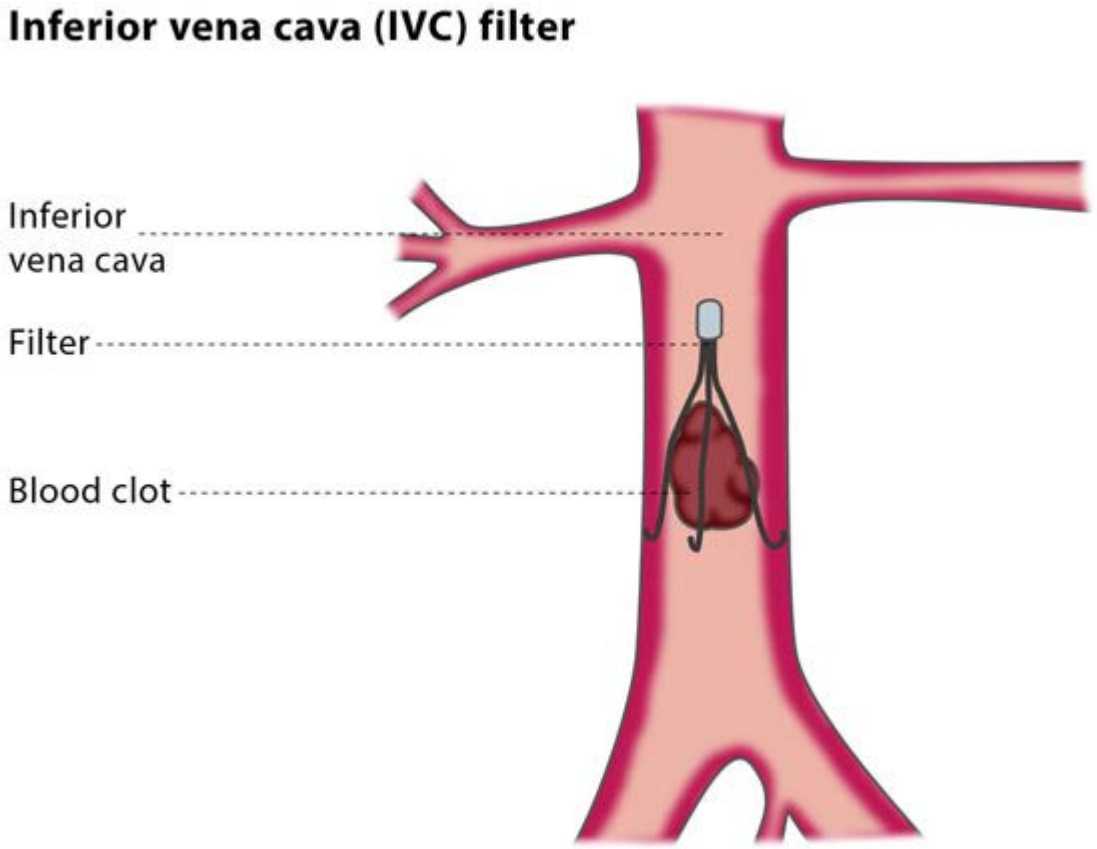
IVC filters in cancer

Maeve Crowley

Guy's and St Thomas' NHS
NHS Foundation Trust

Outline

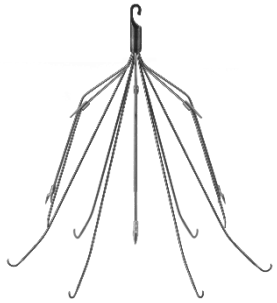
- Cancer associated thrombosis
- IVC filter evidence
- IVC filters in patients with cancer
- Current guidelines
- Complications
- Learning outcomes



Cancer associated thrombosis

- Cancer-associated thrombosis is associated with a 2-6 fold increased risk of mortality in patients with cancer
- Can affect ongoing cancer treatment – delay/discontinuation
- High risk of recurrence and bleeding – filter question commonly occurs

Evidence for IVC filters



- IVC filters are metal alloy devices that mechanically trap emboli *en route* to the pulmonary circulation.

- Cochrane review in 2010 failed to make a recommendation due to inadequate evidence.

- PREPIC study – 400 (14% had cancer) patients with proximal DVT were randomized either to receive or not to receive a filter in addition to standard anticoagulation for 3/12.

PREPIC Study Group. Circulation. 2005 Jul 19;112(3):416-22.

- At 8 years, filters reduced the risk of PE (6.2% vs 15.1%) but increased the risk of DVT (35.7% vs 27.5%) and had no effect on mortality.

- PREPIC2 study – Hospitalized patients with acute PE and 1 criteria for severity (15.5% had active cancer) were randomized to anticoagulation (6/12) with/without a retrievable filter.

- At 3 months, PE had occurred in 6 patients in the filter group (all fatal) and 3 in the no-filter group (2 fatal).

- No other differences were noted between the groups at 3 or 6 months.

Mismetti P, Laporte S, Pellerin O, Ennezat PV, Couturaud F, Elias A, Falvo N, Meneveau N, Quere I, Roy PM, Sanchez O, Schmidt J, Seinturier C, Sevestre MA, Beregi JP, Tardy B, Lacroix P, Presles E, Leizorovicz A, Decousus H, Barral FG, Meyer G; PREPIC2 Study Group. JAMA. 2015 Apr 28;313(16):1627-35.

IVC filters in patients with cancer

- 19.6% of 14,000 cancer patients (rates varied widely across hospitals - 0% - 52% and by cancer type).

- Strongest predictors of IVCF use were a diagnosis of brain cancer (OR=4.6, CI: 3.7-5.6), undergoing major surgery (OR=4.9, CI: 3.9-6.1), and bleeding (OR=2.7, CI: 2.0-3.5).

- 21% had a strong contraindication to anticoagulation (bleeding or major surgery).

Brunson et al. ***Thromb Res. 2016*** *Apr;140 Suppl 1:S132-41.*

- No benefit for 30-day mortality.

- There was a 56% increase in recurrent VTE manifested as DVT at 180 days or less for patients treated with an IVCF (HR: 1.56, CI: 1.26-1.92).

- IVCF treated patients were 1.2-fold more likely to have a bleed occur at 180 days or less (HR: 1.20, CI: 1.04-1.38).

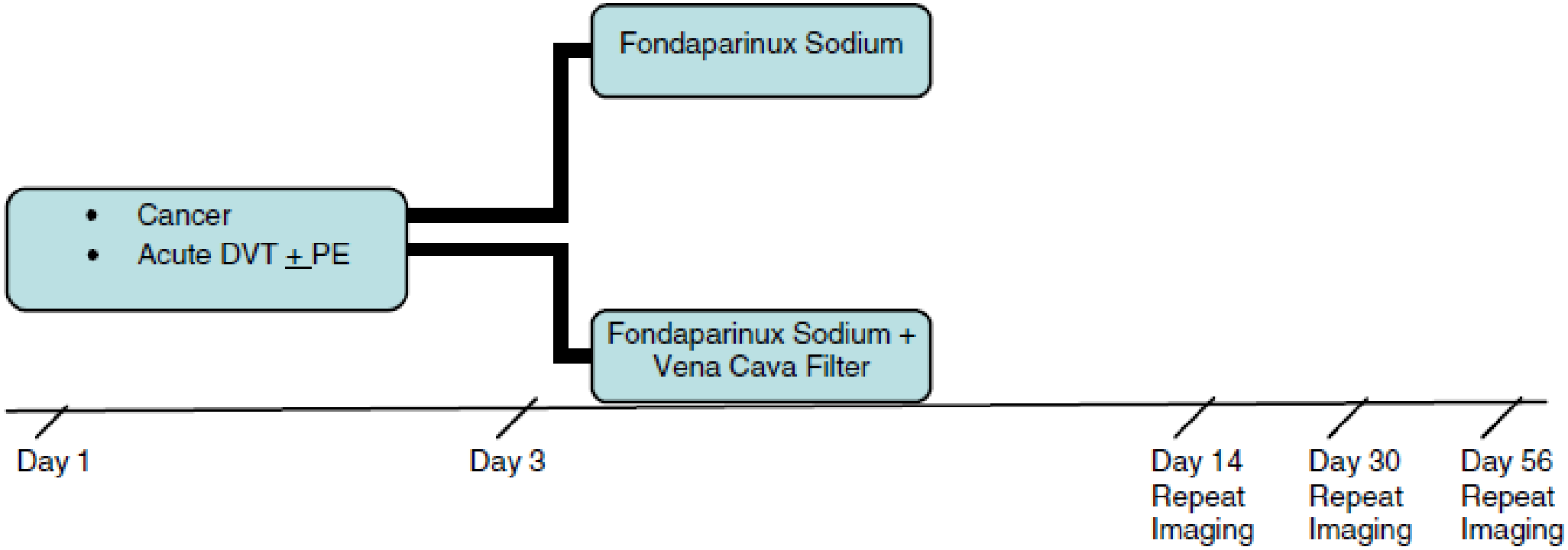
Journal (year published)	JCO (1996) Schwartz et al	AMJCO (2016) Narayan et al	Hematol Oncol Stem Cell Ther (2014) Mansour et al	AmJMed (2014) Abtahian et al
Data source	Retrospective review	Retrospective cohort study	Retrospective review	Retrospective cohort study
Time period	1980-1992	2002-2006	2004-2011	2009-2011
Country	USA (Memorial Sloan-Kettering)	USA (Johns Hopkins)	Jordan	USA
Number of patients	182	246	107	243
Age	Median 59 (15-88)	Mean (SD) 61.9 (13.6)	Mean (SD) 50.8 (14.2)	Mean 60
M/F	103/79	133/113	59/48	124/119
Stage I/II/III/IV	8/22/37/115	No data	2/3/20/61 (Unknown 21)	No data
Cancer subtype Brain/GI/Lung/Prostate/Pancreas	28/29/21/16/4	23/35/29/13/23	16/32/13/UK	42/50/-/-
Indication CI to AC/Prophylaxis/Bleeding/Failure of AC	27/58/61/12	167/17/26/31	38/-/52/18	100/70/55/10
Retrieval	No data	No data	No data	28%
Survival	40% at one year	36% at one year	Median survival 2.39 months (0.03-60.2)	-
Complication type: placement related/ thrombosis	7/15 (4 PEs)	UK/15.9% (at 30d)	0/14 (3 PEs)	41 significant complications (15 PEs)

Outcomes for cancer vs non-cancer patients.

- Abtahian et al 2014 – Retrospective cohort study – 247/666 had cancer. Median follow-up 401 days. Similar rates of complications 19.8% vs 17.7%. Statistical difference in rates of retreival – 28% vs 42%

- Narayan et al 2016 – Retrospective cohort study – 246/702 had cancer. Cancer patients had statistically significant higher rates of VTE – RR 1.9 (1.1-3.2)

Prospective randomised data



*Barginear et al. Support Care **Cancer**. 2012 Nov;20(11):2865-72. doi: 10.1007/s00520-012-1413-z.*

- 64 patients with DVT+/- PE were randomised to fundoparinux +/- IVCF (2007-2010)

- All screened for DVT and PE at baseline

- The primary outcome focused on adverse outcomes: rates of filter complications, bleeding, and recurrent or residual DVTs or PEs.

- Major VCF complications were defined as thrombosis at the filter site, erosion into the wall of the vena cava, infection, prolonged hospitalization, and/or migration of the filter.

Characteristics	Cohorts			
		Fondaparinux sodium (n=33)	Fondaparinux sodium+vena cava filter (n=31)	p value
Gender	Female	24 (73 %)	16 (52 %)	0.0812
	Male	9 (27 %)	15 (48 %)	
Mean age[a]		67±14 years	63±12 years	0.2413
ECOG PS	0	2 (6 %)	2 (6.5 %)	0.6244
	1	14 (42 %)	10 (32 %)	
	2	13 (39 %)	17 (55 %)	
	3	4 (12 %)	2 (7 %)	
Treatment regimens[b]	Chemotherapy	31 (94 %)	28 (90 %)	0.6673
	Hormonal	3 (9 %)	2 (7 %)	1.0000
	Darbepoetin alpha or epoetin alpha	6 (18 %)	3 (10 %)	0.4764
	Anti-angiogenic	0 (0 %)	1 (3 %)	0.4844
Malignancy	Lung cancer	12 (37%)	6 (19%)	0.1825
	Breast cancer	5 (15%)	5 (16%)	
	Pancreatic cancer	3 (9%)	6 (19%)	
	Colon cancer	1 (3%)	6 (19%)	
	Lymphoma	4 (12%)	2 (7%)	
	Ovarian cancer	4 (12%)	1 (4%)	
	Other cancers	4 (12%)	5 (16%)	
TNM stage	II	3 (9%)	1 (3%)	0.7400
	III	5 (15%)	6 (19%)	
	IV	25 (75%)	24 (77%)	
	Brain metastases	5 (15%)	3 (9%)	0.7091

- No patient had a recurrent DVT but two had new PEs, one in each randomized cohort.

- Major bleeding occurred in three patients (1 in IVCF cohort).

- Two patients on the IVCF arm (7%) had complications from insertion (thrombosis requiring a percutaneous thrombectomy and bleeding at the insertion site requiring prolonged hospitalization).

- Complete resolution of VTE occurred in 51% of patients within 8 weeks of initiating anticoagulation.

IVC filter guidelines

- ACCP 2016 - *'In patients with acute DVT or PE who are treated with anticoagulants, we recommended against the use of IVC filters'*
- NICE 2015 – *'offer temporary IVC filters to patients with proximal DVT or PE who cannot have anticoagulant treatment; consider IVC filters for patients with recurrent proximal DVT or PE despite adequate anticoagulation only after considering alternative therapies; ensure there is a strategy for removing the IVC filter at the earliest convenience'*
- SIR 2011 – *'contraindication to anticoagulation, complication of anticoagulation, failure of anticoagulation, prophylactically in high risk situations'*

- ESMO 2011 – *'considered in patients with recurrent PE despite adequate anticoagulant treatment or with a contraindication to anticoagulant therapy. Once the risk of bleeding is reduced, patients with a vena cava filter should receive or resume anticoagulant therapy in order to reduce the risk of recurrent deep vein thrombosis of the lower extremities'*

- BSH 2015 – *'An IVC filter should only be inserted when there is a strong contraindication to anticoagulation and should be removed if possible as soon as anticoagulation is possible'*

- ISTH 2012 – *'Cancer is neither a specific indication nor a special contraindication to vena cava filter placement'; The efficacy of vena cava filters is not proven in cancer patients'; temporary or retrievable (optional) vena caval filters may prove to be particularly valuable in cancer patients , especially when anticoagulation is contraindicated'*

IVC filter complications

- FDA manufacturer and user facility device experience (MAUDE) database
- Between 2000 and 2010 – 842 complications reported
- Most common - IVC perforation, filter migration and filter fracture. More likely to occur if prolonged (>30 day) use
- Likely underestimation – voluntary reporting

US Food and Drug Administration. Inferior Vena Cava (IVC) filters: Risk of Adverse events with long term use. Safety Alert report issued 09 August 2010

- Insertion-related complications (4-15%)
  - Puncture site problems
  - Misplacement
  - Migration
  - Failure to deploy
  - Vena caval perforation
  - Symptomatic access site DVT (uncommon)

- Later complications
  - Filter migration or embolization (3-69%)
  - Strut fracture and penetration (9-24%)
  - IVC thrombosis (6-30%)
  - Lower extremity oedema and PTS (5-70%)
  - DVT (0-20%)
  - Recurrent PE 3-7%

Weinberg et al JACC: Cardiovascular Intervention 2013;6:539-47

Infection

- Rare - few case reports/small case series

- Rottenstreich et al 2015 – 3/406 patients. 1 MSSA infection 1 yr post insertion; 1 MRSA infection 10/7 post insertion; 1 a few days after insertion. All settled quickly after removal of the filter. (1 patient had cancer – APL)

- Assifi et al 2012 – IVDU patient who developed infection – multiple admissions with bacteremia. Vegetations noted on the filter. No further bacteraemia following removal.

- Meda et al 2007 - IVC filter infection with *C. glabrata* following septic thrombophlebitis of the femoral veins.

PRESERVE Study

- Predicting the safety and effectiveness of inferior vena cava filters
- Collaboration between the Society of Interventional Radiologists and Society of Vascular Surgeons
- Study outline – 5 year study aiming to enroll 1800 patients in 60 US centres. Patients will be evaluated up to 24/12 or 1/12 post retrieval. Follow-up: Phone, physical examination, imaging.

- Composite safety endpoint of freedom from clinically significant perforation after successful filter placement, filter embolization, caval thrombotic occlusion, deep vein thrombosis, and perioperative serious adverse event [Time Frame: within first 365 days (± 30 days)].
- Composite effectiveness endpoint of procedural and technical success without occurrence of clinically significant pulmonary embolism [Time Frame: at 12-months in-situ or 1-month post-retrieval (whichever comes first)]

- Expected to finish in 2019

Case

27/1/17

- 56 year old lady with no history of thrombosis
- Presented with a DVT and PE
- Commenced on Rivaroxaban

Feb 2017

- Anticoagulation complicated by PV bleeding – required RCC transfusion
- Changed to OD LMWH
- Underwent gynaecology review – suspicious for malignancy

18/2/17

- Presented with bilateral blindness
- Diagnosed with an occipital stroke
- Changed to BD LMWH

27/2/17

- Bleeding became problematic again
- IVC Filter inserted

13/3/17

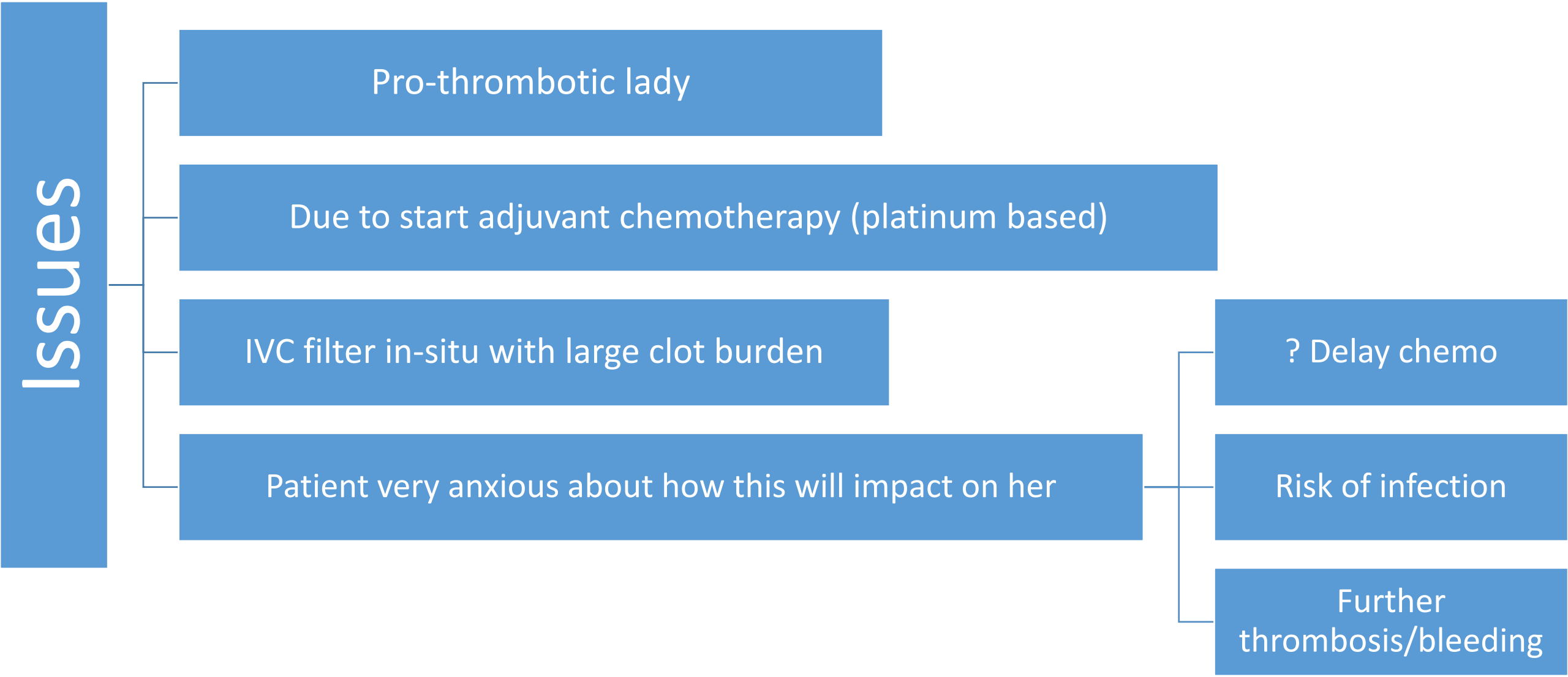
- Surgery managed with UFH
- No immediate complications
- Back on LMWH 16/3/17

22/3/17

- IVC filter removal attempted
- Failed due to thrombus burden

6/4/17

- Post-op imaging shows a new PE
- LMWH dose increased


Issues
Pro-thrombotic lady
Due to start adjuvant chemotherapy (platinum based)
IVC filter in-situ with large clot burden
Patient very anxious about how this will impact on her
? Delay chemo
Risk of infection
Further thrombosis/bleeding

Learning outcomes

- Poor evidence base – mainly based on case reports/case series.
- Evidence often based on non-cancer populations.
- Geographical/institutional variability.
- Importance of multidisciplinary, individualized approach.
- Situations can change quickly so need to frequently re-evaluate.