

Gemelli



Fondazione Policlinico Universitario A. Gemelli
Università Cattolica del Sacro Cuore

COME DISTINGUERE TRA GUAINA FIBROBLASTICA E TROMBOSI

MAURO PITTIRUTI



GAVePed
Gruppo Accessi Venosi Pediatrici



DUE CONSEGUENZE INEVITABILI DEI DISPOSITIVI INTRAVASCOLARI

Guaina fibroblastica (FS)

- Si verifica nel 100% dei casi
- È evidente ecograficamente nel 20-40% dei casi
- Può essere associata al malfunzionamento del catetere in <1%.

Trombosi correlata al catetere (CRT)

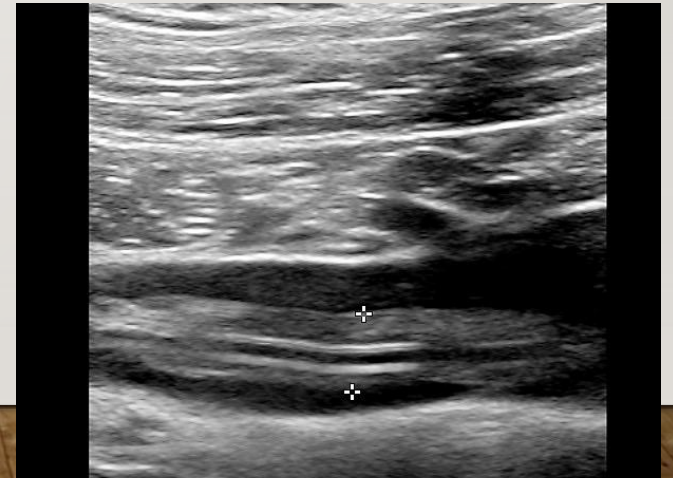
- Si verifica nel 100% dei casi
- È asintomatica ma evidente ecograficamente nel 5-10% dei casi
- Diventa sintomatica in < 5%



DUE CONSEGUENZE INEVITABILI DEI DISPOSITIVI INTRAVASCOLARI

La guaina fibroblastica (FS)

- Inevitabile (catetere = corpo estraneo)
- Ignoriamo perché in alcuni dispositivi o in alcuni pazienti è più rilevante
- Possiamo prevenirla? **NO**



DUE CONSEGUENZE INEVITABILI DEI DISPOSITIVI INTRAVASCOLARI

Trombosi correlata al catetere (CRT)

- Inevitabile (inserimento del catetere = lesione della parete della vena).
- Ignoriamo perché in alcuni dispositivi o in alcuni pazienti la CRT è più rilevante e diventa sintomatica.
- Possiamo prevenirla? **FORSE, IN PARTE, A VOLTE....**



FS VS. CRT

Cosa hanno in comune?

- Il loro sviluppo è innescato dall'inserimento del catetere
- Si sviluppano molto presto, nelle prime ore/giorni dopo l'inserimento
- Ignoriamo il motivo per cui rimangono non rilevabili nella maggior parte dei casi, ma diventano evidenti all'ecografia (e anche clinicamente) in altri casi



FS VS. CRT

Non hanno nient'altro in comune!

FS = un tessuto connettivo (fibroblasti, cellule muscolari lisce, collagene) che avvolge lentamente il catetere

CRT = un tessuto di riparazione in rapida crescita (trombo) innescato da un danno endoteliale



The fibroblastic sleeve, the neglected complication of venous access devices: A narrative review

Giovanna Passaro , **Mauro Pittiruti**  and **Antonio La Greca**

Abstract

The presence of a vascular access device (or of any intravascular foreign body) inside the bloodstream is often associated with the formation of a connective tissue sleeve around the catheter (often named—erroneously—“fibrin sleeve”). Such sleeve is usually a physiological phenomenon with little or no clinical relevance, but its pathogenesis is still unclear, so that it is frequently confused with venous thrombosis; also, its relationship with other major catheter-related complications, such as venous thrombosis and bloodstream infection, is uncertain. This narrative review tries to convey in a systematic form the current knowledge about pathogenesis, incidence, clinical manifestations, diagnosis, and management of this phenomenon.

The Journal of Vascular Access

1–13

© The Author(s) 2020

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/1129729820951035

journals.sagepub.com/home/jva



CRT VS. FS

Table 3. Main differences between catheter-related thrombosis (CRT) and fibroblastic sleeve (FS).

	CRT	FS
Etiopathogenesis	Endothelial damage	Foreign body reaction
Molecular trigger	Tissue thromboplastin	Fibronectin
Type of tissue	Thrombus	Connective tissue
Location	At the site of vein wall damage	Around the catheter
Evolution	Fibrosis/reabsorption	Reabsorption (?)
US imaging	Mass obstructing the vein Anechoic, and then hypo-echoic Mainly attached to the vein wall	Sleeve all around the catheter Hypo- or hyper-echoic Mainly attached to the catheter
Clinical manifestation	Signs and symptoms of venous obstruction + risk of catheter malfunction	Catheter malfunction
Risk of pulmonary embolism	Yes	No
Need for VAD removal	Rare (not responsive to therapy)	Rare (irreversible catheter malfunction)
Preventable with anticoagulants	Yes (not consistently)	No
Sensitive to thrombolysis	Yes (in the initial phase)	No
Pharmacological management	LMW heparin	None

CRT VS. FS

Table 3. Main differences between catheter-related thrombosis (CRT) and fibroblastic sleeve (FS).

	CRT	FS
Etiopathogenesis	Endothelial damage	Foreign body reaction
Molecular trigger	Tissue thromboplastin	Fibronectin
Type of tissue	Thrombus	Connective tissue
Location	At the site of vein wall damage	Around the catheter
Evolution	Fibrosis/reabsorption	Reabsorption (?)
US imaging	Mass obstructing the vein Anechoic, and then hypo-echoic Mainly attached to the vein wall	Sleeve all around the catheter Hypo- or hyper-echoic Mainly attached to the catheter
Clinical manifestation	Signs and symptoms of venous obstruction + risk of catheter malfunction	Catheter malfunction
Risk of pulmonary embolism	Yes	No
Need for VAD removal	Rare (not responsive to therapy)	Rare (irreversible catheter malfunction)
Preventable with anticoagulants	Yes (not consistently)	No
Sensitive to thrombolysis	Yes (in the initial phase)	No
Pharmacological management	LMW heparin	None

CRT VS. FS

Table 3. Main differences between catheter-related thrombosis (CRT) and fibroblastic sleeve (FS).

	CRT	FS
Etiopathogenesis	Endothelial damage	Foreign body reaction
Molecular trigger	Tissue thromboplastin	Fibronectin
Type of tissue	Thrombus	Connective tissue
Location	At the site of vein wall damage	Around the catheter
Evolution	Fibrosis/reabsorption	Reabsorption (?)
US imaging	Mass obstructing the vein Anechoic, and then hypo-echoic Mainly attached to the vein wall	Sleeve all around the catheter Hypo- or hyper-echoic Mainly attached to the catheter
Clinical manifestation	Signs and symptoms of venous obstruction + risk of catheter malfunction	Catheter malfunction
Risk of pulmonary embolism	Yes	No
Need for VAD removal	Rare (not responsive to therapy)	Rare (irreversible catheter malfunction)
Preventable with anticoagulants	Yes (not consistently)	No
Sensitive to thrombolysis	Yes (in the initial phase)	No
Pharmacological management	LMW heparin	None

CRT VS. FS

Table 3. Main differences between catheter-related thrombosis (CRT) and fibroblastic sleeve (FS).

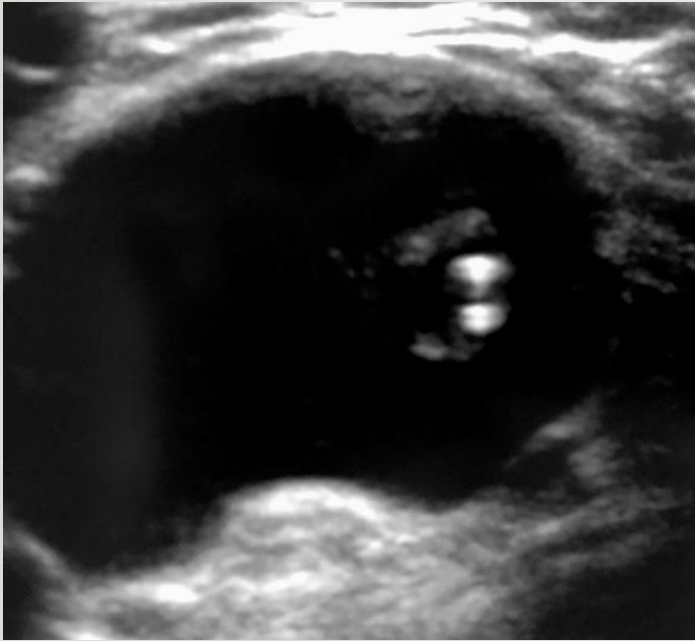
	CRT	FS
Etiopathogenesis	Endothelial damage	Foreign body reaction
Molecular trigger	Tissue thromboplastin	Fibronectin
Type of tissue	Thrombus	Connective tissue
Location	At the site of vein wall damage	Around the catheter
Evolution	Fibrosis/reabsorption	Reabsorption (?)
US imaging	Mass obstructing the vein Anechoic, and then hypo-echoic Mainly attached to the vein wall	Sleeve all around the catheter Hypo- or hyper-echoic Mainly attached to the catheter
Clinical manifestation	Signs and symptoms of venous obstruction + risk of catheter malfunction	Catheter malfunction
Risk of pulmonary embolism	Yes	No
Need for VAD removal	Rare (not responsive to therapy)	Rare (irreversible catheter malfunction)
Preventable with anticoagulants	Yes (not consistently)	No
Sensitive to thrombolysis	Yes (in the initial phase)	No
Pharmacological management	LMW heparin	None

IL PROBLEMA PRINCIPALE

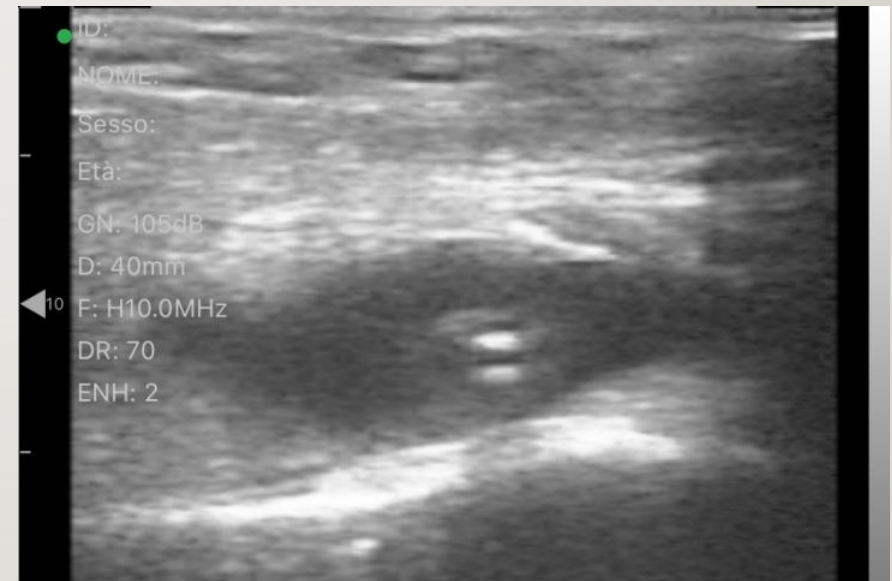
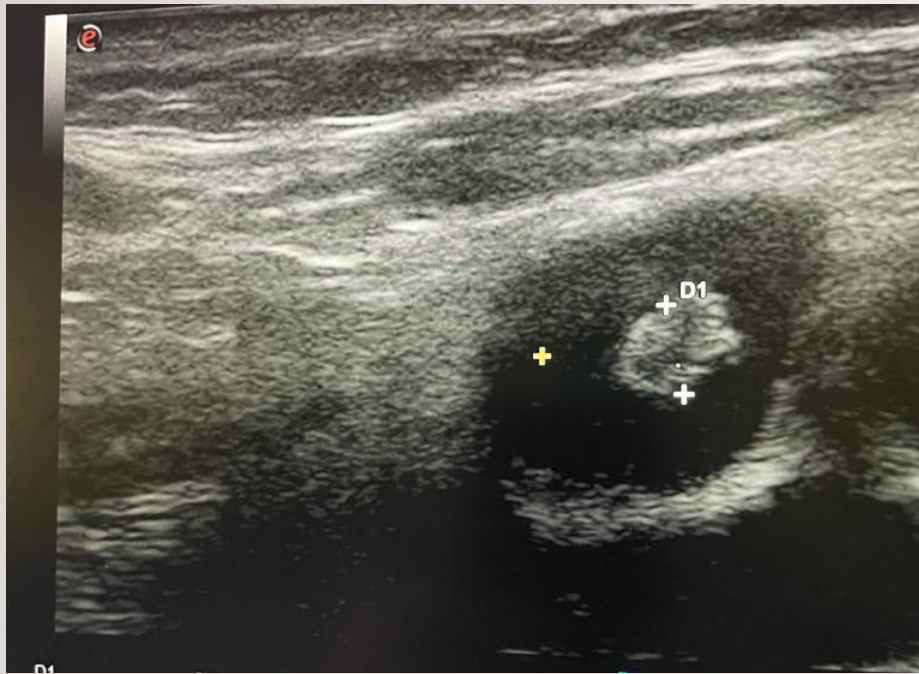
**La FS viene sistematicamente
confuso con la CRT!**



CRT? NO, FS!!!



CRT? NO, FS!!!



LA STORIA DELLA GUAINA INIZIA CON UN'INTERPRETAZIONE ERRATA

I primi studi degli anni '70 identificano questa "guaina" o "manicotto" intorno al catetere venoso e la chiamano 'manicotto di fibrina' (*fibrin sleeve*) o 'guaina di fibrina' (*fibrin sheath*) senza alcuna evidenza istochimica della presenza di "fibrina".



Fibrin Sleeve Formation on Indwelling Subclavian Central Venous Catheters

Verne L. Hoshal, Jr., MD;

Arch Surg/Vol 102, April 1971

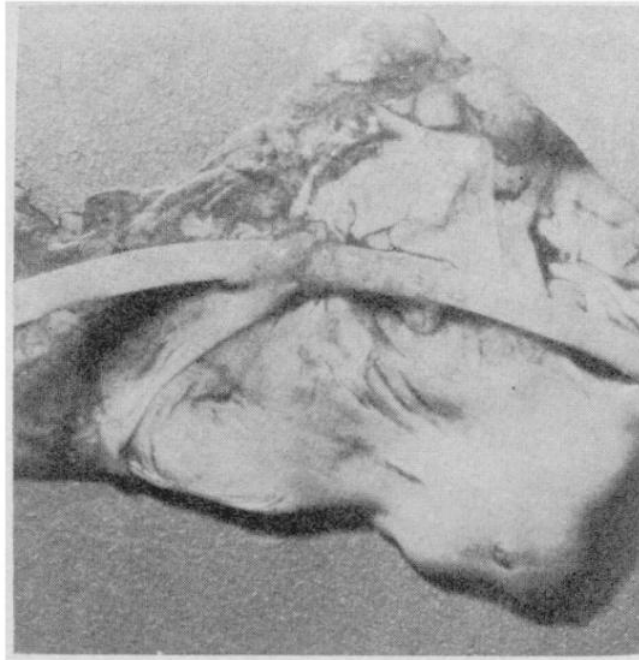


Fig 1.—A 1.5-cm fibrin sleeve encompasses proximal portion of Teflon catheter indwelling only 24 hours in subclavian vein.

Fig 2.—Left clavicle is elevated exposing subclavian, internal jugular, and innominate veins. Probe is positioned in folded-up fibrin sleeve which developed around and to tip of polyethylene catheter indwelling for ten days.



Histologic Development of the Sheath That Forms Around Long-Term Implanted Central Venous Catheters

LAURA O'FARRELL, DVM, PhD; JAMES W. GRIFFITH, DVM; AND C. MAX LANG, DVM

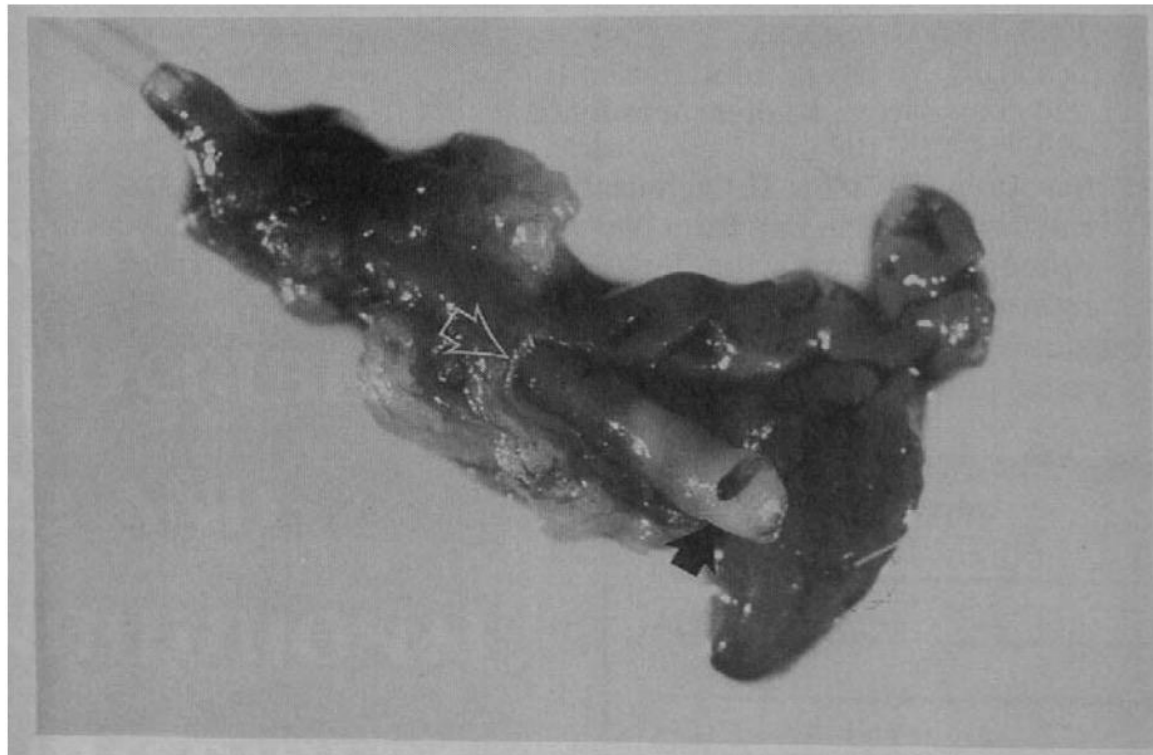


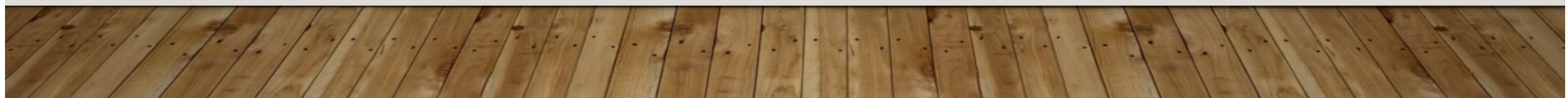
FIG. 2. A white sheath surrounds the catheter (solid arrow) and blocks the tip 8 weeks after implantation. The open arrow indicates the vein wall.

ALLA FINE DEL XX SECOLO...

Nel 1998, Stas e collaboratori (Università di Lovanio, Belgio) studiano seriamente la "guaina" e scoprono che il manicotto è un tessuto connettivo con una componente cellulare (fibroblasti e cellule muscolari lisce) e una componente acellulare (collagene).

Niente fibrina!

1998





Università Cattolica di Lovanio (Belgio)

Composition and formation of the sleeve enveloping a central venous catheter

D.Z. Xiang, MD, E.K. Verbeken, MD, PhD, A.T.L. Van Lommel, PhD, M. Stas, MD, and I. De Wever, MD, PhD, *Leuven, Belgium*

1998

Conclusion: The sleeve around a central venous catheter is not a fibrin sleeve, but a stable cellular-collagen tissue covered by endothelium. It is mainly formed by smooth muscle cells migrating from the injured vein wall into the early pericatheter thrombus. (J Vasc Surg 1998;28:260-271.)

Composition and formation of the sleeve enveloping a central venous catheter

D.Z. Xiang, MD, E.K. Verbeken, MD, PhD, A.T.L. Van Lommel, PhD, M. Stas, MD, and I. De Wever, MD, PhD, *Leuven, Belgium*

Purpose: After catheterization, 42% to 100% of central venous catheters are surrounded by a “fibrin sleeve.” This sleeve has been considered the cause of catheter-related infections, withdrawal occlusion, and pulmonary embolism. The reactions between the vein wall and the catheter were studied.

Methods: A silicone catheter was placed in the anterior caval vein of 123 rats. After in situ fixation at scheduled intervals, the pathologic changes were studied on semi-serial histologic sections by means of light microscopy, transmission electron microscopy, and scanning electron microscopy (SEM). In 36 rats, the catheter was withdrawn immediately; in 72 rats, it was left in situ up to 6 months; and in 15 rats, the study was performed up to 10 months after withdrawal of a catheter that had remained in situ for 6 months.

Results: In the group in which the catheter was withdrawn immediately, mural thrombi disappeared by day 7. In the group in which the catheter remained in situ, thrombi remained around the proximal portion of the catheter. This pericatheter thrombosis (PCT) was invaded by migrating and proliferating smooth muscle cells (SMCs), originating from an injured vein wall, and transformed from day 7 into a tissue composed predominantly of SMCs and collagen and covered by endothelial cells. Later, the number of cells decreased, and the relative amount of collagen increased. Up to 10 months after withdrawal of the catheter, the collapsed sleeve was still present within the vein.

Conclusion: The sleeve around a central venous catheter is not a fibrin sleeve, but a stable cellular-collagen tissue covered by endothelium. It is mainly formed by smooth muscle cells migrating from the injured vein wall into the early pericatheter thrombus. (J Vasc Surg 1998;28:260-271.)

1998

1998

Xiang et al

JOURNAL OF VASCULAR SURGERY
August 1998

Table I. Overview of sleeve formation

Interval	Pathological process	Proposed terms
Day 1-3	A thrombus is formed between the injured vein wall and the catheter. SMCs in injured vein wall modulate their phenotype from contractile to synthetic.	Pericatheter thrombus
Weeks 1-2	Pericatheter thrombus transforms to a tissue: catheter sleeve, composed mainly of synthetic phenotype SMCs and collagen, covered by endothelial cells.	
Weeks 3-4	Synthetic phenotype SMCs are reverting to a contractile phenotype. A spectrum of phenotypes of SMCs is present.	Catheter sleeve
Month 2	The number of SMCs decreases, and the relative volume of collagen increases. SMCs are only of the contractile phenotype.	
Months 4-6	<u>Collagen is the major component of the sleeve.</u>	
10 months after catheter withdrawal	The sleeve is still present as a collapsed structure adherent to the vein wall.	Sleeve remnant

SMCs, smooth muscle cells.

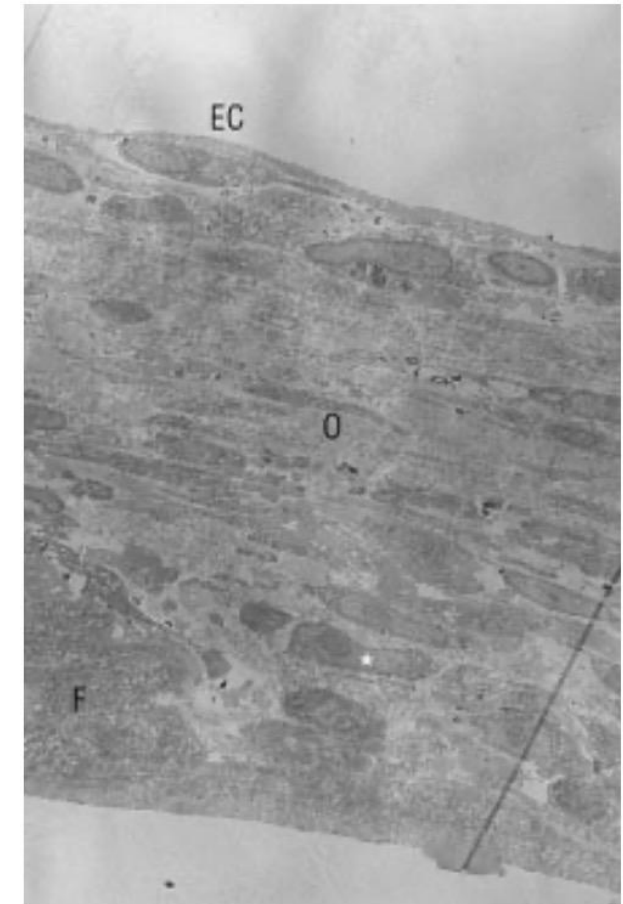


Fig. 6. Day 7: This overview picture of the sleeve shows a layer of endothelial cells (EC) at the luminal side, several layers of smooth muscle cells of the synthetic phenotype (star) with collagen (O) in between, and still some fibrin (F) at the catheter side(TEM, 1440×).

MA È TROPPO TARDI!

- Tutti lo chiamano "manicotto di fibrina"....
- Il termine "fibrina" suggerisce una relazione con la formazione del trombo....
-La maggior parte dei documenti dei primi due decenni del XXI secolo confondono quindi la FS con la CRT.



NON É FIBRINA!

- Il FS è un tessuto connettivo ricoperto da endotelio, che avvolge (in modo piuttosto irregolare) il catetere venoso.
- Possono esserci dei "ponti" che collegano il manicotto con la parete della vena, ma il FS non è aderente alla parete.

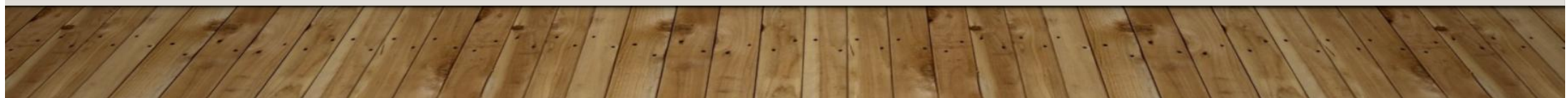
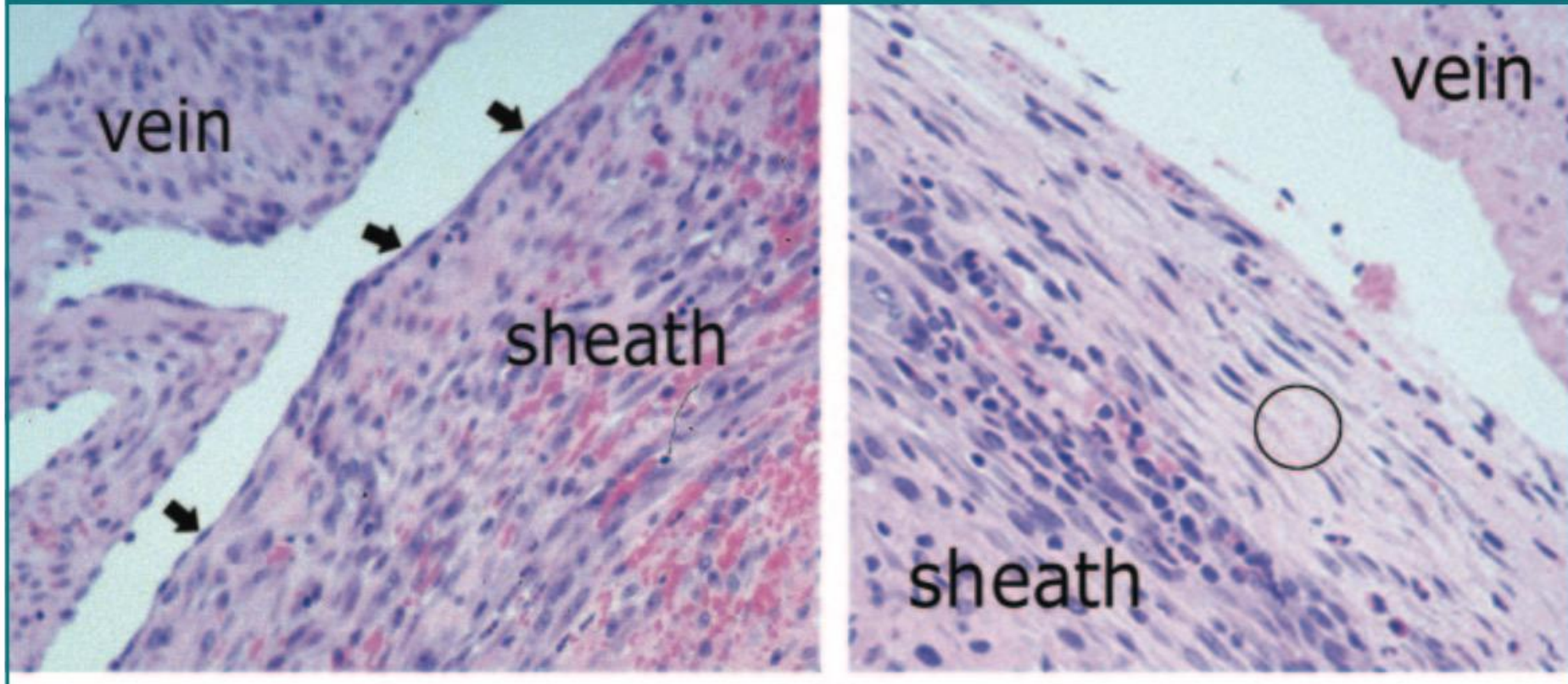
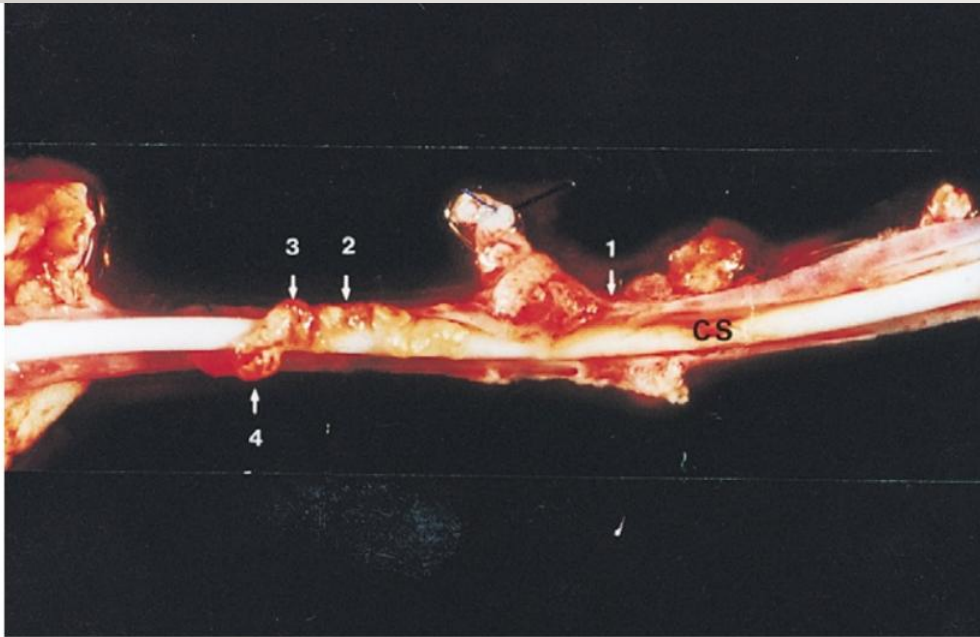


Figure 2



- Forauer AR, Theoharis CGA and Dasika NL. Jugular vein catheter placement: histologic features and development of catheter-related (Fibrin) sheaths in a Swine model. *Radiology* 2006; 240(2): 427–434.



Xiang et al. / *Thromb. Res.* 2001



Passaro et al. / *JVA* 2021

Figure 3

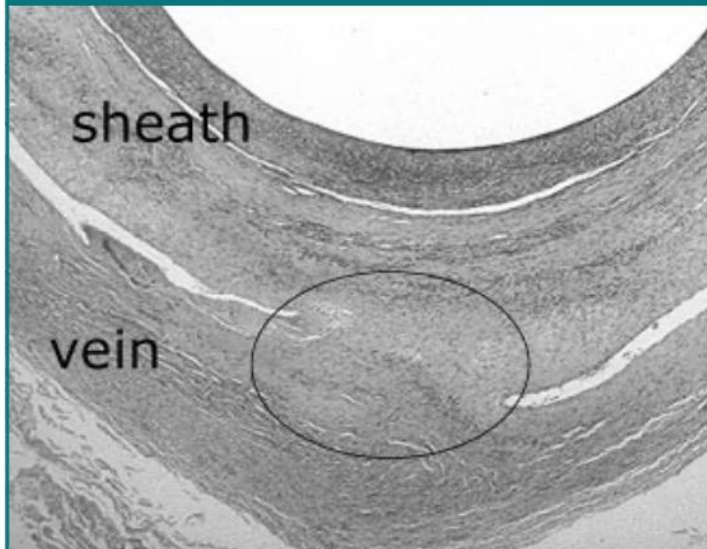


Figure 3: Photomicrograph shows bridge from vein wall to sheath (oval) in 45-day specimen. The connection contains smooth muscle cells and collagen and is covered by endothelial cells that are continuous with the adjacent vein wall. (Hematoxylin-eosin stain; original magnification, $\times 25$.)

Figure 4

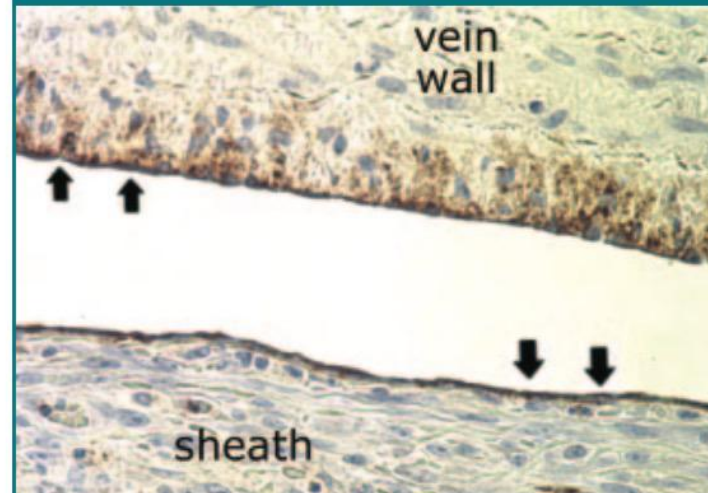
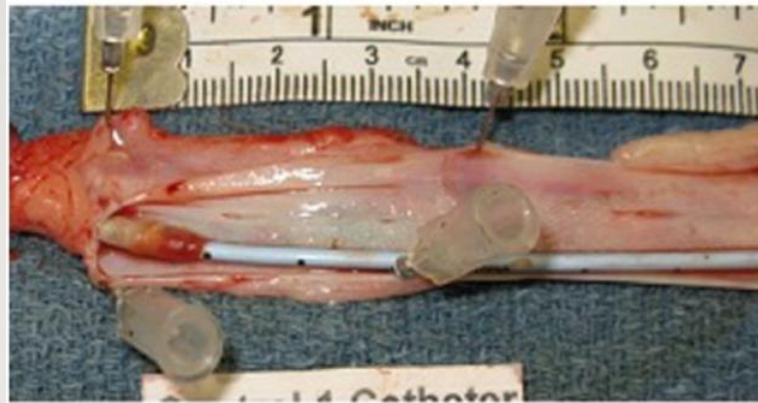
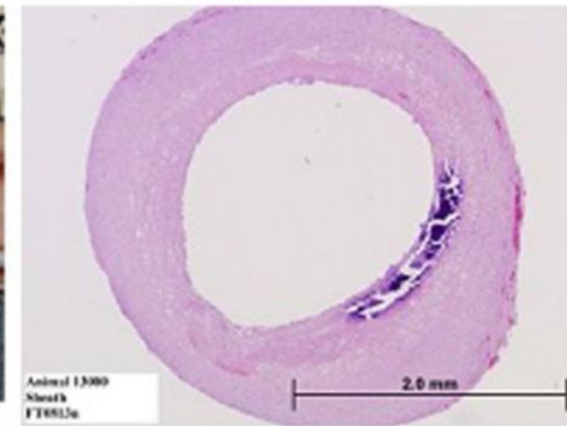


Figure 4: Photomicrograph in 14-day specimen. von Willebrand factor–positive cells stain dark brown. The single-cell-thick endothelial layer (arrows) stains positive on both the luminal surface of the sheath and adjacent vein wall. (Anti–von Willebrand factor stain 1:500; original magnification, $\times 200$.)



(a)



(b)



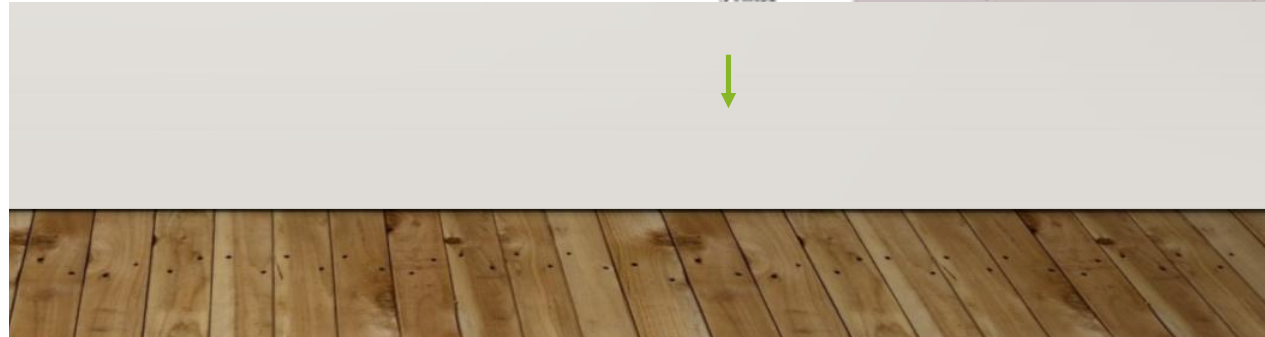
Original research article

Chlorhexidine-coated peripherally inserted central catheters reduce fibroblastic sleeve formation in an in vivo ovine model

Charles J Sylvia Jr¹, Molly A Wagel², Kamna Giare-Patel², Taylor A Spangler³, Eugene M Breznock¹ and Nisha Gupta²

JVA The Journal of
Vascular Access

The Journal of Vascular Access
1-7
© The Author(s) 2018
Reprints and permissions:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/1129729818769033
journals.sagepub.com/home/jva
SAGE



INCIDENZA DI CRT E FS

- All'esame ecografico, la **FS** è molto più frequente della **CRT**
- All'esame ecografico, la **CRT asintomatica** è molto più comune della **CRT sintomatica**
- All'esame ecografico, l'esistenza simultanea di **FS** e **CRT** è un evento raro



INCIDENZA DI CRT & FS

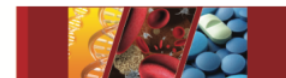
Table 2. Main studies on correlation between fibroblastic sleeve and catheter-related thrombosis.

Author	Diagnosis	Catheter type	FS incidence (%)	CRT incidence
Brismar et al. ³⁰	Venography	CVC for parental nutrition	42	8%
Raad et al. ⁷	Postmortem examination	Non-tunneled CVC	100	38%
Oguzkurt et al. ¹⁴	Venography	Short-term dialysis catheters	56	28%
Alomari and Falk ⁴⁸	Venography	Tunneled dialysis catheters	76	24% of FS

Passaro et al. / JVA 2021

BODDI ET AL., 2015

European Journal of
Haematology



European Journal of Haematology 95 (472–479)

ORIGINAL ARTICLE

Incidence of ultrasound-detected asymptomatic long-term central vein catheter-related thrombosis and fibrin sheath in cancer patients

Maria Boddi¹, Gianluca Villa², Marco Chiostrì¹, Francesco De Antoniis¹, Ilaria De Fanti²,
Alessandra Spinelli¹, Andrea Savino¹, Gian Franco Gensini^{1,3}, Cecilia Pelagatti²

¹Department of Experimental and Clinical Medicine, Careggi Teaching Hospital, Florence; ²Section of Anesthesia and Intensive Care, Department of Human Health Science, Careggi Teaching Hospital, Florence; ³Don Carlo Gnocchi Foundation, IRCCS, Florence, Italy

TREZZA ET AL., 2020

Original research article

JVA

The Journal of
Vascular Access

Incidence of fibroblastic sleeve and of catheter-related venous thrombosis in peripherally inserted central catheters: A prospective study on oncological and hematological patients

**Carmela Trezza¹, Catello Califano², Vincenzo Iovino³,
Carmela D'Ambrosio¹, Giuseppe Grimaldi⁴ and Mauro Pittiruti⁵ **

The Journal of Vascular Access
1–6

© The Author(s) 2020

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/1129729820949411

journals.sagepub.com/home/jva

 SAGE

INCIDENZA DI CRT & FS

		FS	CRT sintomatica	CRT asintomatica	CRT + FS
Boddi 2015	400 CICC	12.8%	0	1.25%	0
Trezza 2020	254 PICC	29.9%	0.39%	5.12%	0.78%

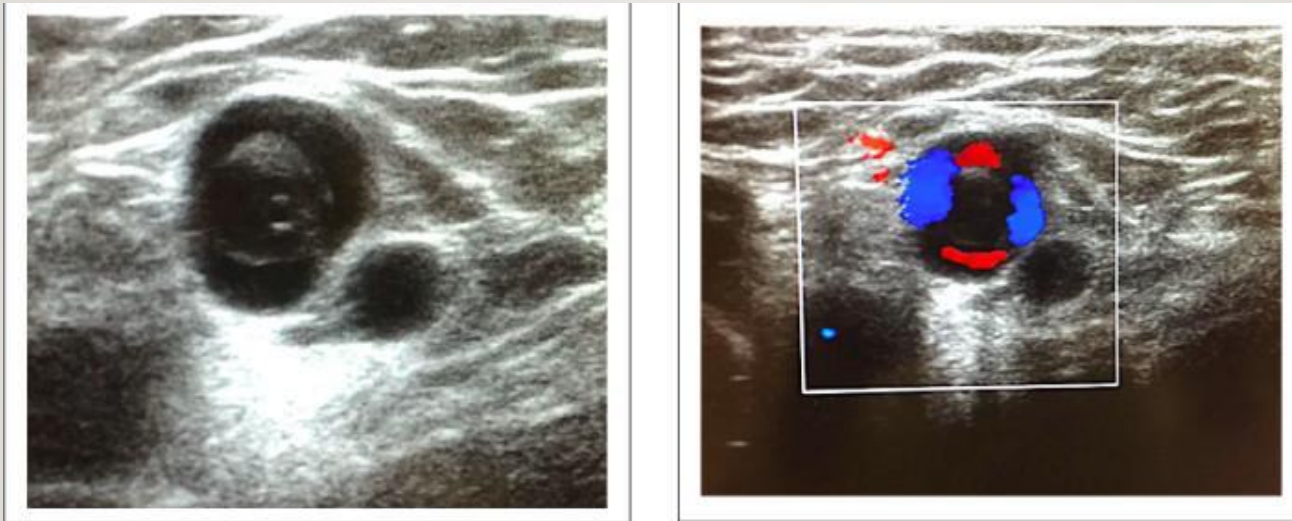
CRT VS. FS

Spesso il FS viene erroneamente interpretato come CRT asintomatica all'ecografia o alla TC, esponendo il bambino ai rischi di un trattamento anticoagulante non necessario.



Molti operatori che utilizzano comunemente la ecografia per la diagnosi delle complicanze legate al catetere adottano ancora il termine "trombosi peri-catetere" quando vedono materiale ecogeno intorno al catetere.

La stragrande maggioranza di queste immagini interpretate come "trombosi peri-catetere" - soprattutto se asintomatiche - sono in realtà guaine fibroblastiche.



DIAGNOSI DIFFERENZIALE DI FS VS. CRT

- Compression Ultrasonography (CUS)
- Rapporto spaziale con il catetere
- Rapporto con la parete della vena (ponti)
- Ecogenicità
- Spessore/lunghezza
- Imaging con color-doppler



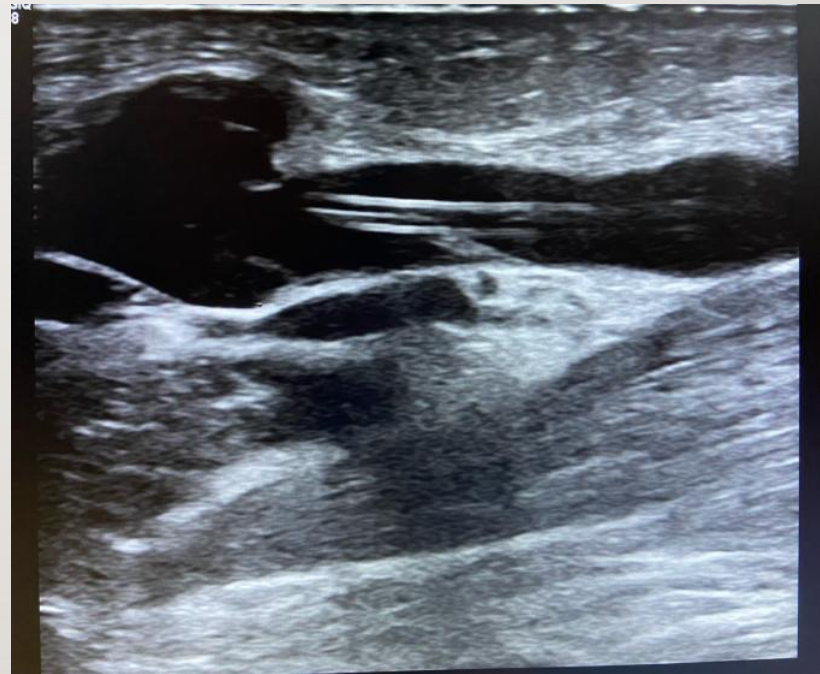
CUS



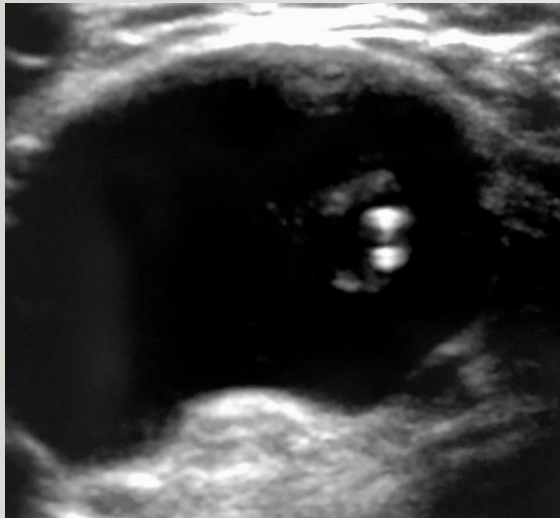
RAPPORTO SPAZIALE CON IL CATETERE



RAPPORTO CON LA PARETE DELLA VENA (PONTI)



ECOGENICITÀ



ipo



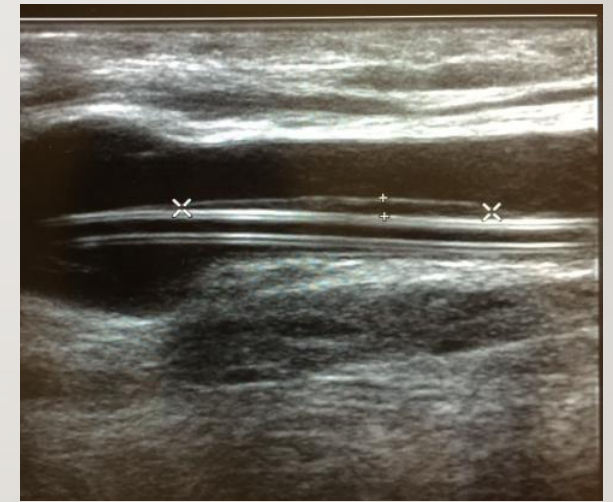
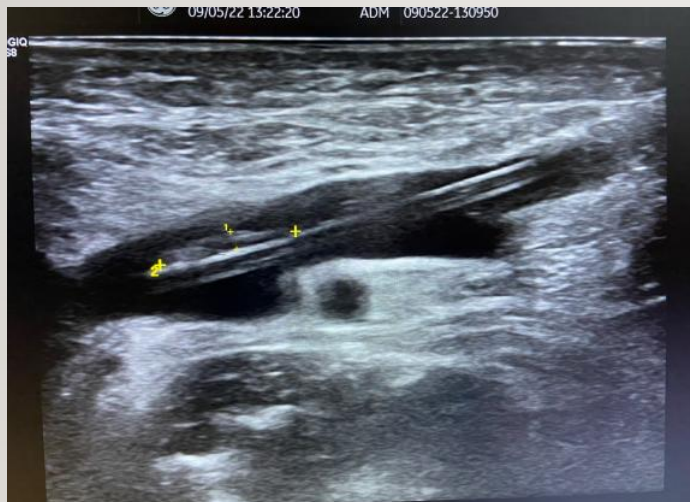
iper



iper

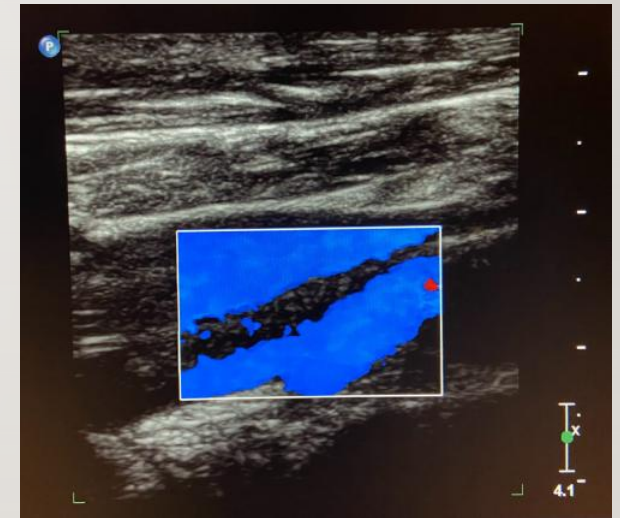


SPESSORE/LUNGHEZZA



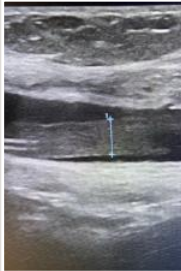
Spessore: 1 – 3 mm
Lunghezza: variabile

COLOR-DOPPLER

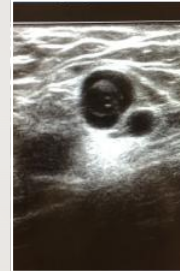


Ring sign

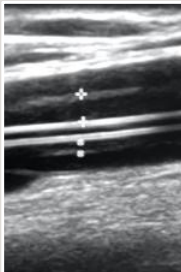
DIAGNOSI DI GUAINA FIBROBLASTICA



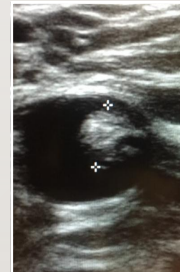
Ecostruttura
omogenea



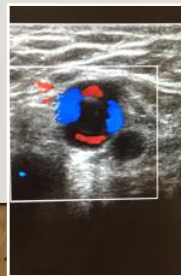
Superficie regolare



spessore 1-3 mm



Ecogenicità
variabile



color – «ring sign»

Per evitare trattamenti antitrombotici inutili e potenzialmente pericolosi, è necessario essere in grado di differenziare la FS dalla CRT asintomatica.

Table 3. Main differences between catheter-related thrombosis (CRT) and fibroblastic sleeve (FS).

	CRT	FS
Etiopathogenesis	Endothelial damage	Foreign body reaction
Molecular trigger	Tissue thromboplastin	Fibronectin
Type of tissue	Thrombus	Connective tissue
Location	At the site of vein wall damage	Around the catheter
Evolution	Fibrosis/absorption	Reabsorption (?)
US imaging	Mass obstructing the vein Anechoic, and then hypo-echoic Mainly attached to the vein wall	Sleeve all around the catheter Hypo- or hyper-echoic Mainly attached to the catheter
Clinical manifestation	Signs and symptoms of venous obstruction + risk of catheter malfunction	Catheter malfunction
Risk of pulmonary embolism	Yes	No
Need for VAD removal	Rare (not responsive to therapy)	Rare (irreversible catheter malfunction)
Preventable with anticoagulants	Yes (not consistently)	No
Sensitive to thrombolysis	Yes (in the initial phase)	No
Pharmacological management	LMW heparin	None

E NON È TUTTO...

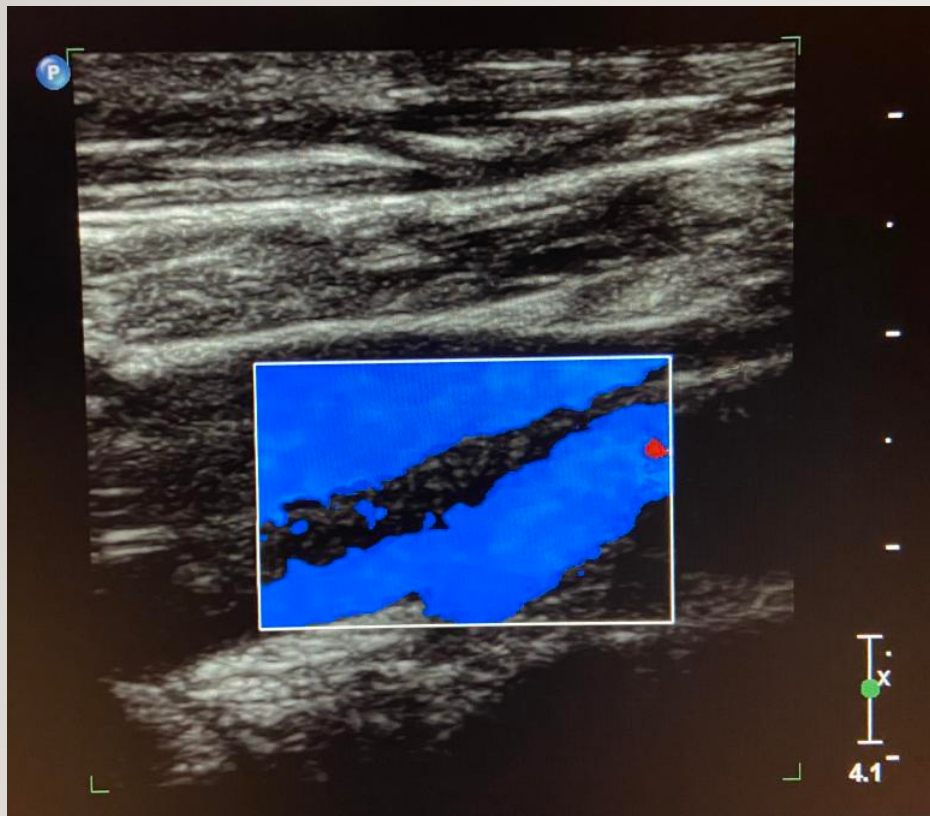
- La guaina può rimanere all'interno dei vasi per un tempo prolungato dopo la rimozione del catetere (il cosiddetto "fantasma del catetere").
- Ebbene, questa guaina residua viene sistematicamente interpretata erroneamente come CRT!



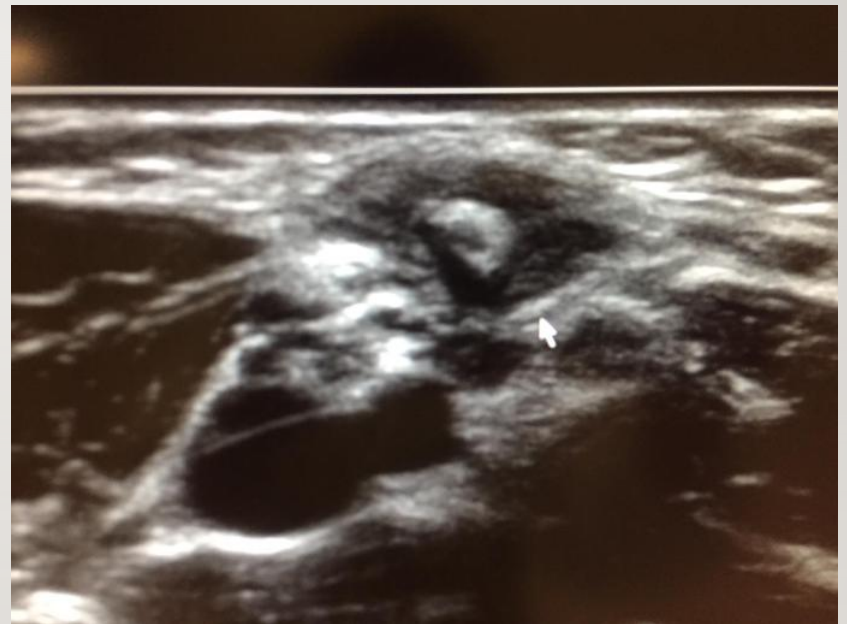
THE GHOST



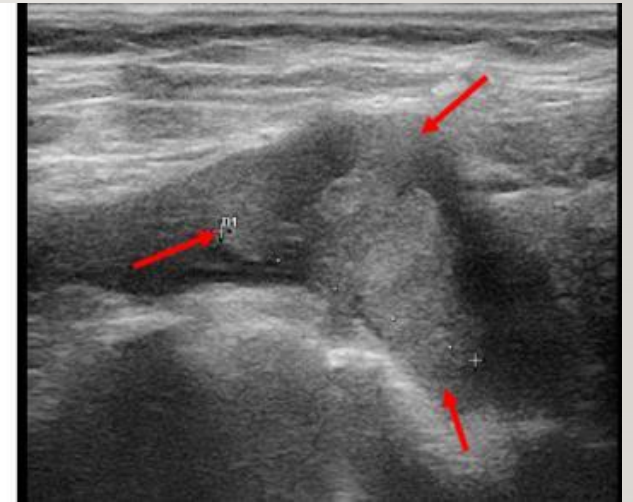
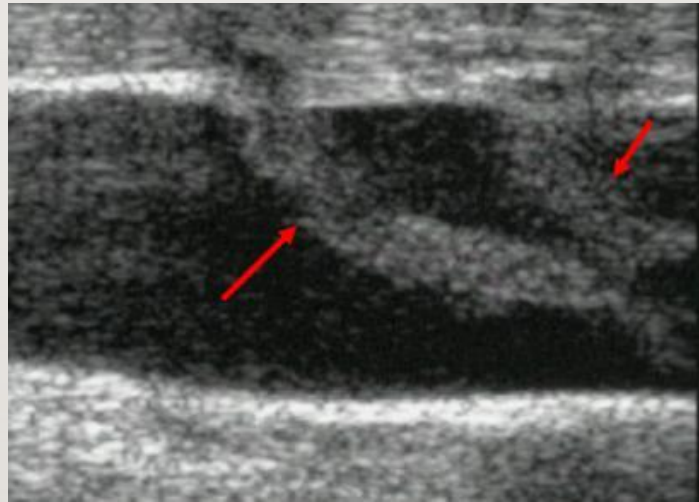
THE GHOST



THE GHOST



THE GHOST



TAKE HOME MESSAGE

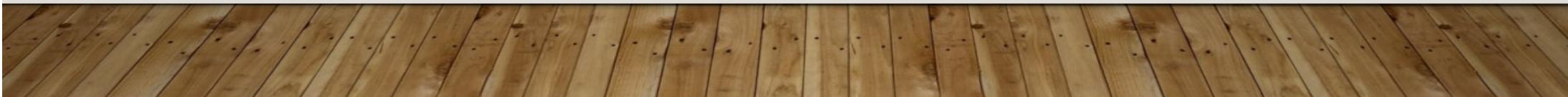
Prendete atto della esistenza della guaina fibroblastica!

- Ditelo ai Vostri colleghi
- Ditelo ai Vostri radiologi
- Ditelo ai Vostri ecografisti
- Ditelo a tutti coloro che si prendono cura di bambini/neonati con dispositivi intravascolari

RICORDARE:

La maggior parte delle "trombosi asintomatiche" sono soltanto guaine.

Imparate a differenziare CRT e FS!



2022



2022



2024



2022

Vascular Access in Neonates and Children

Daniele G. Biasucci
Nicola Massimo Disma
Mauro Pittiruti
Editors

 Springer



www.gavecelt.it

[Home](#) [Chi siamo](#) [Formazione](#) [Biblioteca »](#) [Eventi](#) [Area Video](#) [Links Utili](#) [News](#)

Area Video



RaFeVA in neonato



RaCeVA in neonato



Posizionamento ECC in
T1/T2



Posizionamento CVO in
T1/T2



Posizionamento i PICC-
port Dignity con ecografo
wireless ed ECG wireless



Posizionamento di
ProPICC tunnelizzato
con ecografo wireless ed
ECG wireless

GRAZIE DELL'ATTENZIONE

mauropittiruti@me.com

www.gavecelt.it

