



La trombosi da catetere (Catheter-related thrombosis)

Dott. Igor Giarretta

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Venous Thromboembolism Associated With Long-Term Use of Central Venous Catheters in Cancer Patients

By Melina Verso and Giancarlo Agnelli

The incidence of clinically overt UL-DVT related to CVCs has been reported to vary between **0.3%** and **28.3%**.

The incidence of CVC-related UL-DVT screened by venography reportedly varies between **27%** and **66%**.

In general population the reported incidence of CRT varies from around **5%**, by considering only symptomatic events, up to an overall rate of **30%**.



Peripherally Inserted Central Venous Catheters Are Not Superior to Central Venous Catheters in the Acute Care of Surgical Patients on the Ward

Simon Turcotte, MD, Serge Dubé, MD, MSc, Gilles Beauchamp, MD

Département de Chirurgie, Hôpital Maisonneuve-Rosemont, Centre affilié à l'Université de Montréal, 5415 boul de l'Assomption Montréal, Quebec H1T 2M4, Canada

Thrombotic complications appear to be more significant with PICC and to occur early after catheterization.

Phlebotic complications accounted for premature catheter removal in approximately 6% of PICC. Finally, prospective data suggest that approximately 40% of PICC will have to be removed before completion of therapy, possibly more often and earlier than CVC.

Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis

Vineet Chopra, Sarah Anand, Andy Hickner, Michael Buist, Mary A M Rogers, Sanjay Saint, Scott A Flanders



Annals of Internal Medicine

SUPPLEMENT

The Michigan Appropriateness Guide for Intravenous Catheters (MAGIC): Results From a Multispecialty Panel Using the RAND/UCLA Appropriateness Method

Vineet Chopra, MD, MSc; Scott A. Flanders, MD; Sanjay Saint, MD, MPH; Scott C. Woller, MD; Naomi P. O'Grady, MD; Nasia Safdar, MD, PhD; Scott O. Trerotola, MD; Rajiv Saran, MD, PhD; Nancy Moureau, BSN, RN; Stephen Wiseman, PharmD; Mauro Pittiruti, MD; Elie A. Akl, MD, MPH, PhD; Agnes Y. Lee, MD, MSc; Anthony Courey, MD; Lakshmi Swaminathan, MD; Jack LeDonne, MD; Carol Becker, MHSA; Sarah L. Krein, PhD, RN; and Steven J. Bernstein, MD, MPH

PICC show a high risk of thrombosis in cancer and intensive care unit patients

CRT a real scarecrow?

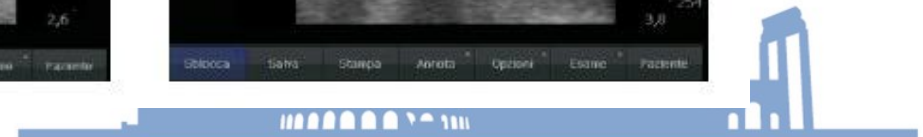
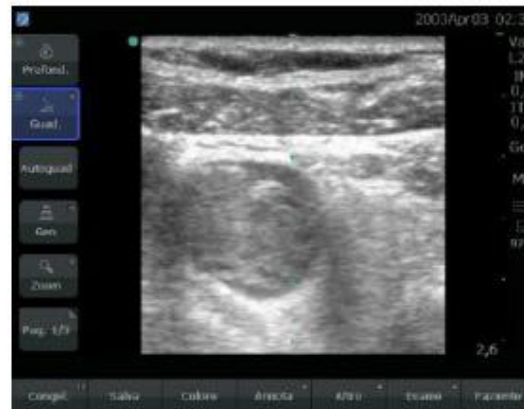
- Confusion between fibroblastic sheath and asymptomatic CRT
- Confusion between asymptomatic and symptomatic CRT
- Several devices included
- Different study population
- Several techniques included



CRT

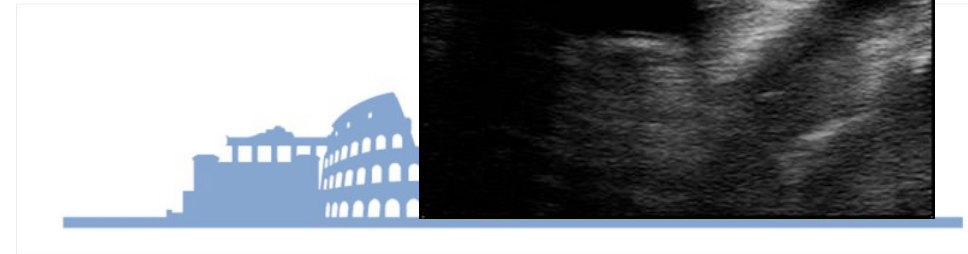
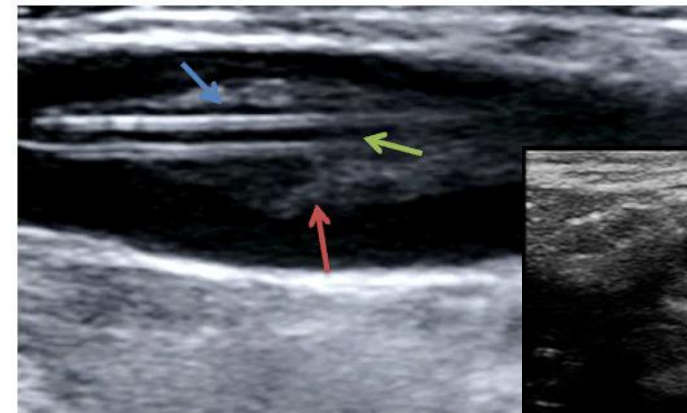
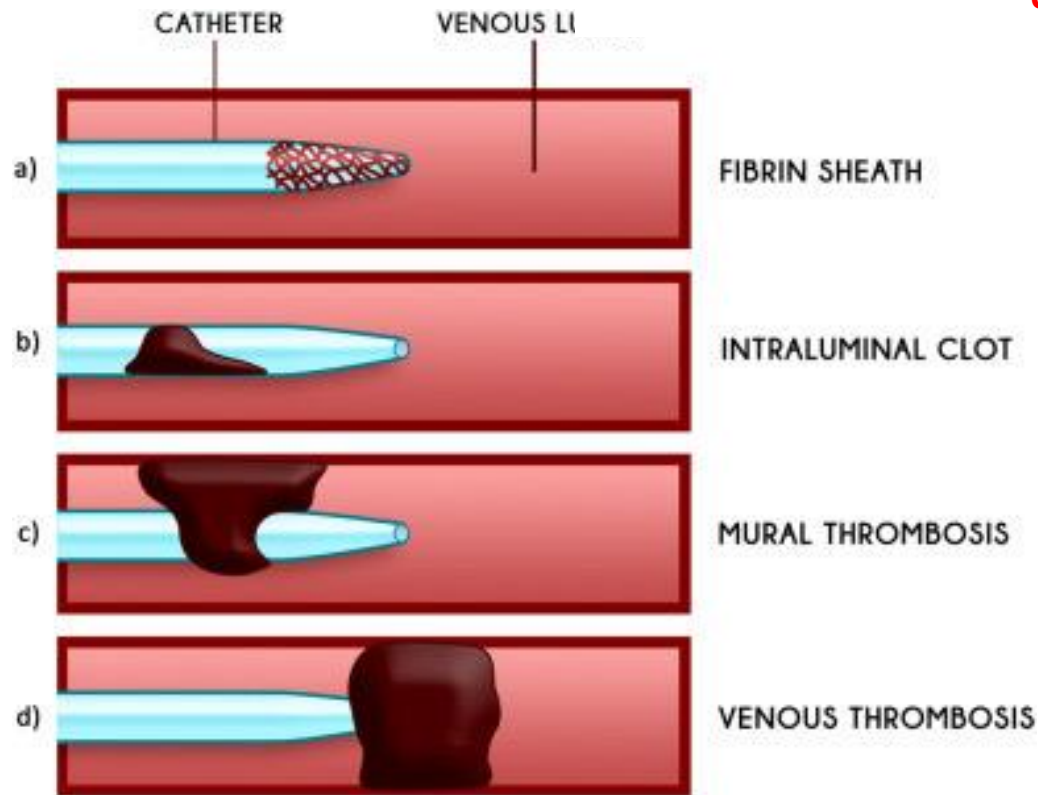
Catheter-related thrombosis occurs as a consequence of endothelial damage:

- From endothelial damage at the site of venipuncture
- As the consequence of traumatism of the catheter against the vein wall
- As the effect of a mechanical trauma of the catheter (and specially the catheter tip) against the venous wall
- As the result of a chemical injury to the endothelium



Catheter-related thrombosis (CRT),

Appearance of a thrombus on the vascular wall, most frequently where the endothelium has been damaged at the catheter introduction site and/or where the contact between vein wall and catheter is traumatic.



Early-CRT (with-in 30 days from implantation)

- Scelta inappropriata della vena
- Tecnica di inserzione inappropriata
- Malposizione della punta
- Fissaggio inappropriato



**RIDUCIBILI UTILIZZANDO UN BUNDLE
DI INSERZIONE**

Late-CRT (beyon 30 days from implantation)

- Neoplasia e/o chemioterapia
- Alterazioni congenite/acquisite della coagulazione



**ELIMINABILI SOLO EVITANDO
L'IMPIANTO DEL CVC**





Werner Forßmann

Poliuretani di
I generazione

Introduzione della venipuntura
ecoguidata delle vene del braccio
(Gavecelt 2003)

1929

'70-'80

'90

2000-03

Impianto del primo
CVC (PICC)

Materiali biocompatibili
(silicone e poliuretani di II
generazione)



Massimo Lamperti
Andrew R. Bodenham
Mauro Pittiruti
Michael Blaivas
John G. Augoustides
Mahmoud Elbarbary
Thierry Pirotte
Dimitrios Karakitsos
Jack LeDonne
Stephanie Doniger
Giancarlo Scoppettuolo
David Feller-Kopman
Wolfram Schummer
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Eric Desruennes
Lawrence A. Melniker
Susan T. Verghese

**International evidence-based
recommendations on ultrasound-guided
vascular access**

Table 6 Recommendations regarding sterility using ultrasound guidance and prevention of infectious and mech using ultrasound-guided cannulation

Sterility during ultrasound vascular procedures					
Domain code	Suggested definition	Level of evidence	Degree of consensus		
D8.S1	Sterile techniques should always be used during the placement of a vascular access device, including hand washing; sterile full body drapes; wearing of sterile gowns, gloves, caps and masks covering both the mouth and nose. Probe and cable sterility have to be maintained using sterile gel and appropriate probe and cable shields	A	Very good		
Prevention of infectious and mechanical complications with ultrasound-guided cannulation					
D8.S2	Ultrasound guidance should be used in order to decrease the rate of CRBSI in adults and children	C	Very good	Strong	
D8.S3–4	A multi-faceted strategy, including the use of ultrasound guidance with specific preventive and educational measures and the promotion of good practices applied by both medical and nursing staff, is suggested in order to reduce the incidence of CRBSI	B	Good	Strong	
D8.S5	Ultrasound guidance should be used to avoid cannulation of thrombotic sites	A	Very good	Strong	
D8.S6	Ultrasound guidance, by reducing puncture attempts, technical failure rates and mechanical complications, has to be preferred because of a reduced incidence of catheter-related thrombosis	A	Very good	Strong	

1. **Dimensioni**
2. **Profondità**
3. **Pervietà**
4. **Rapporti con strutture circostanti**
5. **Collassabilità respiratoria**
6. **Praticità dell'exit-site**

Appropriata scelta della vena

review

Annals of Oncology 20: 1459–1471, 2009
doi:10.1093/annonc/mdp062
Published online 12 June 2009

2008 SOR guidelines for the prevention and treatment of thrombosis associated with central venous catheters in patients with cancer: report from the working group

P. Debourdeau^{1*}, D. Kassab Chahmi², G. Le Gal³, I. Kriegel⁴, E. Desruennes⁵, M.-C. Douard⁶, I. Elalamy⁷, G. Meyer⁸, P. Mismetti⁹, M. Pavic¹, M.-L. Scrobohaci¹⁰, H. Lévesque¹¹, J. M. Renaudin¹² & D. Farge¹³ on behalf of the working group of the SOR

¹Department of Oncology and Internal Medicine, Desgenettes Hospital, Lyons; ²SOR, National Cancer Institute, Boulogne-Billancourt; ³Department of Internal Medicine, La Cavale-Blanche Hospital, Brest; ⁴Department of Anesthesiology, Curie Institute, Paris; ⁵Department of Anesthesiology, Gustave Roussy Institute, Villejuif; ⁶Department of Anesthesiology, Saint Louis Hospital, Paris; ⁷Hemostasis Laboratory, Tenon Hospital, Paris; ⁸Department of Pneumology, Georges Pompidou Hospital, Paris; ⁹Department of Vascular Pathology, Saint-Etienne Hospital, Saint-Etienne; ¹⁰Hemostasis Laboratory, Saint-Louis Hospital, Paris; ¹¹Department of Vascular Pathology, Bois Guillaume Hospital, Rouen; ¹²Department of Vascular Pathology, Georges Pompidou Hospital, Paris and ¹³Department of Vascular Pathology, Saint-Louis Hospital, Paris, France

Received 11 August 2008; revised 30 October 2008; accepted 9 February 2009

The use of Ultrasound has a significantly favorable impact on the infectious and thrombotic risk related to the implantation of VAD



Poliuretani di I
generazione

Introduzione della venipuntura
ecoguidata delle vene del braccio
(Gavecelt 2003)

1929

'70-'80

'90

2000-03

2007

Impianto del
primo CVC
(PICC)

Materiali
biocompatibili
(silicone e poliuretani
di II generazione)

Introduzione della tecnica
dell'ECG intracavitario



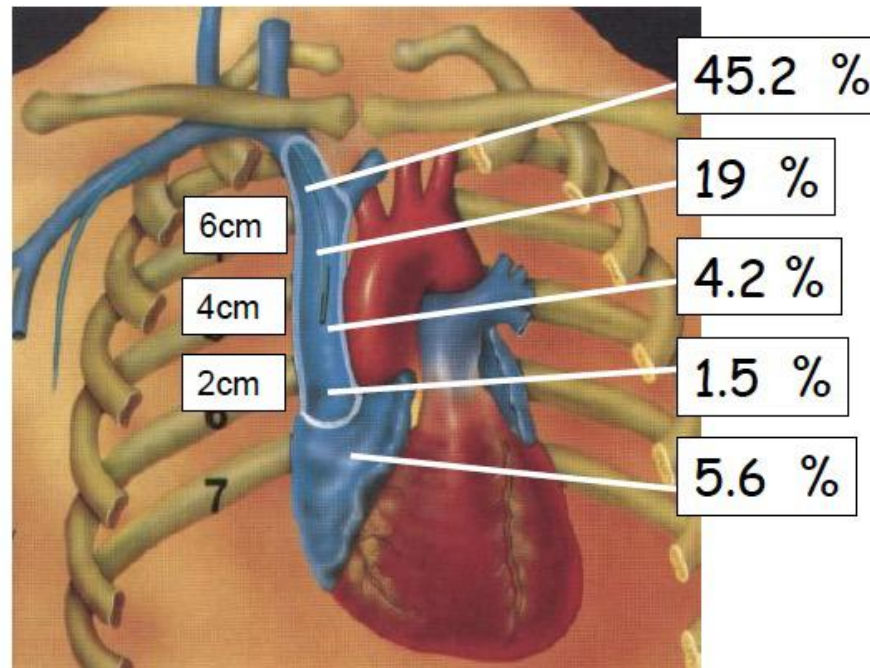
Corretta posizione della punta

Support Care Cancer (2005) 13:325–331
DOI 10.1007/s00520-004-0723-1

ORIGINAL ARTICLE

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

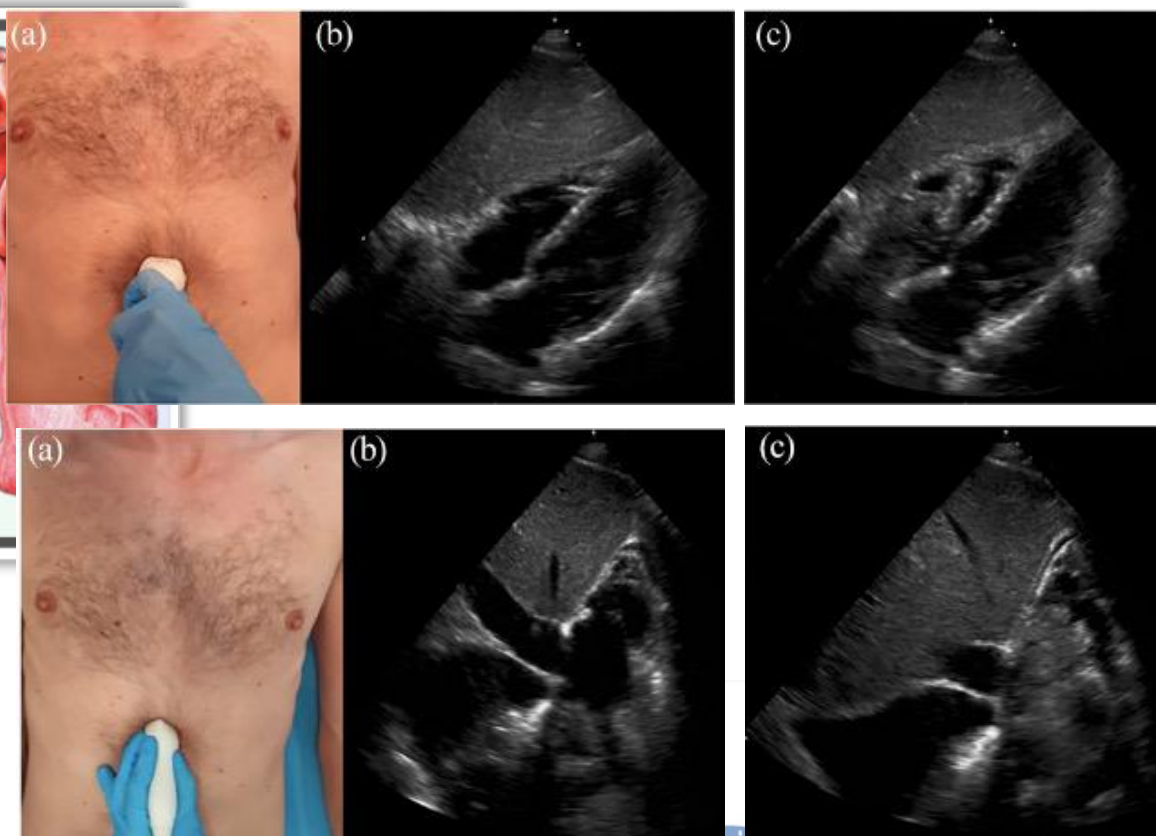
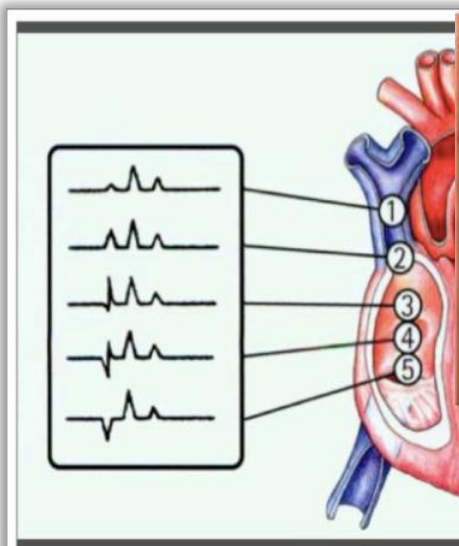
**Catheter tip position as a risk factor
for thrombosis associated with the use
of subcutaneous infusion ports**

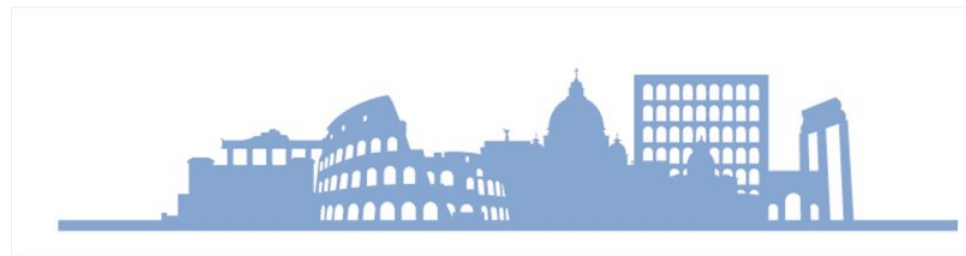


*Petersen Am J Surg 1999
Luciani, Radiology 2001
Puel, Cancer 2003
Melina Verso, J Clin Oncol
2003
Caers, Support Care Cancer
2005*



ECG intracavitario Ecografia intraprocedurale







The Effect of Catheter to Vein Ratio on Blood Flow Rates in a Simulated Model of Peripherally Inserted Central Venous Catheters

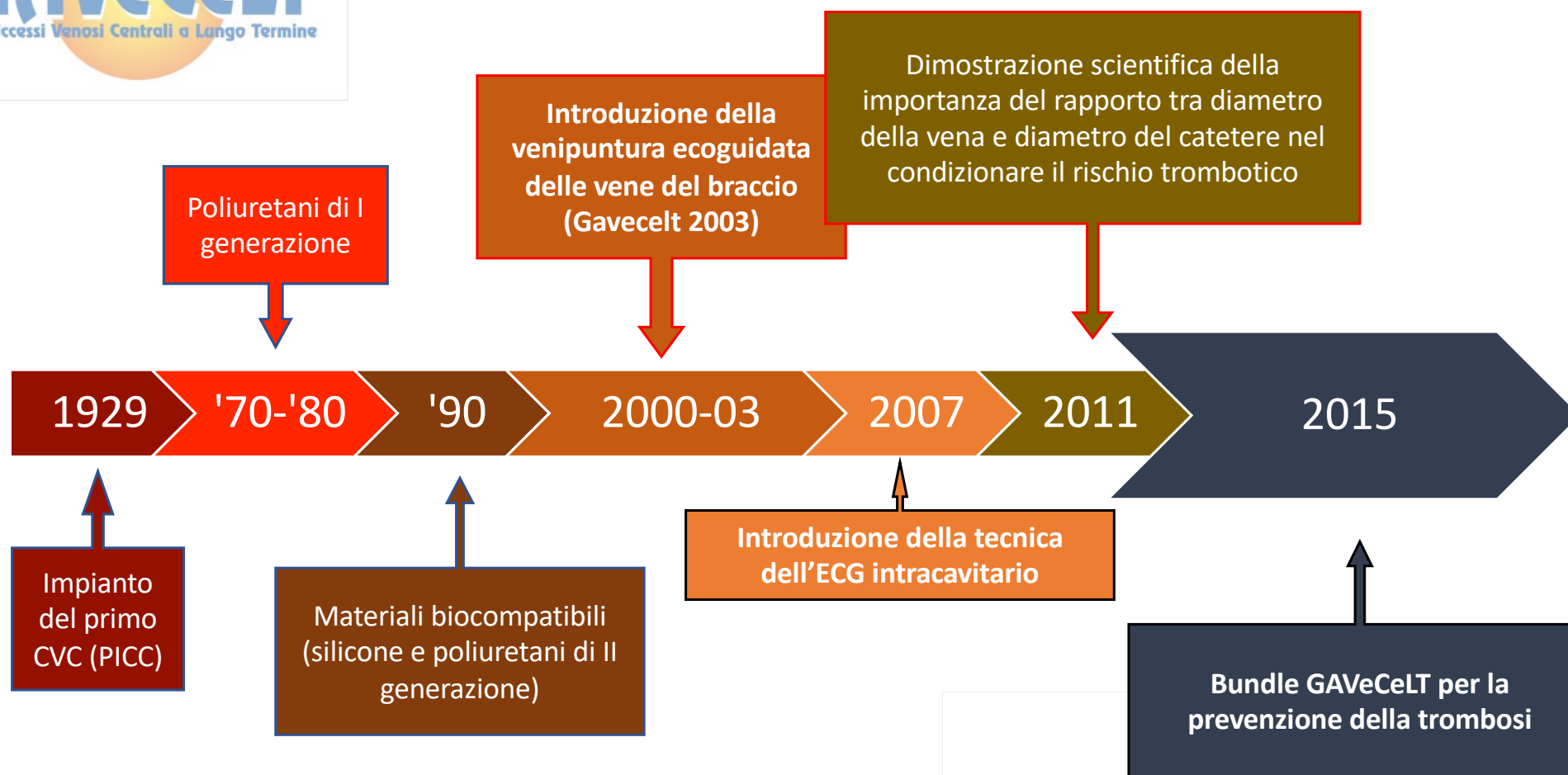
Thomas P. Nifong, MD; and Timothy J. McDevitt, PhD

The risk of thrombosis is related to the ratio between the **diameter of the vein** (visible only with the echo) and the **diameter of the catheter** (which is decided by the operator)

Measure	Unobstructed	Inner Wire 0.67 mm (2F)	Inner Wire 1.33 mm (4F)	Inner Wire 2.0 mm (6F)	Inner Wire 2.6 mm (8F)
Outer tube, 4 mm					
D_{cath}/D_{cvt}	0	0.16	0.32	0.48	0.64
Average flow, mL/min	17	12	8.7	5.4	1.2
Relative flow, %	100	69	40	20	6.9
SD, mL/min	0.42	0.11	0.15	0.03	0.016
P value ^a	...	3.7×10^{-6}	6.8×10^{-11}	3.8×10^{-7}	
Outer tube, 5 mm					
D_{cath}/D_{cvt}	0	0.13	0.25	0.38	
Average flow, mL/min	41	33	25	17	
Relative flow, %	100	81	60	42	
SD, mL/min	0.15	0.75	0.70	0.16	
P value ^a	...	1.0×10^{-8}	8.5×10^{-8}	9.0×10^{-6}	
Outer tube, 6 mm					
D_{cath}/D_{cvt}	0	0.11	0.21	0.32	
Average flow, mL/min	81	52	47	39	
Relative flow, %	100	64	58	49	
SD, mL/min	0.98	0.58	0.40	2.7	
P value ^a	...	5.3×10^{-10}	1.0×10^{-6}	.0028	6.7×10^{-4}

D_{cath} = diameter of the catheter; D_{cvt} = diameter of the catheter

IN ORDER TO REDUCE THE RISK OF CRT, THE OUTER DIAMETER OF THE CATHETER SHOULD NOT EXCEED 1/3 OF THE INNER DIAMETER OF THE VEIN



Bundle GAVeCeLT per la prevenzione della CRT:

- a) Appropriata scelta della vena**
- b) Minimo trauma durante la venipuntura**
- c) Appropriata posizione della punta**
- d) Fissaggio appropriato**



Minimo trauma durante la venipuntura



Kit da microintroduzione:

Ago 21 G ecogenico
Guida soft straight 0,018
Microintroduttore 3,5 Fr



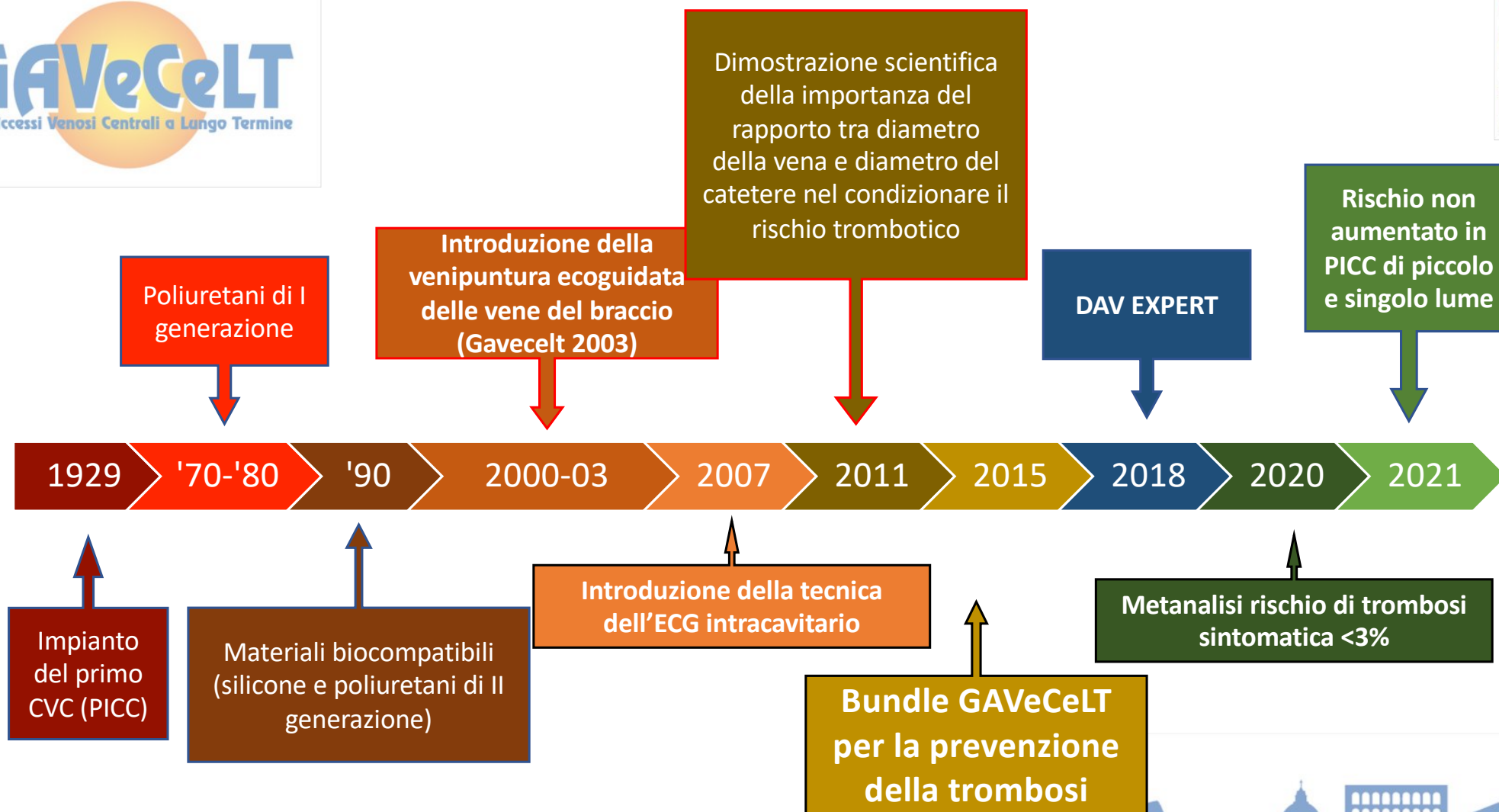
Fissaggio appropriato - Stabilizzare il catetere

Un VAD mobile è più incline al trauma meccanico sulla parete della vena nel sito di venipuntura

Strategie:

1. Scelta appropriata dell'exit
2. Tunnellizzazione
3. SAS
4. Colla istoacrilica
5. Medicazioni trasparenti semipermeabili





**Peripherally inserted central catheters inserted with current best practices have low deep vein thrombosis and central line–associated bloodstream infection risk compared with centrally inserted central catheters:
A contemporary meta-analysis**

Gregory J Schears¹, Nicole Ferko², Imran Syed² ,
John-Michael Arpino² and Kimberly Alsbrooks³

JVA | The Journal of
Vascular Access

The Journal of Vascular Access
2021, Vol. 22(1) 9–25
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DOI: 10.1177/1129729820916113
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The absolute risk of deep vein thrombosis was calculated to **2.3% and 3.9%** for smaller diameter peripherally inserted central catheters and centrally inserted central catheters, respectively. On average, peripherally inserted central catheter patients had 11.6 more catheter days than centrally inserted central catheter patients ($p = 0.064$).

Reconsidering the GAVeCeLT Consensus on catheter-related thrombosis, 13 years later

Fulvio Pinelli¹ , Paolo Balsorano¹ , Benedetta Mura²
and Mauro Pittiruti³ 

JVA | The Journal of
Vascular Access

The Journal of Vascular Access
2021, Vol. 22(4) 501–508
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DOI: 10.1177/1129729820947594
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**CVAD INSERTION SHOULD
REFLECT ACTUAL
CLINICAL NEEDS, WITHOUT
FEARING IATROGENIC
COMPLICATIONS**

Diagnosis

**If CRT is suspected, first step is US scan
(with or without color doppler)**

Diagnosis is easy, even without color doppler
(use **CUS = Compression UltraSonography**), and training is minimal



Treatment goals:

- Relieve the symptoms (usually within 48 hrs)
- Prevent the further growth of the thrombus
- Prevent pulmonary embolism
- Save the venous access device

Estimated risk of symptomatic CRT vs. PE

CICC 0-2 %: low risk of pulmonary embolism

DICC 0-5 %: no risk of pulmonary embolism

high risk of pulmonary embolism

Catheter should be removed in case of
Infected thrombus
Malposition of the tip
Irreversible occlusion of the lumen



Use the VAD, if it works

Start anticoagulation by LMWH 100 units/kg/12hrs

Reconsider possible removal after 7-10 days of treatment with LMWH

Catheter-Related Central Venous Thrombosis: The Development of a Nationwide Consensus Paper in Italy

*Costantino Campisi, MD, Roberto Biffi, MD, and Mauro Pittiruti, MD
on behalf of the GAVeCeLT Committee for the Consensus*

Conclusions of the Consensus

- Thrombolytic drugs should be used in acute cases (diagnosis <24 hours after the first symptoms). The efficacy of systemic versus local thrombolysis is still under debate, especially for large thrombi.
- Chronic symptomatic cases should be treated with a combination of LMWH and then oral anticoagulants, or LMWH long term alone, depending on the clinical setting. Compared with warfarin, the LMWHs exhibit a superior safety profile and more predictable antithrombotic effects and can usually be given once daily in a unit dose without the need for dose monitoring

**Only if
CRT is at the tip,
CRT onset is esteemed to be
very recent (< 24 hrs)**



Central venous access in oncology: ESMO Clinical Practice Guidelines[†]

B. Sousa¹, I. Furlanetto², M. Hutke³, P. Gouveia¹, R. Wuerstlein⁴, I. M. Meriz⁵, D. Pinto¹ &

F. Cardoso
Catheter-related thrombosis —treatment

[†]Breast Unit,
NHS Foundat
Instituto Portu

- Anticoagulation therapy with LMWH is the preferred treatment, as it is more effective in preventing thrombosis and has less risk for bleeding compared with VKA [II, A]
- If the catheter is functional and there are no risks for complications, or severe/rapid progressive symptoms, anticoagulation treatment should be continued for the time length of time the catheter is in use [III, C]
- If the CVC is not necessary or non-functioning, or there is concomitant deep vein thrombosis, sepsis, or if long-term anticoagulation is contraindicated, a short course (3–5 days) of anticoagulation therapy is recommended and then the catheter should be removed [I, A]
- LMWH alone or LMWH followed by warfarin should be used for a minimum of 3–6 months [I, C]
- It is recommended to continue anticoagulation therapy at a prophylactic dose, until the catheter is in place [I, C]
- Thrombolytic (urokinase, streptokinase and alteplase) treatment is not recommended as a first-line therapy, due to a greater risk of thrombosis [I, B]

Unanswered issues

- How to manage asymptomatic/incidental thrombosis?
- Is it useful to perform Doppler ultrasound before any CVC removal?
- Prophylaxis in high-risk patients?
- Duration of treatment?
- Any role for the use of oral anticoagulants?



Unanswered issues

- How to manage asymptomatic/incidental thrombosis?
- Is it useful to perform Doppler ultrasound before any CVC removal?
- Prophylaxis in high-risk patients?
- Duration of treatment?
- Any role for the use of direct oral anticoagulants?



asymptomatic-CRT

My suggestion is:

- Evaluation by a VAD expert
- Close follow-up for patients at low risk of progression
- Short treatment period for patients at high risk of progression

THROMBOSIS AND HEMOSTASIS

CME Article

The natural history of asymptomatic central venous catheter-related thrombosis in critically ill children

Sophie Jones,¹⁻⁴ Warwick Butt,^{1,5} Paul Monagle,¹⁻³ Timothy Cain,⁶ and Fiona Newall^{1-4,7}

Ultrasounds of 146 children determined a 21.9% incidence of acute CVC-related thrombosis. Two children were symptomatic.

No radiological thrombosis extension or clinical embolization occurred at 2 year follow-up.



Oral anticoagulants?

	CLOT Trial ⁸	CATCH Trial ⁹
Number of Patients	676	900
Study Design	Open-label, multicenter, RCT	Open-label, multicenter, RCT
LMWH Preparation*	Dalteparin	Tinzaparin
Mean Age	62 years dalteparin/63 years warfarin	59.7 years dalteparin/58.8 years warfarin
Tumor Types		
Breast	16%	9%
Colorectal	16%	13%
Lung	13%	12%
Genitourinary tract	13%	10%
Gynecologic system	10%	23%
Hematologic	10%	10%

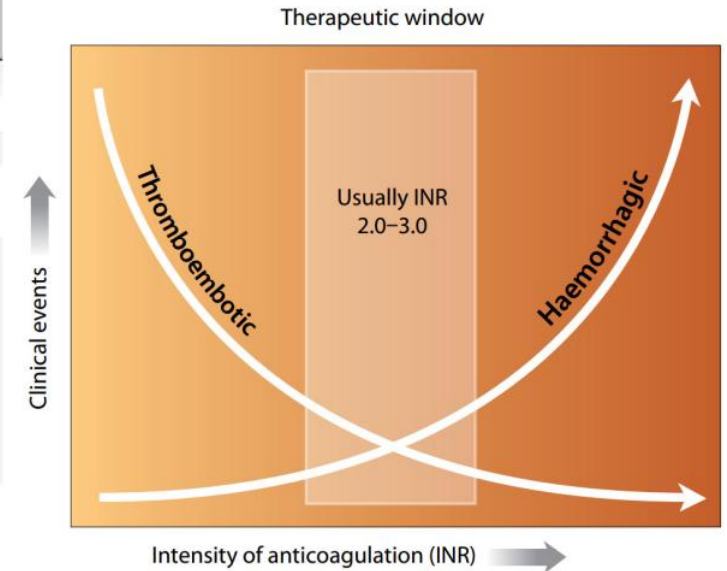
Eastern Cooperative Oncology Group Score**

0-1
2

Active Cancer Treatment***

Metastatic Disease
Time in Therapeutic Range (Warfarin Arm)

	CLOT Trial ⁸		CATCH Trial ⁹	
	Dalteparin	Warfarin	Tinzaparin	Warfarin
Symptomatic VTE	7.9%	15.7%	6.9%	10%
Symptomatic DVT	4.1%	10.9%	2.7%	5.3%
Non-Fatal PE	2.4%	2.7%	0.7%	0.4%
Fatal PE	1.5%	2.1%	3.8%	3.8%
Major Bleeding	6.0%	4.0%	2.7%	2.4%
Death	39.0%	41.0%	33.4%	30.6%

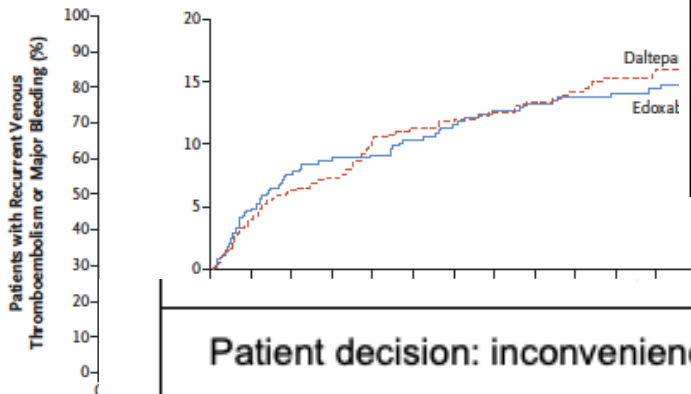


Any role for the use of direct oral anticoagulants?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism



No. at Risk	522	472	429	407	388	360	345	328	310	295	270	237	161
Edoxaban	522	472	429	407	388	360	345	328	310	295	270	237	161
Dalteparin	524	485	449	420	385	364	352	340	324	313	276	241	171

	Edoxaban (N=522)	Dalteparin (N=524)
LMWH lead-in days – median (IQR)	5.0 (5-6)	-
Drug exposure days - median (IQR)	211 (16-357)*	184 (15-341)*
<3 months – no. (%)	139 (26.6)	137 (26.1)
3 months to ≤6 months – no. (%)	80 (15.3)	102 (19.5)
>6 months – no (%)	303 (58.0)	285 (54.4)
Completed treatment for 12 months or until study closure	200 (38.3)	154 (29.4)

Patient decision: inconvenience of dosing

21 (4.0)

78 (14.9)



A Single Center Retrospective Cohort Study Comparing Different Anticoagulants for the Treatment of Catheter-Related Thrombosis of the Upper Extremities in Women With Gynecologic and Breast Cancer

Angelo Porfidia^{1,2}, Giulia Cammà^{1,2}, Nicola Coletta^{1,2}, Margherita Pizzocci^{2,3}, Igor Giarretta¹, Andrea Lupascu^{1,2}, Giuseppe Scaletta^{2,4}, Enrica Pizzocci^{2,3}, Paolo Tondi^{2,5}, Giovanni Scambia^{2,4}, Gabriella Ferrandina^{2,4} and Rocco Giarretta^{1,2}

**Oral direct
anticoagulants?**

	Edoxaban (n = 22)	Enoxaparin (n = 21)	Fondaparinux (n = 31)	P
Residual thrombosis, n (%)	1 (4.5)	1 (4.8)	5 (16.0)	0.25
Preservation of line function, n (%)	22 (100.0)	21 (100.0)	31 (100.0)	na
Recurrent VTE, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	na
MB, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	na
CRNMB, n (%)	0 (0.0)	2 (9.5)	1 (3.2)	0.27
Death, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	na

CRNMB, clinically relevant non-major bleeding; MB, major bleeding; na, not available; VTE, venous thromboembolism.

CRT-Take home messages (1)

- **Catheter removal is not indicated, if the catheter...**
 - is still useful
 - is still well functioning
 - its tip is properly located
 - is not infected
- **Indications for catheter removal are:**
 - Local symptoms worsening during treatment
 - Catheter not useful and/or malpositioned and/or infected and/or malfunctioning
- **Catheter removal should be performed:**
 - After at least 72h of treatment (PICCs and PICC-ports)
 - After at least one week of treatment (CICCs, FICCs, chest-ports)
 - Under US control



Take home messages (2)

- CRT is a pathophysiological phenomenon, quite inevitable during any venous access procedure
- VAD experts can reduce CRT incidence by following existing protocols
- Only symptomatic CRT is clinically relevant and should be treated
- Asymptomatic CRT may be managed by close follow-up in low risk patients
- The main treatment for CRT is LMWH for at least 3 months, however DOAC appears to have similar efficacy and safety with higher patient compliance





**Scuola SIUMB avanzata di ecocolorDoppler
Ospedale di circolo e Fondazione Macchi
Varese**

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