

Evidence-based medicine

102/02/26

Instructor: 鈕聖文醫師, R1 羅融

Presenter: Intern 李柏翰

Patient Profile

- Chart No.: 14598379
- Name: 王麗
- Gender: female
- Age: 50
- Admission: 102/01/10~02/05

Clinical scenario

- This 50-year-old female had history of:
 - CKD stage 5
 - Old stroke with right hemiparesis
 - Hypertension
 - Left ovarian tumor
- Her last hospitalization was during 10/12/12~12/19 due to AV shunt infection s/p removal.
- This time she was admitted for CKD with uremic symptoms, however, during admission, left lower leg pain, tenderness, progressive swelling was noticed since 01/21.

Present Illness

- 
- 1/10 PE: Severe left lower limb non-pitting edema while admission
 - Temporary HD with catheter inserted in left iliac vein
 - 1/21 Left lower leg pain, tenderness and progressive swelling
 - 1/22 CTA: left leg DVT (left external iliac, common femoral, popliteal, ant.&pos. tibial veins, peroneal vein)
 - Heparin → warfarin
 - Consulted CVS/Plasty: kept medical treatment; OP was not considered due to high risk

Present Illness

- 
- 1/25 15pm: Consulted Radiologist: directed thrombolysis; done with **urokinase(4.5M IU)** under direct access at inguinal femoral vein; infused along left common and external iliac vein + **IVC filter** placed
 - Kept **urokinase dripping with 30K IU/hr**
 - 1/25 21pm: follow-up left lower extremity venography
 - 1/27 17pm: con's change
 - 1/27 18pm brain CT: right side ICH
 - 2/5 critical AAD

Asking-提出臨床問題

- Background questions
 - (1)question
 - (2)answer
 - (3)apply
- Foreground questions
 - (1)PICOT
 - (2)search data
 - a. Summary
 - b. Synopses
 - c. Synthesis
 - d. Study

Background Question

- What is **Post-thrombotic syndrome**?
 - pain, swelling, a sensation of heaviness, edema, pigmentation, and deterioration of the skin, and venous ulcers in severe cases.

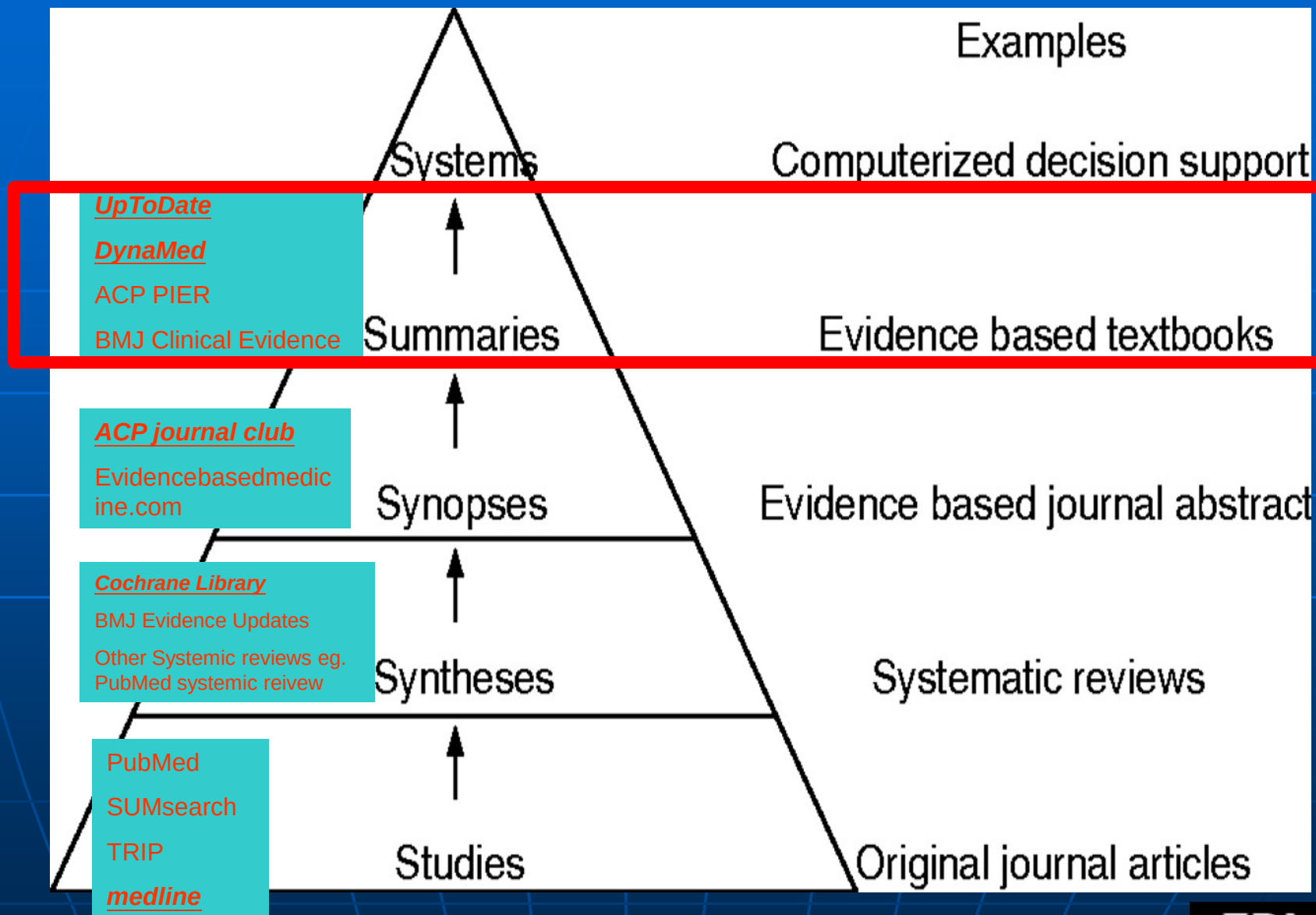
Foreground question

Patient / Problem	patient with ESRD + DVT
Intervention	Thrombolysis
Comparison	Other intervention (such as thrombectomy)
Outcome	Clot reduction / frequency of adverse event
Time	Not confined

Acquire-搜尋最有用的資料

- 先從已經過評讀的database開始找起
(system, synopses, synthesis)
- 最後再找尚未經過嚴格評讀的study

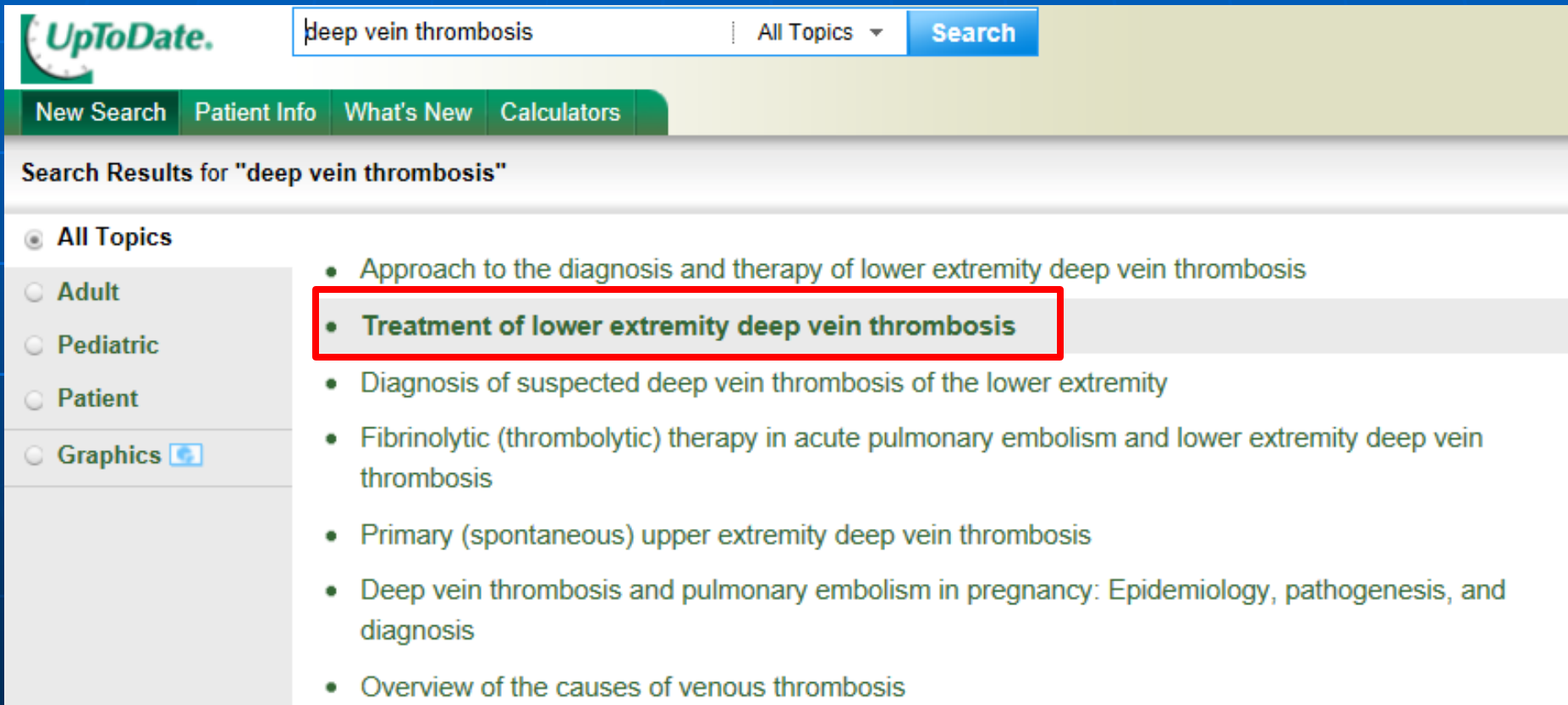
Search strategy: 5S model



Grades of Recommendation

Grade of Recommendation	Level of Evidence	Therapy
[A]	1a	Systemic review of RCTs
	1b	Single RCT
	1c	'All-or-none'
[B]	2a	Systemic review of cohort studies
	2b	Cohort study or poor RCT
	2c	'Outcomes' research
	3a	Systemic review of case-control studies
	3b	Case-control study
[C]	4	Case series
[D]	5	Expert opinion, physiology, bench research

■ Key words: deep vein thrombosis

A screenshot of the UpToDate website showing search results for "deep vein thrombosis". The interface includes a search bar at the top with the query and a dropdown menu set to "All Topics". Below the search bar are navigation tabs for "New Search", "Patient Info", "What's New", and "Calculators". The search results are titled "Search Results for 'deep vein thrombosis'". On the left, there is a sidebar with radio buttons for "All Topics", "Adult", "Pediatric", "Patient", and "Graphics". The main content area displays a list of search results, with the second item, "Treatment of lower extremity deep vein thrombosis", highlighted with a red rectangular border.

UpToDate. deep vein thrombosis All Topics Search

New Search Patient Info What's New Calculators

Search Results for "deep vein thrombosis"

☒ All Topics

☐ Adult

☐ Pediatric

☐ Patient

☐ Graphics 

- Approach to the diagnosis and therapy of lower extremity deep vein thrombosis
- **Treatment of lower extremity deep vein thrombosis**
- Diagnosis of suspected deep vein thrombosis of the lower extremity
- Fibrinolytic (thrombolytic) therapy in acute pulmonary embolism and lower extremity deep vein thrombosis
- Primary (spontaneous) upper extremity deep vein thrombosis
- Deep vein thrombosis and pulmonary embolism in pregnancy: Epidemiology, pathogenesis, and diagnosis
- Overview of the causes of venous thrombosis

Treatment of lower extremity DVT

-- Recommendations



- **proximal DVT**: treated acutely with (Grade **1A**) :
 - LMW heparin
 - unfractionated intravenous heparin
 - subcutaneous heparin
 - subcutaneous fondaparinux
- **severe renal failure** ($\text{ClCr} < 30 \text{ mL/min}$) (Grade **2C**):
 - **intravenous unfractionated heparin** > LMW heparin

Treatment of lower extremity DVT

-- Recommendations



- **IVC filter** (Grade **1C**) :
 - contraindication to or a failure of anticoagulant therapy
- oral anticoagulation with **warfarin** (Grade **1A**):
 - keep INR target of 2.5 (INR range: 2.0 to 3.0)

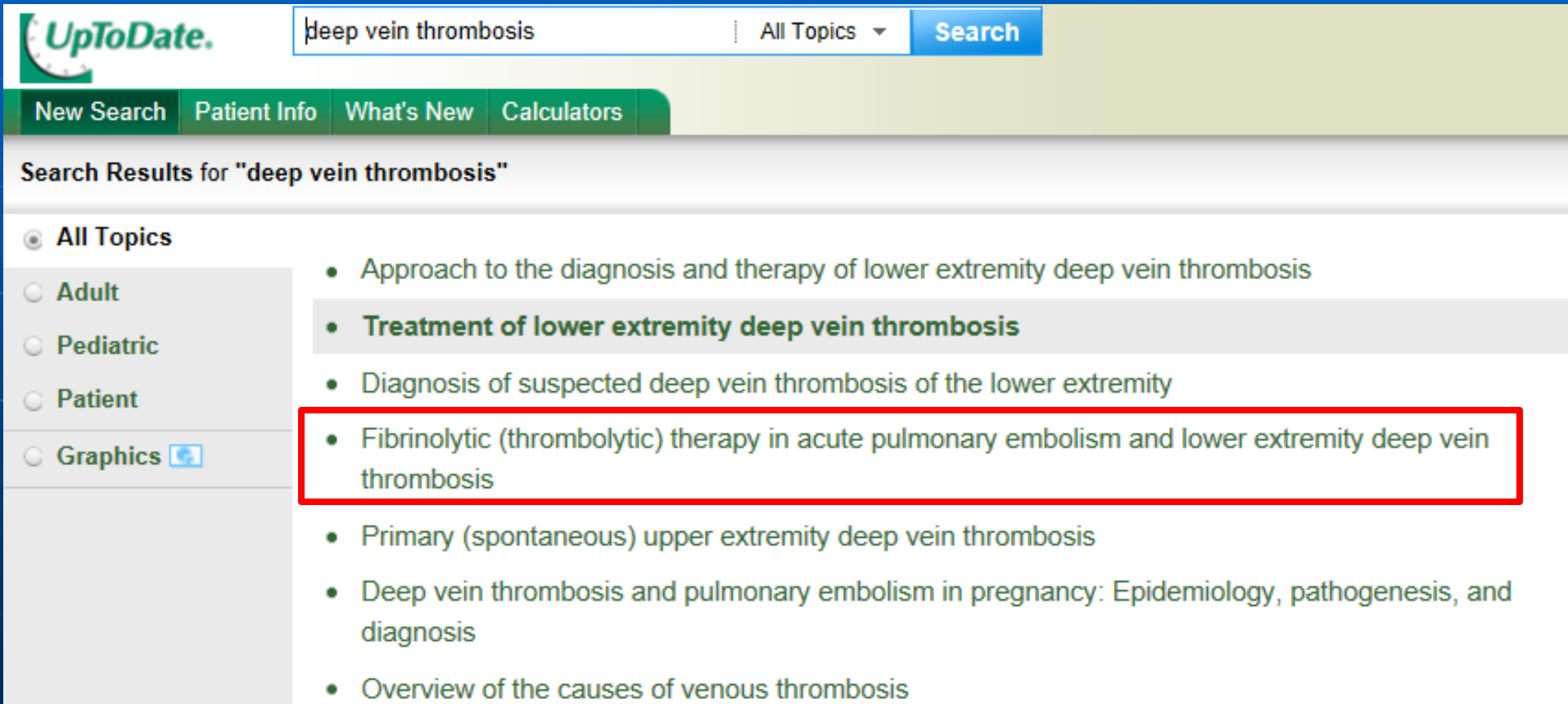
Treatment of lower extremity DVT

-- Recommendations



- **Anticoagulation failure and massive iliofemoral thrombosis:**
 - increasing dosage
 - switching to alternative anticoagulant
 - IVC filter
 - **vascular interventions:** thrombolytic therapy or thrombectomy
- The selected intervention(s) will depend upon **available expertise.**

■ Key words: **deep vein thrombosis**

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UpToDate.

[New Search](#) [Patient Info](#) [What's New](#) [Calculators](#)

Search Results for "deep vein thrombosis"

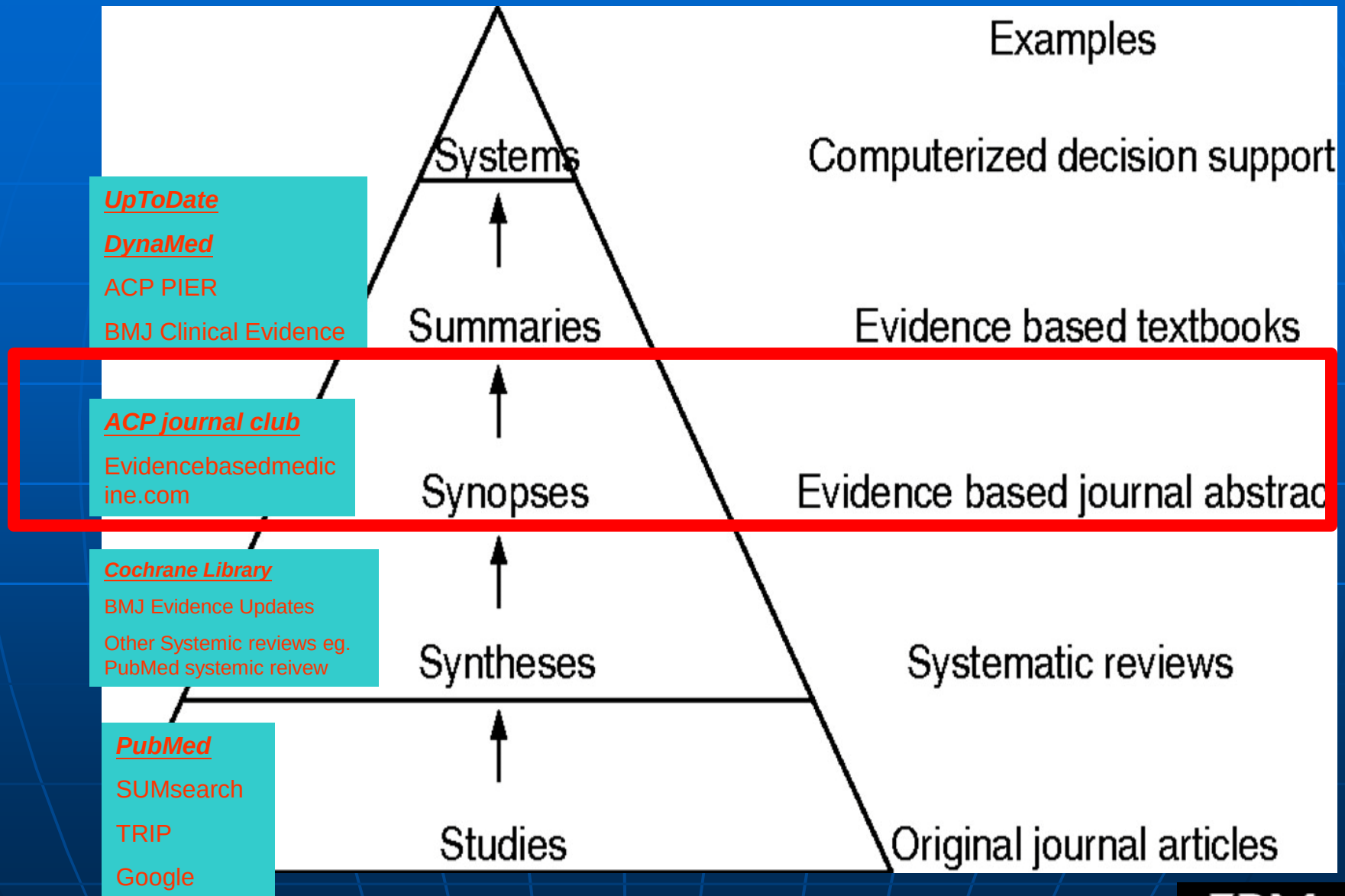
- ☒ All Topics
- ☐ Adult
- ☐ Pediatric
- ☐ Patient
- ☐ Graphics 

- Approach to the diagnosis and therapy of lower extremity deep vein thrombosis
- **Treatment of lower extremity deep vein thrombosis**
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Thrombolysis of DVT-- Recommendations

- **Thrombolytic therapy + anticoagulation** > anticoagulation (Grade **2B**):
 - **massive iliofemoral** or proximal femoral DVT with a high risk of limb gangrene
 - symptomatic for **14 or fewer days**
 - do **not** have an **increased risk of bleeding**
 - accept the risk of bleeding to potentially obtain relief of acute symptoms and reduced post-thrombotic morbidity
- **Catheter-directed** thrombolysis > systemic thrombolysis (Grade **2C**).

Search strategy: 5S model



- Key word: **end-stage renal disease**,
deep vein thrombosis

- 查無相關文獻

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end-stage renal disease AND deep

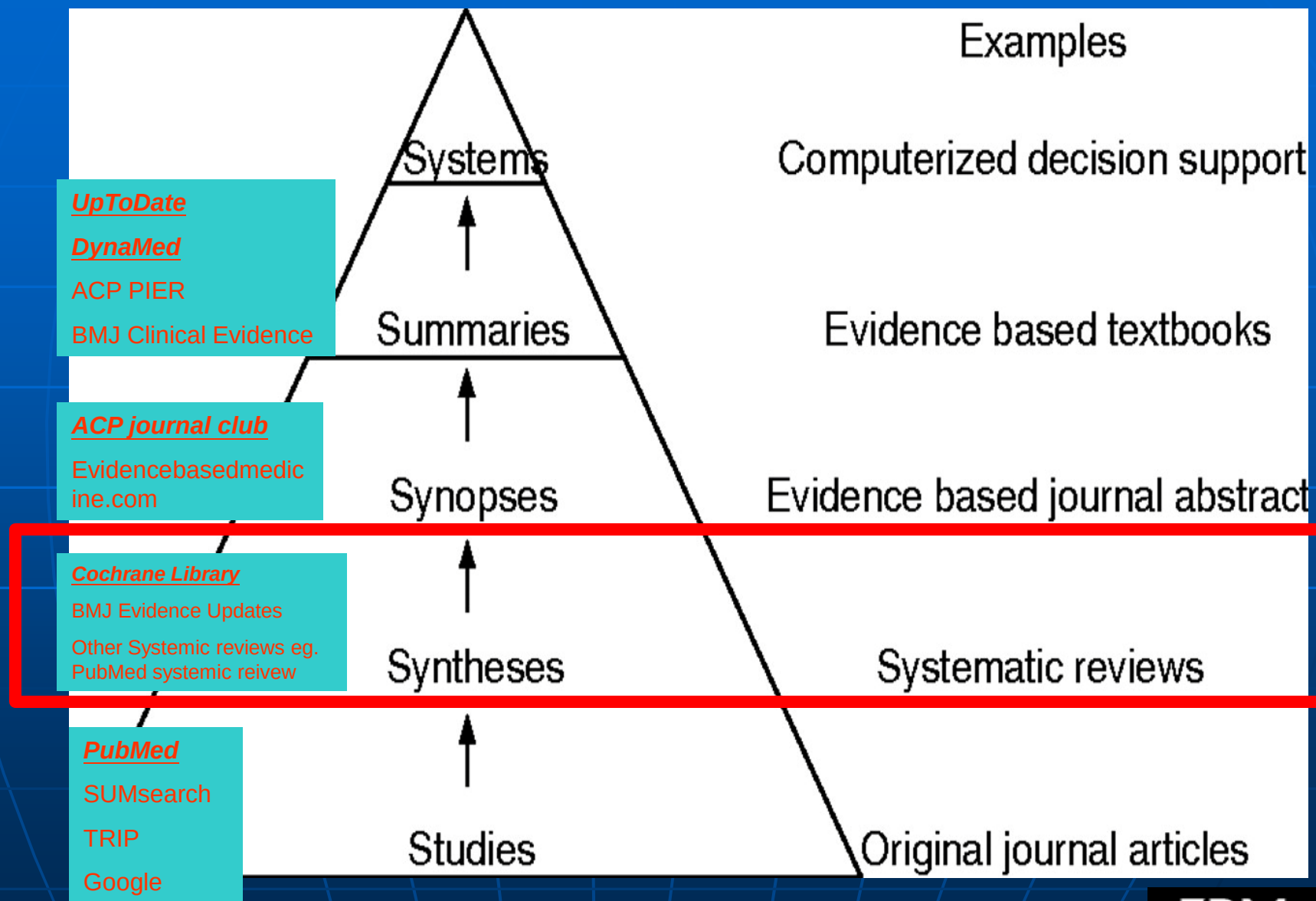
[Search Help](#)

Your search - end-stage renal disease AND deep vein thrombosis - did not match any documents.

Suggestions:

- Make sure all words are spelled correctly.
- Try different keywords.
- Try more general keywords.

Search strategy: 5S model



- Key word:
 - deep vein thrombosis, **end stage renal disease**
 - 無相關的Systemic reviews

Search	Search Manager	Medical Terms (MeSH)	Bro
Abstract, Keywords v	deep vein thrombosis and end stage renal disease		Go
Limits	View search tips (Word variations have been searched)		Add to Search
Cochrane Database of Systematic Reviews : Issue 1 of 12, January 2013			
Reviews (0)	There are 0 results from 0 records for your search on ' deep vein thrombosis and end stage renal disease keywords '		

- Key word:
 - deep vein thrombosis

Search Manager Medical Terms (MeSH)

▼ deep vein thrombosis

View search tips (Word variations have been searched)

Cochrane Database of Systematic Reviews : Issue 1 of 12, January 2013

There are **45** results from **7694** records for your search on '**deep vein thrombosis in title abstracts**'

Pages **1 - 25** | 26 - 45

Select all | Export all | Export selected

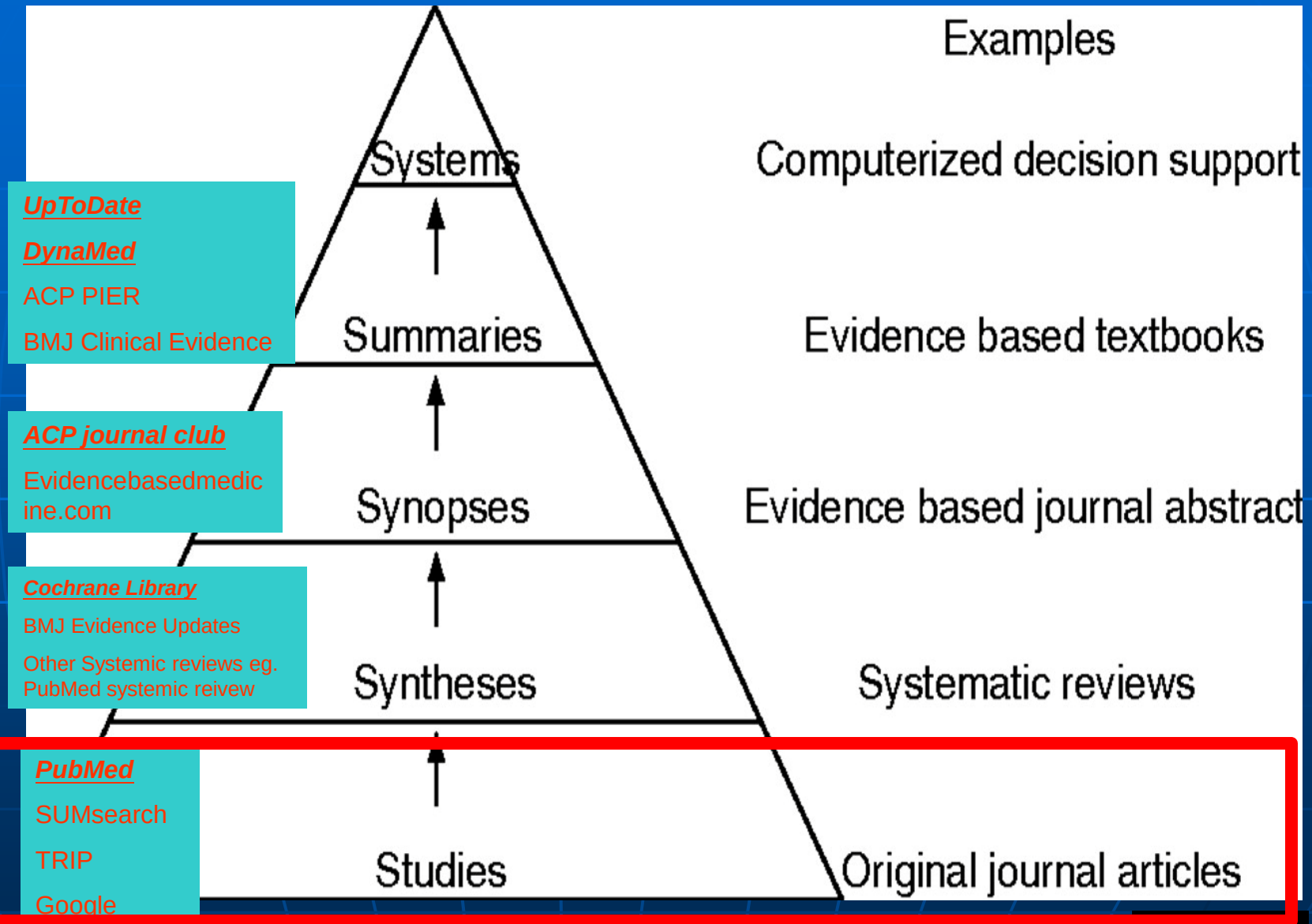
☐ Thrombolysis for acute **deep vein thrombosis**
Lorna Watson and Matthew P Armon
July 2004

☐ Anticoagulant therapy for **deep vein thrombosis** (DVT) in pregnancy
Che Anuar Che Yaakob , Abdulla Abu Dzarr , Ahmad Amir Ismail , Nik Ahmad Zuky Nik Lah and

Cochrane

- Cochrane review comparing **catheter-directed thrombolysis (CDT)** for acute DVT with **traditional AC** in nearly 700 patients revealed the following:
 - Significantly improved **early clot lysis with a relative risk reduction of 4.14**; 95% CI: 1.22–14.01 to late clot lysis (RR: 2.71; 95% CI: 1.84–3.99).
 - **Reduced PTS** (RR: 0.66; 95% CI: 0.47–0.94).

Search strategy: 5S model



**Title: Catheter-Directed Thrombolysis with
Percutaneous Rheolytic Thrombectomy
Versus Thrombolysis Alone in Upper and
Lower Extremity Deep Vein Thrombosis**

**Author: Hyun S. Kim et al; Cardiovasc Intervent
Radiol (2006) 29:1003–1007**

Purpose

- To compare the efficacy of catheter-directed thrombolysis (CDT) alone versus CDT with rheolytic percutaneous mechanical thrombectomy (PMT) for upper and lower extremity deep vein thrombosis (DVT).

Methods

- A **retrospective cohort** of consecutive patients with **acute iliofemoral** or brachiosubclavian DVT (symptom duration less than 14 days) treated with **urokinase CDT** was identified, and a **chart review** was conducted.
 - **1997~2003**
- In patients treated with urokinase CDT alone or combined CDT and rheolytic PMT:
 - Demographic characteristics
 - **treatment duration**
 - **total lytic dose**
 - clot lysis rates
 - **complications**

Thrombolytic technique

- All patients were treated initially with a continuous intravenous infusion of unfractionated heparin,
 - adjusted to maintain aPTT ratio between 2 and 2.5 times control.
- **Contraindications** to percutaneous thrombolysis:
 - a recent stroke
 - surgery or serious gastrointestinal bleeding
 - a primary or metastatic central nervous system malignancy
 - coagulopathy.

Thrombolytic technique

- **CDT with urokinase** in 40 limbs from 36 patients
 - 14 men, 22 women; mean age 45.0 years $\pm$ 16.3.
- Rheolytic PMT using a **6 Fr Angiojet** rheolytic thrombectomy catheter **followed by urokinase CDT** in 27 limbs from 21 patients
 - 11 men, 10 women; mean age 43.1 years $\pm$ 13.8.

Demographic characteristics

Table 1. Patient demographics

	CDT alone (<i>n</i> = 40)	CDT and PMT (<i>n</i> = 27)	<i>p</i> value
Mean age (years)	45.0 ± 16.3	43.1 ± 13.8	0.656
Gender			
Male	39%	52%	0.322
Female	61%	48%	0.322
Risk factors			
Active cancer	28%	59%	0.009
Thrombophilia	18%	7%	0.238
Previous DVT/PE	23%	26%	0.749
Anatomic risk factor	18%	4%	0.087
Immobilization	5%	11%	0.352
Idiopathic	35%	26%	0.430
Upper extremity limbs treated	35%	30%	0.646
Lower extremity limbs treated	65%	70%	0.646

Thrombophilia, documented biochemical hypercoagulable disorder; Anatomic risk factor, May-Thurner syndrome in lower extremities or thoracic outlet syndrome/effort induced thrombosis in upper extremities; Immobilization, immobilization for longer than 4 weeks prior to onset of DVT; Idiopathic, no identifiable DVT risk factor

Results--Clinical efficacy

Table 2. Clinical efficacy

	CDT alone (n = 40)	CDT and PMT (n = 27)	<i>p</i> value
Treatment duration (hr)	48.0 ± 27.1	26.3 ± 16.6	0.0004
Urokinase doses (million units)	5.6 ± 5.3	2.7 ± 1.8	0.008
Clot reduction			
Grade III Complete lysis	73%	82%	0.395
Grade II 50-99% clot lysis	15%	19%	0.704
Grade I <50%	13%	0	0.056
Stent placements	18%	15%	0.772
Major bleeding	5%	4%	0.803
Minor bleeding	3%	0	0.407
Pulmonary embolism	3%	4%	0.779

Results

- In 67 limbs treated, **urokinase CDT with PMT** was associated with:
 - **45% reduction in treatment duration**
 - $(48.0\% - 26.3\%) / 48\% = 45\%$
 - **52% reduction in total lytic dose;**
 - $(5.6 - 2.7) / 5.6 = 52\%$
 - compared with urokinase CDT alone, with a similar safety and efficacy.

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Conclusion

- Percutaneous CDT with rheolytic PMT is as effective as CDT alone for acute proximal extremity DVT but requires significantly shorter treatment duration and lower lytic doses.
 - Randomized studies to confirm the benefits of pharmacomechanical thrombolysis in the treatment of acute proximal extremity DVT are warranted.

對找到的文章
進行CRITICAL APPRAISAL

Level of evidence

Level	與[治療 / 預防 / 病因 / 危害]有關的文獻
1a	用多篇RCT所做成的綜合性分析(SR of RCTs)
1b	單篇RCT(有較窄的信賴區間)
1c	All or none
2a	用多篇世代研究所做成的綜合性分析
2b	單篇cohort及低品質的RCT
2c	Outcome research / ecological studies
3a	SR of case-control studies
3b	Individual case-control studies
4	Case-series(poor quality :cohort / case-control studies)
5	沒有經過完整評讀醫學文獻的專家意見

Validity

- Validity (closeness to the truth):
 - chance (**p value**, power, confident interval)
 - bias (selection, measurement, recall bias)

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Impact (size of the effect)

	Grade III clot reduction	Major bleeding	
CDT+PMT	82%	4%	EER(Experimental event rate)
CDT	73%	5%	CER(Control event rate)

RRR / RRI (Relative risk reduction / increase)	ARR / ARI (Absolute risk reduction / increase)	NNT / NNH (Number needed to treat / harm)
$(\text{CER} - \text{EER}) / \text{CER}$; $\text{EER} - \text{CER} / \text{CER}$	$\text{CER} - \text{EER}$; $\text{EER} - \text{CER}$	$1 / \text{ARR}$; $1 / \text{ARI}$
RRR = $(82\% - 73\%) / 73\% = 12\%$ RRI = 20%	ARR = 9% ARI = 1%	NNT = 11 NNH = 100 LHH = 9.09

AAMPICOT for therapy

Item	AAMPICOT for therapy	Comments
Answer	此文獻有沒有回答我的問題	有
Authors	作者群是這領域的專家嗎？	是 (Radiologist in Johns Hopkins)
Method	本文獻研究設計是屬於那一類	Retrospective cohort
Population	取樣是否為隨機取樣？	否
Intervention	給予實驗組的處置是否描述清楚，並且是臨床可行的？	是
Comparison	給予對照組的處置是否描述清楚，並且是臨床可行的？各種可能比較皆有了？	部分是

AAMPICOT for therapy

Outcome	測量了那些結果？是否用客觀的方式測量？	Treatment duration, urokinase dose, clot reduction, adverse event
	這些結果是否有統計學上的重要性？	部分有
	這些結果是否有臨床上的重要性？	是
	是否呈現結果的「數值」，「p值」，「信賴區間」，「檢力」？	有呈現P值
Time	測量結果的時間點是否合宜？	是
	追蹤時間是否夠長？	是
	文獻發表時間？	2006

Apply

結合醫學倫理方法
將study的結果應用在病人身上

醫療現況(EBM+臨床專業)

50歲女性，ESRD with HD, massive iliofemoral DVT poor response to AC

病人意願

同意接受CDT並承擔出血風險

生活品質

CDT能夠減少PTS，改善生活品質

社會脈絡

此病人因經濟問題無法選擇PMT治療

Thanks for your attention!