

Prevention of Venous Thromboembolism after Injury: An Evidence-Based Report—Part II: Analysis of Risk Factors and Evaluation of the Role of Vena Caval Filters

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Objective: In part II, we describe the results of the literature search and data analysis concerning risk factors for venous thromboembolism and the role of vena caval filters (VCF) in preventing pulmonary embolism.

Methods: The methodology used in part I was used in part II.

Results: Spinal fractures and spinal cord injuries increase the risk for development of deep venous thrombosis (DVT) by twofold and threefold, respectively. Patients with DVT were an average of 9

years older than patients without DVT. No specific age cut-off point for increased risk could be established because data could not be combined across studies. Patients with prophylactically inserted VCF had a lower incidence of pulmonary embolism (0.2%) compared with concurrently managed patients without VCF (1.5%) or historical controls without VCF (5.8%). These results are reported on uncontrolled studies with observational design.

Conclusion: Spinal injuries, spinal

cord injuries, and age are risk factors for development of DVT. Prophylactic placement of VCF in selected trauma patients may decrease the incidence of pulmonary embolism. Future research with well-designed studies is required to provide definitive answers.

Key Words: Trauma, Injury, Venous thromboembolism, Deep venous thrombosis, Pulmonary embolism, Risk factors, Spinal injury, Spinal cord injury, Vena caval filters, Vena cava interruption.

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Venous thromboembolism (VT) is a significant cause of major morbidity and mortality among injured patients.¹ Clinical diagnosis is unreliable and treatment may be delayed, inadequate, or even harmful; therefore, prevention is essential.^{2–5} The literature provides inconsistent data on prevention of VT.^{6–9} As a result, physicians' practices vary and are not based on reliable conclusions.

We produced an evidence-based report to assess the existing literature. Part I of this report addressed the incidence of deep venous thrombosis (DVT) and pulmonary embolism (PE) and the role of different methods of prevention of VT.¹⁰ In part II, we evaluate various risk factors for

the development of VT, and assess the role of vena caval filters (VCF) in preventing PE. We follow the same methodology as in part I. We intend to summarize the evidence on this topic and identify areas where evidence is lacking to stimulate future research.

MATERIALS AND METHODS

A detailed description of the Materials and Methods is reported in part I. The definition of DVT and PE were accepted as stated in each individual article. Data from all studies reporting on risk factors were meta-analyzed, regardless of study quality. We treated the risk factors as either dichotomous or continuous variables, as appropriate. For instance, if three or more studies provided data on VT incidence on patients who were younger or older than 55 years old, then the risk factor was "age > 55," a dichotomous variable. If three or more studies provided data on age of patients with or without DVT by using only a mean and standard deviation, the risk factor was simply "age," a continuous variable.

The evidence on VCF was derived entirely from nonrandomized trials. The study designs frequently included historical controls and used outcomes that were different from study to study. Different periods of time were used for follow-up. Comparison of these studies was difficult because the designs and reported outcomes were not consistent.

All rates were expressed as random-effect estimates.^{11,12} Meta-analysis was performed only if at least three studies examined the same variable. Shrinkage plots were produced to display the effect size of each study and compare it with

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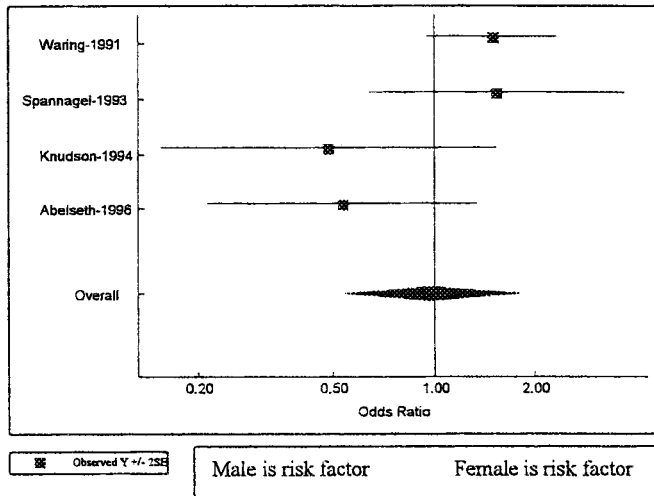


Fig. 1. Shrinkage plot of four studies comparing rates of DVT between male and female patients.

the overall model estimate. The χ^2 test of heterogeneity tested heterogeneity among studies. Funnel plots were created to test for possible publication bias but are not shown in this article. A level of significance at $p < 0.05$ was used for all comparisons.

RESULTS
Risk Factors as Dichotomous Variables

There were sufficient data to assess the effect of the following variables: gender (Fig. 1),¹³⁻¹⁶ head injury (Fig. 2),^{5-7,15,17-20} long-bone fracture (Fig. 3),^{5-7,9,15-17,20-24} pelvic fracture (Fig. 4),^{5,6,9,15,17,20,22,24} spinal fracture (Fig. 5),^{5-7,9,15,18-20,22,24} and spinal-cord injury (Fig. 6).^{5,9,20,22,24} Several studies included age as a risk factor, but the different cut-off points used in each study (age [years] >30, >40, >50, >55, etc.) did not allow analysis of this variable. The only risk

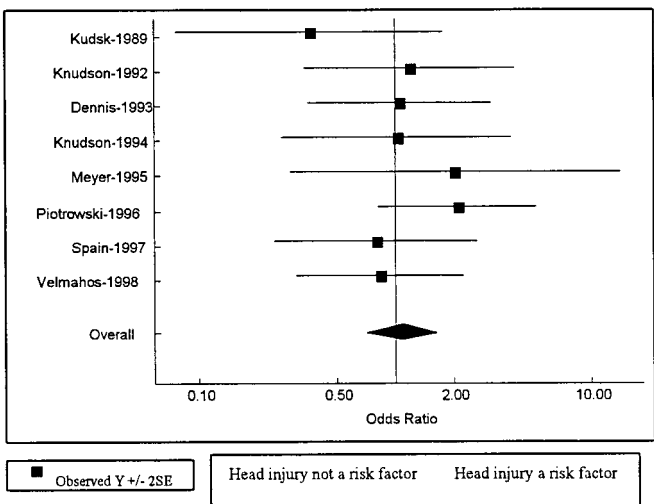


Fig. 2. Shrinkage plot of eight studies comparing rates of DVT between patients with and patients without head injuries.

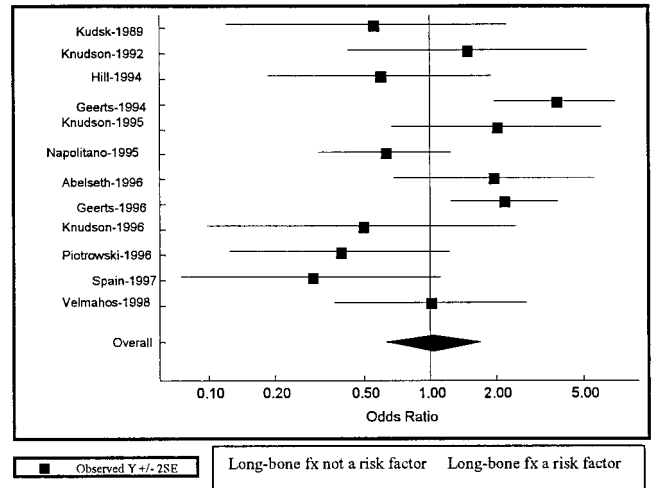


Fig. 3. Shrinkage plot of 12 studies comparing rates of DVT between patients with and patients without long-bone fractures.

factors that had statistically significant effects for increasing the development of DVT were spinal fractures (odds ratio [OR], 2.260; 95% confidence interval [CI], 1.415, 3.610) and, even more, spinal-cord injury (OR, 3.017; 95% CI, 1.794, 5.381). The test of heterogeneity indicates that only the studies used to evaluate long-bone fractures are heterogeneous. For all other comparisons, the test is not significant for heterogeneity among studies.

Risk Factors as Continuous Variables

We found sufficient data to examine three continuous variables: age,^{6,16,17,20,22,25} Injury Severity Score,^{6,15,17,20,22,25} and units of blood transfused.^{15,17,25} The meta-analysis showed that, compared with patients without DVT, patients with DVT are significantly older by 8.133 ± 1.504 (95% CI, 5.115, 11.141) years and have a significantly higher Injury Severity Score by 1.430 ± 0.747 (95% CI, 0.000, 2.924). This statistical difference in Injury Severity Score is mar-

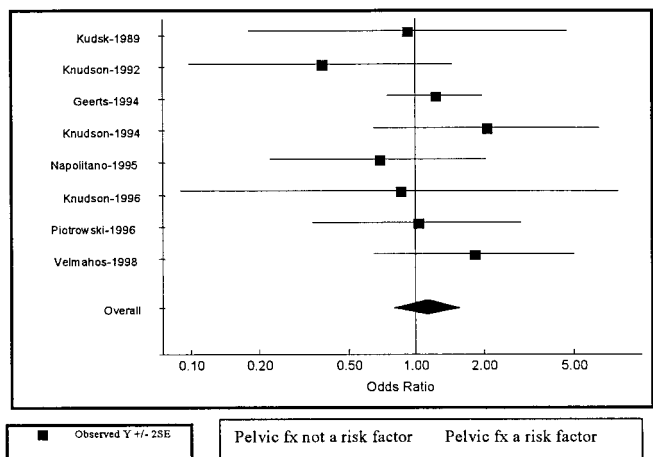


Fig. 4. Shrinkage plot of eight studies comparing rates of DVT between patients with and patients without pelvic fractures.

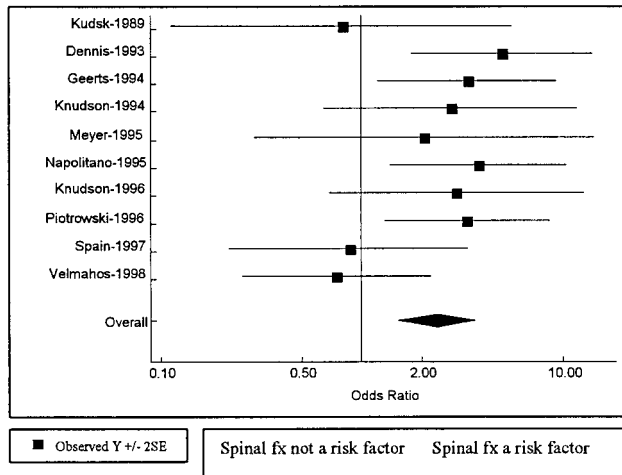


Fig. 5. Shrinkage plot of 10 studies comparing rates of DVT between patients with and patients without spinal fractures.

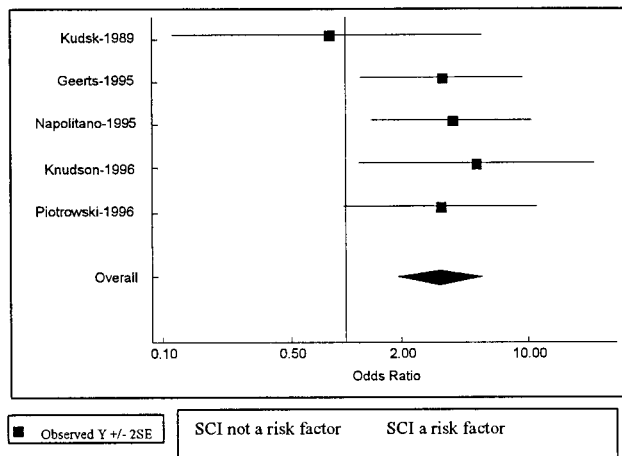


Fig. 6. Shrinkage plot of five studies comparing rates of DVT between patients with and patients without spinal-cord injuries (SCI).

ginal, as shown by the lower limit of the 95% CI, and has minimal clinical significance. The difference in the amount of blood transfused between patients with and without DVT is not statistically significant (1.882 ± 2.815 , 95% CI, -3.637 , 7.401). The heterogeneity test failed to identify heterogeneity among these studies.

Role of VCF

Table 1 presents the incidence of PE among patients who had a VCF placed, patients who were managed contemporaneously without a VCF, and historical control patients without a VCF.²⁶⁻³¹ A total of 321 severely injured patients in these studies received a VCF prophylactically. Random-effect estimates of the incidence of PE and total PE were estimated. Two patients (0.2%) developed PE, with no fatal PEs. Among 1,083 patients who were managed contemporaneously without a VCF, 7 patients (1.5%) developed a PE and 1 patient (0.1%) developed a fatal PE. Among 1,806 historical controls, 57 patients (5.8%) developed a PE and 24 patients (3.3%) developed a fatal PE. In most comparisons, the studies were heterogeneous.

DISCUSSION

This study uses meta-analysis to examine the existing literature data regarding risk factors of VT and the role of VCF in preventing PE. Following the recommendation of our group of national experts, we excluded studies that did not refer exclusively to trauma patients. This restriction decreased significantly the number of studies that could be analyzed but increased the validity of our results for trauma patients by excluding nontrauma patients.

Multiple risk factors have been reported for the development of VT. Our analysis focuses on risk factors included in at least three studies. DVT was examined as the outcome because there was inadequate data to examine PE. Of six risk factors that we identified by the above criteria, only spinal

TABLE 1. Incidence of Pulmonary Embolism in Patients with and without Vena Caval Filters

Study	Total No. of Patients	VCF Group ^a		Prosp No VCF		Hist No VCF	
		N	No. of PE	N	No. of PE	N	No. of PE
Gosin et al., 1997 ²⁶	499	99	0	151	4	249	12
Rogers et al., 1997 ²⁷	2,090	35	1	905	1	1,150	11
Khansarinia et al., 1995 ²⁸	324	108	0	—	—	216	13
Rodriguez et al., 1996 ²⁹	120	40	1	—	—	80	14
Wilson et al., 1994 ³⁰	126	15	0	—	—	111	7
Webb et al., 1992 ³¹	51	24	0	27	2	—	—
Total	3,210	321	2	1,083	7	1,806	57
Random-effect estimates		0.002		0.015		0.058	
95% CI		(-0.007, 0.010)		(-0.011, 0.041)		(0.020, 0.096)	
χ^2 heterogeneity test							
Q statistics		1.93		5.83		35.76	
p value		0.86		0.054		0.000	

VCF, vena caval filter; Hist, historical control group; Prosp, prospective control group; PE, pulmonary embolism; CI, confidence interval.

^a Note: The treatment (VCF) group in each study was compared with a prospective control group, a historical control group, or both.

fractures and spinal-cord injuries were found to increase the odds for development of DVT (by twofold and threefold, respectively) relative to patients without spinal trauma.

We could not confirm that widely assumed risk factors, such as pelvic fractures, long-bone fractures, or head injuries, affect the incidence of DVT. It is possible that the studies we analyzed included multiple trauma patients who were already at the highest risk of VT. Among such patients, individual risk factors might not increase an already high risk. Another explanation is that we lacked sufficient patients to identify existing differences.

Of the continuous variables that were examined as risk factors, only age was statistically and clinically different between patients with and without DVT. Patients with DVT were on average 9 years older than patients without DVT. Unfortunately, a specific age cut-off point at which DVT increases significantly could not be identified because of the lack of consistency of age cut-off points used among studies that examined this risk factor. We can only conclude that DVT is more likely to occur as age progresses.

There are no randomized studies of the effect of VCF on the incidence of PE. The existing studies use prospective observational designs and comparison to historical controls. Results from such studies are prone to bias. Hence, although these studies suggest that VCF decreases the risk of PE and fatal PE in selected groups of trauma patients, firm conclusions about the role of VCF cannot be drawn.

The major limitation of the current report is the quality and quantity of original studies. We made no attempt to give greater importance to studies that had better design and, therefore, presumably more valid results. This was done because, in general, there is a lack of empirical evidence relating study design to bias.³² Additionally, available data were limited because we included only studies on trauma patients. We believe that extrapolations from conclusions on nontrauma patients to the trauma population may be misleading and should be avoided. Finally, the heterogeneity among studies may have influenced the results. The statistical test did not indicate significant heterogeneity for most comparisons; however, the power of this test is known to be poor, and combining different groups of trauma patients with variable characteristics (e.g., spinal-cord injury patients with general trauma patients) may be inappropriate. Again, the limited number of available studies provided little opportunity to isolate these groups for individual study. The strengths and limitations of meta-analysis should be recognized. Meta-analysis is only one component that contributes to an overall judgment about a method, and does not provide the final and irreversible conclusion.^{33,34}

In summary, the available evidence suggests that spinal fractures, spinal-cord injuries, and age are risk factors for DVT in trauma patients. The reported incidence of PE in patients who undergo VCF placement is lower than the incidence of PE among patients without VCF. The observational design of these studies do not allow firm conclusions to be drawn about VCF. Definitive answers can only be given by

future research focused on well-designed prospective randomized trials.

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