Inferior Vena Cava Filters in Stable Patients With Pulmonary Embolism and Heart Failure

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Mortality according to the use inferior vena cava (IVC) filters in patients with pulmonary embolism (PE) and heart failure (HF) has been sparsely studied. In the present investigation, we assess whether IVC filters in stable patients with PE and HF reduce mortality. This is a retrospective cohort study of administrative data from the Premier Healthcare Database, 2009 through 2015. Patients aged ≥18 years hospitalized with a primary diagnosis of PE and a discharge diagnosis of HF were identified by International Classification of Diseases-Ninth Revision-Clinical Modification codes. Exclusions were unstable patients (in shock or on a ventilator), patients who underwent pulmonary embolectomy, and patients with co-morbidities. In-hospital all-cause mortality was 102 of 2,423 (4.2%) with an IVC filter compared with 686 of 14,063 (4.9%) without an IVC filter (p = 0.16). Only patients aged >80 years showed a lower in-hospital all-cause mortality with IVC filters, 38 of 933 (4.1%) with an IVC filter compared with 307 of 4,486 (6.8%) without an IVC filter (p = 0.0012). In conclusion, stable patients with PE and HF, if aged >80 years, showed a reduced in-hospital all-cause mortality with IVC filters. **(Am J Cardiol 2019;124:292−295)**

The only randomized controlled trial of retrievable inferior vena cava (IVC) filters in patients with pulmonary embolism (PE), the Prevention du Risque d'Embolie Pulmonaire par Interruption Cave (PREPIC II) trial, showed a similar all-cause mortality at 3 and 6 months after insertion in those who received an IVC filter and those who did not.[1] This trial, however, did not have enough patients to stratify according to subgroups. Several subgroups of patients with acute PE have been shown by retrospective cohort studies of huge databases to have a lower mortality if the patients received an IVC filter. Unstable patients with PE, defined as those in shock or on a ventilator, had a lower in-hospital all-cause mortality with IVC filters[2,3]; irrespective of age,[4] providing the IVC filters were inserted early, during the period of instability.[5] Several subgroups of stable patients with PE also showed a lower mortality with IVC filters.[6] A subgroup that has been sparsely studied, his that with heart failure (HF).[7] In the present investigation, we further assess whether IVC filters in stable patients with PE and HF reduce mortality.

Methods

This is a retrospective cohort study of administrative data from the Premier Healthcare Database (Charlotte, North Carolina).[8] This investigation was determined by the institutional review board not to meet the definition of "human subjects" because the database includes only deidentified patients.

We identified all patients aged ≥18 years hospitalized with a primary (first-listed) diagnosis of PE from 2009 through 2015. From these, we selected patients with PE who had a discharge diagnosis of HF. We excluded those who were unstable (in shock or on a ventilator), because such patients previously were shown to have a lower in-hospital all-cause mortality if they received an IVC filter.[2−5] For the same reason, we excluded patients who underwent pulmonary embolectomy.[3,9] We matched patients by excluding those with co-morbid conditions listed in the Charlson Comorbidity Index other than HF.[10] International Classification of Diseases-Ninth Revision-Clinical Modification codes were used and are shown in Tables 1 and 2. In-hospital all-cause mortality was assessed according to the use of IVC filters. Guidelines for Strengthening the Reporting of Observational Studies in Epidemiology were followed.[11]

Differences of categorical variables were calculated by the 2-tailed Fisher's exact test or 2-tailed chi-square test with Yates' correction using GraphPad Software (San Diego, California). Differences of means of continuous variables were reported as mean ± standard deviation and differences of means were assessed by Student's unpaired *t* test. Relative risk and 95% confidence intervals (CI) of relative risk were calculated using MedCalc statistical software (Ostend, Belgium). Linear regression analyses were performed using InStat 3.0; GraphPad Software, San Diego, California.

Results

From 2009 through 2015, 16,486 patients were hospitalized with a primary diagnosis of PE, had HF, were stable, and had no co-morbid conditions (Figure 1). Those who received an IVC filter were older than those who did not, aged 74 ± 13 years compared with 70 ± 15 years ($p < 0.0001$). The proportion of females in those who received IVC filters and those who did not was similar, 58% females

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Table 1
ICD-9-CM codes used

Condition	ICD-9-CM code
Pulmonary embolism	415.1, 415.13, 415.19
Vena cava filter	38.7
Shock	785.50, 785.59
Ventilator dependence	V46.1, V46.11
Pulmonary embolectomy	38.05
Heart failure	428.0, 428.1, 428.2, 428.3, 428.4, 428.1

ICD-9-CM = International Classification of Diseases-Ninth Revision-Clinical Modification.

with ICV filters compared with 57% without IVC filters ($p = 0.38$).

The proportion of patients with PE and HF who received an IVC filter increased linearly with age (Figure 2). In-hospital all-cause mortality increased linearly with age in those who did not receive an IVC filter (Figure 3). In those who received an IVC filter, mortality was not age-related.

Among patients of all ages, in-hospital all-cause mortality was 102 of 2,423 (4.2%) with an IVC filter compared

Table 2
ICD-9-CM codes in co-morbid conditions other than heart failure listed in the Charlson Comorbidity Index[7]

Condition	ICD-9-CM codes
Acute myocardial infarction	410
Peripheral vascular disease	440.2, 443.9
Cerebrovascular disease	430-438
Dementia	290
Chronic obstructive pulmonary disease	490-496
Rheumatologic disease	710.0, 710.1, 710.4, 714.0, 714.1, 714.2, 714.8
Ulcer disease	531-534
Acute or chronic liver disease	570, 571
Diabetes mellitus	250.0-250.3
Hemiplegia and hemiparesis	342.0-342.9
Paraplegia	344.1
Moderate or severe renal disease	580-586, 588
Diabetes with chronic complications	250.4-250.6
Any neoplasms, leukemia, lymphoma	140-195, 200-208
Metastatic cancer	196-199
HIV and AIDS	042

HIV = human immunodeficiency virus; ICD-9-CM = International Classification of Diseases-Ninth Revision-Clinical Modification.

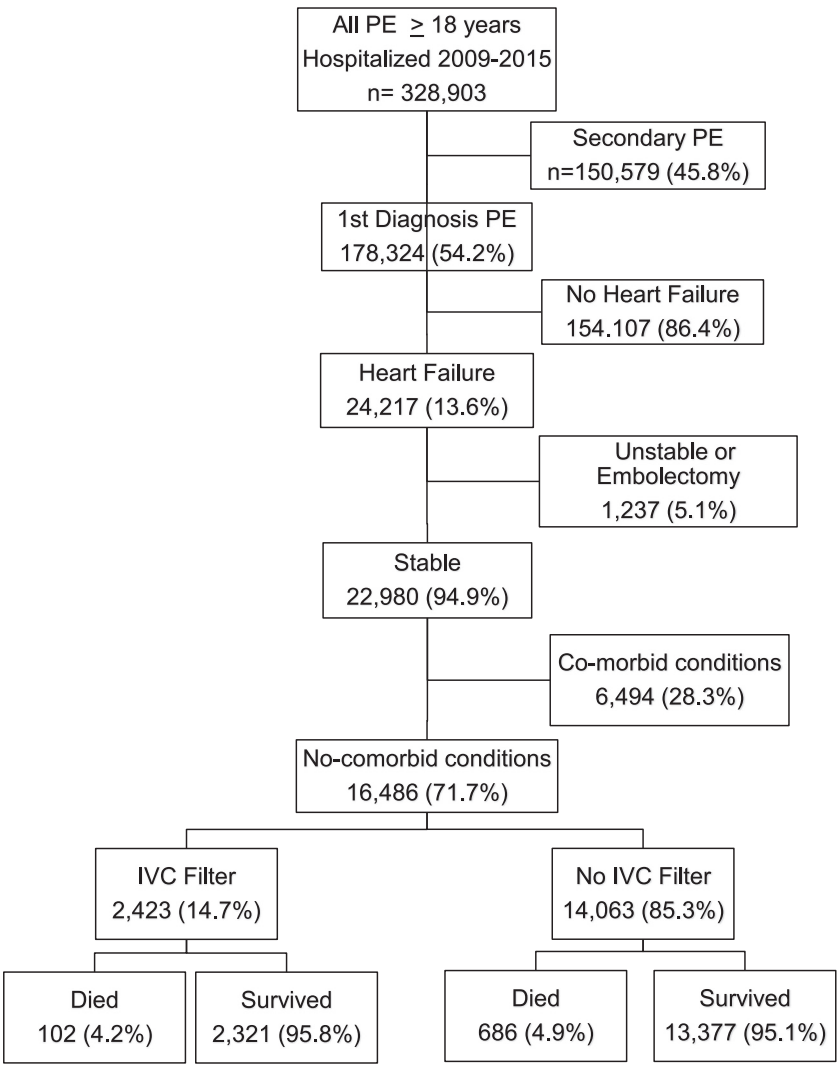

Figure 1. Flow chart. IVC = inferior vena cava; PE = pulmonary embolism.

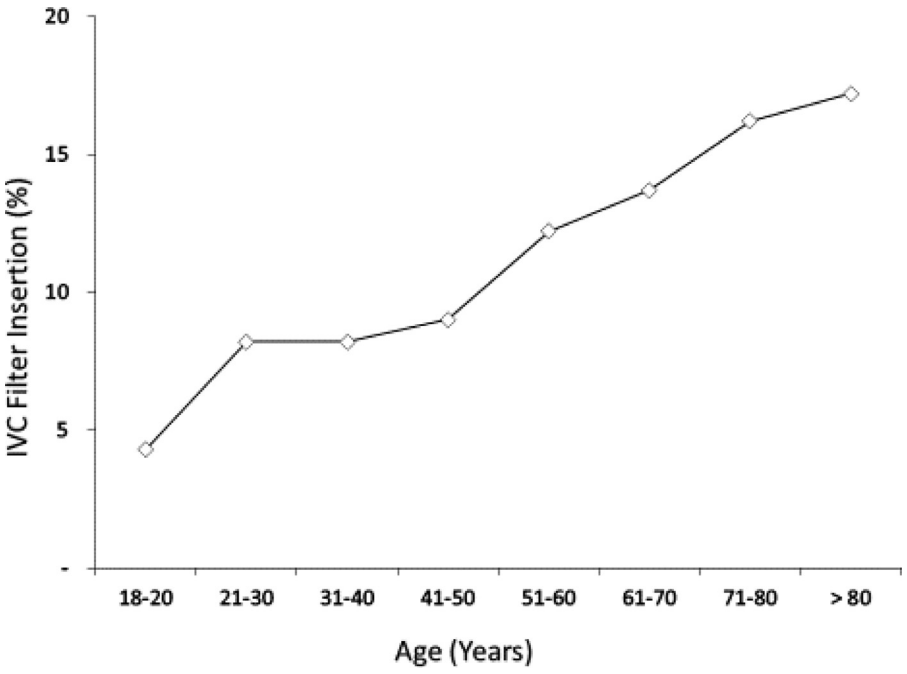

Figure 2. Proportion of patients who received an inferior vena cava (IVC) filter in relation to age groups. The proportion of patients who received an IVC filter increased linearly with age. Correlation coefficient (r) = 0.9828, $p < 0.0001$.

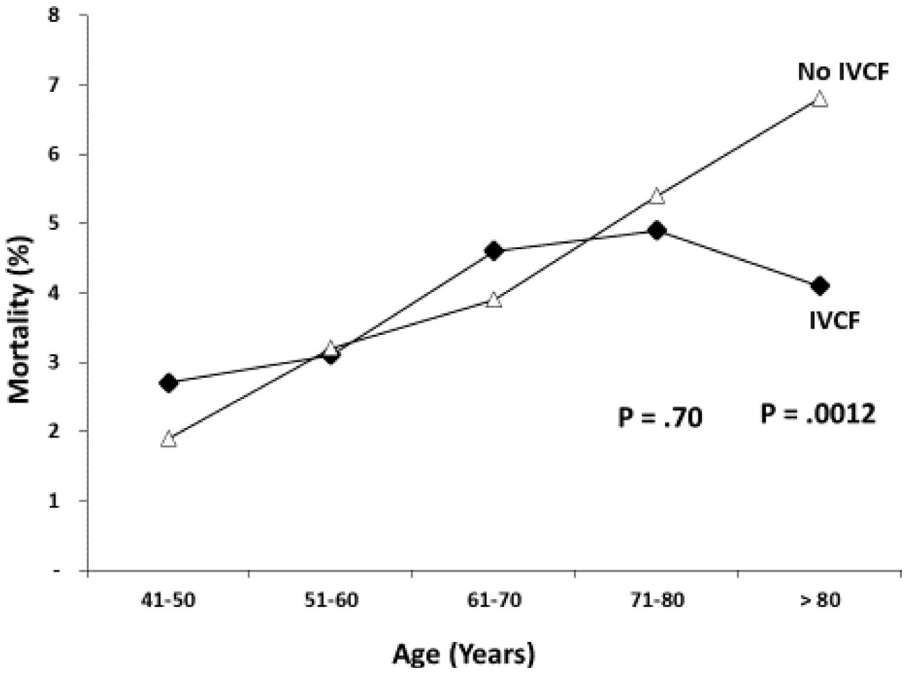

Figure 3. In-hospital all-cause mortality in relation to age groups. In those who did not receive an inferior vena cava (IVC) filter, mortality increased linearly with to age, correlation coefficient (r) = 0.9941, p = 0.0005. Mortality did not increase with age in those who received an IVC filter, r = 0.7658, p = 0.13.

with 686 of 14,063 (4.9%) without an IVC filter (p = 0.16), relative risk 0.87 (95% CI = 0.71 to 1.07). Only patients aged >80 years showed a lower in-hospital all-cause mortality with IVC filters, 38 of 933 (4.1%) with an IVC filter compared with 307 of 4,486 (6.8%) without an IVC filter (p = 0.0012), relative risk 0.80 (95% CI = 0.43 to 0.87; Figure 3).

Discussion

Among stable patients with PE and HF, those who received an IVC filter showed a lower in-hospital all-cause mortality only if aged >80 years.

In a previous retrospective cohort study based on administrative data from the Nationwide Inpatient Sample, 2005

to 2014, patients aged >80 years had the largest absolute risk reduction with IVC filters, 4.9%.[7] This is concordant with our observation of a lower mortality with IVC filters in patients aged >80 years. However, significant absolute risk reductions with IVC filters that ranged from 0.4% to 2.1% were also shown in patients aged ≤80 years.[7] We showed no risk reduction in such patients. We believe that a lower mortality with IVC filters in patients aged ≤80 years resulted from inclusion of unstable patients in the population. This skews the results in favor of IVC filters. It is not clear that mortality would have been reduced with IVC filters in patients aged ≤80 years if the population had been limited to stable patients.

We are not certain that the lower mortality with IVC filters in stable patients aged >80 years with HF represents a benefit of IVC filters in HF or is a reflection of the benefit of IVC filters in the very elderly, irrespective of HF. We previously showed a lower in-hospital all-cause mortality with IVC filters in stable patients with PE aged >80 years irrespective of which co-morbid conditions were present or whether no co-morbid conditions were present.[12] We presume that patients aged >80 years are fragile, and, therefore, more likely than younger patients to succumb to even a small recurrent PE.

Strengths of our investigation include the large number of patients evaluated. Patients were matched by including only those with HF and PE and excluding those with other co-morbid conditions. Patients were further matched according to decades of age. Interpretation of the results of cohort studies, however well-done, must be circumspect,[13] as indeed we are circumspect, in inferring cause. However, in most cases, the estimates of the treatment effects from observational studies and randomized controlled trials are similar.[14,15]

In conclusion, stable patients with PE and HF, if aged >80 years, showed a reduced in-hospital all-cause mortality with IVC filters.

Disclosures

The authors have no conflicts of interest to disclose.

1. Mismetti P, Laporte S, Pellerin O, Ennezat PV, Couturaud F, Elias A, Falvo N, Meneveau N, Quere I, Roy PM, Sanchez O, Schmidt J, Seinturier C, Sevestre MA, Beregi JP, Tardy B, Lacroix P, Presles E, Leizorovicz A, Decousus H, Barral FG, Meyer G, PREPIC2 Study Group. Effect of a retrievable inferior vena cava filter plus anticoagulation vs anticoagulation alone on risk of recurrent pulmonary embolism: a randomized clinical trial. *JAMA* 2015;313:1627–1635.
2. Stein PD, Matta F, Keyes DC, Willyerd GL. Impact of vena cava filters on in-hospital case fatality rate from pulmonary embolism. *Am J Med* 2012;125:478–484.
3. Stein PD, Matta F, Lawrence FR, Hughes MJ. Usefulness of inferior vena cava filters in unstable patients with acute pulmonary embolism and patients who underwent pulmonary embolectomy. *Am J Cardiol* 2018;121:495–500.
4. Stein PD, Matta F. Vena cava filters in unstable elderly patients with acute pulmonary embolism. *Am J Med* 2014;127:222–225.
5. Stein PD, Matta F, Lawrence FR, Hughes MJ. Importance of early insertion of inferior vena cava filters in unstable patients with acute pulmonary embolism. *Am J Med* 2018;131:1104–1109.
6. Stein PD, Matta F, Hughes MJ. Vena cava filters in stable patients with acute pulmonary embolism. *Am J Cardiol* 2019. https://doi.org/10.1016/j.amjcard.2019.02.054.
7. Wadhwa V, Gutta NB, Trivedi PS, Chatterjee K, Ahmed O, Ryu RK, Kalva SP. In-hospital mortality benefit of inferior vena cava filters in patients with pulmonary embolism and congestive heart failure. *AJR Am J Roentgenol* 2018;211:672–676.
8. Premier Inc. Premier healthcare database whitepaper. Available at: https://learn.premierinc.com/pharmacy-and.../premier-healthcare-database-whitepaper. Accessed on February 17, 2017.
9. Stein PD, Matta F. Case fatality rate with pulmonary embolectomy for acute pulmonary embolism. *Am J Med* 2012;125:471–477.
10. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–383.
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg* 2014;12:1495–1499.
12. Stein PD, Matta F, Hughes MJ. Inferior vena cava filters in elderly patients with stable acute pulmonary embolism. *Am J Med* 2017;130:356–364.
13. Curtis JP, Krumholz HM. The predicament of comparative effectiveness research using observational data. *Ann Intern Med* 2015;163:799–800.
14. Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. *N Engl J Med* 2000;342:1878–1886.
15. Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. *N Engl J Med* 2000;342:1887–1892.