

[B]	[처 방 내 역]	용량	단위	횟수	일수	용
	Artery Bypass(인조혈관이용)[대퇴-슬와동맥]					

처방코드	00164	X
처 방 명	Artery Bypass(인조혈관이용)[대퇴-슬와동맥]	
의 보 수 가		555,477
일 반 수 가		1,281,870

[B]	[처 방 내 역]	용량	단위	횟수	일수	용
	Lower Extremity Arteriography [흉부외과]					
	혈관내 스텐트 삽입술(기타혈관)[흉부외과용]					

처방코드	RA149CS	X
처 방 명	Lower Extremity Arteriography [흉부외과]	
의 보 수 가		354,069
일 반 수 가		819,810

처방코드	M6609CS	X
처 방 명	혈관내 스텐트 삽입술(기타혈관)[흉부외과]	
의 보 수 가		967,577
일 반 수 가		2,232,870



# C-arm vs Cath room vs Hybrid-room



**Hybrid-room**



**Operation-room**



**Cath-room**



# Field of Vascular Care !!



## **Lower Extremity Disease**

Iliac artery disease

SFA ds – long occlusion, femoropopliteal disease

Below the Knee

## **Renal, Carotid, Subclavian Artery Stenosis**

**Venous disease** – SVC, DVT, Vein occlusion

**Aorta Disease** – Aortic dissection, aneurysm, AAA

**Adult congenital and structural heart disease (TAVI,  
ASD closure, percutaneous MVP)**

# Summary

# Venous Thromboembolic Disorder

- Deep Vein thrombosis / Pulmonary embolism
  - Possible cause of mortality
    - First year mortality of acute DVT; 19-21%
    - PE death; 15% hospital death, 150,000-200,000 death/year in USA
  - Significant morbidity due to progression to chronic venous insufficiency



▶유럽에서는 매년 유방암, 교통사고, AIDS환자 보다 더 많은 환자가 DVT나 PE\*로 사망하고 있습니다.

# Isolated calf vein thrombosis

- Differences in
  - Rates of PE / post-thrombotic complications
- **Recanalize more rapidly**
- Lower reflux in involved calf vein segments
- Lower long term complication
  - PE : 10%, 33% by V/Q scan
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- Proximal propagation : 15% to 23%
  - in the absence of treatment
    - 1/4 - 1/3 by Kearon
- **However, Need anticoagulation & Compression stocking!!!**



# Acquired Risk Factors - Surgery

Basic



	Calf DVT	Proximal DVT	Fatal PE
<b>High risk</b>	40-80%	10-30%	>1%
<ul style="list-style-type: none"> <li>• Surgical patients with history of venous thromboembolism</li> <li>• Major pelvic or abdominal surgery for malignancy</li> <li>• Major trauma</li> <li>• Major lower limb orthopedic surgery</li> </ul>			
<b>Moderate risk</b>	10-40%	1-10%	0.1-1%
<ul style="list-style-type: none"> <li>• Geberak surgery in patients &gt;40 years</li> <li>• Patients on oral contraception</li> <li>• Neurosurgical patients</li> </ul>			
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<ul style="list-style-type: none"> <li>• Uncomplicated surgery in patients &lt;40 years without any other risk factors</li> <li>• Minor surgery in patients &gt;40 years without any other risk factors</li> </ul>			

# Lecture



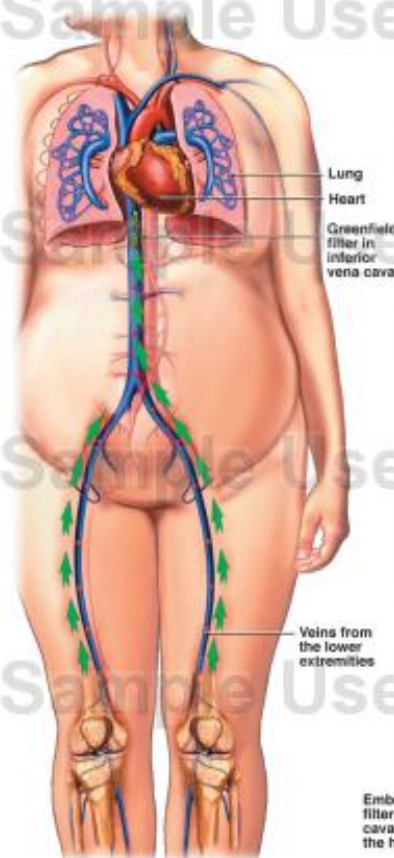
# **Deep Vein Thrombosis & Pulmonary Embolism : overview & treatment**

**Department of Thoracic and Cardiovascular Surgery  
Mediplex Sejong Hospital  
Joon Hyuk Kong**

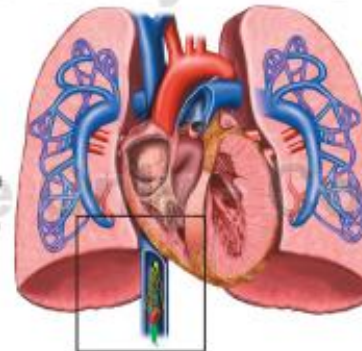
# 심부정맥 혈전증의 위험성

## DVT and Pulmonary Embolism - Greenfield Filter Placement

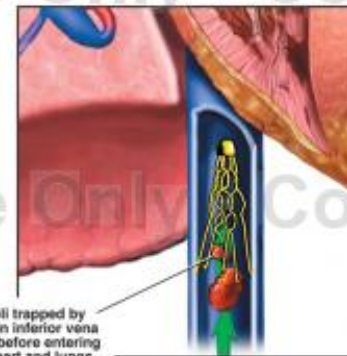
Path of Emboli from the Lower Extremities to the Lungs



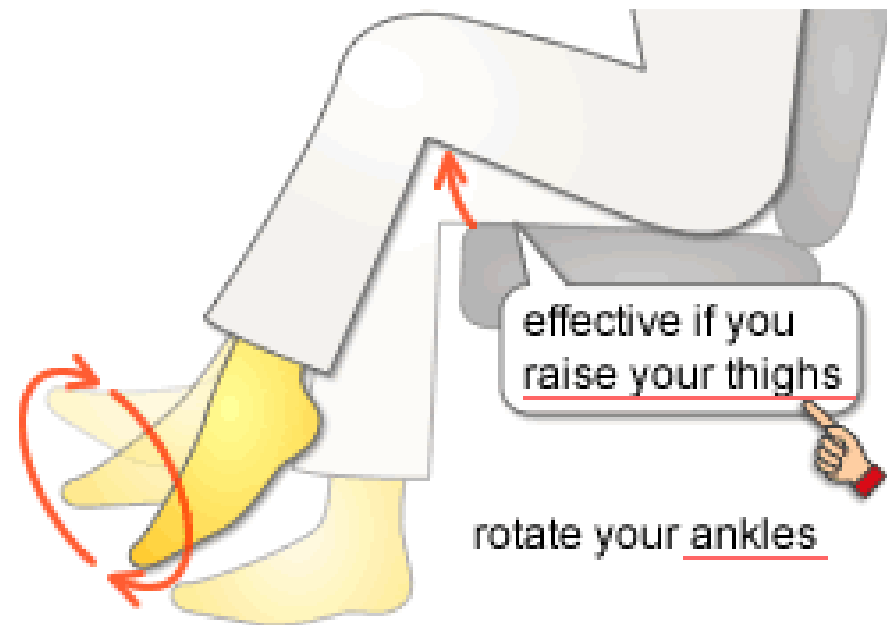
Greenfield Filter, Heart and Lungs



Greenfield Filter

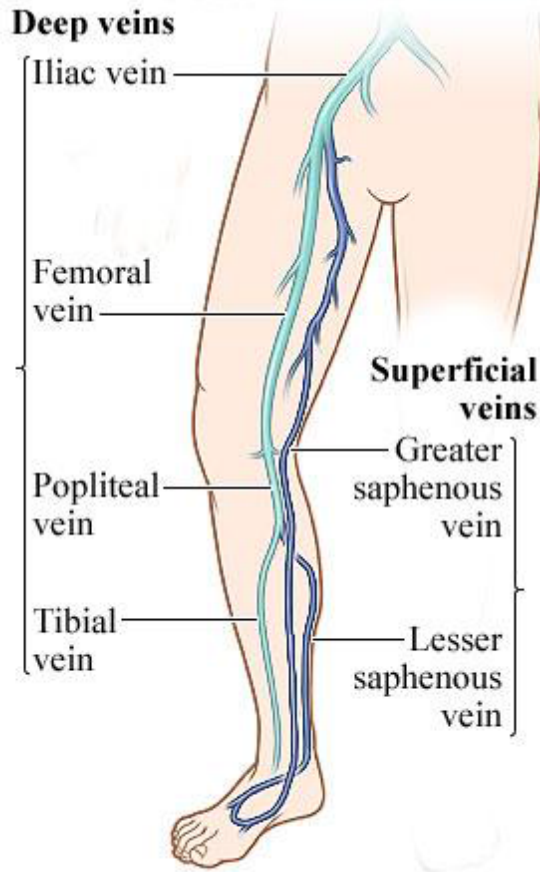


# Economy class syndrome



# **Anatomy**

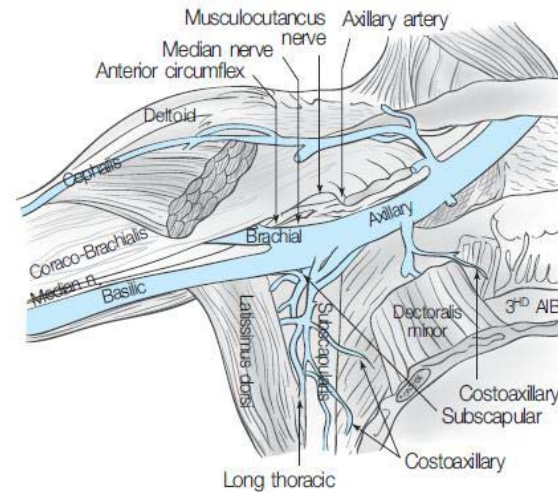
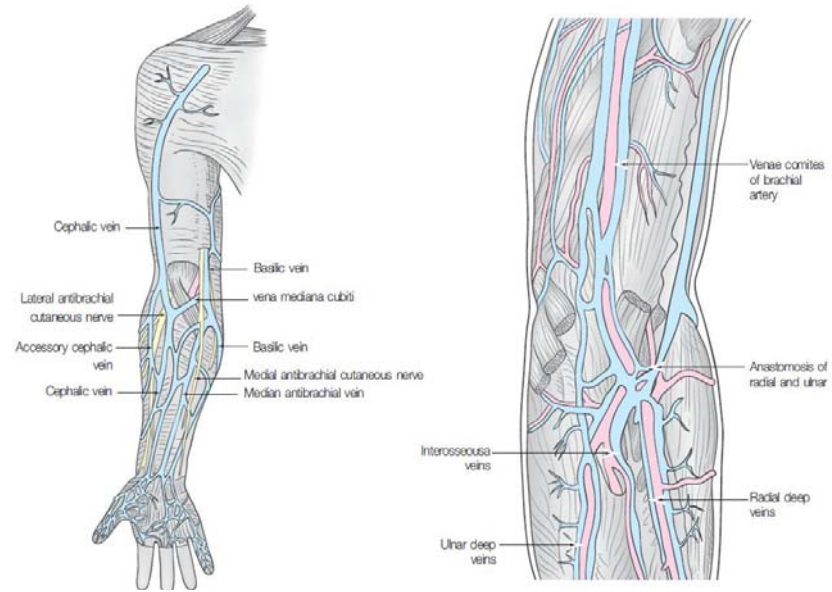
# Venous System



great

small

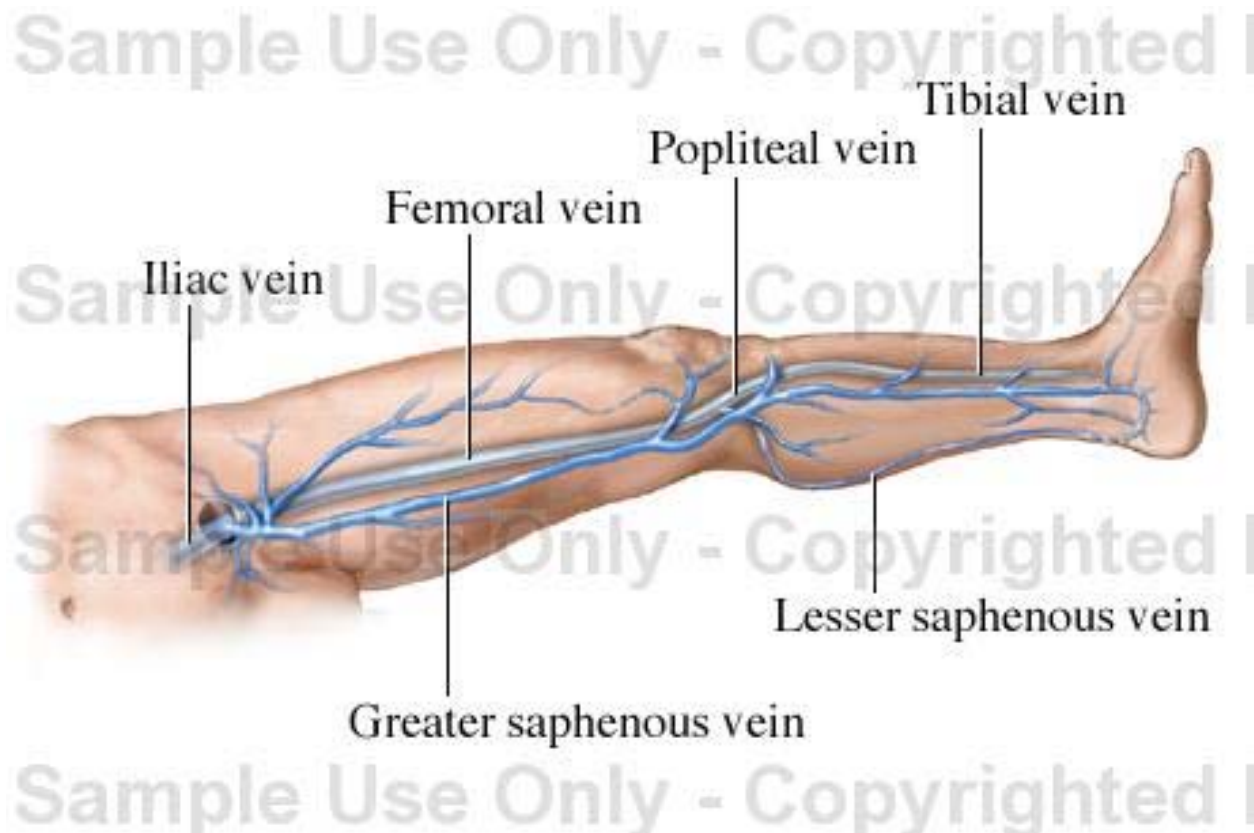
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# **Pathophysiology**

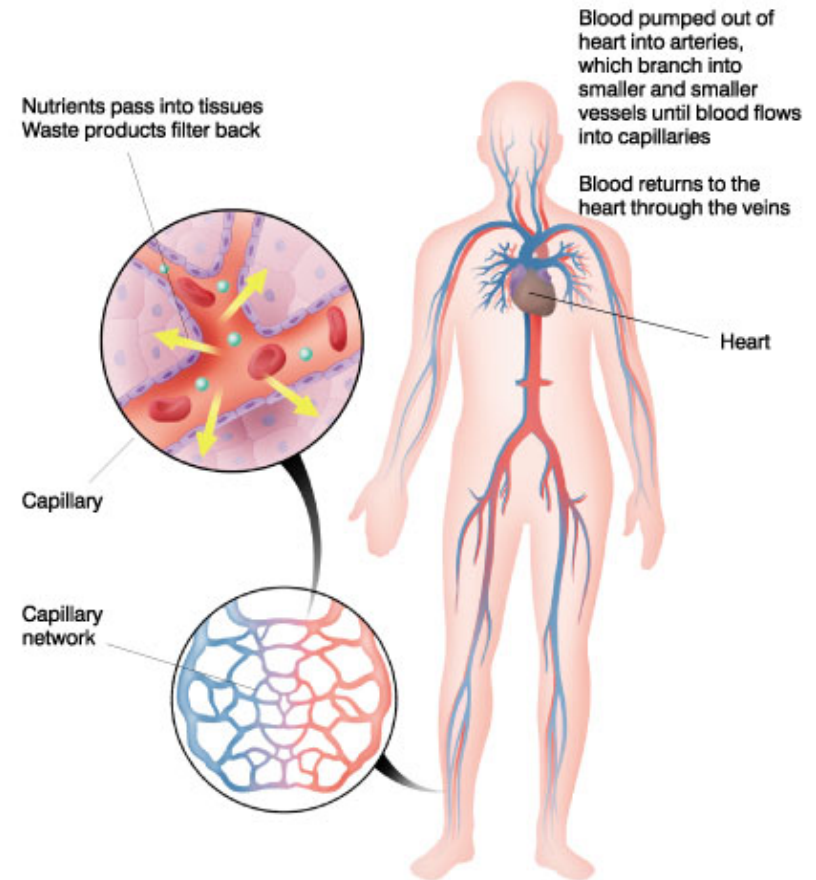
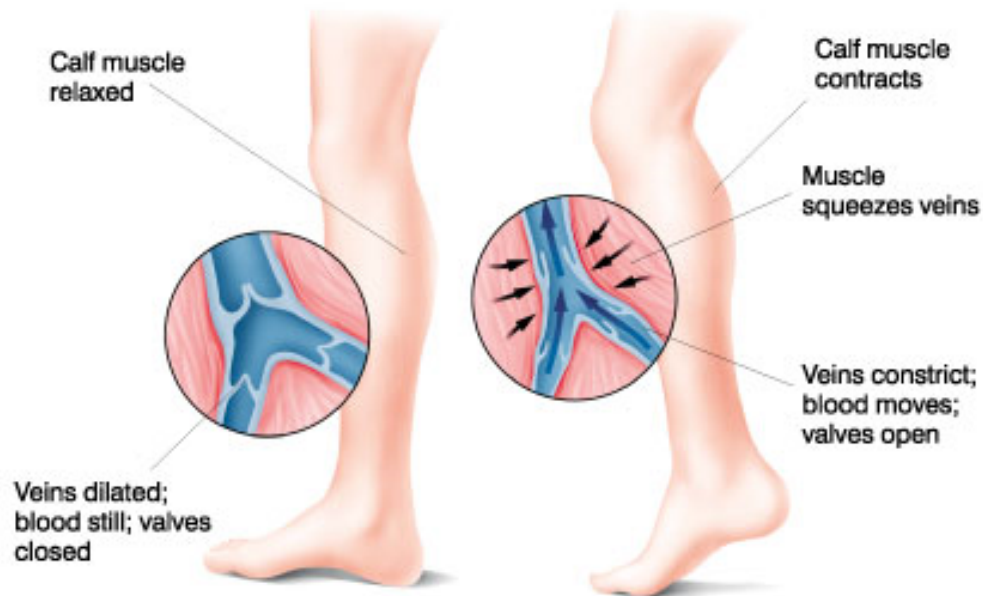
# Summary

# 하지정맥의 구조





# 하지정맥의 순환



# Venous Thrombosis Disorder

참고하세요.

- **Deep Vein thrombosis / Pulmonary embolism**

- Traveler's thrombosis (Economy class syndrome)
- Chronic venous insufficiency



- **Other forms of venous thrombosis**

- Superficial thrombophlebitis
- Axillary-Subclavian thrombosis
- Mesenteric venous thrombosis



참고하세요.

# Superficial Thromb

- Cause ; Spontaneous, Trauma, Varicose vein, Buerger's disease, Malignancy, Hypercoagulability
- Not related with bacterial infection, except caused by recent iv catheterization
- Symptoms ; localized pain, erythema, warmth, tenderness, swelling, palpable cord
- **Asymptomatic Synchronous DVT(+)** in **35%** => Check venous duplex study!
- Indication for treatment
  - Isolated superficial thrombophlebitis with encroachment on the S-F junction
  - Purulent infection
  - >5cm involvement: 45 days LMWH



# Venous Thromboembolic Disorder

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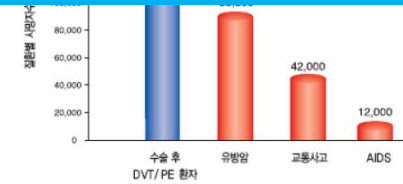


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# Venous Thromboembolic Disorder

참고하세요.

- Incidence of acute DVT
  - Autopsy cases ; 35-52%
  - Community-based, venography, symptomatic ; 1.6 /1000 residents, yearly
  - Postoperative DVT; GS(19%), NS(24%), hip fracture(48%), hip arthroplasty(51%), knee arthroplasty(61%)
  - Trauma; autopsied casualties(62%), venography(58%) -- duplex(4-20%)



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# Epidemiology and history

참고하세요.

- The incidence of **recurrent, fatal, and non fatal VTE** has been estimated to exceed 900,000 cases annually in the united state alone.
- In the United States of America, 200,000 new cases of **pulmonary embolism(PE)** occur each year, and 50,000 of these result in death.
- **VTE** kills four to five more people annually than dose breast cancer or acquired Immunodeficiency syndrome.
- **PE** is the third most common fatal vascular disorder following coronary artery disease (CAD) and cerebrovascular accident (CVA).
- The in-hospital mortality rate is 12%, and it is thus the number one preventable death in hospitalized patients.

(\*Rutherford's Vascular Surgery 7th edition, section 7 venous disease, chapter 48, p 736, chapter 50, p 770, Saunders 2010)

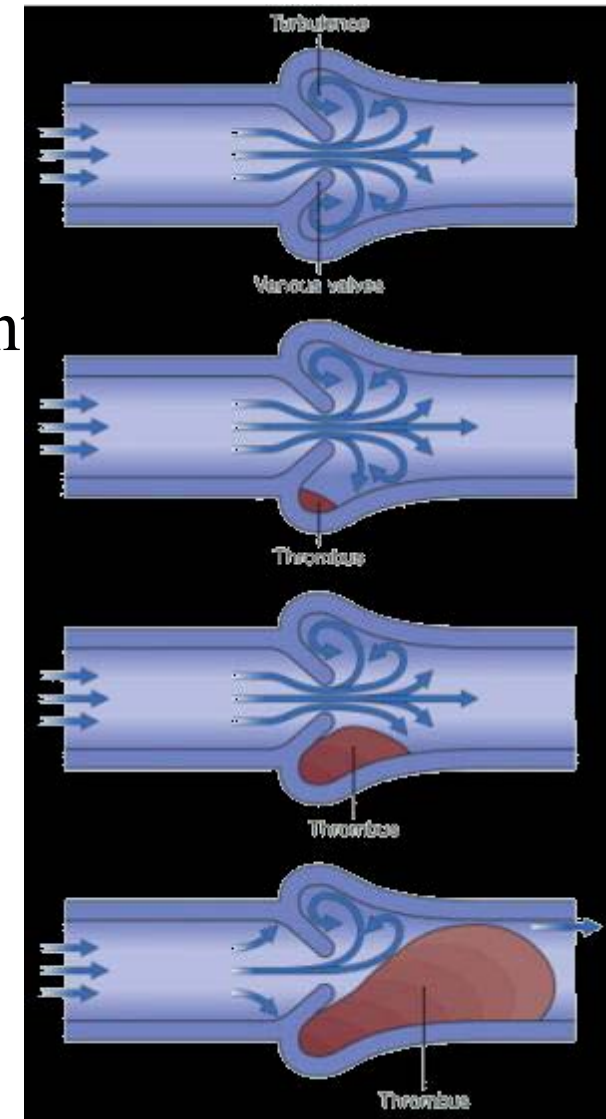
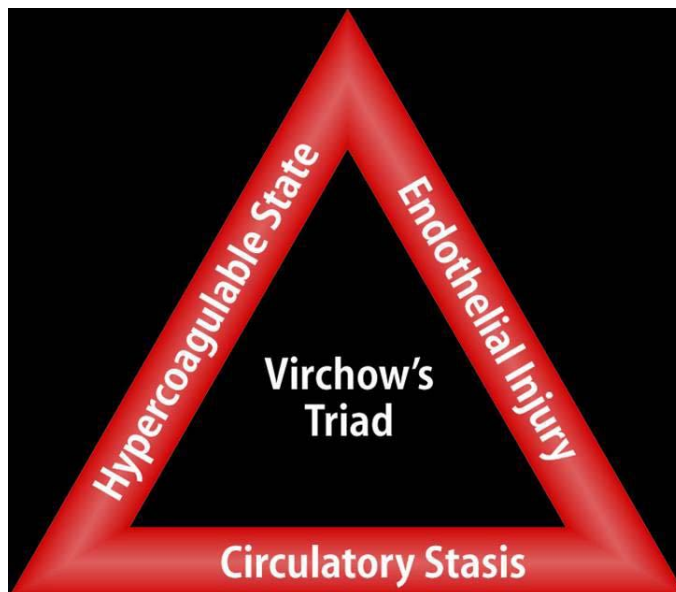
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# Pathophysiology

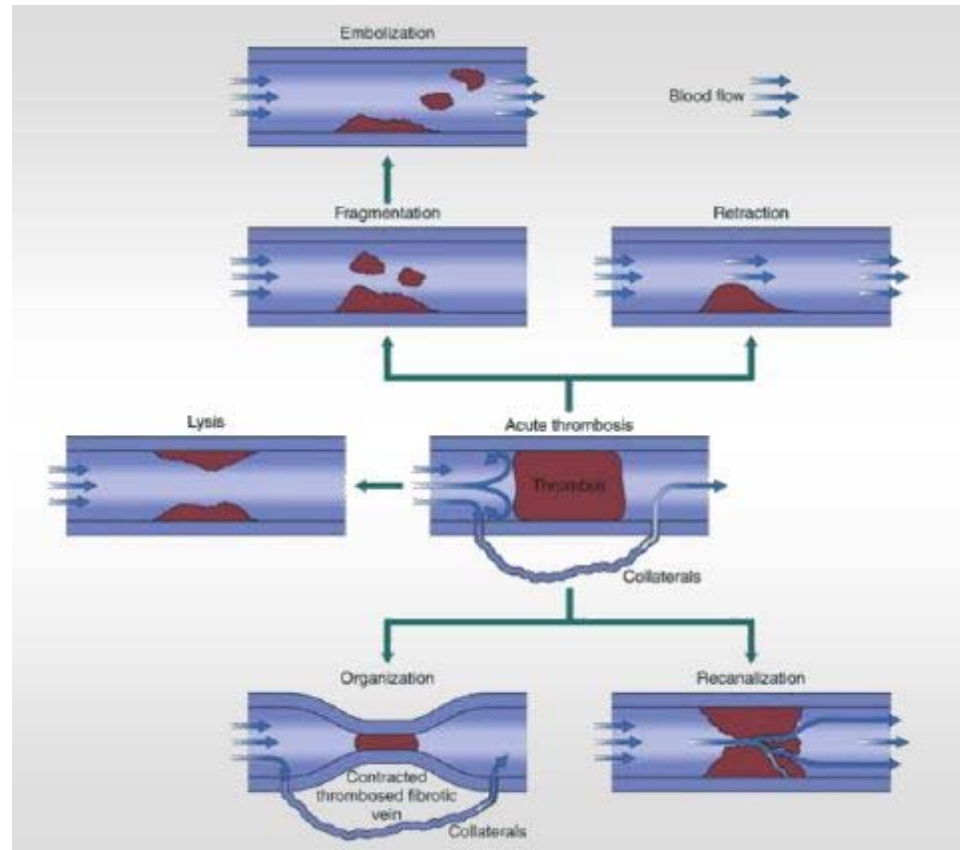
- **Virchow's triad**
  - Endothelial abnormality
  - Stasis of blood flow (predominant)
  - Hypercoagulability of blood





# Pathophysiology consequences

참고하세요.



# Clinical spectrum of acute DVT

1. Asymptomatic calf vein thrombosis
2. Symptomatic calf vein thrombosis
3. Femoropopliteal DVT
4. Phlegmasia Alba Dolens
5. Phlegmasia Cerulea Dolens
6. Venous gangrene

# Clinical Course

- **Acute (<2wks)**
  - Flow void, low echogenic thrombus, venous distension, loss of compression
- **Subacute (2-4wks)**
  - Increased echogenecity, decreased venous size, resumption of flow
- **Chronic (>4wks)**
  - Echogenic thrombus, wall irregularity, valve abnormality, collateral veins

# Clinical Course

- Acute DVT
  - Symptomless, warmness, redness, pain, swelling
- Phlegmasia alba dolens (=milk leg, white leg)
  - Increased tissue pressure exceeds the capillary perfusion pressure, causing pallor
- Phlegmasia cerulea dolens(=blue leg)
  - Deoxyhemoglobin in stagnat vein imparts a cyanotic hue to the limb

# **Phlegmasia alba dolens (=white leg)**



# Phlegmasia cerulea dolens (=blue leg)



# **Risk Factors**

# Risk factor hypercoagulable

참고하세요.

Inherited	Acquired
<b>Common</b>	<b>Age</b>
Factor V Leiden	Surgery and trauma
Prothrombin gene mutation (G20110A)	Immobilization
Homozygous C677T mutation in methylene tetrahydrofolate reductase gene	Malignant disease
	Previous venous thromboembolism
	Pregnancy and puerperium
	Oral contraceptive
	Hormone replacement therapy
	Antiphospholipid antibodies
<b>Rare</b>	<b>Unknown (probably multifactorial)</b>
Antithrombin deficiency	Elevated levels of factor VIII, IX, and XI and fibrinogen
Protein S deficiency	
Protein C deficiency	
Dysfibrinogenemia	
Homozygous homocystinuria	



# Acquired Risk Factors - Surgery

Basic



	Calf DVT	Proximal DVT	Fatal PE
<b>High risk</b>	40-80%	10-30%	>1%
<ul style="list-style-type: none"> <li>• Surgical patients with history of venous thromboembolism</li> <li>• Major pelvic or abdominal surgery for malignancy</li> <li>• Major trauma</li> <li>• Major lower limb orthopedic surgery</li> </ul>			
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## Acquired Risk Factors

참고하세요.

- **Old age**
  - a major risk factor of VTE
- **Prior venous thromboembolism**
  - independent risk factor for future VTE / adequate prophylaxis
- **Immobilization**
  - 60% of the paralyzed limb / 7% contralateral normal control leg
  - air travel
- **Malignancy**
  - resulting from activation of the coagulation cascade?
- **Superficial thrombophlebitis**
  - an independent risk factor for VTE
- **Antiphospholipid antibody syndrome**
  - anticardiolipin antibody / lupus anticoagulant antibody
  - 2% of population / 30-50% of patients with SLE
  - 50% frequency of DVT/ half having PE

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## Inherited Thrombophilia

참고하세요.

### Epidemiology

Thrombophilia	General population (%)	Patients with VTE (%)
Factor V Leiden*	5	20
Prothrombin G20210A	3	7
Elevated factor VIII**	6-8	10-15
Protein C deficiency	0.2-0.5	3
Protein S deficiency	0.2-0.5	3
Antithrombin deficiency	0.01	1
Hypofibrinogenemia**	5	10

\*Rare in the Asian and African populations

\*\* Mildly raised and/or normal

- **Diagnosis of inherited thrombophilia**
  - Should be considered in **any patient with VTE**

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## Inherited Thrombophilia

참고하세요.

### Regulation of coagulation pathway



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## Inherited Thrombophilia

참고하세요.

### Mechanism of thrombosis



- **Investigation for suspected inherited thrombophilia**
  - age less than 45 years
  - recurrent episodes of VTE
  - Family history of VTE
  - thrombosis at unusual venous sites such as dural sinuses
  - recurrent miscarriages

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참고하세요.

# Acquired Risk F

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Hyperhomocysteinemia**	5	10

- Diagnosis of inherited thrombophilia

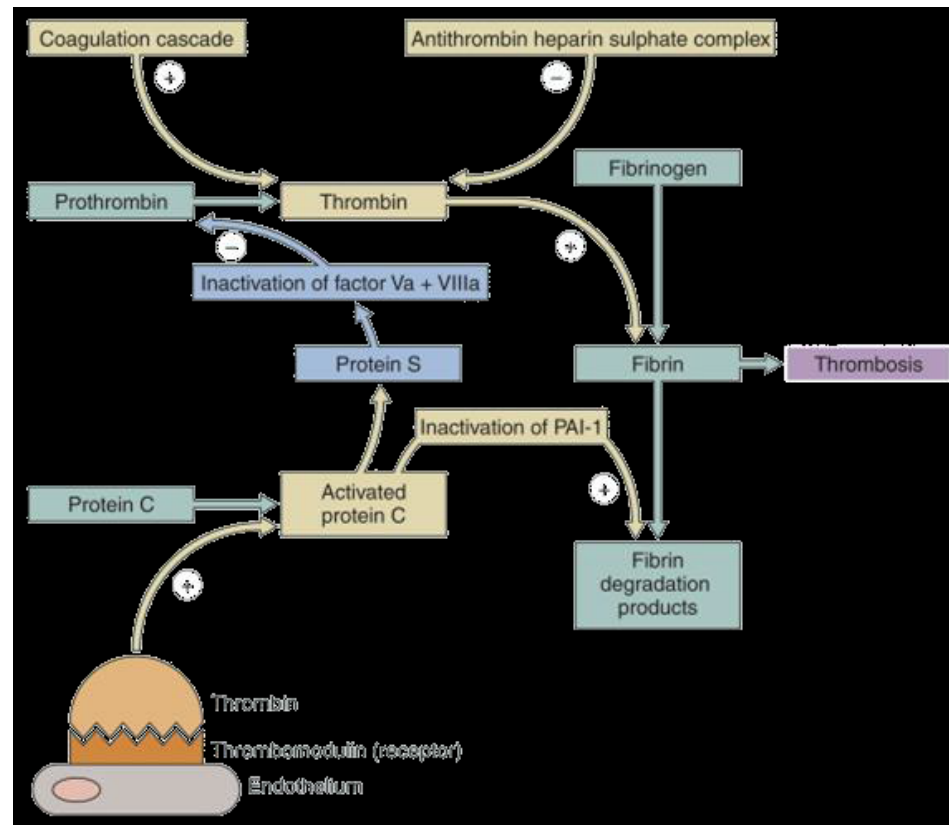
\*Rare in the Asian and African populations

\*\*Likely to be multifactorial

Should be considered in any patient with VTE

# Inherited Thrombophilia

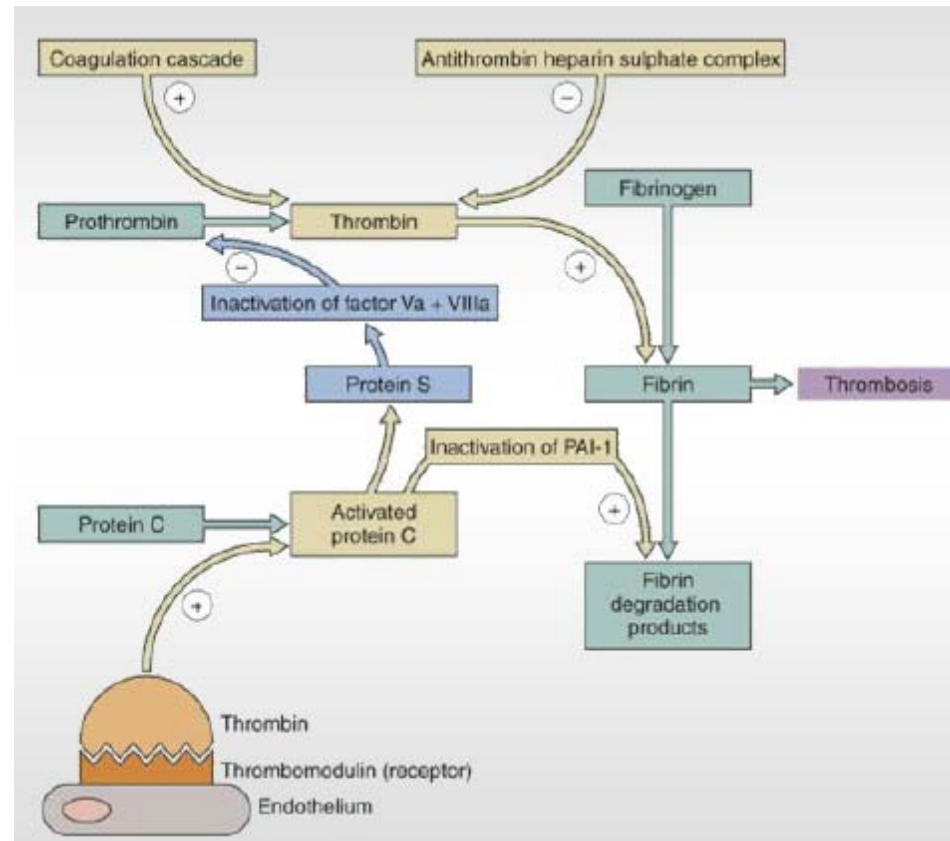
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참고하세요.

# Inherited Throm

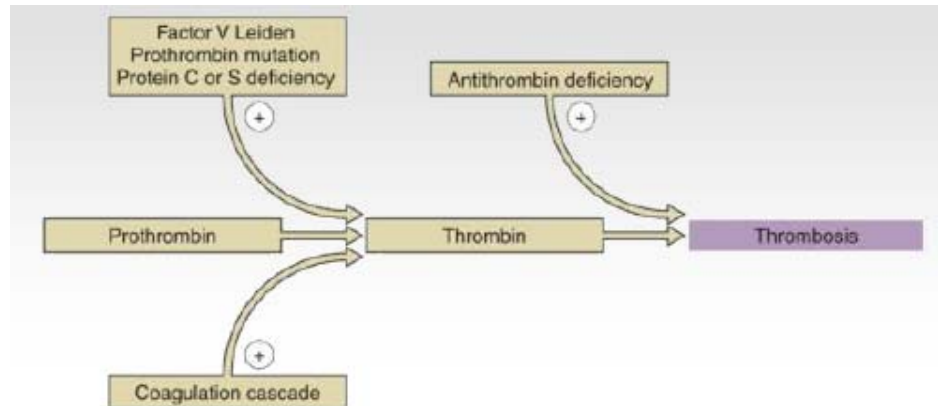
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참고하세요.

# Inherited Throm

- Mechanism of thrombosis



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  - recurrent miscarriages

ombophilia

# **Clinical Features**



# Clinical Features – L/E DVT

- **Mostly asymptomatic**
- Pain, Edema
  - due to vein obstruction, inflammation of perivascular tissue, lymphatic obstruction
- Distention of superficial veins
- Cutaneous erythema
- Homan's sign
  - pain in calf with forced dorsiflexion of foot



참고하세요.

# Clinical Features –

- **Less common (2-5% of population)**
- **Indwelling mechanical devices**
  - pacer lead, central venous catheters
  - 30-40% of cases
- **Conditions of venous compression**
  - lymphadenopathy, tumors
- **Paget-Schroetter syndrome**
- **10-30% risk for PE (similar to leg DVT)**



# Clinical Features – PE

- Classification of PE

Pulmonary embolism	History	Pathophysiology	Therapy
Acute massive	Acute	Circulatory collapse	Thrombolysis, thrombectomy
Acute submassive	Acute	Stable, echocardiographic signs of RV overload	Thrombolysis?, heparin
Acute nonmassive	Acute	Stable	Heparin
CTEPH (Chronic thromboembolic pulmonary Hypertension)	Chronic	RV overload	Medical or elective thromboendarterectomy

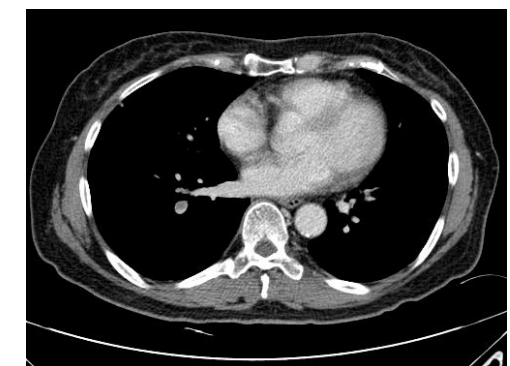
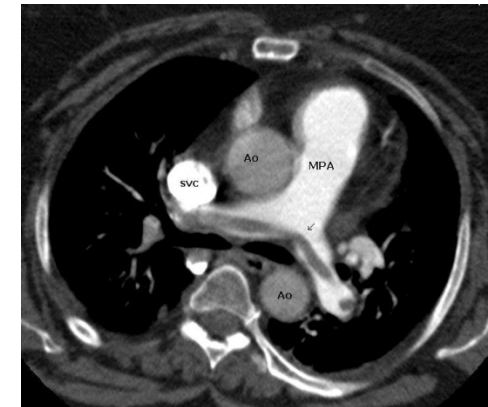
- Acute massive: >50% PA occlusion**

- sudden death in 10%, within 1 hr,
    - severe acute dyspnea, syncope

- Acute submassive**

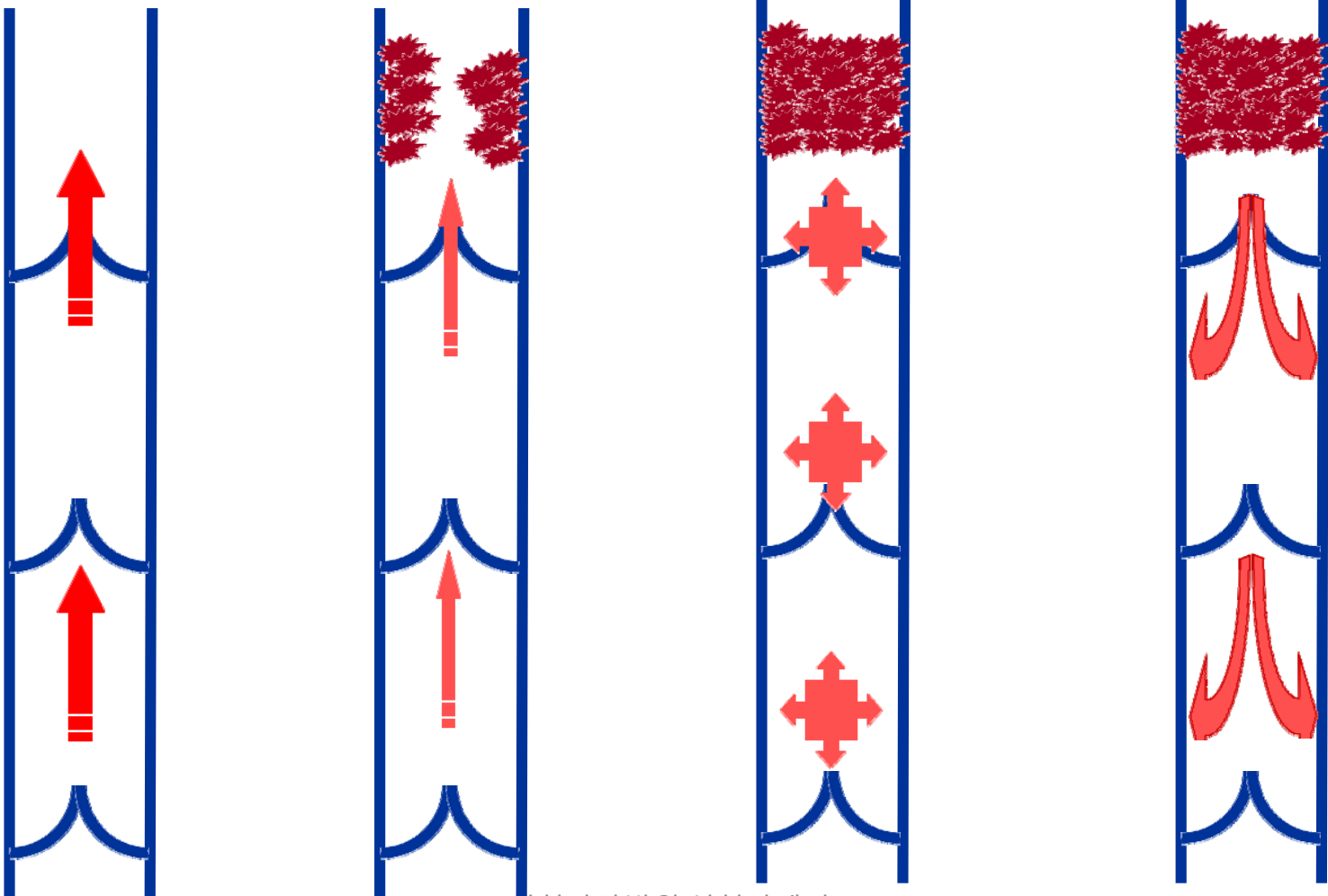
- Acute nonmassive: <50% PA occlusion**

- asymptomatic or tachypnea, dyspnea, pleuritic pain

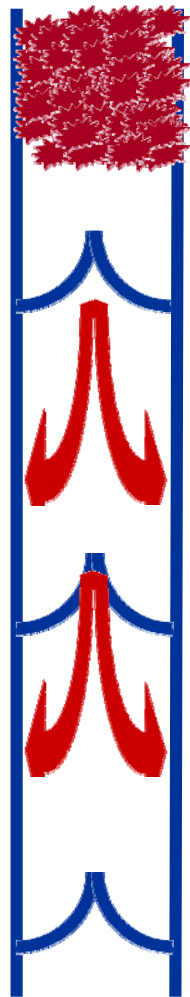


# Complication

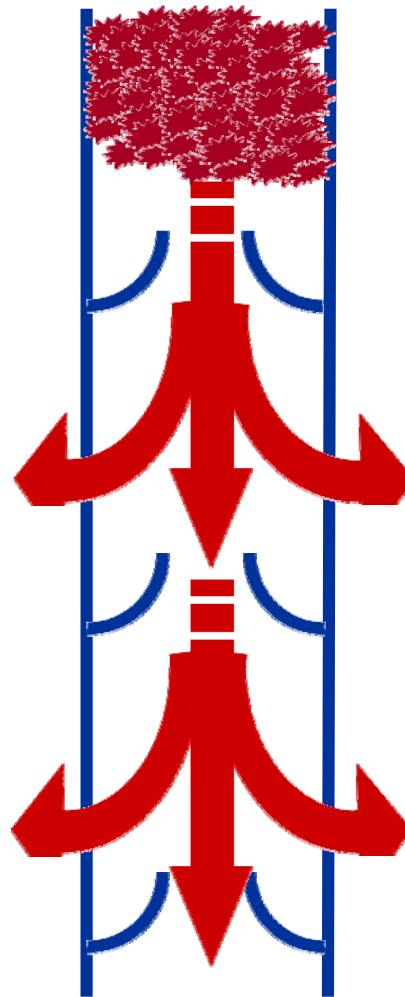
# 합병증 발생기전-01



# 합병증 발생기전-02



- **Venous valvular incompetence**



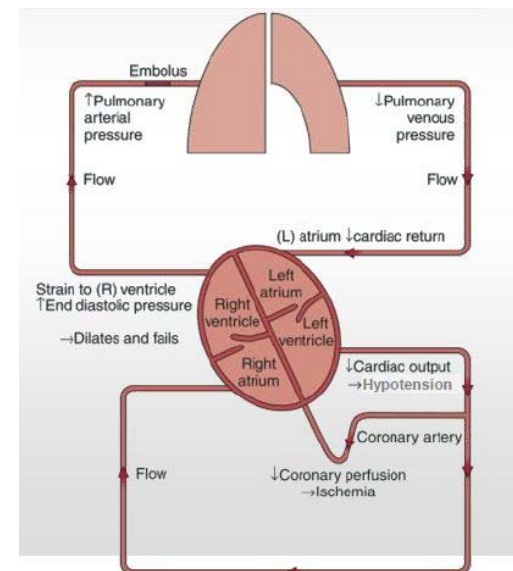
- **Post-thrombotic syndrome (PTS) symptoms**
  - Chronic leg heaviness, leg aching
  - Venous claudication,
  - Leg edema, varicosities,
  - hyperpigmentation, nonhealing ulcers
- **PTS more frequently**
  - extensive multilevel DVT
  - recurrent DVT
  - oral anticoagulant regimen was inadequate

# PTS



# Complications (I)

- **Pulmonary Embolism**
  - **most devastating complication**
    - obstruction of blood flow distal to the clot
    - rapid increase in pulmonary arterial and right heart pressure





# Complications (II)

- **Pulmonary Embolism**
  - Inadequate tx. of proximal venous thrombosis
    - 20% to 50% risk of significant recurrent VTE
    - 90% of thromboemboli arising from L/Ex veins
  - Sx PE: 7% to 17% of proximal U/Ex thrombi
  - Lung scan: + in 25- 51% of Asx patients
  - Autopsy : [DVT + PE] = [1.8 X DVT alone]
  - **PE contributes to approx. 15% of hospital deaths**
  - 1-week survival rate after a PE : 71%
  - 25% of PE manifest as sudden death
  - Mortality in adequate Dx. and Tx.: 8% to 9%

# Complications (III)

- **Post-thrombotic Syndrome**

- less dramatic than PE
- greater degree of chronic socioeconomic morbidity
- 29% to 79% of patients
  - pain, edema, hyperpigmentation, or ulceration
- Severe manifestations
- ambulatory venous hypertension
  - valvular reflux / persistent venous obstruction / anatomic distribution of these abnormalities
- X6 risk of post-thrombotic syndrome with recurrent DVT

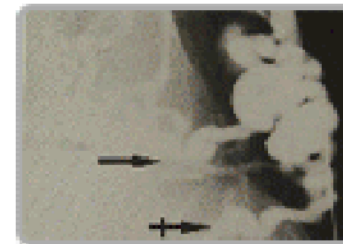
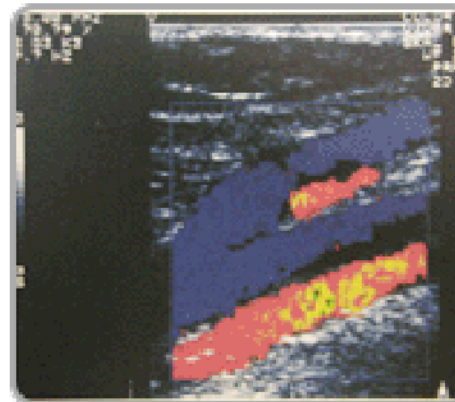
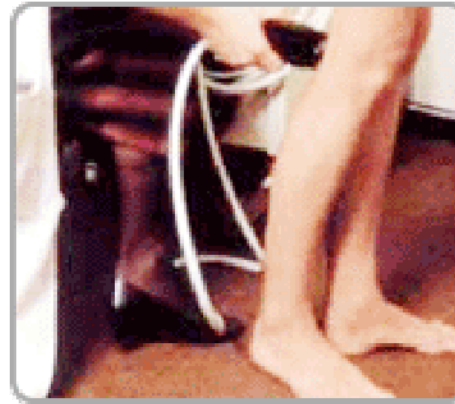
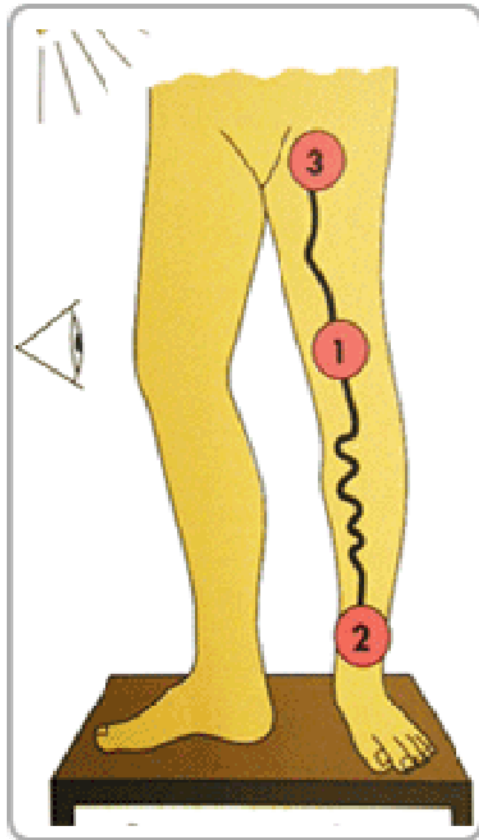
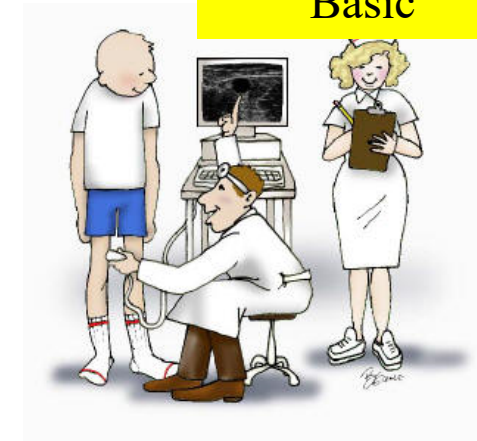
# Post-Thrombotic Syndrome (PTS)

- Painful heavy leg
- Cramps
- Paresthesia
- Pruritus
- Formation of varicosities
- Edema
- Hyperpigmentation of the skin

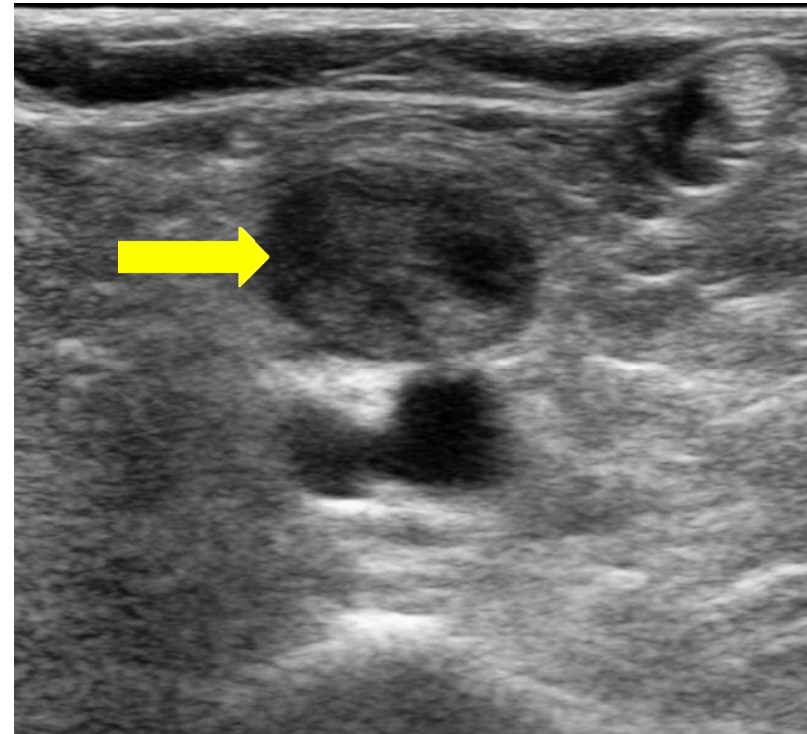
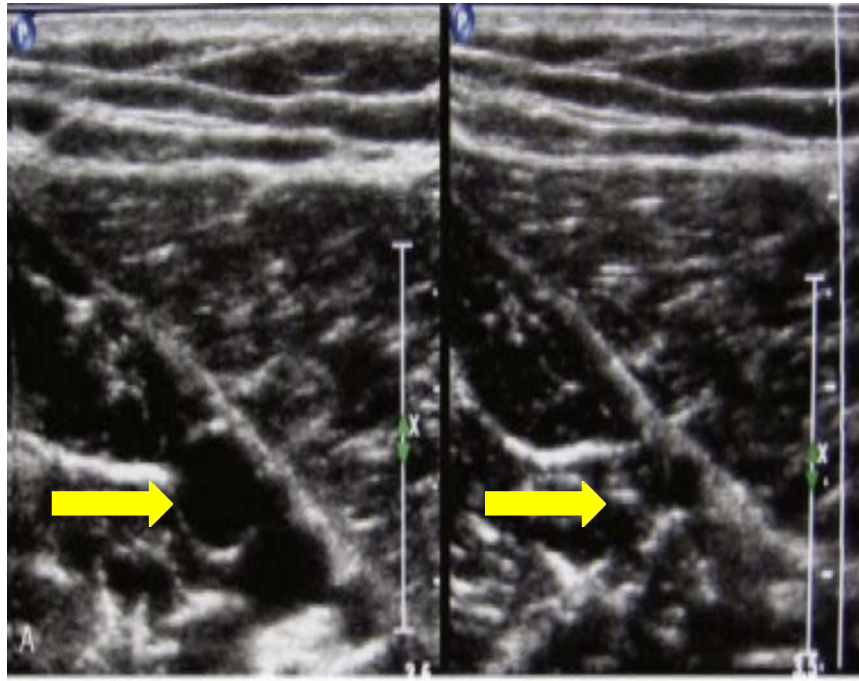
⇒ **Reduced quality of life (QoL)**

# Diagnosis

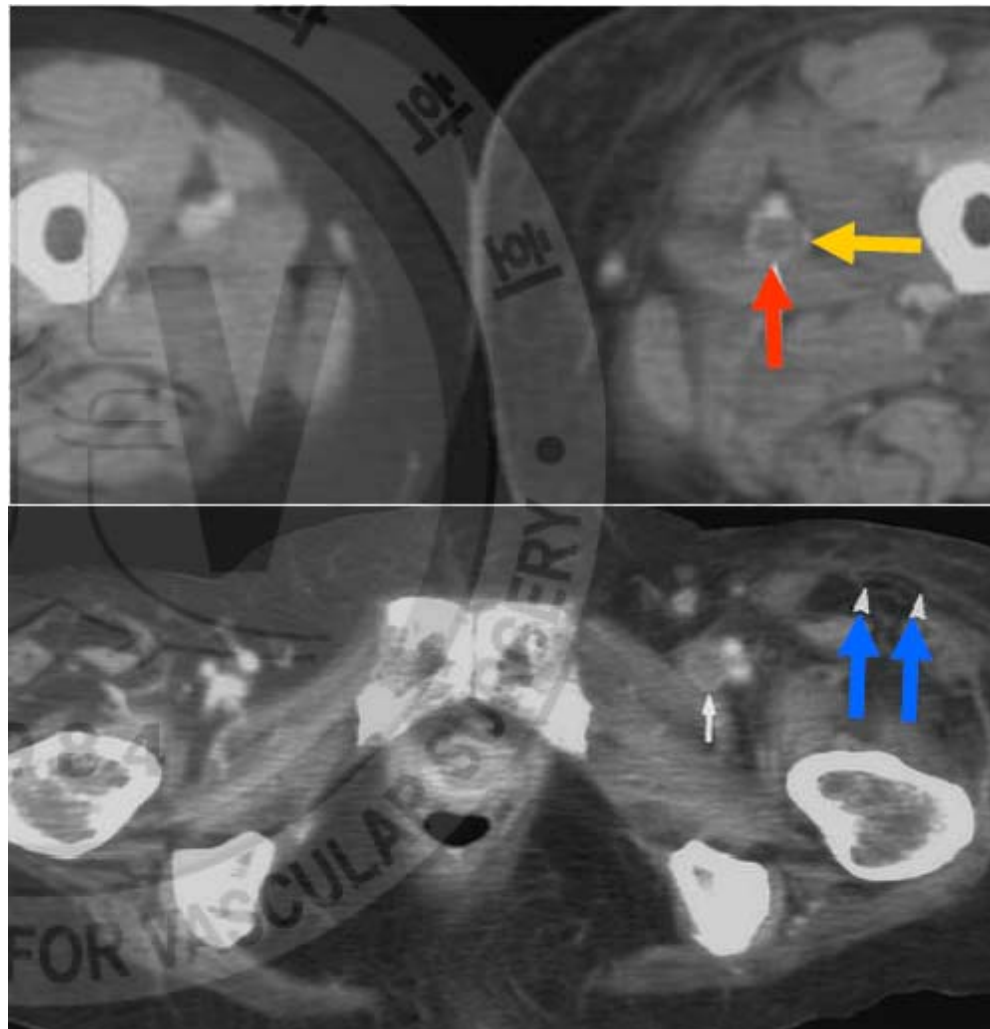
# 초음파검사



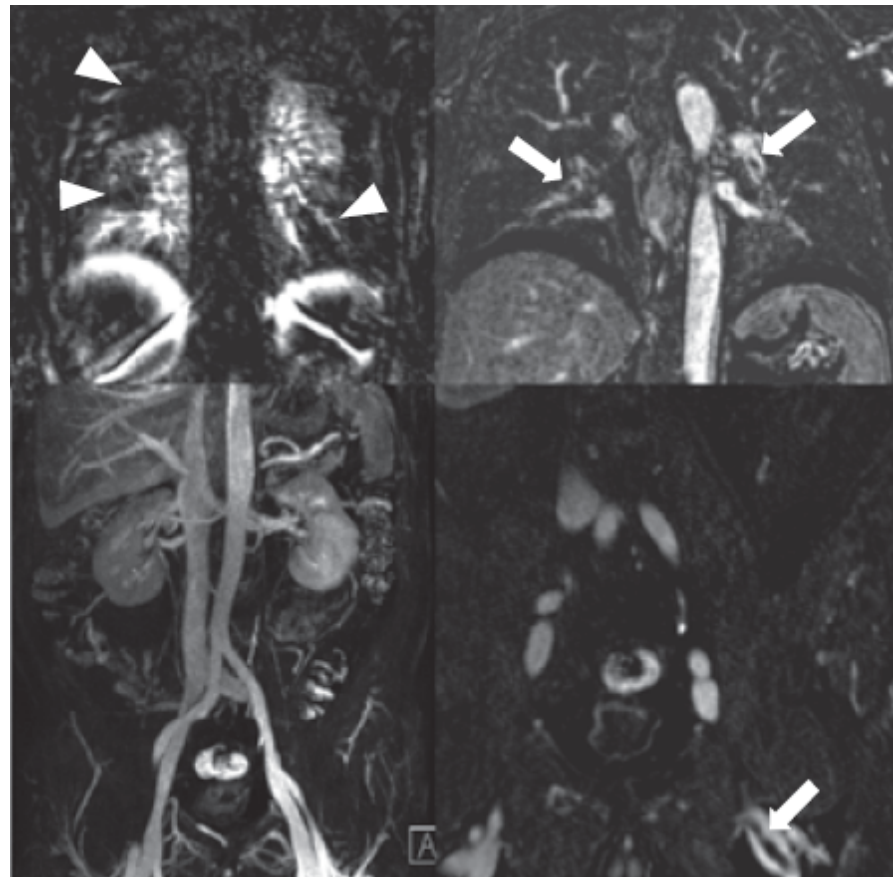
# 초음파검사



# CT



# MRI





# 혈관촬영



# Diagnosis of DVT

- **D-dimer** ; cross-linked degradation product of fibrin.
  - Sensitivity 44-72%, specificity 44-70%
  - High negative predictive value; 97-99%
- **Duplex USG** ; test of choice (Accuracy >95%)
- **CT venography** ; pelvic vein evaluation, PE study
- Impedence phlethysmography
- Ascending venography
- MR Venography
- Lung ventilation & perfusion scan

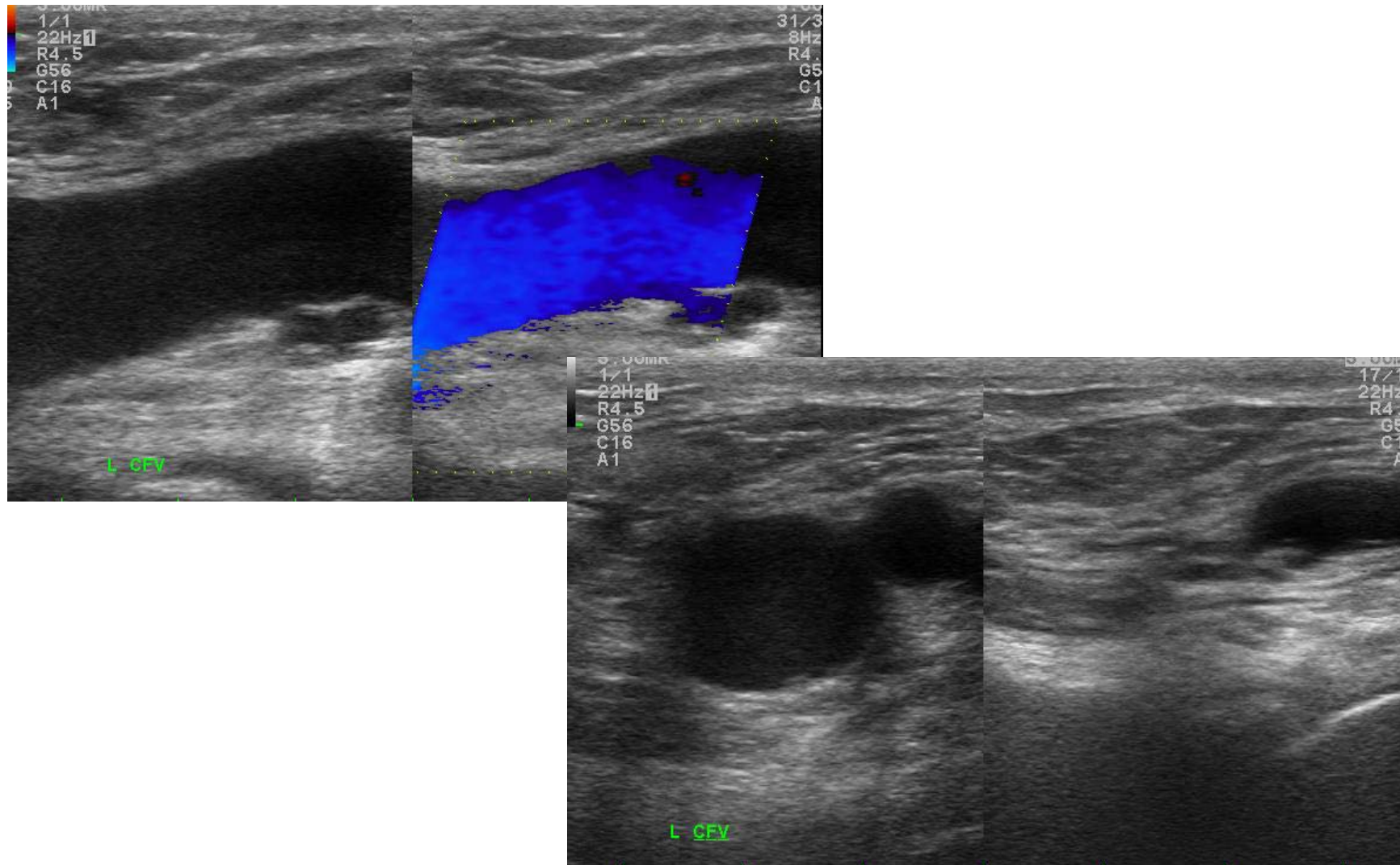
# DVT ; Diagnosis

- **Before anticoagulation, Check coagulation profiles !**
  - CBC ; Hb, Hct, platelet
  - BT / PT / aPTT
  - AT-III, protein C, protein S
  - Coagulation factors VIII, IX, XI
  - Fibrinogen, FDP, D-dimer, homocysteine
  - Lupus anticoagulant, anticardiolipin Ab, antiphospholipid Ab
- **Family study in hereditary or familiar tendency**
  - Factor V Leiden, Prothrombin gene mutation ; rare in KOREA

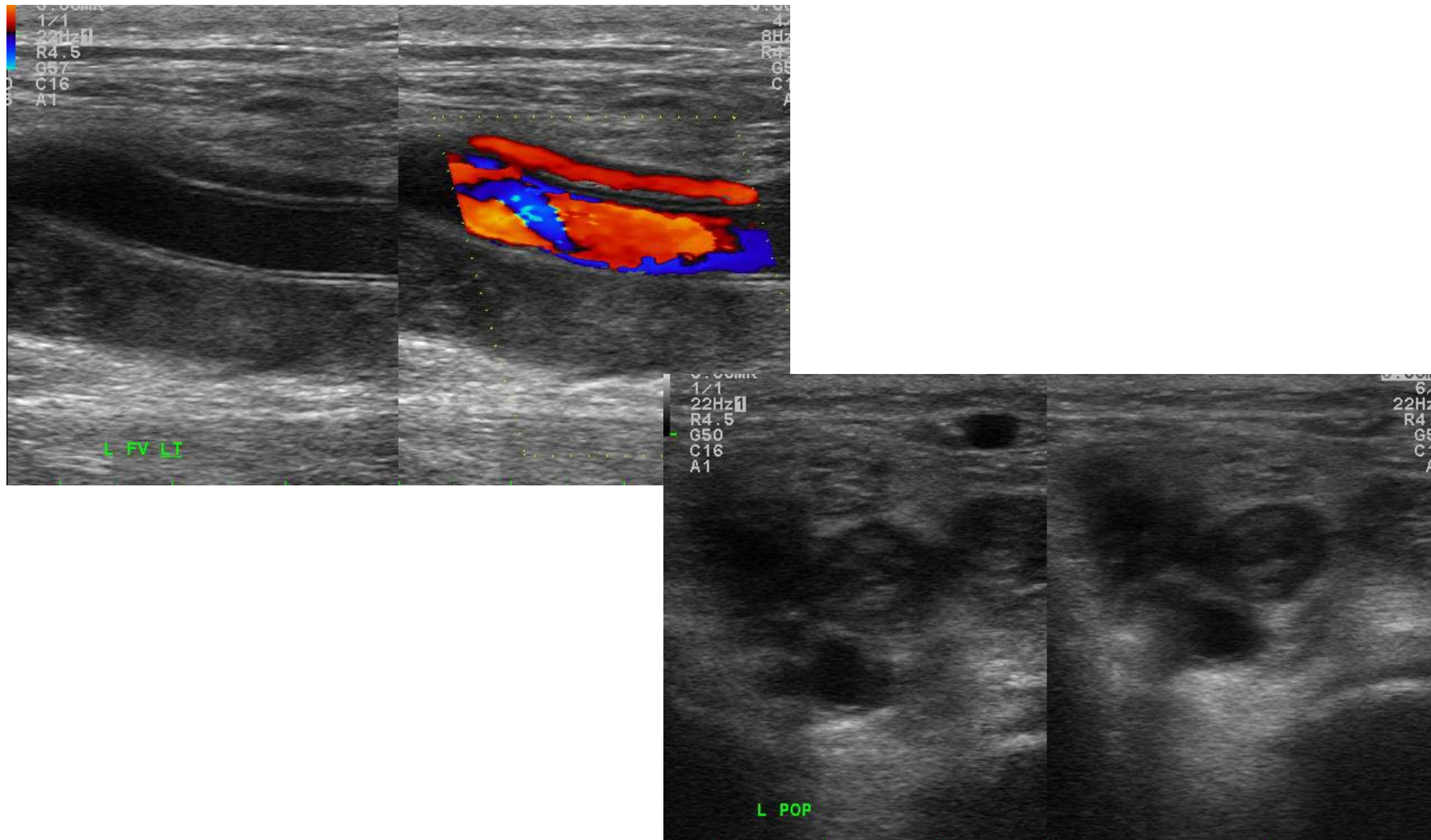
# Duplex criteria for DVT

- Negative for DVT
  - Complete approximation of the vein wall during compression
  - Complete color filling of the lumen without any defect
- **Positive** for DVT
  - Partially compressible or noncompressible vein
  - **Echogenic material** within the vein
  - **Filling defect** on color imaging
  - Absence of doppler signal

# Duplex USG ; normal finding



# Duplex USG ; abnormal finding





# Conditions that **mimic acute**

참고하세요.

---

Muscle strain or blunt trauma  
Ruptured muscle with subfascial hematoma  
Spontaneous hemorrhage or hematoma  
Ruptured synovial cysts (Baker's cysts)  
Arthritis, synovitis, or myositis  
Cellulitis, lymphangitis, or inflammatory lymphedema  
Superficial thrombophlebitis  
Arterial insufficiency  
Pregnancy or oral contraceptive use  
Lymphedema  
Lipedema  
Chronic venous insufficiency or venous reflux syndromes  
Extrinsic venous compression: lymphadenopathy, tumors, lymphomas,  
hematomas, abscesses, right iliac artery  
Systemic edema: congestive heart failure, metabolic, nephrotic syndrome,  
post-arterial reconstruction  
Dependency or leg immobilization (casts)  
Arteriovenous fistula

---



참고하세요.

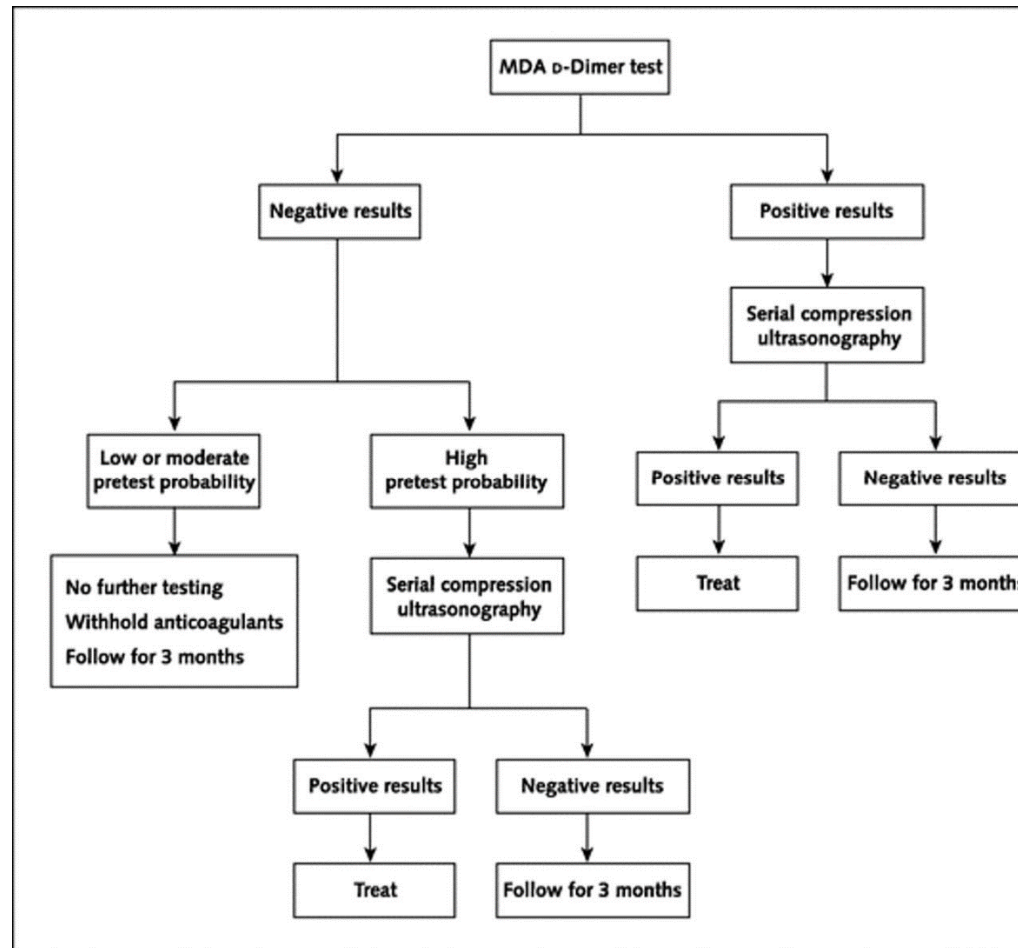
# Diagnostic strategie

- Assessment of risk of venous thrombosis; [Modified wells Criteria](#)

Criteria	Score
Active cancer (receiving treatment within previous 6 months or receiving palliative treatment)	1
Paralysis, paresis, or recent immobilization of lower extremity	1
Recently bedridden for $\geq 3$ days, or major surgery within 12 weeks requiring any type anesthesia	1
Localized tenderness along distribution of deep venous system	1
Entire leg swollen	1
Calf swelling $\geq 3$ cm increased compared to asymptomatic leg (measured 10cm below tibial tuberosity)	1
Pitting edema confined to symptomatic leg	1
Collateral superficial veins (nonvaricose)	1
Previously documented DVT	1
Alternative diagnosis at least as likely as DVT	-2
Risk Assessment	Score
Low risk	$\leq 0$
Intermediate risk	1-2
Likely	$> 2$

# Diagnostic strategy DVT

참고하세요.



# Summary of Pathophysiology

- Deep vein thrombosis (DVT) and pulmonary embolism (PE) are a single clinicopathological entity
  - > venous thromboembolic disease, VTE
- The incidence: 1 (DVT) and 0.5 (PE) cases per **1000 population per year** in the **Western world**
- In a hospital setting, 15% of medical and 30-50% of surgical patients develop VTE if no prophylaxis is initiated
- Clinical feature: nonspecific and inaccurate
- Serious complications; 30-40% mortality in **untreated PE**, ~50% PTS in DVT
- Clinical risk assessment and plasma D-dimer testing with duplex study and pulmonary CT angiography

# Treatment

# 치료방법

- 약물치료
- 혈관내 시술
- 수술적 방법

# **Concerns in a patient with DVT**

참고하세요.

- **Pulmonary embolism**
- **Symptoms**
- **Extension of thrombosis**
- **Recurrence**
- **Post-thrombotic syndrome**

=> Aim of DVT treatment

# Goals of DVT Therapy

- Diminish the severity and duration of lower extremity **symptoms**
- Prevent **Pulmonary embolism**
- Minimize the risk of recurrent venous thrombosis
- Prevent the **postthrombotic syndrome (PTS)**

# Overview of Treatment

1. **Systemic Anticoagulation**
2. **Systemic Thrombolysis**
3. **Surgical Thrombectomy**
4. **IVC filter**
5. **Catheter Directed Thrombolysis (CDT)**
6. **Percutaneous Mechanical Thrombectomy (PMT?)**
7. **PharmacoMechanical Thrombolysis (PMT)**
8. **Adjuvant Venous Angioplasty and Stenting**



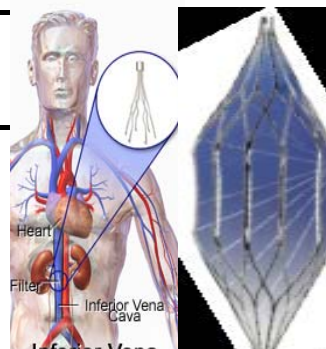
참고하세요.

# DVT: Treatment

- Anticoagulants
- Thrombolytic therapy
- Pharmacomechanical thrombectomy
- Surgical thrombectomy
- Vena cava filter
- Conservative treatment

# ★ DVT: Treatment options ★

Goal	Caval filter	Anti-Coagulation	Thrombolytic Therapy	Venous Thrombectomy
reduce PE	+	+	+	+
prevent thrombus extension		+	+	+/-
reduce DVT recurrence		+	+	+/-
restore venous patency			+	+
restore venous valve			+	+
reduce chronic venous insufficiency		+/-	+	+

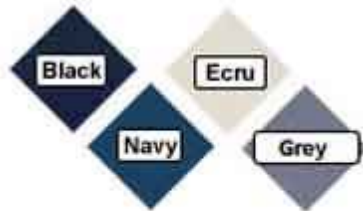


# **Treatment**

- **Conservative Treatment**

# 심부정맥 혈전증의 예방

Protect yourself from Deep Vein Thrombosis.



# 심부정맥 혈전증의 예방



aimclub®



aimclub®



참고하세요.

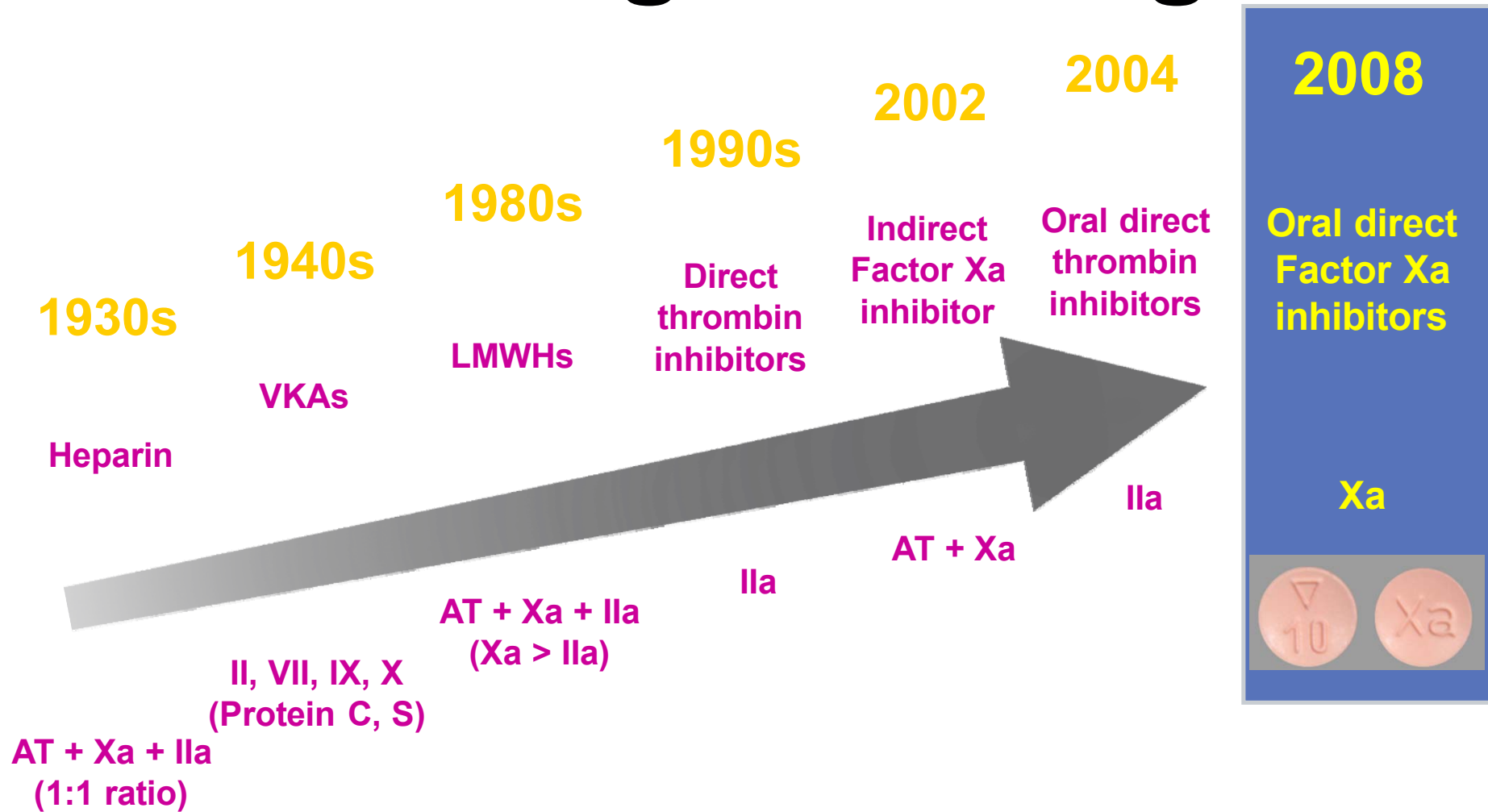
# Conservative Tre

- **Bed rest and leg elevation**
  - 1289 prospective cohort study
  - Bed rest **does not prevent PE**
  - LMWH + early ambulation + compression bandage or ES, faster improvement of pain and swelling w/o increasing risk of PE, decreased PTS
    - Partsch H, JVS 2002
- **Graduated compression stocking**
  - Graduated compression stocking for 24 months post-5 yr cumulative data of incidence of **PTS 26% vs. 49%**
    - Prandoni P et al, Ann Int Med 2004
- Below-the-knee stocking is equivalent to the thigh one

# **Treatment**

- **Anticoagulation**

# The evolution of anticoagulant drugs





## Outpatient Anticoagulation Therapy: Relative

- PE with hemodynamic or respiratory instability
- Extensive iliofemoral thrombus
- Known potential for non-compliance
- Active bleeding
- Severe renal impairment
- Thrombocytopenia
- High risk of falls

## Anticoagulation

- UFH (Unfractionated heparin)
- LMWH (low molecular weight heparin)
- Fondaparinux

## Clotting Cascade



## Clotting Cascade



## Heparin (UF)

- Heterogenous mixture of polysaccharide fragments w/ molecular weight 12,000-15,000
- Bind to the **antithrombin**, results **conformational change of AT**, thereby enhance AT's inhibitory effect on thrombin and other coagulation factors (II, V, X, XI, XII)

## Low Molecular Weight Heparin (LMWH)

- Obtained by various fractionation or depolymerisation of polymeric heparin
- Molecular weight < 8000

## Low Molecular Weight Heparin (LMWH)

Agent	Trade Name	Mean MW	Anti-Xa: Anti-IIa Ratio
UFH	-	12,000-15,000	1
Acetylsalicylic acid	Noralflo	6,000	1.9
Dalteparin	Fogarin	6,000	2.7
Enoxaparin	Clexane	4,500	3.8
Nadroparin	-	-	-
Reviparin	-	-	-
Tinzaparin	-	-	-

## Advantages of Heparin

Pharmacokinetic Characteristics	Clinical advantages
Reduced protein binding	Good bioavailability
Predictable dose response	Predictable dose response
Predictable dose response	Resistance not encountered
	If used or w/based dosing possible
	Monitoring not required

## Heparin vs. LMWH



## Meta-Analysis LMWH vs UFH for Treatment of Venous Thromboembolism



## Fondaparinux

- Synthetic pentasaccharide
- Factor Xa inhibitor
- For injection
- Fondaparinux vs enoxaparin in hip/knee

## UFH vs LMWH vs Fondaparinux

	UFH	LMWH	Fondaparinux
Mechanism	Enhances AT effect on Na & thrombin	Enhances AT effect more selectively on Na than on thrombin	Enhances anti-Xa activity of AT
Half-life	1-2 hr	4.5-7hr	17-21 hr
Dosing	Continuous drip	SC or oral daily	Once daily
Reversal agents	Protacimin sulfate	Protacimin sulfate neutralizes 60% of	Not reversible by

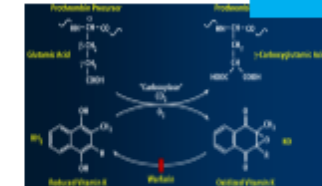
## LMWH vs. UFH

Recurrences rate	Enoxaparin	UF Heparin	RR (>0.75)
Vein thrombosis event	4.5 %	5.7 %	0.81
DVT	3.1 %	4.4 %	0.79
PE	0.95 %	1.8 %	0.63

## LMWH vs. UFH

Complication (%)	Enoxaparin	UF Heparin	RR (> 0.75)
Major bleeding	10days: 2.2 % 30days: 2.9 %	2.0 % 4.3 %	NS 0.74 (28%)
Death	3.3 %	5.8 %	NS
Mortality			0.69 (31%)

## Warfarin : Mechanism



- Inhibit carboxylation of coagulation factor II, VII, IX, X in the liver
- Also inhibits natural anticoagulant protein C/S

# Outpatient Anticoagulation Therapy: **Relative**

참고하세요.

- PE with hemodynamic or respiratory instability
- Extensive iliofemoral thrombus
- Known potential for non-compliance
- Active bleeding
- Severe hypertension (HTN)
- Renal clearance  $<30$  mL/min or SCr  $>2.5$  mg/dL
- Thrombocytopenia  $<100,000$
- History of heparin-induced thrombocytopenia

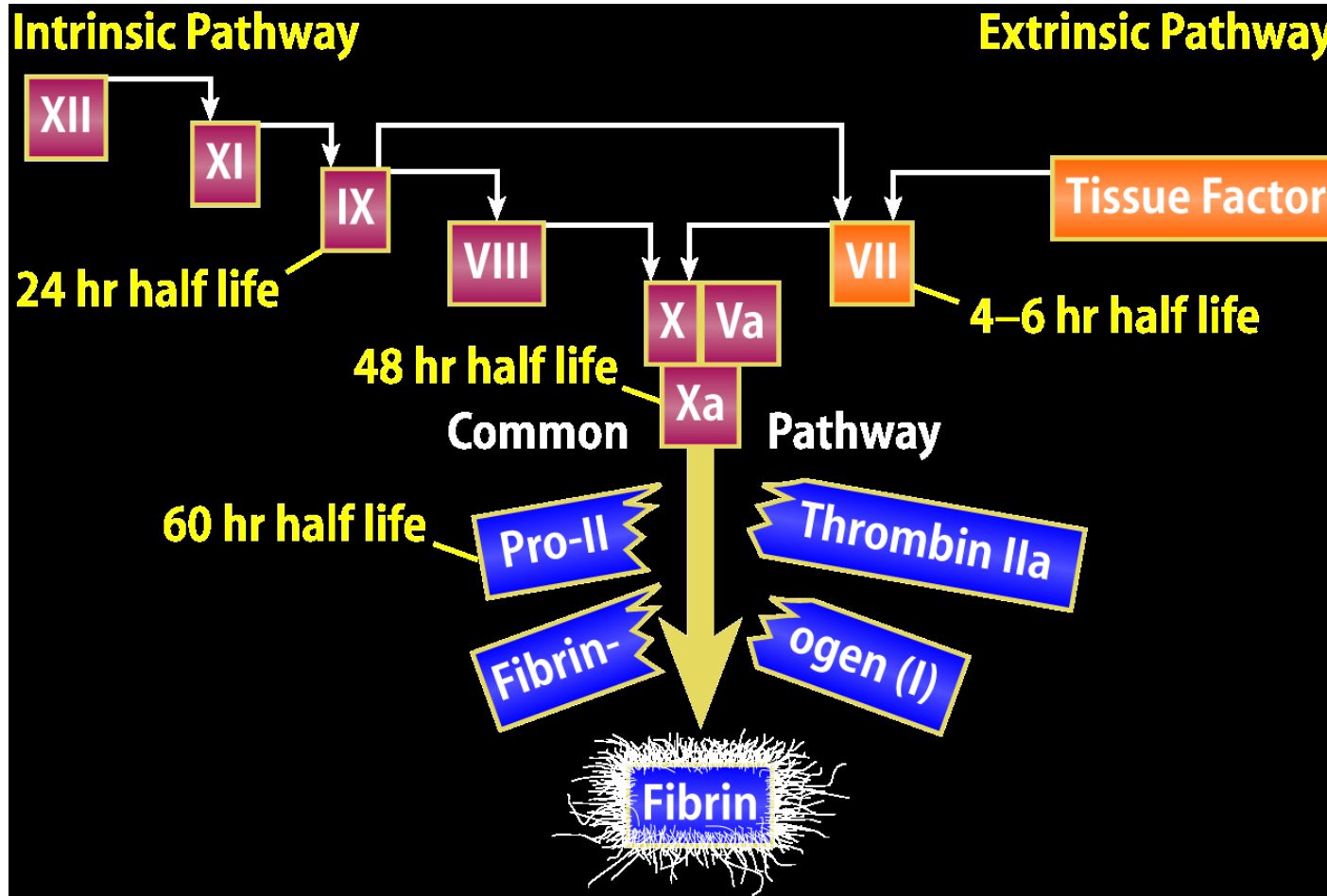
참고하세요.

# Anticoagula

- UFH (Unfractionated heparin)
- LMWH (low molecular weight heparin)
- Fondaparinux
- Vitamin K antagonist
- Direct thrombin inhibitor
- Factor Xa inhibitor

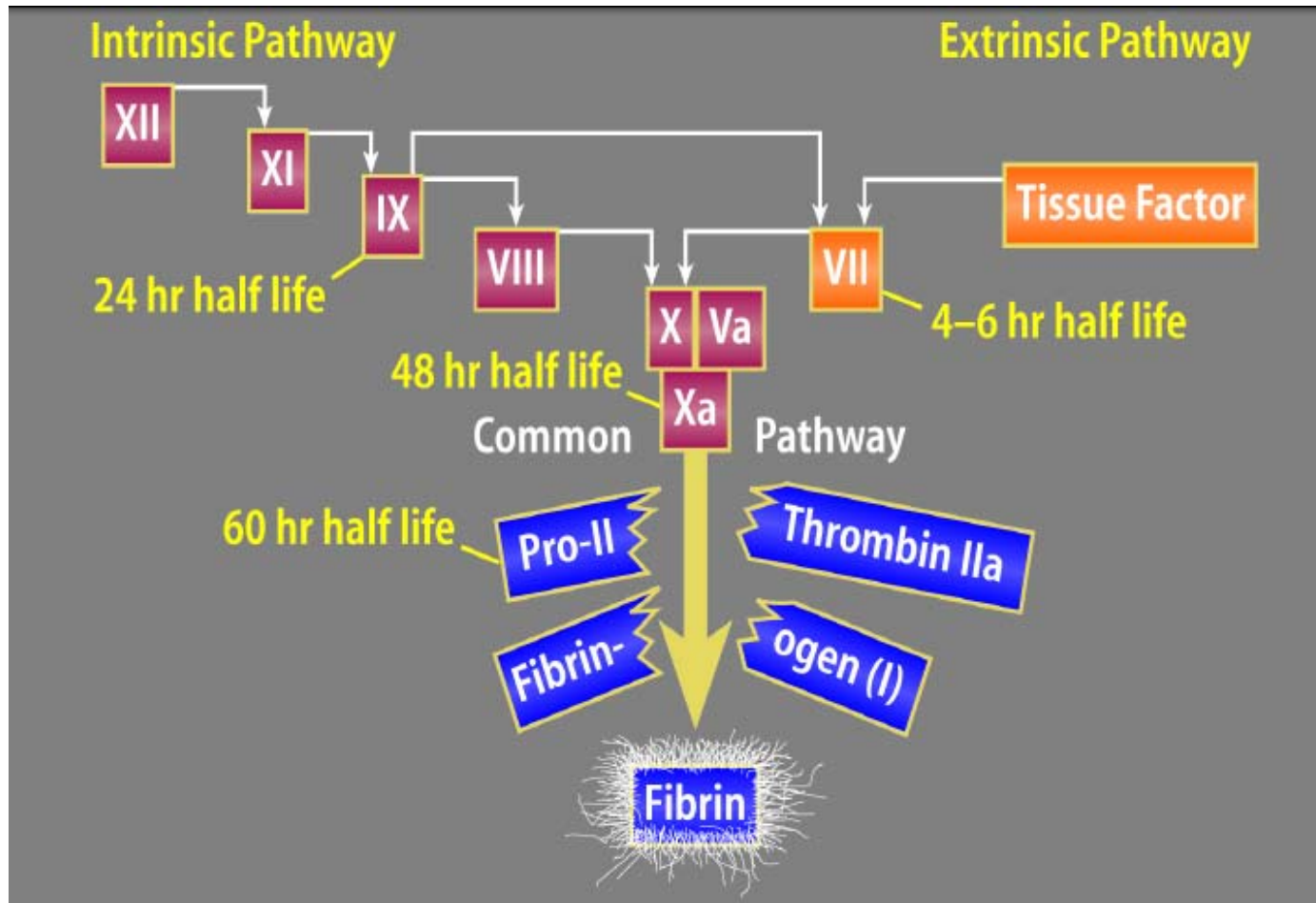
참고하세요.

# Clotting Case



참고하세요.

# Clotting Case



참고하세요.

# Heparin (UFH)

- **Heterogenous mixture** of polysaccharide fragments w/ molecular weight 12,000~15,000
- **Bind to the antithrombin**, results **conformational change of AT**, thereby enhance AT's inhibitory effect on thrombin and other coagulation factors esp., Xa
- Drawbacks of unfractionated heparin (UFH)
  - Need to administer heparin by continuous IV infusion
  - Unpredictable activity, requiring laboratory monitoring
  - Heparin induced thrombocytopenia (HIT)

# Low Molecular Weight Heparin (LMWH)

참고하세요.

- Obtained by various fractionation or depolymerisation of polymeric heparin
- Molecular weight < 8000
- Various activity to the **AT and Xa**
- Constant release → predictable effect, do not need monitoring

# Low Molecular Weight Heparin (LMWH)

참고하세요.

Agent	Trade Name	Mean MW	Anti-Xa:Anti-IIa Ratio
UFH	-	12,000~15,000	1
Ardeparin	Normiflo	6,000	1.9
Dalteparin	Fragmin	6,000	2.7
Enoxaparin	Clexane	4,200	3.8
Nadroparin	Fraxiparin	4,500	3.6
Reviparin	Clivarine	4,000	3.5
Tinzaparin	Innohep	4,500	1.9



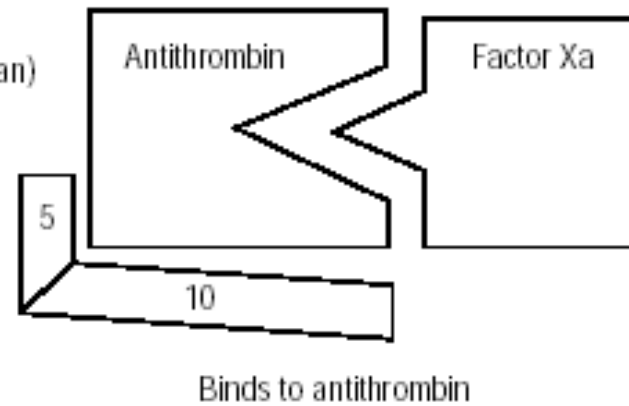
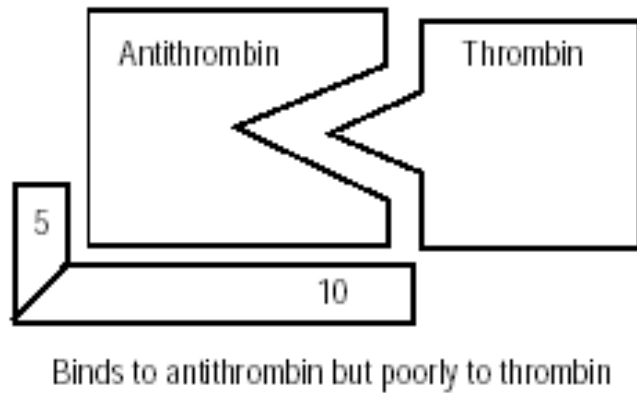
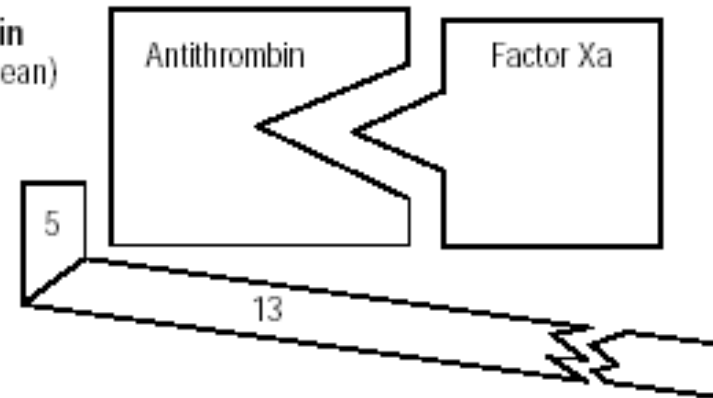
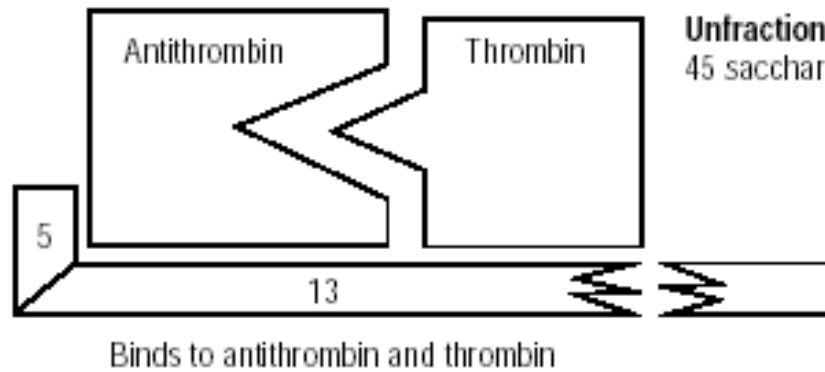
참고하세요.

# Advantages of

Pharmacokinetic Characteristic	Clinical advantage
Reduced protein binding	Good bioavailability
	Predictable dose response
	Resistance not encountered
Predictable dose response	Fixed or wt-based dosing possible
	Monitoring not required
Longer plasma half-life	Once- or twice-daily dose possible
Smaller molecule	Improved subcutaneous absorption
Less effect on platelets and endothelium	Reduced incidence of HIT and, possibly, bleeding

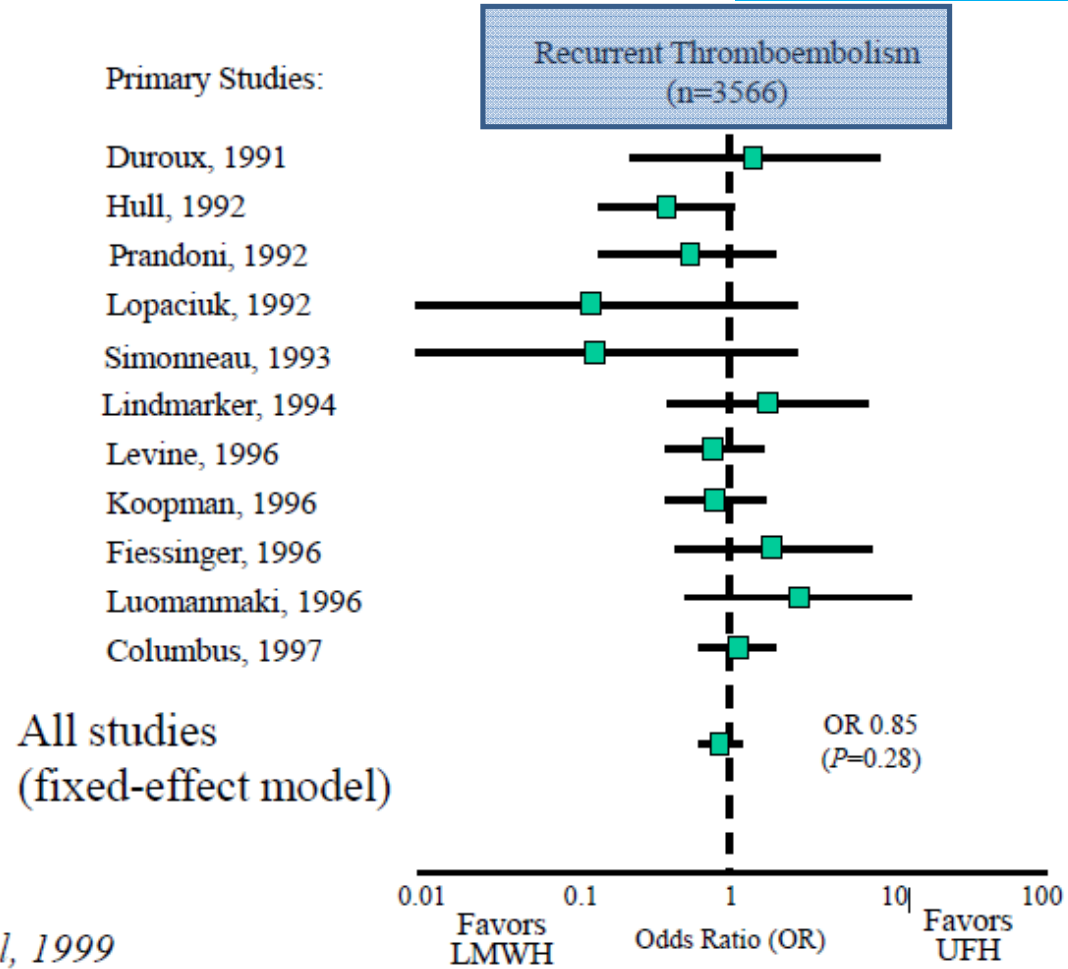
참고하세요.

# Heparin vs. LMWH



# Meta-Analysis LMWH vs UFH for Treatment of Deep Vein Thrombosis

참고하세요.



Gould et al, 1999

참고하세요.

# Fondaparinux

- Synthetic pentasaccharide
- Factor Xa inhibitor
- For injection
- Fondaparinux vs enoxaparin in hip/knee surgery
  - More effective at preventing VTE
  - No difference in major bleeding
- no report of HIT

참고하세요.

## UFH vs LMWH vs Fondaparinux

	UFH	LMWH	Fondaparinux
Mechanism	Enhances AT effects on Xa & thrombin	Enhances AT effects more selectively on Xa than on thrombin	Enhances anti-Xa activity of AT
Half-life	1-2 hr	4.5-7hr	17-21 hr
Dosing	Continuous drip	BID or once daily	Once daily
Reversal agents	Protamin sulfate 1mg neutralizes 100u of heparin	Protamin sulfate neutralizes 60% of activity	Not reversible by protamin
Monitoring	aPTT, heparin assays	none	none
Clearance	Hepatic & RES, No renal adjustments	Renal Adjust for CrCl<30mL/min	Renal contraindicated in CrCL<30mL/min
Cause HIT	yes	yes	no

# LMWH vs. UF Heparin

참고하세요.

Recurrences rate	Enoxaparin	UF Heparin	RR (>0.75)
Vein thrombosis event	4.5 %	5.7 %	0.81
DVT	3.1 %	4.4 %	0.79
PE	0.95 %	1.8 %	0.63

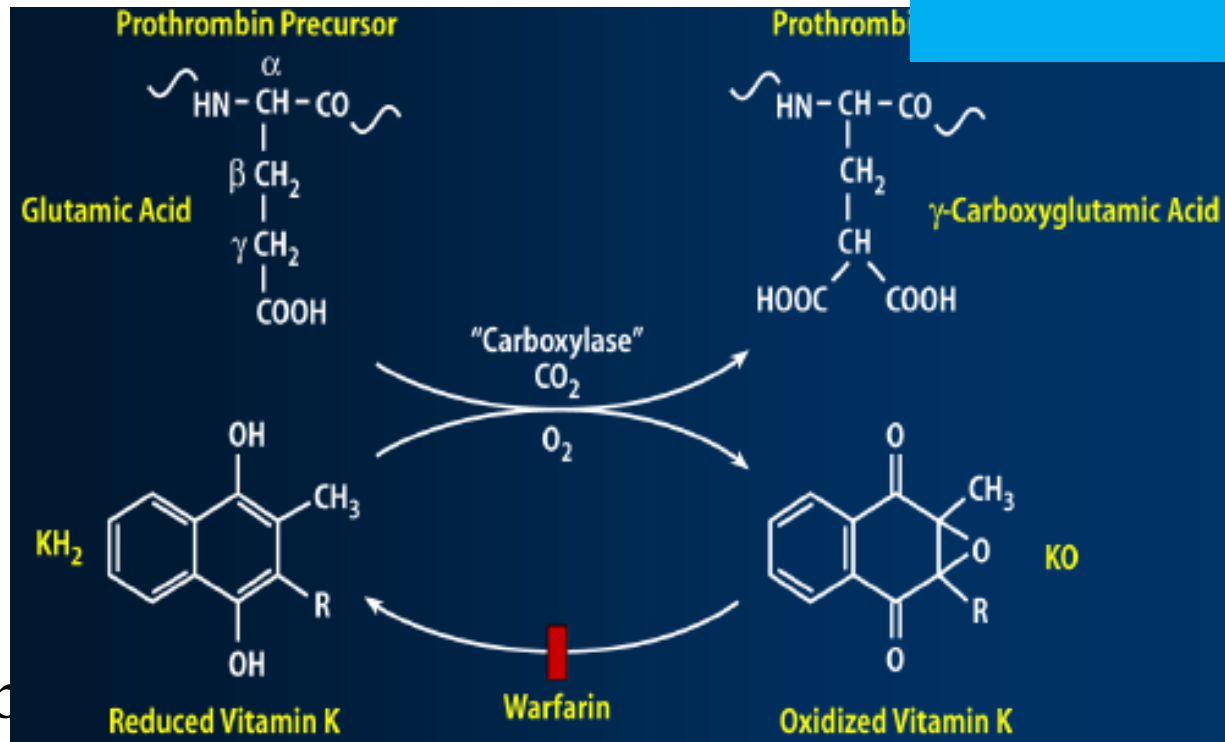
# LMWH vs. UF Heparin

참고하세요.

Complication (%)		Enoxaparin	UF Heparin	RR (> 0.75)
Major bleeding	10days	2.2 %	2.0 %	NS
	30days	2.9 %	4.3 %	0.74 (28%)
Death		3.3 %	5.8 %	NS
Mortality				0.69 (31%)

참고하세요.

# Warfarin : Mechanism



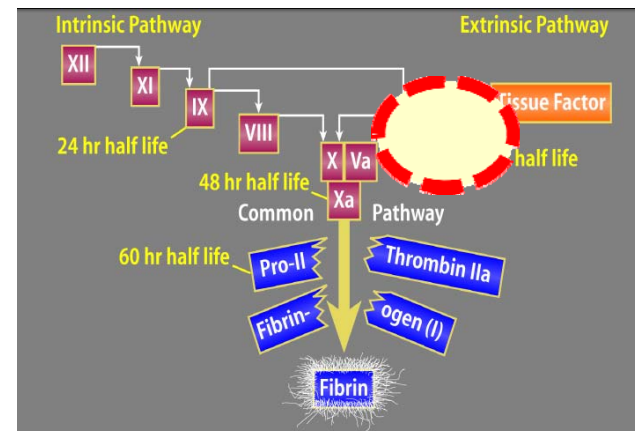
- Inhibits synthesis of factors II, IX, X in the liver
- Also inhibits natural anticoagulant protein C/S



# VKA should be given with heparin at the beginning

참고하세요.

- Slow action of VKA
- Relatively hypercoagulable state due to short half life of natural anticoagulants (protein C/S)
- Very short half life of factor VII → initial INR may not reflect effect of VKA



# New Oral Anticoagulants (**NOACs**)

- Factor Xa inhibitors
  - Rivaroxaban
  - Apixaban
  - Edoxaban
- Direct thrombin inhibitors
  - Dabigatran

# New ERA of NOAC in VTE treatment

Rivaroxaban  
(Xarelto®)



**EINSTEIN-PE** 2012 NEJM  
**EINSTEIN-DVT** 2010 NEJM



Dabigatran  
(Pradaxa®)

**RE-COVER** 2009 NEJM  
**RE-COVER II** 2014 Circulation

**WFR**

Apixaban  
(Eliquis®)



**AMPLIFY** 2013 NEJM



Edoxaban  
(Lixiana®)

**Hokusai-VTE** 2013 NEJM

# Pharmacokinetics of NOACs

	Dabigatran	Rivaroxaban	Apixaban
Administration	bid	QD	bid
Bioavailability	6.50%	80%	66%
Tmax	1.25-3 h	2-4 h	1-3 h
Half life	12.14 h	5-13 h	8-15 h
Renal excretion	80%	66%	25%
Plasma protein binding	35%	>90%	87%
Dialysability	Yes	Not expected	Unlikely

# Anticoagulant th

## Contraindicat

참고하세요.

- Active bleeding
- Recent CNS surgery : 2 mo
- Recent major surgery : 2 wk
- Recent hemorrhagic stroke 2 mo
- Severe uncontrolled hypertension
- Severe renal and/or hepatic dysfunction

# Optimal Duration of Ant Therapy for Symptomatic Thrombosis

참고하세요.

Indication	Duration
DVT with provocative events	3 months
DVT without provocative cause	6 months to > 1 year
DVT with malignancy	until resolution of malignancy
Hypercoagulable state	life long
Recurrent DVT	life long

# 보험인증기준

자렐토 보험급여 가이드

## 심재성 정맥혈전증의 치료 및 재발성 심재성 정맥혈전증과 폐색전증의 위험 감소

- 보험 인정 투여기간
  - 급성 심재성 정맥혈전증 치료 초기: **3주 이내**
  - 심재성 정맥혈전증 치료 (초기 치료 이후 유지),  
재발성 심재성 정맥혈전증과 폐색전증의 위험감소: **6개월 이내**

- 질병코드 및 보험코드

질병명	질병코드	보험코드
정맥염, 혈전정맥염, 정맥 색전증 및 혈전증	I 80 - I 82	자렐토 20mg / 641105730 자렐토 15mg / 641105740
폐색전증	I 26	

- 보험약가 : 3,750원 / 정
- 환자부담금 : 5%~30% (188원~1125원/정)

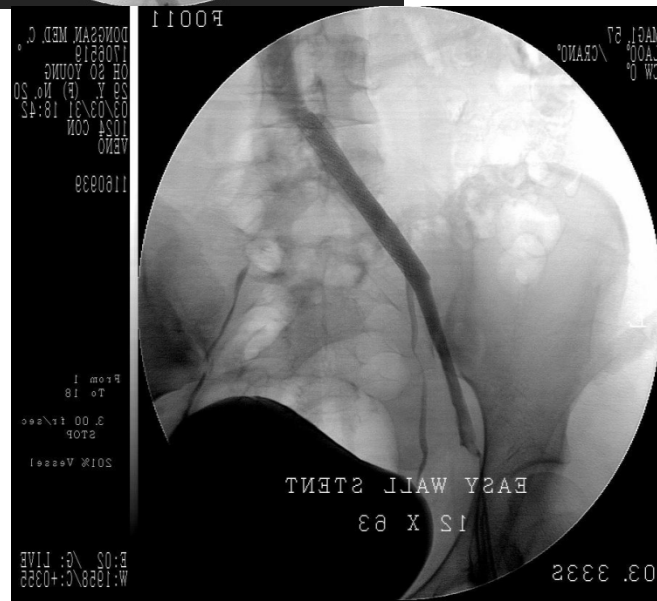
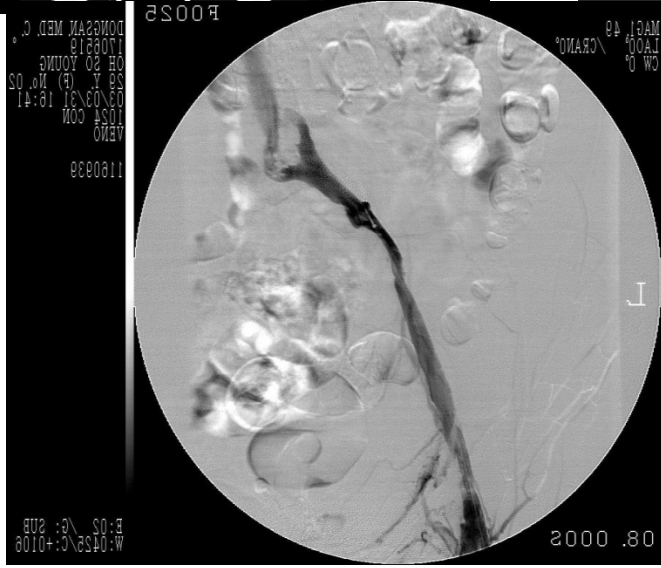
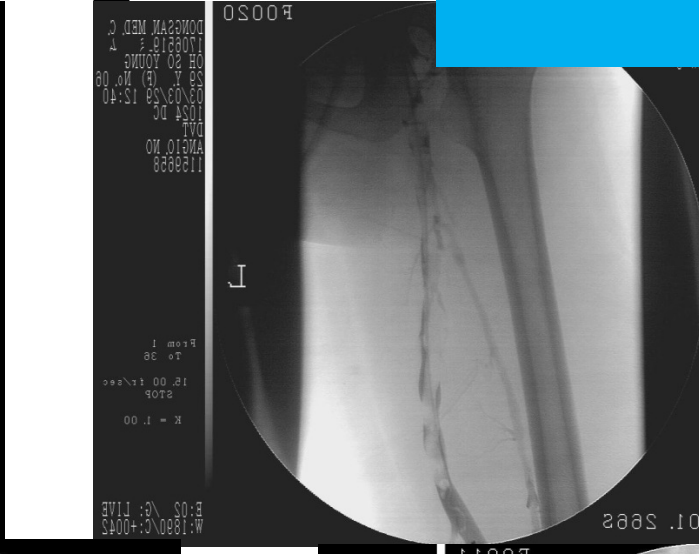
# **Treatment**

- **Catheter Directed  
Thrombolysis (CDT)**



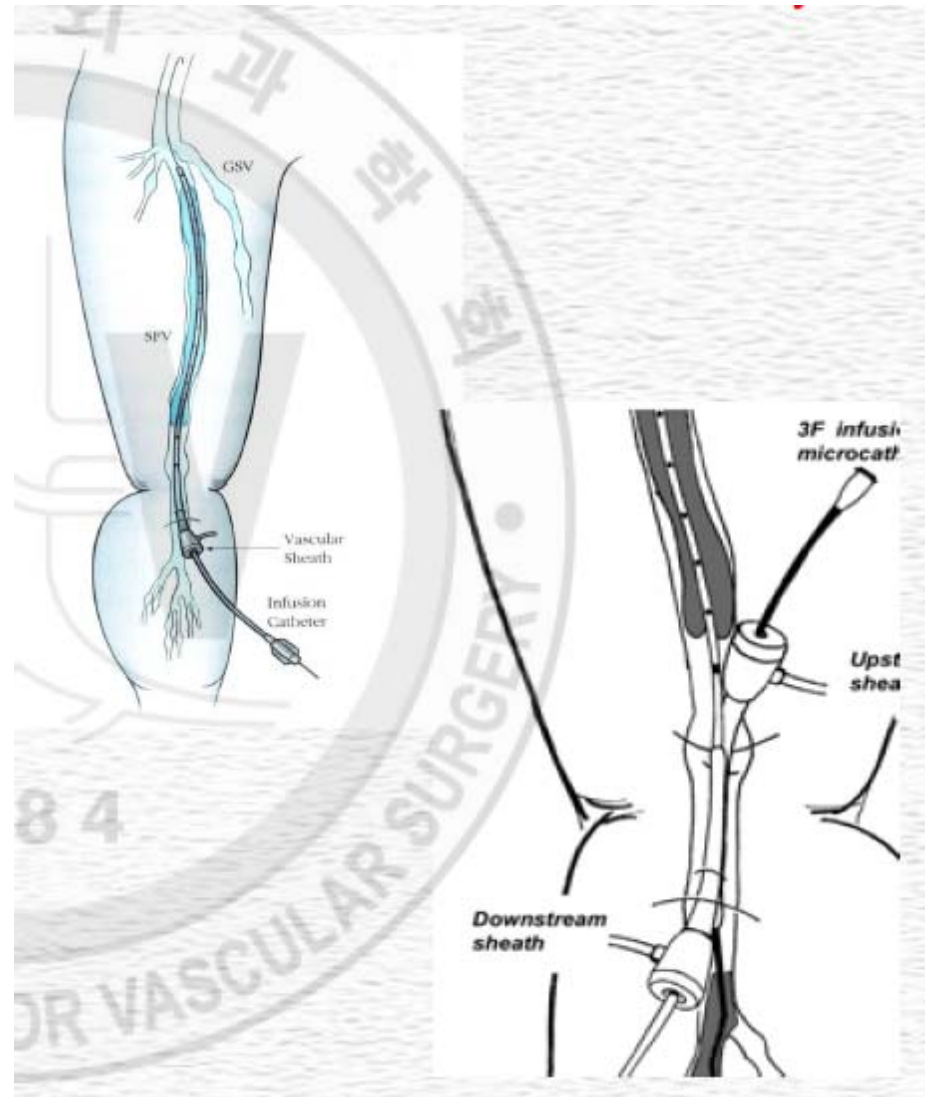
# Thrombolytic th

참고하세요.



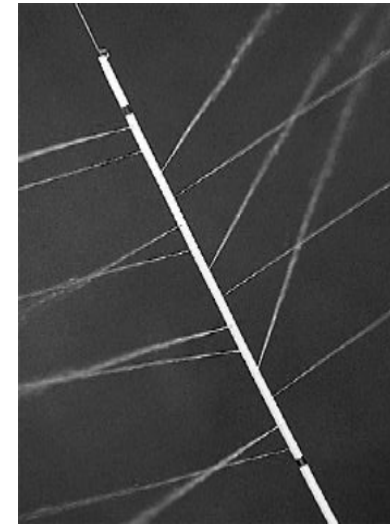
# Catheter directed thrombolytic therapy (CDT)

- **Access**
  - Ipsilateral Popliteal vein
  - Contralateral Femoral vein
  - Internal Jugular vein
- **6-F sheath : Heparin**
- **5F multi-sideportcatheter : UK**
  - Heparin 500 unit/hr
  - Urokinase 30~100 x 10<sup>3</sup>IU/hr



# Catheter directed thrombolytic therapy (CDT)

- Delivery of thrombolytics into the thrombus
- Popliteal approach
- Urokinase >> streptokinase, rtPA – more bleeding
- Pulsed spray catheter



# National Multicenter Radiology 1999

참고하세요.

- 287 patients
  - Acute 188, 45 chronic, 54 acute on chronic
- Results
  - Complete lysis 31%, significant(50-99%) 52%, incomplete(<50%) 17%
  - 7.8 million U of UK during 53.4 hrs
  - Higher complete lysis rate in patients with symptoms of less than 10days
  - Major non-fatal bleeding complication 11%
  - Pulmonary embolism in 6 patients, 1 death
  - Overall mortality 0.4%
  - Improved 1 yr patency in treated w/ stent(74%) than w/o stent(53%)

참고하세요.

# Limitations of

- **Time to lysis**
- Need to hospitalization and intensive monitoring
- **Risk of hemorrhage**
- Cost

# **Treatment**

- **PharmacoMechanical  
Thrombolysis (PMT)**

# Pharmacomechanical thrombectomy(PMT)

- Reduce dosage of thrombolytic Tx
- Reduce treatment time
- Increase safety
  - narrows contraindications
  - decrease complications
- Reduced cost

# PMT Devices

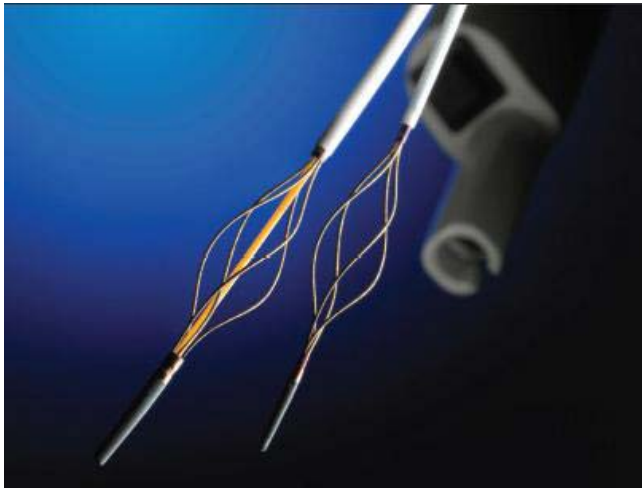
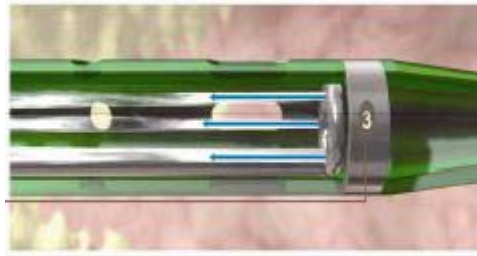
- Aspiration thrombectomy device
- Rotational device
  - Arrow PTD
- Rheolytic thrombectomy
  - **angiojet**, oasis, hydrolyser
- Isolated PMT
  - **trellis**
- Ultrasound accelerated thrombolysis
  - Ekos



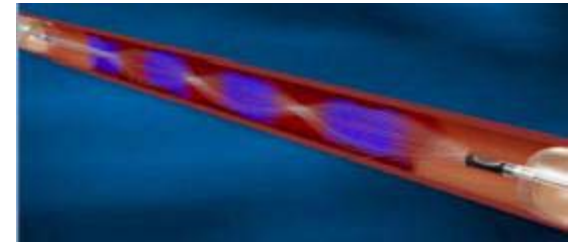
# PMT Devices



angioje



trellis

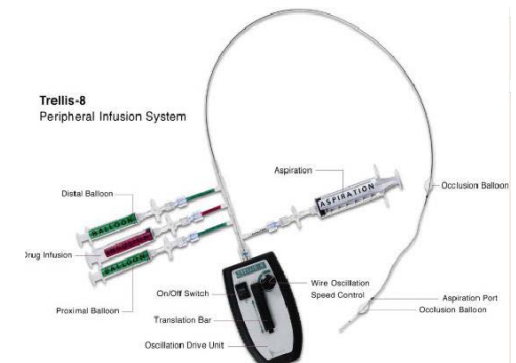


**EKOS**  
2<sup>nd</sup> Generation

Control Unit

5.2 fr side-hole drug delivery catheter

Device

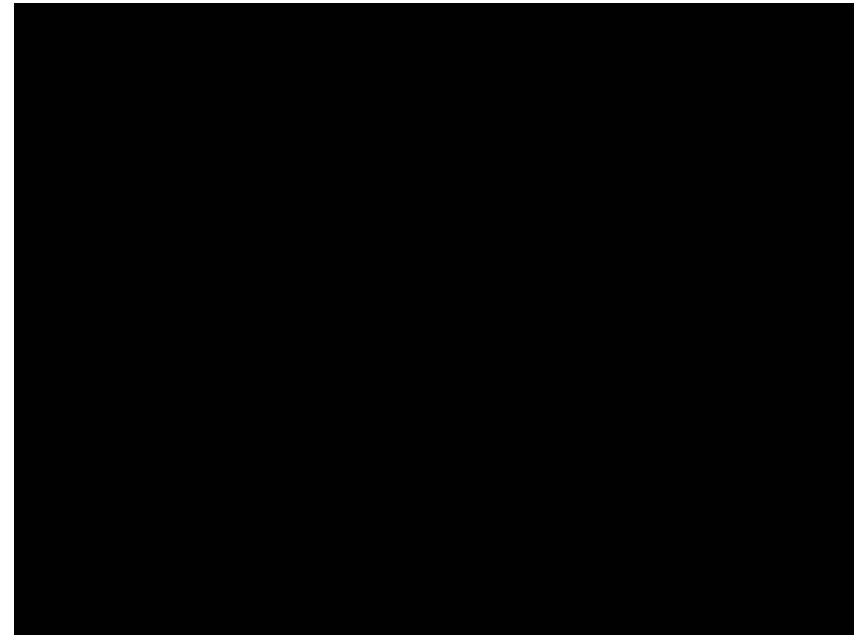
A photograph of the EKOS 2nd Generation system. On the left is the Control Unit, a blue and white device with a screen and various buttons. On the right is the Device, a long, thin, flexible catheter with a handle and a distal tip. The background is blue.

# PMT

**Trellis**



**Angiojet**



# CDT vs. PMT

	complete thrombus remove	partial thrombus remove	angioplasty & stenting
CDT	70 %	30 %	78 %
PMT	75 %	25 %	82 %

Lin PH et al. Am J Surg 2006

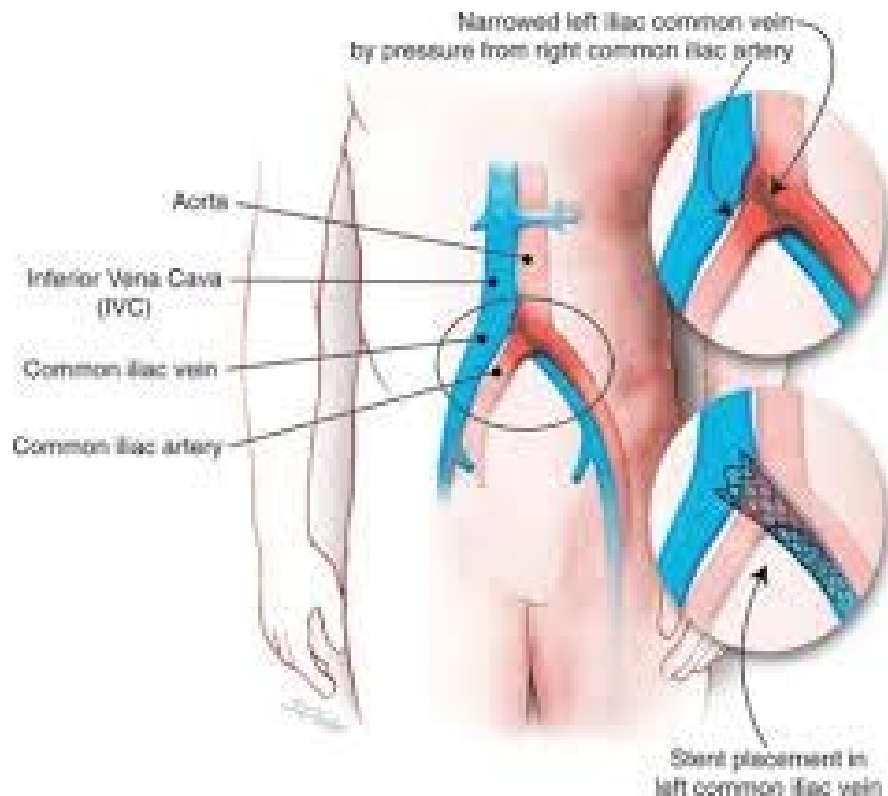
- ❖ Compared to CDT, it provided similar treatment success, with reduced ICU, total hospital length of stay, and hospital costs

# **Treatment**

- **Adjuvant Venous Angioplasty and Stenting**

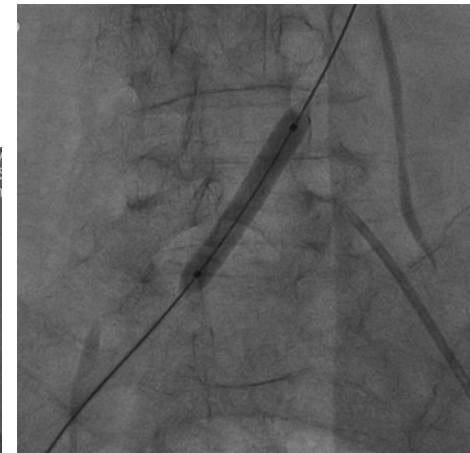
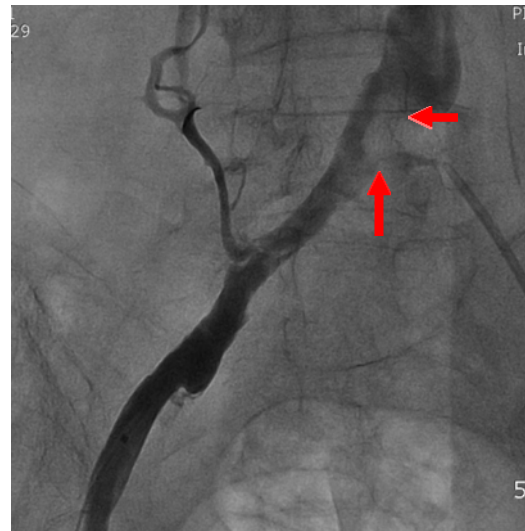
# May-Thurner Syndrome

- Iliac vein compression syndrome
  - Compression of the left common iliac vein by the overlying right common iliac artery

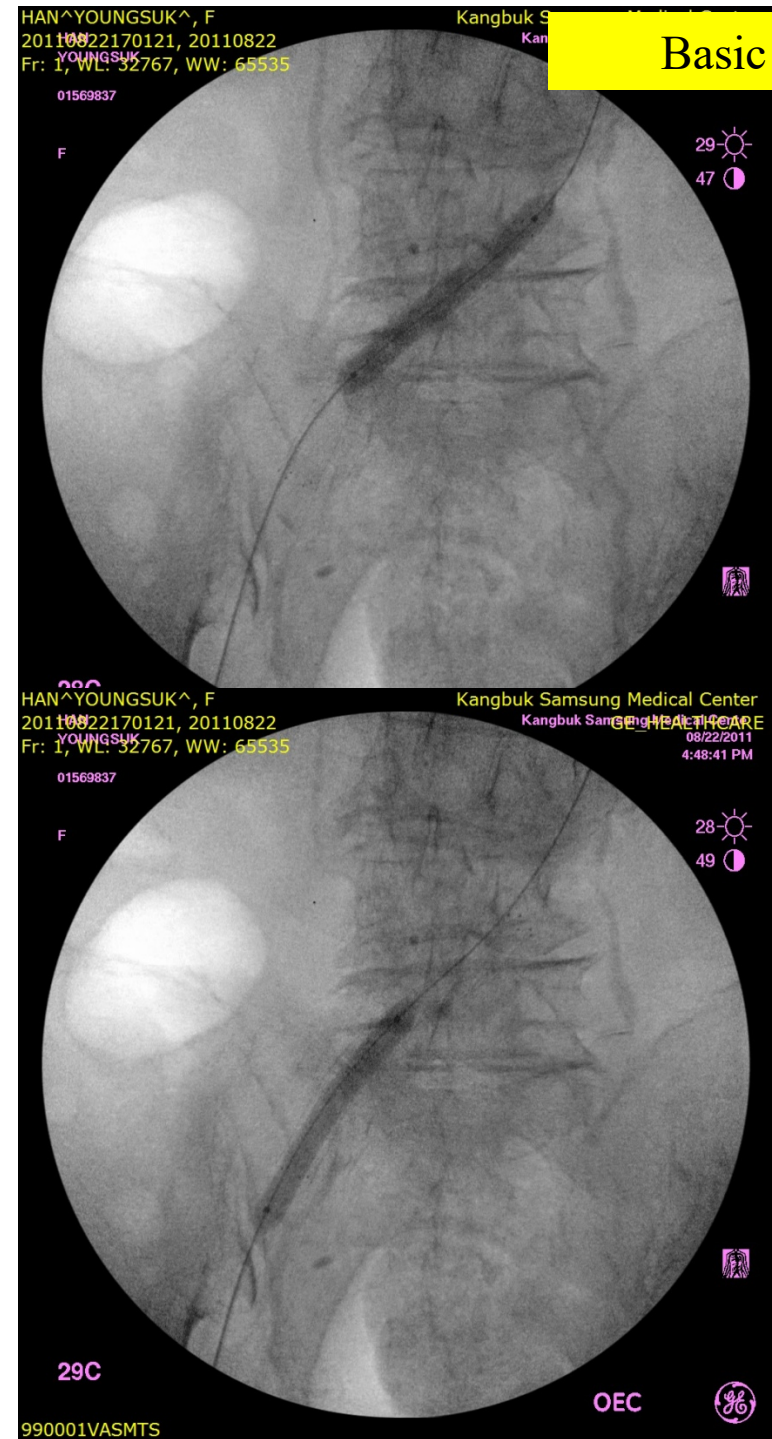
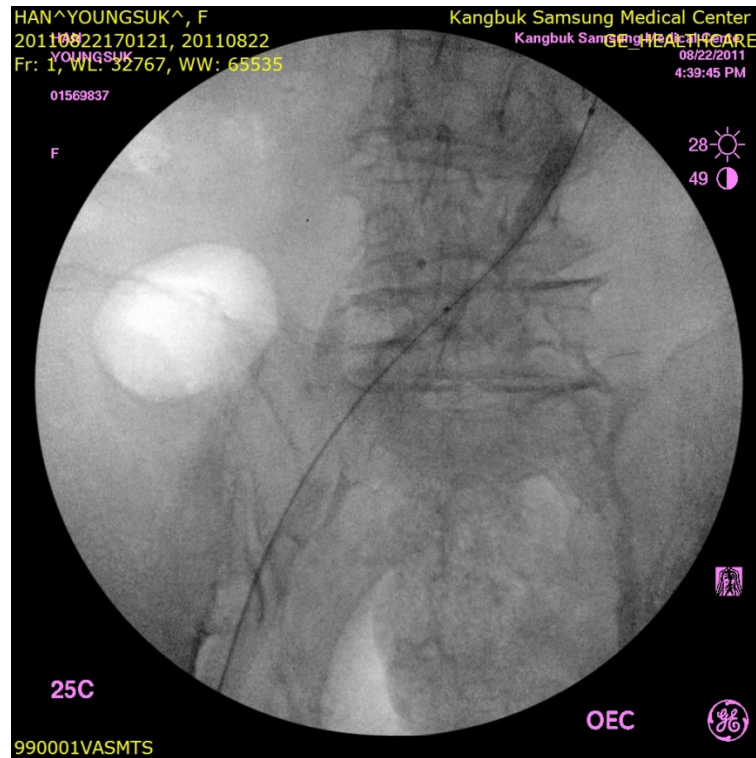


# Adjuvant Venoplasty & Stenting

- **Technique**
  - Popliteal vein approach
  - Venoplasty balloon (8~10 mm)
  - Self-expanding stents (10~16 mm)
  - After the procedure, oral warfarin for 6 months



# Balloon angioplasty & Stent insertion



# Balloon angioplasty insertion

참고하세요.

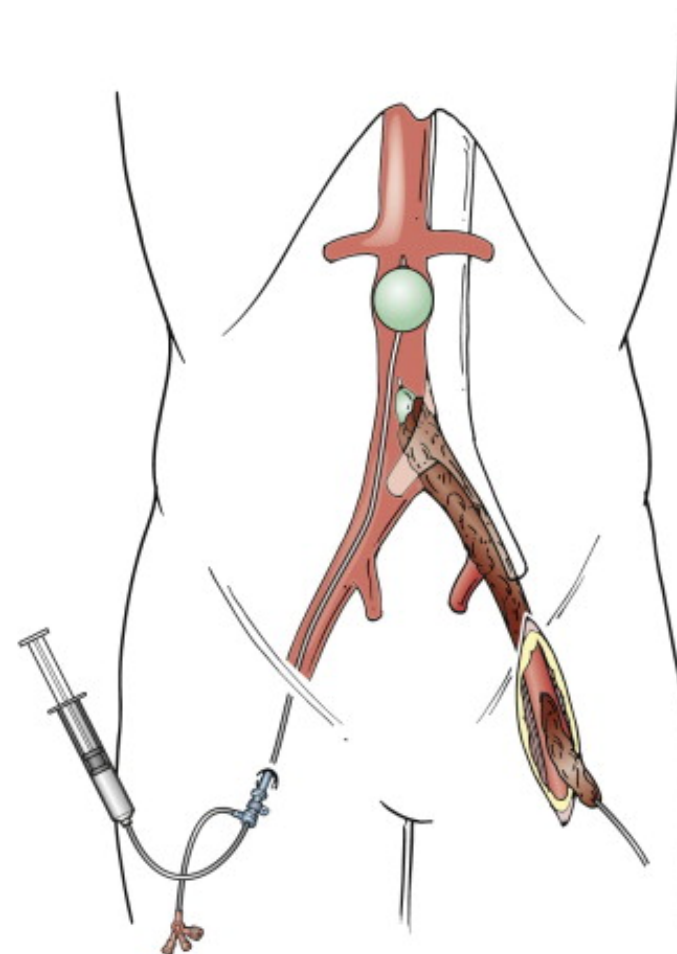
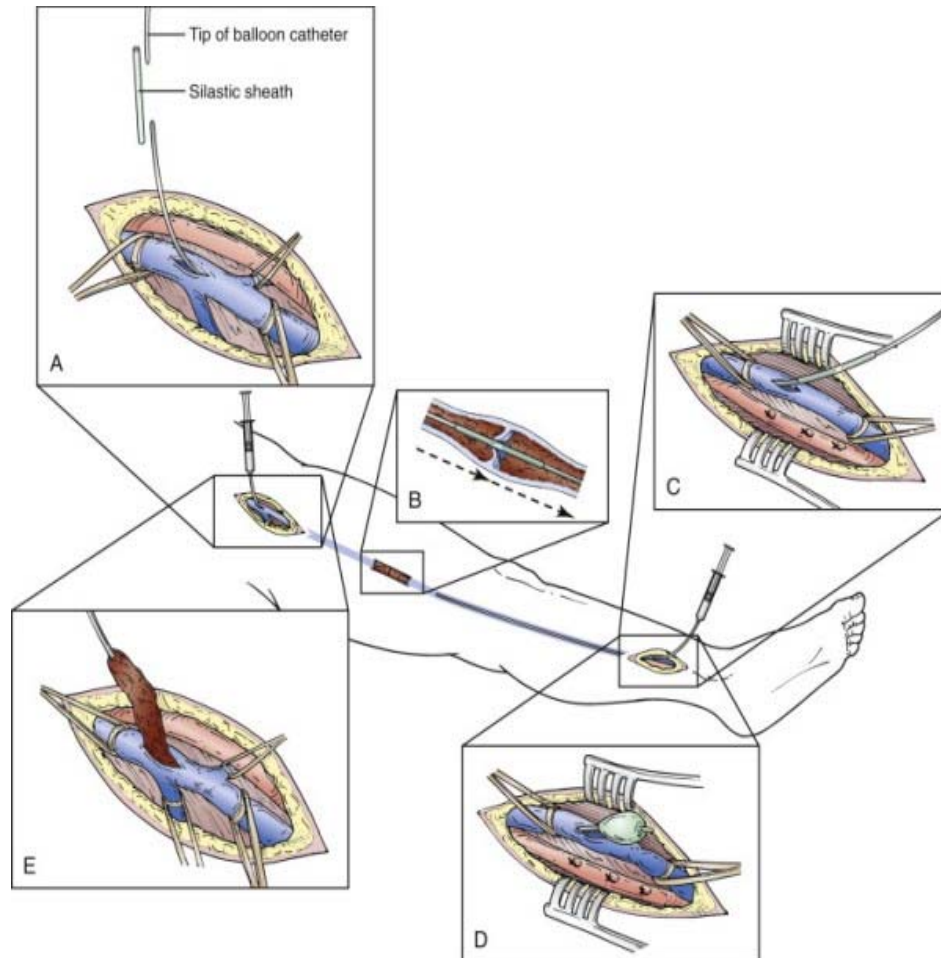
Author (year)	N	Success rate	Primary patency				Sx resolution	Compl ication
			6 mts	1 yr	2 yrs	4 yrs		
O'Sullivan GJ (2000)	39	87%		92% (A) 94% (C)			85%	17%
Hurst DR (2001)	18		89%	79%				
Kwak HS (2005)	22	96%		95%	95%			9%
Husmann MJ (2007)	11	100%		90%	82%		90%	
Oguzkurt L (2008)	36	94%		85%		80%	85% (A) 25% (C)	3%



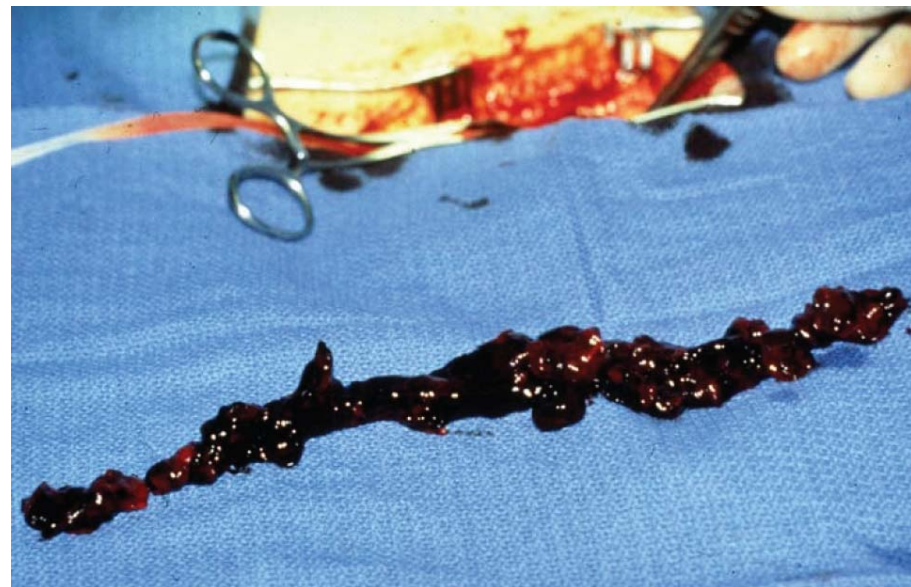
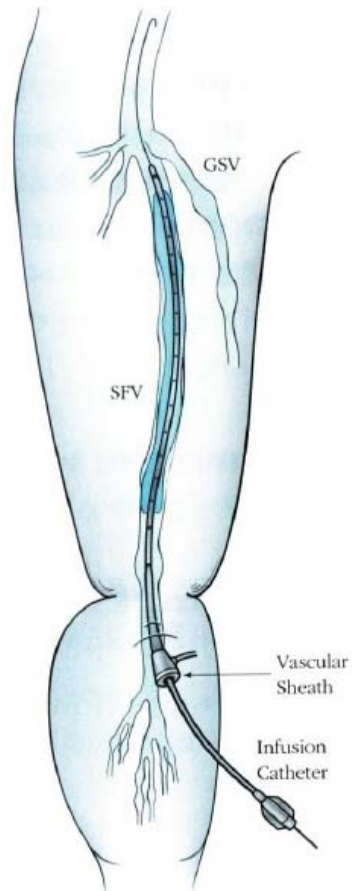
# **Treatment**

- **Surgical Thrombectomy**

# Operative thrombectomy

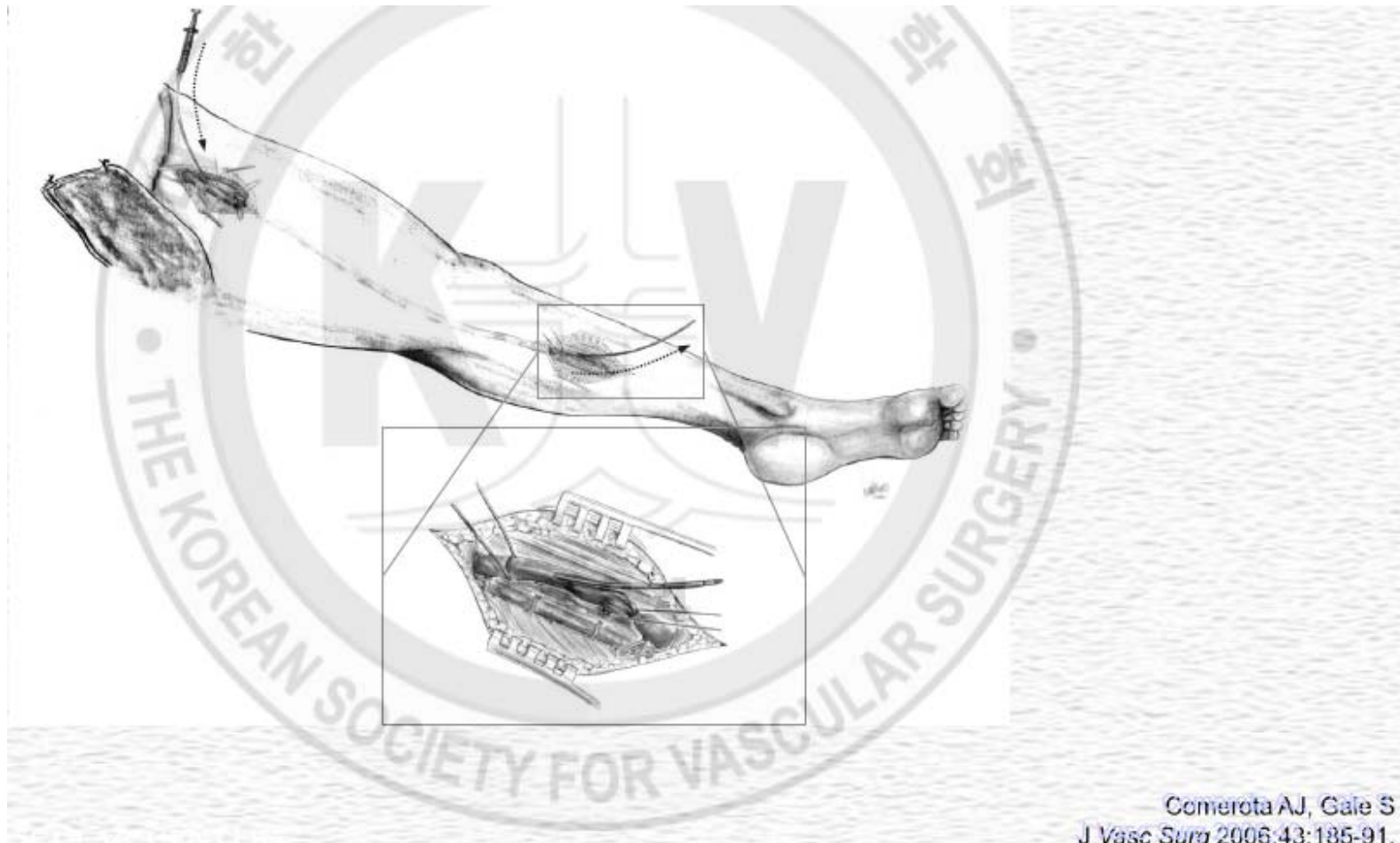


# 기계적 혈전제거술



# Venous Thrombectomy

## - infrainguinal Ballon Cathter Passage -



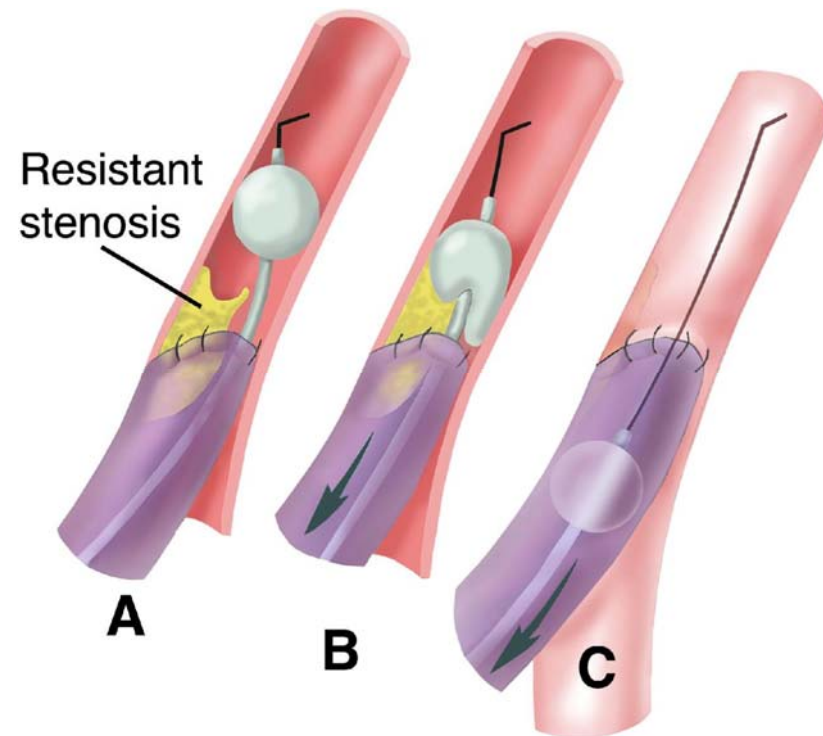
- 소병준, 원광대

# Over-wire-Fogarty

Old type



Over-the-wire



참고하세요.

# Venous Thromb

- Revival of thrombectomy in the management of acute iliofemoral venous thrombosis.
  - 230 thrombectomy
  - No fatal PE
  - 1 operative mortality
  - Early & long-term patency 80% vs 30% of anticoagulated pts
    - Eklof B, Contemp Surg 1992

참고하세요.

# Venous Thromb

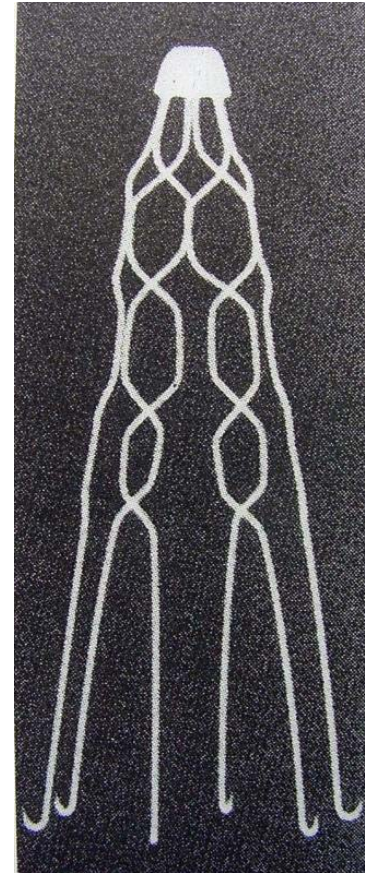
- AVF treatment guidelines for acute DVT
  - Accurate definition preoperatively of the extent of thrombosis, including routine contralateral iliocavography
  - Completion phlebography after thrombectomy to insure the adequacy of thrombectomy & examine residual venous lumen
  - Construction of a small arteriovenous fistula to increase velocity through a thrombogenic iliofemoral venous segment which assists in maintaining patency
  - Immediate & prolonged anticoagulation

# Treatment

- **IVC filter**

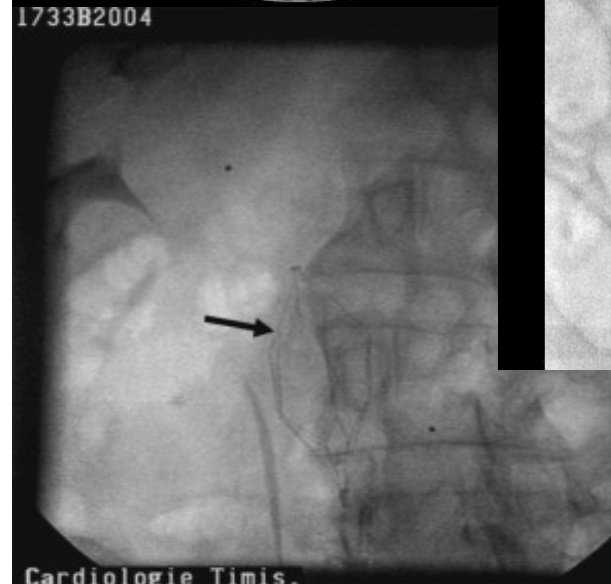
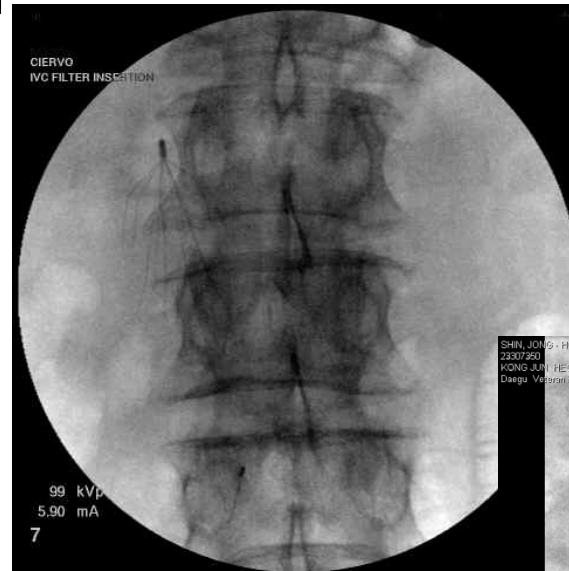
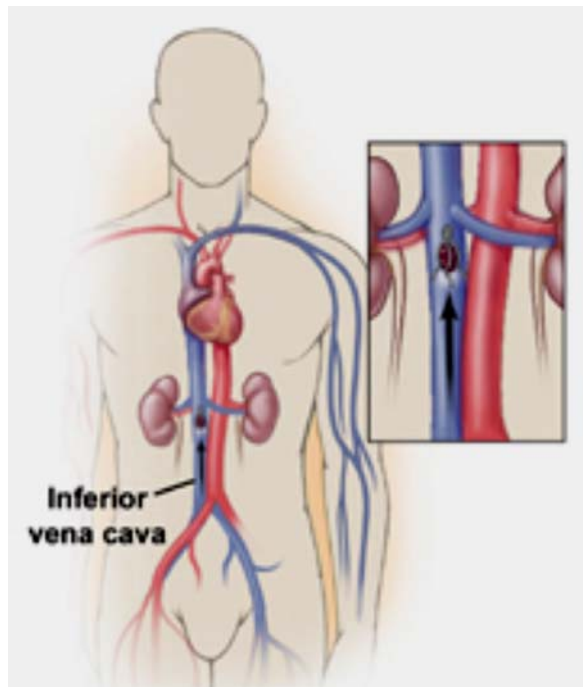


# Inferior Vena Cava Filter



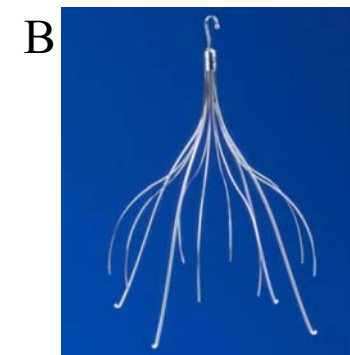
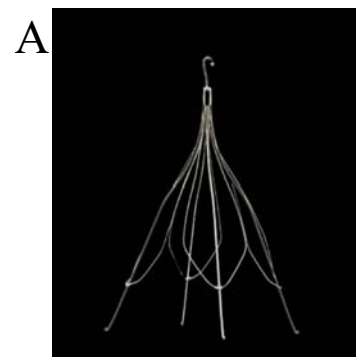
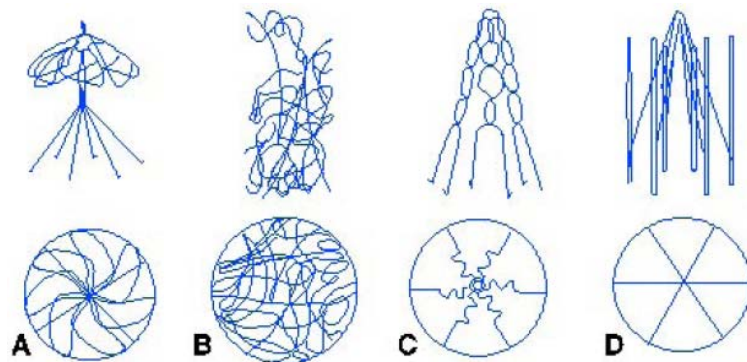
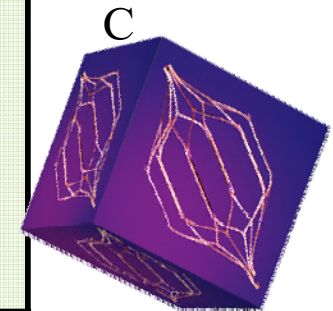
# Technique of IVC Filter

- Approach
  - Rt or Lt femoral,
  - Rt internal jugular approach

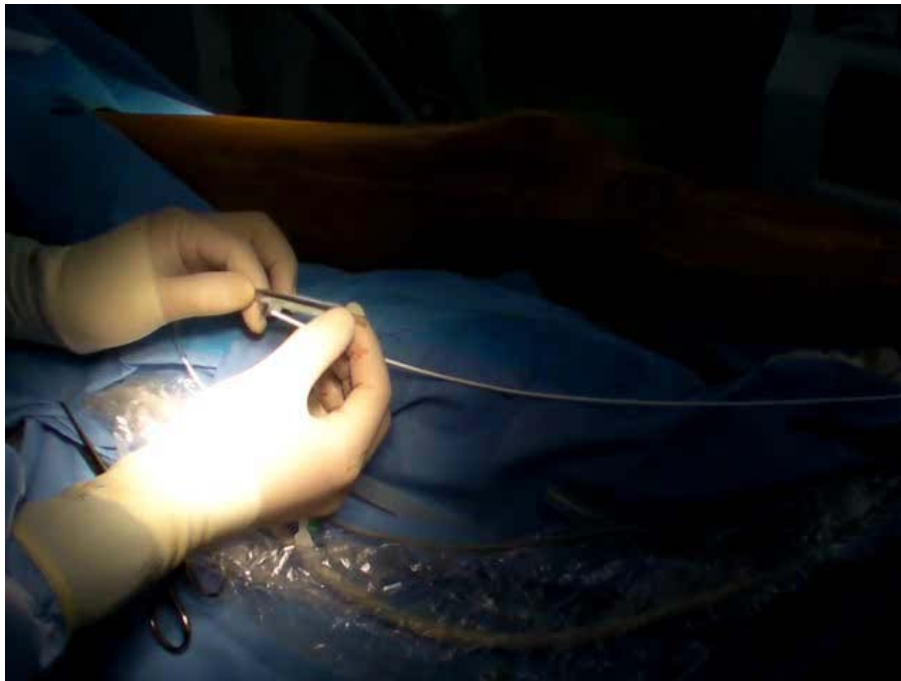


# Inferior Vena Cava Filters

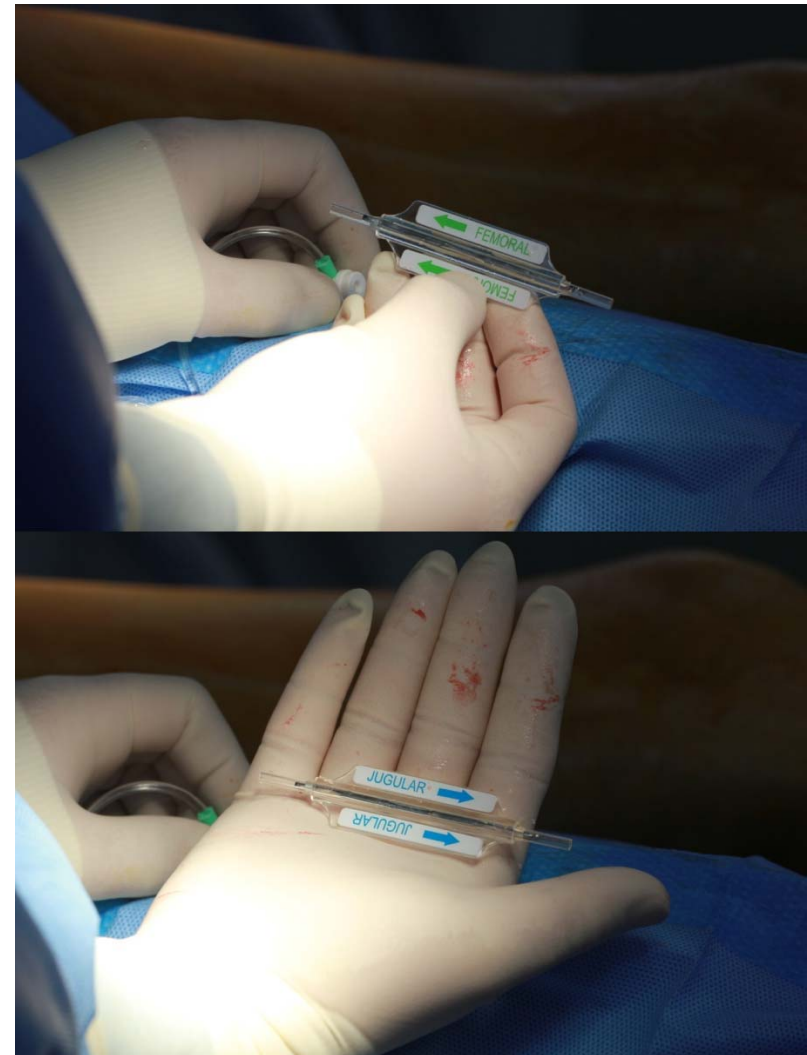
Permanent filter	Optional retrievable filter
Simon Nitinol (A) Bird's Nest (B) Greenfield (C) VenaTech (D) TrapEase	Gunther Tulip (A) Cook Celect Filter (B) OptEase (C) Recovery Filter



# I. IVC filter

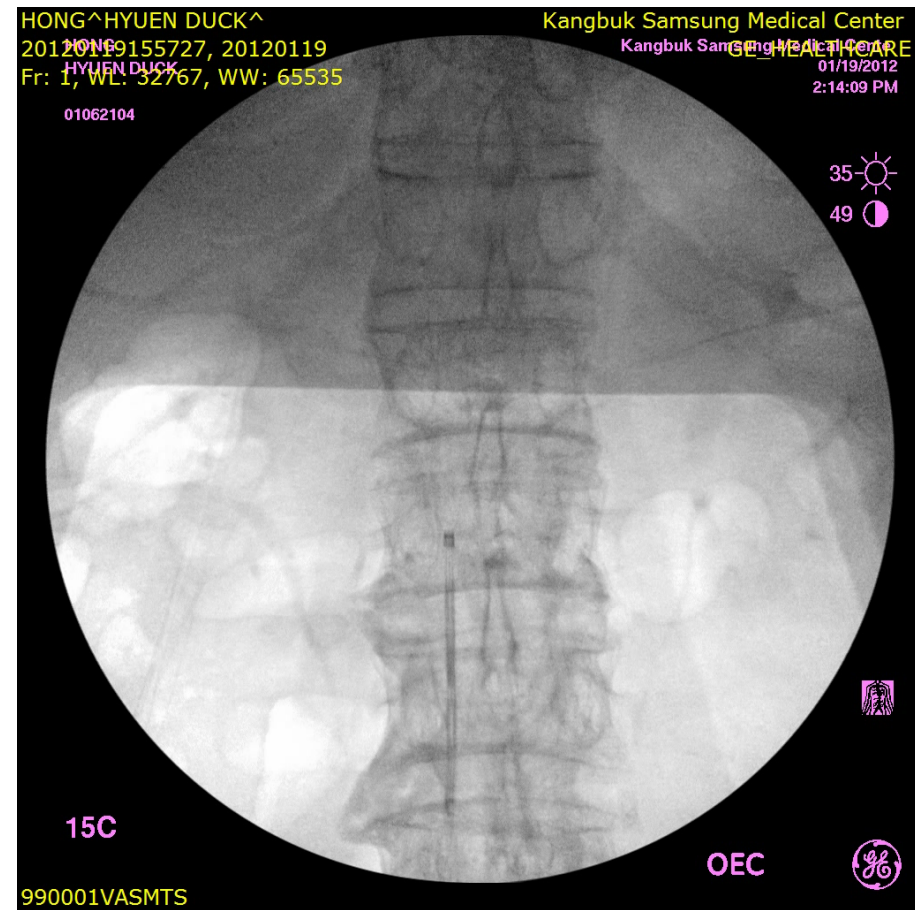
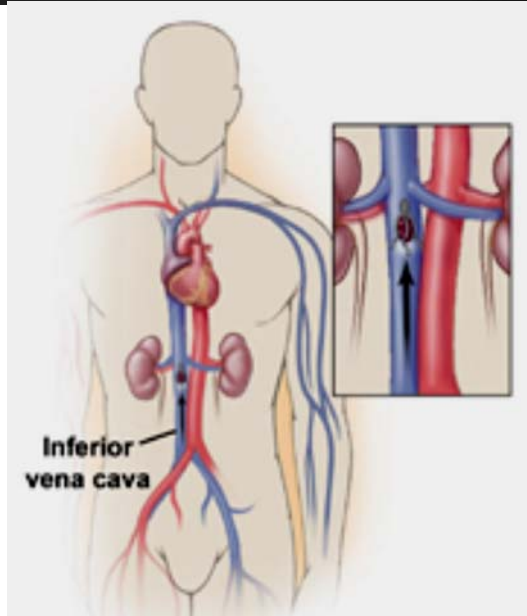


**Medial view**



# I. IVC filter

OptEase filter



# Permanent IVC filter Indication

- **Contraindication to anticoagulation**
- Patients who experience a complication to anticoagulation treatment
- Recurrent PE
- DVT pts who have cancer, burns
- DVT during Pregnant
- High-risk surgical and trauma patients with a contraindication for anticoagulation

참고하세요.

# Inferior Vena Caval

- **Absolute** Indication
  - **Contraindications to anticoagulation**
  - **Recurrent** thromboembolism despite adequate anticoagulation
  - **Complications** of anticoagulations that have to be forced the therapy to be discontinued
  - Immediately after pulmonary embolectomy
  - Failure of another form of caval interruption, demonstrated by recurrent thromboembolism

참고하세요.

# Inferior Vena Caval

- **Relative** indications
  - A large free-floating iliofemoral thrombus demonstrated on venography in a high-risk patient
  - Propagating ilio-femoral thrombus despite adequate anticoagulation
  - Chronic pulmonary embolism in a patient with pulmonary hypertension and cor pulmonale
  - Occlusion of more than 50% of pulmonary bed and would not be tolerate any additional thrombus
  - Recurrent septic embolism



# Summary

- **IVC filters**

- are *not considered* indicated for thrombolysis,
- **strongly considered**
  - in case of loose (free-floating) thrombi or patients with poor cardiopulmonary reserve, filter placement **before thrombolysis or mechanical thrombectomy** should be strongly considered.

\* Optimal or **retrievable filters** should be considered for this purpose.

# Summary (cont'd)

- **CDT** for lower extremity DVT
  - are *not established*,
  - **seriously considered**
    - patients with iliac and proximal femoral vein thrombosis, especially who are younger,
    - patients with thrombosis of short duration (less than 10 – 14 days)

# Summary (cont'd)

- **Mechanical thrombectomy**
  - may turn out to shorten the treatment time
  - possibly decrease the risk of complications, but this remains to be proved
- **Endovascular stents**
  - are used almost only in the iliac veins

# Highlights in Thrombolytic Management of DVT

- WHAT'S **IN**?
  - **Cather-directed thrombolysis**: good effect and low rate of bleeding complications
- WHATS'S **OUT**?
  - **Systemic thrombolysis**: because of a high rate of bleeding complications

# Highlights in Thrombolytic Management of DVT

- WHAT'S **NEW**?
  - **Pharmacomechanical thrombolysis**:
    - is associated with reduced thrombolysis time
    - allows aggressive treatment of underlying pathology
- WHAT'S **CONTROVERSIAL**?
  - Aggressive thrombolysis combined with immediate treatment of underlying obstructions or other causes

## Acute DV

참고하세요.

### Studies

- Thrombolysis registry 1999
- **CaVenT study 2012, 2016**
- PEAR
- **Attr**
- VIDR

### Guidelines

- SIR 2006
- SIR 2009

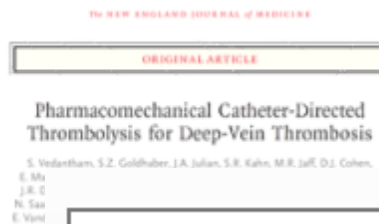
## CaVenT trial (

참고하세요.

- Additional CDT resulted in a persistent and increased **clinical benefit during follow-up for up to 5 years**, supporting the use of additional CDT in patients with extensive proximal DVT

## ATTRACT trial

참고하세요.



## ATTRACT T

참고하세요.

- recombinant tissue plasminogen activator (rt-PA) (Activase, Genentech, South San Francisco, CA)
- Good flow to popliteal vein
  - Isolated thrombolysis using **30 mg** rt-PA
  - **CaVenT-like** Thrombolysis using **100 mg** rt-PA
- Poorer inflow to popliteal vein
  - Infusion-first Thrombolysis using **multicatheter catheter**
- PTS, defined as a score of  $\geq 5$  on the Villalta PTS Scale

## ATTRACT trial

참고하세요.

- **Leg pain and swelling significantly improved** in PCDT vs no-PCDT out to **30 days** ( $p=0.019$  and  $p=0.05$ )
- In **IFDVT** mod-severe PTS 18.4% vs 28.2% in PCDT vs no-PCDT

143

## ATTRACT trial

참고하세요.

- **PTS** : 46.7% for PCDT vs 48.2% for no-PCDT ( $p=0.56$ )
- **Recurrent VTE** : 12.5% for PCDT vs 8.5% for no-PCDT ( $p=0.09$ )
- **Major and any bleeding** rates statistically higher in PCDT arm (**1.7% vs 0.3%**;  $p=0.49$  and **4.5% vs 1.7%**;  $p=0.034$ )

## ATTRACT trial

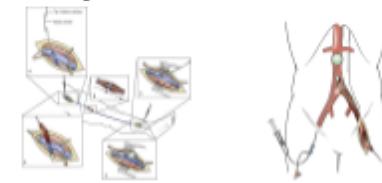
참고하세요.

- PCDT (pharmacomechanical catheter directed thrombolysis)
  - Helpful for **acute symptoms**
  - More benefit in **IFDVT**
  - **Did not** result in a lower risk of the PTS
  - Higher risk of **major bleeding**

## Hybrid is non-inferior

참고하세요.

- novel single-incision approach that combines operative and endovascular techniques to maximize thrombus resolution.



145

148

## Hybrid is non-inferior

참고하세요.

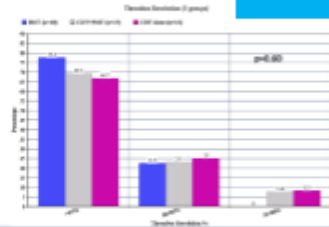


Fig 1. Comparison of degree of thrombus resolution between the groups of catheter-directed thrombolysis, hybrid operative thrombolysis, and pharmacomechanical thrombolysis.

**HOT thrombolysis established complete ( $\geq 90\%$ ) thrombus resolution more frequently than PT did (70% vs 67%;  $P = .11$ )**

## Hybrid Operative Thrombolysis (HOT) (youtube: joonhyuk)

참고하세요.



## DVT: Treatment options

Goal	Caval Filter	Anti-Coagulation	Thrombolytic Therapy	Systemic Thrombolysis
reduce PE	++	++	++	++
prevent thromboembolism	+	++	++	++
reduce DVT recurrence	+	+	+	++
restore venous patency	+	+	+	+
restore venous valve	+	+	+	+
reduce chronic venous insufficiency	++	+	+	+

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참고하세요.

# Acute DV

## Studies

- Thrombolysis registry 1999
- **Cavent study 2012, 2016**
- PEARL registry 2015
- **Attract study 2013, 2017**
- VIDIO trial 2016

## Guidelines

- SIR 2006
- SIR 2009
- SVS 2012
- AHA 2011
- ACCP 2012 9th
- **ACCP 2016 9th update**
- **ESC 2017**

참고하세요.

# CaVenT trial (

- Additional CDT resulted in a persistent and increased **clinical benefit during follow-up for up to 5 years**, supporting the use of additional CDT in patients with extensive proximal DVT
- However, allocation to this therapy **did not lead to better quality of life**



# ATTRACT trial

참고하세요.

*The* NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

## Pharmacomechanical Catheter-Directed Thrombolysis for Deep-Vein Thrombosis

S. Vedantham, S.Z. Goldhaber, J.A. Julian, S.R. Kahn, M.R. Jaff, D.J. Cohen, E. Magnuson, M.K. Razavi, A.J. Comerota, H.L. Gornik, T.P. Murphy, L. Lewis, J.R. Duncan, P. Nieters, M.C. Derfler, M. Filion, C.-S. Gu, S. Kee, J. Schneider, N. Saad, M. Blinder, S. Moll, D. Sacks, J. Lin, J. Rundback, M. Garcia, R. Razdan, E. VanderWoude, V. Marques, and C. Kearon, for the ATTRACT Trial Investigators\*

N Engl J Med 2017;377:2240-52.

참고하세요.

# ATTRACT T

- recombinant tissue plasminogen activator (rt-PA) (Activase, Genentech, South San Francisco, CA)
- Good flow to popliteal vein
  - Isolated thrombolysis using Trellis
  - PowerPulse Thrombolysis using the AngioJet
- Poor inflow to popliteal vein
  - Infusion-First Thrombolysis using a multisidehole catheter
- PTS, defined as a score of  $\geq 5$  on the Villalta PTS Scale

Assessment	Baseline	Initial Tx	10 d	30 d	6 m	12 m	18 m	24 m
Leg pain (Likert)	X		X	X				
Leg circumference	X		X	X				
Venous QOL (VEINES)	X			X	X	X	X	X
General QOL (SF-36 version 2)	X			X	X	X	X	X
Duplex ultrasonography	X			X		X*		
Venogram (PCDT arm only)		X†						
Cost diary review			X	X	X	X	X	X
Villalta Scale to assess PTS	X		X	X	X	X	X	X
VCSS					X	X	X	X
CEAP classification					X	X	X	X

Abbreviations: VEINES, Venous insufficiency epidemiological and economic study; SF-36, short-form 36; VCSS, venous clinical severity score; CEAP, clinical-etiological-pathophysiological-anatomic classification.

\* Performed in a subgroup of patients.

† Performed pre- and post-PCDT

참고하세요.

# ATTRACT trial

- **Leg pain and swelling** significantly improved in PCDT vs no-PCDT out to 30 days (p=0.019 and p=0.05)
  - In IFDVT mod-severe PTS  
18.4% vs 28.2% in PCDT vs no-PCDT
  - In FPDVT mod-severe PTS  
17.1% vs 18.1% in PCDT vs no-PCDT

참고하세요.

# ATTRACT trial

- **PTS** : 46.7% for PCDT vs 48.2% for no-PTCD (p=0.56)
- **Recurrent VTE** : 12.5% for PCDT vs 8.5% for no-PCDT (p=0.09)
- **Major** and **any bleeding** rates statistically higher in PCDT arm (1.7% vs 0.3% ; p=0.49 and 4.5% vs 1.7%; p=0.034)

참고하세요.

# ATTRACT trial

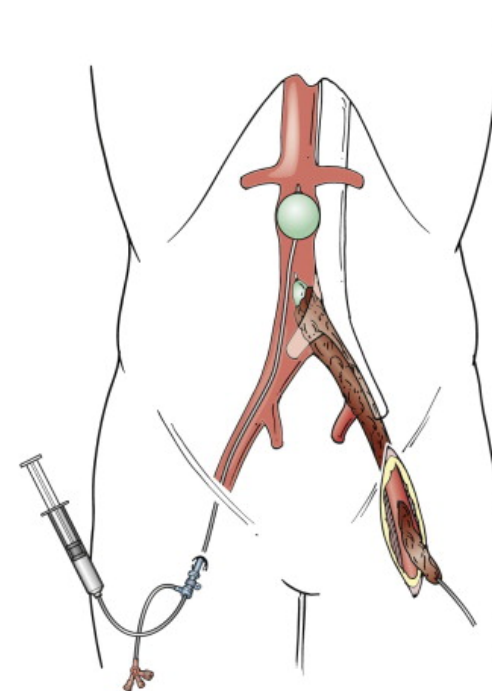
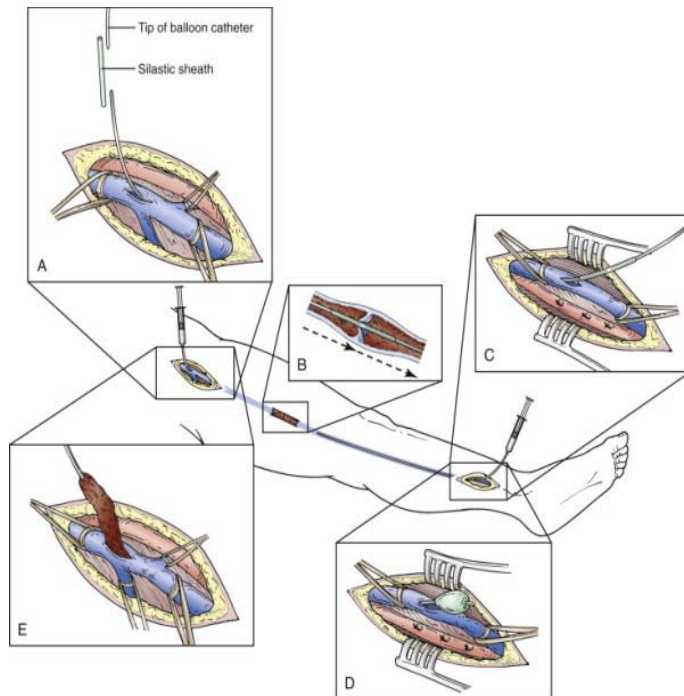
## PCDT (pharmacomechanical catheter directed thrombolysis)

- Helpful for **acute symptoms**
- More benefit in **IFDVT**
- **Did not** result in a **lower risk of the PTS**
- Higher risk of **major bleeding**

참고하세요.

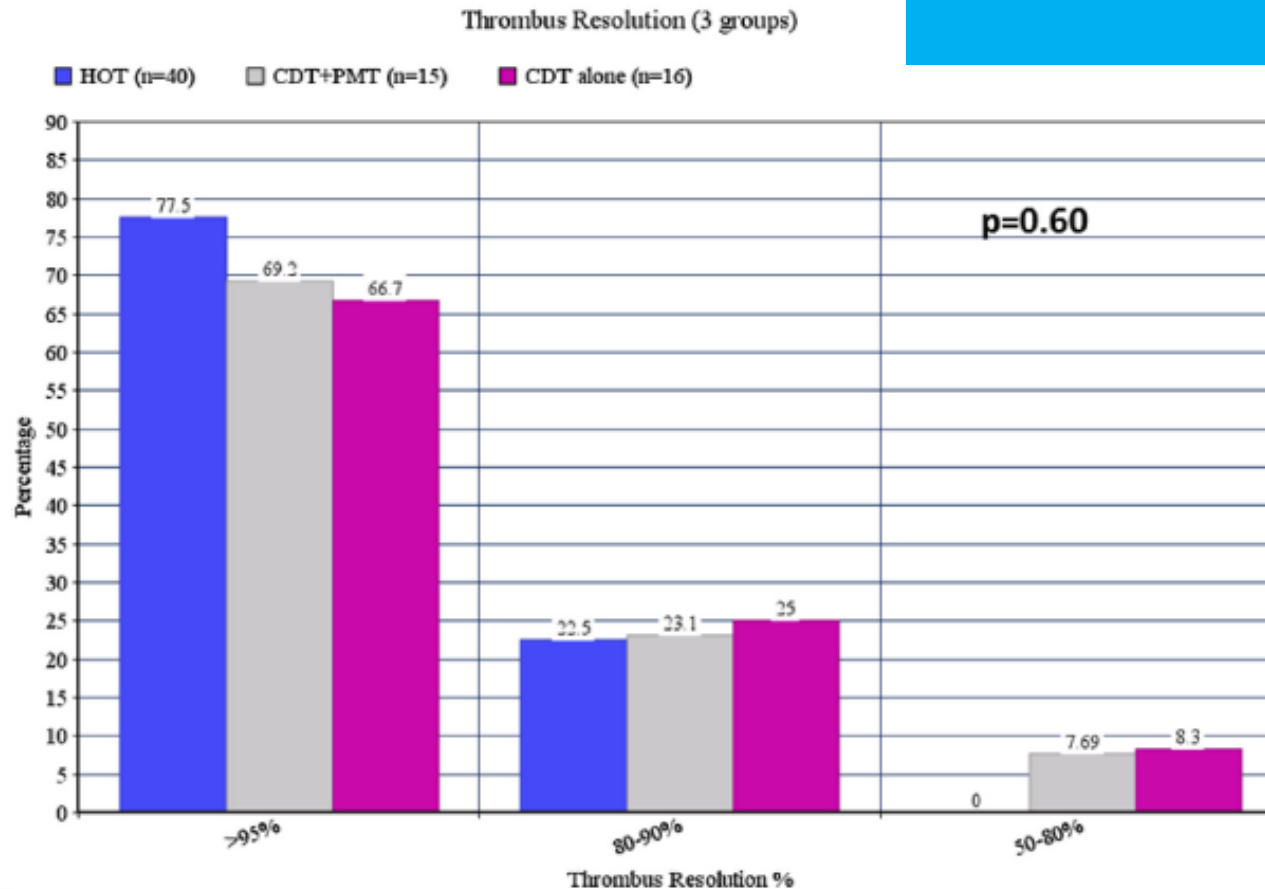
# Hybrid is non-inferior

- novel single-incision approach that combines operative and endovascular techniques to maximize thrombus resolution.



참고하세요.

# Hybrid is non-inferior



**Fig 1.** Comparison of degree of thrombus resolution between the groups at completion venography. *CDT*, Catheter-directed thrombolysis; *HOT*, hybrid operative thrombectomy; *PMT*, pharmacomechanical thrombectomy.

HOT thrombectomy established complete ( $\geq 95\%$ ) thrombus resolution more frequently than PT did (78% vs 67%;  $P = .11$ )

# Hybrid Operative Thrombolysis + IAT

(youtube: joonhyuk)

참고하세요.







# DVT: Treatment options



Goal	Caval filter	Anti-Coagulation	Thrombolytic Therapy	Venous Thrombectomy
reduce PE	+	+	+	+
prevent thrombus extension		+	+	+/-
reduce DVT recurrence		+	+	+/-
restore venous patency			+	+
restore venous valve			+	+
reduce chronic venous insufficiency		+/-	+	+



# **Calf Vein Thrombo**

참고하세요.

참고하세요.

# Calf Vein Thrombo

- CVT usually do not cause major sequelae & high risk of PE
- But CVT can embolize, propagation to large veins substantially increases the risk of PE & post-thrombotic syndrome
- Propagation rate : 6-30%
- If not treated, recurrent VTE occurred in 30% of pts.
- 29% recurrent VTE in pts treated w/ 5 days IV heparin vs. no recurrence in pts receiving 3 mo of anticoagulation

*Lagerstedt CI, Lancet 1985*

# Guideline

참고하세요.

# Acute DV

참고하세요.

**Studies**

- Thrombolysis registry 1999
- Caveat study 2012, 2016
- PEARL registry 2015
- Attract study 2013, 2017
- VIDIO trial 2016

**Guidelines**

- SIR 2006
- SIR 2009
- SVS 2012
- AHA 2011
- ACCP 2012 9th
- ACCP 2016 9th update
- ESC 2017

# ACCP 9th update 2

참고하세요.

Study	Year	Population	Intervention	Control	Primary Outcome	Secondary Outcome
Attract	2013	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...
Attract	2017	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...
Attract	2017	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...
Attract	2017	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...
Attract	2017	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...
Attract	2017	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...
Attract	2017	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...
Attract	2017	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...
Attract	2017	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...
Attract	2017	Acute proximal DVT	CDT	Anticoagulation	Recanalization	...

The **CAVEND** Study has reported that CDT reduced VTE, did not alter quality of life, and appears to be cost-effective.

A retrospective analysis of CDT (2019 patients) was associated with increase in recanalization(23%), incremental bleeding (30%), PE(5.3%), and vena savaal filter insertion(20%)

This new evidence has not led to a change in our recommendation for the use of CDT in patients with DVT since ACCP 2012

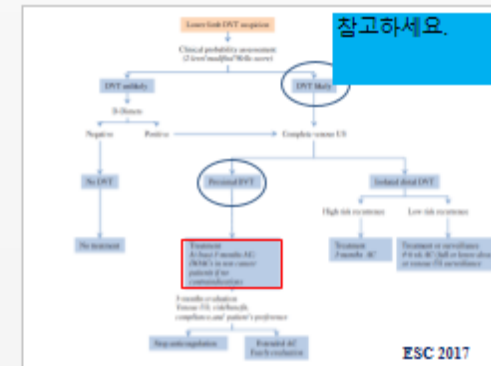
ESC 2016, 149(2), 319-325

# ACCP Guideline 2

참고하세요.

**Catheter-Directed Thrombolysis for Acute DVT of the Leg**

- In patients with **acute proximal DVT of the leg**, we suggest **anticoagulant therapy alone over CDT (Grade 2C)**
- We propose that the patients who are most likely to **benefit from CDT** have
  - **Iliofemoral DVT**
  - **Symptoms for <14 days**
  - **Good functional status**
  - **Life expectancy of >1 year**
  - **Low risk of bleeding**



참고하세요.

참고하세요.

# Acute DV

## Studies

- Thrombolysis registry 1999
- **Cavent study 2012, 2016**
- PEARL registry 2015
- **Attract study 2013, 2017**
- VIDIO trial 2016

## Guidelines

- SIR 2006
- SIR 2009
- SVS 2012
- AHA 2011
- ACCP 2012 9th
- **ACCP 2016 9th update**
- **ESC 2017**

# ACCP 9<sup>th</sup> update 2

참고하세요.

Outcomes	No. of Participants (Studies) Follow-up	Quality of the Evidence (GRADE)	Relative Effect (95% CI)	Anticipated Absolute Effects	
				Risk with Anticoagulation Alone	Risk Difference with Catheter-Assisted Thrombus Removal (95% CI)
All-cause mortality	209 (1 study) 3 mo	⊕⊕⊕⊕ <b>Low</b> <sup>a,b</sup> because of imprecision	RR 0.43 (0.08-2.16)	46 per 1,000 <sup>c</sup>	26 fewer per 1,000 (from 43 fewer to 54 more)
Recurrent VTE	189 (1 study) 3 mo	⊕⊕⊕⊕ <b>Low</b> <sup>a,b</sup> because of imprecision	RR 0.61 (0.3-1.25) <sup>d</sup>		Moderate-Risk Population <sup>e</sup>
				48 per 1,000	19 fewer per 1,000 (from 34 fewer to 12 more)
Major bleeding	224 (2 studies) 3 mo	⊕⊕⊕⊕ <b>Low</b> <sup>a,b</sup> because of imprecision	RR 7.69 (0.4-146.9) <sup>d</sup>		Moderate-Risk Population <sup>e,f</sup>
				29 per 1,000	194 more per 1,000 (from 17 fewer to 1000 more)
PTS	189 (1 study) 2 y	⊕⊕⊕⊕ <b>Moderate</b> <sup>a</sup> because of imprecision	RR 0.74 (0.55-1) <sup>g</sup>		Moderate-Risk Population <sup>h</sup>
				588 per 1,000	153 fewer per 1,000 (from 265 fewer to 0 more) <sup>i</sup>
Patency	189 (1 study) 6 mo	⊕⊕⊕⊕ <b>Moderate</b> <sup>b</sup> because of imprecision	RR 1.42 (1.09-1.85)	455 per 1,000 <sup>j</sup>	191 more per 1,000 (from 41 more to 386 more)
QoL	189 (1 study) 24 mo	⊕⊕⊕⊕ <b>Moderate</b> <sup>k</sup> because of risk of bias			The mean quality of life in the intervention groups was 0.2 higher (2.8 lower to 3 higher) <sup>l,m</sup>

The CAVENT Study has reported that CDT reduced PTS, did not alter quality of life, and appears to be cost-effective

A retrospective analysis of CDT (3649 patients) was associated with increase in **transfusion(2X), intracranial bleeding (3X), PE(1.5X), and vena caval filter insertion(2X)**

This new evidence has not led to a change in our recommendation for the use of CDT in patients with DVT since ACCP 2012

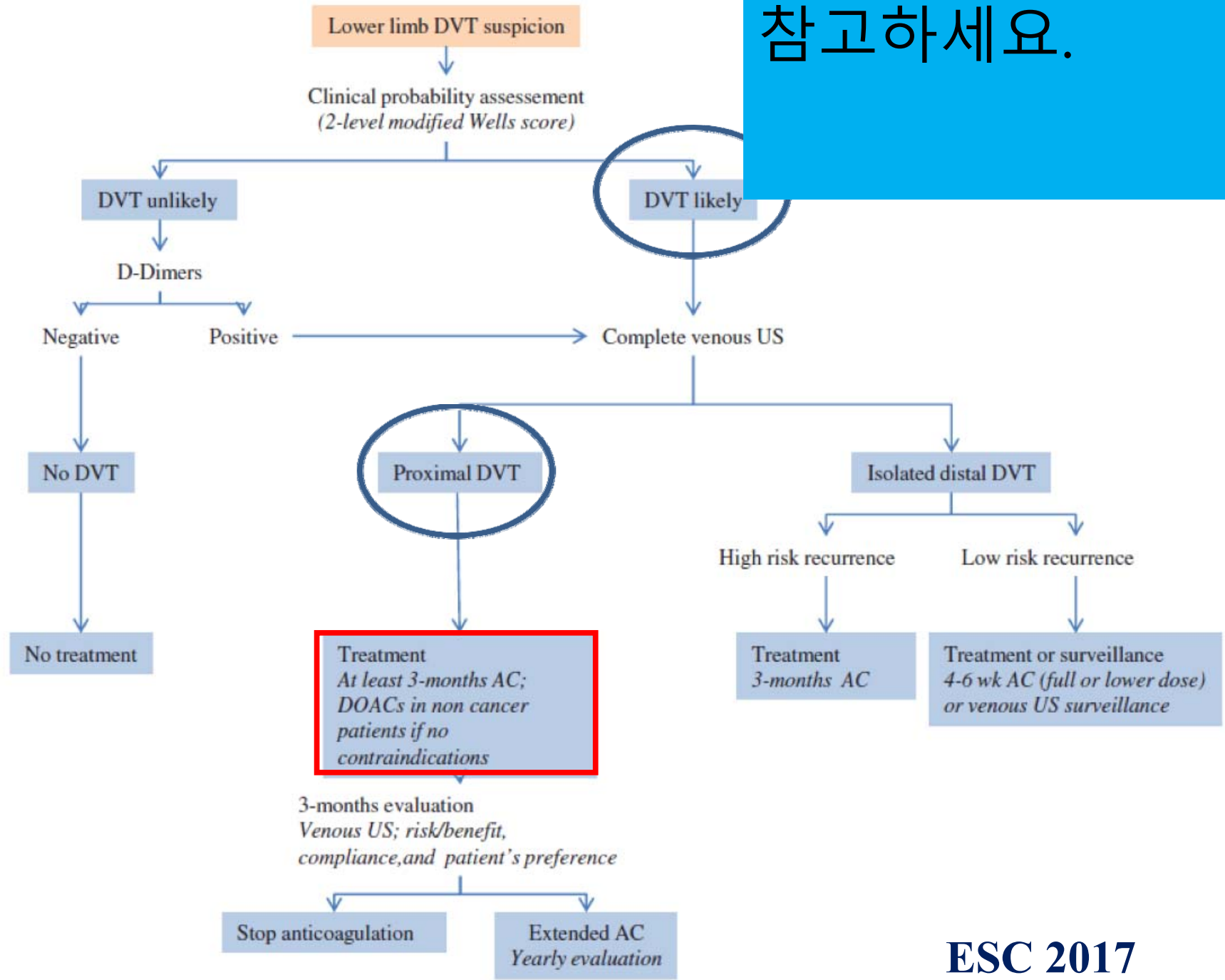
참고하세요.

# ACCP Guideline 2

- **Catheter-Directed Thrombolysis for Acute DVT of the Leg**
  - In patients with **acute proximal DVT of the leg**, we suggest **anticoagulant therapy alone over CDT (Grade 2C)**
  - We propose that the patients who are most likely to **benefit from CDT** have
    - Iliofemoral DVT
    - Symptoms for <14 days
    - Good functional status
    - Life expectancy of >1 year
    - Low risk of bleeding



참고하세요.



**Pregnanc**

참고하세요.

참고하세요.

## **DVT in pregnancy**

- Increased risk of VTE in pregnancy
- Warfarin – teratogenic
- LMWH until delivery

**Malignanc**

참고하세요.

# Anticoagulant therapy with malignancy

참고하세요.

- Risk of VTE : 11%, 2nd leading cause of death in pt w/ overt malignancy
- Recurrence rate is higher in pts w/ malignancy than without malignancy
- Bleeding complication is higher in pts c malignancy than without malignancy
  
- Anticoagulant therapy LMWH>VKA
- NOAC – no data available
- Extended anticoagulation

# Anticoagulant therapy with brain tumor

참고하세요.

- High risk of **VTE : 7.5~25%**
  - esp., age  $\geq 60$  years, glioblastoma, large tumor size, subtotal resection, use of chemotherapy, neurosurgery  $\leq 2$  mo, leg paresis
- Risk of **bleeding: 2~4%** in pts w/ glioma,
  - esp., pituitary adenoma, metastatic tumor from melanoma, choriocarcinoma, thyroid ca., renal cell ca.
- Anticoagulant therapy LMWH > VKA

**Prophylax**

참고하세요.

# DVT: Prophylaxis



	Calf DVT	Proximal DVT	Fatal PE
<b>High risk</b>	40-80%	10-30%	>1%
<ul style="list-style-type: none"> <li>• Surgical patients with history of venous thromboembolism</li> <li>• Major pelvic or abdominal surgery for malignancy</li> <li>• Major trauma</li> <li>• Major lower limb orthopedic surgery</li> </ul>			
<b>Moderate risk</b>	10-40%	1-10%	0.1-1%
<ul style="list-style-type: none"> <li>• Geberak surgery in patients &gt;40 years</li> <li>• Patients on oral contraception</li> <li>• Neurosurgical patients</li> </ul>			
<b>Low risk</b>	<10%	<1%	<0.1%
<ul style="list-style-type: none"> <li>• Uncomplicated surgery in patients &lt;40 years without any other risk factors</li> <li>• Minor surgery in patients &gt;40 years without any other risk factors</li> </ul>			



참고하세요.

# DVT: Prophyl

- **Pharmacologic**
  - UFH
  - LMWH
  - Fondaparinux
  - Oral direct thrombin inhibitor
  - Factor Xa inhibitor
  - VKA
  - Aspirin
- **Mechanical**
  - Intermittent pneumatic compression

# Summary

참고하세요.

# **Therapeutic Goals Treatment**

참고하세요.

- **Relieve the patient's symptoms**
- **Prevent further thrombus propagation**
- **Prevent pulmonary embolism & CTEPH**
- **Prevent DVT recurrence**
- **Prevent postthrombotic syndrome**

# **Acute Pulmonary Embolism**

참고하세요.

# Clinical point

acute, major PE → 20% die within 48hrs  
→ most remaining, resolve over days to weeks

**minor: <30% occlusion**

PaO<sub>2</sub> 65~80mmHg

PaCO<sub>2</sub> 35mmHg

**major: 30~50% occlusion**

at least 2 lobar pulmonary obstruction

PaO<sub>2</sub> 50~60mmHg

PaCO<sub>2</sub> <30mmHg

**massive: >50% occlusion → 50% mortality**

PaO<sub>2</sub> <50mmHg

PaCO<sub>2</sub> <30mmHg

\* chronic massive embolism → severe PHTN

\* acute embolism in normal RV function → PA pressure may be normal

↳ 30~40mmHg = severe PHTN

참고하세요.

# Supportive & throm

## O2, ventilator support

**heparin:** IV heparin 70U/kg bolus → 18~20U/kg/hr  
monitor aPTT 50~70sec every 6~8hr  
PLT every 2~3days for HIT

## LMWH

**Thrombolytic:** UK 4400U/kg over 10min → 4400U/kg for 12hr  
heparin+thrombolytics=more effective & lower mortality rate

contraindication

- fresh surgical wound
- anemia
- recent stroke
- peptic ulcer
- bleeding tendency

# Acute PTE Embolectomy

## Indication

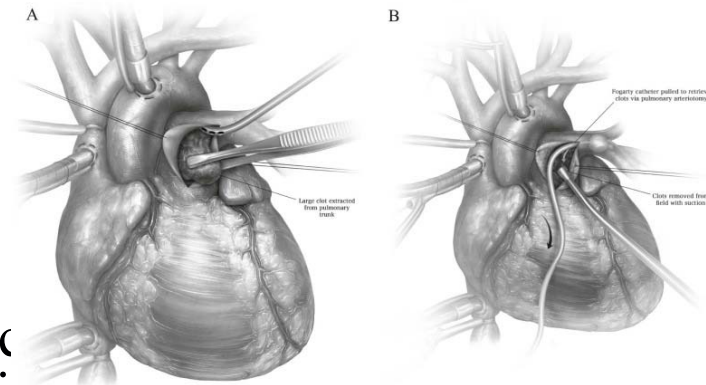
hemodynamic unstable  
major PE c ↓ O<sub>2</sub> gas exchange  
contraindication to thrombolytics or heparin  
large trapped clot in RA or RV

## Postop treatment

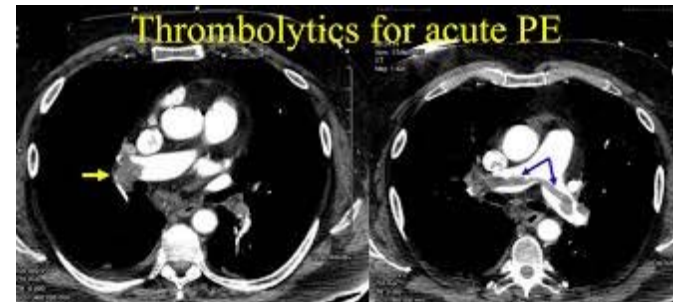
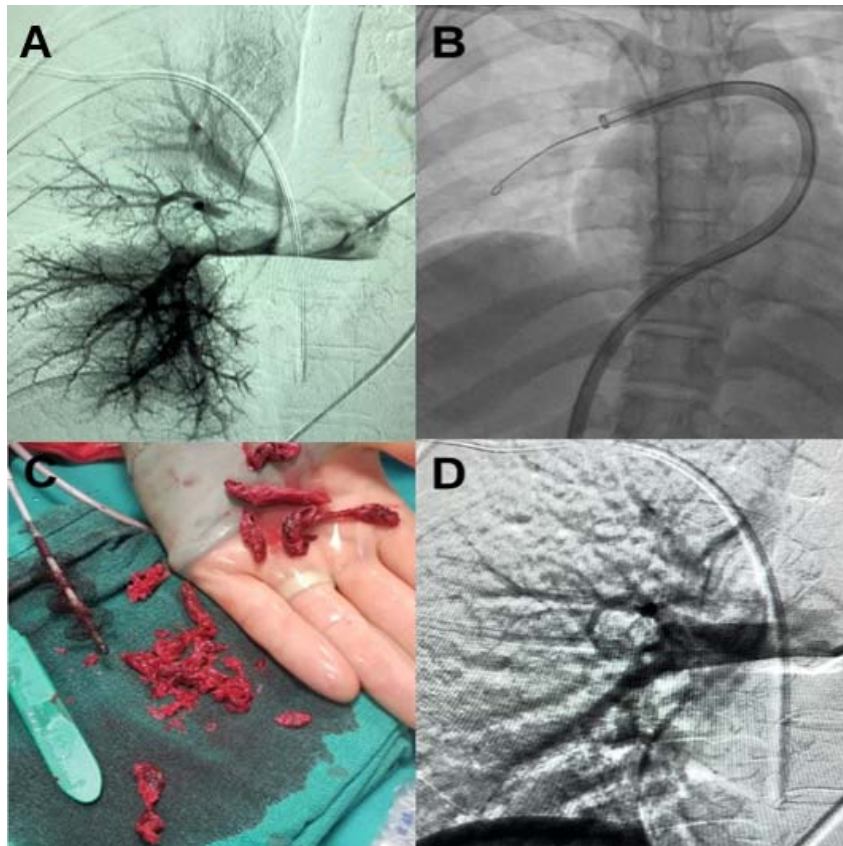
no caval procedures  
wafarin for 6mon

## IVC filter indication

contraindication to thrombolytic  
to recurrent PE on anticoagulation



# Acute PTE





# **Chronic Pulmonary Embolism**

# Natural history

**acute emboli**, not lysed--1~2wk→attach to arterial wall  
--with times→converted into connective & elastic tissues  
--a few weeks→vessel narrowing, fibrosis

why acute emboli fail to resolve

-unclear

-lupus anticoagulant

-deficiency of protein C, S, AT-III

**PHTN** >40mmHg→30% will survive at 5 years

>50mmHg→10% will survive at 5 years

chronic process involve proximal PA from pul. trunk to sublobar PA

infarction is infrequently

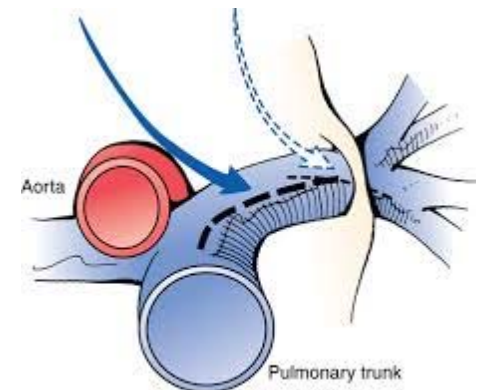
# Surgical indication

## Purpose

- hemodynamic goal: ameliorate RV compromise d/t PHTN
- respiratory goal: improve lung function by removal of non-functioning space
- prophylactic goal: prevent progress RV dysfunction, retrograde extension of clot  
prevent secondary vasculopathy

## Indication

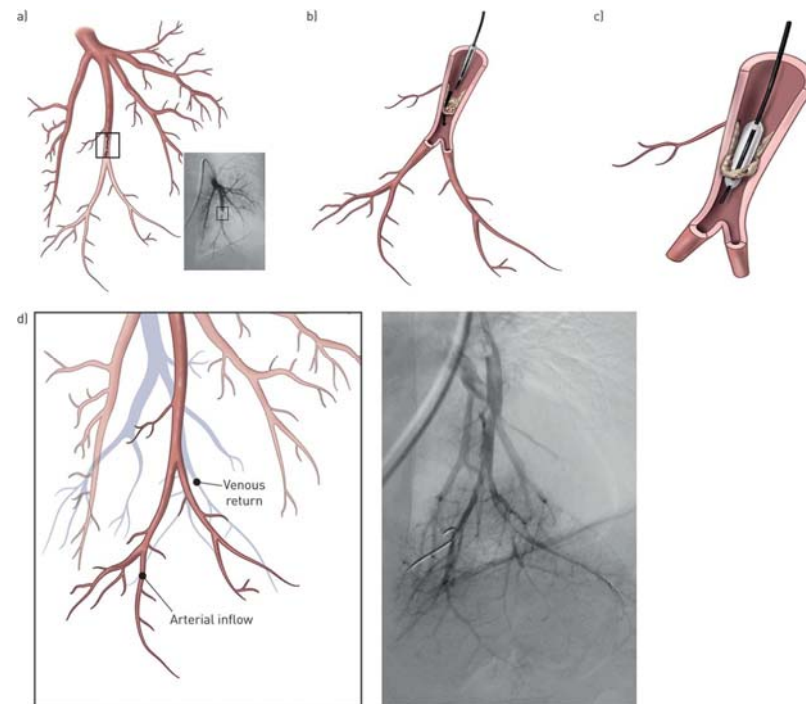
- symptomatic & hemodynamic or ventilatory impairment
- increased PVR
- lobar, segmental, PA occlusion



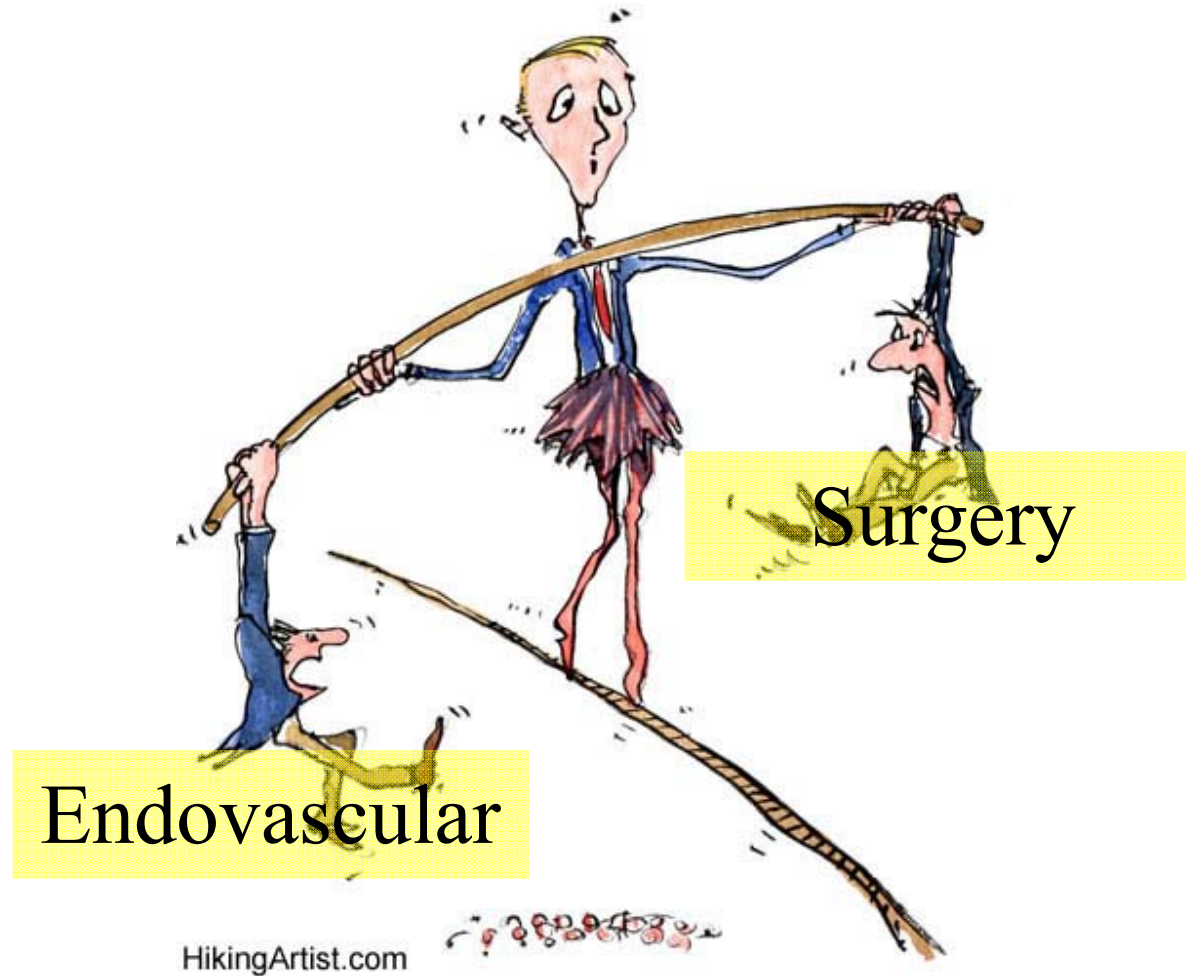
Source: Cohn LH: Cardiac Surgery in the Adult, 4th Edition.  
www.accesssurgery.com

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# Chronic PTE Endo



# Vascular Surgeon with Balance



Endovascular

Surgery