IVC filters in cancer

Maeve Crowley
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.

• 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.

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).

• 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).
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Data source</td>
<td>Retrospective review</td>
<td>Retrospective cohort study</td>
<td>Retrospective review</td>
<td>Retrospective cohort study</td>
</tr>
<tr>
<td>Country</td>
<td>USA (Memorial Sloan-Kettering)</td>
<td>USA (Johns Hopkins)</td>
<td>Jordan</td>
<td>USA</td>
</tr>
<tr>
<td>Number of patients</td>
<td>182</td>
<td>246</td>
<td>107</td>
<td>243</td>
</tr>
<tr>
<td>Age</td>
<td>Median 59 (15-88)</td>
<td>Mean (SD) 61.9 (13.6)</td>
<td>Mean (SD) 50.8 (14.2)</td>
<td>Mean 60</td>
</tr>
<tr>
<td>M/F</td>
<td>103/79</td>
<td>133/113</td>
<td>59/48</td>
<td>124/119</td>
</tr>
<tr>
<td>Stage I/II/III/IV</td>
<td>8/22/37/115</td>
<td>No data</td>
<td>2/3/20/61 (Unknown 21)</td>
<td>No data</td>
</tr>
<tr>
<td>Cancer subtype</td>
<td>Brain/GI/Lung/Prostate/Pancreas</td>
<td>28/29/21/16/4</td>
<td>23/35/29/13/23</td>
<td>42/50/-/-</td>
</tr>
<tr>
<td>Indication CI to AC/Prophylaxis/Bleeding/Failure of AC</td>
<td>27/58/61/12</td>
<td>167/17/26/31</td>
<td>38/-/-/52/18</td>
<td>100/70/55/10</td>
</tr>
<tr>
<td>Retrieval</td>
<td>No data</td>
<td>No data</td>
<td>No data</td>
<td>No data</td>
</tr>
<tr>
<td>Survival</td>
<td>40% at one year</td>
<td>36% at one year</td>
<td>Median survival 2.39 months (0.03-60.2)</td>
<td>-</td>
</tr>
<tr>
<td>Complication type</td>
<td>placement related/ thrombosis</td>
<td>7/15 (4 PEs)</td>
<td>UK/15.9% (at 30d)</td>
<td>0/14 (3 PEs)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>41 significant complications (15 PEs)</td>
<td></td>
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</table>
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 retrieval – 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

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