A Cohort Study of Inferior Vena Cava Thrombosis in Taiwan: An Under-recognized Entity

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Research

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Abstract

Background: Inferior vena cava thrombosis (IVCT) is a rare clinical condition. Herein, we report eight cases of IVCT in Taiwanese patients.

Methods: Eight Taiwanese patients diagnosed with IVCT between May 2012 and December 2019 were included in this study. The patients' demographics, presenting characteristics, additional sites of venous thromboembolism, extent of IVCT, prothrombotic risk factors, and IVCT-related adverse events were evaluated.

Results: All eight patients with IVCT presented with other coexisting venous thromboembolic manifestations, such as deep venous thrombosis (DVT, 100%) or pulmonary embolism (62.5%). The clinical presentations, including DVT in both lower extremities coexisting with the dilatation of the superficial veins of the abdominal wall (50%), were reported. No congenital anomalies of the inferior vena cava (IVC) were noted. Various thromboembolic risk factors, such as unretrieved IVC filters (25%), pregnancy (37.5%), lupus anticoagulants (37.5%), surgery (25%), antithrombin deficiency (12.5%), hemoglobin H disease (12.5%), and essential thrombocythemia (12.5%), were identified. All patients were administered anticoagulants. One patient (12.5%) developed post-thrombotic syndrome. No mortality was reported in our cohort.

Conclusions: This is the first report of IVCT in Taiwanese patients. Typical clinical features of IVC occlusion coexisting with predisposing factors of venous thrombosis, such as lupus anticoagulants, pregnancy, or unretrieved IVC filters, could indicate a diagnosis of IVCT. Moreover, IVCT presenting as a complication resulting from the unretrieved IVC filter was observed, highlighting the potential risks of chronic indwelling filters.

Background

Inferior vena cava thrombosis (IVCT) is a clinically rare condition [1]. According to the United States National Hospital Discharge Survey, vena cava thrombosis (presumed to be predominantly IVCT) accounted for only 1.3% of all hospitalized patients who were diagnosed with venous thrombosis between 1979 and 2005 [2]. In Asia, a low incidence of IVCT is plausible, as lower risk and incidence of venous thromboembolism (VTE) in the Asian ethnic population have been demonstrated [3]. However, the true incidence of IVCT could be underestimated due to a lack of standardized detection methods and insufficient clinical awareness. Therefore, IVCT may be an under-recognized entity owing to its uncommon occurrence.

Although IVCT is not commonly identified, the associated acute or chronic complications are significant and alarming. They include post-thrombotic syndrome (90%), venous claudication (45%), pulmonary embolism (PE) (30%), and venous ulceration (15%) [4]. Furthermore, the mortality rate of IVCT has been reported to be two-fold higher than that of deep vein thromboses confined to the lower extremities. This implies that the consequences of IVCT can be serious [5]. Cautious clinical identification followed by adequate anticoagulant treatment can decrease IVCT-associated morbidity and mortality. Hence, this specific VTE entity must be recognized and addressed.

Since 2010, IVCT has become an emerging issue. The United States Food and Drug Administration (FDA) released an inferior vena cava (IVC) filter-related device safety communication. It indicated the potential risk of IVC filter-related complications [6], including IVCT. The FDA also recommended that the implanting physicians and clinicians responsible for the ongoing care of patients with retrievable IVC filters should consider removing the filter as soon as protection from PE is no longer required [7]. This is to reduce the risks associated with chronic indwelling IVC filters.

In this study, eight Taiwanese patients from two medical centers diagnosed with IVCT were enrolled, including two patients who presented with complications after implantation of unretrieved IVC filters. The primary clinical information, coexisting thrombotic risk factors, additional sites of venous thrombosis, and treatment outcomes were investigated.

Patients And Methods

Eight patients diagnosed with IVCT between May 2012 and December 2019 at the Changhua Christian Hospital and National Taiwan University Hospital were included in this study. All laboratory tests and radiological imaging examinations were performed as part of routine clinical evaluations. The patients were classified into the following two groups based on the etiology of the IVCT: those with IVCT that occurred de novo and those with IVCT resulting from prior IVC filter implantation. Patient demographics, presenting characteristics, additional sites of venous thrombosis, location with the extent of the IVCT, treatment outcome, and related adverse events were investigated. Furthermore, two patients who did not develop IVCT were included as controls. These patients initially had IVC filters that were later retrieved. All patients provided informed consent to participate in this study, and the research was conducted in accordance with the Declaration of Helsinki.

Results

In our cohort, out of the eight patients with IVCT, three were men and five were women. Their ages ranged from 30 to 54 years (median age, 35.5 years). DVT associated with unilateral lower extremity swelling was detected in four patients (in the left lower extremity in two patients, and in the right lower extremity in the other two patients). Bilateral lower extremity swelling was detected in the remaining four patients who also presented with dilatation of the superficial veins of the abdominal wall. Five patients were found to have PE. Collateral circulation within the abdomen was observed in six patients. The clinical presentations, extent of the IVCT, and risk factors are summarized in Table 1.

Table 1

Clinical presentation and characteristics of Taiwanese patients with inferior vena cava thrombosis and inferior vena cava filter placement

Patient no.	Age (year)	Sex	Main clinical presentation		Site of thrombosis					Collaterals inside the abdomen	Risk factors
			Swelling of LE	Dilatation of SAV	IVC	IVs	PDV	DDV	PE		
De novo inferior vena cava (IVC) thrombosis											
1	30	F	L + R	Present	IHCT	L + R	L + R	L + R	(+)	Present	ET + pregnancy
2	35	M	L + R	Present	IHCT	L + R	L + R	(-)	(+)	Present	LA
3	32	F	L	None	IRPT	(-)	L	L	(-)	None	LA + pregnancy + surgery
4	36	F	L	None	IRPT	L	L	(-)	(-)	None	Surgery
5	54	F	L + R	Present *	IRCT	L + R	L + R	L + R	(-)	Present	Unknown
6	32	M	R	None	IRCT**	R	R	R	(+)	Present	AT deficiency
IVC thrombosis after IVC filter placement											
7	38	M	L + R	Present	IRCT	L + R	L + R	(-)	(+)	Present	LA + IVC filter
8	46	F	R	None	IRPT	(-)	R	R	(+)	Present	Hb H disease + pregnancy + IVC filter
Preventive IVC filter placement without occurrence of IVC thrombosis											
9+	57	M	L + R	None	(-)	(-)	(+)	(+)	(+)	None	Surgery
10+	57	M	R	None	(-)	(-)	(+)	(+)	(-)	None	Unknown

Clinical pictures of 10 patients with inferior vena cava thrombosis and IVC filter implantation seen at Changhua Christian Hospital and National Taiwan University Hospital

LE, lower extremity; SAV, superficial abdominal wall vein; IVC, inferior vena cava; IVs, iliac veins; PDV, proximal deep vein; DDV, distal deep vein; PE, pulmonary embolism; F, female; M, male; R, right; L, left; IHCT, infrahepatic complete thrombosis; IRCT, infrarenal complete thrombosis; IRPT, infrarenal partial thrombosis; ET, essential thrombocythemia; LA, lupus anticoagulant; AT, antithrombin.

*Also experienced abdomen pain

** IVC thrombosis was detected 9 days prior to implantation of the IVC filter

⁺IVC filter was removed on Jan 24, 2019 and in 2018

No congenital IVC anomalies were detected in our cohort. Prior placement of an IVC filter was found to be an important risk factor for IVCT (25%). Other VTE risk factors, including pregnancy (37.5%), presence of lupus anticoagulants (37.5%),

surgery (25%), essential thrombocythemia (12.5%), antithrombin deficiency (12.5%), and hemoglobin H disease (12.5%), were observed in our cohort. No known risk factors were identified in one patient. Four patients had more than one prothrombotic risk factor.

We evaluated the association between the filters and IVCT. Two patients developed IVCT as a complication of prior placement of an unretrieved IVC filter, and PE was detected in both patients. De novo IVCT was found in the other six patients, including one (patient 6) who experienced IVCT and was subsequently treated with an IVC filter implantation at 9 days later. In addition, two other patients (patients 9 and 10) received retrievable IVC filters to prevent PE. These filters were eventually retrieved. Neither patient experienced an IVCT nor a PE during the follow-up period.

All patients with IVCT in this study received anticoagulants. One patient (patient 6) underwent both catheter-directed mechanical thrombectomy and IVC filter placement. The decision of which investigational methods were used during IVCT treatment was made by the attending physician. One patient developed post-thrombotic syndrome (12.5%). No IVCT-related mortality was reported in our cohort.

The clinical presentation and characteristics of one patient with IVCT in this study are briefly described below.

Patient 7 was a 38-year-old man. He experienced VTE with repeated episodes of painful swelling in his right lower extremity, accompanied by upper back pain and cough. He was diagnosed with DVT and PE. Treatment with anticoagulants was initiated. An IVC filter was placed after the second VTE event. However, 6 months after filter placement, he had swelling in both lower extremities. The superficial veins of the abdominal and chest walls were also dilated. Retrieval of the filter was attempted twice; however, it was unsuccessful. A positive result for lupus anticoagulant was the only significant finding from the thrombotic screening tests. Compression ultrasonography revealed a partial thrombosis in both common femoral veins, superficial femoral veins, and popliteal veins. Computed tomography revealed a complete thrombosis in the infrarenal IVC with the presence of an IVC filter and blood clots within both iliac veins. Collateral circulation was present (Fig. 1).

Discussion

This study analyzed eight Taiwanese patients with IVCT. To the best of our knowledge, this is the first report that has examined the presentation and characteristics of IVCT in Taiwanese patients.

Based on the pathogenesis of VTE, IVCT could be caused by congenital or acquired abdominal pathophysiological changes combined with the presence of various prothrombotic factors. Venous thrombus formation tends to increase if congenital IVC anomalies are present. A recent systemic review reported that congenital IVC anomalies, with a weighted prevalence of 6.8%, could lead to a 50- to 100-fold increase in the risk of DVT [8]. However, no congenital IVC anomaly was detected in our cohort, as only a limited number of adult cases were enrolled.

With respect to IVCT-affiliated VTE manifestation, all our patients had DVT, while five (62.5%) also had PE. Typical clinical features of IVCT include bilateral lower extremity DVT, scrotal swelling, unexplained back pain, pelvic pain, and renal failure [9–12]. Most of these features were present in this cohort. When coexisting with predisposing factors, such as a congenital IVC anomaly or prior placement of an unretrieved IVC filter, these classic presentations strongly indicate the probability of IVCT. Furthermore, four of our patients presented with bilateral lower extremity swelling (due to DVT) simultaneously with abdominal wall superficial venous dilatation. This is a pathognomonic manifestation of IVCT, based on our experience and the reports of other studies [9]. In addition, six patients developed collateral circulation within the abdomen, indicating the chronically long-standing nature of their condition.

Various risk factors for VTE were observed in our patients. Specifically, two patients developed IVCT after an IVC filter implantation was not removed. The complication did not occur in the other two patients whose filters were later retrieved. Our data confirmed the emerging risk of IVCT as a potential complication after an un retrieved IVC filter placement in

Taiwanese patients. This corresponds to accumulating evidence from other Asian countries with a reported long-term lower risk of VTE [13–15]. Our experience also indicates that the identification of IVCT in Taiwan should no longer be an under-recognized issue. The incidence could be raised due to the potential hazards of the increasing use of IVC filters.

The effectiveness of IVC filters in preventing PE in patients with VTE remains controversial and inconclusive. According to the PREPIC study [16], an IVC filter was shown to have the potential benefit of protecting against short-term PE (at 12 days, 1.1% with PE in the filter group versus 4.8% in the no-filter group, $p = 0.03$). However, it had a higher risk of symptomatic DVT in the long term (at 2 years, 20.8% in the filter group vs. 11.6% in the no-filter group, $p = 0.02$). However, according to the study, there was no difference in the mortality rates during the 8-year follow-up [17]. Furthermore, increased mortality and incidence of subsequent DVT were observed in patients with IVC filters, according to the American Society of Hematology (ASH) 2020 guidelines for the management of venous thromboembolism [18]. This contained an evaluation of seven systemic reviews and two randomized trials, indicating low confidence in the evidence for IVC filter efficacy. A similar conclusion of insufficient evidence to support IVC filter effectiveness was also reported from the National Institutes for Health and Care Excellence (NICE) review in 2020 [19].

The American College of Chest Physicians (ACCP) 2016 guidelines recommended the use of an IVC filter in patients with acute proximal DVT but in whom anticoagulants are contraindicated, such as those with active uncontrollable bleeding [20]. It is also considered reasonable that IVC filters be used for those thromboembolic patients in whom anticoagulation is perceived to have failed [21]. However, ACCP advises against the initial use of an IVC filter in addition to anticoagulants in patients with acute DVT of the leg [20]. This is primarily due to the efficacy and safety concerns regarding IVC filters. A similar recommendation was also advocated by the ASH guidelines [18]. In our opinion, the application of filter devices in clinical thrombotic conditions without approved indications, such as prophylactic use in patients without a history of PE, should be strongly discouraged. Moreover, a low retrieval rate after the placement of retrievable types of filters has further aggravated real-world adverse event-related conditions [22].

Various significant complications related to indwelling IVC filters have been noted [23], including thrombus formation related to the filter. The incidence of permanent filter-associated IVCT is approximately 13% after 8 years of follow-up [17]. Filter-related thromboembolism is known to be a complicated process and may be influenced by various filter types and designs, patient-specific underlying conditions, such as pregnancy or malignancy, and the intrinsic thrombogenicity of the device. A filter thrombus can be formed from entrapped emboli within the filter. Besides, the filter could induce thrombus formation, as it is a foreign body. A thrombus could also be formed by the extension of DVT to the veins of the lower extremities and iliac veins. Therefore, IVC filters should be judiciously used and retrieved whenever possible.

The goals of treating IVCT include reducing the risk of PE, decreasing chronic complications such as post-thrombotic syndrome, and decreasing venous insufficiency and the related symptoms. The management of IVCT consists of in-time administration of anticoagulants, if not contraindicated. Catheter-directed thrombolysis or thrombectomy may have rapid direct thrombolytic advantages [24], while percutaneous transluminal angioplasty with a stent may also be a reasonable choice [25]. The advantage of the investigational clot-removal strategy is to reduce post-thrombotic syndrome, although it is dependent on the physician's experience.

Conclusion

Eight cases of IVCT in Taiwanese patients were reported, although IVCT in Taiwan is uncommon. All patients had DVT, and the majority (62.5%) had PE. Typical clinical manifestations associated with IVCT, including bilateral lower extremity DVT coexisting with superficial abdominal wall dilatation (in four of our patients), were reported. Moreover, various VTE risks were demonstrated. Two patients presented with complications after the placement of unretrieved IVC filters, highlighting the potential risks of IVCT associated with chronic indwelling filters.

Abbreviations

ACCP American College of Chest Physicians

ASH American Society of Hematology

DVT Deep venous thrombosis

FDA Food and Drug Administration

IVC Inferior vena cava

IVCT Inferior vena cava thrombosis

NICE National Institutes for Health and Care Excellence

PE Pulmonary embolism

VTE Venous thromboembolism

Declarations

Ethics approval and consent to participate:

All patients provided informed consent to participate in this study, and the research was conducted in accordance with the Declaration of Helsinki. The study design was approved by the ethics review board of Changhua Christian Hospital.

Consent for publication:

All patients provided informed consent for the publication of this study.

Availability of data and materials:

All data generated or analyzed during this study are included in this published article.

Competing interests:

The authors declare that they have no competing interests.

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Authors' contributions:

HY and CY collected and interpreted the patient data. MC proposed the study design and supervised the entire study process. HY was a major contributor to the writing of the manuscript. All authors have read and approved the final manuscript.

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Figures

Figure 1

Bilateral lower extremity DVT and IVC thrombosis occurred in a 38-year-old man. (A) Computed tomography demonstrated a filter bearing IVC thrombosis. In the follow-up at 21 months (B) and 33 months (C) later, computed tomography revealed a

residual thrombosis. DVT, deep venous thrombosis; IVC, inferior vena cava