Vai trò của can thiệp nội mạch điều trị HKTMSCD trong kỷ nguyên thuốc chống đông

Ths. BS. Lê Tuấn Minh

Phòng C2 – Viện Tim Mạch Việt Nam

TỔNG QUAN

Thuyên tắc huyết khối tĩnh mạch (VTE) là **1 trong 3** nguyên nhân tim mạch phổ biến và gây tử vong hàng đầu (sau Nhồi máu cơ tim và Đột quỵ não)

Number of people affected per year

900,000

The precise number of people affected by deep vein thrombosis (DVT) or pulmonary embolism (PE) is unknown, although as many as 900,000 people could be affected each year in the United States.

Sudden death

25%

Sudden death is the first symptom in about one-quarter (25%) of people who have a PE.

Deaths per year

60,000 - 100,000

Estimates suggest that 60,000-100,000 Americans die of DVT/PE (also called venous thromboembolism, or VTE)

10% – 30% of people will die within one month of diagnosis.

Long-term complications

33%

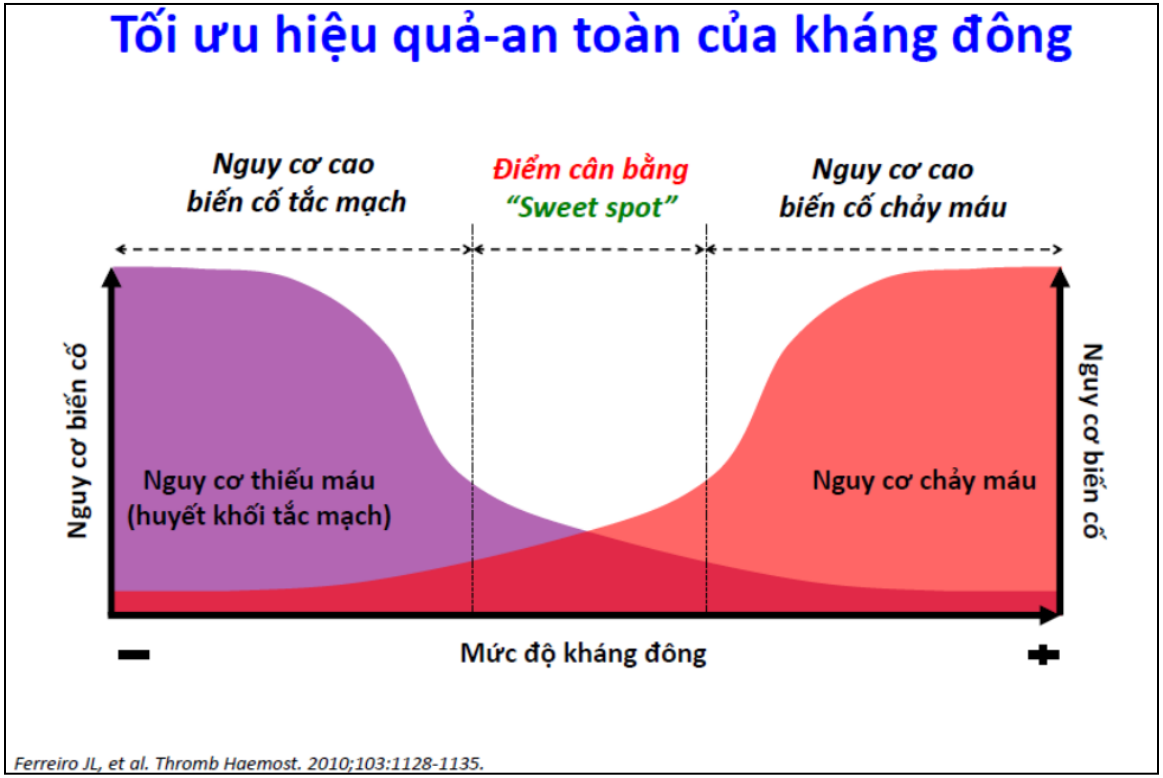
Among people who have had a DVT, one third to one half will have long-term complications (post-thrombotic syndrome) such as swelling, pain, discoloration, and scaling in the affected limb.

One-third (about 33%) of people with DVT/PE will have a recurrence within 10 years.

Data and Statistics on Venous Thromboembolism | CDC

Các thuốc chống đông: Nền tảng trong điều trị VTE

- Dự phòng huyết khối tiến triển và lan rộng trong giai đoạn cấp
- Dự phòng tái phát trong giai đoạn mở rộng

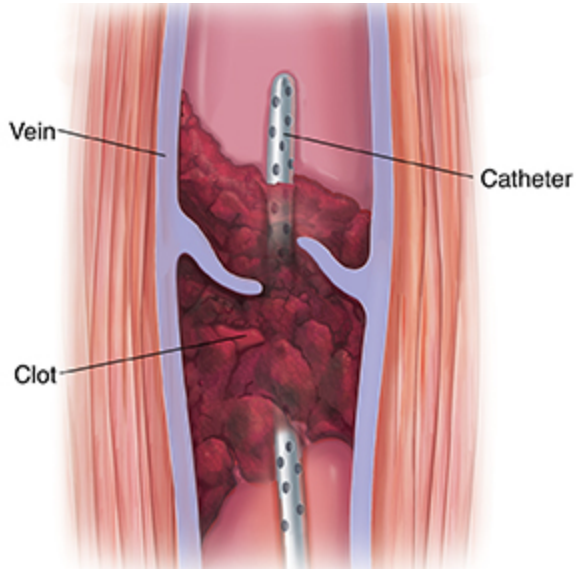


Vai trò của can thiệp nội mạch?

MỘT SỐ VAI TRÒ CỦA CAN THIỆP

Tại sao can thiệp nội mạch?

- Giảm nhanh triệu chứng
- Giảm TT ĐM phổi
- Bảo tồn chức năng van
- Giảm nguy cơ HC hậu HK
- Xử trí nguyên nhân



Viêm tắc tĩnh mạch xanh (Phlegmasia Cerulea Dolens)

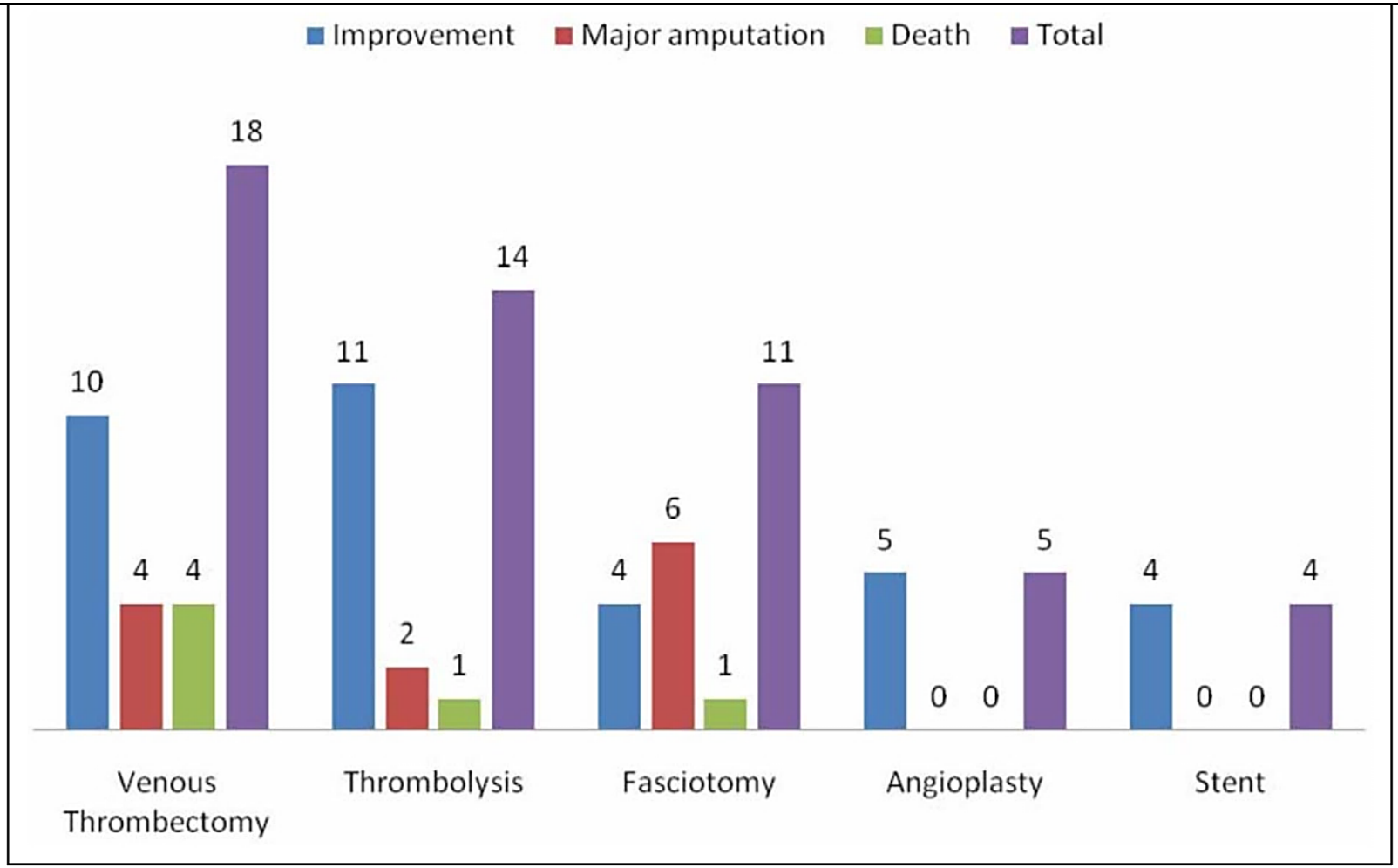
- Là biến chứng **hiếm gặp** của DVT
- Được mô tả trong y văn từ năm **1593** (BS. Fabricus Hildanus)
- Tỷ lệ tử vong và cắt cụt chi lần lượt từ **25 - 40%** và **20 - 50%**

VASC ENDOVASCULAR SURG 2011 45: 5

Radiology. 2015 Jul;276(1):31-53

Trends in Management of Phlegmasia Cerulea Dolens

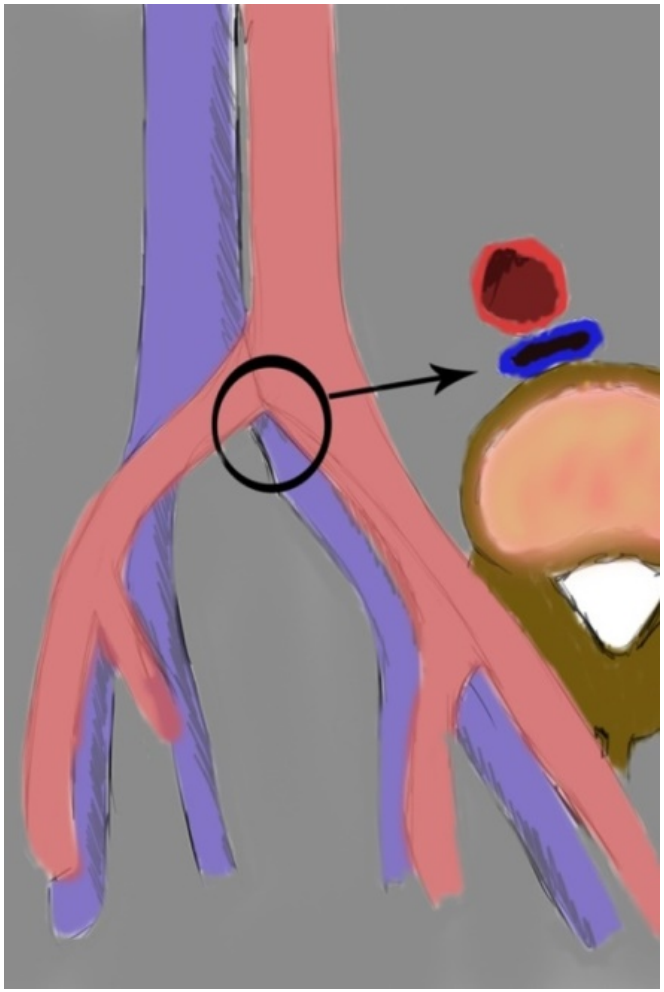
Khamin Chinsakchai, MD[1], Kaj ten Duis, MD[1], Frans L. Moll, MD, PhD[1], and Gert J. de Borst, MD, PhD[1]



VASC ENDOVASCULAR SURG 2011 45: 5

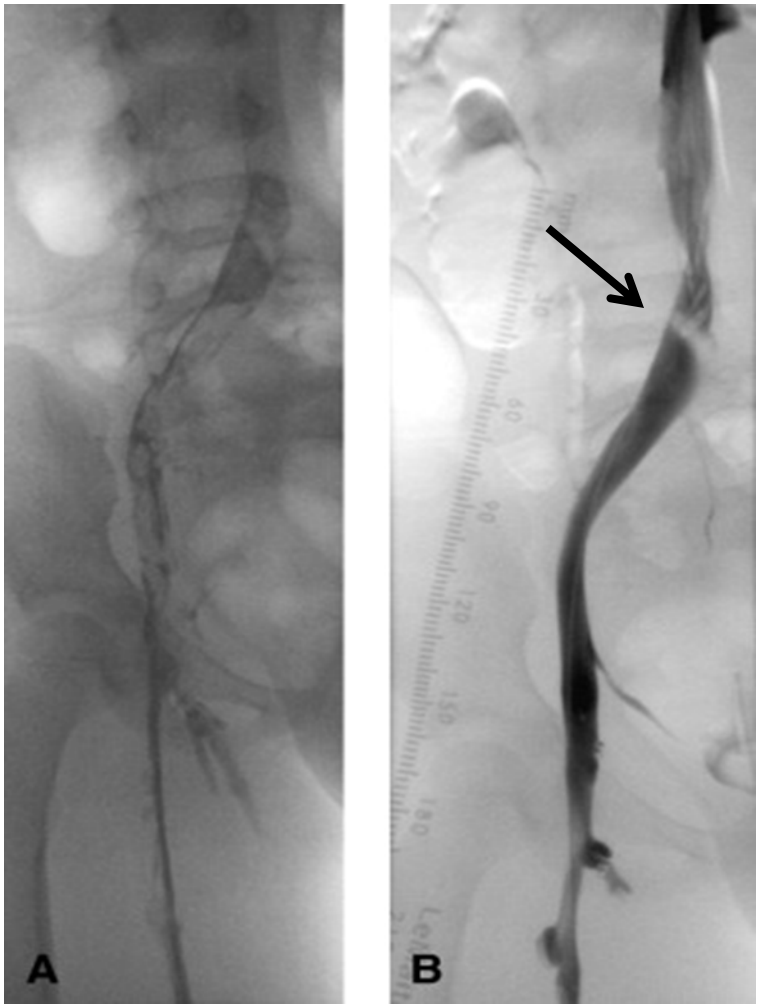
Hội chứng May-Thurner (MTS)

- Hay còn gọi là **Hội chứng Cockett hoặc HC chèn ép tĩnh mạch chậu**
- Tỷ lệ **2-5%** DVT
- Phần lớn không gây triệu chứng
- Đe dọa tính mạng khi liên quan đến **vỡ tĩnh mạch chậu** hoặc huyết khối **thuyên tắc phổi**



J Vasc Surg. 2010;52(5):1278–82.

Ca lâm sàng



AngioJet + CDT + Ballon

Sau 15 ngày: AngioJet + Stent

J Vasc Surg. 2011, 53(1), 212-215

Outcomes of endovascular intervention for May-Thurner syndrome

Eric S. Hager, MD,[a] Theodore Yuo, MD,[a] Robert Tahara, MD,[b] Ellen Dillavou, MD,[a] Georges Al-Khoury, MD,[a] Luke Marone, MD,[a] Michel Makaroun, MD,[a] and Rabih A. Chaer, MD,[a]
Pittsburgh and Bradford, Pa

Background: Endovascular interventions for May-Thurner syndrome (MTS) have become first-line therapy, often performed in a young patient population despite the lack of robust supportive data. This article reports on long-term outcomes from a large series of patients treated in the setting of de novo or postthrombotic presentation.

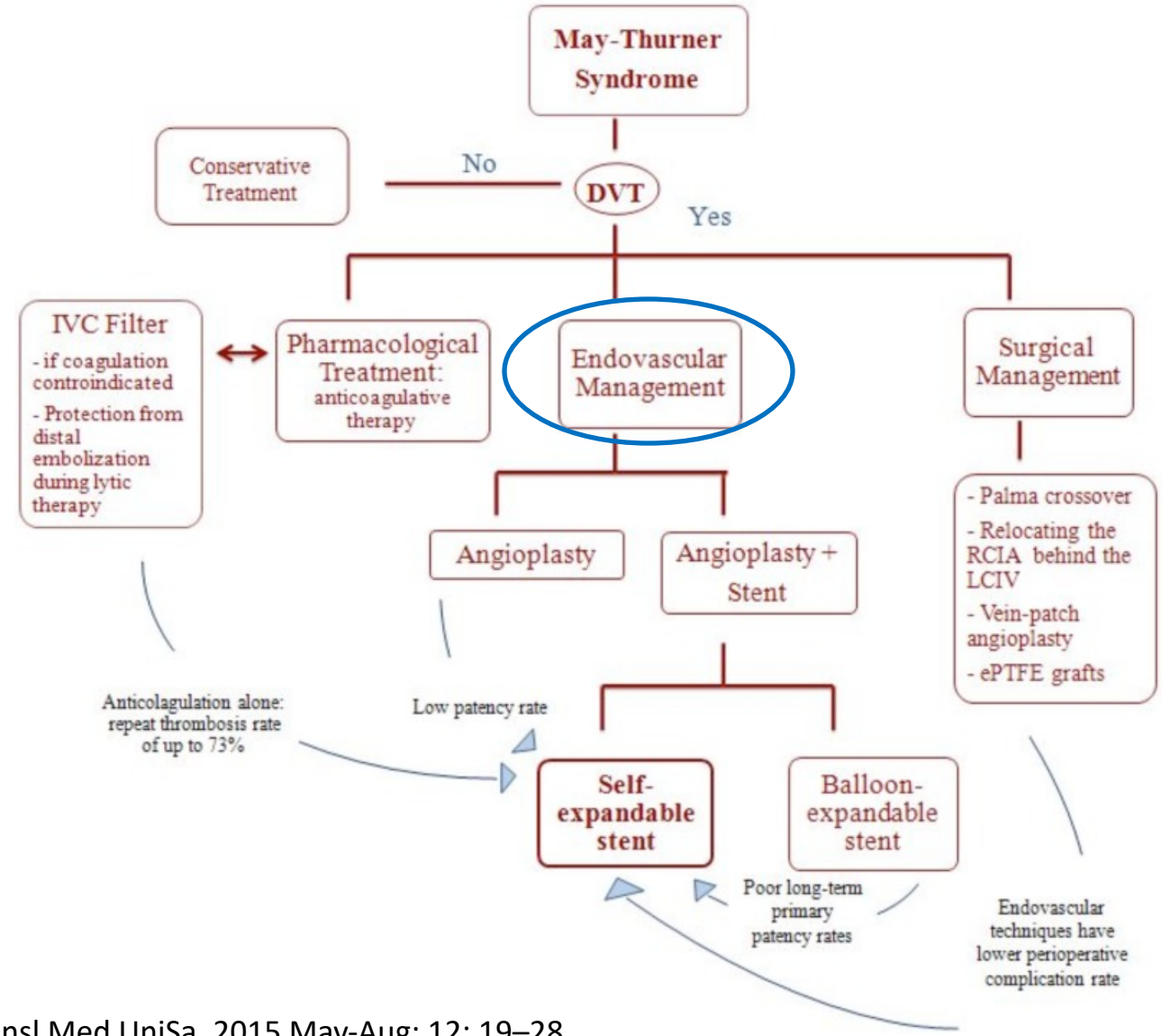
Methods: A retrospective review of MTS patients treated between 2006 and 2010 was conducted at two institutions. Patients who presented with acute iliofemoral deep vein thrombosis (DVT) were treated with either catheter-directed thrombolysis (CDT) and/or pharmacomechanical thrombolysis and identified as having a venous stenosis by venogram or intravascular ultrasound (IVUS). Patients who presented with chronic venous insufficiency symptoms or recalcitrant ulceration but no DVT and evidence of MTS on duplex ultrasound, magnetic resonance venography, or computerized tomography venography were evaluated by venography. IVUS was selectively utilized. Stenting of the iliocaval junction was performed in all patients with a >50% diameter stenosis by IVUS or venogram.

Results: Seventy patients with MTS underwent 77 lower extremity interventions. They were divided into two groups: postthrombotic (group 1) and de novo presentation of chronic swelling/pain or ulceration but no DVT (group 2). There were 56 extremities in group 1 and 21 extremities in group 2. Both groups were comparable in terms of gender distribution and comorbidities, but hypercoagulable state was more common in group 1 ($P = .014$), and average CEAP and Villalta scores on presentation were higher in group 2 ($P < .001$). There were left-sided symptoms in 40 (78%) patients in group 1 and 15 (79%) in group 2 ($P = 1.00$). Female patients were more likely to have left-sided symptoms compared with male patients (odds ratio, 4.88; 95% confidence interval, 1.49-15.89; $P = .014$). The average stent size was significantly different among the groups ($P < .027$), with different types used in each group. There was one patient in group 1 who had significant periprocedural bleeding (1 unit transfused) during the CDT portion of the procedure. Mean follow up was 29.7 months in group 1 (range, 18.4-58.3 months) and 22.4 months in group 2 (range, 17.1-42 months). Complete or partial symptom relief was reported for 52 (92.9%) extremities in group 1 and 20 (95.2%) extremities in group 2 ($P = 1.00$). The overall primary patency of group 1 at 36 months by life-table analysis was 91% with a secondary patency of 95%. The primary and secondary patency for group 2 was 91% at 36 months.

Conclusions: Stenting of MTS has proven to be safe, efficacious, and durable for up to 36 months in both the postthrombotic patient as well as those treated for edema alone. (J Vasc Surg: Venous and Lym Dis 2013;1:270-5.)

J Vasc Surg Venous Lymphat Disord. 2013 Jul;1(3):270-5

Chiến lược điều trị MTS



Transl Med UniSa. 2015 May-Aug; 12: 19–28.

Hội chứng hậu huyết khối (PTS)

- Là những triệu chứng của **bệnh tĩnh mạch mạn tính** xuất hiện **thứ phát** sau HKTMSCD.
- Mặc dù điều trị chống đông tối ưu, có tới **20 - 40% bệnh nhân DVT** phát triển PTS các mức độ trong **2 năm**[1]
- **Gánh nặng điều trị:**
  - Canada: $4527
  - Mỹ: ≈ $7000
  - **Điểm QoL thấp hơn** các bệnh mạn tính khác như viêm xương khớp, đau thắt ngực và bệnh phổi mạn[2]

1. Br J Haematol 2006; **134**: 357– 65.2. *J Thromb Haemost*. 2008;6:1105–1112

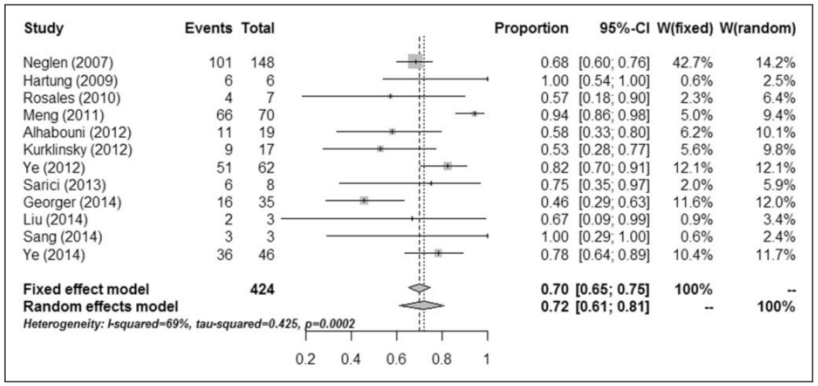
Stenting for chronic obstructive venous disease: A current comprehensive meta-analysis and systematic review

Wang Wen-da, Zhao Yu and Chen Yue-xin

Table 8. Proportion meta-analysis plot of patency rate.

Follow-up time		Patency rate (rate with 95% CI) PTS and NIVL	PTS	*P*
12 Months	PP	91.4% [87.8%, 94.0%]	90.1% [72.9%, 97.3%]	0.5285
	aPP	95.0% [89.4%, 97.7%]	92.8% [88.6%, 95.5%]	0.6108
	SP	97.8% [95.6%, 98.9%]	97.3% [81.6%, 99.7%]	0.2239
36 Months	PP	77.1% [69.1%, 83.5%]	82.3% [62.5%, 92.8%]	0.1725
	aPP	92.3% [86.9%, 95.6%]	86.9% [78.4%, 92.4%]	0.3152
	SP	94.3% [89.4%, 97.0%]	88.8% [80.4%, 93.9%]	0.2513

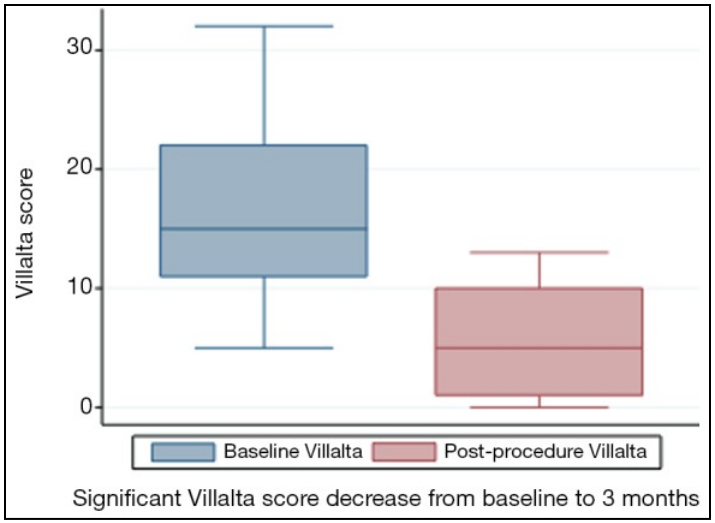
Note: PP: primary patency; aPP: assisted-primary patency; SP: secondary patency; PTS: postthrombotic syndrome; NIVL: non-thrombotic iliac vein lesion; CI: confidence interval.



- Nhóm stent giảm điểm CEAP có ý nghĩa
- Tỷ lệ liền loét ở nhóm PTS là 70,3%
- Giữ thông mạch đạt 90,1% sau 12 tháng và 82,3% sau 36 tháng

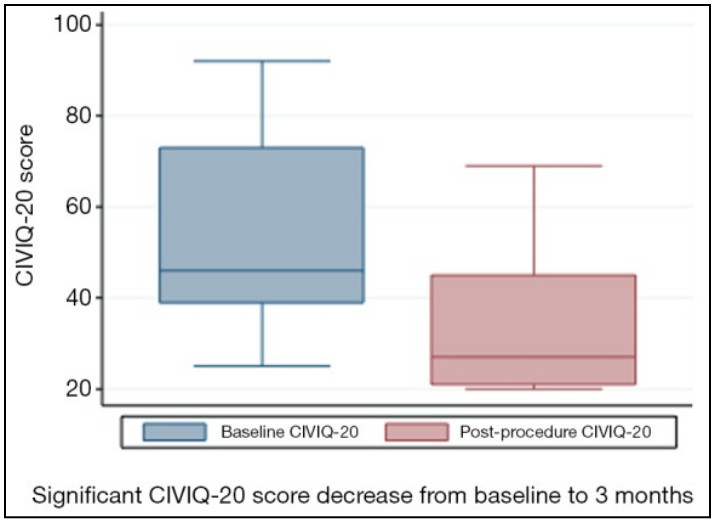
Phlebology 2016;31:376-89

Cải thiện chất lượng cuộc sống



Significant Villalta score decrease from baseline to 3 months

≠



Significant CIVIQ-20 score decrease from baseline to 3 months

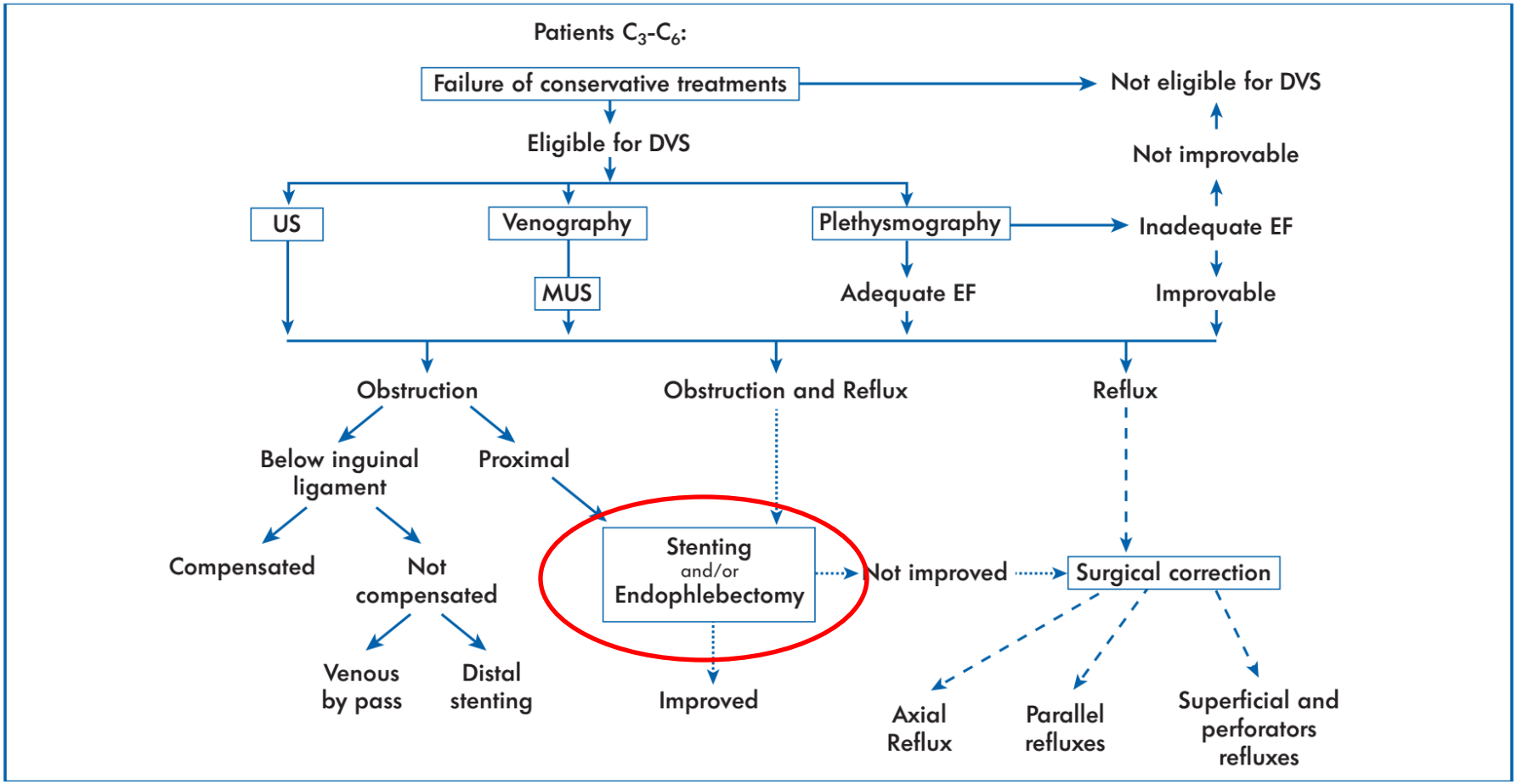
CIVIQ category	Stented group	Non-stented group	*p*
Leg pain (0–5) Q1–4	9.38 ± 4.37	9.70 ± 4.17	0.74
Physical activity (0–5) Q5–7, 9	9.84 ± 5.05	10.93 ± 5.41	0.36
Psychological activity (0–5) Q12–20	18.69 ± 9.03	20.07 ± 9.15	0.51
Social activity (0–5) Q8, 10, 11	7.69 ± 4.09	7.63 ± 4.23	0.95

CIVIQ: Chronic Venous Insufficiency Quality of Life Questionnaire.

Quant Imaging Med Surg. 2016 Aug; 6(4): 342–352

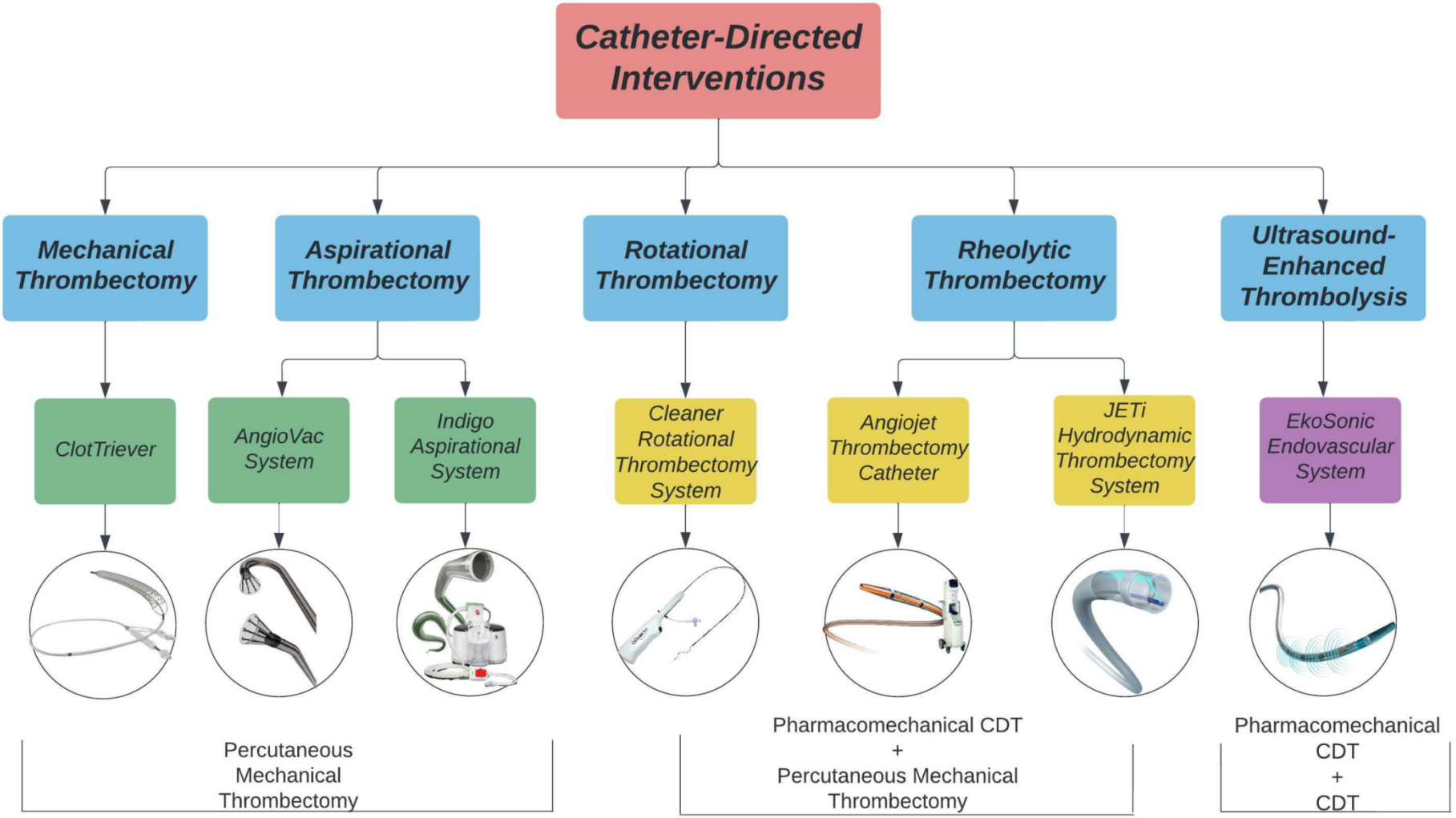
JRSM Cardiovascular Disease. 2019. Volume 8: 1–5

Chiến lược điều trị PTS



Maleti O, Lugli M, Perrin M. Syndrome post-thrombotique. EMC – Cardiologie 2013;8:1-12

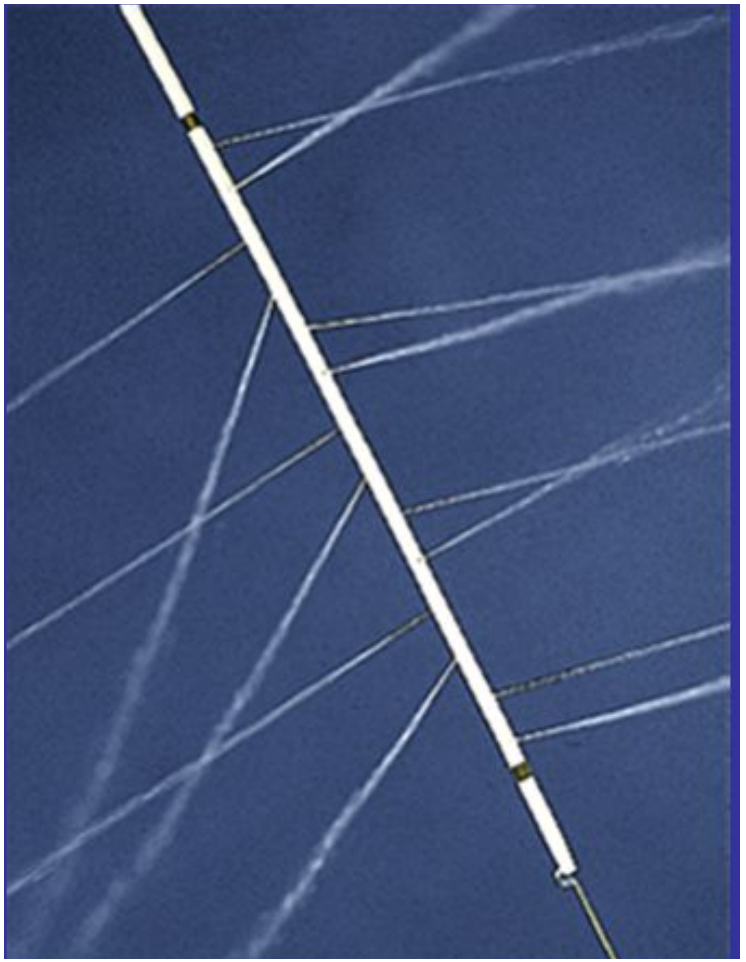
CÁC PHƯƠNG PHÁP CAN THIỆP



Life **2022**, *12*(12), 1984

Tiêu sợi huyết trực tiếp

- Tiêu sợi huyết bơm trực tiếp qua hướng dẫn của cathteter (catheter directed throbolysis – CDT)
- **Catheter nhiều lỗ bên** (multi side holes): Fountain (Merit), Unifuse Infusion (AngioDynamics)
- **Thuốc tiêu sợi huyết**: urokinase, tPA, rtPA

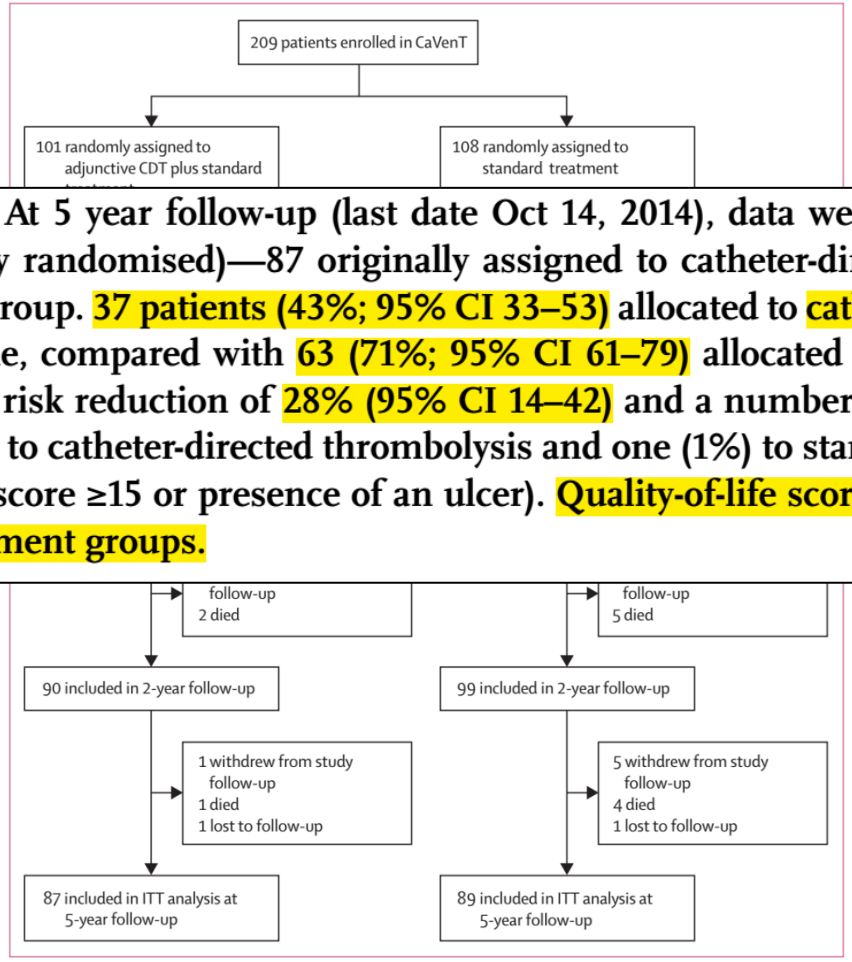


Tiêu sợi huyết hóa – cơ học

- *Pharmacomechanical techniques* – PMT: phối hợp giữa tiêu sợi huyết và biện pháp làm vỡ HK
- **EKOS** : CDT có sóng siêu âm hỗ trợ
- **AngioJet**: sử dụng nguyên lý Bernoulli để phá vỡ và hút huyết khối

Post-thrombotic syndrome after catheter-directed thrombolysis for deep vein thrombosis (CaVenT): 5-year follow-up results of an open-label, randomised controlled trial

*Ylva Haig, Tone Enden, Ole Grøtta, Nils-Einar Kløw, Carl-Erik Slagsvold, Waleed Ghanima, Leiv Sandvik, Geir Hafsahl, Pål Andre Holme, Lars Olaf Holmen, Anne Mette Njaaastad, Gunnar Sandbæk, Per Morten Sandset, on behalf of the CaVenT Study Group**



Findings At 5 year follow-up (last date Oct 14, 2014), data were available for 176 patients (84% of the 209 patients originally randomised)—87 originally assigned to catheter-directed thrombolysis and 89 originally assigned to the control group. 37 patients (43%; 95% CI 33–53) allocated to catheter-directed thrombolysis developed post-thrombotic syndrome, compared with 63 (71%; 95% CI 61–79) allocated to the control group (p<0·0001), corresponding to an absolute risk reduction of 28% (95% CI 14–42) and a number needed to treat of 4 (95% CI 2–7). Four (5%) patients assigned to catheter-directed thrombolysis and one (1%) to standard treatment had severe post-thrombotic syndrome (Villalta score ≥15 or presence of an ulcer). Quality-of-life scores with either assessment scale did not differ between the treatment groups.

	Adjunctive catheter-directed thrombolysis group (n=87)	Standard treatment only group (n=89)
Baseline		
Age (years)	58 (41–66)	53 (37–63)
Three risk factors for venous thrombosis	10 (11%)	13 (15%)
Thrombophilia	33 (38%)	30 (34%)
Combined thrombophilia	4 (5%)	2 (2%)
At 5 year visit		
Daily wear of compression stockings, classII	49 (56%)	52 (58%)
Recurrent venous thromboembolism	13 (15%)	21 (24%)
Diagnosed with cancer	5 (6%)	7 (8%)

Data are median (IQR), n (%), or mean (SD). *Based on routine diagnostic imaging before recruitment (missing n=9).

***Table 1*: Demographic and clinical characteristics**

Cochrane Library

Cochrane Database of Systematic Reviews

Thrombolytic strategies versus standard anticoagulation for acute deep vein thrombosis of the lower limb (Review)

Broderick C, Watson L, Armon MP

- 19 RCTs với 1943 bệnh nhân DVT (TM chậu đùi ± khoeo)
- **Chảy máu cao hơn** ở nhóm tiêu sợi huyết (6,7% với 2,2%)
- 6 nghiên cứu (N=1393): **giảm nhẹ PTS** sau 6 tháng ở nhóm tiêu sợi huyết (50% với 53%)
- 2 nghiên cứu (N=211) theo dõi hơn 5 năm cho kết quả tương tự
- **Tiêu sợi huyết không chọn lọc tương đương CDT**

Cochrane Database of Systematic Reviews 2021, Issue 1. Art. No.: CD002783

NGHIÊN CỨU ATTRACT

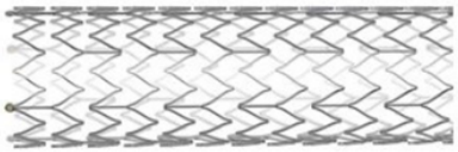
ATTRACT 2017

- RCT (N=692) chia 2 nhóm: NOACs vs NOACs + CDT
- Tuổi trung bình 53
- HK tắc TM đùi ± TM chậu
- Theo dõi 6 tháng – 2 năm
- Kết luận: **CDT/PMT không những không làm giảm triệu chứng hậu HK mà còn làm tăng nguy cơ chảy máu**

N Engl J Med 2017; 377:2240-2252

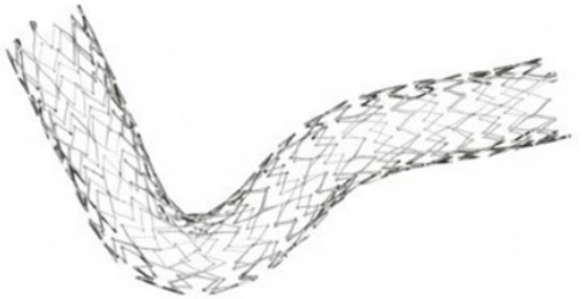
Stent tĩnh mạch

VENOVO BARD



ZILVER VENA COOK MEDICAL

VICI BOSTON SCIENTIFIC



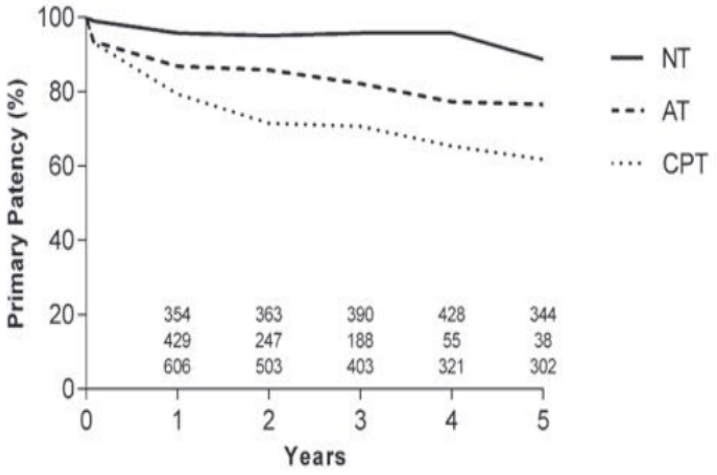
ABRE MEDTRONIC

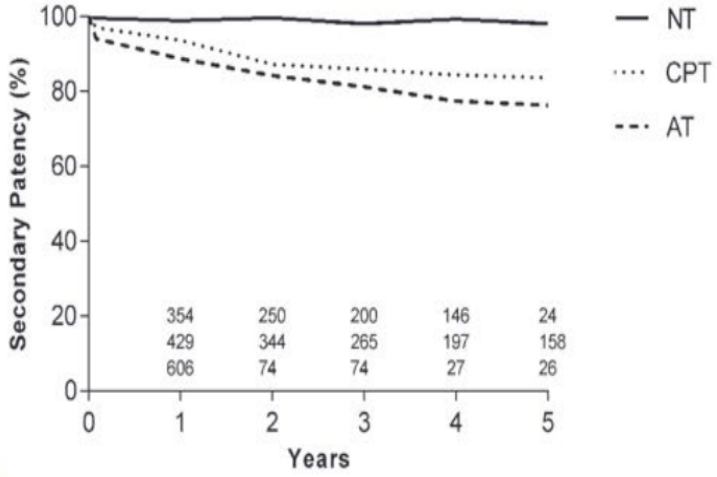
	Vein	Artery
Compliance	High	Low
Elasticity	High	Low
Pressure	Low	High
Valves to prevent reflux	Present	Absent
Important changes of the cross-sectional area because of postural changes	Present	Absent
Lesion	Post-thrombotic fibrosis	Atherosclerotic lesion

Meta-Analysis: Venous Stenting

- Non-thrombotic (NT)
  - Iliac vein compression
  - May Thurner
- Acute Thrombosis (AT)
- Chronic Post Thrombotic (CPT)

- Technical success 94-96%
- Complications
  - 0.3% to 1.1% major bleeding
  - 0.2% to 0.9% for pulmonary embolism
  - 0.1% to 0.7% for periprocedural mortality

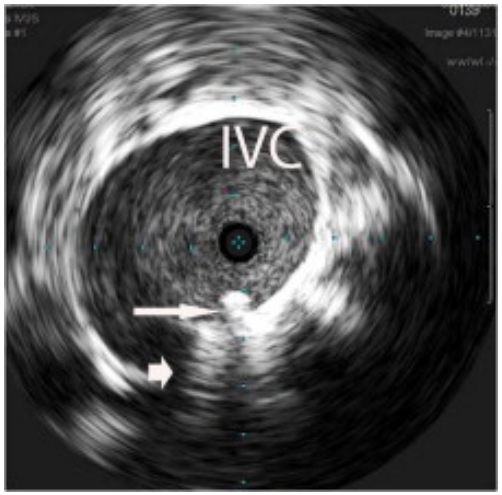


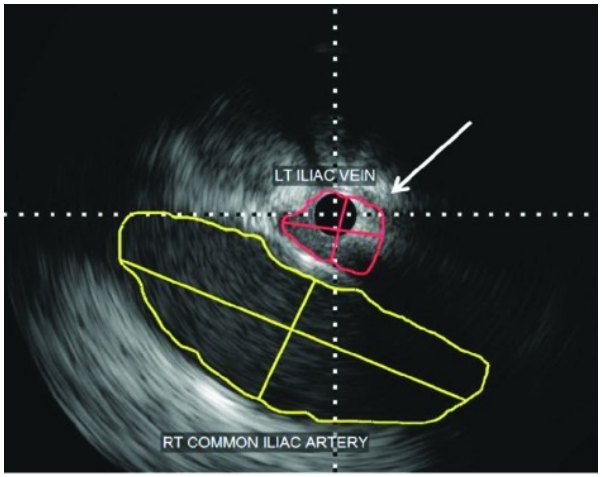


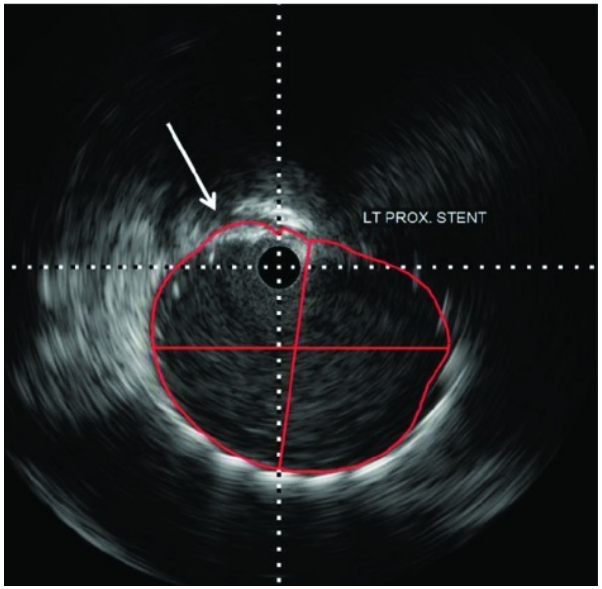
*Razavi MK, et al. *Circ Cardiovasc Interv*. 2015;8:e002772.

IVUS trong can thiệp tĩnh mạch

- Đánh giá đường kính lòng mạch và cấu trúc thành mạch, các tổn thương bất thường
- Hỗ trợ các biện pháp điều trị (lựa chọn stent)
- Đặt lưới lọc IVC tại giường

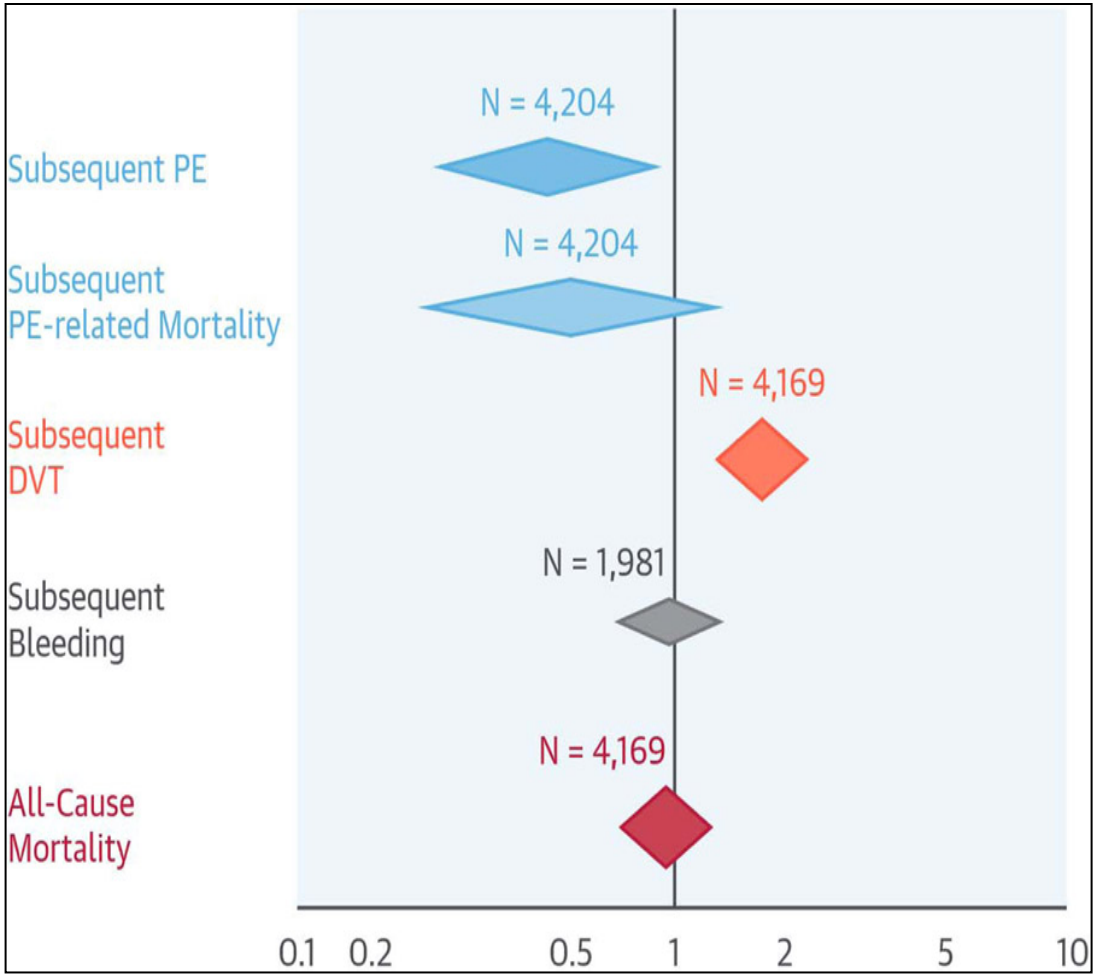




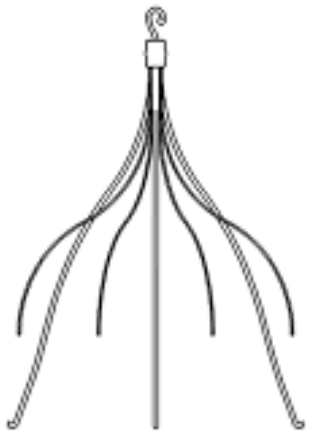


Semin Intervent Radiol. 2012 Mar; 29(1): 10–15

Lưới lọc tĩnh mạch chủ dưới



Günther Tulip™



Celect™

VenaTech

J Am Coll Cardiol. 2017; 70(13): 1587-1597

KHUYẾN CÁO HƯỚNG DẪN ĐIỀU TRỊ

Table 2
Recommendations for CDT/PMT provided by current guidelines.

Guideline	Recommendation	Grade of recommendation/Level of evidence
Scientific statement From the American Heart Association [39]	CDT or PCDT should be given to patients with IFDVT associated with limb-threatening circulatory compromise (ie, phlegmasia cerulea dolens)	I/C
	Patients with IFDVT at centers that lack endovascular thrombolysis should be considered for transfer to a center with this expertise if indications for endovascular thrombolysis are present	I/C
	CDT or PCDT is reasonable for patients with IFDVT associated with rapid thrombus extension despite anticoagulation and/or symptomatic deterioration from the IFDVT despite anticoagulation	IIa/C IIa/B
	CDT or PCDT is reasonable as first-line treatment of patients with acute IFDVT to prevent PTS in selected patients at low risk of bleeding complications	IIa/B
Clinical practice guidelines of the society for vascular surgery and the american venous forum [40]	Early thrombus removal strategies is recommended as the treatment of choice in patients with limb threatening venous ischemia due to iliofemoral deep venous thrombosis with or without associated femoropopliteal venous thrombosis (phlegmasia cerulea dolens)	1/A
	It is recommended that patients with isolated femoropopliteal deep venous thrombosis be managed with conventional anticoagulation therapy because there is currently insufficient evidence to support early thrombus removal strategies in this patient population.	1/C
	Percutaneous catheter-based techniques (pharmacologic or pharmacomechanical) is suggested as first-line therapy for early thrombus removal in patients meeting the criteria selection	2/C
	Strategy of pharmacomechanical thrombolysis be considered over catheter-directed pharmacologic thrombolysis alone if expertise and resources are available	2/C
	Patients managed with early thrombus removal be treated with a standard course of conventional anticoagulation after the procedure	1/A
Interdisciplinary expert panel on iliofemoral deep vein thrombosis (InterEPID) [41]	Patients with phlegmasia cerulea dolens should undergo urgent surgical thrombectomy	IIa/C
	Alternatively, patients with phlegmasia cerulea dolens should undergo endovascular thrombus removal	IIb/C
	Endovenous techniques may be reasonable as first-line therapy for early thrombus removal	IIb/C
	Among patients with iliofemoral DVT but without phlegmasia cerulea dolens, open surgical venous thrombectomy may be reasonable for selected patients who are candidates for thrombus removal but have contraindications to thrombolytic therapy	IIb/C
Antithrombotic therapy for VTE disease: CHEST guideline [1]	- In patients with acute proximal DVT of the leg anticoagulant therapy alone is suggested over catheter-directed thrombolysis. *Patients who are most likely to benefit from CDT (see*Table 3*), who attach a high value to prevention of post thrombotic syndrome and a lower value to the initial complexity, cost, and risk of bleeding with CDT, are likely to choose CDT over anticoagulation alone*	2/C

Eur J Intern Med. 2018 Jun;52:13-21

esvs GUIDELINES

Recommendation 34

In selected patients with symptomatic iliofemoral deep vein thrombosis, early thrombus removal strategies should be considered.

Class	Level	References
IIa	A	Enden *et al.* (2012),[222] Vedantham *et al.* (2017),[223] Notten *et al.* (2020),[226] Sharifi *et al.* (2012),[230] Comerota *et al.* (2019),[233] Kahn *et al.* (2020)[237]

Recommendation 36

For patients with deep vein thrombosis treated by early thrombus removal, with or without stenting, it is recommended that the duration of anticoagulation should be at least as long as if the patients were treated by anticoagulation alone and at the discretion of the treating physician.

Class	Level	References
I	C	Kearon *et al.* (2019),[234] Eijgenraam *et al.* (2014)[236]

Eur J Vasc Endovasc Surg (2021) 61, 9-82

American Heart Association®

Recommendations for Endovascular and Surgical Treatment of PTS

1. **For the severely symptomatic patient with iliac vein or vena cava occlusion, surgery (eg, femoro-femoral or femoro-caval bypass) (*Class IIb; Level of Evidence C*) or percutaneous endovenous recanalization (eg, stent, balloon angioplasty) (*Class IIb; Level of Evidence B*) may be considered.**

Circulation. 2014;130:1636-1661

HỘI TIM MẠCH HỌC VIỆT NAM

Khuyến cáo VNHA 2022

Khuyến cáo	Nhóm	Mức độ bằng chứng
Can thiệp hóa cơ học, hút huyết khối hoặc tiêu sợi huyết tại chỗ được cân nhắc chỉ định trong trường hợp HKTMSCD cấp tính (< 14 ngày) tầng chậu - đùi, có nguy cơ đe dọa hoại tử chi do chèn ép động mạch *(phlegmasia cerulea dolens)*, ở BN tiên lượng sống > 1 năm, không có chống chỉ định (1), (3)	IIa	A
Không được chỉ định can thiệp hóa cơ học, hút huyết khối hoặc tiêu sợi huyết tại chỗ cho BN bị HKTMSCD tầng đùi khoeo hoặc đoạn xa (cẳng - bàn chân)	III	B

Khuyến cáo của Hội tim mạch học Việt Nam về chẩn đoán, điều trị và dự phòng thuyên tắc huyết khối tĩnh mạch 2022

HỘI TIM MẠCH HỌC VIỆT NAM

Khuyến cáo VNHA 2022

Khuyến cáo	Nhóm	Mức độ bằng chứng
Can thiệp nội tĩnh mạch nên là phương pháp điều trị được lựa chọn đầu tiên ở BN hậu huyết khối bị tắc tĩnh mạch tầng chậu và có triệu chứng/dấu hiệu trầm trọng	IIa	B
Cân nhắc dùng siêu âm trong lòng mạch (IVUS) để hướng dẫn điều trị can thiệp cho bệnh nhân tắc nghẽn tầng chậu	IIa	C
Can thiệp hoặc phẫu thuật không được chỉ định cho bệnh nhân tắc nghẽn tầng chậu không có triệu chứng/dấu hiệu trầm trọng	III	C

Khuyến cáo của Hội tim mạch học Việt Nam về chẩn đoán, điều trị và dự phòng thuyên tắc huyết khối tĩnh mạch 2022

LỰA CHỌN ĐỐI TƯỢNG CDT/PMT

Table 3
criteria for selecting patients candidated to CDT/PMT provided by current guidelines.

Guideline	Recommendation	Grade of recommendation/level of evidence
Scientific statement From the American Heart Association [39]	CDT or PCDT should not be given to most patients with chronic DVT symptoms (> 21 days) or patients who are at high risk for bleeding complications	III/B
Clinical practice guidelines of the society for vascular surgery and the american venous forum [40]	Patients meeting the following criteria: - a first episode of acute iliofemoral deep venous thrombosis - symptoms < 14 days in duration - a low risk of bleeding - ambulatory with good functional capacity and an acceptable life expectancy	2/C
Interdisciplinary expert panel on iliofemoral deep vein thrombosis (InterEPID) [41]	Patients with: - symptomatic acute iliofemoral DVT - prevent or reduce post-thrombotic syndrome - onset of symptoms within 21 days - good functional status - reasonable life expectancy - low risk of bleeding	IIb/B
Antithrombotic therapy for VTE disease: chest guideline [1]	Patients with: - iliofemoral DVT - symptoms for < 14 days - good functional status - life expectancy of ≥1 year - low risk of bleeding	nd

- **Huyết khối cấp tính TM chậu-đùi**
- **Thời gian: 14 – 21 ngày**
- **Hợp tác được, kỳ vọng sống tốt**
- **Nguy cơ chảy máu thấp**

Eur J Intern Med. 2018 Jun;52:13-21

KẾT LUẬN

- Can thiệp nội mạch hiệu quả trong điều trị HKTMSCD: giảm nhanh triệu chứng, giảm nguy cơ PTS
- Phù hợp với các trường hợp HKTM chậu-đùi, nguy cơ chảy máu thấp
- Stent tĩnh mạch xử lý tổn thương tại TM chậu-đùi (nguyên nhân HKTM hoặc PTS)
- Cần nhiều các nguyên cứu có chất lượng