins.

Once deployed, permanent filters are left in situ; they become endothelialised and are eventually incorporated within the blood vessel wall. Temporary or retrievable (also known as optional) filters are recent developments in which filters can be removed within a certain time interval (specified by the manufacturer) if their use is no longer required. This time period may extend to approximately 12 weeks, depending on the clinical experience of the interventional radiologist. There are currently approximately 12 filter designs, several of which are retrievable. Retrievable filters have potential advantages over the permanent filters; one is the opportunity for subsequent removal if no longer needed, thus avoiding longer term sequelae of DVT. They can also be repositioned within the vena cava if significant incorporation into the endothelium/endothelialisation has not occurred. Despite being called 'retrievable', these filters can become permanent implants if their subsequent removal becomes complicated due to endothelialisation, or if there is a significant amount of trapped thrombus within the filter such that the filter cannot be retracted back into its sheath, thus preventing percutaneous removal.

Why it is important to do this review

Pulmonary embolism is a major cause of hospital morbidity and mortality.

The majority of retrievable filters have been designed for temporary use only. Whilst reports suggest that they can be left in situ longer term (Kirilcuk 2005), the safety of this practice has not been extensively evaluated.

Filters are strongly recommended for two groups of people: those who have a proximal DVT or pulmonary embolism, or both, where it is too dangerous for them to receive anticoagulation; and those who continue to have recurrent emboli despite already receiving appropriate levels of anticoagulation (Buller 2004).

There is controversy in the literature about whether other groups of people may potentially benefit from having a vena caval filter inserted (Hann 2005; Kinney 2003). These include:

- people with extensive trauma without established venous thromboembolism;
- people with large free-floating ilio-femoral thrombosis who do or do not subsequently receive thrombolytic therapy for this;
- people with cancer and concurrent venous thromboembolism;
- pregnant women who have venous thromboembolism.

The studies and the interventions examined in this review were to assess the efficacy and safety of filters; whether efficacy and safety varied amongst the different filter designs, and with different concurrent antithrombotic drugs.

We intended the comparisons in this review to be as follows.

1. Filters versus no filter in those people for whom anticoagulation is contraindicated.
2. Filters and anticoagulants versus anticoagulants alone.
3. Filters with anticoagulation versus filters with no anticoagulation, seeking to answer the question as to whether long-term anticoagulation is recommended with permanent filters in situ; there is considerable debate about this (Gomes 2003).
4. Trials of filters with newer antithrombotic drugs, of interest as these newer agents may have greater antithrombotic action or

less haemorrhagic complications. Both of these effects are relevant to current indications for filters and fondaparinux appears to have fewer haemorrhagic complications (Yusuf 2006).

5. Permanent versus temporary filters to look at which type of filter is most effective, but also to investigate respective rates of complications.

6. Direct comparison of filter brands, to see if any one filter is superior in terms of its filtering efficiency or low rate of complications.

Comparisons of filters versus no filters also examine the complications and adverse effects from having filters in situ. Pooled case series data indicate a recurrent PE rate of 2% to 5% with a fatal PE rate of 0.7%, despite the presence of a filter. The mortality rate from complications related to filter insertion is 0.12%. Filter migration has been estimated to occur at rates up to 69% and inferior vena caval perforation up to 24%, though these figures reflect radiological findings and not necessarily clinical events. Deep vein thrombosis was reported to occur at rates up to 45.7%, and post-thrombotic syndrome up to 59% (Kinney 2003); these problems occurred more frequently with longer durations of follow up. It is controversial as to whether these lower limb complications are the result of having a filter in situ, or are part of the intrinsic pro-thrombotic tendency these people may have.

OBJECTIVES

To evaluate the evidence for vena caval filters in preventing pulmonary embolism.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials and controlled clinical trials that studied the effectiveness of vena caval filters in preventing pulmonary embolism.

Types of participants

Participants were considered for inclusion in trials if they were aged 18 or older and:

- had radiologically confirmed proximal deep venous thrombosis or pulmonary embolism, or both;

or

- were considered to be at high risk of deep venous thrombosis or pulmonary embolism, with contraindications to anticoagulation.

Trials were excluded from the review if the participants had a life expectancy of less than four weeks when given treatment or if they had previous permanent vena caval filter placement.

Types of interventions

We searched for studies in which participants aged 18 or older with radiologically confirmed proximal deep venous thrombosis or pulmonary embolism, or both, received:

- vena caval filter versus no filter in people for whom anticoagulation was contraindicated;
- vena caval filter and anticoagulation (heparin, low molecular weight heparin (LMWH), and vitamin K antagonists) versus anticoagulation (and no filter);
- permanent vena caval filter versus temporary vena caval filter;
- direct comparisons between filter brands;
- vena caval filter with newer antithrombotic drugs (fondaparinux, hirudin) versus newer antithrombotic drugs (without filter).

Participants aged 18 or older at high risk of deep venous thrombosis and pulmonary embolism and in whom anticoagulation was contraindicated receiving:

- vena caval filter with mechanical prophylaxis versus no filter and mechanical prophylaxis (includes graded compression stockings, intermittent pneumatic compression, venous foot pump).

Types of outcome measures

Primary outcomes

- Pulmonary embolus as demonstrated by computer tomography (CT), pulmonary angiography or ventilation-perfusion lung scan.

Secondary outcomes

- Mortality.
- Filter-related complications - mortality, embolisation, clinical perforation.
- Distal (to filter) thrombosis - vena caval thrombosis and limb deep venous thrombosis as documented by ultrasonography impedence.

Search methods for identification of studies

Electronic searches

The Cochrane Peripheral Vascular Diseases Group searched their Specialised Register (last searched October 2009) and the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* (last searched 2009, Issue 4), see Appendix 1 for details of the search strategy used to search CENTRAL. The Specialised Register is maintained by the Trials Search Co-ordinator and is constructed from weekly electronic searches of MEDLINE, EMBASE, CINAHL, AMED, and through handsearching relevant journals. The full list of the databases, journals and conference proceedings which have been searched, as well as the search strategies used are described in the Specialised Register section of the Cochrane Peripheral Vascular Diseases Group module in *The Cochrane Library.*

Searching other resources

Citations within identified studies were analysed. In addition, specialists known to be involved with trials of vena caval filters, individual authors, and biomedical companies manufacturing vena caval filters were contacted for details of unpublished or ongoing trials.

Data collection and analysis

Selection of studies

Randomised controlled and controlled clinical trials of vena caval filters looking at their efficacy in preventing pulmonary embolism were included.

We collected the following information:

- incidence of radiologically confirmed pulmonary embolism;
- mortality;
- rates of distal (to filter) venous thrombosis;
- filter-related complications.

Subgroups of interest that were analysed consisted of:

- people who had a contraindication to anticoagulation;
- people who had another episode of pulmonary embolism despite being anticoagulated;
- people who had cancer and co-existing venous thromboembolism;
- pregnant women who had venous thromboembolism;
- people who had superior vena caval filters inserted for upper limb venous thrombosis;
- people who had supra-renal vena caval filters inserted;
- people who had filters inserted versus those receiving the newer antithrombotic drugs;
- comparisons between permanent and temporary filters;
- comparisons between filter brands.

Three authors (TY, HT and RH) independently identified all studies which satisfied the inclusion criteria; TY obtained the full text of the identified studies; TY, HT and RH independently assessed trials for inclusion in the review. If there was disagreement, RH was consulted. Trial authors were contacted for further information in the context of missing or incomplete data.

Data extraction and management

Two authors (TY and HT) independently extracted data according to the PVD Group's data extraction sheet. Incidence figures of desired outcomes were transcribed from the data tables provided.

Assessment of risk of bias in included studies

We used the criteria for assessing risk of bias as provided in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2008). The following domains were assessed as 'Yes' (low risk of bias), 'Unclear' (uncertain risk of bias) or 'No' (high risk of bias):

- randomisation;
- concealment of allocation;
- blinding (of participants, personnel and outcome assessors);
- incomplete outcome data;
- selective outcome reporting;

For the original review each trial was evaluated for quality according to the Jadad scale (Jadad 1996). This is a 5-point score which is based on the adequacy of randomisation, blinding and follow up. A maximum of two points was awarded if the word randomised or randomisation was stated and the sequence of number generation was described and was truly unpredictable. A maximum of two points was also allocated if the intervention was double blinded, no points were given for open trials; and one point was scored for adequate description of participant withdrawals and drop-outs during the study.

Measures of treatment effect

Dichotomous data were assessed by relative risk estimates and hazard ratios.

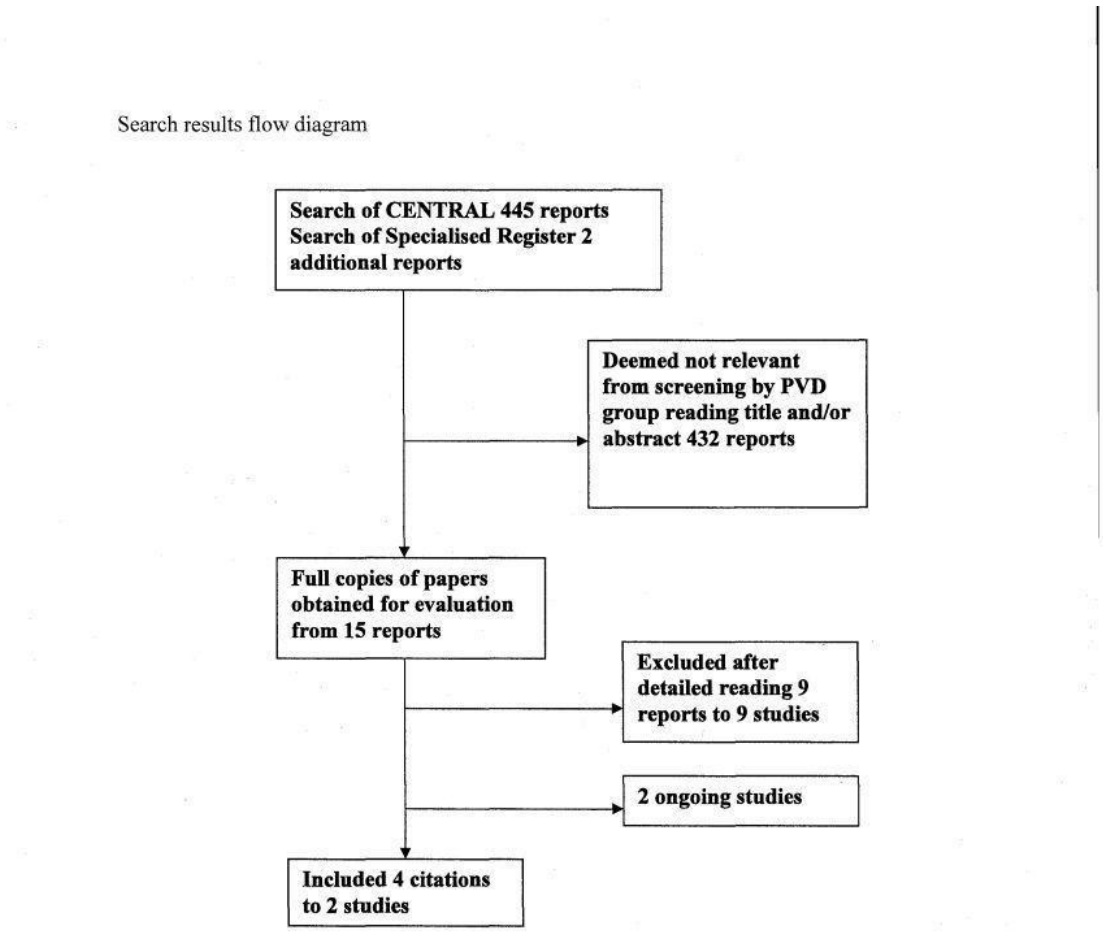
RESULTS

Description of studies

Results of the search

See the flow diagram of the search results, Figure 1.

Figure 1. Flow diagram of search results



The search for trials found two randomised controlled trials, one of which had an eight-year follow up, and nine clinical trials for assessment. Three controlled clinical trials had major methodological flaws as the interventional and control groups were not comparable or details were not stated; three others used a prospective cohort against an historical control. Two clinical trials were, in fact, case series. One was a cost-effectiveness analysis.

Included studies

Summary details of included studies are given in the Characteristics of included studies.

Fullen 1973 was a quasi-randomised open trial with 129 participants in a single centre in the US. All participants who had a traumatic hip fracture were asked to be involved in the study. The mean ages in the filter group and control group were 69 and 67 years respectively. The gender distribution was not documented. There seemed to be a greater proportion of people with atherosclerotic heart disease and cardiac failure allocated to the filter group. Exclusion criteria was refusal to consent to participating in the trial.

People included in the trial were randomised to receive a (Mobin-Uddin) caval filter. Primary outcomes were pulmonary embolism on a definite, probable or possible occurrence (based on clinical, imaging and post-mortem data), and mortality. Secondary outcomes were complications from surgery or the filter. Dates of outcome assessments were not stated; investigations for pulmonary embolic disease were performed when clinically suspected. The average length of stay was 33 and 34 days between the two groups; no range values were listed.

There was a reduction in pulmonary embolism in the filter group; with the only case in the filter group occurring prior to filter insertion.

Seven people could not have internal fixation, one in the filter group and six in the control group.

Filters could not be inserted into seven people randomised to the filter group. A jugular approach was used. Filters could not be placed into these seven people due to narrow central veins or difficulty negotiating the filter through the right atrium in severe kyphosis. No anticoagulation was used by any participant. Small doses of aspirin may have been taken by a number of control participants (no figure given but described as "occasional").

The PREPIC study was a randomised controlled open trial with 400 participants from multiple (44) centres in France. Participants consisted of consecutive hospitalised people, made up of 64% males with an average age of 73 years, with documented proximal DVT or pulmonary embolism and considered by the referring physician to be at high risk of pulmonary embolism. There were numerous exclusion criteria; notably people were excluded if they failed or had contraindications to anticoagulation, or if they were pregnant. PREPIC had a 2 x 2 factorial design with interventions of (permanent) caval filter versus no filter, and low molecular weight heparin (LMWH) versus unfractionated heparin. Primary outcomes were: pulmonary embolism, mortality, and deep venous thrombosis. Secondary outcomes were: bleeding, post-thrombotic syndrome, and filter-related complications. Outcomes were assessed at 12 days, two years, and eight years.

Analysis of the rates of pulmonary embolism showed that they were not statistically different between the LMWH and unfractionated heparin groups, so they were considered to be equivalent treatments.

Both study groups received vitamin K antagonists for the first three months; at eight years, 35% of people in both study groups were still receiving vitamin K antagonists. Similar proportions of people In both groups wore elastic stockings (45% and 47% in the filter and no-filter group respectively) at eight years.

Excluded studies

Details of excluded studies are given in the Characteristics of excluded studies. Three studies (Khansarinia 1995, Rodriguez 1996, and Rosner 2004) were excluded as they were designed to compare prospective interventional cohorts with historical controls. Brasel 1997 was excluded as it was a cost-effectiveness study. Midy 1994 and Rosenthal 1994 were case series. Gosin 1997 and Rogers 1997 did not have comparable prospective interventional and control groups; only selected high-risk people received filters, and prospective interventional cohorts were compared with historical controls. In Webb 1992, only selected high-risk people received filters, and there were no data regarding baseline characteristics of the intervention and control groups. These people also received concurrent prophylactic anticoagulation in the setting of trauma (acetabular fracture).

Several large case series were considered but could not be included within this review due to their methodology (primarily related to their lack of an adequate control group).

Risk of bias in included studies

See Figure 2 and Figure 3.

Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

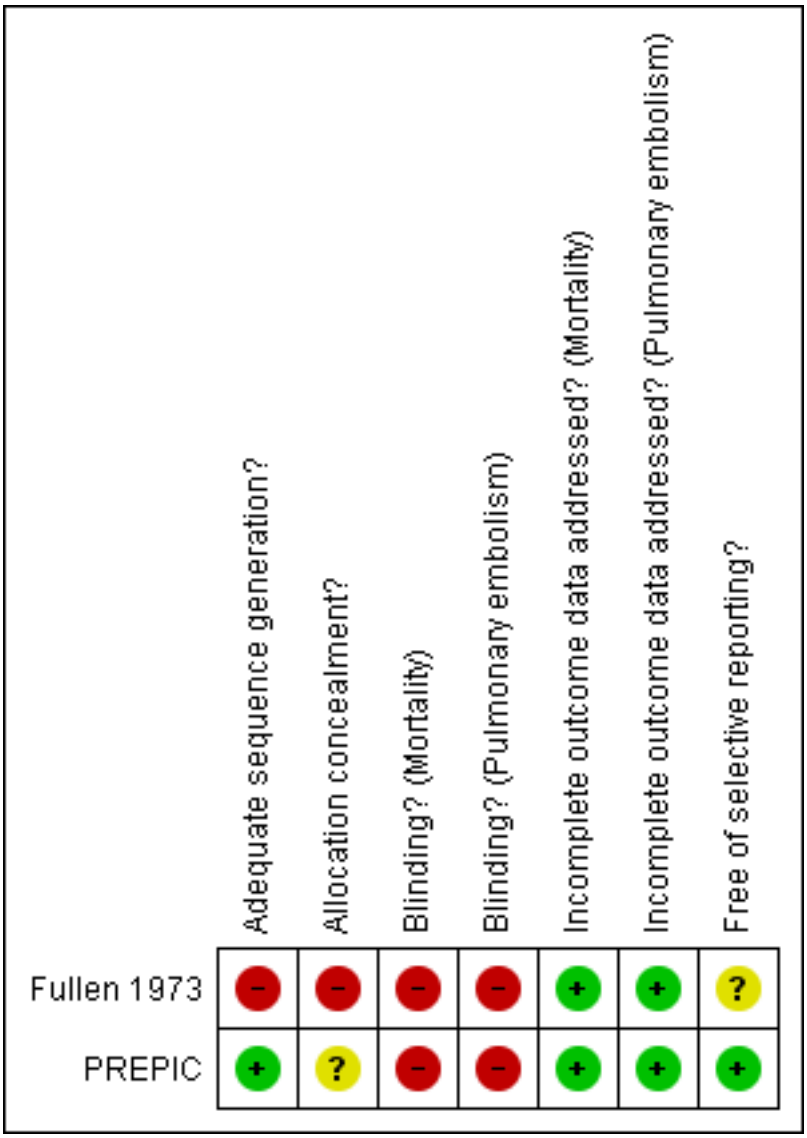
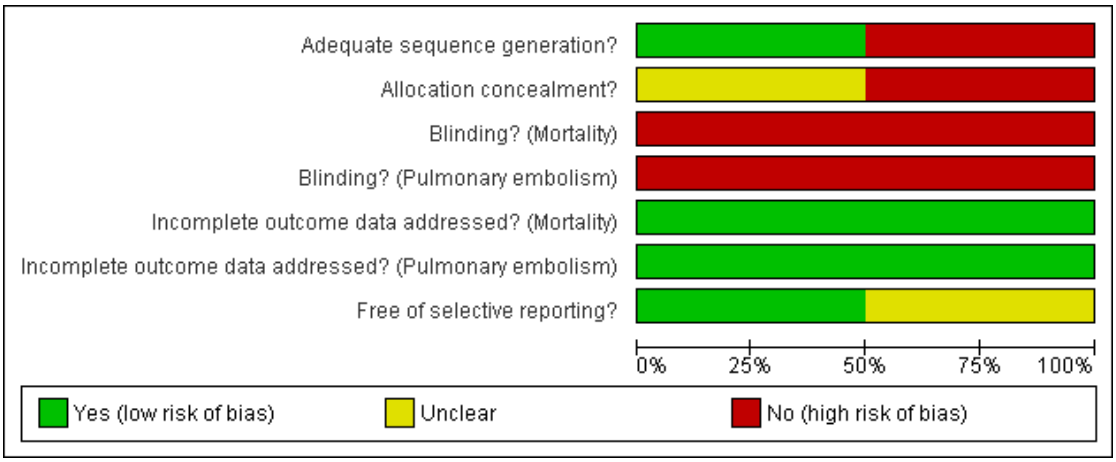


Figure 3. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.



Fullen 1973 was randomised on the basis of hospital numbers (odd or even). The study was an open design. Participation in the filter group required consent and the insertion procedure. Baseline characteristics were scarce. A higher rate of atherosclerotic heart disease and cardiac failure was noted in the filter group. Co-interventions (usage of anticoagulation) was similar between the groups, as was time from admission-to-filter insertion and admission-to-fracture fixation. Seven people could not undergo fracture fixation - six of these were in the control group. It is not stated whether the outcome assessors were blinded or not. Diagnostic imaging for PE was not stated as being a routine part of the trial. The use of plain chest radiography for the diagnosis of PE is inaccurate. Follow up was complete as this was an in-hospital population. Analysis was not by intention to treat. Inclusion and exclusion criteria were briefly stated. Primary outcomes of mortality and PE were given, as were details related to filter complications. No DVT rates were reported.

The PREPIC study was randomised by a centralised computer telephone system. The study was an open design. An independent adjudication committee who assessed all radiological and clinical outcomes was blinded to the treatment status of the participants. Baseline characteristics and co-interventions (including the proportion of people receiving vitamin K antagonists and wearing elastic stockings) were similar between the intervention and control groups. Withdrawals and drop outs were few and appropriately described in the manuscript. Participant cross over was 10% (19 people initially assigned to the no-filter group subsequently received a filter). An intention-to-treat analysis was performed. Inclusion and exclusion criteria were clearly stated. Primary and secondary outcomes were reported.

Effects of interventions

Fullen 1973 demonstrated caval filters were effective in reducing PE but not mortality in a quasi-randomised trial of 129 patients with proximal femoral fractures, over a 33 to 34 day period. Anticoagulation was not given in either arm. Mortality was 4/41 in the filter group and 14/59 in the control group (RR 0.41, 95% CI 0.15 to 1.16). Rate of pulmonary embolism in the filter group was 4/41, and 19/59 in the control group (RR 0.3, 95% CI 0.11 to 0.82). No details about long term complication rates were given.

The PREPIC study demonstrated the efficacy of caval filters in preventing pulmonary embolism in a group of people with proximal DVT or PE and receiving concurrent anticoagulation, at eight years (hazard ratio 0.37, 95% CI 0.17 to 0.79 in favour of a filter) (see Figure 4). At eight years, there was a significant increase in the rate of DVT in the filter group (hazard ratio 1.52, 95% CI 1.02 to 2.27) (see Figure 5).

Figure 4. Kaplan-Meier analysis of time to pulmonary embolism

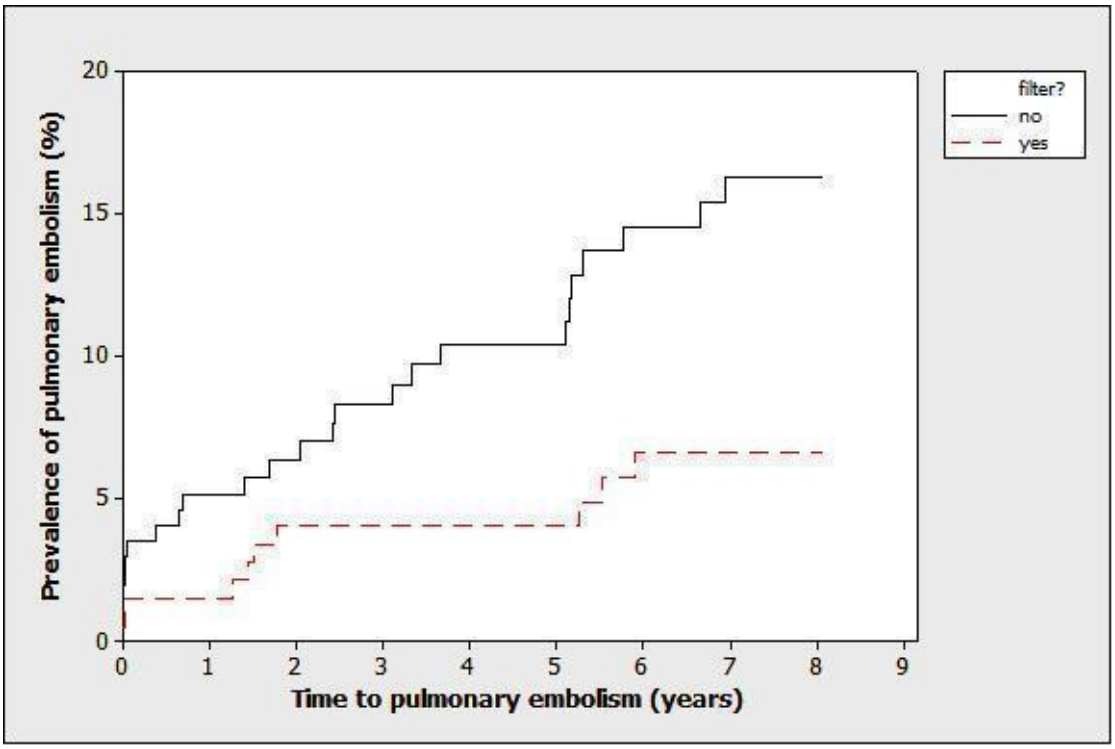
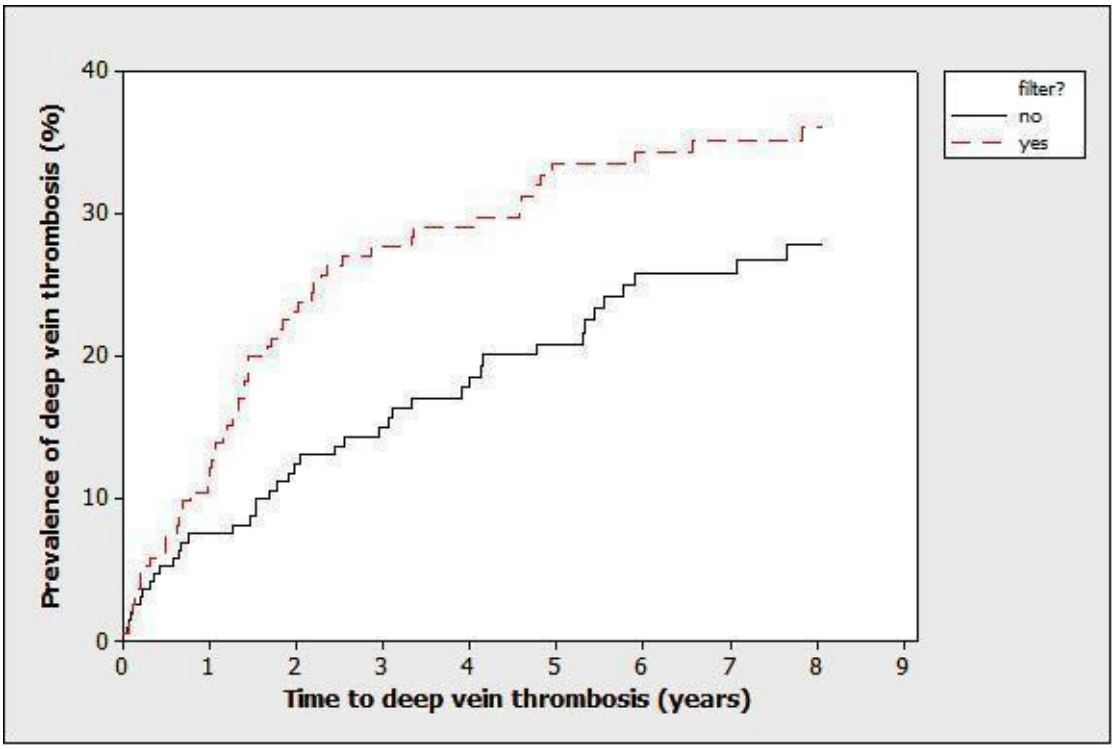


Figure 5. Kaplan-Meier analysis of time to deep vein thrombosis



Post-thrombotic syndrome was a common complication (defined as the appearance or worsening of oedema, varicose veins, trophic disorders, or ulcers) in both groups, affecting 68% to 70% of people in each study group. No data were collected on filter-related complications as the sample sizes were not powered to detect them. The PREPIC study included small subgroups of people with cancer, and used four permanent filter designs. It lacked statistical power to be able to draw any conclusions.

DISCUSSION

No firm conclusions regarding filter efficacy in the prevention of pulmonary embolism can be drawn from either of the RCTs.

Fullen 1973 showed a reduction in PE in high risk people following a traumatic hip fracture who did not receive DVT prophylaxis. However, it was inadequately randomised; there were more people with fractures in the control group which could not undergo internal fixation, and the outcome assessors were not blinded. It also used a filter that was subsequently removed from clinical use because of its occasional fatal filter embolism risk and high late caval thrombosis rate (Greenfield 1992).

In the PREPIC study, the group of people who received filters in the study varied significantly from the wider application in current clinical practice, notably those patients with DVT or PE and in whom anticoagulation has failed or cannot be administered. This limits the generalisability of the study's conclusion. In addition, the PREPIC study used permanent filters. There is an increasing trend towards the use of retrievable filters in practice, although it would seem many of these are left in situ (Karmy-Jones 2007). The PREPIC study also lacked statistical power to detect a reduction in the incidence of pulmonary embolism over shorter and more clinically significant time periods.

No recommendations can be made for other subgroups of people who might benefit from filters as they have not been studied in this or any other RCT. There are several large case series reporting long-term experiences of filters for various indications but none of these studies fulfilled the inclusion criteria for this review. These groups of people include those with cancer and pregnant women, with concurrent venous thromboembolism; patients with proven DVT or PE in whom anticoagulation has failed; patients with upper limb thrombosis and superior vena caval filters; those with supra-renal caval filters; and people with trauma who do not have established venous thromboembolism but have a filter inserted for

prophylaxis.

The failure of the PREPIC study to demonstrate a survival advantage was due to the older study population (mean age 73 years) with multiple other co-morbidities; the majority of deaths were attributed to cancer or cardiovascular-related causes. Pulmonary embolism accounted for seven deaths, but the PREPIC study lacked statistical power to detect a difference in PE-related mortality.

The PREPIC study did show an increasing incidence of DVT that correlated to the length of time the filter was in situ. The study demonstrated an increased risk of DVT in the filter group at eight years. Given the current lack of evidence in people who have a permanent filter inserted due to a perceived bleeding risk, observations from the PREPIC study suggest that consideration should be given to long-term anticoagulation when or if the risk of bleeding resolves. However, further data are required to confirm this observation. The placement of filters in people with major trauma without established DVT or PE is not as straightforward as it seems and continues to be a source of controversy and debate.

Retrievable filters have variable retrieval rates as reported in the literature, from 22% (Karmy-Jones 2007) to between 88% and 100% (Imberti 2005). The true rate of filter retrieval is not known as these figures are likely to reflect publication bias. Local rates of removal are influenced by the clinical situation, the experience of the individual interventionist, and institutional protocols. Drug-eluting filters have extended the recommended implantation period to 12 weeks, enabling the scenario in which the filter was indicated to resolve or diminish; before this their retrieval would be compromised. It is envisaged that retrievable filters may avoid the long-term thrombogenic problems seen with permanent filters but this remains to be seen.

There are no long-term clinical trials directly comparing the efficacy of permanent filters to temporary filters, nor comparing between different filter designs.

Superior vena caval filters are inserted for upper limb thrombosis; the majority of upper limb venous thromboses occur in the setting of an intravascular device within a central vein. Filters, being foreign objects within the body, potentially promote thrombosis. The superior vena cava is much shorter than the inferior vena cava, theoretically increasing the risk of clinically significant filter embolisation. Further information is needed before their placement in the superior vena cava is considered.

Filters have a relatively low rate of serious adverse outcome; these data come from large pooled case series and registry data of permanent filters, with one pooled series totaling over 3000 participants. Twenty year follow-up figures are available from another filter registry (Greenfield 1995). This information is subject to incomplete rates of participant follow up in a heterogeneous study population over varying time periods, and provides details generally pertaining to a single filter design. Thus, there is likely to be significant inherent bias in the conclusions based on this information. Despite the limitations of this registry, some insight into the safety profile of permanent filters can be gleaned: the mortality rate from filter insertion was 0.12%; migration occurred in 3% to 69% of patients depending on the definition of migration; filter migration is usually of little clinical significance. Perforation occurred at a rate of 9% to 24%; radiological features of perforation were common and in the majority of cases did not lead to any clinical sequelae. Inferior vena caval thrombosis occurred at a rate of 4% to 30%, but not all series had routine, follow-up Doppler examinations. It is unknown whether caval thrombosis reflects an efficient filter which has performed its task and trapped thrombus en route; or reflects in situ thrombosis due to altered blood flow from the mere presence of a filter in addition to a thrombogenic tendency inherent with any foreign object within the body, occurring in a group of people with a thrombotic predisposition. Thrombi may then propagate across a filter, with subsequent emboli from fragmentation of the thrombus beyond the filter. Small emboli can also pass between the filter struts or travel through a collateral circulation if this has developed. Recurrent PE in the presence of a filter, occurs at a rate of 2% to 5%; fatal PE rates are 0.7% (Hann 2005; Kinney 2003). There are case reports of a second filter placed above the first to prevent further embolisation (Arbogast 1994; Hann 2005). Again, there is no evidence currently available to support this practice.

Smaller case series on retrievable filters are being collated; the largest series to date totals 169 participants (Stein 2004).

AUTHORS' CONCLUSIONS

Implications for practice

No recommendations can be drawn from the two RCTs of filters included in this review.

Fullen 1973 was inadequately randomised, had more people unable to have surgical fixation of their fracture in the control group, and the outcome assessors were not blinded. It has limited generalisability as it is now considered standard practice for DVT prophylaxis to be administered in people with traumatic hip fractures.

PREPICs generalisability is also limited. This RCT also lacked statistical power to detect a reduction in the rate of PE at clinically significant time periods of less than eight years and used permanent filters. Retrievable filters are increasingly used when a filter is indicated. Filters are an adjunctive treatment with anticoagulation in patients with (or at high risk of) proximal DVT or PE. Anticoagulation remains the mainstay of treatment for venous thromboembolism provided there are no contraindications to this. Caval filters are associated with an increased risk of DVT in the longer term and this will likely influence the duration of anticoagulation. Caval filters are associated with a low rate of serious adverse events and, therefore, cannot be recommended for all people with venous

thromboembolism. Their use is recommended to be restricted to certain high-risk situations until more information becomes available.

In the absence of evidence for other groups of people for whom filters are potentially beneficial and for the use of retrievable filters the American College of Chest Physicians Guidelines (Buller 2004) remain valid; the current accepted indications for filters remain as failure of, or contraindication, to, anticoagulation. Clinical judgment is required for other indications in which filters may be considered, such as for patients with venous thromboembolism and diminished cardiopulmonary reserve, those undergoing high-risk surgery, or those who receive thrombolysis for a proximal DVT.

It would appear to be prudent to scan the lower limbs to confirm the presence of residual thrombus before contemplating filter insertion.

Implications for research

Information regarding the indications, timing of insertion and removal, and short and long-term complications of permanent and retrievable filters is lacking.

Large randomised controlled trials are required in groups of people who have failed or have contraindications to anticoagulation, to confirm the efficacy of caval filters in this group; similarly in people who have cancer and concurrent venous thromboembolism, pregnant women who have PE or DVT, and in those with upper limb thrombosis and superior vena caval filters.

There are newer antithrombotic agents available and trials are required of these agents compared to filters with or without anticoagulation. Similarly, information regarding filter efficacy and complications in conjunction with other anticoagulation regimens (for example, low dose vitamin K antagonist protocols or long-term low molecular weight heparin-based protocols).

Large RCTs are also required to compare permanent versus retrievable filters; these should include subgroup analyses of various filter brands.

Outcomes should include rates of PE and DVT, mortality, post-thrombotic syndrome and its effects on quality of life; and filter-related complications: mortality from filter insertion, clinical filter embolism and perforation, and caval thrombosis.

The time duration of these trials should be at least two years to provide an indication of long-term complication rates.

ACKNOWLEDGEMENTS

Thanks to the Cochrane Review Group on Peripheral Vascular Diseases for assisting with the search for relevant articles, Mr Andrew J Wawrzyniak and Dr Karen Welch for their invaluable assistance, the University of Queensland Library for obtaining articles, and Dr Harry Bartlett (QUT) for statistical advice and input. Tim Young would like to thank Professor Alf Steinbeck for being a tremendous personal source of inspiration and support.

REFERENCES

References to studies included in this review

Fullen 1973 *{published data only}*
Fullen WD, Miller EH, Steele WF, McDonough JJ. Prophylactic vena caval interruption in hip fractures. *Journal of Trauma* 1973;**13**(5):403–10.

PREPIC *{published data only}*
Decousus H. Eight-year follow-up of a randomized trial investigating vena cava filters in the prevention of PE in patients presenting a proximal DVT: The PREPIC trial. *Journal of Thrombosis & Haemostasis* 2003;**1**(Suppl 1): Abstract OC440. [MEDLINE: 6457]
* Decousus H, Barral F, Buch-muller A, Charbonnier B, Girard P, Lamer C, et al. Eight-year follow-up of patients with permanent vena cava filter in the prevention of pulmonary embolism. *Circulation* 2005;**112**:416–22.
Decousus H, Leizorovicz A, Parent F, Page Y, Tardy B, Girard P, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. *New England Journal of Medicine* 1998;**338**(7):409–15.

References to studies excluded from this review

Brasel 1997 *{published data only}*
Brasel K, Borgstrom DC, Weigelt JA. Cost-effective prevention of pulmonary embolus in high-risk patients. *The Journal of Trauma, Injury, Infection and Critical Care* 1997;**42**(3):456–62.

Gosin 1997 *{published data only}*
Gosin JS, Graham AM, Ciocca RG, Hammond JS. Efficacy of prophylactic vena caval filters in high-risk trauma patients. *Annals of Vascular Surgery* 1997;**11**:100–5.

Khansarinia 1995 *{published data only}*
Khansarinia S, Dennis JW, Veldenz HC, Butcher LC, Hartland L. Prophylactic Greenfield filter placement in selected high-risk trauma patients. *Journal of Vascular Surgery* 1995;**22**:231–6.

Midy 1994 *{published data only}*
Midy D, Pheline P, Baste JC. Antheor percutaneous filter endocaval filter. Multicentre evaluation based on 300 cases [Filtre endocave percutane antheor. Evaluation multicentrique a propos de 300 cas]. *Journal de Maladies Vasculaires* 1994;**19**(4):308–13.

Rodriguez 1996 *{published data only}*
Rodriguez JL, Lopez JM, Proctor MC, Conley JL, Gerndt SJ, Marx VM, et al. Early placement of prophylactic vena caval filters in injured patients at high risk for pulmonary embolism. *The Journal of Trauma, Injury, Infection and Critical Care* 1996;**40**(5):797–804.

Rogers 1997 *{published data only}*
Rogers FB, Shackford SR, Ricci MA, Huber BM, Atkins T. Prophylactic vena caval filter insertion in selected high-risk orthopaedic trauma patients. *Journal of Orthopaedic Trauma* 1997;**11**(4):267–72.

Rosenthal 1994 *{published data only}*
Rosenthal D, McKinsey JF, Levy AM, Lamis PA, Clark MD. Use of the Greenfield filter in patients with major trauma. *Cardiovascular Surgery* 1994;**2**(1):52–5.

Rosner 2004 *{published data only}*
Rosner MK, Kuklo TR, Tawk R, Moquin R, Ondra SL. Prophylactic placement of an inferior vena cava filter in high-risk patients undergoing spinal reconstruction. *Neurosurgical Focus* 2004;**17**(4):1–6.

Webb 1992 *{published data only}*
Webb LX, Rush PT, Fuller SB, Meredith WJ. Greenfield filter prophylaxis of pulmonary embolism in patients undergoing surgery for acetabular fracture. *Journal of Orthopaedic Trauma* 1992;**6**(2):139–45.

References to ongoing studies

Anon 2009 *{published data only}*
Anon. Anticoagulation and Inferior Vena Cava Filters in Cancer Patients With a Venous Thromboembolism. ClinicalTrials.gov (http://clinicaltrials.gov/ct2/show/NCT00423683?term=NCT00423683&rank=1) (accessed 3 Nov 2009) 2009.

PREPIC 2 2009 *{published data only}*
Anon. PREPIC 2 : Prevention of Recurrent Pulmonary Embolism by Vena Cava Interruption (PREPIC2). ClinicalTrials.gov (http://clinicaltrials.gov/ct2/show/NCT00457158?term=NCT00457158&rank=1) (accessed 3 Nov 2009) 2009.

Additional references

Arbogast 1994
Arbogast JD, Blessed WB, Lacoste H, Gross WS, Gonde RL Jr, Welch RA. Use of two Greenfield filters to prevent pulmonary embolism in a heparin-allergic gravida. *Obstetrics and Gynaecology* 1994;**84**(4 part 2):652–4.

Buller 2004
Buller HR, Agnelli G, Hull HD, Hyers TM, Prins MH, Raskob GE. Antithrombotic therapy for venous thromboembolic disease: the seventh ACCP Conference on antithrombotic and thrombolytic therapy. *Chest* 2004;**126 (3 Suppl)**:401–28.

Douketis 1998
Douketis JD, Kearon C, Bates S, Duku EK, Ginsberg JS. Risk of fatal pulmonary embolism in patients with treated venous thromboembolism. *JAMA* 1998;**279**(6):458–62.

Gomes 2003
Gomes MPV, Kaplan KL, Deitcher SR. Patients with inferior vena cava filters should receive chronic thromboprophylaxis. *The Medical Clinics of North America* 2003;**87**:1189–203.

Greenfield 1992
Greenfield LJ. Evolution of venous interruption for pulmonary thromboembolism. *Archives of Surgery* 1992; **127**(5):622–6. [MEDLINE: 1575633]

Greenfield 1995
Greenfield LJ, Proctor MC. Twenty year clinical experience with the Greenfield filter. *Cardiovascular Surgery* 1995;**3**(2): 199–205.

Hann 2005
Hann CL, Streiff MB. The role of vena caval filters in the management of venous thromboembolism. *Blood Reviews* 2005;**19**:179–202.

Higgins 2008
Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.2 [updated September 2009] . *The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org*.

Imberti 2005
Imberti D, Ageno W, Carpenedo M. Retrievable vena caval filters: a review. *Current Opinion in Haematology* 2006;**13**: 351–6.

Jadad 1996
Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds JM, McQuay HJ. Clinical trials: Is blinding necessary?. *Controlled Clinical Trials* 1996;**17**:1–12.

Karmy-Jones 2007
Karmy-Jones R, Jurkovich GJ, Velmahos GC, Burdick T, Spaniolas K, Todd SR, et al. Practice patterns and outcomes of retrievable vena cava filters in trauma patients: an AAST multicenter study. *Journal of Trauma Injury, Infection and Critical Care* 2007;**62**:17–25.

Kinney 2003
Kinney TB. Update on inferior vena caval filters. *Journal of Vascular and Interventional Radiology* 2003;**14**:425–40.

Kirilcuk 2005
Kirilcuk NN, Herget EJ, Dicker RA, Spain DA, Hellinger JC, Brundage SI. Are temporary inferior vena caval filters really temporary?. *American Journal of Surgery* 2005;**190**: 858–63.

Norris 1985
Norris CS, Greenfield LJ, Hermann JB. Free-floating iliofemoral thrombus: a risk of pulmonary embolism. *Archives of Surgery* 1985;**120**:806–8.

Radomski 1987
Radomski JS, Jarrell BE, Carabasi RA, Yang S-L, Koolpe H. Risk of pulmonary embolus with inferior vena caval thrombosis. *American Surgeon* 1987;**53**:97–101.

Stein 2004

Stein PD, Alnas A, Skaf E, Kayali F, Siddiqui T, Olson RE, et al. Outcomes and complications of retrievable inferior vena cava filters. *American Journal of Cardiology* 2004;**94**: 1090–3.

Yusuf 2006

Yusuf S, Mehta SR, Chrolavicius S, Afzal R, Pogue J, Granger CB, et al. Comparison of fondaparinux and enoxaparin in acute coronary syndromes. *New England Journal of Medicine* 2006;**354**(14):1464–76. [MEDLINE: 16537663; : ClinicalTrials.gov number, NCT00139815]

References to other published versions of this review

Young 2007

Young T, Aukes J, Hughes R, Tang H. Vena caval filters for the prevention of pulmonary embolism. *Cochrane Database of Systematic Reviews* 2007, Issue 3. [DOI: 10.1002/14651858.CD006212.pub2]

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Fullen 1973

Methods	Study design: A single centre study. Country: United States. Follow up was adequate.
Participants	Number: 129 participants with proximal femoral fractures. Age: Average age 69 and 67 years (filter and control group respectively) Sex: Gender distribution not stated. Inclusion criteria: Proximal femoral fractures were invited to participate in the study Exclusion criteria: Refusal to participate in the trial.
Interventions	Treatment: Permanent caval filter. Control: No filter.
Outcomes	Primary outcomes. 1. Mortality. 2. Pulmonary embolism. Secondary outcomes. 1. Complications from filter insertion. Outcomes assessed when clinically indicated and at discharge
Notes	Jadad score 2/5. Anticoagulation was not used in either the intervention (filter) or control arm Not an intention to treat analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	High risk	Randomisation based on odd or even hospital number.
Allocation concealment?	High risk	Open study design; participation in filter group based on consent
Blinding? Mortality	High risk	Open study design; blinding of outcome assessors not stated.
Blinding? Pulmonary embolism	High risk	Open study design; blinding of outcome assessors not stated.
Incomplete outcome data addressed? Mortality	Low risk	Cause of death and numbers reported. Follow-up complete as in-hospital population

Fullen 1973 (*Continued*)

Incomplete outcome data addressed? Pulmonary embolism	Low risk	Definite, probable and possible pulmonary embolism rates reported. Blinding of outcome assessors not stated. Use of chest radiography in diagnosis of PE is inaccurate. Not stated whether all patients had routine imaging, or only when clinically indicated
Free of selective reporting?	Unclear risk	Protocol brief. Mortality, PE and filter complication outcomes documented. Rates of DVT not reported

PREPIC

Methods	Study design: Multicentre study; randomised control open trial using a 2x2 factorial design Country: France. Intention-to-treat analysis.
Participants	Number: 400 participants. Age: 73 +/- 11. Sex: 64% were male. Inclusion criteria: Age >18 with documented proximal DVT or PE, and considered high risk for pulmonary embolism Exclusion criteria: 1. previous filter; 2. contraindication or failure of anticoagulation; 3. curative anticoagulation > 48 hours duration; 4. indication for thrombolysis; 5. short life expectancy; 6. allergy to iodine; 7. hereditary thrombophilia; 8. severe renal or hepatic failure; 9. pregnancy; 10. likely non-compliance.
Interventions	(Permanent) caval filter vs no filter LMWH vs unfractionated heparin
Outcomes	Primary outcomes. 1. Pulmonary embolism. 2. Mortality. 3. Deep venous thrombosis. Secondary outcomes. 1. Bleeding. 2. Post-thrombotic syndrome. 3. Filter-related complications. Outcomes assessed at 12 days, two years, eight years.

PREPIC (*Continued*)

Notes	Study had low power. Jadad score 3/5

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Randomisation was based on a centralised computer system.
Allocation concealment?	Unclear risk	Not described.
Blinding? Mortality	High risk	Open study design.
Blinding? Pulmonary embolism	High risk	Open study design.
Incomplete outcome data addressed? Mortality	Low risk	Negligible losses to follow up (only 4 of 400 participants). No missing outcome data. Causes of death reported. Mortality reported at 12 days, two years and eight years
Incomplete outcome data addressed? Pulmonary embolism	Low risk	No missing outcome data. Pulmonary embolism reported at12 days, two years and eight years
Free of selective reporting?	Low risk	Primary and secondary outcomes were reported.

DVT: deep vein thrombosis
LMWH: low molecular weight heparin
PE: pulmonary embolism

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Brasel 1997	Cost-effectiveness analysis.
Gosin 1997	Prospective interventional cohort with historical control; selected high-risk people received filters; no data on baseline characteristics of the interventional cohort and the control group

(*Continued*)

Khansarinia 1995	Prospective interventional cohort with historical control.
Midy 1994	Case series.
Rodriguez 1996	Prospective interventional cohort with historical control.
Rogers 1997	Prospective interventional cohort with historical control; selected high-risk people received filters; interventional and cohort groups unmatched according to baseline characteristics
Rosenthal 1994	Case series.
Rosner 2004	Prospective interventional cohort with historical control.
Webb 1992	Selected high-risk patients received filters; no data on baseline characteristics of interventional and control groups; people received concurrent DVT prophylaxis

DVT: deep vein thrombosis

Characteristics of ongoing studies *[ordered by study ID]*

Anon 2009

Trial name or title	A randomized control trial of anticoagulation and inferior vena cava filters in cancer patients with a venous thromboembolism
Methods	Study design: Randomized, open label, active control, parallel assignment, safety/efficacy study
Participants	Cancer patients, over 18 years of age, acute radiographically confirmed denovo DVT or PE
Interventions	Arixtra (fondaparinux) alone vs. arixtra with filter.
Outcomes	Primary outcomes: Death due to any cause, event free survival. Secondary outcomes: Occurrence of pulmonary embolism, major bleeding, thrombophlebitis, cellulitis secondary to IV filter, thrombosis of the IVC filter and quality of life
Starting date	January 2007
Contact information	Myra Barginear, MD
Notes	NCT00423683

PREPIC 2 2009

Trial name or title	PREPIC 2 : Interruption of inferior vena cava by a retrievable filter for the prevention of recurrent pulmonary embolism : a randomised, open label study
Methods	Study design: Randomized, open label, active control, parallel assignment, safety/efficacy study
Participants	Age: > 18 years. Inclusion criteria. • Informed consent. • Acute symptomatic pulmonary embolism; and • Deep or superficial vein thrombosis; and At least one of the risk factors below : • More than 75 years old. • Cancer (excepting locally cutaneous cancer). • Known chronic heart failure treated. • Chronic respiratory insufficiency treated. • Bilateral deep vein thrombosis. • Ilio-cava thrombosis. • Ischemic stroke > 3 days and < 6 months, with lower limb deficit. • Cardiac repercussion of pulmonary embolism assessed by echocardiography or increasing troponin I or T, or Brain Natriuretic Peptide (BNP) or proBNP. Exclusion Criteria: • Contrindication to an anticoagulant treatment or recurrent thromboembolic event despite adequate anticoagulation. • Vena cava filter already inserted. • Filter insertion impossible due to caval thrombosis. • More than 72 hours pre-randomised treatment with therapeutic dosage of anticoagulant therapy. • Non carcinologic surgery within three months prior randomisation. • Carcinologic surgery within 10 days prior randomisation. • Hypersensitivity to contrast media. • Access port in place or programmed within 3 months. • Woman who are child bearing. • Life expectancy < 6 months
Interventions	Treatment: optional/retrievable filter. Control: No filter.
Outcomes	Primary outcomes: at three months, combined criteria including recurrent PE confirmed by objective tests and fatal PE confirmed by autopsy and death which cannot be attributed to a documented cause and for which PE/DVT cannot be ruled out. Secondary outcomes: Recurrent pulmonary embolism, fatal or not, at six months (combined criteria including recurrent pulmonary embolism confirmed by objective tests and fatal PE confirmed by autopsy and death which cannot be attributed to a documented cause). Current or new symptomatic DVT confirmed by objective tests. Mechanical complication of filter (migration, tilt, transfixion) and or puncture site hematoma, and/or local or general infection due to filter. Filter thrombosis. Filter retrieval failure. Total death.

PREPIC 2 2009 (*Continued*)

Starting date	July 2006
Contact information	Patrick Mismetti, MD PhD, Karine Rivron Guillot, MD
Notes	NCT00457158

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. Search strategy for CENTRAL

#1 MeSH descriptor Vena Cava Filters explode all trees
#2 ven* near cav*
#3 Tempofilter
#4 VenaTech
#5 Bard near G2
#6 "Bard Recovery"
#7 "Boston Greenfield"
#8 "Birds Nest"
#9 Cook near Celect
#10 "Gunther Tulip"
#11 OptEase
#12 TrapEase
#13 Mobin-Uddin
#14 (ALN)
#15 (Rex Medical Option)
#16 Simon near Nitinol
#17 IVC near filter
#18 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17

WHAT'S NEW

Last assessed as up-to-date: 20 October 2009.

Date	Event	Description
22 October 2009	New search has been performed	Searches updated and one additional RCT included. Conclusions remain unchanged
22 October 2009	New citation required but conclusions have not changed	John Aukes removed as author from the updated review.

HISTORY

Protocol first published: Issue 4, 2006

Review first published: Issue 3, 2007

Date	Event	Description
21 April 2008	Amended	Converted to new review format.
9 November 2007	New search has been performed	One additional reference (conference abstract) added to the included study (PREPIC). No change to conclusions
22 August 2007	New citation required but conclusions have not changed	Citation order revised on request of review author.

CONTRIBUTIONS OF AUTHORS

TY wrote the protocol and review with input from RH and HT.

TY, HT, RH searched for trials.

TY contacted relevant biomedical companies and clinicians involved with filters, and obtained full text articles.

TY, HT and RH selected and assessed trials for inclusion; and analysed, and interpreted results of these.

TY and HT independently extracted, entered, and analysed data in Revman.

DECLARATIONS OF INTEREST

None declared

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Chief Scientist Office, Scottish Government Health Directorates, Scottish Government, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

*Vena Cava Filters [adverse effects]; Pulmonary Embolism [mortality; *prevention & control]; Randomized Controlled Trials as Topic; Vena Cava, Inferior; Venous Thrombosis [complications]

MeSH check words

Humans