

Vena cava filters reduced long-term risk for pulmonary embolism in proximal deep venous thrombosis

The PREPIC Study Group. Eight-year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism: the PREPIC (Prévention du Risque d'Embolie Pulmonaire par Interruption Cave) randomized study. *Circulation*. 2005;112:416-22.

Clinical impact ratings: Hospitalists ★★★★★☆ Hematol/Thrombo ★★★★★☆

QUESTION

In patients with acute proximal deep venous thrombosis (DVT), do inferior vena cava (IVC) filters reduce long-term risk for pulmonary embolism (PE)?

METHODS

Design: 2 × 2 factorial randomized controlled trial (*Prévention du Risque d'Embolie Pulmonaire par Interruption Cave* [PREPIC] study).

Allocation: Concealed.*

Blinding: Blinded (data collectors and the adjudication committee that reviewed all documented outcome events).*

Follow-up period: 8 years.

Setting: 44 hospitals in France.

Patients: 400 patients ≥ 18 years of age (mean age 73 y, 52% women) who had objectively confirmed proximal DVT and were at risk for PE. {Exclusion criteria included previous filters, short life expectancy, hereditary thrombophilia, severe renal or hepatic failure, and pregnancy.}†

Intervention: IVC filter ($n = 200$) or no filter ($n = 200$) and either low-molecular-weight heparin (enoxaparin) subcutaneously ($n = 195$) or intravenous unfractionated heparin with adjusted dosing ($n = 205$) for 8 to 12 days. Beginning at day 4 and for ≥ 3

months, patients received graded compression stockings and warfarin or acenocoumarol or, if necessary, unfractionated heparin.

Outcomes: Symptomatic PE. Secondary outcomes included recurrent DVT, total clinical venous thromboembolism, filter complications, major bleeding, and all-cause mortality.

Patient follow-up: 99% (intention-to-treat analysis).

MAIN RESULTS

The rate of PE was lower in the filter group than in the no-filter group (Table). However, the rate of symptomatic recurrent DVT was greater in the filter group than in the no-

filter group (Table). Groups did not differ for any other outcomes (Table).

CONCLUSION

In patients with acute proximal deep venous thrombosis (DVT), inferior vena cava filters reduced long-term risk for pulmonary embolism but increased risk for recurrent DVT.

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For correspondence: Dr. H. Decousus, Hôpital Bellevue, Saint-Etienne, France. E-mail decousus@chu-st-etienne.fr.

*See Glossary.

†Decousus H, Leizorovicz A, Parent F, et al. *N Engl J Med*. 1998;338:409-15.

Vena cava filter vs no filter in acute proximal deep venous thrombosis (DVT) at 8 years‡

Outcomes	Filter	No filter	RRR (95% CI)	NNT (CI)
Symptomatic pulmonary embolism	6.2%	15.1%	61% (20 to 82)	11 (9 to 34)
All-cause mortality	48.1%	51.0%	2% (-17 to 20)	Not significant
Major bleeding	15.4%	18.5%	15% (-36 to 47)	Not significant
			RRI (CI)	NNH (CI)
Symptomatic recurrent DVT	35.7%	27.5%	41% (2 to 88)	9 (5 to 216)
Symptomatic venous thromboembolism	36.4%	35.4%	9% (-18 to 43)	Not significant

‡Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from hazard ratios in article.

COMMENTARY

Conservative indications for insertion of a permanent IVC filter in patients with acute proximal DVT or PE include a contraindication for anticoagulants and, less commonly, recurrent venous thromboembolism that occurs despite "adequate" anticoagulant therapy (1). The use of a filter for these indications is based on the premise that the device will prevent fatal PE. Although the validity of this premise has not been established in the clinical settings for which caval interruption is usually recommended, the trial by the PREPIC study group provides valuable indirect support.

The results showed that IVC filter placement reduced risk for symptomatic PE but at the cost of increased risk for recurrent DVT. 35% of patients in both groups received vitamin K antagonists for the 8-year period of follow-up, and more recurrences occurred when patients were off rather than on anticoagulant therapy. Given the study strengths (concealed allocation, blinded adjudication of outcomes, adequate sample size, and an extended 8-year follow-up period), confidence in the results is relatively high. However, some methodological limitations, such as incomplete blinding, crossover of approximately 10% of patients to the filter cohort, and 1 questionable recurrence of PE, are noteworthy.

The results support the conservative recommendations but do not support the use of IVC filters as first-line treatment for venous thromboembolism, either as an adjunct to or as a replacement for anticoagulant therapy. The overall risk for fatal PE was low in both groups, and filter placement had no effect on mortality or the overall rate of recurrent venous thromboembolism. Although PE is potentially more serious than recurrent DVT, the latter complication is associated with at least as much morbidity as nonfatal PE. The findings do not clearly influence decisions on duration of long-term anticoagulants in patients with an IVC filter, because the benefit derived from a reduction in PE is countered by an increase in recurrent DVT.

Jack Hirsh, MD
McMaster University
Hamilton, Ontario Canada

Reference

- Büller HR, Agnelli G, Hull RD, et al. Antithrombotic therapy for venous thromboembolic disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. 2004;126:401S-428S.