

# Radiologia interventistica nella prevenzione dell'embolia polmonare: quando?

Dott. Francesco Modestino



Unità Operativa Radiologia Malpighi Azienda Ospedaliero-Universitaria di Bologna Policlinico S. Orsola - Malpighi



# **EPIDEMIOLOGY**

- 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.

# 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.

# **PREVENTION**

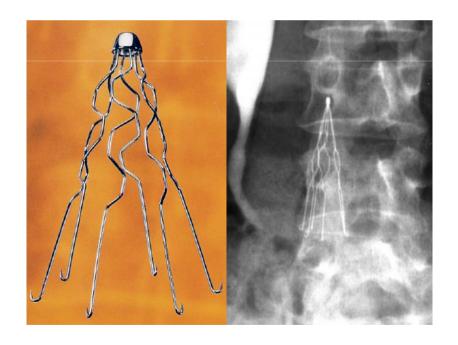
- Surgical Vena caval interruption (1893).
- Currently percutaneous (IVC) filter insertion, is largely used therapeutic option in the management of selected patients with VTE.
- Two general types of IVC filters currently available: permanent and retrievable.
- Permanent filters have been used since the 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.



Kazi Mobin-Uddin et al. N Engl J Med 1972; 286:55-58

# **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  $\mu$ L]), 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.

# **INDICATIONS**

# 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-bon3 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 trails, and additional data are needed.

Prophylactic indications now account more than half of all filter!

- 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.

- 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).

- 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!!

SAME INDICATIONS

DOCUMENTED VTF

- 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.

### **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?

### **ACR/SIR GUIDELINES**

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

Abbreviations: ACR, American College of Radiology; DVT, deep venous thrombosis; IVC, inferior vena cava; PE, pulmonary embolism; SIR, Society of Interventional Radiology; VTE, venous thromboembolism.

### **AHA GUIDELINES**

- Adult patients with any acute proximal DVT (or acute PE) with contraindications to anticoagulation or active bleeding complication should receive an IVC filter (Class I: Level of Evidence B)
- 2. Anticoagulation should be resumed in patients with an IVC filter once contraindications to anticoagulation or active bleeding complications have resolved (Class I; Level of Evidence B)
- 3. Patients who receive retrievable IVC filters should be evaluated periodically for filter retrieval within the specific filter's retrieval window (Class I; Level of Evidence C)
- 4 For patients with recurrent PE despite therapeutic anticoagulation, it is reasonable to place an IVC filter (Class IIa; Level of Evidence C)
- 5. For IFDVT patients who are likely to require permanent IVC filtration (e.g., long-term contraindication to anticoagulation), it is reasonable to select a permanent nonretrievable IVC filter device (Class IIa; Level of Evidence C)
- For IFDVT patients with a time-limited indication for an IVC filter (e.g., a short-term contraindication to anticoagulant therapy), placement of a retrievable IVC filter is reasonable (Class IIa; Level of Evidence C)
- For patients with recurrent DVT (without PE) despite therapeutic anticoagulation, it is reasonable to place an IVC filter (Class IIb: Level of Evidence C)
- 8. An IVC filter should not be used routinely in the treatment of IFDVT (Class III; Level of Evidence B)

Abbreviations: AHA, American Heart Association; DVT, deep venous thrombosis; IFDVT, iliofemoral deep venous thrombosis; IVC, inferior vena cava; Abbreviations; IVC, inferior vena cava; PE, pulmonary embolism; VTE, venous thromboembolism.

### **ESC GUIDELINES**

Indicated for	
Documented VTE and contraindication to anticoagulation	
Recurrent PE despite anticoagulation	
Not recommended for	
Prophylactic placement	
Free-floating thrombus	
Prior to systemic thrombolysis, surgical embolectomy, or pulmonary thromboendarterectomy	

### **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 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)

Abbreviations: CTPH, chronic thromboembolic pulmonary hypertension; DVT, deep venous thrombosis; IVC, inferior vena cava; PE, pulmonary embolism.

### BRITSH COMMITTEE FOR STANDARDS IN HAEMATOLOGY GUIDELINES

IVC filter Indicated
For patients with VTE and contraindication to anticoagulation
Consider IVC filter placement
In select patients with PE despite anticoagulation
In pregnant patient with VTE and contraindications to anticoagulation (including estimated delivery within 2 wk)
Preoperatively (retrievable) for patients with recent VTE (1 mo) and need to stop anticoagulation therapy for surgery
IVC filters not recommended for
Unselected patients with VTE who can receive anticoagulation
Free-floating thrombus
Thrombolysis

N. C.	Recommendations	Classa	Levelb	
	IVC filters should be considered in			
	patients with acute PE and absolute	lla	С	
	contraindications to anticoagulation.			
	IVC filters should be considered in			
	case of recurrence of PE, despite	lla	С	
	therapeutic levels of anticoagulation.			
	Routine use of IVC filters in patients			
	with PE is not recommended.	III	A	

### SIZE OF TREATMENT EFFECT

SIZE OF TREATMENT EFFECT								
Recommenda	tions	Classa	Levelb	014001	01 400 11	01 100 111	01.000 111.11.00 111	
IVC filters should be considered in				CLASS I	CLASS IIa	CLASS IIb	CLASS III No Benefit or CLASS III Harm	
patients with acute PE and absolute		lla	С	Benefit >>> Risk	Benefit >> Risk	Benefit ≥ Risk	And the second second second second	
contraindications to anticoagulation.				Procedure/Treatment	Additional studies with	Additional studies with broad	Procedure/ Test Treatment	
IVC filters should be considered in				SHOULD be performed/	focused objectives needed	objectives needed; additional		
case of recurrence of PE, despite		lla	С	administered	IT IS REASONABLE to per-	registry data would be helpful	COR III: Not No Proven No benefit Helpful Benefit	
	els of anticoagulation.				form procedure/administer	Procedure/Treatment	COR III: Excess Cost Harmful	
Routine use of IVC filters in patients with PE is not recommended.		Ш	A		treatment	MAY BE CONSIDERED	Harm w/o Benefit to Patients or Harmtui	
F TREATMENT EFFECT	LEVEL A  Multiple popula evaluated*  Data derived fr randomized clir or meta-analys	om mul nical tri		■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	Recommendation that procedure or treatment is not useful/effective and may be harmful  Sufficient evidence from multiple randomized trials or meta-analyses	
CERTAINTY (PRECISION) OF	evaluated* Data derived fr single randomi	ited populations		<ul> <li>■ Recommendation that procedure or treatment is useful/effective</li> <li>■ Evidence from single randomized trial or nonrandomized studies</li> </ul>	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized ctudies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies	
ESTIMATE OF CERT	Very limited po evaluated* Only consensus of experts, cas or standard of	s opinio e studio	n	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care	

# PREPIC-1

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NUMBER 7



A CLINICAL TRIAL OF VENA CAVAL FILTERS IN THE PREVENTION OF PULMONARY EMBOLISM IN PATIENTS WITH PROXIMAL DEEP-VEIN THROMBOSIS

Decousus H et al. N Engl J Med. 1998 Feb 12;338:409-15.

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

The PREPIC (Prévention du Risque d'Embolie Pulmonaire par Interruption Cave) Randomized Study

The PREPIC Study Group\*

Circulation 2005 Jul 19;112:416-22.

- 400 patients with proximal DV To-Filter Groups.\*
- All anticoagulated (heparin followed by warfarin)
- Halfwere and an inverse to receive a percent local filter.

Symptomatic pulmonary		
embolism†		
Enrollment-3 mo	2	6
>3 mo-1 yr	0	4

**TABLE 2.** PRINCIPAL END POINTS WITHIN THE FIRST 12 DAYS AFTER RANDOMIZATION TO THE FILTER OR NO-FILTER GROUP.

END POINT	FILTER	No FILTER	ODDS RATIO (95% CI)*	P VALUE	
	number	(percent)			
Pulmonary embolism Symptomatic† Asymptomatic	2 0	5			
All‡	2 (1.1)	9 (4.8)	0.22	0.03	
			(0.05-0.90)		
Major bleeding	9 (4.5)	6 (3.0)	1.49 (0.53-4.20)	0.44	
Death	5 (2.5)	5 (2.5)	$0.99 \\ (0.29-3.42)$	0.99	

- Difference in a symptomatic embolisher in the property of the pro
- (ACINATION DE LA CONTROL DE LA
- patients who received a filter.

  This approach may have detected small and

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

**VOLUME 338** 

# PREPIC-2

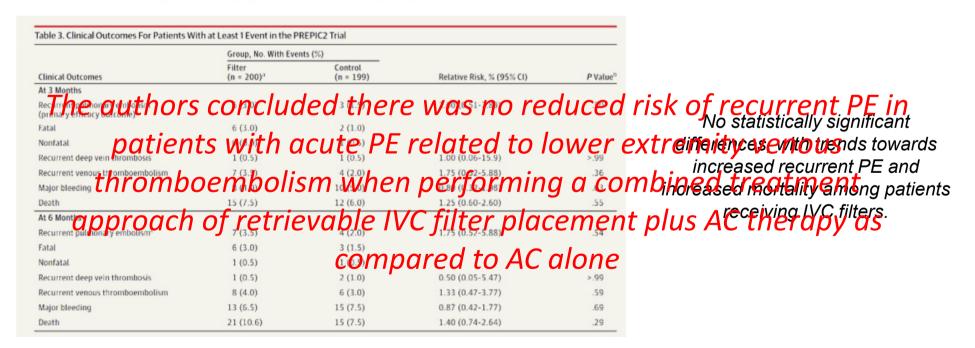
Jama 2015 Apr 28;313:1627-35.

### **Original Investigation**

# 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, PhD; Silvy Laporte, MS, PhD; Olivier Pellerin, MD, MSc; Pierre-Vladimir Ennezat, MD, PhD; Francis Couturaud, MD, PhD; Antoine Elias, MD, PhD; Nicolas Falvo, MD; Nicolas Meneveau, MD, PhD; Isabelle Quere, MD, PhD; Pierre-Marie Roy, MD, PhD; Olivier Sanchez, MD, PhD; Jeannot Schmidt, MD, PhD; Christophe Seinturier, MD; Marie-Antoinette Sevestre, MD; Jean-Paul Beregi, MD, PhD; Bernard Tardy, MD, PhD; Philippe Lacroix, MD; Emilie Presles, MSc; Alain Leizorovicz, MD; Hervé Decousus, MD; Fabrice-Guy Barral, MD; Guy Meyer, MD; for the PREPIC2 Study Group

- BBOPpatie tBEwith Vacciulters/12 days simple with a tic PE and DVT
- Retrieved bell and fictors or a retrievable IVC filter.



# **LIMITS**

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VOLUME 338

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- AC therapy in both groups was possible and effective.
- In clinical practice, common indications for IVC filter placements are AC not effective or controllicated.
- 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.

# In addition to lack of benefit, IVC filters are associated with complications!

# Immediate complications

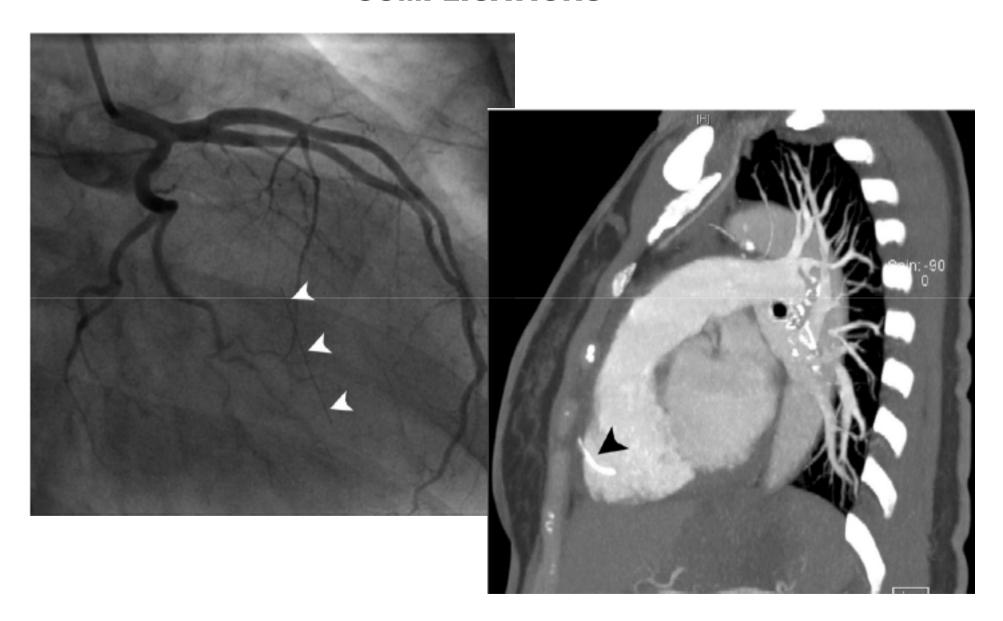
- Misplacement (1.3%)
- Peumothorax (0.02%)
- Haematoma (0.6%)
- Air embolism (0.2%)
- Carotid artery puncture (0.04%)
- Arteriovenous fistula (0.02%)

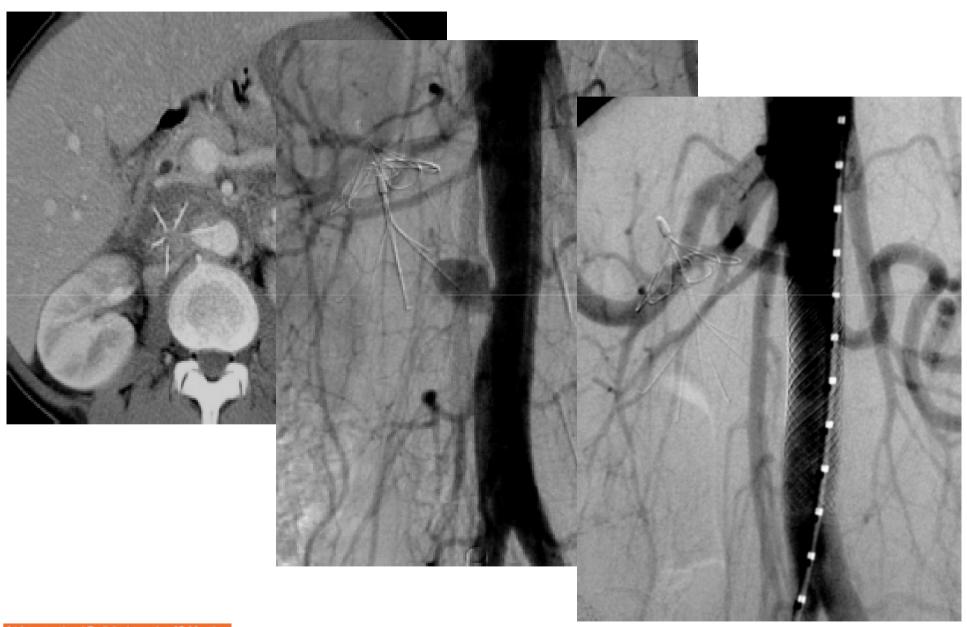
# Early complications

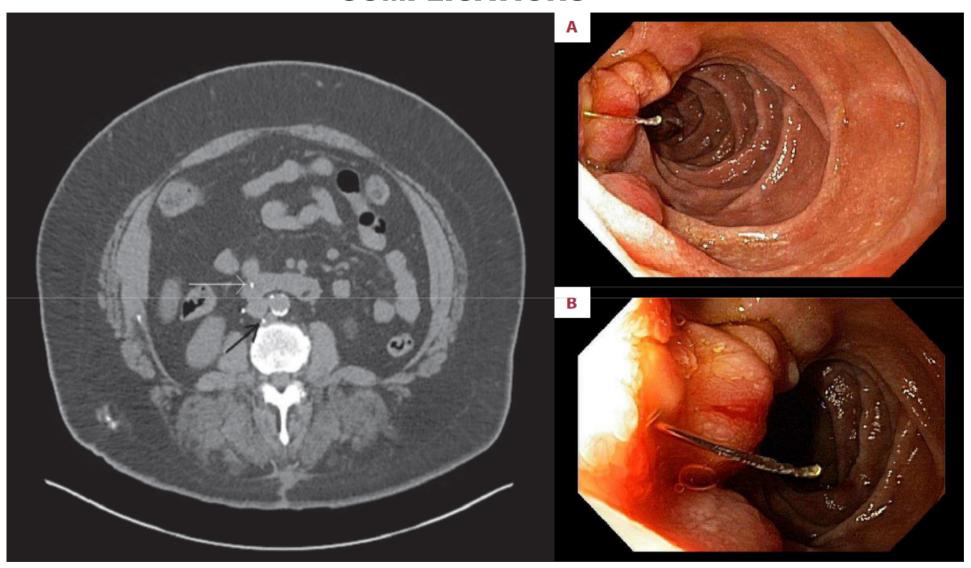
- Insertion site thrombosis (8.5%)
- Infection

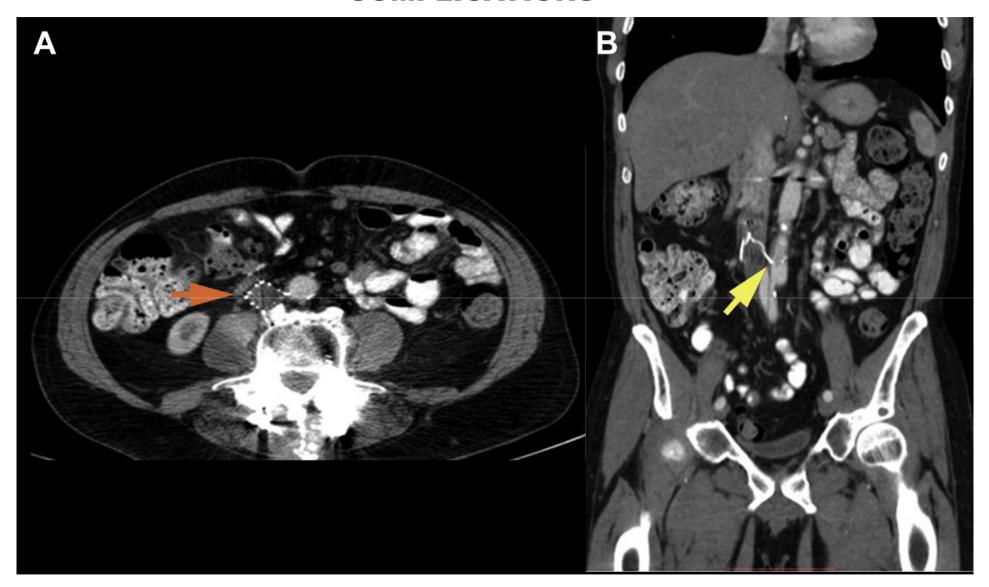
# Late complications

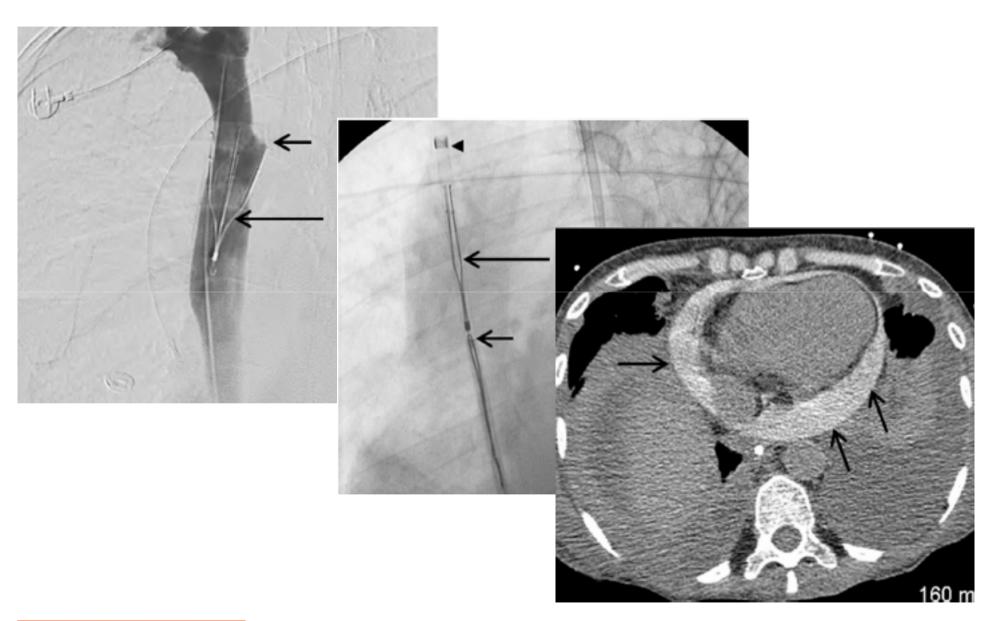
- Recurrent DVT (21%)
- IVC thrombosis (2–10%)
- Post-thrombotic syndrome (15–40%)
- IVC penetration (0.3%)
- Filter migration (0.3%)
- Filter tilting and fracture
- Entrapment of guidewires

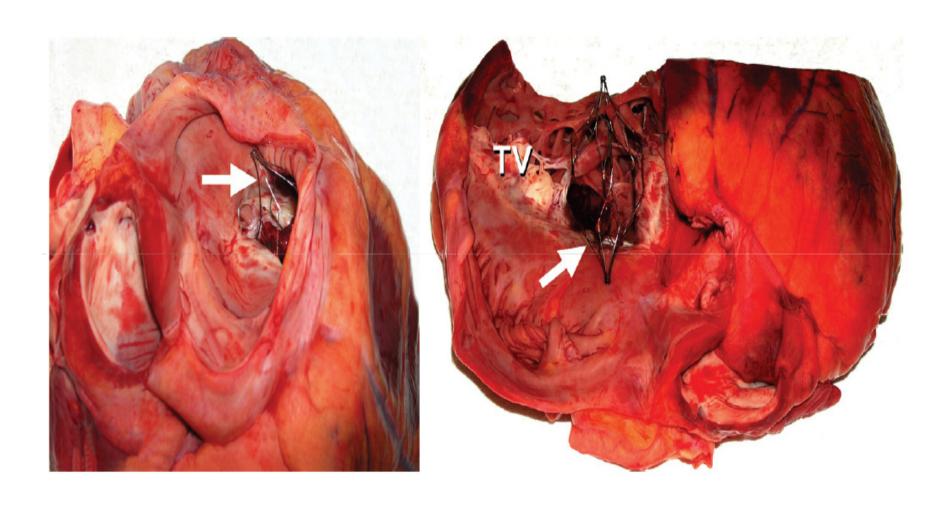












# **CONCLUSIONS**

- Theorically 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 pubblications: 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....

Recommendations	Classa	Levelb
IVC filters should be considered in patients with acute PE and absolute contraindications to anticoagulation.	lla	O
IVC filters should be considered in case of recurrence of PE, despite therapeutic levels of anticoagulation.	IIa	С
Routine use of IVC filters in patients with PE is not recommended.	Ш	A





# **CONCLUSIONS**

Prasad V et al. Jama intern med 2013 Apr 8;173:493-5

# The Inferior Vena Cava Filter

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

# Grazie per l'attenzione