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# Dilemmas in anticoagulation and use of inferior vena cava filters in venous thromboembolism; a survey of Respiratory Physicians, Haematologists and Medical Oncologists and a review of the literature

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## Abstract

Twenty percent of patients with Cancer Associated Thrombosis receive an inferior vena cava filter annually. Insertion is guided by practice guidelines, which do not specify or discuss the use of inferior vena cava filters in malignancy. Adherence to these guidelines is known to be variable. We aimed to see if there was consistent management of venous thromboembolism among Medical Oncologists/Haematologists and Respiratory Physicians, with respect to inferior vena cava filter use in the setting of suspected and confirmed malignancy. Medical Oncologists, Haematologists and Respiratory Physicians were surveyed with four theoretical cases. Case 1 concerns a patient who develops a pulmonary embolism following spinal surgery. Cases 2 and 4 explore the use of inferior vena cava filters in the setting of malignancy. Case 3 covers the role of inferior vena cava filters in recurrent thrombosis despite systemic anticoagulation. There were 56 responses, 32 (57%) Respiratory Physicians and 24 (43%) Haematologists/Oncologists. Respiratory Physicians were significantly more likely to insert an inferior vena cava filter in case 1 ( $p = 0.04$ ) whilst Haematologists/Medical Oncologists were more likely to insert an inferior vena cava filter in case 3 ( $p = 0.03$ ). No significant differences were found in cases 2 and 4. There were significant disparities in terms of type and timing of anticoagulation. Consistency of recommendations with guidelines was variable likely in part because guidelines are themselves inconsistent. The heterogeneity in responses highlights the variations in venous thromboembolism management, especially in Cancer Associated Thrombosis. International Societies should consider addressing inferior vena cava filter use specifically in the setting of Cancer Associated Thrombosis. Collaboration between interested specialities would assist in developing consistent, evidence-based guidelines for the use of inferior vena cava filters in the management of venous thromboembolism.

## Keywords

Thrombosis, cancer, anticoagulants, pulmonary embolism

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## Introduction

Venous thromboembolism (VTE) is a potentially lethal event. Systemic anticoagulation is the main modality of treatment. Inferior vena cava filters (IVCFs) may be used as an adjunct to anticoagulation or when anticoagulation is contraindicated.

The development of retrievable IVCFs led to increased use when compared to permanent IVCFs.<sup>1,2</sup> Few prospective

controlled studies, with limited quality of evidence, exist regarding the efficacy and safety of IVCFs.<sup>3</sup> Guidelines published by different international societies are inconsistent,

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with no recommendations made for IVCFs and Cancer Associated Thrombosis (CAT) (Fig. 1).<sup>4-11</sup>

In 2010, after reviewing 921 adverse events over a five-year period, the US Food and Drug Administration (FDA) issued a safety statement recommending ‘that implanting physicians and clinicians responsible for the ongoing care of patients with retrievable IVCFs consider removing the filter as soon as protection from pulmonary embolism is no longer needed’.<sup>12</sup> This resulted in a fall in the rate of IVCF placement.<sup>2</sup> Retrievable IVCFs result in more frequent complications than their permanent counterparts with complication rates directly linked to the length of time the IVCF remains in situ.<sup>13</sup>

The burden of VTE in malignancy is high, with VTE accounting for approximately 9% of cancer deaths.<sup>14</sup> Furthermore, patients with CAT tend to have more advanced cancer correlating to an increased bleeding risk and a higher rate of recurrent VTE, both of which are considerations for IVCF insertion.<sup>8,9,15,16</sup> It is estimated that 30,000–40,000 filters are deployed annually in patients with malignancy in the US alone,<sup>17</sup> accounting for over 30% of total IVCF placements.<sup>2</sup> In one study, 25% of patients diagnosed with a Pulmonary Embolism (PE) in association with a solid organ malignancy received an IVCF.<sup>18</sup> The most common reason provided for their use was a contraindication to

Guidelines	ACCP	SIR/ACR	AHA	CIRSE	BCSH
1. Acute DVT/PE with contraindication to Anticoagulation	✓	✓	✓	✓	✓
2. Failure of Anticoagulation					
a. Recurrent/progressive DVT despite Anticoagulation	ND	✓	ND	ND	ND
b. Recurrent PE despite anticoagulation	ND	✓	✓	✓	✓ ¶
c. Inability to achieve/maintain adequate anticoagulation	ND	✓	ND	✓	ND
3. Massive PE with residual DVT	ND	✓	✓	✓	ND
4. Free floating ileofemoral or inferior vena cava thrombus	ND	ND	ND	✓	✗
5. Severe cardiopulmonary disease and DVT (e.g. pulmonary hypertension, cor pulmonale)	ND	✓	ND	✓	ND
6. Prophylactic use, in patients without documented DVT/PE at high risk of developing DVT/PE and/or complications from anticoagulation	✗	✓	ND	✓	ND
¶ - only after increasing INR or switching to LMWH			NM =Not Discussed		
✗ - Not recommended			✓ Recommended		
American College of Chest Physicians (ACCP), American Heart Association (AHA), British Committee for Standards in Haematology, Cardiovascular and Interventional Radiology Society of Europe (CIRSE) and American College of Radiology/Society of International Radiology (ACR/SIR).					

**Fig. 1.** Summary of recommendations for IVCF insertion from international societies. BCSH: British Committee for Standards in Haematology; LMWH: low molecular weight heparin.

anticoagulation (39%); however, no indication was documented in 23%.

We have previously published our experience with IVCF use at our centre where we found a preponderance of use outside established guidelines.<sup>19</sup> This drove our interest in understanding how Australian specialists approached common clinical dilemmas around IVCF use in VTE.

## Methods

We surveyed specialists involved in VTE management on four fictional cases adapted from patients seen in our hospital to ascertain whether there was a consistency in the clinical approach and how closely this aligned with existing guidelines (Fig. 2).

## Survey development

Based on the available guidelines for the use of IVCFs, four cases were created, each with a series of multiple-choice questions. The scenarios presented were designed to consider the type and timing of anticoagulation and/or whether IVCFs would be recommended, including situations in which the guidelines may be considered to provide conflicting recommendations (supplementary Appendix A).

Broadly the cases may be summarised as follows:

1. A patient following cervical laminectomy who develops a symptomatic PE and Deep Vein Thrombosis (DVT) three days post operatively – presenting a conflict between the risk of bleeding and the need for urgent anticoagulation.

<b>Case 1</b>	A 70-year-old man underwent an uncomplicated anterior cervical laminectomy procedure. Day 3 post-operatively, he develops pleuritic chest pain, hypoxia (SaO <sub>2</sub> 91% on room air) however he remains hemodynamically stable. His VTE prophylaxis is calf compressors only. A CTPA shows bilateral subsegmental PE. A Doppler USS shows a left sided above knee DVT, extending from the popliteal to distal femoral veins. The surgeon is reluctant to start full dose anticoagulation.
<b>Case 2</b>	A 55-year-old female, underwent a staging CT of her Chest Abdomen and Pelvis, following diagnosis of a cystic ovarian mass during abdominal US. Incidental finding of small bilateral segmental PE. Doppler USS: Bilateral below knee DVTs. She is treated with Dalteparin (200iu/kg). The surgeon wants to perform a total abdominal hysterectomy, bilateral salpingoophorectomy and debulking of the tumour as soon as possible.
<b>Case 3</b>	A 63-year-old female is diagnosed with a first episode of a right lower limb DVT extending from the posterior tibial veins to 4 cm above the knee. She is treated with Rivaroxaban 15mg BD for 21 days then 20mg once daily. 5 weeks later, she is admitted to hospital with shortness of breath and pleuritic chest pain. A CTPA shows bilateral filling defects in the main pulmonary arteries, with a moderate thrombotic burden bilaterally.
<b>Case 4</b>	A 76-year-old male with metastatic colorectal adenocarcinoma is found on routine surveillance to have a large PE at the bifurcation of the pulmonary arteries. He is asymptomatic, not hypoxic and has no haemodynamic compromise. A Bilateral Doppler USS of his lower limbs is performed showing; Bilateral DVT's - a 10cm above knee DVT on the right and 11cm below knee DVT on the left

**Fig. 2.** Case descriptions.  
VTE: venous thromboembolism.

2. A patient with a recently diagnosed gynaecological malignancy who develops a PE before a planned procedure – highlighting the perioperative management of known recent VTE in association with need for semi-urgent surgical resection of a malignancy.
3. A patient with recurrent VTE despite adequate anticoagulation – highlighting anticoagulation in recurrent VTE and need for further investigation for occult malignancy.
4. A patient with known metastatic malignancy with extensive VTE (both a large PE and extensive DVT) on myelosuppressive chemotherapy – highlighting therapeutic options, including type of anticoagulation and potential use of IVCF.

### Survey distribution

Ethical approval was obtained from the St John of God Human Research Ethics Committee. The survey was then circulated electronically to Respiratory Physicians, Medical Oncologists and Haematologists at major teaching hospitals in Western Australia, New South Wales and Victoria, via heads of departments of several institutions.

### Statistical analysis

Odds ratio, for inserting an IVCF compared with choosing not to, are reported with their 95% confidence interval from separate univariable logistic regression models. All analyses were conducted using Stata v 15.0. A  $p$  value of  $<0.05$  was considered statistically significant.

## Results

There were 56 complete survey responses from 32 Respiratory Physicians (57%) and 24 Haematologists/Medical Oncologists (43%) with a response rate of 66%. All Haematologists surveyed had an interest in thrombosis.

### Case 1: symptomatic PE and DVT three days post cervical laminectomy

Of the physicians surveyed, half chose to prescribe anticoagulation immediately, with half choosing to delay anticoagulation. Intravenous (IV) heparin was the most commonly prescribed anticoagulant. Thirty physicians (56%) chose to insert an IVCF, all retrievable and to be removed within six months (Table 1).

Those who delayed anticoagulation were eight times more likely to insert an IVCF than those who were anticoagulated immediately ( $p < 0.05$ ).

### Case 2: development of PE before a planned procedure for gynaecologic malignancy

Thirty-seven physicians (66%) recommended deferring the surgery for 1–3 weeks, with a further 19 (34%) respondents

recommending delaying the surgery for 4–6 weeks. Twenty-one (38%) (13 Respiratory/8 Haematologist/Oncologists) recommended the insertion of an IVCF (Table 1). Numerically clinicians recommending deferred surgery were more likely to recommend IVCF insertion, but this did not reach statistical significance ( $p = 0.277$ ) (Table 2).

### Case 3: recurrent VTE despite adequate anticoagulation

The majority of respondents (82%) chose to switch the patient to low-molecular-weight heparin (LMWH,  $n = 46$ ) either immediately ( $n = 29$  (63%)) or after IV heparin ( $n = 17$  (37%)), nine (16%) chose to switch to warfarin usually after IV heparin ( $n = 8$ ) with only one person choosing to continue the direct oral anticoagulant (DOAC).

Eleven respondents (20%) chose to insert an IVCF, 10 (91%) of which were retrievable (50% electing to retrieve within six months). Ten (91%) of these respondents opted to switch to LMWH, while one (9%) continued with the DOAC (Table 1).

The development of a recurrent VTE despite anticoagulation raises the suspicion of an occult malignancy. We asked respondents what (if any) investigations they would arrange in this circumstance. Details of recommended further investigations are shown in Fig. 3. Most respondents elected to screen for occult malignancy.

### Case 4: metastatic malignancy with extensive VTE

This case highlights the management of extensive VTE in the setting of known solid organ malignancy. Only three (7%) respondents recommended management with a DOAC. The remainder (93%) chose to treat either with LMWH initially or IV heparin initially then transitioning to LMWH. Of the 12 respondents (21%) who recommended insertion of an IVCF, four (33%) chose a permanent filter (Table 1).

### Differences between specialties

Compared to Haematology/Oncology Physicians, Respiratory Physicians were significantly more likely to insert an IVCF for case 1 (PE post-surgery), and less likely to do so for case 3 (recurrent VTE on anticoagulation). No statistical difference was noted between the specialties in cases 2 and 4 with regards to IVCF insertion (Table 3).

## Discussion

The use of IVCFs has remained topical in recent years since an FDA safety statement and a 2015 RCT which recommended against their use where anticoagulation could be more effective.<sup>12,20</sup> Furthermore, the indications for IVCF use in patients with malignancy-associated VTE is complicated by a lack of prospective clinical trial data to guide decision making.

**Table 1.** Survey responses for each case.

Case responses	Respiratory (n = 32)	Haematology/oncology (n = 24)	Total (n = 56)
<b>Case 1</b>			
Timing to anticoagulation (says post-surgery)			
Day 3 (on diagnosis of VTE)	15 (267%)	16 (28.5%)	31 (55%)
Days 4–10	17 (30.3%)	8 (14.2%)	25 (45%)
Choice of anticoagulation			
IV heparin Infusion	19 (34%)	19 (34%)	38 (68%)
LMWH (Treatment dose)	6 (10.7%)	3 (5.3%)	9 (16%)
LMWH (Prophylactic dose)	6 (10.7%)	2 (3.5%)	8 (14%)
DOAC	1 (1.7%)	0 (0%)	1 (2%)
VKA	0 (0%)	0 (0%)	0 (0%)
Choice of anticoagulation			
Yes	<b>21 (37.5%)</b>	<b>9 (16%)</b>	<b>30 (54%)</b>
Permanent	0 (0%)	0 (0%)	
Retrievable	21 (38%)	9 (34%)	
No	<b>11 (19.6%)</b>	<b>15 (26.7%)</b>	<b>26 (46%)</b>
<b>Case 2</b>			
Timing to surgery			
1–3 weeks	23 (41%)	14 (25%)	37 (66%)
4–6 weeks	9 (16%)	10 (17.8%)	19 (34%)
> 6 weeks	0 (0%)	0 (0%)	0 (0%)
Choice of anticoagulation			
IV heparin infusion cease 4–6 h before surgery	19 (34%)	11 (19.6%)	30 (54%)
LMWH (treatment dose) cease 24 h before surgery	13 (23.2%)	13 (23.2%)	26 (46%)
Decision to insert an IVCF			
Yes	<b>13 (23.2%)</b>	<b>8 (14.2%)</b>	<b>21 (37%)</b>
Permanent	1 (1.7%)	1 (1.7%)	
Retrievable	12 (21.4%)	7 (12.5%)	
No	<b>19 (34%)</b>	<b>16 (28.5%)</b>	<b>35 (63%)</b>
<b>Case 3</b>			
Choice of anticoagulation			
Vitamin K antagonist (VKA)	1 (1.7%)	0 (0%)	1 (2%)
DOAC	0 (0%)	1 (1.7%)	1 (2%)
LMWH	17 (30.3%)	12 (21.4%)	29 (52%)
IV heparin followed by DOAC	0 (0%)	0 (0%)	0
IV heparin followed by LMWH	7 (12.5%)	10 (17.8%)	17 (30%)
IV heparin followed by VKA	7 (12.5%)	1 (1.7%)	8 (14%)
Decision to insert an IVCF			
Yes	<b>3 (5.3%)</b>	<b>8 (14.2%)</b>	<b>11 (20%)</b>
Permanent	0 (0%)	1 (1.7%)	
Retrievable	3 (5.3%)	7 (12.5%)	
No	<b>29 (51.7%)</b>	<b>16 (28.5%)</b>	<b>45 (80%)</b>
<b>Case 4</b>			
Choice of anticoagulation			
Vitamin K antagonist (VKA)	0 (0%)	0 (0%)	0 (0%)
DOAC	2 (3.5%)	1 (1.7%)	3 (5%)
LMWH	21 (37.5%)	14 (25%)	35 (63%)
IV heparin followed by DOAC	0 (0%)	0 (0%)	0 (0%)
IV heparin followed by LMWH	9 (16%)	9 (16%)	18 (32%)
IV heparin followed by VKA	0 (0%)	0 (0%)	0 (0%)

(continued)

Table 1. Continued

Case responses	Respiratory (n = 32)	Haematology/oncology (n = 24)	Total (n = 56)
Decision to insert an IVCF			
Yes	<b>3 (5.3%)</b>	<b>8 (14.2%)</b>	<b>11 (20%)</b>
<i>Permanent</i>	<i>0 (0%)</i>	<i>1 (1.7%)</i>	
<i>Retrievable</i>	<i>3 (5.3%)</i>	<i>7 (12.5%)</i>	
No	<b>29 (51.7%)</b>	<b>16 (28.5%)</b>	<b>45 (80%)</b>

IV: intravenous; LMWH: low-molecular-weight heparin; DOAC: direct oral anticoagulant; VKA: vitamin K antagonist; IVCF: inferior vena cava filters; DOAC: direct oral anticoagulant.

Note: Bold values refer to the total number of responses for that question. Whereas italic values show the breakdown of responses.

Table 2. Relationship between timing of anticoagulant/timing of surgery and insertion of IVCF.

Case	Insert IVCF	Immediate anticoagulation	Delayed anticoagulation	OR (95% CI)	p
Case 1	No	21	5	8.4 (2.44–28.9)	0.001
	Yes	10	20		
Case 2	No	25	10	1.88 (0.60–5.83)	0.277
	Yes	12	9		

IVCF: inferior vena cava filter.

Note: Odds ratio for inserting an IVCF, compared with choosing not to, are reported with their 95% confidence interval (95% CI).

We created four scenarios representative of dilemmas faced by clinicians in clinical practice. All cases were adaptations of cases seen in our hospital over the previous 12 months.

In case 1, there is a compelling contraindication to anticoagulation due to the relatively high risk of an epidural haematoma. The use of an IVCF in this setting has unanimous support from available guidelines (Fig. 3). The risk of VTE following spinal surgery is recognised to be considerable with neurosurgery recognised as a transient risk factor for VTE.<sup>21,22</sup> The risks of spinal haematoma and major complications from therapeutic anticoagulation are high.<sup>23,24</sup> IVCFs have been proven to reduce the rate of recurrent PE significantly in this situation.<sup>17</sup> In spite of this, 46% of respondents would not elect to insert an IVCF in this case; 55% of respondents (15 Respiratory Physicians and 16 Medical Oncologists/Haematologists) elected to initiate anticoagulation therapy on Day 3 immediately upon diagnosis of VTE. This obviates the need for an IVCF if anticoagulation is tolerated without complication. This likely accounts for why only 46% of respondents elected not to insert an IVCF. The American College of Chest Physicians (ACCP) suggest resuming therapeutic-dose LMWH 48–72 h after surgery.<sup>25</sup> However no clear consensus exists from with specific regard to spinal surgery with wide variability of surgeons' practices.<sup>25,26</sup>

There is still an ongoing debate as to the timing of anticoagulation in patients following spinal surgery,<sup>27</sup> with the differences in practices evident in the responses. Of the physicians surveyed, half chose to delay anticoagulation by up to four weeks. These physicians were eight times more likely to insert an IVCF likely reflecting concerns around delayed anticoagulation.

In case 2, a patient requires major oncological surgery in the setting of a recent VTE. The rates of VTE recurrence tend to be greatest following the initial month after diagnosis and remain high for 6–12 months post diagnosis.<sup>9</sup> Conversely, delaying surgery may also have prognostic implications from the malignancy.

Following surgery for ovarian malignancy, the post-operative VTE risk is as high as 13.5%. The development of VTE has a negative impact on overall survival with PE being the leading cause of death in ovarian malignancy.<sup>28,29</sup> The type and timing of therapeutic anticoagulation has to be balanced against the perioperative bleeding risk and the risk of further VTE. Two retrospective case series have shown reduced rates of PE with the use of IVCFs preoperatively in gynaecological and other malignancies.<sup>30,31</sup>

The British Committee for Standards in Haematology (BCSH) guidelines recommend considering IVCF use in patients scheduled for surgery with recent VTE (<1 month) in whom anticoagulation must be interrupted.<sup>5</sup> This is consistent with previously published experience at our centre.<sup>19</sup> In this setting, there is a relative indication for IVCF use. In our survey, only 21 (38%) of the physicians surveyed opted to insert an IVCF, reflecting the lack of consensus.

We examined the relationship between timing of surgery and the insertion of an IVCF. Numerically physicians choosing to delay surgery by 4–6 weeks were more likely to recommend insertion of an IVCF; however, this did not reach statistical significance. This likely reflects personal preference and the risk-averse nature of some clinicians. Delayed surgery was likely preferred to further mitigate the risk of VTE in an already high-risk population. As the risk of recurrent VTE remains highest in the month following diagnosis, delaying surgery and allowing a patient to

	ACCP	AHA	BCSH	SIR/ACR	CIRSE
Case 1 (PE post-spinal surgery)	✓	✓	✓	✓	✓
Case 2 (Pre-Op VTE in Gynae Cancer)	-	-	✓	✓	✓
Case 3 (Recurrent PE with anticoagulation)	✗	✓	✓ †	✓	✓
Case 4 (Metastatic Cancer with DVT and PE)	✗	-	-	-	-

- ✗ Not Recommended
- ✓ Recommended
- ✓ † Reasonable to insert if recurrent acute PE despite therapeutic anticoagulation
- Not discussed

ACCP American College of Chest Physicians

AHA American Heart Association

BCSH British Committee for Standards in Haematology

SIR/ACR Society of Interventional Radiology/American College of Radiology

CIRSE Cardiovascular Interventional Radiology Society of Europe

**Fig. 3.** Recommendations from international societies regarding IVCF insertion with regards to each individual case.

become established on therapy may be a reasonable approach. Furthermore, IVCF insertion may theoretically reduce the risks involved with the necessary interruption of anticoagulation in the immediate perioperative period.

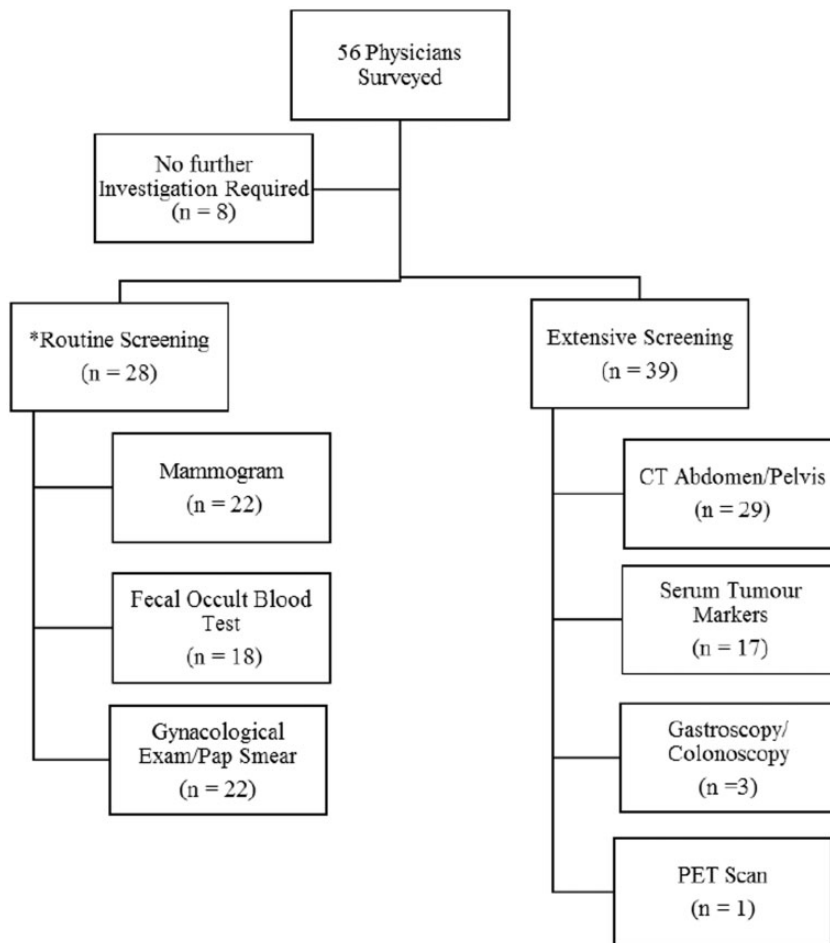
In the absence of anticoagulation, the risk of recurrence is about 40% in the first month.<sup>32</sup> Surgery itself necessitates the interruption of anticoagulation while in itself is a major acquired risk factor for VTE.<sup>33</sup> Understandably, the BCSH guidelines consider this a relative indication for IVCF insertion, but only based on expert opinion (Grade C evidence).

Case 3 has two facets to consider. The first part focuses on the development/propagation of a thrombus despite adequate anticoagulation with a DOAC. Eleven respondents (20%) chose to insert an IVCF of whom 10 opted to switch to LMWH, while 1 continued with the DOAC.

In this circumstance, the Society of Interventional Radiology/American College of Radiology (SIR/ACR), American Heart Association (AHA) and Cardiovascular Interventional Radiology Society of Europe (CIRSE) guidelines support the insertion of an IVCF.<sup>6-8</sup> The ACCP guidelines however recommend against their use.<sup>4</sup> The BCSH guidelines recommend switching to LMWH before considering an IVCF.<sup>5</sup> The varied responses in our survey understandably reflect these inconsistencies.

Mellado et al. examined the effectiveness of IVCFs in the setting of recurrent symptomatic VTE on anticoagulation. They found a statistically significant survival advantage for the patients who received an IVCF whilst on systemic anticoagulation.<sup>34</sup> This may be of particular relevance in oncology, where there is an increased risk of PE recurrence despite anticoagulation.





**Fig. 4.** Investigation for malignancy in the setting of recurrent VTE.

\*Routine screening was defined as compliance with age/gender appropriate government run cancer screening strategies.

**Table 3.** Relationship between decision to insert an IVCF and specialty.

Case	Insert IVCF	Respiratory	Haematology/oncology	OR (95% CI)	p
1	No	11	15	3.18 (1.06–9.58)	0.040
	Yes	21	9		
2	No	19	16	1.37 (0.45–4.13)	0.577
	Yes	13	8		
3	No	29	16	0.21 (0.05–0.89)	0.034
	Yes	3	8		
4	No	24	20	1.67 (0.44–6.36)	0.455
	Yes	8	4		

Note: Odds ratio for inserting an IVCF compared with choosing not to, are reported with their 95% confidence interval (95% CI).

Whether to alter the dose or change anticoagulant for VTE occurring on therapeutic anticoagulation is largely based on expert opinion.<sup>34</sup> Only two guidelines comment on this. The ACCP guidelines recommend switching the patient to a LMWH if they are on a vitamin K antagonist and if they are already on LMWH, they recommend increasing the dose (grade 2 evidence).<sup>4</sup> The BCSH guidelines

recommend considering an IVCF after the target INR has been increased to 3.5 or the patient has been switched to LMWH. As these guidelines were derived prior to the widespread use of the DOACs, the recommendation in such an instance of DOAC failure is not known.<sup>5</sup> Unfortunately, The ACR/SIR, CIRSE and the AHA guidelines provide no further advice.<sup>6–8</sup>

The development of a recurrent VTE despite anticoagulation raises the suspicion of an occult malignancy.<sup>35,36</sup> Eighty-six percent of respondents recommended investigating for an occult malignancy (Fig. 4). More than half of physicians that we surveyed recommended performing a CT chest/abdomen/pelvis to further investigate for malignancy. At present, the extensive investigation of malignancy in patients with an unprovoked VTE (and in the absence of further signs or symptoms to suggest malignancy) is not routinely recommended, as the yield of uncovering an underlying malignancy is low.<sup>35–37</sup>

Case 4 involves a substantial PE and DVT in the setting of known metastatic disease in a patient undergoing chemotherapy. The presence of malignancy is an independent risk factor for fatal PE when compared to non-cancer populations.<sup>38,39</sup> The majority of physicians elected to anticoagulate with LMWH. Three physicians (5%) elected to prescribe a DOAC. In our experience, the use of a DOAC in this situation is often a pragmatic consideration based on patient preference against prolonged injections. The DOAC edoxaban (a Factor Xa inhibitor) has demonstrated non-inferiority for treatment of malignancy associated VTE when compared to dalteparin with an acceptable rate of bleeding complications.<sup>40</sup> A similar study (SELECT-D) compared rivaroxaban (a DOAC) to dalteparin (LMWH). Relatively low rates of VTE were seen in both arms with more clinically relevant non-major bleeding in the rivaroxaban arm.<sup>41</sup> Thus we believe that it is likely that DOACs will soon become an acceptable standard of care in patients with VTE-associated malignancy.

No current guidelines advocate for upfront IVCF insertion for large PE alone as described in case 4. In our survey, 12 (21%) respondents recommended IVCF insertion with a third of them opting for a permanent IVCF. Oncology patients are a unique group with the potential for heightened risk of both VTE and bleeding. The available RCTs published to date are underpowered to guide clinical decision making in the setting of CAT. The PREPIC2 study examined anticoagulation with or without the use of a retrievable IVCF in 399 patients. Only 62 subjects (15%) of those on the study had active malignancy. Another study comparing the use of IVCF and fondaparinux (a LMWH) with or without an IVCF had a sample size of 64 patients.<sup>20,39</sup> The use of IVCFs in this cohort may represent a cautious but invasive strategy to avoid hypothetical under treatment, which is reflected in our survey.

Respiratory Physicians were more likely to insert an IVCF for case 1 (PE post operatively). This case has the most compelling indication for IVCF insertion. In the absence of anticoagulation, all guidelines recommend the use of an IVCF. With the absence of malignancy, Haematologists/Oncologists may be less familiar with this scenario.

However, in case 3 (recurrent VTE despite anticoagulation), Haematologists/Oncologists were more likely to insert an IVCF. This likely reflects the differences between guidelines. The ACCP guidelines, which would be better known

to Respiratory Physicians, recommend against their use in this setting. On the other hand, the BCSH would consider it a reasonable approach to insert an IVCF in the setting of treatment failure. While these guidelines were published in 2006, a more recent consensus from the International Society of Thrombosis and Haemostasis (ISTH) state IVCFs should not be systematically inserted in cancer patients with recurrent VTE, and should be reserved for patients with contraindications to anticoagulation.<sup>42</sup>

A detailed set of guidelines on the diagnosis and management of VTE have recently been published by Thrombosis and Haemostasis Society of Australia and New Zealand.<sup>43</sup> This paper was not available to respondents at the time of surveying. The authors conduct a detailed discussion on the assessment, diagnosis and management of VTE and agree with our previously published supposition that the use of DOACs is acceptable in the setting of CAT. Within the guidelines, however, there is limited discussion on the use of IVCFs in general, nor detailed specific management of oncology-associated VTE. We would respectfully submit that these otherwise excellent guidelines would be improved by the presence of non-haematological physicians involved in the process and we would recommend greater collaboration between specialists in drafting future guidelines as a positive step to ensure a consistency of approach in this complex area of medicine.

### Limitations

The major limitation of this study was the small sample size; however, most respondents were consultants (> 77%), which is beneficial given the relative complexity of the cases. Another potential limitation was that vascular surgeons, interventional radiologists and cardiologists were not surveyed. In the Australian context, the decision around insertion of temporary IVCF is primarily the remit of Haematologists, Medical Oncologists and Respiratory Physicians – although we accept that the responsibility for such decisions may vary by specialty and by country.

Our survey of Australian Respiratory Physicians, Haematologists and Oncologists highlights the variability in the management of VTE, particularly CAT. This variability is in part driven by inconsistencies between the available guidelines, which in turn occurs due to gaps in the completed research. IVCFs are an important tool in CAT management but they have their limitations. There remains a need for better powered studies to answer clinically relevant questions.

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### Author contributions

All authors have contributed to the work as per the authorship criteria.

**Conflict of interest**

The author(s) declare that there is no conflict of interest.

**Ethical approval**

The study has been approved by St John of God Human Research Ethics Committee.

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**Supplemental material**

Supplemental material for this article is available online.

**References**

- Cohoon KP, McBride J, Friese JL, et al. Retrievable inferior vena cava filters can be placed and removed with a high degree of success: initial experience. *Catheter Cardiovasc Interv* 2015; 86: 719–725.
- Shah M, Alnabelsi T, Patil S, et al. IVC filters – trends in placement and indications, a study of 2 populations. *Medicine (Baltimore)* 2017; 96: e6449.
- Bikdeli B, Chatterjee S, Desai NR, et al. Inferior vena cava filters to prevent pulmonary embolism: systematic review and meta-analysis. *J Am Coll Cardiol* 2017; 70: 1587–1597.
- Kearon C, Akl EA, Ornella J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. *Chest* 2016; 149: 315–352.
- Baglin TP, Brush J, Streiff M and British Committee for Standards in Haematology Writing Group. Guidelines on use of vena cava filters. *Br J Haematol* 2006; 134: 590–595.
- Jaff MR, McMurtry MS, Archer SL, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. *Circulation* 2011; 123: 1788–1830.
- American College of Radiology/Society of Interventional Radiology. *ACR-SIR-SPR practice parameter for the performance of inferior vena cava filter placement for the prevention of Pulmonary Embolism*. Fairfax, VA: American College of Radiology/Society of Interventional Radiology, 2016.
- Reekers JA. *Quality improvement guidelines for percutaneous inferior vena cava filter placement for the prevention of pulmonary embolism*. Vienna, Austria: CIRSE, 2009.
- Lyman GH, Khorana AA, Falanga A, et al. American Society of Clinical Oncology guideline: recommendations for venous thromboembolism prophylaxis and treatment in patients with cancer. *J Clin Oncol* 2007; 25: 5490–5505.
- Mandala M, Falanga A and Roila F; Group EGW. Management of venous thromboembolism (VTE) in cancer patients: ESMO Clinical Practice Guidelines. *Ann Oncol* 2011; 22(Suppl 6): vi85–vi92.
- Lyman GH, Bohlke K, Khorana AA, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update 2014. *J Clin Oncol* 2015; 33: 654–656.
- U.S. Food and Drug Administration. *Removing retrievable inferior vena cava filters: initial communication*. Silver Spring, MD: U.S. Food and Drug Administration, 2010.
- Andreoli JM, Lewandowski RJ, Vogelzang RL, et al. Comparison of complication rates associated with permanent and retrievable inferior vena cava filters: a review of the MAUDE database. *J Vasc Interv Radiol* 2014; 25: 1181–1185.
- Stein PD, Beemath A, Meyers FA, et al. Incidence of venous thromboembolism in patients hospitalized with cancer. *Am J Med* 2006; 119: 60–68.
- Prandoni P, Lensing AW, Piccioli A, et al. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. *Blood* 2002; 100: 3484–3488.
- Sorensen HT, Mellekjaer L, Olsen JH, et al. Prognosis of cancers associated with venous thromboembolism. *N Engl J Med* 2000; 343: 1846–1850.
- Becker DM, Philbrick JT and Selby JB. Inferior vena cava filters. Indications, safety, effectiveness. *Arch Intern Med* 1992; 152: 1985–1994.
- Coombs C, Kuk D, Devlin S, et al. Outcomes after inferior vena cava filter placement in cancer patients diagnosed with pulmonary embolism: risk for recurrent venous thromboembolism. *J Thromb Thrombolysis* 2017; 44: 489–493.
- Craven P, Daly C, Oates R, et al. Inferior vena cava filters (IVCFs): a review of uses and application to international guidelines at a single Australian center; implications of venous thromboembolism associated with malignancy. *Pulm Circ* 2018; 8: 2045894018776505.
- Mismetti P, Laporte S, Pellerin O, et al. 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.
- Heit JA, Mohr DN, Silverstein MD, et al. Predictors of recurrence after deep vein thrombosis and pulmonary embolism: a population-based cohort study. *Arch Intern Med* 2000; 160: 761–768.
- Barnes B, Alexander JT and Branch CL Jr. Postoperative Level 1 anticoagulation therapy and spinal surgery: practical guidelines for management. *Neurosurg Focus* 2004; 17: E5.
- Cain JE Jr, Major MR, Lauerman WC, et al. The morbidity of heparin therapy after development of pulmonary embolus in patients undergoing thoracolumbar or lumbar spinal fusion. *Spine (Phila Pa 1976)* 1995; 20: 1600–1603.
- Kou J, Fischgrund J, Biddinger A, et al. Risk factors for spinal epidural hematoma after spinal surgery. *Spine (Phila Pa 1976)* 2002; 27: 1670–1673.
- Douketis JD, Spyropoulos AC, Spencer FA, et al. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. [published correction appears in *Chest* 2012; 141: 1129]. *Chest* 2012; 141: e326S–e350S.
- Glottzbecker MP, Bono CM, Harris MB, et al. Surgeon practices regarding postoperative thromboembolic prophylaxis after high-risk spinal surgery. *Spine (Phila Pa 1976)* 2008; 33: 2915–2921.

27. Cheng JS, Arnold PM, Anderson PA, et al. Anticoagulation risk in spine surgery. *Spine (Phila Pa 1976)* 2010; 35: S117–S124.
28. Clarke-Pearson DL, Jelovsek FR and Creasman WT. Thromboembolism complicating surgery for cervical and uterine malignancy: incidence, risk factors, and prophylaxis. *Obstet Gynecol* 1983; 61: 87–94.
29. Gunderson CC, Thomas ED, Slaughter KN, et al. The survival detriment of venous thromboembolism with epithelial ovarian cancer. *Gynecol Oncol* 2014; 134: 73–77.
30. Babu SB, Maheen Khan A and Coates PJB. Three-year experience of prophylactic placement of inferior vena cava filters in women with gynecological cancer. *Int J Gen Med* 2013; 6: 671–674.
31. Bhargava AK, Dubey M, Naithani BK, et al. Experience with the use of IVC filters for prevention of peri-operative pulmonary venous thrombo-embolism in cancer patients. *J Anaesthesiol Clin Pharmacol* 2010; 26: 83–86.
32. Kearon C and Hirsh J. Management of anticoagulation before and after elective surgery. *N Engl J Med* 1997; 336: 1506–1511.
33. Spencer FA, Emery C, Lessard D, et al. The Worcester Venous Thromboembolism study: a population-based study of the clinical epidemiology of venous thromboembolism. *J Gen Intern Med* 2006; 21: 722–727.
34. Mellado M, Pijoan JI, Jiménez D, et al. Outcomes associated with inferior vena cava filters among patients with thromboembolic recurrence during anticoagulant therapy. *JACC Cardiovasc Interv* 2016; 9: 2440–2448.
35. Robin P and Carrier M. Revisiting occult cancer screening in patients with unprovoked venous thromboembolism. *Thromb Res* 2018; 164: S7–S11.
36. Carrier M, Lazo-Langner A, Shivakumar S, et al. Screening for occult cancer in unprovoked venous thromboembolism. *N Engl J Med* 2015; 373: 697–704.
37. Khan F, Vaillancourt C and Carrier M. Should we screen extensively for cancer after unprovoked venous thrombosis? *BMJ* 2017; 356: j1081.
38. Laporte S, Mismetti P, Decousus H, et al. Clinical predictors for fatal pulmonary embolism in 15,520 patients with venous thromboembolism: findings from the Registro Informatizado de la Enfermedad TromboEmbolica venosa (RIETE) Registry. *Circulation* 2008; 117: 1711–1716.
39. Barginear MF, Gralla RJ, Bradley TP, et al. Investigating the benefit of adding a vena cava filter to anticoagulation with fondaparinux sodium in patients with cancer and venous thromboembolism in a prospective randomized clinical trial. *Support Care Cancer* 2012; 20: 2865–2872.
40. Raskob GE, van Es N, Verhamme P, et al. Edoxaban for the treatment of cancer-associated venous thromboembolism. *N Engl J Med* 2018; 378: 615–624.
41. Young AM, Marshall A, Thirlwall J, et al. Comparison of an oral factor Xa inhibitor with low molecular weight heparin in patients with cancer with venous thromboembolism: results of a randomized trial (SELECT-D). *J Clin Oncol* 2018; 36: 2017–2023.
42. Carrier M, Khorana AA, Zwicker JI, et al. Subcommittee on haemostasis and malignancy for the SSC of the ISTH. Management of challenging cases of patients with cancer-associated thrombosis including recurrent thrombosis and bleeding: guidance from the SSC of the ISTH: a reply to a rebuttal. *J Thromb Haemost* 2014; 12: 116–117.
43. Tran HA, Gibbs H, Merriman E, et al. New guidelines from the Thrombosis and Haemostasis Society of Australia and New Zealand for the diagnosis and management of venous thromboembolism. *Med J Aust* 2019; 210: 227–235.