



GAVeCeLT 2022

XV PICC Day



LA TROMBOSI DA PICC: IL PUNTO DELLA SITUAZIONE

Dr.ssa Giovanna Passaro

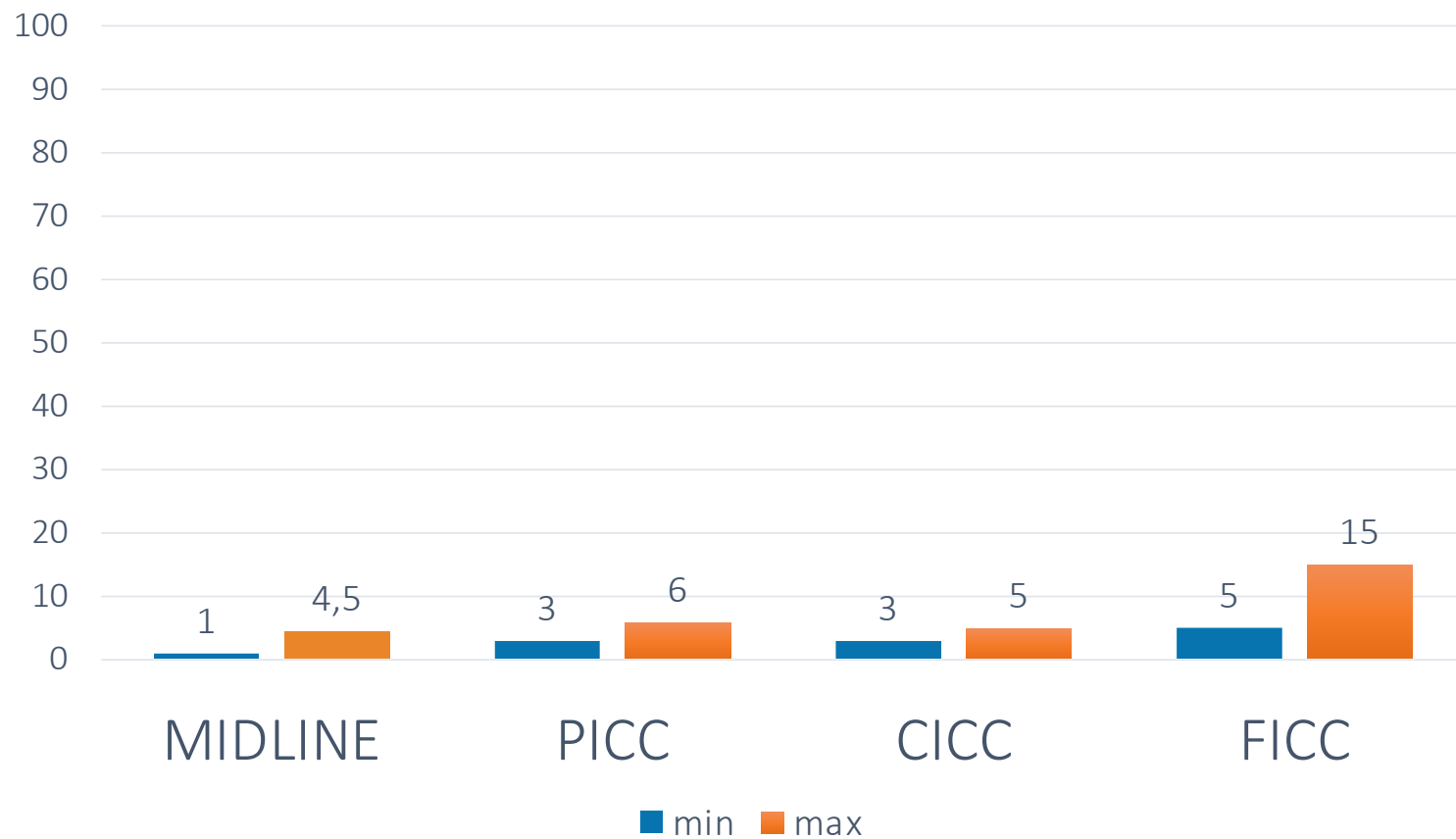
U.O.C. Medicina Interna - P.O. «San Filippo Neri» - ASL RM1



*« The best way to prevent DVT
is to avoid a device unless absolutely necessary »*



INCIDENZA CRT SINTOMATICA

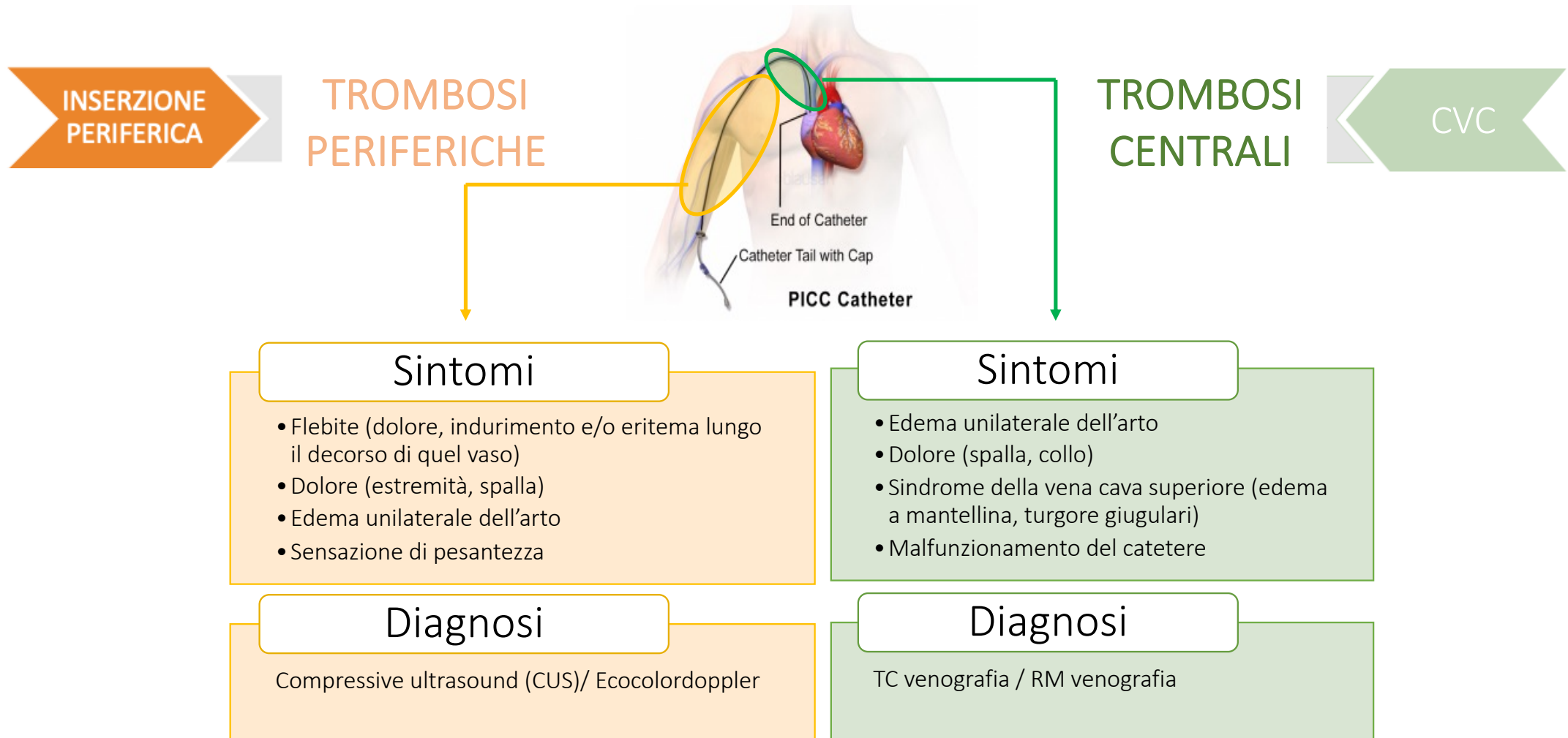


Pinelli F, et al. (2021). / *J Vasc Access*. 22(4), 501-508.

Lisova K, et al. (2018) / *J Vasc Access*. 19(5):492–495.

Chopra V, ET AL (2019) / *BMJ Qual Saf*. 28(9):714-720.

TROMBOSI VENOSA DA PICC



Peripherally inserted central catheter–related thrombosis rate in modern vascular access era—when insertion technique matters: A systematic review and meta-analysis

Paolo Balsorano¹, Gianni Virgili², Gianluca Villa³, Mauro Pittiruti⁴,
Stefano Romagnoli¹, Angelo Raffaele De Gaudio³
and Fulvio Pinelli¹

The Journal of Vascular Access
1–10
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INCIDENZA



PICC-TVP sintomatica 2.4%

PICC-TVP sintomatica in pazienti oncologici 2.2%

PICC-TVP sintomatica in pazienti oncoematologici 5.9%

Il rischio di trombosi da catetere aumenta entro i primi 10 giorni, e poi rimane stabile fino a 30 giorni. La maggior parte delle trombosi viene rilevata entro le prime 2 o 3 settimane.

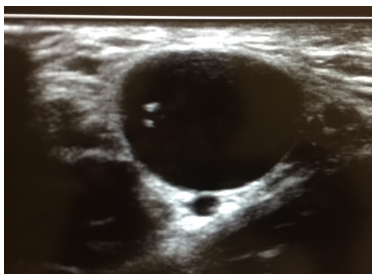
White D et al. (2018) / *Thromb Res*; 172: 54–60



RACCOMANDAZIONI GAVeCeLT 2021
PER LA INDICAZIONE, L'IMPIANTO E LA GESTIONE
DEI DISPOSITIVI PER ACCESSO VENOSO

a cura di Mauro Pittiruti e Giancarlo Scoppettuolo

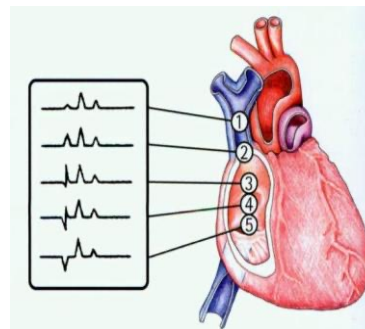
VERIFICARE CHE IL
CALIBRO DELLA VENA
SIA ADEGUATO AL
CALIBRO DEL
CATETERE



UTILIZZARE
VENIPUNTURA
ECOGUIDATA (+ kit da
microintroduzione)



VERIFICARE CHE LA
PUNTA DEL CATETERE
SIA IN PROSSIMITA'
DELLA GIUNZIONE
CAVO-ATRIALE



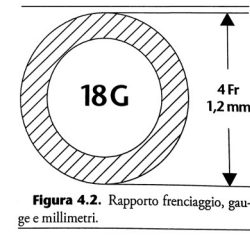
STABILIZZARE IN
MODO ADEGUATO IL
CATETERE (EXITE SITE
APPROPRIATO +
SUTURELESS DEVICE +
MEDICAZIONE
TRASPARENTE)



CATHETER TO VEIN RATIO



«The rule of the 33% has also the advantage of being easy to remember, easy to teach, easy to learn, and easy to apply»



French

Unità di misura del diametro del esterno del lume di un catetere

$$1 \text{ Fr} = 0,33 \text{ mm}$$

3Fr PICCs = vena di 9Fr (3mm) o più grande

4Fr PICCs = vena di 12Fr (4mm) o più grande

5Fr PICCs = vena di 15Fr (5mm) o più grande

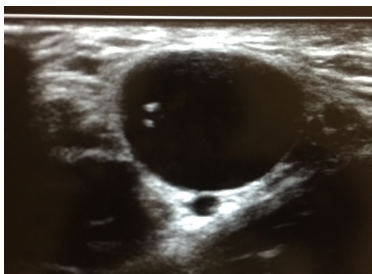
Il diametro del catetere (in Fr) dovrebbe essere uguale o inferiore al diametro della vena (in mm)



RACCOMANDAZIONI GAVeCeLT 2021
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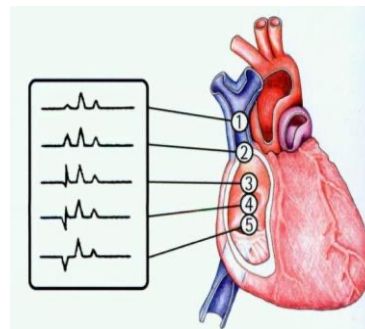
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CAVO-ATRIALE

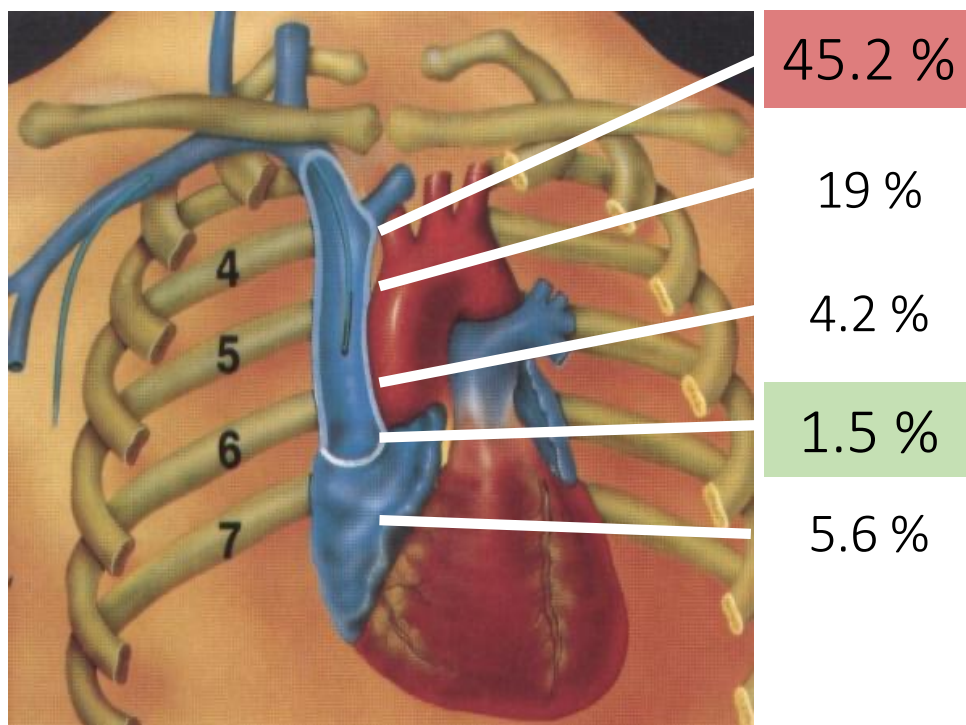


STABILIZZARE IN
MODO ADEGUATO IL
CATETERE (EXITE SITE
APPROPRIATO +
SUTURELESS DEVICE +
MEDICAZIONE
TRASPARENTE)

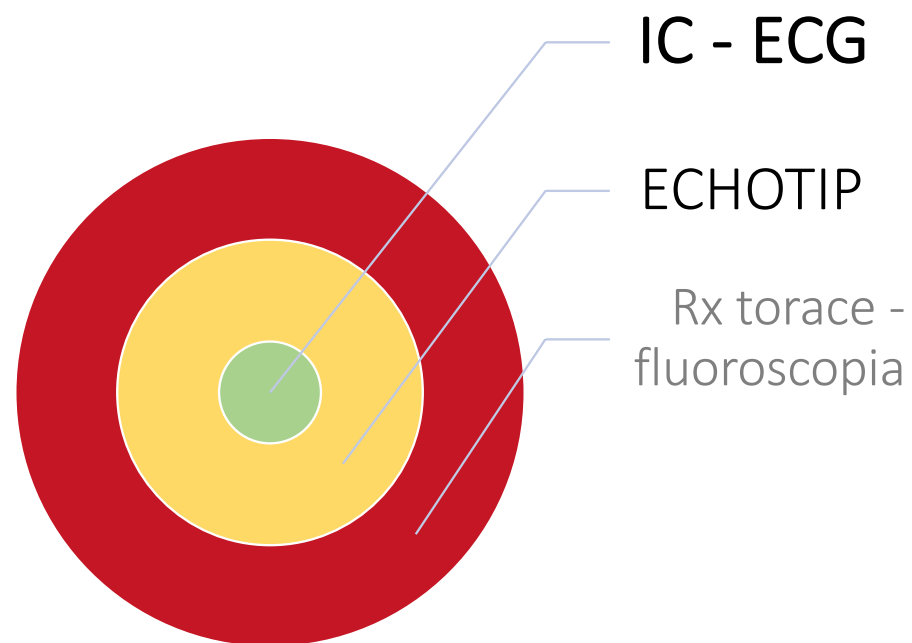


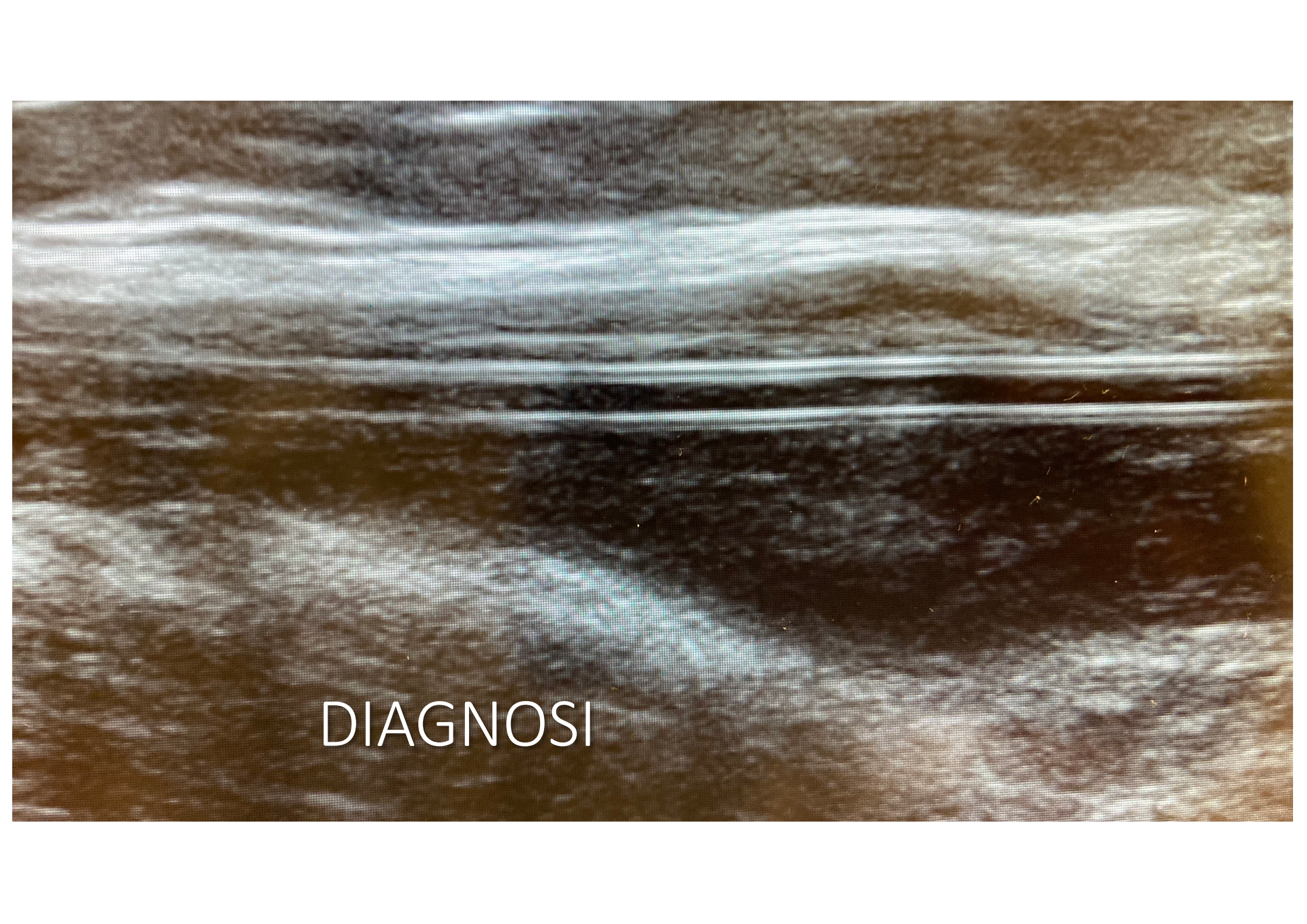
Jo Caers
Christel Fontaine
Vincent Vinh-Hung
Johan De Mey
Gerrit Ponnet

Catheter tip position as a risk factor for thrombosis associated with the use of subcutaneous infusion ports



POSIZIONE DELLA PUNTA





DIAGNOSI

CUS

Compression

UltraSonography



Sensibilità e specificità della ecografia con compressione
97% (95% CI, 90–100) - 96% (95% CI, 87–100)

Di Nisio et al. (2010) / *J Thromb Haemost*; 8: 684–92.

RECOMMENDATIONS AND GUIDELINES

Catheter-associated deep vein thrombosis of the upper extremity in cancer patients: guidance from the SSC of the ISTH

Guidance statements on diagnosis of catheter-associated upper extremity thrombosis in patients with cancer

- 1 We recommend ultrasonography as the initial test of choice for the diagnosis of suspected upper extremity thrombosis.
- 2 We recommend against the utilization of D-dimer to exclude the diagnosis of suspected catheter-associated upper extremity deep vein thrombosis.
- 3 We suggest evaluation of deep vein thrombosis by standard contrast venography in cases of high clinical suspicion and negative (or non-diagnostic) ultrasound testing. Less invasive radiographic methods such as CT venography or MRI venography can be considered if contrast venography is not available or practical.

Zwicker et al. (2014) / *J Thromb Haemost*; 12: 796–800



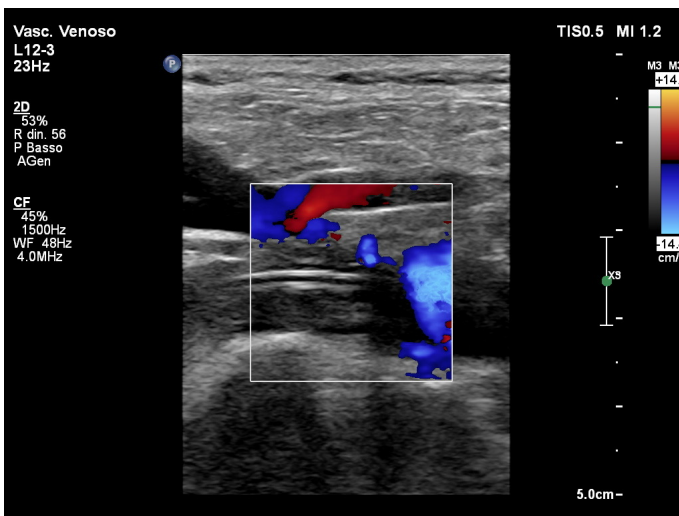
TROMBOSI VENOSA



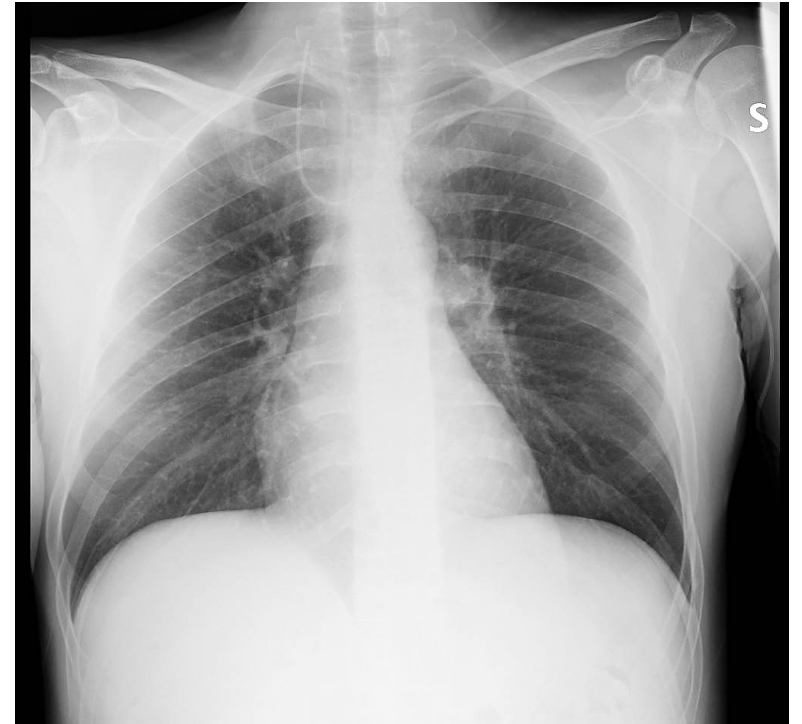
CUS scansione trasversale
Incomprimibilità della vena



Scansione longitudinale
Visualizzazione diretta del trombo



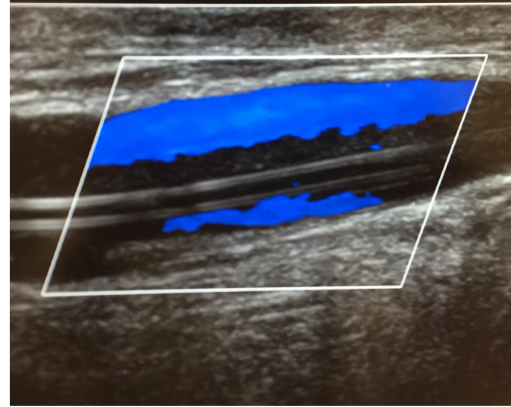
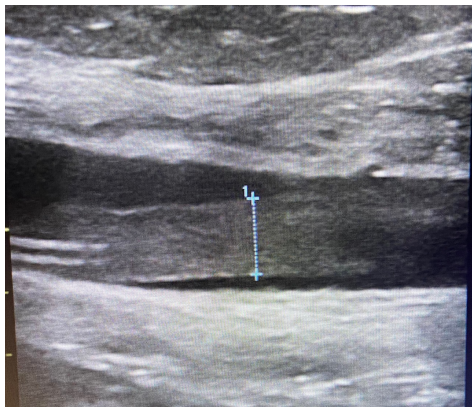
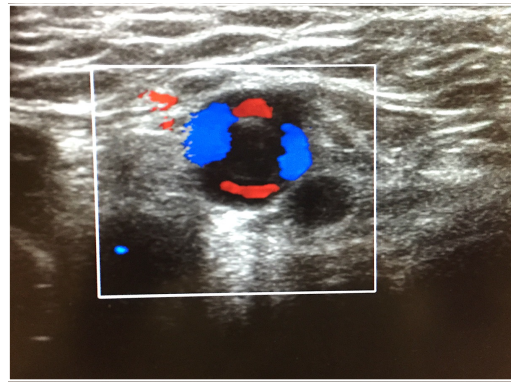
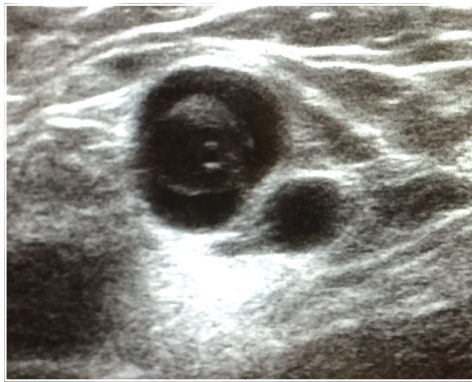
Anomalie del flusso
Trombi ipoecogeni
Indicazione indiretta sulla pervietà della vena



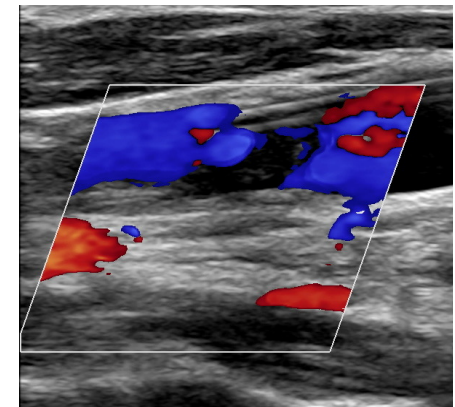
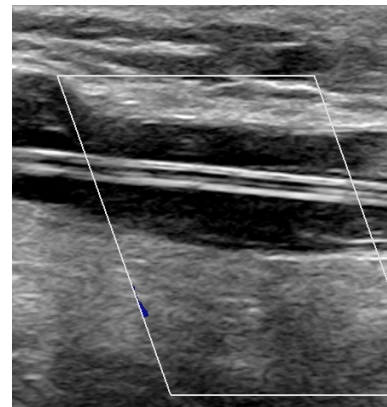
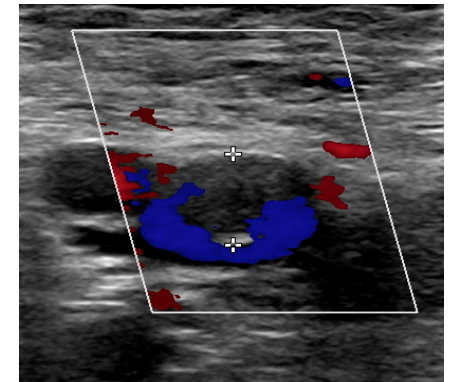
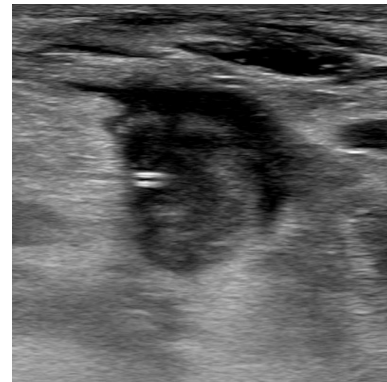
CUS POSITIVA NON SIGNIFICA
SEMPRE TROMBOSI

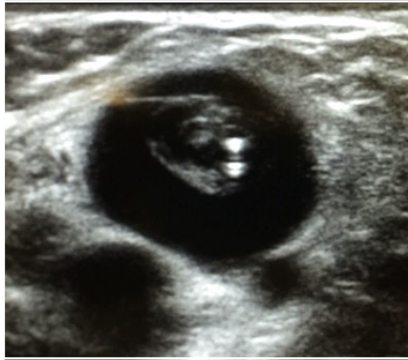


GUAINA FIBROBLASTICA



TROMBOSI VENOSA



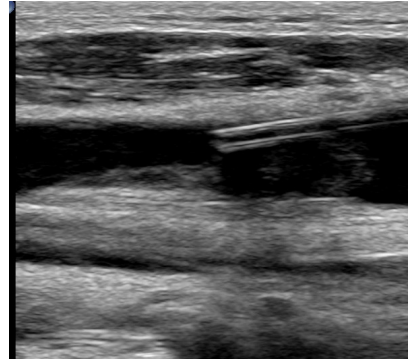


GUAINA
FIBROBLASTICA



Paziente
asintomatico
Catetere
normofunzionante

CUS +

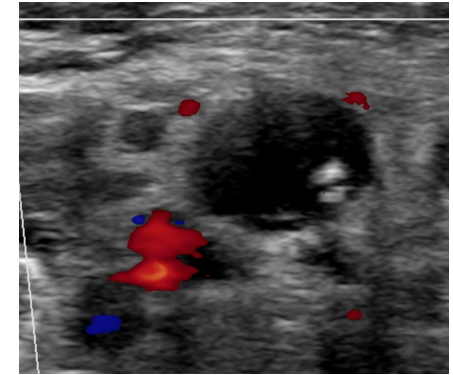


TROMBOSI MURALE
NON OSTRUTTIVA



Paziente
asintomatico
Catetere
normofunzionante

CUS +



TROMBOSI
OSTRUTTIVA



Paziente +/-
sintomatico
Catetere
normofunzionante

CUS +

TROMBOSI VENOSA DA PICC

Chi trattare?

Come trattare?

Per quanto tempo?

Con quali farmaci?



LINEE GUIDA e CRT



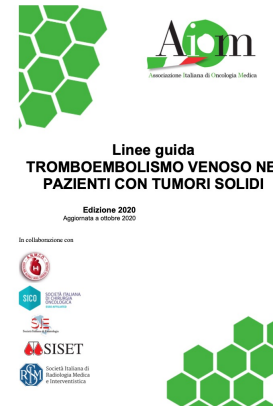
Nessuna indicazione specifica

Chest, 2021, 160.6: e545-e608

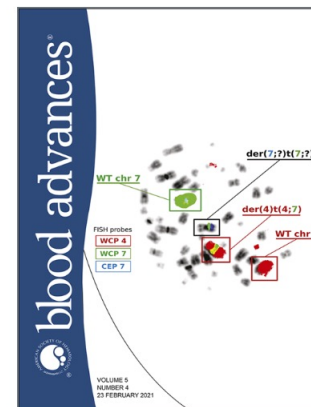


Nessuna indicazione specifica

Journal of Clinical Oncology, 2020, 38.5: 496-520.



L'impiego routinario di una profilassi con EBPM non deve essere preso in considerazione. Nei pazienti oncologici con CRT il trattamento anticoagulante per tre mesi può essere preso in considerazione



Suggerisce di non usare la tromboprofilassi parenterale o orale per pazienti con cancro e catetere venoso e mantenere il CVC piuttosto che rimuoverlo in caso di CRT

Blood advances, 2021, 5.4: 927-974.



NCCN Guidelines Version 1.2022

Acute Deep Vein Thrombosis (DVT)

CATHETER-RELATED DVT: DIAGNOSIS AND TREATMENT

DIAGNOSIS

WORKUP/IMAGING

TREATMENT

Clinical suspicion of catheter-related DVT:

- Unilateral limb swelling
- Pain in supra-clavicular space or neck
- Dysfunctional catheter

- Venous US
- CT venogram with contrast
- MRV with contrast
- X-ray venogram with contrast

DVT

No contraindication to anticoagulation^d

Contraindication to anticoagulation

No DVT

- Anticoagulation for at least 3 months or as long as central venous access device (CVAD) is in place^{c,e,l}
- Consider catheter removal if symptoms persist or if the catheter is infected or dysfunctional or no longer necessary
- Consider catheter-directed therapy (pharmacomechanical thrombolysis or mechanical thrombectomy) in appropriate candidates^{f,h,k}

Remove catheter or follow with serial imaging

Follow for change in contraindication as clinically indicated

Contraindication resolved

Anticoagulation for at least 3 months^{c,e,l}

Contraindication persists

Re-evaluate for risk/benefit of anticoagulation^j

- Evaluate for other causes
- Consider further diagnostic imaging/testing if initial testing is unrevealing and clinical suspicion remains high



2022 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer, including patients with COVID-19

Dominique Farge*, Corinne Frere*, Jean M Connors, Alok A Khorana, Ajay Kakkar, Cihan Ay, Andres Muñoz, Benjamin Brenner, Pedro H Prata, Dialina Brilhante, Darko Antic, Patricia Casais, María Cecilia Guillermo Esposito, Takayuki Ikezoe, Syed A Abutalib, Luis A Meillon-García, Henri Bounameaux, Ingrid Pabinger, James Douketis, the International Initiative on Thrombosis and Cancer (ITAC) advisory panel

Lancet Oncol 2022; 23: e334–47

Prophylaxis of catheter-related thrombosis

International Advisory Panel ranking: 8.52 out of 9.00

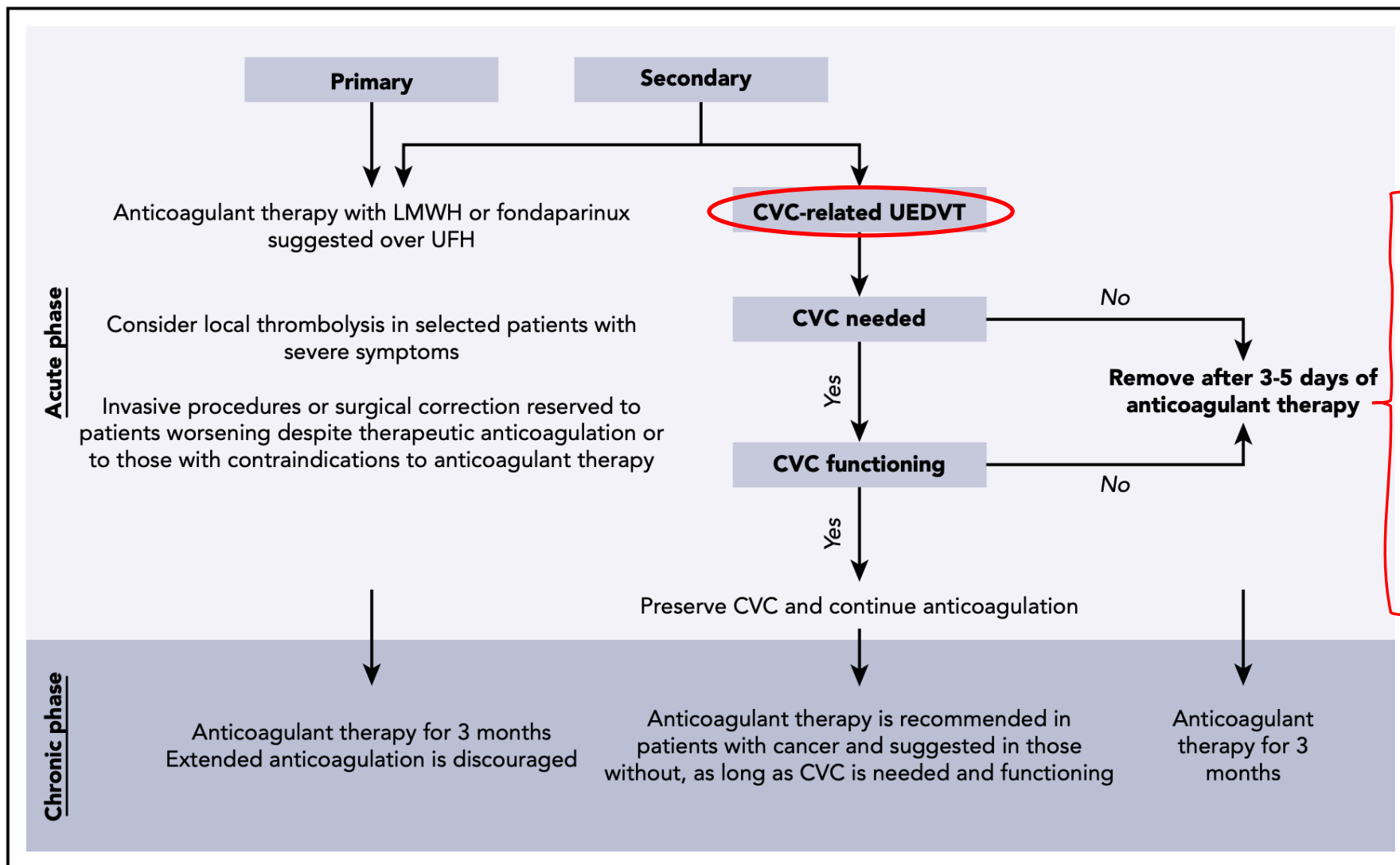
- 1 Use of anticoagulation for routine prophylaxis of catheter-related thrombosis is not recommended (grade 1A). Values and preferences: bleeding risk with anticoagulants.
- 2 Catheters should be inserted on the right side, in the jugular vein, and the distal extremity of the central catheter should be located at the junction of the superior vena cava and the right atrium (grade 1B).
- 3 In patients requiring central venous catheters, we suggest the use of implanted ports over peripherally inserted central catheter lines (guidance).

Best clinical practice (guidance): in the absence of any clear scientific evidence and because of an undetermined balance between desirable and undesirable effects, judgment was based on the professional experience and consensus of the international experts within the working group

Treatment of established catheter-related thrombosis

International Advisory Panel ranking: 8.61 out of 9.00

- 1 For the treatment of symptomatic catheter-related thrombosis in patients with cancer, anticoagulant treatment is recommended for a minimum of 3 months and as long as the central venous catheter is in place; in this setting, LMWHs are suggested and direct comparisons between LMWHs, direct oral anticoagulants, and vitamin K antagonists have not been made (guidance).
- 2 In patients with cancer and with catheter-related thrombosis, the central venous catheter can be kept in place if it is functional, well positioned, and not infected, with good resolution of symptoms under close surveillance while anticoagulation therapy is administered. No standard approach in terms of duration of anticoagulation is established (guidance).

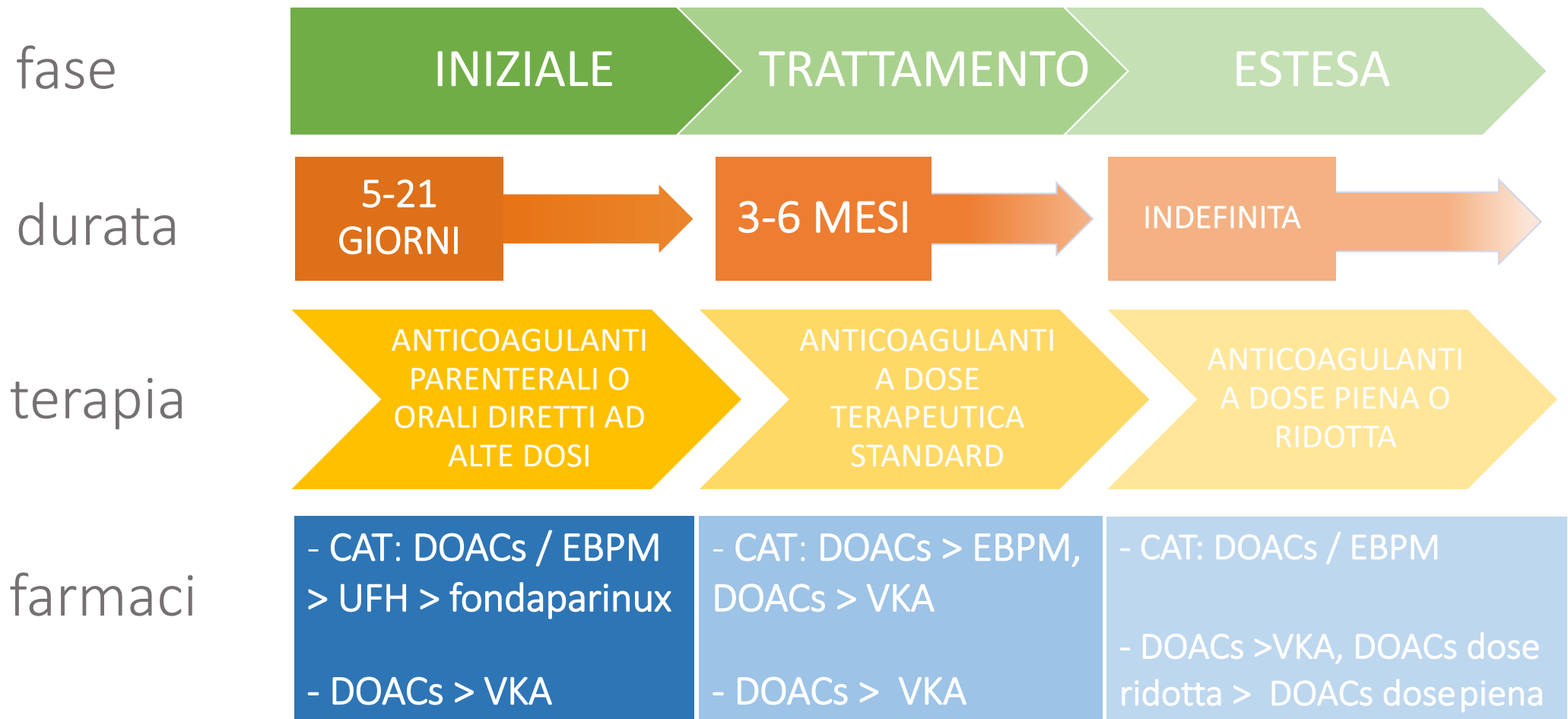


Sousa, B et al. (2015). Central venous access in oncology: ESMO Clinical Practice Guidelines. *Annals of Oncology*, 26, v152-v168.

Zwicker, J. I. et al. (2014). Catheter-associated deep vein thrombosis of the upper extremity in cancer patients: guidance from the SSC of the ISTH. *Journal of Thrombosis and Haemostasis*, 12(5), 796-800.

Abbattista M., et al. (2020). Treatment of unusual thrombotic manifestations. *Blood, The Journal of the American Society of Hematology*, 135(5), 326-334.

TRATTAMENTO TROMBOEMBOLISMO VENOSO



American College of Chest Physicians / CHEST 2021

DOACs – TVP arto superiore



Esclusione delle TVP arti superiori da RCTs DOAC

Dati mancanti

Utilizzo clinico in base all'estrapolazione dei risultati per TVP arti inferiori

Dose e durata ottimale dovrebbero essere individualizzate

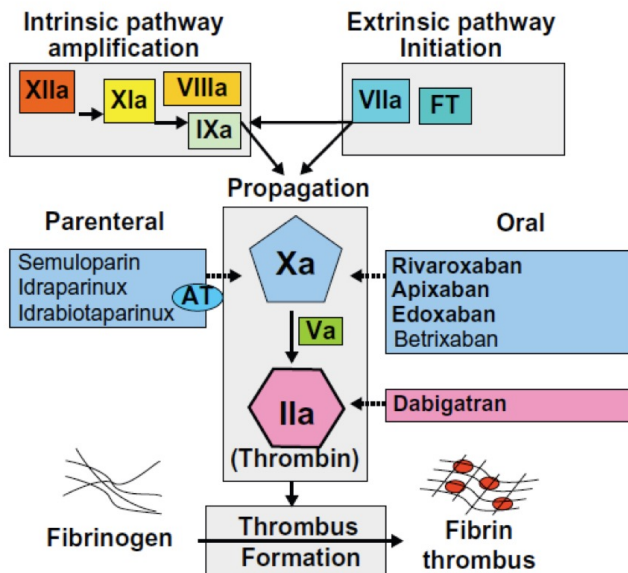


Table 2. Direct oral anticoagulants for the treatment of upper extremity deep vein thrombosis.

Author	Study Design	Patients	Duration	Treatment	Patient Characteristics	Outcomes
Laube (2017) [48]	Retrospective cohort	n = 83	3 months	Rivaroxaban (100%)	Age: 62 Male: 28% CVC: 83 (100%) Malignancy: 100%	Recurrence: 3 (3.6%) CRNMB: 1 (1.2%) MB: 2 (2.4%)
				No control	-	-
Fan (2017) [46]	Prospective cohort	n = 84	3 months	Rivaroxaban n = 44 (52%)	Age: 50 Male: 57% CVC: 100% Malignancy: 100%	Recurrence: 0 CRNMB: 7.3% MB: 0
				LMWH/Warfarin n = 40 (48%)	Age: 51 Male: 56% CVC: 100% Malignancy: 100%	Recurrence: 0 CRNMB: 11.4% MB: 0
Montiel (2017) [17]	Retrospective cohort	n = 55	3–6 months	Rivaroxaban (84%) Apixaban (13%) Dabigatran (4%)	Age: 49 Male: 49% CVC: 20 (36%) Malignancy: 10 (18%)	Recurrence: 1 (2%) CRNMB: 1 (2%) MB: 0
				No control	-	-
Davies (2018) [47]	Prospective cohort	n = 70	3 months	Rivaroxaban (100%)	Age: 54.1 Male: 33% CVC: 100% Malignancy: 100%	Recurrence: 1 (1.43%) CRNMB: 4 (5.7%) MB: 7 (10%)
				No control	-	-
Schastlivtsev (2019) [49]	Prospective cohort	n = 30	6 months	Rivaroxaban (100%)	Age: 52 Male: 43% CVC: 4 (13.3%) Malignancy: 2 (6.7%)	Recurrence: 0 CRNMB: 2 (6.7%) MB: 0
				No control	-	-
Houghton (2020) [50]	Retrospective cohort	n = 210	3 months	Apixaban/ Rivaroxaban n = 102 (49%)	Age: 57 Male: 55% CVC: 45 (44%) Malignancy: 53 (52%)	Recurrence: 0 CRNMB: 5 (6.8%) MB: 0
				LMWH/Warfarin n = 108 (51%)	Age: 62 Male: 63% CVC: 62 (57%) Malignancy: 72 (67%)	Recurrence: 1 (1.6%) CRNMB: 1 (1.6%) MB: 2 (3.3%)

CVC, central venous catheter; CRNMB, clinically relevant non-major bleeding; MB, major bleeding.

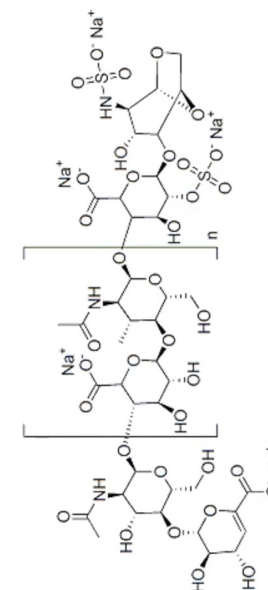
DOACs

TVP arto superiore

Bosch, F., et al. (2020). / *Journal of Clinical Medicine*, 9(7), 2069.

Eparine a basso peso molecolare

Subcutaneously administered anticoagulants	Daily dose	
	Prophylaxis	Treatment
Enoxaparin	2.000 U.I. (0,2 ml)/24h - 4.000 U.I. (0,4 ml)/24h	100 U. I./kg/12h*
Nadroparin ^o	2850 U.I./die (≤70 kg) 3800 U.I./die (>70Kg)	Weight-based dosing 171 U.I./kg/24h ^{oo} Fixed dosing: 40 to 49 kg: 7,600 U. I. (0,4 ml)/24h 50 to 59 kg: 9,500 U. I. (0,5 ml)/24h 60 to 69 kg: 11,400 U. I. (0,6 ml)/24h 70 to 79 kg: 13,300 U. I. (0,7 ml)/24h 80 to 89 kg: 15,200 U. I. (0,8 ml)/24h ≥90 kg: 17,100 U. I. (0,9 ml)/24h
Dalteparin [^]	5000 U.I. /24h	200 U.I./kg/24h or 100 U.I./kg/24h
Bemiparin	2.500 U.I. (0,2 ml)/24h 3.500 U.I. (0,2 ml)/24h	115 U.I./kg/24h
Parnaparin	3.200 U.I. (0.3 ml)/24h - 4.250 U.I. (0.4 ml)/24h	6.400 U.I. (0.6 ml)/12 h 8.500 U.I. (0.8 ml)/24h 6.400 U.I. (0.6 ml)/24h 4.250 U.I. (0.4 ml)/24h
Reviparin**	4.200 U.I. (0,6 ml)/24h	175 U.I./kg/12h
Tinzaparin §	3.500 U.I. - 4.500 U.I./24h	175 U.I./kg/24h



* CrCl: 15-30 mL/min: Prophylaxis 2000 UI/24 h; Treatment 100 U.I. (1 mg)/kg/24h.

^o CrCl ≥30 to <50 mL/minute: Decrease dose by 25% to 33%. CrCl <30 mL/minute: Prophylaxis: reduce dose by 25% to 33%, Treatment: use is contraindicated.

^{oo}For patients with higher-than-average bleeding risk, may administer the same total daily dose in 2 equally divided doses.

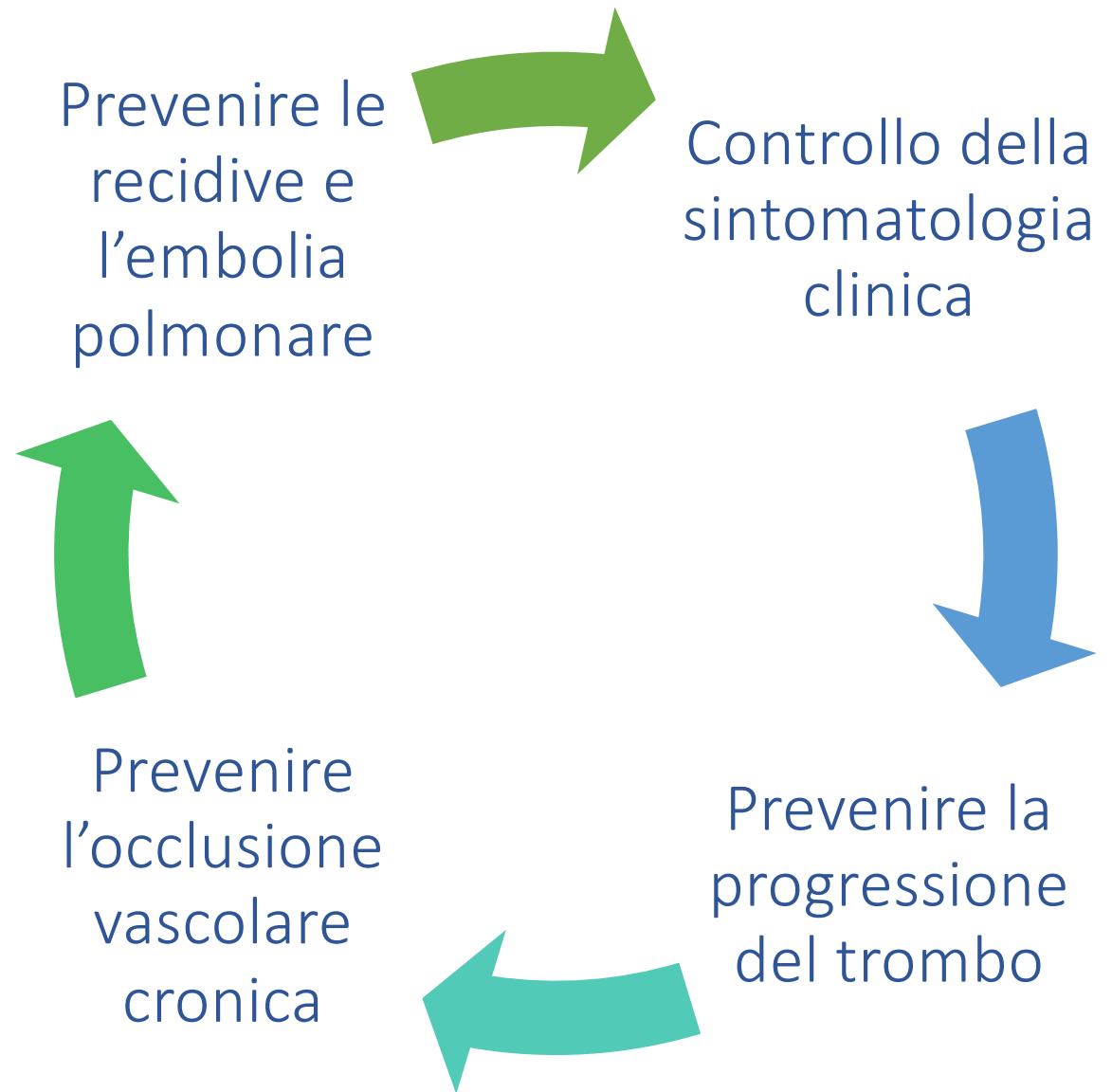
[^] CrCl ≥30 mL/minute: no dosage adjustment. CrCl <30 mL/minute: switching to an alternative anticoagulant.

** CrCl <30 mL/minute: use is contraindicated.

§ CrCl <30 mL/minute: Evidence suggests no accumulation in patients with CrCl ≥20 mL/minute, but there are limited data available in patients with a CrCl <20 mL/minute. While the manufacturer recommends that a dose reduction be considered in patients with CrCl <30 mL/minute, there are no specific dosage adjustments provided in the manufacturer's labeling; use with caution.

Finalità del trattamento

TROMBOSI VENOSA PROFONDA



EMBOLIA POLMONARE

ARTI SUPERIORI

Embolia polmonare 4.6 volte più comune nelle TVP arti inferiori

Frequenza di embolia polmonare sintomatica associata a TVP arti superiori **5.4%**

Embolia polmonare meno frequente nelle TVP arti superiori vs arti inferiori (**3%** vs 16%, $p < 0.001$)

Owens CA et al. (2010) / *J. Vasc. Interv. Radiol*, 21(6), 779-787
Joffe H.V., et al. (2004) / *Circulation*, 110(12), 1605-1611

TROMBOSI DA CATETERE

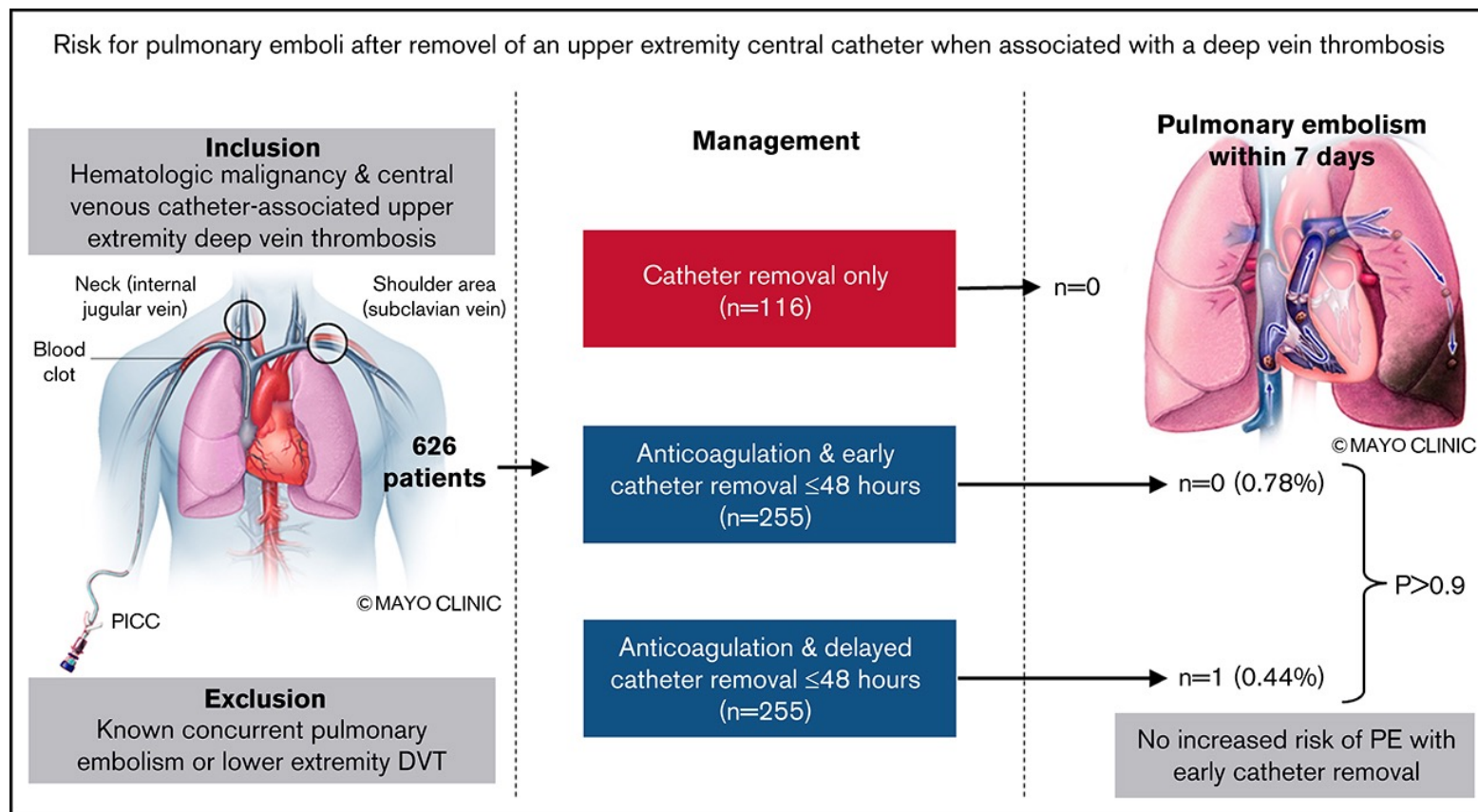
EP nei cateteri in PVC o polietilene (10/38, 26%) >>> catetere poliuretano o silicone (3/41, 7%; $p < 0.05$)

Il 7% dei pazienti con CRT in terapia anticoagulante sviluppa ricorrente TVP e il **2.8%** embolia polmonare

In 558 pazienti con CRT, 45 (**8%**) presentavano una concomitante EP. Il tipo di catetere era influente sul rischio di EP

Monreal M., et al. (1994) / *Thrombosis and haemostasis*, 72(10), 548-550. Kreuziger LB et al. (2015) / *J. Vasc. Surg. Venous. Lymphat. Disord.*, 3(3), 243-250 Kreuziger L.B. et al (2015) / *Thrombosis Research*, 136(6), 1103-1109.

Risk of pulmonary emboli after removal of an upper extremity central catheter associated with a deep vein thrombosis



Houghton et al. (2021) / *Blood Adv*, 27;5(14):2807-2812

Should ultrasound evaluation for catheter-related thrombosis always be required before PICC removal?

Pinelli Fulvio¹ , Muzzi Mirko²  and Pittiruti Mauro³ 

- b. An ultrasound scan should be considered before removal in the following situations:
- PICC inserted less than 2–3 weeks before: in this case, if a thrombus has developed, it might be “fresh” and prone to be mobilized during PICC removal;
 - PICC removal performed by the vascular access team (specifically trained to use ultrasound);
 - PICC in hospitalized patients, particularly in intensive care units or in non-intensive oncological wards;
 - High risk patients (critically ill, history of previous thrombosis, hematological disease, COVID-19,³⁸ renal failure).³⁹

The Journal of Vascular Access
1–6
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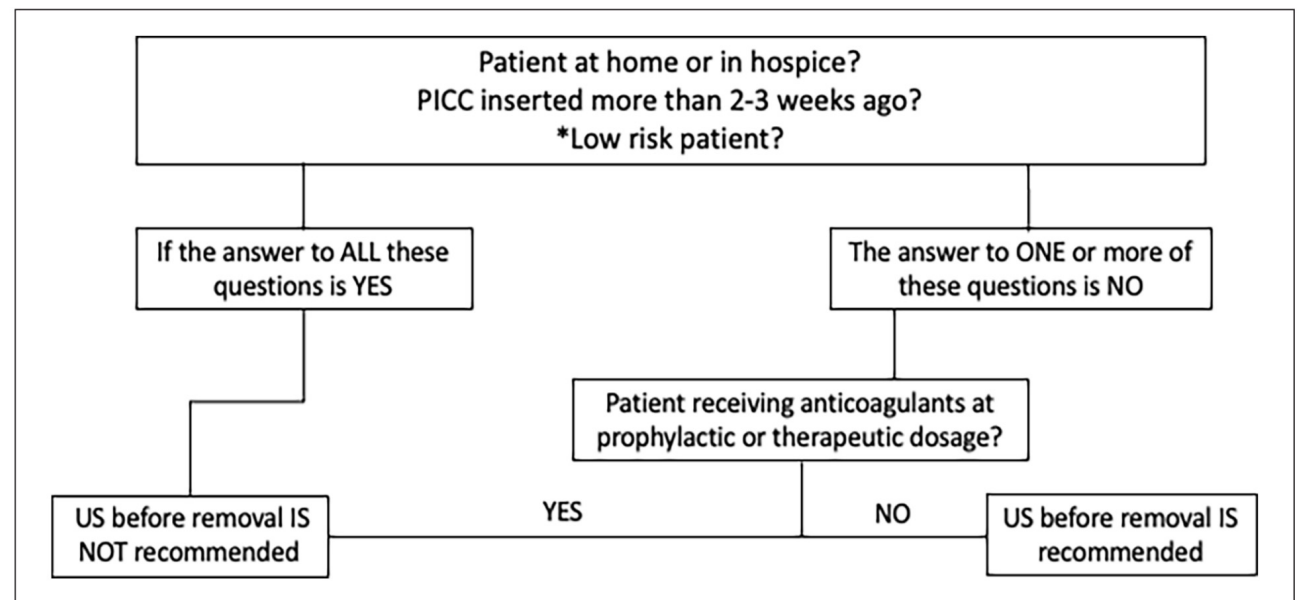
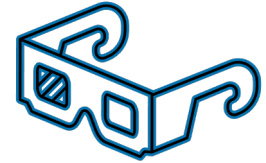



Figure 2. Flow chart representing the clinical scenario of a PICC without signs or symptoms suggestive of a CRT.

*Low risk patient = not critically ill, no history of previous thrombosis, no hematological disease, no COVID-19

CONCLUSIONI



PREVENZIONE

- Bundle di impianto
- Profilassi farmacologica esclusivamente per i pazienti ad alto rischio trombotico



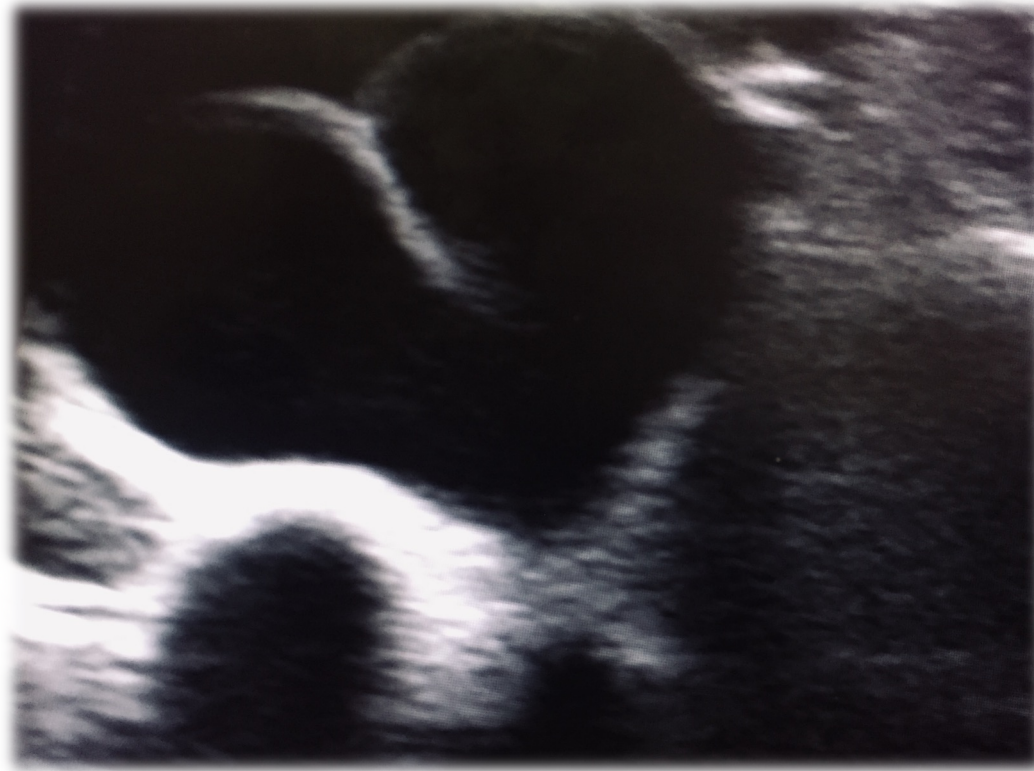
DIAGNOSI

- Sospetto clinico
- Diagnosi ecografica (diagnosi differenziale con guaina fibroblastica nei pazienti asintomatici con CUS positiva)



TERAPIA

- Terapia anticoagulante per almeno 3 mesi, da prolungare finché il catetere è in sede
- Non rimuovere il catetere se necessario, normofunzionante, ben posizionato e non infetto



Grazie per l'attenzione