ORIGINAL ARTICLE

A Multicenter Trial of Vena Cava Filters in Severely Injured Patients

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ABSTRACT

BACKGROUND

Whether early placement of an inferior vena cava filter reduces the risk of pulmonary embolism or death in severely injured patients who have a contraindication to prophylactic anticoagulation is not known.

METHODS

In this multicenter, randomized, controlled trial, we assigned 240 severely injured patients (Injury Severity Score >15 [scores range from 0 to 75, with higher scores indicating more severe injury]) who had a contraindication to anticoagulant agents to have a vena cava filter placed within the first 72 hours after admission for the injury or to have no filter placed. The primary end point was a composite of symptomatic pulmonary embolism or death from any cause at 90 days after enrollment; a secondary end point was symptomatic pulmonary embolism between day 8 and day 90 in the subgroup of patients who survived at least 7 days and did not receive prophylactic anticoagulation within 7 days after injury. All patients underwent ultrasonography of the legs at 2 weeks; patients also underwent mandatory computed tomographic pulmonary angiography when prespecified criteria were met.

RESULTS

The median age of the patients was 39 years, and the median Injury Severity Score was 27. Early placement of a vena cava filter did not result in a significantly lower incidence of symptomatic pulmonary embolism or death than no placement of a filter (13.9% in the vena cava filter group and 14.4% in the control group; hazard ratio, 0.99; 95% confidence interval [CI], 0.51 to 1.94; P=0.98). Among the 46 patients in the vena cava filter group and the 34 patients in the control group who did not receive prophylactic anticoagulation within 7 days after injury, pulmonary embolism developed in none of those in the vena cava filter group and in 5 (14.7%) in the control group, including 1 patient who died (relative risk of pulmonary embolism, 0; 95% CI, 0.00 to 0.55). An entrapped thrombus was found in the filter in 6 patients.

CONCLUSIONS

Early prophylactic placement of a vena cava filter after major trauma did not result in a lower incidence of symptomatic pulmonary embolism or death at 90 days than no placement of a filter. (Funded by the Medical Research Foundation of Royal Perth Hospital and others; Australian New Zealand Clinical Trials Registry number, ACTRN12614000963628.)

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Venous thromboembolism is common after major trauma. A prospective surveillance study involving 349 consecutive severely injured patients showed that without prophylactic anticoagulation, proximal deep-vein thrombosis occurred in 18% of patients, and pulmonary embolism occurred in 11%.[1] More important, it has been shown that up to 37% of all symptomatic pulmonary emboli occur within the first 4 days after trauma.[2] Fatal pulmonary embolism is less common (0.4 to 4.2%)[1,3-5]; however, it accounts for 12% of all deaths after major trauma, and half of these deaths are considered preventable.[6] Therefore, effective thromboprophylaxis is of paramount importance.

Observational studies have suggested that a delay of more than 1 to 3 days in initiating thromboprophylaxis in severely injured patients triples the risk of venous thromboembolism and possibly increases mortality.[7-9] However, prophylactic anticoagulation has also been reported to be associated with an odds ratio of more than 13 for progressive enlargement of hematoma in patients with traumatic brain injury.[10] A recent randomized, controlled trial assessing the benefits of erythropoietin after traumatic brain injury showed that up to 43% of the patients did not receive prophylactic anticoagulation within 7 days after admission for the injury.[11] To address this challenging issue, retrievable inferior vena cava filters have been developed and are now widely used in many trauma centers as a primary means to prevent pulmonary embolism.[12-14] This approach has been taken despite the limited high-quality data to guide the use of these devices, including data on issues such as appropriate patient selection and the timing of insertion and removal of the device.[15-19] Prophylactic use is the most contentious application of vena cava filters.[20] Although there are numerous published observational studies,[21] concerns remain about the long-term complications of these filters, with the recognition that a substantial number of retrievable filters are not removed.[22] There are also important implications for health care resources associated with their ongoing use. The U.S. market for vena cava filters was valued at under $200 million in 2007, and the global market value was estimated to reach $435 million in 2016.[23]

High-quality evidence from randomized, controlled trials is needed to support continued use of these devices as a primary means of thromboprophylaxis when prophylactic anticoagulation is contraindicated. We hypothesized that early placement of a vena cava filter might reduce the risk of symptomatic pulmonary embolism in severely injured patients in whom prophylactic anticoagulation is contraindicated. In this multicenter, randomized, controlled trial, we assessed whether insertion of a retrievable vena cava filter within 72 hours after admission for trauma would result in a lower incidence of pulmonary embolism than no filter in this group of patients.

A Quick Take is available at NEJM.org

METHODS

TRIAL DESIGN AND OVERSIGHT

The design of this trial has been published previously.[24] The trial was designed and conducted by clinical investigators at the four tertiary hospitals in Australia where patients were treated after enrollment. The trial was funded by the Medical Research Foundation of Royal Perth Hospital, the Western Australia Department of Health, and the Raine Medical Research Foundation. No financial or nonmonetary (in-kind) support was received from any companies that manufacture vena cava filters or from commercial entities. The funders were not involved in the design of the trial, the analysis of the data, or the decision to submit the manuscript for publication. The ethics review board at each participating institution approved the protocol (available with the full text of this article at NEJM.org). Written informed consent was obtained before enrollment from all patients who were assessed as being competent to provide consent. If patients were not competent to provide consent, their next of kin agreed to enrollment and signed an acknowledgment document; patients provided written informed consent after they regained competence. An independent data and safety monitoring committee provided safety oversight. An independent statistical company maintained the Web-response randomization portal, held the clinical database, and conducted all analyses independent of the investigators. The authors vouch for the completeness and accuracy of the data and analyses and for the fidelity of the trial to the protocol.

TRIAL POPULATION

Eligible patients were 18 years of age or older and had an estimated Injury Severity Score of more than 15 and a contraindication to receipt of prophylactic anticoagulation within 72 hours after admission for the injury. The Injury Severity Score

is an anatomical scoring system that measures the severity of an injury.[25] Each of six regions of the body (head, face, chest, abdomen, extremities [including the pelvis], and external) is assigned a score of 0 to 6 on the Abbreviated Injury Scale (with a score of 0 indicating no injury and a score of 6 indicating an unsurvivable injury), and the Injury Severity Score is calculated as the sum of the squares of the highest three scores on the Abbreviated Injury Scale. Injury Severity Scores range from 0 to 75, with higher scores indicating more severe injury. If there is an unsurvivable injury in any region, the maximum score of 75 is automatically assigned. Key exclusion criteria were imminent death, confirmed pulmonary embolism on admission to the trial center, systemic anticoagulant treatment before injury, pregnancy, and unavailability of an interventional radiologist to insert the filter within 72 hours after admission.

RANDOMIZATION AND PROCEDURES

Patients were randomly assigned to receive either a retrievable filter (vena cava filter group) or no filter (control group). Randomization was performed with the use of a permuted-block scheme, with stratification according to trial center. For safety reasons, patients and the treating clinicians were aware of the group assignments. To minimize detection bias, the trial used a proactive approach to detect symptomatic pulmonary embolism, with strict guidelines regarding when computed tomographic (CT) pulmonary angiography should be performed (Table S1 in the Supplementary Appendix, available at NEJM.org).[24]

All patients underwent routine Doppler and compression ultrasonography of the legs 2 weeks after enrollment. The trial was designed to avoid unnecessary radiation from routine CT pulmonary angiography in asymptomatic patients and to ensure the clinical safety of patients assigned to the control group through early detection of mildly symptomatic pulmonary embolism and deep-vein thrombosis, thus reducing the risk of fatal pulmonary embolism in these patients.[6,26] All deaths in the trial were referred to the Coroner's Court of Western Australia; if deemed necessary, a full postmortem examination was performed to determine whether pulmonary embolism was the cause of death.

The type of filter used was at the discretion of the interventional radiologists who performed the procedure. All filters were removed as soon as prophylactic anticoagulation was safely established or before 90 days, unless there was a strong indication to leave the filter longer than this prespecified period. All filters retrieved from patients in the trial centers in Western Australia were analyzed for integrity at the Centre for Implant Technology and Retrieval Analysis.

The trial protocol recommended initiation of prophylactic anticoagulation as soon as clinically feasible. The decision to initiate prophylactic anticoagulation and the doses were at the discretion of the clinicians. All patients received intermittent pneumatic compression to uninjured legs.[27] Clinicians were allowed to insert a filter for patients assigned to the control group if there was a well-established indication.

END POINTS

The primary end point was a composite of symptomatic pulmonary embolism (segmental pulmonary embolism on CT pulmonary angiography, confirmed by an independent consultant radiologist or by postmortem examination) or death from any cause at 90 days after enrollment. An additional primary end point was the cost-effectiveness of the use of vena cava filters in severely injured patients; the results of that analysis are not reported here. Prespecified secondary end points included symptomatic pulmonary embolism in the subgroup of patients who survived at least 7 days and who did not receive prophylactic anticoagulation within 7 days after injury, complications related to the vena cava filters, death at 90 days, and major and nonmajor bleeding at 90 days. An additional secondary end point, which was not prespecified in the protocol, was deep-vein thrombosis at 90 days, including deep-vein thrombosis detected by protocol-mandated ultrasonography of the legs at 2 weeks. The primary and secondary end points assessed in this trial are described in Table S2 in the Supplementary Appendix.

STATISTICAL ANALYSIS

A previous study showed that pulmonary embolism occurred in more than 9% of severely injured patients who did not receive prophylactic anticoagulation.[1] A similar incidence was anticipated in this trial because of the proactive approach used to detect symptomatic pulmonary embolism in patients with a high Injury Severity Score and a high Trauma Embolic Scoring System score (which

is used to predict the risk of deep-vein thrombosis and nonfatal pulmonary embolism in severely injured patients).[28,29] We determined that a sample size of 240 patients would be needed to provide the trial with 80% power to show the superiority of the filter, as indicated by an 8.5-percentage-point lower incidence of symptomatic pulmonary embolism with the filter than with no filter (0.5% vs. 9.0%), allowing for 20% crossover between the two groups.

The analyses of the primary and secondary end points were performed according to the intention-to-treat principle and included all patients who had undergone randomization, regardless of their adherence to the protocol or subsequent crossover to receive or decline the filter. One patient withdrew consent 6 weeks after enrollment, and data for this patient from the time of randomization to withdrawal of consent were included in the analysis.

For the primary end point, Cox proportional-hazards regression was used to generate the hazard ratio and 95% confidence interval, and the log-rank test was used to generate the P value. All secondary end points were analyzed with the use of the Miettinen and Nurminen method at day 90 without the exclusion of deaths, in accordance with the intention-to-treat principle, and are reported as relative risks and 95% confidence intervals.[30] In addition, two analyses were performed in the subgroup of patients who survived at least 7 days and did not receive prophylactic anticoagulation within 7 days after injury: an analysis of the time to symptomatic pulmonary embolism with the use of Cox proportional-hazards regression, with data for patients who died censored at the time of death, and an analysis of the time to symptomatic pulmonary embolism with the use of Cox regression, with death treated as a competing risk. Complications related to the vena cava filters are reported. Finally, Cox regression was used to assess the effect of other covariates on the primary end point (Table S3 in the Supplementary Appendix). All tests were two-sided. There was no prespecified plan to adjust analyses of secondary end points for multiple comparisons. Those results are reported without P values and with 95% confidence intervals that have not been adjusted for multiple comparisons, and inferences drawn from them may not be reproducible.

According to a prespecified plan, the trial would be stopped if a total of four fatal pulmonary emboli (which were defined as serious adverse events) occurred in the control group. An interim analysis was not planned to preserve the statistical power.

RESULTS

PATIENTS

From June 2015 through December 2017, a total of 1714 patients were screened, and 240 patients were enrolled and underwent randomization (Fig. 1). Two patients in each group crossed over to the other group, and data from these patients were assessed according to the intention-to-treat principle. The median age was 39 years (interquartile range, 27 to 57), and the median Injury Severity Score was 27 (interquartile range, 22 to 34). A total of 138 patients (57.5%) had traumatic intracranial hematoma or contusions.[31] The characteristics of the patients were balanced between the two groups (Table 1, and Table S4 in the Supplementary Appendix). Of the 122 patients assigned to the vena cava filter group, 89% had the filter inserted within 24 hours after enrollment (median, 15.6 hours [interquartile range, 3.0 to 22.3]). Data for 1 patient who withdrew consent before the 90-day follow-up were censored at the time consent was withdrawn. For all other patients, data on all primary and secondary end points were available at 90 days after enrollment, or earlier for those who died.

PRIMARY AND SECONDARY EFFICACY END POINTS

A total of 27 patients died after enrollment; the causes of death are shown in Table S6 in the Supplementary Appendix. A full postmortem examination was deemed necessary and conducted in 9 patients (33%). One patient assigned to the control group was found to have had a fatal saddle pulmonary embolism with deep-vein thrombosis in the calf of each leg. This occurred 16 days after the injury and 8 days after the initiation of prophylactic anticoagulation.

Overall, the incidence of symptomatic pulmonary embolism or death (the primary composite end point) was not significantly lower among those in whom a vena cava filter was placed than among those in whom no filter was placed (13.9% vs. 14.4%; hazard ratio, 0.99; 95% confidence interval [CI], 0.51 to 1.94; P=0.98 by log-rank test) (Fig. 2 and Table 2). Only age and Injury Severity Score were significantly associated with the pri-

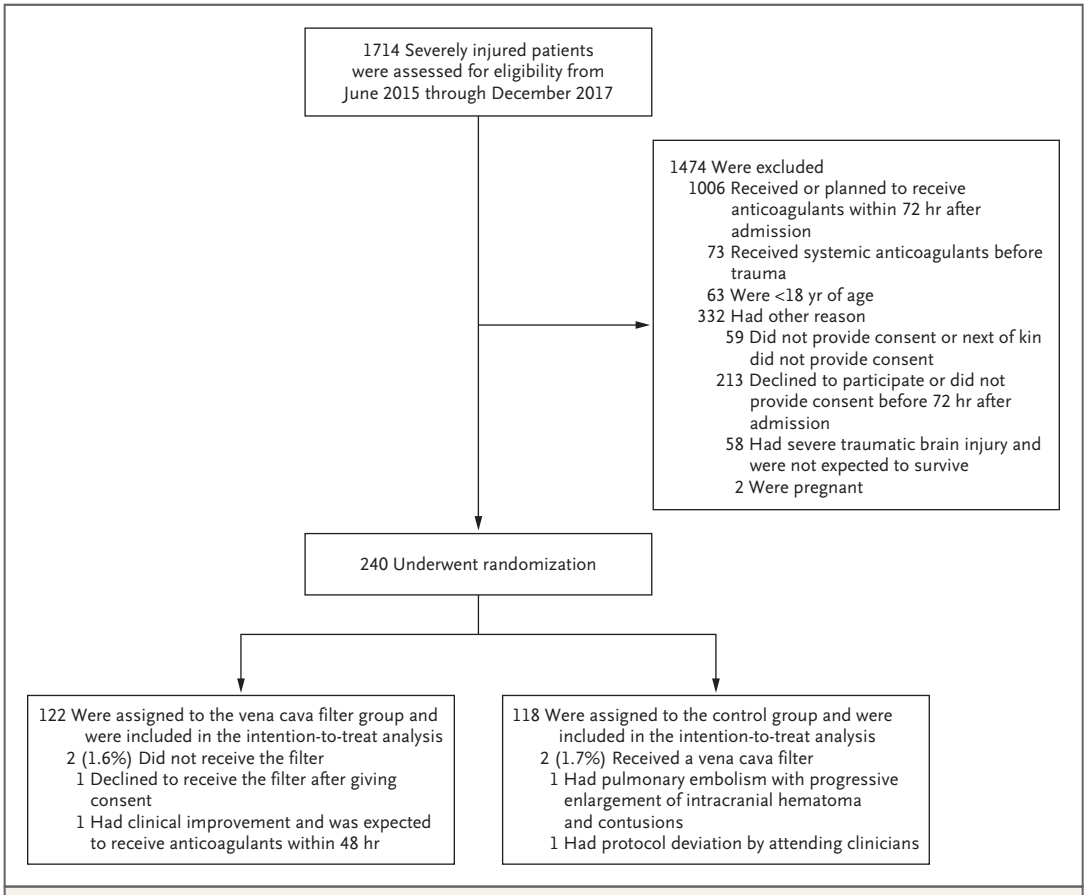

Figure 1. Enrollment and Randomization.

Severely injured patients had an Injury Severity Score of more than 15 (scores range from 0 to 75, with higher scores indicating more severe injury).

mary end point (Table S3 in the Supplementary Appendix). In the prespecified subgroup of patients who survived 7 days and did not receive prophylactic anticoagulation within 7 days after injury (46 patients in the vena cava filter group and 34 in the control group), none of the patients in the vena cava filter group had symptomatic pulmonary embolism between day 8 and day 90, whereas 5 patients (14.7%) in the control group had a symptomatic pulmonary embolism during that period (all occurred between day 9 and day 19 after the injury) (relative risk with the filter, 0; 95% CI, 0.00 to 0.55) (Table 2). The result regarding the occurrence of symptomatic pulmonary embolism in this subgroup remained unchanged in time-to-event analyses in which data from patients were censored at the time of death and in which death was treated as a competing risk (Figs. S9 and S10 in the Supplementary Appendix).

SAFETY END POINTS

The incidence of major and nonmajor bleeding, the incidence of deep-vein thrombosis in a leg (which occurred in 11.4% of patients in the vena cava filter group and in 10.1% in the control group; relative risk, 1.1; 95% CI, 0.6 to 2.3), and transfusion requirements did not differ significantly between the two groups (Table 2, and Table S7 in the Supplementary Appendix). Up to day 90, filters were left in situ for a median duration of 27 days (interquartile range, 11 to 90). The complications associated with inferior vena cava filters are shown in Table 3. Entrapped thrombus within the filter was noted at the first attempt to remove the filter in 6 of the 122 patients (4.9%; 95% CI, 2.2 to 9.8) in the safety population, which included 120 patients in the vena cava filter group and 2 patients in the control group who received a vena cava filter. In 1 patient (0.8%; 95% CI,

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Vena Cava Filter Group (N=122)	Control Group (N=118)
Median age (IQR) — yr	35 (25–56)	41 (29–58)
Male sex — no. (%)	94 (77.0)	90 (76.3)
Median weight (IQR) — kg	80 (70–91)	83 (72–95)
Median height (IQR) — cm	176 (170–181)	176 (170–180)
Median BMI (IQR)†	25.8 (23.3–30.0)	27.2 (24.2–30.5)
Race or ethnic group — no. (%)‡		
White	107 (87.7)	105 (89.0)
African	0	2 (1.7)
Asian	5 (4.1)	4 (3.4)
Aboriginal or Torres Strait Islander	5 (4.1)	4 (3.4)
Other	5 (4.1)	3 (2.5)
Median time from injury to trial enrollment (IQR) — hr§	34.3 (24.5–47.3)	32.5 (22.0–49.5)
Median Injury Severity Score (IQR)¶	27 (22–33)	26 (22–35)
Median Trauma Embolic Scoring System score (IQR)‖	9 (6–10)	9 (6–11)
Median Charlson Comorbidity Index score (IQR)**	0 (0–1)	0 (0–0)
Intracranial-pressure monitor present — no. (%)	47 (38.5)	42 (35.6)
Median initial Glasgow Coma Scale score (IQR)††	9 (3–15)	11 (3–15)
History of deep-vein thrombosis — no.	0	0
History of pulmonary embolism — no.	0	0
Smoking status — no. (%)		
Current: within 3 mo	50 (41.0)	46 (39.0)
Previous	30 (24.6)	21 (17.8)
Never	41 (33.6)	51 (43.2)
Missing data	1 (0.8)	0
Trial site of admission — no. of patients (%)‡‡		
Royal Perth Hospital	117 (95.9)	113 (95.8)
Sir Charles Gairdner Hospital	4 (3.3)	3 (2.5)
Royal Brisbane and Women's Hospital	1 (0.8)	2 (1.7)

* There were no significant differences between the two groups in any of the characteristics listed here ($P<0.05$). IQR denotes interquartile range.
† The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.
‡ Race or ethnic group was determined from the trial site administrative health data systems.
§ Data were missing for 7 patients in each group.
¶ The Injury Severity Scores range from 0 to 75, with higher scores indicating more severe injury.[25]
‖ Scores on the Trauma Embolic Scoring System are the sum of the scores of each of five components (age, Injury Severity Score, obesity, ventilator use, and lower-extremity trauma); total scores range from 0 to 14, with higher scores indicating a higher risk of thromboembolic events after injury.[28,29]
** The Charlson Comorbidity Index assesses 17 medical conditions; total scores range from 0 to 35, with higher scores indicating more coexisting illnesses (see Fig. S8 in the Supplementary Appendix).[31]
†† The Glasgow Coma Scale scores range from 3 to 15, with lower scores indicating lower levels of consciousness.
‡‡ Many patients stayed in more than one trial hospital during the 90 days after enrollment (see Table S4 in the Supplementary Appendix).

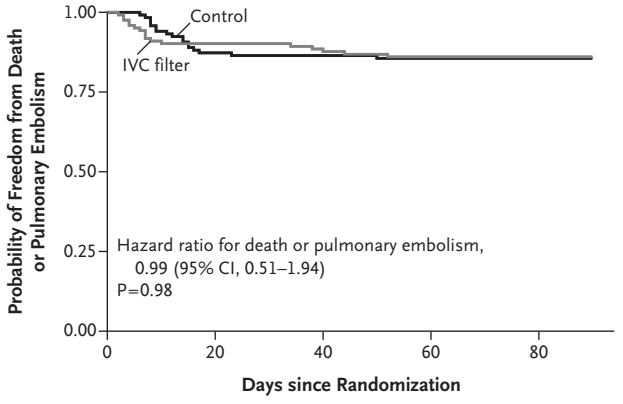

Figure 2. Kaplan–Meier Analysis of the Primary End Point.

Severely injured patients were assigned to receive an inferior vena cava (IVC) filter or no filter. The primary end point was a composite of symptomatic pulmonary embolism or death from any cause at 90 days. The P value was generated with the use of a log-rank test, and the hazard ratio was generated with Cox proportional-hazards regression.

0.1 to 4.5), the filter was adherent to the caval wall and was removed surgically.

DISCUSSION

The use of vena cava filters has become widespread in many trauma centers as a primary means to prevent pulmonary embolism in patients who are at high risk for bleeding.[32] The American College of Chest Physicians, the Eastern Association for the Surgery of Trauma, and the Society of Interventional Radiology provide conflicting recommendations in this patient population.[33-35]

Most studies evaluating the clinical efficacy of vena cava filters in trauma patients have been observational.[3-5,8,13-16,19,22,32] The current trial showed that in patients who have a contraindication to prophylactic anticoagulation, the early placement of a prophylactic filter (within the first 72 hours after injury) did not result in a lower incidence of symptomatic pulmonary embolism or death at 90 days (the primary composite end point) than no placement of a filter. Our findings are consis-

Table 2. Primary and Secondary End Points.

End Point	Vena Cava Filter Group (N=122)	Control Group (N=118)	Hazard Ratio or Relative Risk (95% CI)*
Primary end point: composite of symptomatic pulmonary embolism or death from any cause at 90 days — no. (%)	17 (13.9)	17 (14.4)	0.99 (0.51–1.94)
Secondary end points			
Symptomatic pulmonary embolism from day 8 to day 90 among patients who did not receive prophylactic anticoagulation within 7 days after injury — no./total no. (%)†	0/46	5/34 (14.7)	0 (0.00–0.55)
Death from any cause at 90 days — no. (%)	16 (13.1)	11 (9.3)	1.41 (0.69–2.87)
Major bleeding at 90 days — no. (%)‡	86 (70.5)	78 (66.1)	1.07 (0.90–1.27)
Nonmajor bleeding at 90 days — no. (%)§	29 (23.8)	21 (17.8)	1.34 (0.81–2.20)

* The hazard ratio is shown for the primary end point, and the relative risks are shown for the secondary end points. Relative risks were calculated with the use of the Miettinen and Nurminen method.[30] Confidence intervals have not been adjusted for multiplicity, and therefore inferences drawn from these intervals may not be reproducible. No data on primary and secondary end points were missing.

† A total of 46 patients (38%) in the vena cava filter group and 34 (29%) in the control group did not receive anticoagulant prophylaxis within 7 days after injury (between-group difference, 9 percentage points; 95% CI, −3.0 to 20.4). Of the 5 symptomatic pulmonary emboli in the control group, 4 were diagnosed by means of computed tomographic pulmonary angiography (3 bilateral and 1 unilateral), and 1 through postmortem examination (this patient had a saddle pulmonary embolism that was not diagnosed before death).

‡ Major bleeding was defined as bleeding that contributed to death; occurred at a critical site (e.g., intracranial, intraspinal, epidural, or lung hemorrhage); led to transfusion of 2 or more units of red cells, platelets, or fresh frozen plasma; or was associated with a decrease in the hemoglobin level of more than 2 g per deciliter within any 24-hour period after injury.

§ Nonmajor bleeding was defined as bleeding that led to new medical interventions (e.g., gastrointestinal endoscopy or local or systemic drugs to control bleeding [including tranexamic acid]). Minor bleeding that did not result in medical intervention was not included.

Table 3. Safety End Points Related to the Inferior Vena Cava Filters.*

End Point	Patients (N=122)
Clots were noted in the filter at the first attempt to remove the filter — no. (%)	6 (4.9)
The filter was adherent to the inferior vena caval wall at the first attempt to remove the filter — no. (%)	2 (1.6)
The filter was tilted within the inferior vena cava at the time of removal, but the filter was successfully removed at the first attempt — no. (%)	3 (2.5)
More than one attempt was needed to remove the filter — no. (%)	7 (5.7)
The filter was not removed within 90 days — no./total no. (%)†	
The filter had clots that resulted in systemic anticoagulation beyond day 90	2/108 (1.9)
The filter was adherent and was surgically removed	1/108 (0.9)
The filter was not removed because of technical reasons or because of loss to follow-up‡	34/108 (31.5)

* Included are 120 patients in the vena cava filter group and 2 patients in the control group who received a vena cava filter. The median time the filter was left in situ until the 90-day follow-up was 27 days (interquartile range, 11 to 90). A total of 117 patients (95.9%) received Bard Denali retrievable vena cava filters, and 5 (4.1%) received Cook retrievable vena cava filters.

† This category excludes 14 patients who died before removal of the vena cava filter was attempted.

‡ Technical reasons included the presence of an ongoing clinical indication for a vena cava filter (e.g., a contraindication to anticoagulation for pulmonary embolism or deep-vein thrombosis) (6 patients) and difficulty in accessing the internal jugular vein because the cervical spine was immobilized (e.g., with halo traction or a jacket) (27 patients). One patient became pregnant and was lost to follow-up. Except in the case of the last patient, all filters were removed before day 232.

tent with the results of a recent meta-analysis of the use of vena cava filters in various clinical situations.[36] Anticoagulation was initiated within 7 days after severe injury in 67% of the patients enrolled in our trial. However, among the 33% of patients with ongoing contraindications to prophylactic anticoagulation in whom anticoagulation could not be started within 7 days after severe injuries, symptomatic pulmonary embolism developed in none of the patients assigned to the vena cava filter group.

Given the cost and risks associated with a vena cava filter,[22,37] our data suggest that there is no urgency to insert the filter in patients who can be treated with prophylactic anticoagulation within 7 days after injury. Unnecessary insertion of a vena cava filter has the potential to cause harm. In this trial, an entrapped thrombus was found within the filter in almost 5% of the patients in whom a filter was placed, and the filter had to be surgically removed in one patient. Nonetheless, in patients with multiple injuries, repeated surgical procedures may delay initiation or interrupt the continued use of prophylactic anticoagulation. The concern regarding bleeding risk with anticoagulants is particularly relevant in patients with multiple, large, intracranial hematomas or contusions.[10,38-40] In this trial, among patients who did not receive anticoagulation within 7 days, 69% had intracranial hematomas or contusions (Table S8 in the Supplementary Appendix). This patient cohort may benefit from the use of a vena cava filter as a temporizing measure to prevent symptomatic pulmonary embolism.

Previous studies have suggested that vena cava filters are associated with an increased risk of deep-vein thrombosis in the legs.[22,37] This complication was not confirmed in this trial — perhaps because of the use of intermittent pneumatic compression in the legs,[27] the initiation of prophylactic anticoagulation, and the removal of the filter as early as possible.[22,24] We noted that in patients with spinal injury in whom the cervical spine was immobilized (often for up to 3 months or longer), the difficult access to the internal jugular veins was a major barrier to early retrieval of the filter. The use of vena cava filters that can be removed through femoral veins would thus be preferable in these patients.

This trial has limitations. First, it was designed on the premise that a sizable protective effect is needed to justify the costs and risks of a vena cava

filter, and it was underpowered to detect a modestly lower incidence of symptomatic pulmonary embolism or death in the vena cava filter group than in the control group. Second, several caveats should be considered in interpreting the results of the secondary end point, which showed a benefit with vena cava filters. A patient had to survive to 7 days to qualify for inclusion in this prespecified subgroup; this criterion introduced survivor bias, since this subgroup could be relatively less sick and conceivably at a lower risk for pulmonary embolism than patients who died earlier.[6] In addition, the presence of filters may have influenced decisions to initiate anticoagulation, which introduces potential bias by having more patients with a higher bleeding risk in the control group. Finally, the trial was not conducted in a blinded manner. Nonetheless, a similar number of patients underwent CT pulmonary angiography in the two groups, which suggests that the prespecified criteria used to mandate CT pulmonary angiography were successful in minimizing detection bias.

In conclusion, early placement of a vena cava filter after major trauma did not result in a lower incidence of symptomatic pulmonary embolism or death at 90 days (the primary composite end point) than no placement of a filter.

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Dr. Ho reports serving on an advisory board for Medtronic and serving as an advisor for Cardinal Health; and Dr. Lipman, receiving advisory board fees, paid to his institution, from Bayer and MSD, lecture fees from Pfizer South Africa and MSD South Africa, and honoraria from Pfizer. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

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