Usefulness of Inferior Vena Cava Filters in Stable Patients with Acute Pulmonary Embolism

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Retrospective cohort studies using administrative data from national databases or a registry suggest that there are subcategories of stable patients with acute pulmonary embolism who would show a reduced mortality with an inferior vena cava (IVC) filter in addition to anticoagulants. These subcategories are those who underwent pulmonary embolectomy, receiving thrombolytic therapy, suffering recurrent pulmonary embolism while on treatment, hospitalized with solid malignant tumors if aged >60 years, hospitalized with chronic obstructive pulmonary disease (COPD) if aged >50 years, and very elderly (aged >80 years). The following is a review of these studies. It is important to be circumspect in inferring a lower mortality with IVC filters based on comparative effectiveness research that uses national observational data. On the other hand, the likelihood of a randomized controlled trial in any of these subcategories of stable patients is remote. Whether patients are better served by inserting an IVC filter on the basis of retrospective cohort studies, or by withholding IVC filters until a randomized controlled trial can be obtained is a matter for consideration. **(Am J Cardiol 2019;123:1874−1877)**

The PREPIC II (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) Trial is the only randomized controlled trial of retrievable inferior vena cava (IVC) filters in patients with acute pulmonary embolism (PE),[1] although randomized controlled trials of IVC filters also have been performed in patients with deep venous thrombosis (DVT),[2,3] DVT who underwent percutaneous interventions,[4] venous thromboembolism (VTE) and cancer[5] and prophylactically in high-risk trauma patients.[6] In the PREPIC II trial, 200 stable patients with PE plus DVT or superficial venous thrombosis plus at least 1 additional criterion for high risk received a retrievable IVC filter with anticoagulants, and 199 received only anticoagulants.[1] At 3 months and 6 months after insertion, any recurrent PE, fatal PE and all-cause mortality were similar in those who received an IVC filter and those who did not. Does this indicate that there are no subcategories of stable patients who would have a lower mortality with an IVC filter in addition to anticoagulants? Might larger investigations identify such subcategories? Retrospective cohort studies using administrative data from the Nationwide Inpatient Sample (renamed the National Inpatient Sample), Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality,[7] the Premier Healthcare Database (Charlotte, North Carolina), and a retrospective cohort study using prospectively collected data from the Registro Informatizado de la Enfermedad Tromboembólica registry suggest that there are subcategories of stable patients with PE who have a lower mortality with an IVC filter in addition to anticoagulants. The following is a review of these retrospective cohort studies. The results of IVC filters in unstable patients with PE (those in shock or on a ventilator), were reviewed previously.[8]

Methods

We reviewed PubMed for articles in all languages using search terms "IVC filters and stable PE," 4 citations, "vena cava filters and stable pulmonary embolism," 40 citations, "inferior vena cava filters," 4,846 citations, and "IVC filters in pulmonary embolism," 611 citations. In these, 13 references met the criteria for inclusion. In addition there were 12 review articles or meta-analyses that were relevant and written in the last 8 years. References in previous investigations and references in review articles and meta-analyses were reviewed. Exclusions were investigations of patients with DVT exclusive of PE, investigations of patients with VTE unless patients with PE were separately evaluated, investigations that did not stratify according to whether the patients were stable (not in shock or on a ventilator) or unstable, investigations in which in-hospital mortality was not shown, and single center observational studies with <125 patients in each arm.

Results

Subcategories of stable patients who showed a lower mortality with IVC filters and in-hospital all-cause mortality according to the use of IVC filters in these patients are shown in Table 1.

Stable patients with PE who underwent pulmonary embolectomy, 1999 to 2008, based on data from the NIS database, had a lower in-hospital all-cause mortality if they received an IVC filter, 210 of 1,500 (14%) compared with 480 of 1,320 (36%)(p <0.0001).[11] During more recent years, 2010 to 2014, based on the Premier Healthcare

Department of Osteopathic Medical Specialties, College of Osteopathic Medicine, Michigan State University, East Lansing, Michigan. Manuscript received December 26, 2018; revised manuscript received and accepted February 20, 2019.

Funding: None.

See page 1876 for disclosure information.

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0002-9149/
https://doi.org/10.1016/j.amjcard.2019.02.054

Table 1
All-cause in-hospital mortality according to use of IVC filters in stable patients with pulmonary embolism

Subgroup	Database	Years	All-cause in-hospital mortality IVC filter	All-cause in-hospital mortality no IVC filter	p Value	Ref
Pulmonary embolectomy	NIS	1999-2008	210/1500 (14%)	480/1320 (36%)	<0.0001	11
	Premier	2010-2014	20/245 (8.2%)	49/124 (40%)	<0.0001	12
Thrombolytic therapy	NIS	1999-2008	550/8550 (6.4%)	2950/19,050 (15%)	<0.0001	10
	Premier	2010-2014	139/2660 (5.2%)	697/4332 (16.1%)	<0.0001	14
Recurrent pulmonary embolism	RIETE	2001-2005	1/48 (2.1%)	23/ 91 (25.3%)	0.02	15
while on treatment	Premier	2009-2014	18/603 (3.0%)	83/211 (39.3%)	<0.0001	16
Solid malignant tumors aged >30 years	NIS	1998-2009	7070/69,350 (10.2%)	36,875/247,125 (14.9%)	<0.0001	17
Solid malignant tumors aged >60 years	Premier	2010-2014	346/4,648 (7.4%)	2,216/19,847 (11.2%)	<0.0001	18
Chronic obstructive pulmonary disease aged >50 years	NIS	1998-2009	5650/65,160 (8.7%)	37,480/340,550 (11.0%)	<0.0001	20
Very elderly aged > 80 years	NIS	2003-2012	5043/82,706 (6.1%)	40,748/386,507 (10.5%)	<0.0001	21
Congestive heart failure*	NIS	2005-2014	6541/67,237 (9.7%)	43,796/358,638 (12.2%)	<0.001	22

IVC = inferior vena cava; NIS = National Inpatient Sample; Prob = probability; Ref = Reference; RIETE = Registro Informatizado de la Enfermedad Tromboembólica.

* Some of these patients were unstable, so there is uncertainty about the value of IVC filters in stable patients. Absolute risk duction with IVC filters was highest, 4.9%, in patients aged >80 years old.

database, stable patients with PE who underwent pulmonary embolectomy also had a lower in-hospital all-cause mortality if they received an IVC filter, 20 of 245 (8.2%) with an IVC compared with 49 of 124 (40%) without a filter (p <0.0001).[12] All-cause mortality at 3 months was also lower in those who received an IVC filter.[12]

After matching the embolectomy patients in the IVC filter group with those in the no filter group by eliminating all patients with any co-morbidities according to the Charlson Comorbidity Index[13] those who received an IVC filter still showed a lower mortality.[11,12] Presumably, deaths in patients with no co-morbid conditions were due to PE. Based on data from the NIS database, 1999 to 2008, in-hospital mortality due to PE in embolectomy patients with an IVC filter was 35 of 440 (8.0%) compared with 55 of 175 (31%)(p <0.0001).[11] Based on the Premier Healthcare database, 2010 to 2014, in-hospital mortality due to PE was 2 of 211(0.9%) compared with 38 of 105 (36%)(p <0.0001).[12]

In stable patients with acute PE who received thrombolytic therapy, irrespective of the reason, the additional use of an IVC filter resulted in a lower in-hospital mortality.[10,14] In stable patients with PE who received thrombolytic therapy, based on the NIS, 1999 to 2008, in-hospital all-cause mortality in those who received an IVC was 550 of 8,550 (6.4%) compared with 2,950 of 19,050 (15%) in those who did not receive a filter (p <0.0001).[10] In stable patients with PE who received thrombolytic therapy based on the Premier Healthcare Database, 2010 to 2014, in-hospital all-cause mortality in those who received an IVC was 139 of 2,660 (5.2%) compared with 697 of 4,332 (16.1%) in those who did not receive a filter (p <0.0001).[14]

A propensity-matched retrospective cohort study using prospectively collected data from the Registro Informatizado de la Enfermedad Tromboembólica registry, 2001 to 2005, showed mortality according to the use of IVC filters in patients who suffered PE within 3 months of an index diagnosis of VTE.[15] All-cause mortality with an IVC filter was 1 of 48 (2.1(%) compared with 23 of 91 (25.3%) without a filter (p = 0.02).[15]

In patients rehospitalized for recurrent PE within 3 months of an index PE in 2009 to 2014, based on the Premier Healthcare Database, mortality with an IVC filter was 18 of 603 (3.0%) compared with 83 of 211(39.3%) (p <0.0001) without a filter.[16] In patients with recurrent PE who were stable and did not receive thrombolytic therapy or undergo pulmonary embolectomy, mortality with an IVC filter was 15 of 572 (2.6%) compared with 72 of 169 (42.6%) (p <0.0001) without a filter.[16]

Stable patients with PE and solid malignant tumors may be a special population in whom IVC filters reduce all-cause mortality. Data from the NIS, 1998 to 2009, showed that all-cause in-hospital mortality in stable patients aged >30 years who had PE with a solid malignancy was lower in those who received an IVC filter that those who did not, 7,070 of 69,350 (10.2%) compared with 36,875 of 247,125 (14.9%) (p <0.0001).[17] Data from the Premier Healthcare Database, 2010 to 2014 also showed a lower in-hospital all-cause mortality in patients with PE and solid malignant tumors who received an IVC filter, although those who showed a lower mortality were older than shown previously, aged >60 years.[18] This may be because the more recent investigation was not powered to show differences of mortality in younger patients.[18] In-hospital all-cause mortality with IVC filters in those aged >60 years was 346 of 4,648 (7.4%) compared with 2,216 of 19,847 (11.2%) in those who did not receive a filter (p <0.0001).[18] All-cause mortality within 3 months in those aged >60 years was 704 of 4,648 (15.1%) with an IVC filter compared with 3,444 of 19,847 (17.4%) among those who did not receive a filter (p <0.0001).[18]

A lower overall survival (7.3 months) was shown in cancer patients with PE who received an IVC filter compared with 13.2 months in cancer patients who did not receive an IVC filter.[19] It was believed that this may

reflect a poorer cancer prognosis and greater contraindication to anticoagulants.[19]

Based on data from the NIS, 1998 to 2009, in-hospital all-cause mortality in stable patients aged >50 years with PE and chronic obstructive pulmonary disease (COPD) who received an IVC filter was 5,650 of 65,160 (8.7%) compared with 37,480 of 340,550 (11.0%) in those who did not receive an IVC filter (p <0.0001).[20] The greatest reduction of mortality was in patients aged >80 years, 1,570 of 17,220 (9.1%) with an IVC filter compared with 11,720 of 81,600 (14.4%) without a filter (p <0.0001).[20]

Stable patients with PE if aged >80 years have a higher mortality than younger patients.[21] Such patients, being fragile in view of their age, were shown to have a lower in-hospital all-cause mortality if they received an IVC filter.[21] In−hospital all-cause mortality among stable patients aged >80 years with acute PE, based on data from the NIS, 2003 to 2012, in those who received an IVC filter was 5,043 of 82,706 (6.1%) compared with 40,748 of 386,507 (10.5%) in those who did not receive an IVC filter (p <0.0001).[21] Stable patients aged ≤80 years with a primary diagnosis of PE did not show a lower mortality with IVC filters.[21]

After matching the patients who received IVC filters with those who did not by eliminating all who had co-morbidities listed in the Charlson Comorbidity Index[13] stable patients aged >80 years still showed a lower mortality with IVC filters.[21] In-hospital mortality with an IVC filter in these matched patients was 648 of 19,511 (3.3%) compared with 6,465 of 102,060 (6.3%)(p <0.0001).[21] Death presumably was due to PE in these patients.

Some found no lower in-hospital all-cause mortality with IVC filters in patients aged ≥65 years, but they did not stratify according to whether patients were aged >80 years.[9]

Patients with congestive heart failure and acute PE who received an IVC filter showed a lower in-hospital all-cause mortality than those who did not, 6,541/67,237 (9.7%) compared with 43,796/358,638 (12.2%)(p <0.001).[22] Some of these patients were unstable, so it is not clear that stable patients with PE and congestive heart failure had a lower mortality with IVC filters. Patients aged >80 years old showed the highest absolute risk reduction with IVC filters, 4.9%.

Discussion

The lower mortality with IVC filters was confirmed in some of these subcategories of stable patients (pulmonary embolectomy,[11,12] thrombolytic therapy,[10,14] patients with recurrent PE while on treatment,[15,16] solid malignant tumors aged >60 years[17,18]) by investigations performed with different databases during different years. In some of these investigations (pulmonary embolectomy,[11,12] very elderly aged >80 years,[21]) patients with and without IVC filters were matched by eliminating those with any co-morbid conditions. In 1 investigation, patients with recurrent PE while on treatment, there was control for immortal time bias.[16] Even so, results from observational studies are criticized for being vulnerable to influence by unpredictable factors.[23] It is believed by some that interpretation of the results of cohort studies, however well done, must be circumspect, as indeed we are circumspect, in inferring cause.[24] Critics believe that comparative effectiveness research that uses national observational data cannot strongly support causal inference.[24] This notion has been challenged, however.[25,26] There is little evidence that observational studies reported after 1984 give results that are qualitatively different from those obtained in randomized controlled trials.[25] The results of well-designed cohort studies do not systematically overestimate the magnitude of the effects of treatment as compared with those in randomized controlled trials on the same topic.[26] Irrespective of the strength of cohort studies, the likelihood of a randomized controlled trial in any of these subcategories of stable patients is remote due to cost and difficulties in recruitment. Whether patients are better served by inserting IVC filters on the basis of these investigations or by withholding IVC filters until a randomized controlled trial can be obtained is a matter for consideration.

Disclosures

All authors had access to the data and participated in preparation of the manuscript. None of the authors have a conflict of interest.

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