Radiologia interventistica nella prevenzione dell’embolia polmonare: quando?

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Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is one of the most common cardiovascular diseases occurring for the first time in about 1 in 1000 people.

Its incidence rises with increasing age, for example to about 5 per 1000 people among those over 70 years of age.

VTE is associated with significant morbidity and mortality with the 30-day mortality rate in the absence of treatment of about 3% for DVT and 31% for PE.

It is a leading cause of preventable hospital death in the United States.

White RH. *Circulation* 2003;107:14–18
TREATMENT

- Anticoagulants are the mainstay treatment of VTE and are given in three phases of acute, long-term (in the first 3 months), and extended treatment.

- For many years initial treatment was started with a parenteral anticoagulant, low-molecular-weight heparin + vitamin K antagonist.

- The DOACs compared with conventional therapy as effective in prevention of VTE recurrence and associated with less bleeding.

Surgical Vena caval interruption (1893).

Currently percutaneous (IVC) filter insertion, is largely used therapeutic option in the management of selected patients with VTE.

Two general types of IVC filters currently available: permanent and retrievable.

Permanent filters have been used since the 1967 and are placed in patients with a long-term need for mechanical prophylaxis against PE and absolute contraindications to anticoagulation.

VENA CAVA FILTERS

• Mobin-Uddin Filter 1967
  The device was plagued by high rates of IVC occlusion (in over half of patients), pulmonary embolism (PE) and migration.

• It was replaced by the stainless steel Kimray-Greenfield filter in 1973, a device with lower complication rates.

VENA CAVA FILTERS

- Over the past 3 decades, use of the IVC filter has climbed steadily.
- Although only 2000 filters were placed in 1979, by 1990, over 120,000 Kimray-Greenfield filters had been implanted in the United States.
- By the 1990s, nearly 30,000 to 40,000 filters were placed annually.
- At the 90’s decade’s end, nearly 50,000 filters were being placed each year.
- In 2012 259,000 filters were placed in U.S.

VENA CAVA FILTERS

• Optional filters have been available since the late 1990s and are designed to be retrieved or left in place after the temporary risk of PE or contraindication to anticoagulation has resolved.

• If retrieved, these devices offer the theoretical benefit of fewer long-term complications associated with permanent IVC filters, such as increased risk of subsequent DVT, filter migration/embolization, and IVC stenosis or occlusion.

• The availability of optional filters, has altered the practice patterns for IVC filters, with an increase in filter placement rates and expansion of indications for filter placement.

INDICATIONS

Classic DOCUMENTED VTE

1. Absolute contraindication to anticoagulation
   * major bleeding diathesis (e.g., coagulation defects, severe thrombocytopenia [platelet count < 50,000 μL]), uncontrollable active bleeding (e.g., gastrointestinal bleeding from any cause), acute hemorrhagic stroke, cerebral lesions at high risk of bleeding, severe uncontrolled hypertension, severe renal and/or hepatic dysfunction.

2. Complication of anticoagulation resulting in cessation of therapy
   * Spontaneous or significant unprovoked hemorrhage while on anticoagulant therapy is not uncommon in the elderly or in patients with comorbidities such as chronic kidney disease, in which the pharmacokinetics of anticoagulant drugs may be altered.

3. Failure of anticoagulation
   * Inability to reach or maintain therapeutic levels of anticoagulation and/or documented progression of DVT or recurrent PE while on therapeutic anticoagulation

INDICATIONS

Relative

1. Iliocaval DVT or large, free-floating proximal DVT
2. Difficulty establishing therapeutic anticoagulation
3. Massive PE treated with thrombolysis/thrombectomy
4. Chronic PE treated with thromboendarterectomy
5. Thrombolysis for iliocaval DVT
6. VTE with limited cardiopulmonary reserve
7. Recurrent PE with filter in place
8. Poor compliance with anticoagulation
9. High risk of complication of anticoagulation (e.g., risk for frequent falls)

optional filters ↓ lowering of thresholds for filter placement ↓ retrievable

The rate of filter retrieval varies significantly among institutions with a recent systematic review noting on average a 34% retrieval rate.

Angel LF et al. J Vasc Interv Radiol. 2011;22
Prophylactic  

**NO DOCUMENTED VTE**

- At risk of developing DVT and/or PE and no anticoagulation.

1. Surgical procedure in patient at high risk of VTE
2. Severe craniospinal injury (prolonged immobilization or plegic limbs)
3. Pelvic/long-bone fractures
4. Intra-abdominal mass/hemorrhage compressing pelvic veins or the IVC

TRAUMA PATIENTS

• (EAST) 2002 guidelines suggesting prophylactic IVC filters be considered for high-risk trauma patients with suspected prolonged immobilization who cannot receive prophylactic anticoagulation (Glasgow Coma Score < 8, incomplete spinal cord injury, closed head injury, complex pelvic and long-bone fractures, and paresis).

• A systematic review of prophylactic IVC filters, including 24 studies with 2,492 patients, cited a lack of conclusive data to support prophylactic use in trauma patients.

BARIATRIC SURGICAL PATIENTS

• Review 2015: there is conflicting evidence and heterogeneous data about prophylactic IVC filter placement in this population. As is true for other subpopulations, there are no good prospective, randomized trials, and additional data are needed.

Prophylactic indications now account more than half of all filter!

PREGNANT PATIENTS

- VTE during pregnancy 5-6 times greater than in the non-pregnant state.

- Hypercoagulability begins in the first trimester and persists for up to 2 months postpartum. In the third trimester, the gravid uterus can cause compression of the iliac veins and IVC, further increasing risk of VTE.

- The standard treatment is anticoagulation with low molecular weight heparin until at least 6 weeks postpartum.

- Warfarin is avoided in pregnancy because it can cross the placental barrier and lead to fetal complications, including malformations and death.

- Urokinase may precipitate labor and produce an atonic uterus because of the interference of fibrin degradation products with uterine contraction and is therefore confined to treat life-threatening pulmonary embolism.

Barbour LA. *Int J Gynaecol Obstet* 2001;75:203–212
Royal College of Obstetricians and Gynaecologists. *Green-top guideline*. 2015
Anticoagulation, especially with impending childbirth, carries a risk of haemorrhage. **Discontinue anticoagulation to reduce the risk of bleeding and epidural hematoma.**

The risk of pulmonary embolism increases due to the discontinuance of anticoagulation and the hemodynamic changes accompanying the rapid decompression of the venous system after delivery.

A smaller number of these patients may have complications for which anticoagulation is absolutely contraindicated (e.g., placenta previa).

Salonen Ros H et al *Epidemiology* 2001;12:456-60
Royal College of Obstetricians and Gynaecologists. *Green-top guideline*. 2009
**PREGNANT PATIENTS**

- The first reported IVC filter placed in a pregnant patient occurred in 1981.

- The Royal Society of Obstetricians and Gynaecologists VTE guidelines recommend to “consider use of a temporary IVC filter in the peripartum period for patients with iliac vein VTE or in patients with proven DVT and who have recurrent PE despite adequate anticoagulation.

- SIR guidelines recommend suprarenal IVC filter placement in pregnant patients, if the filter is clinically indicated.

*Optimally, retrieval should be performed as soon as appropriate in the postpartum period!!*

-Royal College of Obstetricians and Gynaecologists. Green-top guideline. 2009
PREGNANT PATIENTS

SAME INDICATIONS DOCUMENTED VTE

- Contraindication to anticoagulation.

- Failure of medical therapy for VTE despite adequate anticoagulation.

- Complications of anticoagulation (heparin-induced thrombocytopenia, heparin allergy, significant bleeding during anticoagulation).

SUPRARENAL PLACEMENT PREFERRED

• The IVC can be compressed by the gravid uterus, which could displace the filter particularly when contracting (migration/fracture of the filter or damage to the IVC wall).

• Suprarenal placement also provides additional protection from thrombus that has developed in the dilated ovarian veins.

• Additionally, with the volume of renal blood flow, there is the added advantage of accelerated venous flow, which should promote lysis of trapped thrombi.

• Jugular access preferred.
PREGNANT PATIENTS

CESARIAN SECTION RECOMMENDED

• Lower risk of EP.

• Shorter time without anticoagulation.

• Difficulties in vaginal delivery as a result of swelling of the lower extremities.

• Contractions experienced during labor are more likely to cause filter complications such as migration, tilt, or fracture.

GL?
**AHA GUIDELINES**

<table>
<thead>
<tr>
<th>Patients with documented VTE</th>
<th>No documented VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute or relative contraindication to anticoagulation</td>
<td>Severe trauma without documented PE or DVT</td>
</tr>
<tr>
<td>Complication of anticoagulation</td>
<td>Closed head injury</td>
</tr>
<tr>
<td>Recent PE (within 4 days)</td>
<td>Spinal cord injury</td>
</tr>
<tr>
<td>Inability to achieve/maintain adequate anticoagulation</td>
<td>Multiple long-bone or pelvic fractures</td>
</tr>
<tr>
<td>Propagation/progression of DVT during therapeutic anticoagulation</td>
<td>Patients at high risk (e.g., immobilized or in an intensive care unit)</td>
</tr>
<tr>
<td>Massive PE with residual DVT in a patient at risk for further PE</td>
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</tr>
<tr>
<td>Severe cardiopulmonary disease and DVT (e.g., cor pulmonale with pulmonary hypertension)</td>
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</table>

**ACCP GUIDELINES**

1. Vena caval filters for the initial treatment of DVT: for patients with acute proximal DVT, if anticoagulant therapy is not possible because of the risk of bleeding, placement of an IVC filter is recommended (grade 1C).

2. In children weighing >10 kg with lower-extremity DVT and a contraindication to anticoagulation, placement of a temporary IVC filter is suggested (grade 2C).

3. Vena caval filters for the initial treatment of PE: in patients with acute PE, if anticoagulant therapy is not possible because of the risk of bleeding, placement of an IVC filter is recommended (grade 1C).

4. For patients with CTPH undergoing pulmonary thromboendarterectomy, placement of a permanent vena caval filter before or at the time of the procedure is suggested (grade 2C).

**BRITISH COMMITTEE FOR STANDARDS IN HEMATOLOGY GUIDELINES**

1. IVC filter indicated
   - For patients with PE and contraindication to anticoagulation
   - Consider IVC filter placement
   - In select patients with PE despite anticoagulation

2. Preoperatively (retrievable) for patients with recent VTE (1 mo) and need to stop anticoagulation therapy for surgery

3. IVC filters not recommended for
   - Undiagnosed patients with VTE who can receive anticoagulation
   - Thrombolytic therapy

**ESC GUIDELINES**

<table>
<thead>
<tr>
<th>Indicated for</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased VTE/contraindication to anticoagulation</td>
<td>IIA</td>
<td>C</td>
</tr>
<tr>
<td>Recent PE (high risk anticoagulation)</td>
<td>IIA</td>
<td>C</td>
</tr>
</tbody>
</table>

| Not recommended for | |
|---------------------| |
| Prophylactic placement | |
| Risk-bearing tandem | |

| Prior to systemic thrombolysis, surgical embolectomy, or pulmonary thromboendarterectomy | |

**Recommendations**

- IVC filters should be considered in patients with acute PE and absolute contraindications to anticoagulation.
- IVC filters should be considered in case of recurrence of PE, despite therapeutic levels of anticoagulation.
- Routine use of IVC filters in patients with PE is not recommended.

**Abbreviations:** AHA, American Heart Association; DVT, deep venous thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism; ACCP, American College of Chest Physicians; ESC, European Society of Cardiology; AHA, American Heart Association; VTE, venous thromboembolism; PE, pulmonary embolism; IVC, inferior vena cava.
<table>
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<tr>
<th>Recommendations</th>
<th>Class①</th>
<th>Level②</th>
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<td>III</td>
<td>A</td>
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**LEVEL A**
- Multiple populations evaluated*
- Data derived from multiple randomized clinical trials or meta-analyses

**CLASS I**
- Benefit >> Risk
- Recommendation that procedure or treatment is useful/effective
- Sufficient evidence from multiple randomized trials or meta-analyses

**LEVEL B**
- Limited populations evaluated*
- Data derived from a single randomized trial or nonrandomized studies

**CLASS IIa**
- Benefit >> Risk
- Recommendation in favor of treatment or procedure being useful/effective
- Some conflicting evidence from multiple randomized trials or meta-analyses

**LEVEL C**
- Very limited populations evaluated*
- Only consensus opinion of experts, case studies, or standard of care

**CLASS IIb**
- Benefit ≥ Risk
- Recommendation’s usefulness/efficacy less well established
- Greater conflicting evidence from multiple randomized trials or meta-analyses

**CLASS III**
**No Benefit or CLASS III**
**Harm**
- Procedure/ Test
- Treatment
  - COR III: Not Helpful
  - COR III: Excess Cost w/o Benefit or Harmful

**LEVEL A**
- Recommendation that procedure or treatment is not useful/effective and may be harmful
- Sufficient evidence from multiple randomized trials or meta-analyses

**LEVEL B**
- Recommendation that procedure or treatment is not useful/effective and may be harmful
- Evidence from single randomized trial or nonrandomized studies

**LEVEL C**
- Recommendation that procedure or treatment is not useful/effective and may be harmful
- Only diverging expert opinion, case studies, or standard of care
A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis


Eight-Year Follow-Up of Patients With Permanent Vena Cava Filters in the Prevention of Pulmonary Embolism

The PREPIC (Prévention du Risque d’Embole Pulmonaire par Interruption Cave) Randomized Study

The PREPIC Study Group*


- 400 patients with proximal DVT
- All anticoagulated (heparin followed by warfarin)
- Half were randomized to receive a permanent IVC filter.

Table 2. Principal End Points within the First 12 Days after Randomization to the Filter or No-Filter Group.

<table>
<thead>
<tr>
<th>End Point</th>
<th>Filter</th>
<th>No Filter</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary embolism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>2 (1.1)</td>
<td>5</td>
<td>0.22 (0.05-0.90)</td>
<td>0.03</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>0</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>2 (1.1)</td>
<td>9 (4.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>9 (4.5)</td>
<td>6 (3.0)</td>
<td>1.49 (0.53-4.20)</td>
<td>0.44</td>
</tr>
<tr>
<td>Death</td>
<td>5 (2.5)</td>
<td>5 (2.5)</td>
<td>0.99 (0.29-3.42)</td>
<td>0.99</td>
</tr>
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- Difference in asymptomatic emboli detected using an aggressive screening protocol (including both ventilation-perfusion scans and invasive angiography).
- An increase in recurrent DVT was noted in patients who received a filter.
- This approach may have detected small and clinically insignificant emboli.

"because of the observed excess rate of recurrent DVT and the absence of any effect on mortality among patients receiving filters, their systemic use cannot be recommended."

The dark side of the guidelines
PREPIC-2

Effect of a Retrievable Inferior Vena Cava Filter Plus Anticoagulation vs Anticoagulation Alone on Risk of Recurrent Pulmonary Embolism:
A Randomized Clinical Trial

Patrick Mismetti, MD; Silvy Laporte, MS; Philippe Lefebvre, MD; Pierre-Charles Gauthier, MD; Francis Couturaud, MD; Marc-Antoine Testa, MD; Antoine Eille, MD; Patrick Gauthier, MD; Nicolas Meneveauau, MD; Christiane Saurin, MD; Christophe Sudrie, MD; Marie-Antoinette Sevestre, MD; Jean-Paul Beregi, MD; Bernard Tardy, MD; Philippe Lacroix, MD; Emile Presles, MSc; Alain Leizorovich, MD; Hervé Decousus, MD; Fabrice-Guy Barral, MD; Guy Meyer, MD, for the PREPIC2 Study Group

899 patients with acute symptomatic PE and DVT
Retrievable IVC filters may avoid long-term complications?

399 patients with acute symptomatic PE and DVT
Patients all anticoagulated and randomized to receive a retrievable IVC filter.

The authors concluded there was no reduced risk of recurrent PE in patients with acute PE related to lower extremity venous thromboembolism when performing a combined treatment approach of retrievable IVC filter placement plus AC therapy as compared to AC alone.
• AC therapy in both groups was possible and effective.

• In clinical practice, common indications for IVC filter placements are AC not effective or controindicated.

• These patients may benefit the most from retrievable IVC filter placement??

• PREPIC 1-2 studies did not provide answers for this patient group commonly seen on our practice.
Immediate complications

- Misplacement (1.3%)
- Peumothorax (0.02%)
- Haematoma (0.6%)
- Air embolism (0.2%)
- Carotid artery puncture (0.04%)
- Arteriovenous fistula (0.02%)

Late complications

- Recurrent DVT (21%)
- IVC thrombosis (2–10%)
- Post-thrombotic syndrome (15–40%)
- IVC penetration (0.3%)
- Filter migration (0.3%)
- Filter tilting and fracture
- Entrapment of guidewires

Early complications

- Insertion site thrombosis (8.5%)
- Infection

Streiff, MB. Blood, 2000;95, 3669–3677
Crochet DP et al. J Vasc Interv Radiol, 1999;10, 137–142
COMPLICATIONS
COMPLICATIONS


The dark side of the guidelines
COMPLICATIONS

COMPLICATIONS

COMPLICATIONS

CONCLUSIONS

• Theoretically inferior vena cava filter should work. Placed between the main source of venous emboli and the right side of the heart, the IVC filter should capture a blood clot before it reaches the pulmonary circulation.

• 30 years publications: this theory has never been validated by empirical studies.

• 2 RCT’s: IVC filter no benefit….not applicable to common clinical practice

• Complications…rare but….

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CONCLUSIONS


The Inferior Vena Cava Filter

How Could a Medical Device Be So Well Accepted Without Any Evidence of Efficacy?

Grazie per l'attenzione