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Original Article

Risk factors for thrombosis associated with retrievable inferior vena cava filter placement

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Abstract: Objective: The aim of this study was to investigate the associated risk factors for thrombosis after retrievable inferior vena cava (IVC) filter placement. Methods: A retrospective study of 164 consecutive patients with retrievable IVC filter placement during June 2008 to June 2014 was performed. We recorded the morphology, size and location of the retrievable inferior vena cava filter associated thrombus, and analyzed the relationship between the thrombus and filter tilt, filter hook wall apposition, dwell time, vena cava dilation rate or ancoagulation factors. Results: The total risk of filter associated thrombosis was 31.1%. In the setting of filter tilt ≥ 15°, hook wall apposition, vein expansion rate ≥ 50% and dwell time > 2 weeks, the risk of filter associated thrombosis was 70.3%, 79.6%, 64.7% and 86.2%, respectively, and the presence of filter related thrombosis were significantly higher than the control group in these settings. The mean length of thro bus was 8.6 ± 1.7 mm, 5.3 ± 1.4 mm, 10.1 ± 2.2 mm and 3.6 ± 0.9 mm in the setting of filter tilt ≥ 15°, hook wall apposition, vena cava dilation rate ≥ 50% and dwell time > 2 weeks and a significant difference was found between dwell time > 2 weeks and filter tilt ≥ 15° or vena cava dilation rate ≥ 50%. Conclusions: Filter tilt ≥ 15°, hook wall apposition, vena cava dilation rate ≥ 50% and dwell time > 2 weeks were positively associated to the filter related thrombosis, and these factors were considered as the risk factor of the presence of filter thrombosis.

Keywords: Inferior vena cava filter, thrombosis, complication

Introduction

Venous thromboembolism (VTE) which is characterized by a blood clot formed in a vein deep in the body is a major medical problem worldwide. It is reported the annual incidence and mortality of VTE is about 1% and 6% [1], respectively, making it one of the most common and severe form cardiovascular diseases. Among patients with symptomatic VTE, approximately one third manifest pulmonary embolism (PE) [2, 3]. With the social aging, the increasing incidence of PE is expected. Therefore, effective measurements to prevent PE in VTE patients are urgently needed.

Anticoagulation, the standard treatment for VTE, is often used as the active treatment of thrombosis. However, it is infeasible in patient with anticoagulation contraindications or low extremity injuries [4]. Inferior vena cava (IVC) filter insertion is a safe and efficacy measure for preventing PE in such cases [5]. Moreover, novel retrievable IVC filters have developed to minimize the potential negative long-term effect of permanent IVC filter. However, with the increasing use of the filters, certain complications such as filter fracture, migration and perforation were also presented [6, 7]. According to the report by Corriere et al [8], the incidence of vena cava thrombosis was 12.5% in patients placed with retrievable IVC filters. However, little study has focus on the risk factor in filter related vena cava thrombosis.

The purpose of this retrospective study was to assess the risk factors associated with thrombosis after retrievable inferior vena cava filter placement.

Materials and methods

Patients

After obtaining approval from institutional review board of the second affiliated hospital of

Table 1. Patient demographic data

Variables	Patients (n = 164)
Age (years, mean [range])	55.6 (21-88)
Gender	
Male	106 (64.6%)
Female	58 (35.4%)
Comorbidities	
Lower extremity DVT	85 (51.8%)
Lower extremity DVT with PE	23 (14.0%)
Trauma	13 (7.9%)
Post-surgery	11 (6.7%)
Gynecological malignant tumor	10 (6.1%)
Lung cancer	7 (4.3%)
Digestive tract malignant tumor	4 (2.4%)
Intracerebral hemorrhage	4 (2.4%)
Gastrointestinal hemorrhage	4 (2.4%)
Anticoagulation	
Low molecular weight heparin calium	47 (28.7%)
None	117 (71.3%)

DVT: deep vein thrombosis.

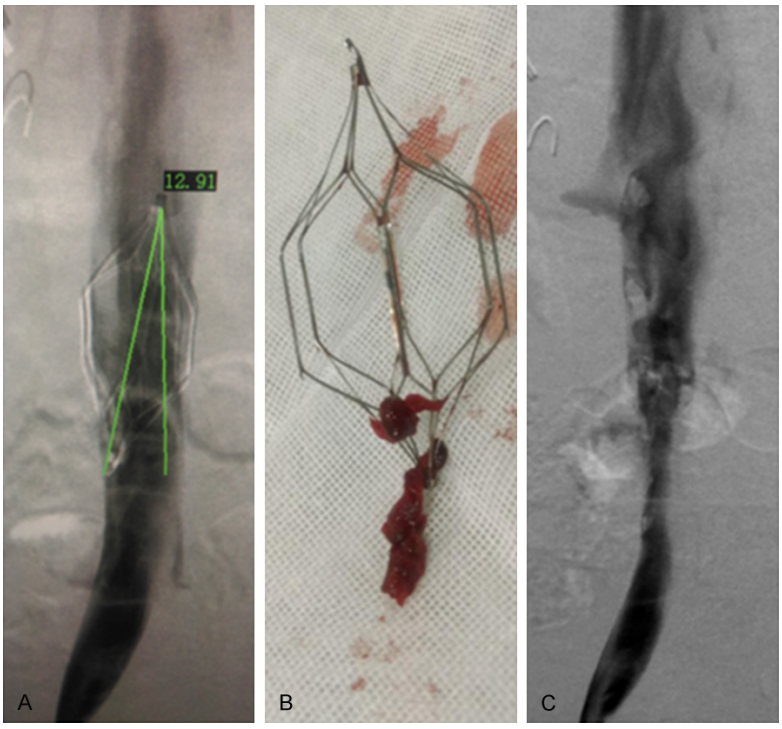

Figure 1. Vena cava thrombosis at the level of a filter. A. Venography before removal of retrievable inferior vena cava (IVC) filter. The tilt angle was 12.91°. Good filter hook wall apposition and a perfusion defect strip could be found on the right side of non-trapping zone. B. Attached thrombus was observed after removal of filter and the thrombus length was 13 mm. C. Venography after removal of filter. Stenosis with multiple perfusion defects (arrow) around the vessel wall was found at the location of filter placement, regional blood flow disorder was also found.

Nantong University, we performed a retrospective review in 164 consecutive patients who underwent IVC filter retrievals between June 2008 and June 2014. Of 164 patients, 106 (64.6%) were men and 58 (35.4%) were women, with a mean age of 55.6 years (range, 21-88 years). Patients were further classified by comorbidities, including 85 (51.8%) patients with low extremity DVT, 23 (14.0%) with low extremity DVT with PE, 13 (7.9%) with trauma, 11 (6.7%) with surgery, 10 (6.1%) with gynecological malignant tumor, 7 (4.3%) with lung cancer, 4 (2.4%) with digestive tract malignant tumor, 4 (2.4%) with intracerebral hemorrhage, 4 (2.4%) with gastrointestinal hemorrhage. In addition, anticoagulation with low molecular weight heparin calium (5000 U) was applied in 47 (28.7%) patients. Optic Patient demographics and medical comorbidities are listed in **Table 1**.

Filter placement was performed in patients with PE and/or DVT in the lower extremities, followed by catheter-directed thrombolysis (CDT) with urokinase (300-000-600000 U/day) for 7 days. The mean dwell time was 18.9 (10-56) days.

Methods

Parameter definition: Vena cave filter trapping region was defined as the zone from proximal segment of filter to the region comprised of distal segment of filter and vena cava wall. Digital Subtraction Angiography (Artis zee multipurpose system; Siemens Healthcare, Erlangen, Germany) was per-

Table 2. Association between filter characteristics and thrombus formation after retrievable inferior vena cava (IVC) filter

Characteristics	No thrombus (n=113)	Thrombus (n=51)	χ^2	*P* value
Tilt angle			75.3297	< 0.0001
Highest tilt angle < 15°	94 (83.2%)	6 (11.8%)		
Highest tilt angle ≥ 15°	19 (16.8%)	45 (88.2%)		
Filter hook wall apposition			88.4997	< 0.0001
Yes	11 (9.7%)	43 (84.3%)		
No	102 (90.2%)	8 (15.7%)		
Dwell time			49.9779	< 0.0001
≤ 2 weeks	109 (96.4%)	26 (51.0%)		
2-4 weeks	3 (2.7%)	17 (33.3%)		
≥ 4 weeks	1 (0.9%)	8 (15.7%)		
Dilation rate of filter			22.6106	< 0.0001
< 50%	101 (89.4%)	29 (56.9%)		
≥ 50%	12 (10.6%)	22 (43.1%)		
Anticoagulation			1.8198	0.177
Yes	36 (31.9%)	11 (21.6%)		
No	77 (68.1%)	40 (78.4%)		

Table 3. The length of thrombus according to the filter characteristics

Characteristics	Length of thrombus (mm)
Highest tilt angle ≥ 15° (n = 64)	8.6 ± 1.7 mm*
Filter hook wall apposition (n = 54)	5.3 ± 1.4 mm
Dwell time > 2 weeks (n = 29)	3.6 ± 0.9 mm
Dilation rate of filter ≥ 50%	10.1 ± 2.2 mm**

*p < 0.05 compared to those with highest tilt angle; **p < 0.01 compared to those with dilation rate of filter < 50%.

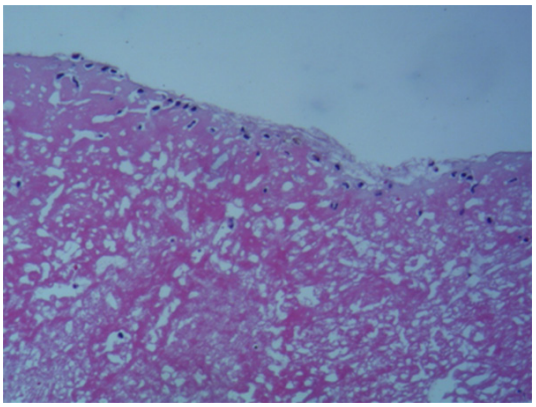

Figure 2. Hematoxylin-eosin (H&E) staining of thrombus (100×). Part of thrombus was covered with endothelial cells and intimal hyperplasia could be observed (arrow).

formed to identify the filter related thrombosis and perfusion defects in the non-trapping zone.

Attached thrombus was determined after removal of filter. The highest tilt angle was determined by measuring the angle between the central longitudinal axis of the filter and vena cava wall in the pictures captured by 3D-digital subtraction angiography (DSA). Filter hook wall apposition was noted when the hook was embedded in the caval wall. IVC dilation rate was determined as follows: (largest diameter of IVC after IVC filter placement-diameter of adjacent normal vessel)/diameter of adjacent normal vessel × 100%.

Filter retrieval: Retrieval was performed using. One day before retrieval, a B mode vena cava ultrasound (Philips, HD15 Pure Wave Ultrasound System, Bothell, WA) was performed to measure the largest diameter at site of filter placement and diameter of adjacent normal vena cava. A 10 Fr sheath is introduced into the femoral vein by the Seldinger technique. 3-D rotational DSA was then performed and 60 mL of contrast agent (Ioversol; Optiray 320; Mallinckrodt, St Louis, MO) was injected at 10 mL/s for 6 seconds to obtain the information about highest tilt angle, filter hook wall apposition and perfusion defect in the non-trapping region. A snare kit was used (Amplatz Goose Neck Snare Kit; ev3 Inc., Plymouth, MN, USA). After snaring the filter hook, the sheath was advanced over the filter and the device removed leaving the sheath to perform a control cavography. For the control cavography, 12 mL of contrast agent (Ioversol) was injected at 6 mL/s for 2 seconds to confirm the patency of the vessel and thrombus at the location of filter placement. After the sheath withdrawal and washed with 0.9% NaCl, the location, length of attached thrombus were determined and collected for pathological analysis. A scanning electron microscopy (SEM, Hitachi S-3400N, Tokyo, Japan) was employed to examine the surface of filter.

If the above retrieval technique failed, the buddy wire technique was applied. A stiff guide

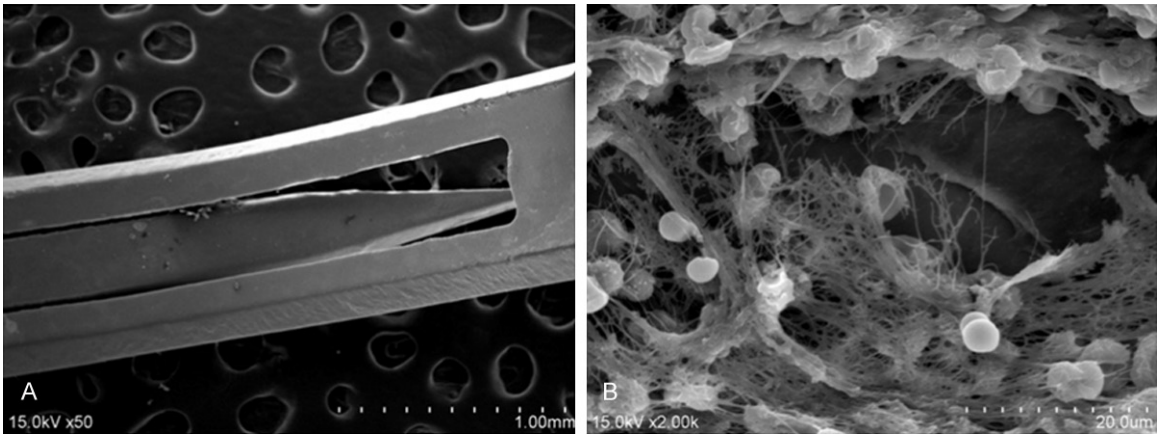

Figure 3. Scanning electron microscopy results. A large amount of fibrin and collagen was located on the surface of filter with embedded red cell. A. 50× Magnification; B. 2000× Magnification.

wire with the help of 5F catheter (Cobra; Cook) was used to catch the filter hooklet. After removal of the stiff buddy wire, the sheath is advanced over the filter while it is retained with the snare.

Statistical analysis

The measurement data and counting data was expressed as mean ± SD and number (percentage), respectively. The one wan ANOVA and Chi square test was used to analyze the difference in measurement data and counting data. All the statistical analysis was performed with SPSS 18.0 software (SPSS Inc. Chicago, IL). $P < 0.05$ was considered as statistical significance.

Results

Filter placement was performed in patients with DVT and/or PE in the lower extremities, followed by catheter-directed thrombolysis (CDT) with urokinase (300000-600000 U/day) for 7 days. The mean dwell time was 18.9 days, ranging from 10 to 56 days. The success rate of filter retrieval was 100% in this study.

Among 164 cases of filter retrieval, 64 (39.0%) cases were with the highest angle ≥ 15°, including 45 (70.3%) cases filter related thrombosis with a mean 8.6±1.7 mm length of thrombus. Filter hook wall apposition was found in 54 (32.9%) cases, including 43 (79.6%) filter related thrombosis with a mean 5.3±1.4 mm length of thrombus (**Figure 1**). Filter dwell time > 2 weeks was found in 29 (17.7%) cases, including 25 (86.2%) filter related thrombosis with a mean 3.6±0.9 mm length of thrombus. Vena cava dilation rate > 50% was presented in 34 (20.7%) cases, including 22 (64.7%) filter related thrombosis with a mean 10.1±2.2 mm length of thrombus. Compared to the no thrombus control group, significant differences were found on highest tilt angle ≥ 15°, filter hook wall apposition, filter dwell time > 2 weeks, vena cave dilation rate > 50% in patients with thrombosis ($P < 0.001$). No significant difference was found on filter related thrombosis between the patients with or without anticoagulation ($P = 0.177$) (**Table 2**). On the thrombus length, the patients with highest tilt angle ≥ 15° and vena cave dilation rate > 50% was significantly higher than in patients with filter dwell time > 2 weeks ($P < 0.05$) (**Table 3**).

Discussion

Although IVC filters are beneficial in PE prevention, the potential negative long-term effect has result in the development of retrievable IVC filter. Currently, many retrievable IVC filter have come to market, and most have exhibited excellent properties [9, 10]. However, occurrence of filter complications, such as migration, strut perforation through the IVC wall, fracture, and tip embedding, has reported in these filters [11]. In present study, our result demonstrated that filter tilt ≥ 15°, hook wall apposition, vena cava dilation rate ≥ 50% and dwell time > 2 weeks were positively associated to the filter related thrombosis, and we identified these factors as the risk factor of the presence of filter thrombosis.

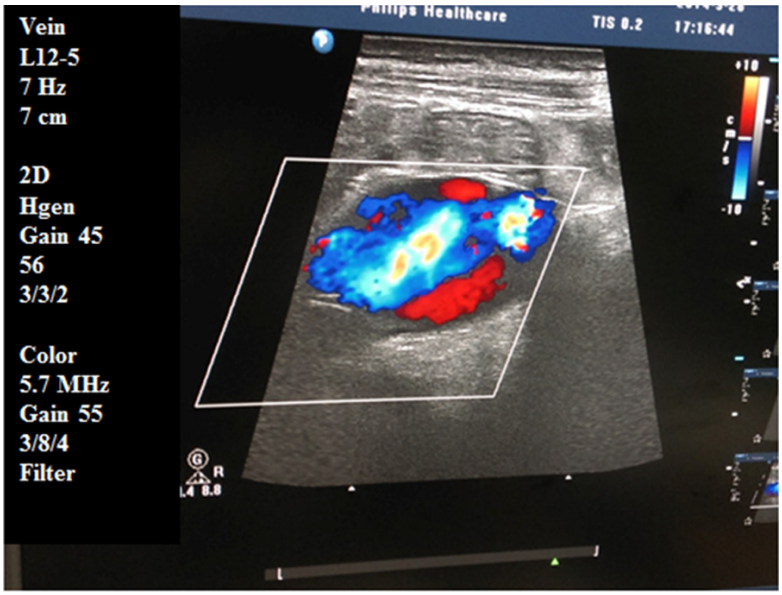

Figure 4. Color Doppler ultrasound of retrievable inferior vena cava (IVC) filter placement. Opposite (vortex flow, red) flow was found between the central longitudinal axis of the filter (axial flow, blue) and the dilated IVC wall.

In the patients with IVC filter insertion, the incidence of IVC thrombosis is between 1% and 32%. This variance is caused by multiple factors, including the type of filter, length of follow-up, degree of surveillance for thrombosis, and concurrent use of prophylactic anticoagulation therapy [6, 12, 13]. In this study, the incidence of IVC thrombosis was 31.1% (51/164), which is a relative high number. We attributed the reasons as follows: 1. There is no consensus on the criteria of filter thrombosis. Here, we defined the thrombosis as the perfusion defect in non-trapping region according to DSA imaging or the attached thrombus after removal of the filter. The presence of trapped thrombus in filter could result in inaccurate results. 2. The type of filter. In this study, we used the OptEase retrieval IVC filter and inverted conical design of these filters marginates captured thrombus to the wall of the cava where flow is the lowest and may predispose to thrombosis [14, 15]. 3. Other factors such as differences in patient populations, selection criteria for filter insertion, duration of follow-up, management of anticoagulation, and technical factors may also attribute to the results.

Minimizing tilt angle plays an important role in quality improvement [16] and ongoing filter design modification, highlighting the concern that excessive tilt can theoretically compromise filtration of embolic materials [17, 18]. As higher tilt angle could lead to closer apposition of the filter tip to the IVC wall, resulting in greater difficulty in filter retrieval [19] and increased risk of tip incorporation into the IVC wall [20], a close relationship between tilt and embedding has been suggested. In this study, 64 (39.0%) patients were presented with highest tilt angle ≥ 15° with a significantly increased incidence (70.3%) of thrombus compared to the patient with highest tilt angle < 15°. By using 3D DSA, the tilt angle could be determined by 360° measurement, which could minimize the measurement error by a single detection [21]. The filter hook wall apposition was presented in 32.9% of the patients, resulting in a 79.6% filter thrombus. Endothelial injury caused by the tip incorporation into the vessel wall could increase the incidence of thrombosis and intimal hyperplasia. According to the pathological analysis of thrombus, intimal hyperplasia was actually existed (**Figure 2**). The SEM results showed that the filter was covered with large amount of fibrin and collagen (**Figure 3**). Vena cave dilation ≥ 50% is another important factor for thrombosis. Over dilation of the vessel by the filter could lead to the filter embedding into the vessel wall and blood flow retardation, eventually resulting in thrombosis (**Figure 4**). In addition, in the patients with filter dwell time > 2 weeks, thrombosis was found in 86.2% with a shortest mean length of 3.6 ± 0.9 mm among all the risk factors, and the distribution of thrombus was mainly on the tip or interconnection part of the filter. We did not observe a significant difference between patients with or with our anticoagulation ($P > 0.05$) and the reason may attribute to the ineffective anticoagulation with heparin.

There are also some limitations in our study. Relative small number of patients could result in conclusion bias on the results. The properties of retrospective review of this study could

lead to incomplete information on the follow-up and long-term effect, and what we presented here were only eventual results. Furthermore, varying levels of experience of interventional radiologists could also influence the outcome of complicated retrievals.

In conclusion, increased filter tilt, hook wall apposition, increased vena cava dilation rate and longer dwell time are factors associated with IVC filter related thrombosis. Awareness of these factors prior to retrieval attempt maybe used to optimize retrieval approach and set appropriate patient expectations. In addition, large sample study with multiple variable analyses should be performed in the near future to confirm the conclusion conducted here.

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Disclosure of conflict of interest

None.

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References

[1] Augustinos P and Ouriel K. Invasive approaches to treatment of venous thromboembolism. Circulation 2004; 110: I27-34.

[2] Imberti D, Ageno W, Manfredini R, Fabbian F, Salmi R, Duce R and Gallerani M. Interventional treatment of venous thromboembolism: a review. Thromb Res 2012; 129: 418-425.

[3] White RH. The epidemiology of venous thromboembolism. Circulation 2003; 107: I4-8.

[4] Hoff WS, Hoey BA, Wainwright GA, Reed JF, Ball DS, Ringold M and Grossman MD. Early experience with retrievable inferior vena cava filters in high-risk trauma patients. J Am Coll Surg 2004; 199: 869-874.

[5] Rosenthal D, Swischuk JL, Cohen SA and Wellons ED. OptEase retrievable inferior vena cava filter: initial multicenter experience. Vascular 2005; 13: 286-289.

[6] Athanasoulis CA, Kaufman JA, Halpern EF, Waltman AC, Geller SC and Fan CM. Inferior vena caval filters: review of a 26-year single-center clinical experience. Radiology 2000; 216: 54-66.

[7] Ferris EJ, McCowan TC, Carver DK and McFarland DR. Percutaneous inferior vena caval filters: follow-up of seven designs in 320 patients. Radiology 1993; 188: 851-856.

[8] Corriere MA, Sauve KJ, Ayerdi J, Craven BL, Stafford JM, Geary RL and Edwards MS. Vena cava filters and inferior vena cava thrombosis. J Vasc Surg 2007; 45: 789-794.

[9] Binkert CA, Drooz AT, Caridi JG, Sands MJ, Bjarnason H, Lynch FC, Rilling WS, Zambuto DA, Stavropoulos SW, Venbrux AC and Kaufman JA. Technical success and safety of retrieval of the G2 filter in a prospective, multicenter study. J Vasc Interv Radiol 2009; 20: 1449-1453.

[10] Lyon SM, Riojas GE, Uberoi R, Patel J, Lipp ME, Plant GR, De Gregorio MA, Gunther RW, Voorhees WD and McCann-Brown JA. Short- and long-term retrievability of the Celect vena cava filter: results from a multi-institutional registry. J Vasc Interv Radiol 2009; 20: 1441-1448.

[11] Nicholson W, Nicholson WJ, Tolerico P, Taylor B, Solomon S, Schryver T, McCullum K, Goldberg H, Mills J, Schuler B, Shears L, Siddoway L, Agarwal N and Tuohy C. Prevalence of fracture and fragment embolization of Bard retrievable vena cava filters and clinical implications including cardiac perforation and tamponade. Arch Intern Med 2010; 170: 1827-1831.

[12] Fox MA and Kahn SR. Postthrombotic syndrome in relation to vena cava filter placement: a systematic review. J Vasc Interv Radiol 2008; 19: 981-985.

[13] Schleich JM, Morla O, Laurent M, Langella B, Chaperon J and Almange C. Long-term follow-up of percutaneous vena cava filters: a prospective study in 100 consecutive patients. Eur J Vasc Endovasc Surg 2001; 21: 450-457.

[14] Leask RL, Johnston KW and Ojha M. Hemodynamic effects of clot entrapment in the TrapEase inferior vena cava filter. J Vasc Interv Radiol 2004; 15: 485-490.

[15] Couch GG, Johnston KW and Ojha M. An in vitro comparison of the hemodynamics of two inferior vena cava filters. J Vasc Surg 2000; 31: 539-549.

[16] Caplin DM, Nikolic B, Kalva SP, Ganguli S, Saad WE and Zuckerman DA. Quality improvement guidelines for the performance of inferior vena cava filter placement for the prevention of pulmonary embolism. J Vasc Interv Radiol 2011; 22: 1499-1506.

[17] Kinney TB, Rose SC, Weingarten KE, Valji K, Oglevie SB and Roberts AC. IVC filter tilt and

asymmetry: comparison of the over-the-wire stainless-steel and titanium Greenfield IVC filters. J Vasc Interv Radiol 1997; 8: 1029-1037.
[18] Shelgikar C, Mohebali J, Sarfati MR, Mueller MT, Kinikini DV and Kraiss LW. A design modification to minimize tilting of an inferior vena cava filter does not deliver a clinical benefit. J Vasc Surg 2010; 52: 920-924.
[19] Geisbusch P, Benenati JF, Pena CS, Couvillon J, Powell A, Gandhi R, Samuels S and Uthoff H. Retrievable inferior vena cava filters: factors that affect retrieval success. Cardiovasc Intervent Radiol 2012; 35: 1059-1065.
[20] Stavropoulos SW, Dixon RG, Burke CT, Stavas JM, Shah A, Shlansky-Goldberg RD and Trerotola SO. Embedded inferior vena cava filter removal: use of endobronchial forceps. J Vasc Interv Radiol 2008; 19: 1297-1301.
[21] Jou LD, Mohamed A, Lee DH and Mawad ME. 3D rotational digital subtraction angiography may underestimate intracranial aneurysms: findings from two basilar aneurysms. AJNR Am J Neuroradiol 2007; 28: 1690-1692.