
# Venous Access in Oncology

## Fibroblastic sleeve (so called “fibrin sleeve”): still a mistery?

Antonio La Greca
Emergency and Trauma Surgery
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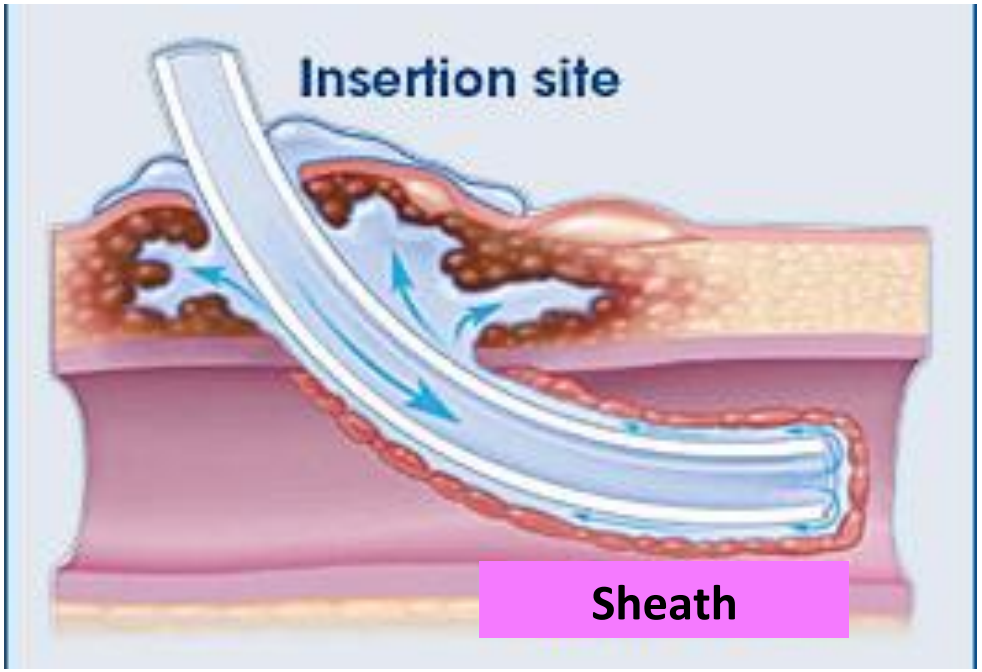
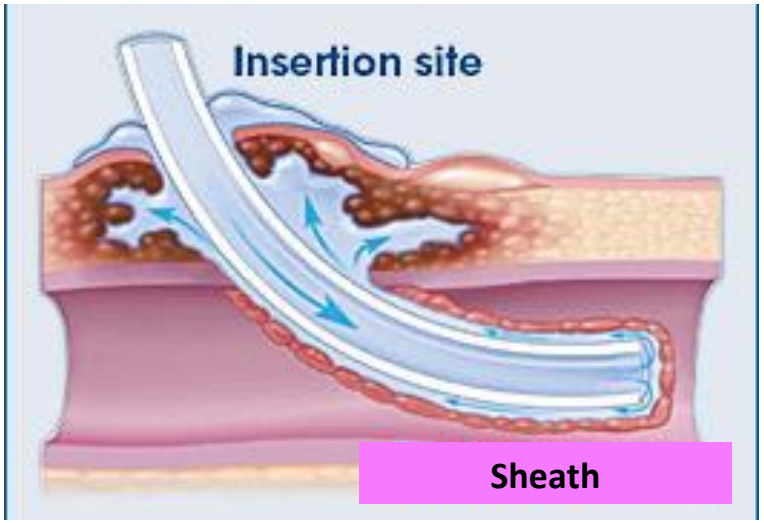
Gemelli

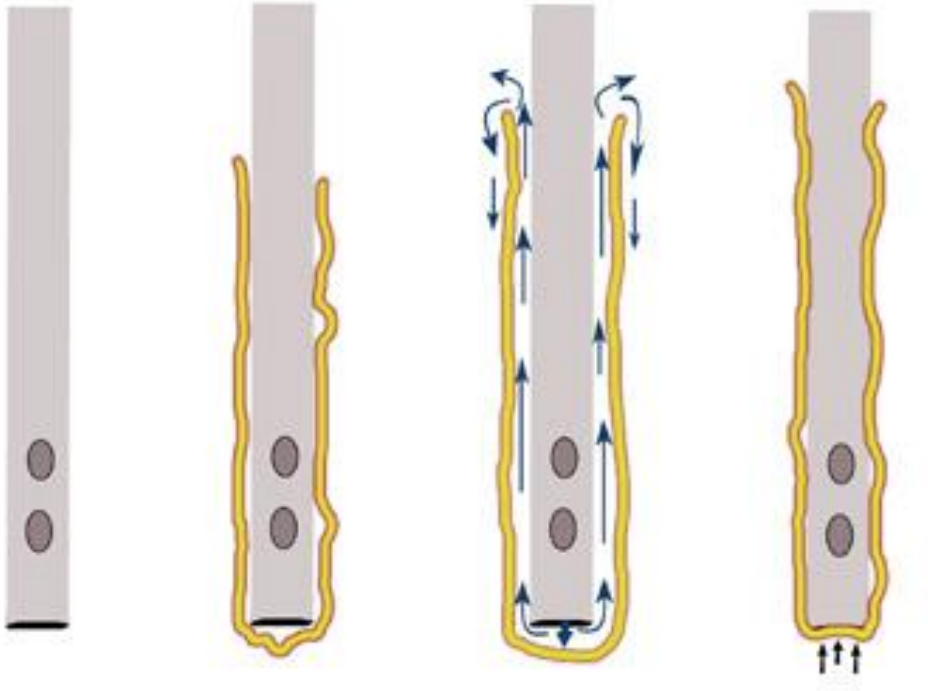
# Guaina pericatetere




Manicotto di materiale collagenico rivestito da endotelio (già "fibrina") che avvolge il CVC generalmente nel suo percorso endovenoso, ma estendendosi talvolta anche al tratto sottocutaneo (reservoir incluso nel caso dei port)

# Guaina pericatetere



Clinicamente rilevante in quanto potenziale causa di malfunzionamento del VAD

(**withdrawal occlusion, stravaso**)

# “Fibrin” sleeve


Motin J, Fischer G, Evreux J. Interet de la voie sous-claviculaire en reanimation prolongee. Lyon Med 1964;40 583–593.

Lyon Med. 1964 Oct 4;212:583-93.

IMPORTANCE OF THE SUBCLAVICULAR ROUTE IN PROLONGED RESUSCITATION (APROPOS OF 154 CASES)].

MOTIN J, FISCHER G, EVREUX J.

# Fibrin Sleeve Formation on Indwelling Subclavian Central Venous Catheters

Verne L. Hoshal, Jr., MD;
Robert G. Ause, MD; and
Phillip A. Hoskins, MD,
Ann Arbor, Mich

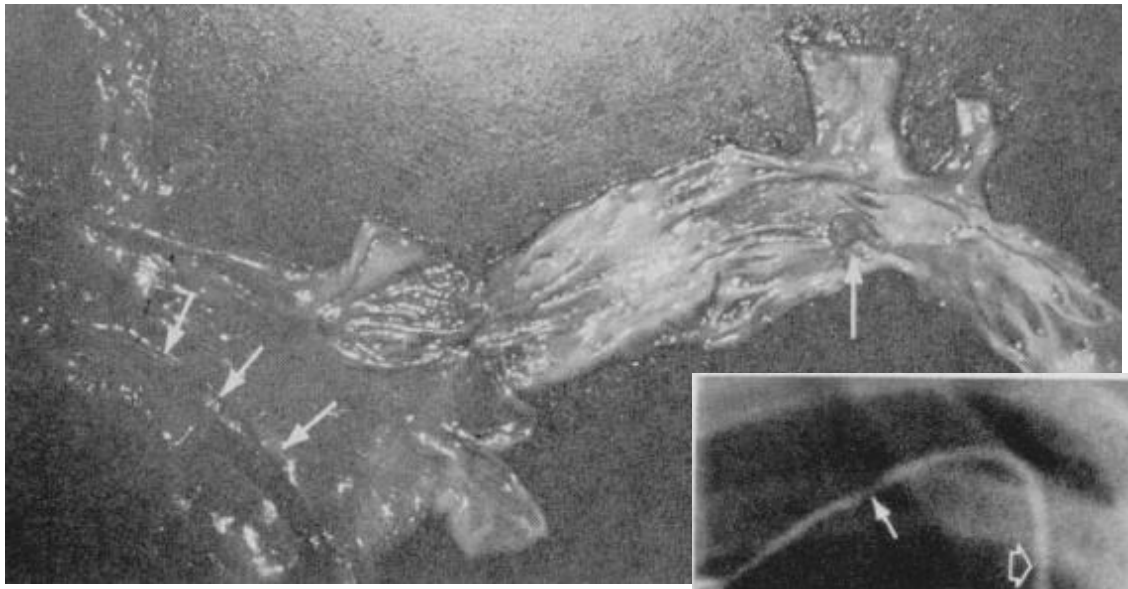
*Fifty-five subclavian veins with previous indwelling catheters were dissected at autopsy. Two groups of subclavian catheters injected with contrast material during removal were studied by cinefluoroscopy. Group 1 consisted of 25 patients with indwelling Teflon and polyethylene catheters. Group 2 comprised six patients with indwelling graphite-benzakonium chloride-heparin sodium (GBH) bonded polyethylene catheters. The vein dissections and the cinefluoroscopic studies in group 1 revealed that totally circumferential fibrin sleeves consistently and extensively formed on indwelling subclavian catheters. They developed on polyethylene, Teflon, nylon, and siliconized rubber catheters. These fibrin sleeves were noted at dissection on catheters within 24 hours after insertion. Two associated thrombi were discovered. Cinefluoroscopy detected one additional thrombus. These findings are an undesirable potential hazard and concern of thromboembolism is certainly warranted. Methods to eliminate fibrin sleeves seem justified. Evidence suggests that GBH-bonded catheters significantly inhibit fibrin sleeve formation.*

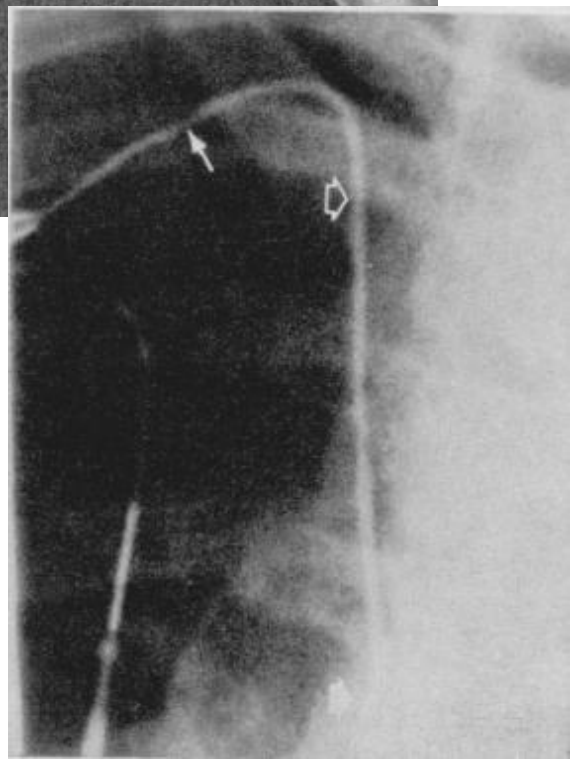
Accepted for publication Dec 15, 1970.

From St. Joseph Mercy Hospital, Ann Arbor, Mich.

Read before the 78th annual meeting of the Western Surgical Association, Colorado Springs, Colo, Nov 20, 1970.

Reprint requests to St. Joseph Mercy Hospital, 326 N Ingalls St, Ann Arbor, Mich 48104 (Dr. Hoshal).





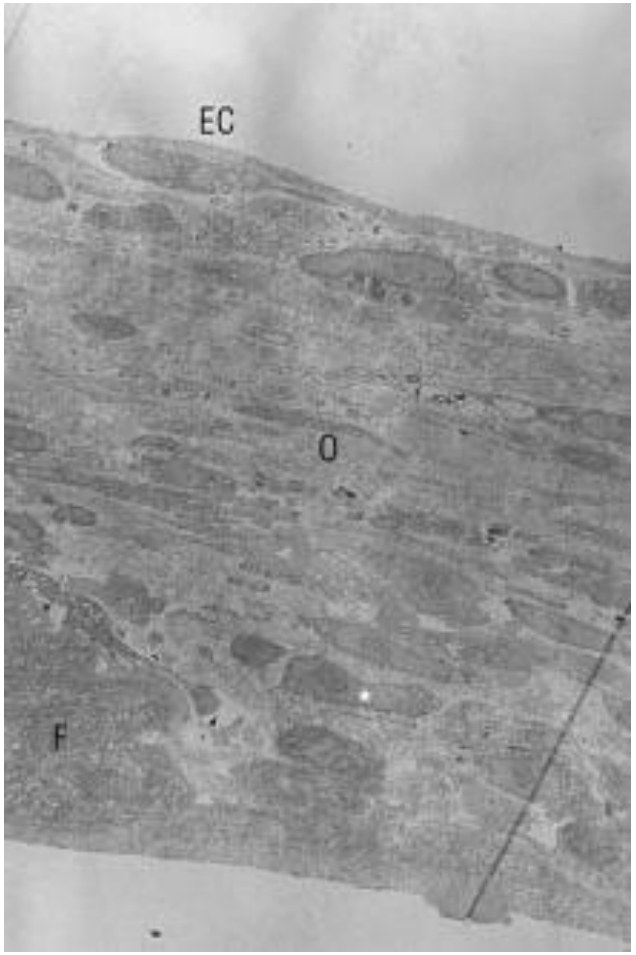
# Composition and formation of the sleeve enveloping a central venous catheter

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*

JOURNAL OF VASCULAR SURGERY
Volume 28, Number 2 *1998*

The tissue around the catheter is a thrombus in the early stage, but a cellular-collagen tissue covered by endothelium after 1 week. Migration and proliferation of activated SMCs from the vein wall to the PCT is an important step in its transformation.

Motin introduced the term "fibrin sleeve" to describe a visible sheath around the catheter seen at autopsy. Although fibrin coating occurs, the visible sleeve is not composed of fibrin. Therefore it is appropriate to distinguish fibrin coating and catheter sleeve.



0148-0671/96/2002-0156$03.00/0
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*Brief Communication*

# 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

*Department of Comparative Medicine, The Mitlon S. Hershey Medical Center of Pennsylvania State University, Hershey, Pennsylvania*

Radiology

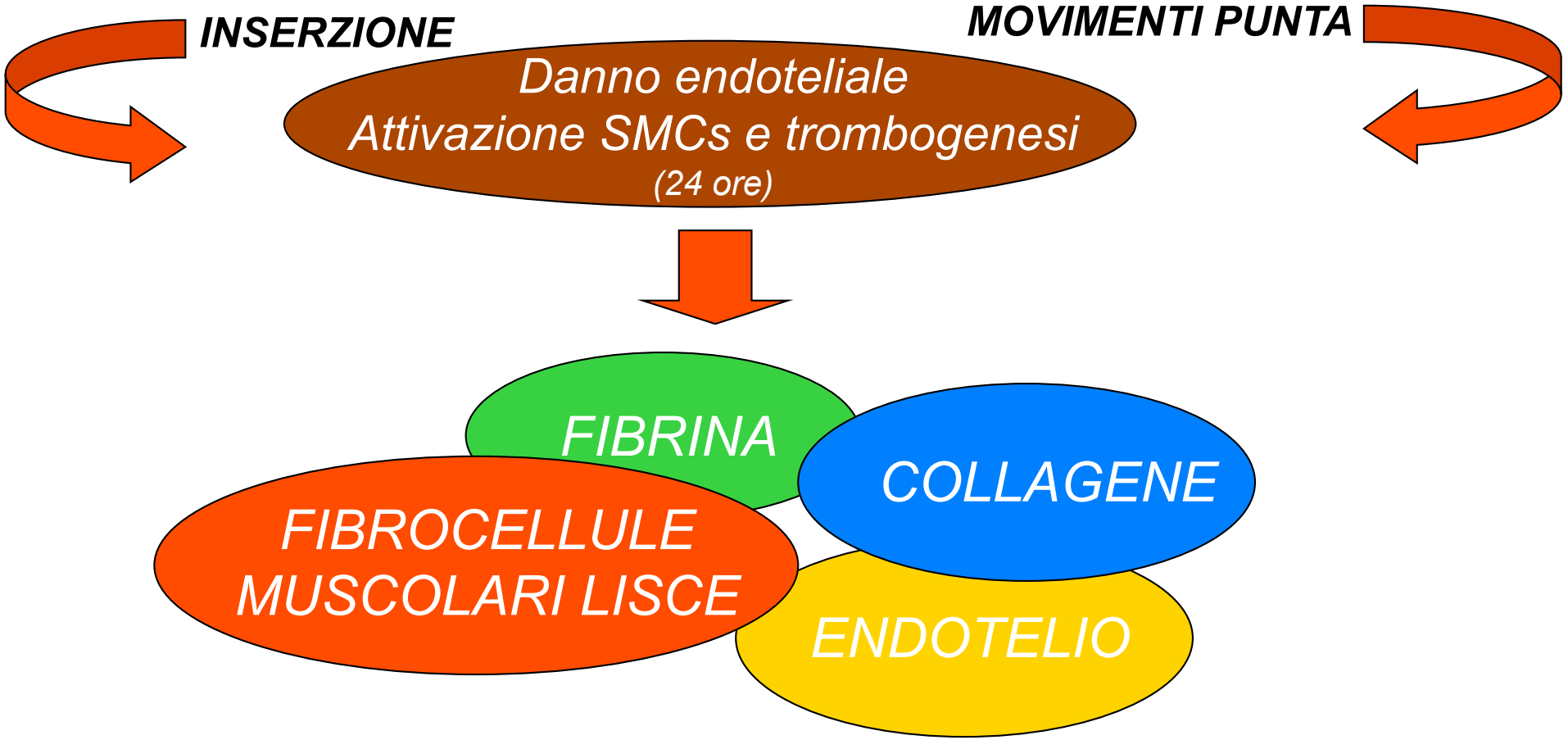
**Radiology:** Volume 240: Number 2—August 2006

# Jugular Vein Catheter Placement: Histologic Features and Development of Catheter-related (Fibrin) Sheaths in a Swine Model[1]

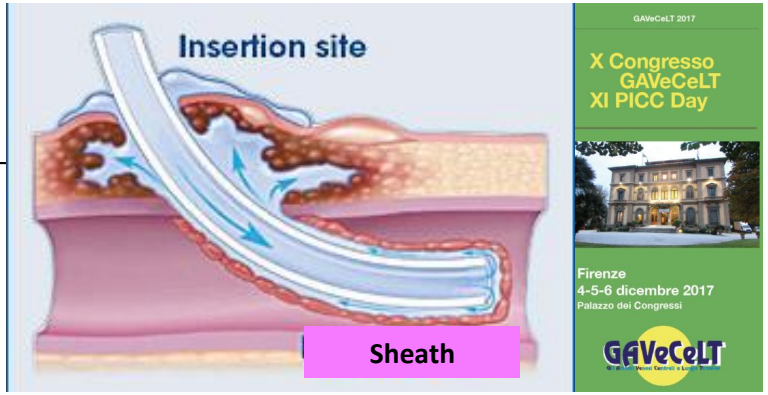
Andrew R. Forauer, MD
Constantine G. A. Theoharis, MD
Narasimham L. Dasika, MD

**Purpose:** To evaluate the development and histologic features of jugular vein catheter–related (fibrin) sheaths in a swine model.

# Patogenesi


INSERZIONE
MOVIMENTI PUNTA
Danno endoteliale
Attivazione SMCs e trombogenesi
(24 ore)
FIBRINA
COLLAGENE
FIBROCELLULE
MUSCOLARI LISCE
ENDOTELIO

# Sleeve: patogenesi




***Giorno 1: trombo pericatetere (TP)***

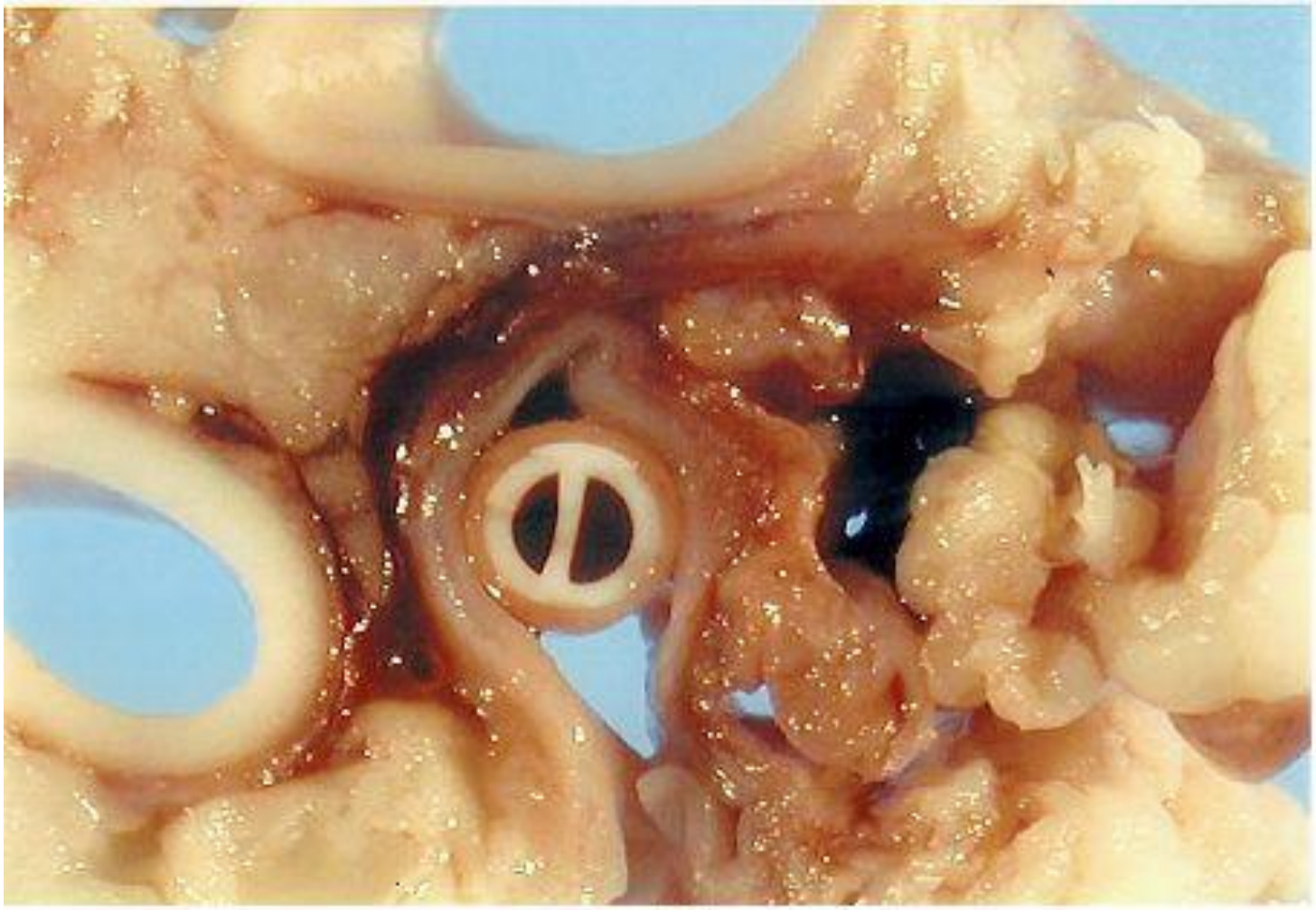
- rete di fibrina e piastrine
- GR e GB intrappolati nella rete
- sulla superficie del catetere a partire da aree di parete venosa disendotelizzate con esposizione delle fibrocellule muscolari liscie (SMC)

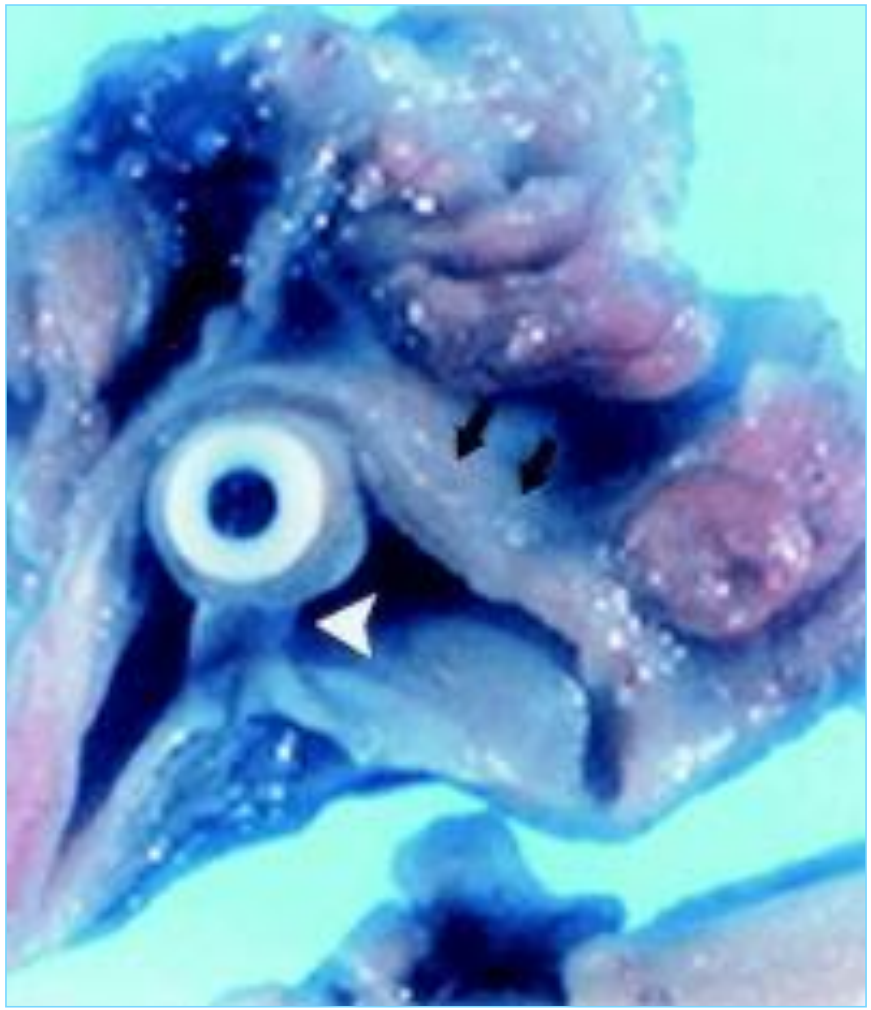
***Giorni 3-7: ispessimento e protrusione del (TP)***

- ponti di collegamento rete-parete venosa
- modificazione fenotipo SMC della parete venosa dalla fase contrattile a quella sintetica

***Giorni 7-28: maturazione dello sleeve cellulo-collagenico***

- infiltrazione della rete da parte delle SMC attivate
- matrice extracellulare e fibrina scarse
- comparsa di collagene, progressivamente predominante sulla quota cellulare
- comparsa di cellule endoteliali fino a quasi completo rivestimento dello sleeve in direzione del flusso (giorno 14)





## *SLEEVE PERICATETERE*

### *Patogenesi*

***In prossimità di aree endoteliali con caratteristiche da insulto cronico (ispessimenti intimali a placca o papillari)***

***“Prossimale”, “distale”, “intermedio”***

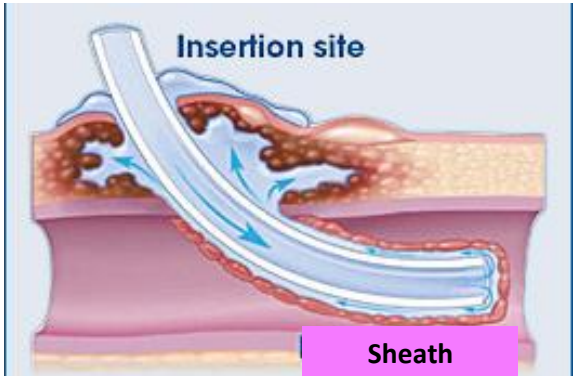
# Sleeve: patogenesi


## Central Venous Catheter Tip Position: A Continuing Controversy

Thomas M. Vesely, MD J Vasc Interv Radiol 2003; 14:527–534

A catheter inserted into a vein will be recognized as a foreign object and quickly covered with fibrin and plasma proteins (29). This is often followed by the deposition of platelets and fibrin. Although the deposition of plasma proteins and platelets onto the surface of a catheter is an expected event, in certain situations, this process may further evolve into catheter thrombosis or fibrin sheath formation.

Vascular injury is considered a primary initiating event for catheter-related thrombosis (30). Vascular damage may occur early at the time of catheter insertion, or the injury may be progressive, as in the setting of a malpositioned catheter tip.



# Sleeve: patogenesi


- Risposta dinamica della parete venosa e del plasma alla presenza del catetere e all'associato trombo inserzionale / di punta / di dorso
- Step patogenetici simili nell'uomo e nell'animale: cellule endoteliali, infiammatorie e muscolari lisce attivate (elementi biologicamente attivi)
- Evoluzione "costante" del processo trombotico in presenza di un supporto sintetico (il catetere)
- Diferisce dal trombo venoso perché a presenza del catetere consente la progressione del processo anche al di là del contatto focale del catetere con la parete venosa

**(Percarpio, 2013)**

# Confusion will be my epitaph … (The King Crimson, 1969)

| New Paradigms in Anticoagulation and Thrombolysis | Hematology 2014

## Central venous catheter–related thrombosis

*William Geerts*[1]

American Society of Hematology

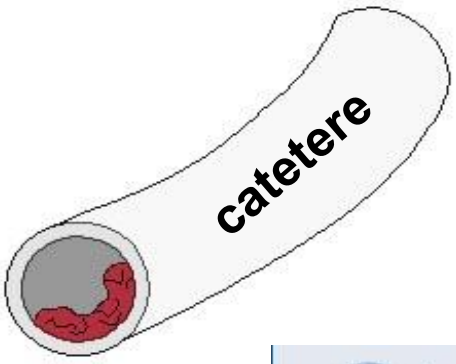
[1] *Thromboembolism Program, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada*

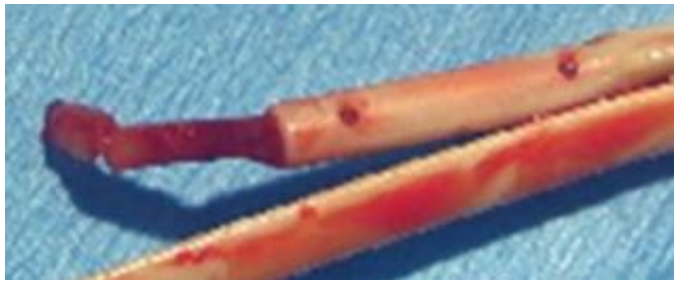
?

### Pathophysiology of CRT

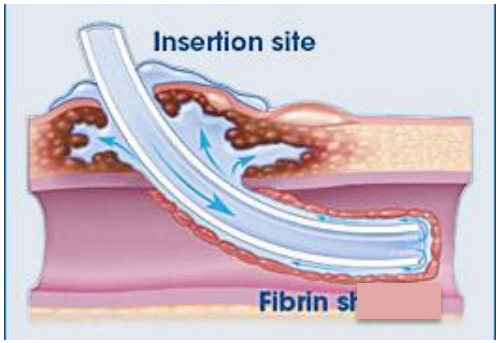
Thrombosis associated with a CVC can be classified into 3 types: pericatheter sheath ("fibrin sleeve"), thrombotic occlusion of the catheter lumen, and mural thrombosis, either superficial (SVT) or deep vein thrombosis (DVT). Insertion of a CVC produces local venous injury at the access site. Deposition of fibrin on the thrombogenic catheter surface and the subsequent in-growth of smooth muscle and endothelial cells are universal and begin within hours of insertion.[2] This pericatheter sheath grows along the catheter from the venotomy site. Blood flow is reduced up to 60% around the CVC, which leads to further cellular adhesion to the catheter and vein walls.[3] Ongoing movement of the catheter within

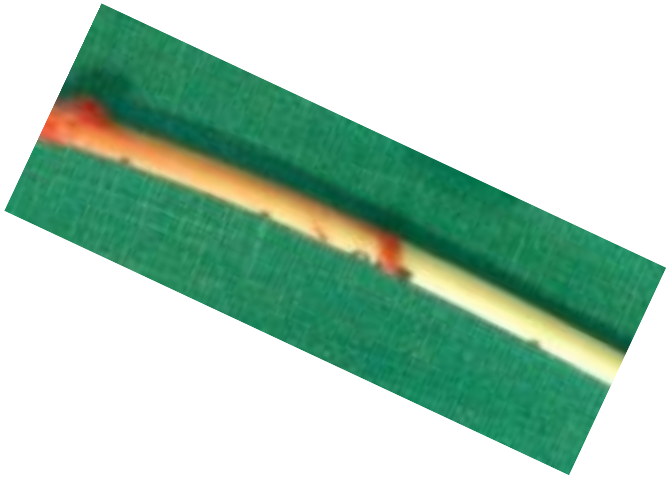
- Occlusione



- Guaina fibroblastica



- Trombo parietale

# Sleeve: incidenza ed evoluzione clinica


## Ist. Tumori Genova 1990/2001 – 1680 pazienti

| | | |
|---|---|---|
| ***SLEEVE*** | ***62*** | ***(3.69 %)*** |
| ***TROMBOSI VENOSA PROF.*** | ***29*** | ***(1.72 %)*** |
| ***MALPOS. CATETERE*** | ***15*** | ***(0.89 %)*** |
| ***STRAVASO FARMACI*** | ***14*** | ***(0.83 %)*** |
| ***ESPULSIONE CAMERA*** | ***13*** | ***(0.77 %)*** |
| ***OCCLUSIONE/ROTTURA CAT.*** | ***12*** | ***(0.71 %)*** |
| ***TOTALE*** | ***142*** | ***(8.53 %)*** |

***Prima causa di complicanze tardive del cateterismo venoso centrale***

# Sleeve: incidenza ed evoluzione clinica


## Ist. Tumori Genova 1990/2001 – 1680 pazienti

| | Incidenza |
|---|---|
| **Port** | **58/1522 (3.8%)** |
| **CVC tunnellizzati esterni** | **4/ 158 (2.5%)** |
| **CVC a media e lunga durata** | **62/1680 (3.7%)** |

***74% dei casi entro i primi 6 mesi*** → **EVENTO PRECOCE**

***71% dei casi in pazienti sottoposti ad infusione continua > 24 ore***

# Sleeve: incidenza ed evoluzione clinica


Ist. Tumori Genova 1990/2001 – 1680 pazienti

| | Incidenza |
|---|---|
| **Distanza punta - atrio Dx <3 cm** | **20/62 (32.2%)** |
| **Distanza punta - atrio Dx >3 cm** | **42/62 (67,8%)** |
| | ***p<0.05*** |

***Fattori di rischio:*** ***il corretto posizionamento della punta del catetere in vena cava superiore sembra ridurre l'incidenza del fenomeno***

# Sleeve: incidenza ed evoluzione clinica


Ist. Tumori Genova 1990/2001 – 1680 pazienti

***Analisi statistica monofattoriale:***

| | |
|---|---|
| ***Infusione continua vs. intermittente*** | ***(p<.005)*** |
| ***Pompe peristaltiche vs elastomeri*** | ***(p<0.05)*** |
| ***Infusione di 5FU vs Adri/Ifosfamide/Taxani*** | ***(p<0.005)*** |

***Analisi statistica multifattoriale:*** ***???***

# Sleeve: incidenza ed evoluzione clinica


Altri fattori di rischio specifici ???

# Sleeve: incidenza ed evoluzione clinica


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 Boddi[1], Gianluca Villa[2], Marco Chiostri[1], Francesco De Antoniis[1], Ilaria De Fanti[2], Alessandra Spinelli[1], Andrea Savino[1], Gian Franco Gensini[1,3], Cecilia Pelagatti[2]

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

400 consecutive patients candidate to CHT and referred to CVC service for insertion of a LT-CVC

# Sleeve: incidenza ed evoluzione clinica

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innominate, and axillary veins). Features suggestive of fibrin sheaths were considered echogenic signal longer than 20 mm and thicker than 10 mm around CVC in the tract directly explorable at the junction between jugular and sub-clavian vein, without venous wall involvement(17, 18). A

The incidence of CVC-related fibrin sheaths was 0.71 events per 1000 catheter days; specifically, 44 of 400 patients (12.8%) presented fibrin sheaths at the 1st month US test (Table 3). Twenty-five of the 42 patients who repeated US examination at 6 months, started a 3-month course of therapy with LWMH, whereas the remaining 17 did not, following the decision independently taken by their oncologist. Of the patients with fibrin sheaths on LWMH therapy, one patient developed subocclusive DVT; at the 6th month, US check-up in 11 of 25 patients on LWMH, fibrin sheaths persisted, whereas in the remaining 13 fibrin sheaths were no longer detectable. Among patients with fibrin sheaths who had not been on LWMH, at the 6th month US check-up in five patients fibrin sheaths showed no change, whereas in the remaining 12 were no longer detectable. Furthermore, at 6th month US check-up, an additional 12 patients who had a 1st month negative US test for DVT or fibrin sheaths showed new onset CVC-RFS. In no patients fibrin sheaths were associated with CVC dysfunction or removal.

**Table 3** Characteristics of patients with or without CVC-related fibrin sheath (RFS) at 1st-month ultrasound check-up

| | CVC-RFS $n = 45$ | No CVC-RFS $n = 350$ | $P$ |
|---|---|---|---|
| Age (yr) | 63 (55–68) | 60 (48–68) | 0.088 |
| Male gender (%) | 23 (51.1) | 101 (28.9) | 0.002 |
| Body mass index (kg/m$^2$) | 23.4 (22.4–26.7) | 24.2 (21.6–27.5) | 0.453 |
| Previous implantation (%) | 2 (4.4) | 24 (6.9) | 0.539 |
| No- sinus rithm at basal ECG (%) | 1 (2.2) | 2 (0.6) | 0.230 |
| Left side of implantation (%) | 7 (15.6) | 71 (20.3) | 0.453 |
| Vein area (mm$^2$) | 126 (86–162) | 99 (69–140) | 0.029 |
| Number of venipuncture | | | |
| $N = 1$ | 44 (97.8) | 331 (94.6) | 0.356 |
| $N > 1$ | 1 (2.2) | 19 (5.4) | |
| Platelet count (10$^3$/μL) | 274 (201–341) | 251 (199–313) | 0.308 |

# Sleeve: incidenza ed evoluzione clinica

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- Fibrin sheaths showed a high incidence (about 12%) and early onset (1° month)
- In only one patient evolved in DVT
- Never caused CVC dysfunction
- Resolution of fibrin sheaths occurred independently of LMWH therapy.

# Sleeve: incidenza ed evoluzione clinica

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- IL COSIDDETTO ”TROMBO PERICATETERE” DEGLI ECOGRAFISTI E’ L’QUIVALENTE ECOGRAFICO DELLO SLEEVE
- Il “trombo pericatetere” non coincide con la trombosi venosa PARIETALE
- Risvolti terapeutici: NON TRATTARE SE NON SINTOMATICO
- Possibile evoluzione in trombosi IN CASO DI SLEEVE “FLORIDO”, TALE DA AUMENTARE L’IMPEGNO VOLUMETRICO DELLA VENA

# Sleeve: clinica


***Parziale o totale difetto di pervietà del catetere:***

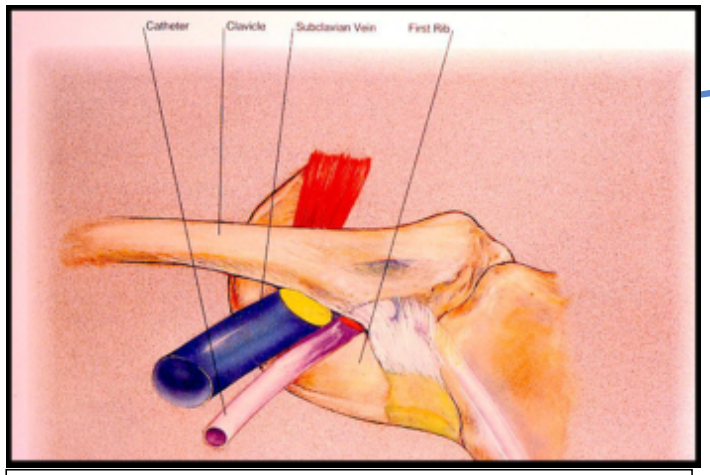
- impossibilità a prelevare sangue (*withdrawal occlusion*)
- impossibilità di infondere

***Stravaso in corrispondenza del sito di venipuntura***

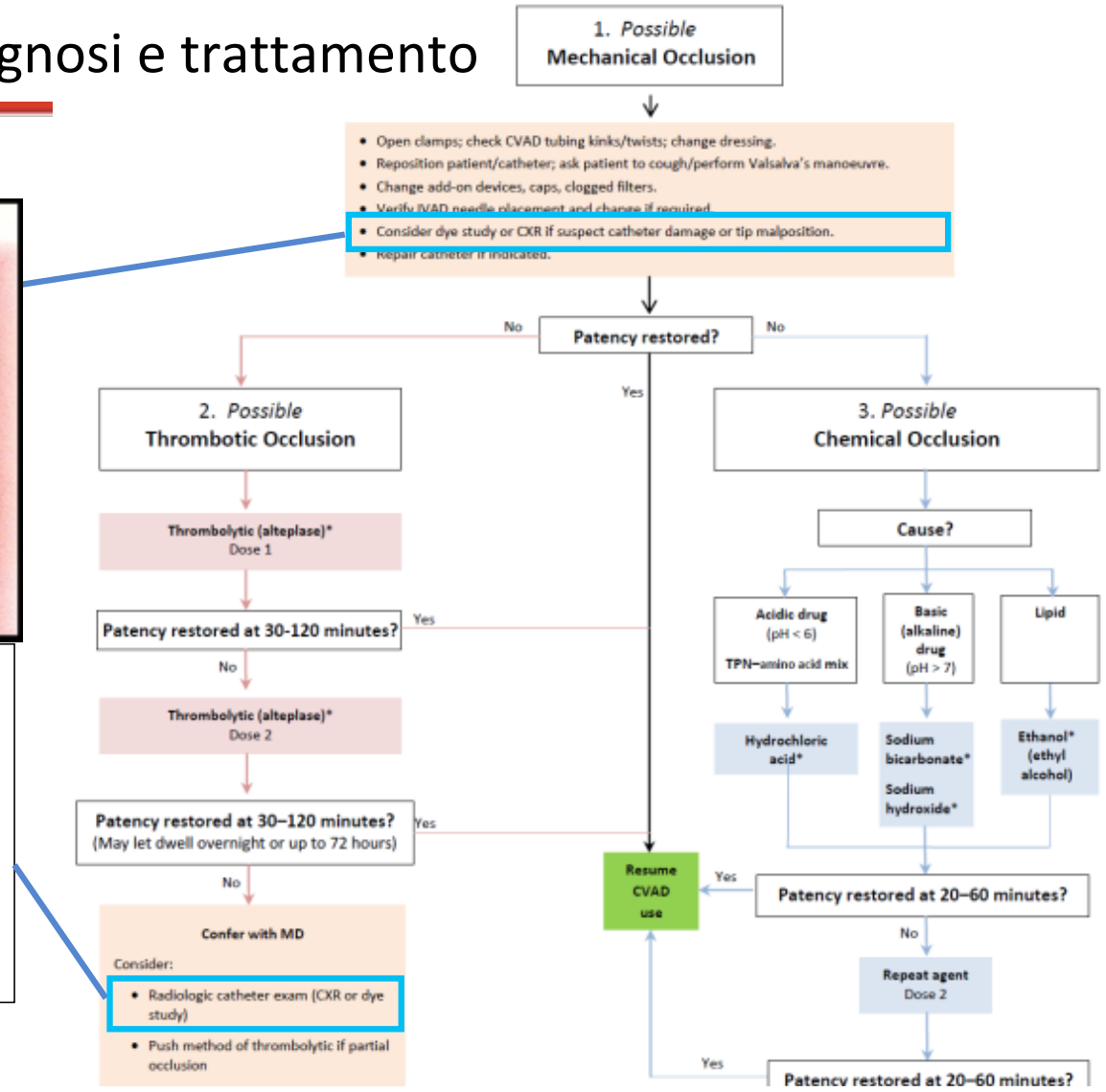
***Stravaso lungo il tunnel sottocutaneo***

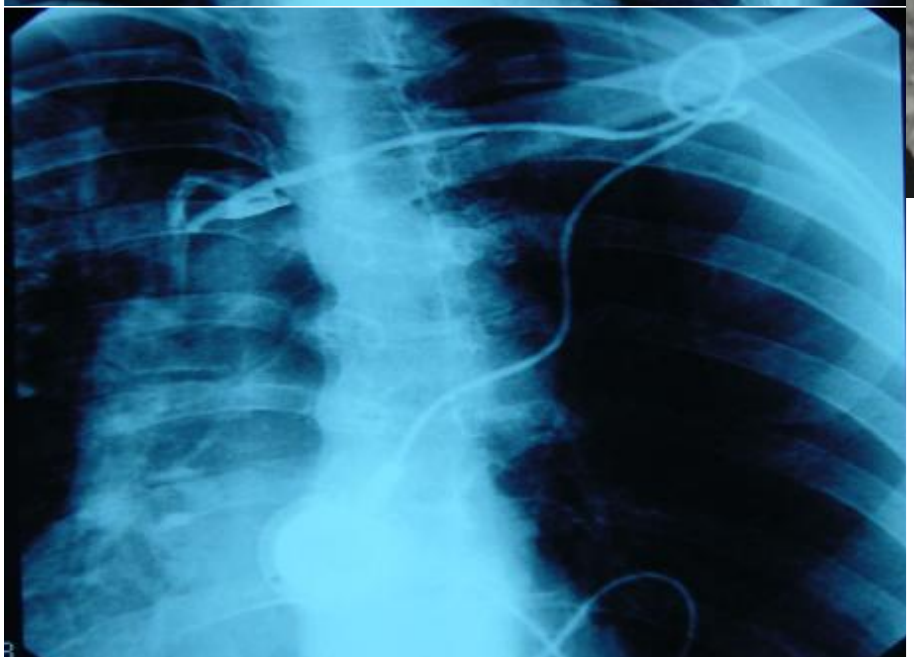
***Stravaso nella tasca del reservoir***

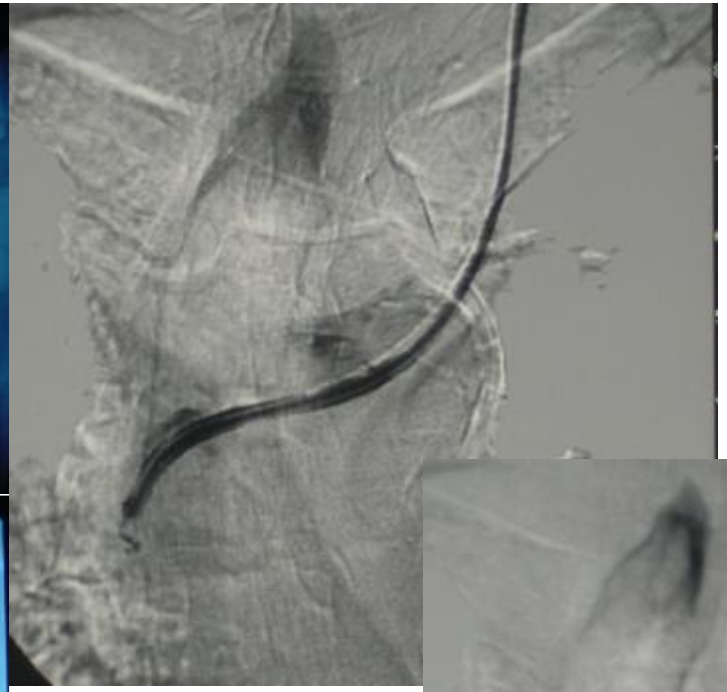
# OCCLUSIONE: diagnosi e trattamento

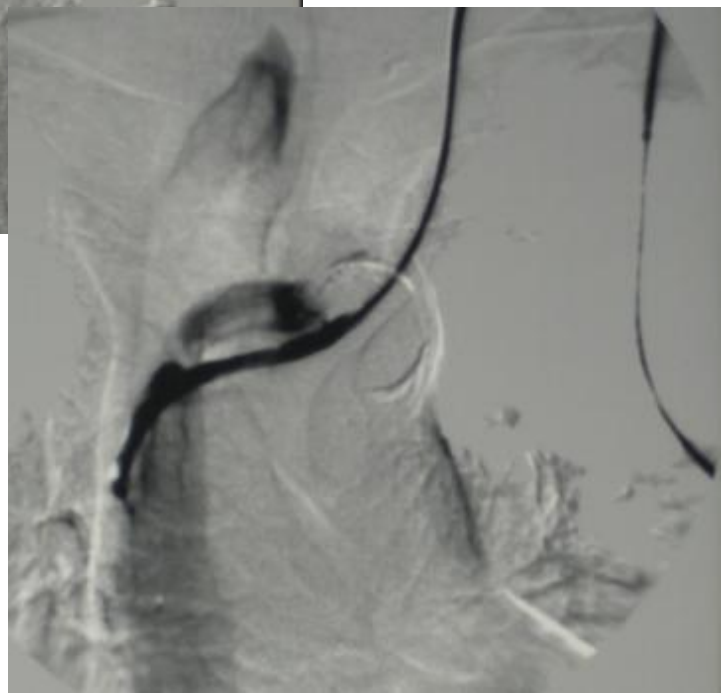



Consider chest X-Ray and/or line-o-gram (expecially if catheter placed via subclavear access):
- PINCH OFF ?
- KINKING ?
- TIP MALPOSITION ?
- **SLEEVE ?**

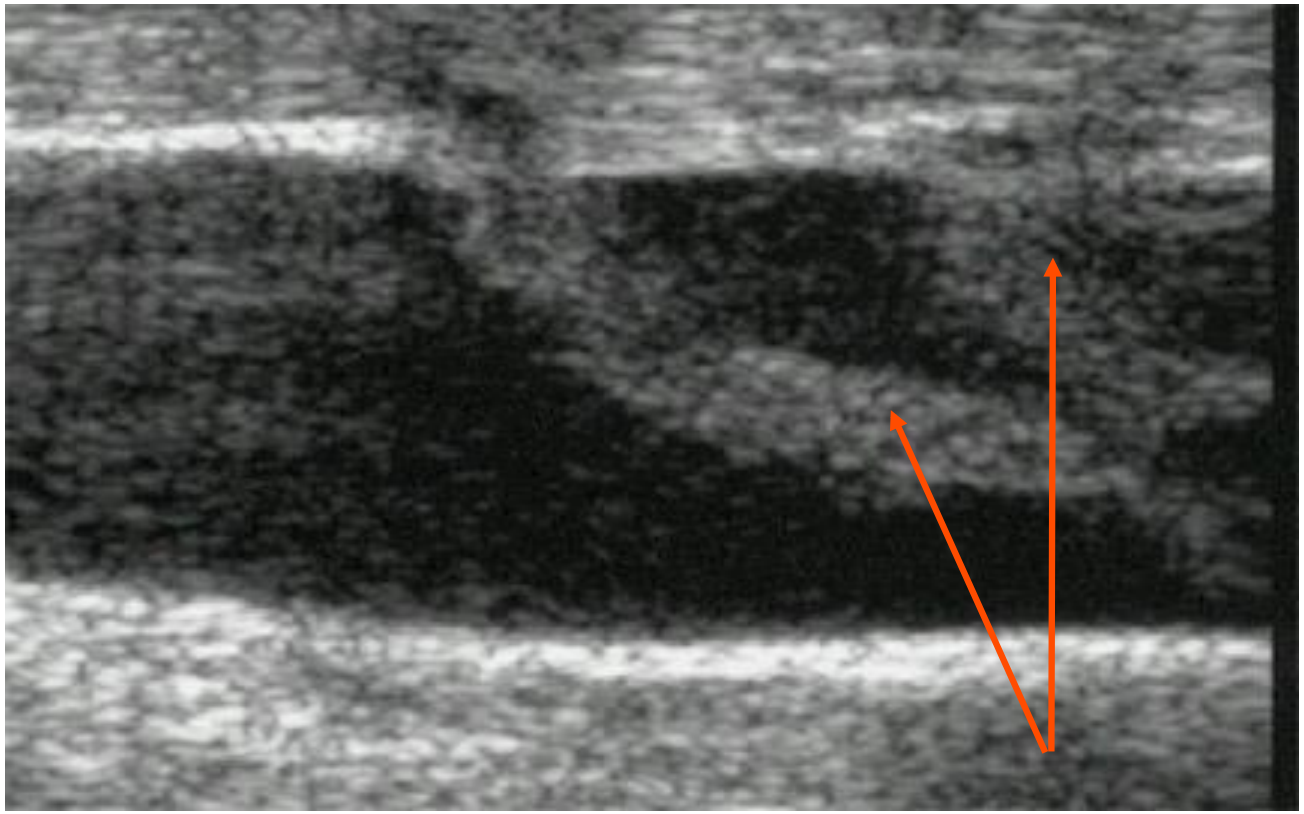








# Sleeve: dopo rimozione del catetere



# Sleeve sintomatico: trattamento


“Peeling” o “stripping” angiografico

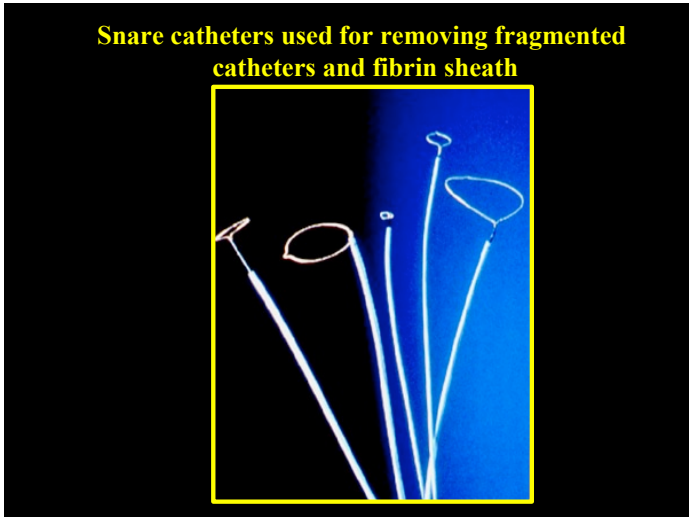
Dilatazione con palloncino

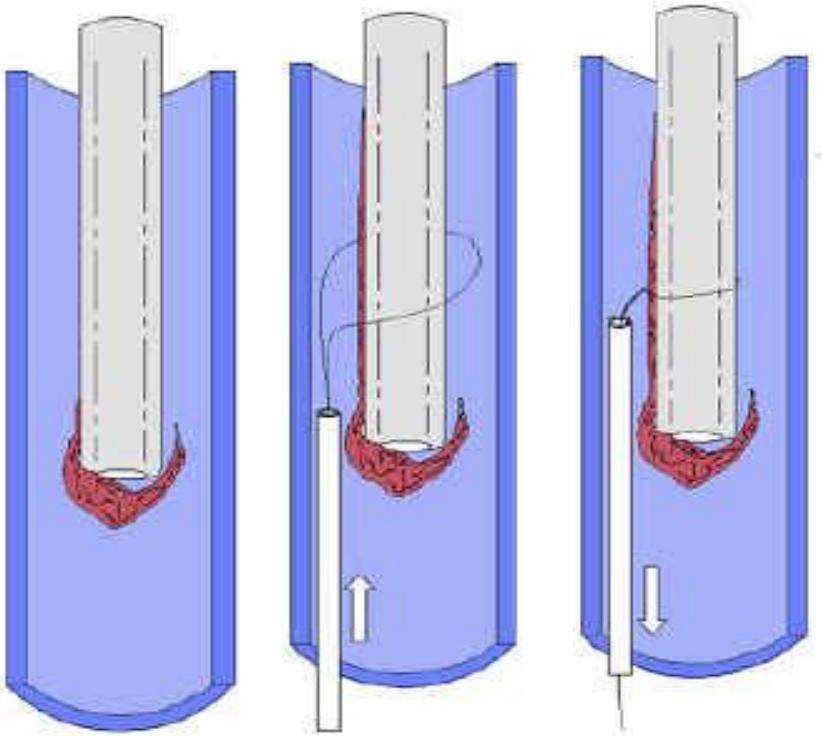
Fibrinolisi infusionale

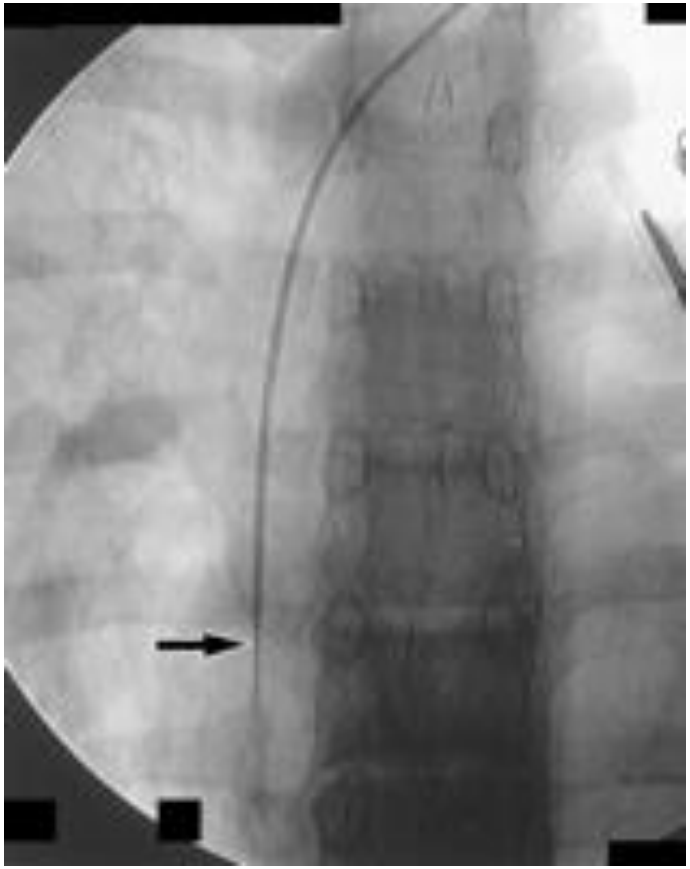
Sostituzione CVC su guida (eventuale conservazione reservoir in caso di port)

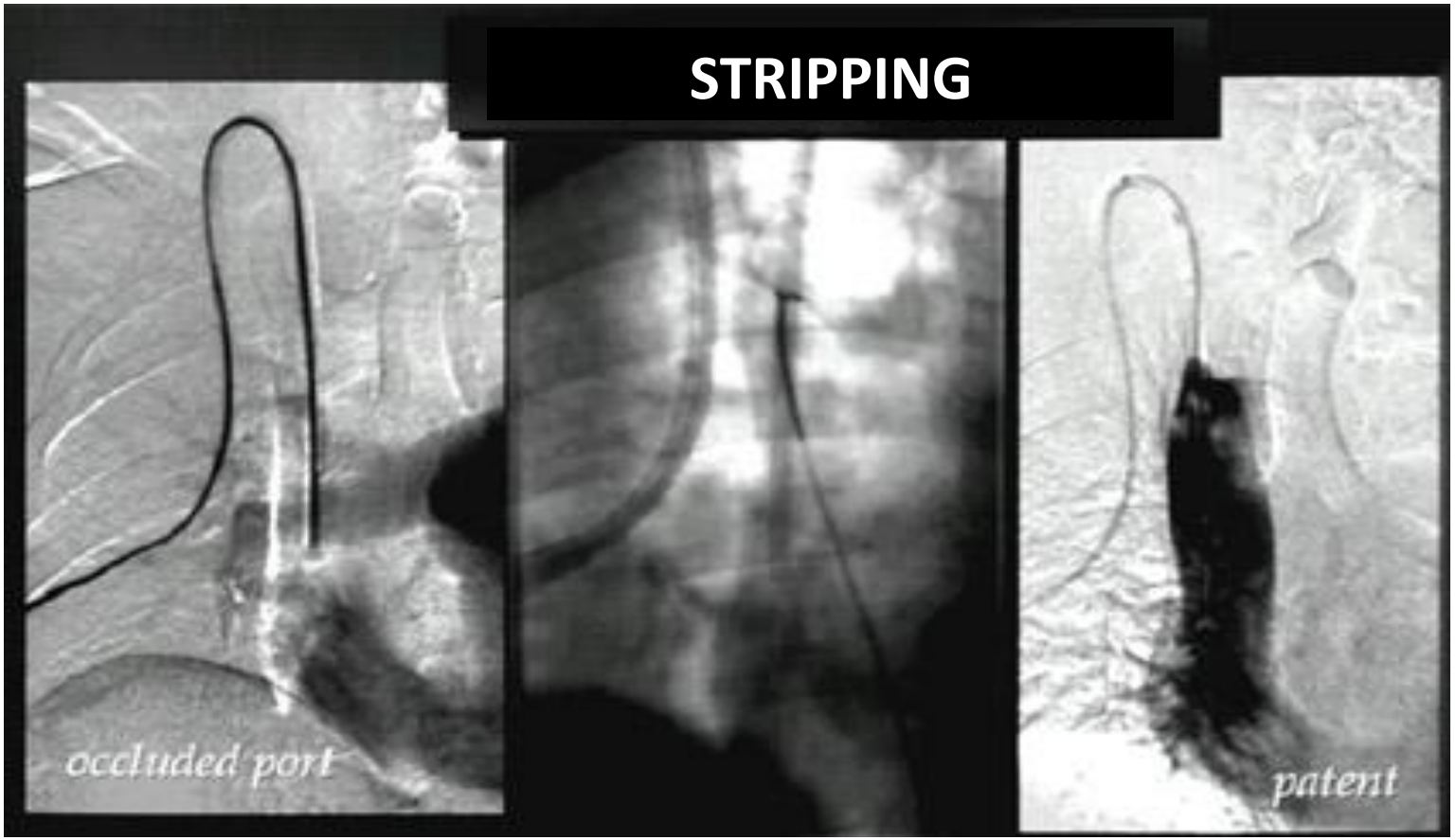
**ESPERIENZE IN AMBITO DIALITICO**

# *“Peeling” o “stripping” angiografico*






STRIPPING
occluded port
patent

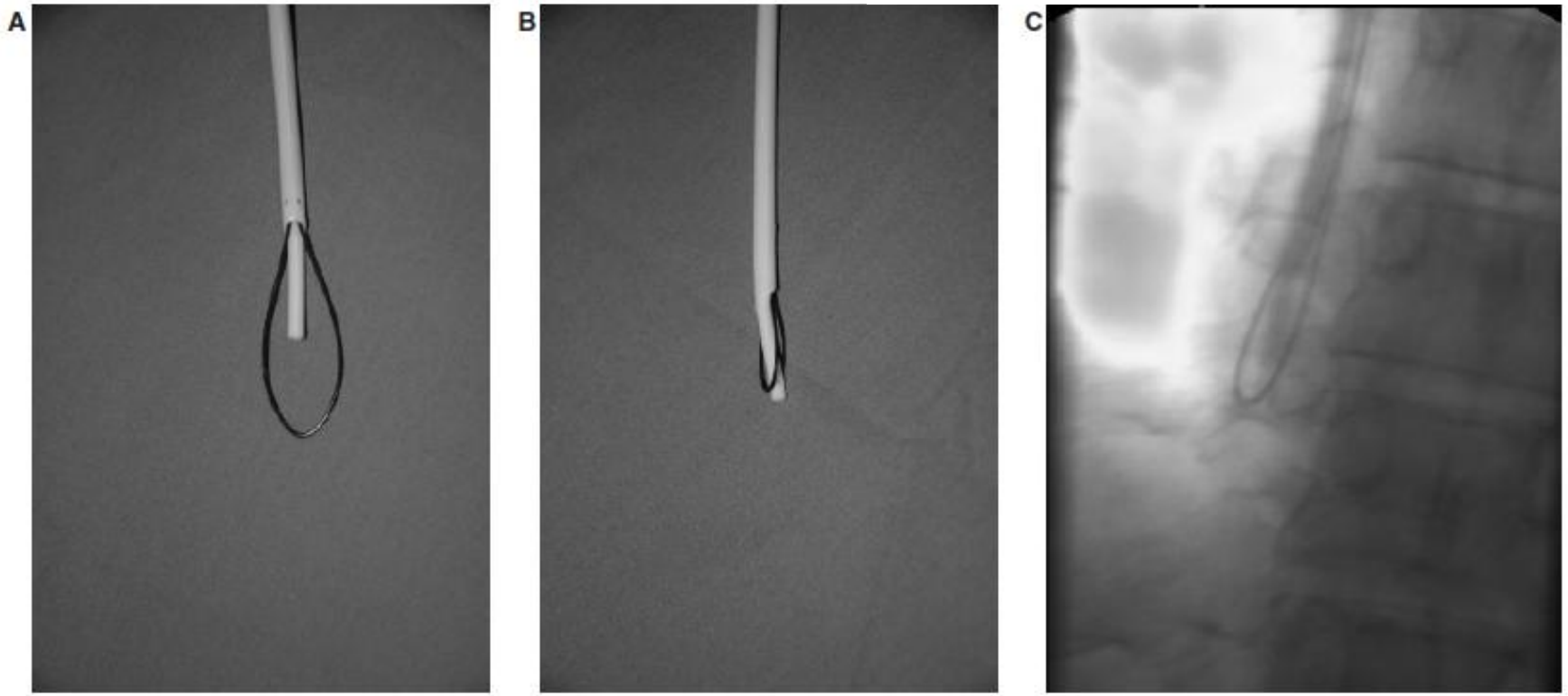
# *Internal snare peeling*

Nephrol Dial Transplant (2007) 22: 1762–1765
doi:10.1093/ndt/gfm154
Advance Access publication 1 April 2007

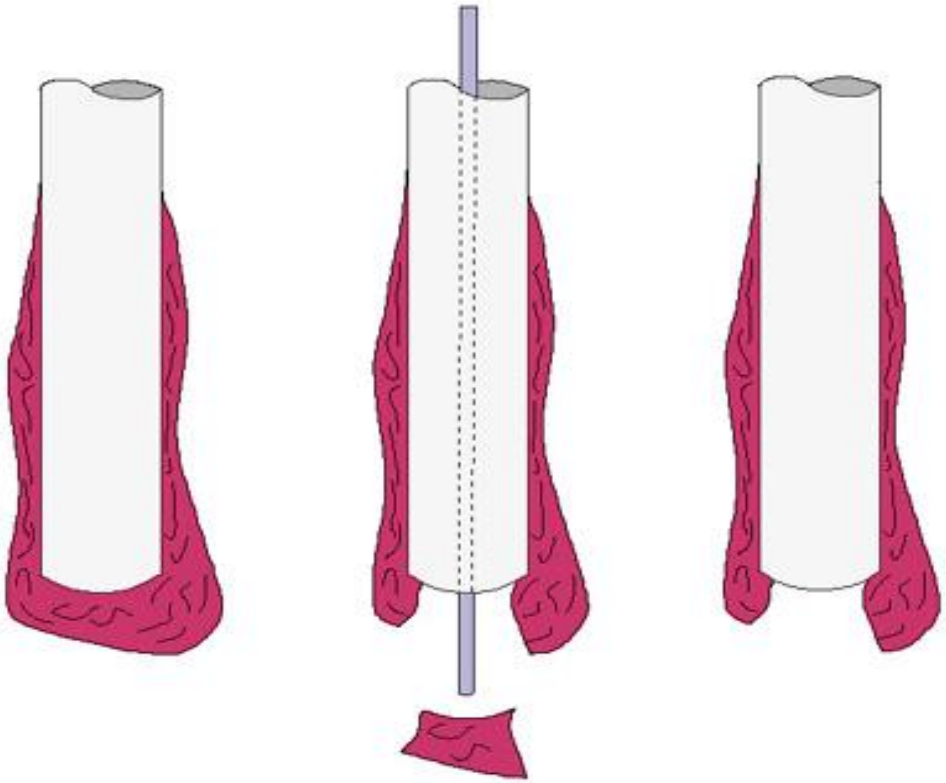
*Technical Note*

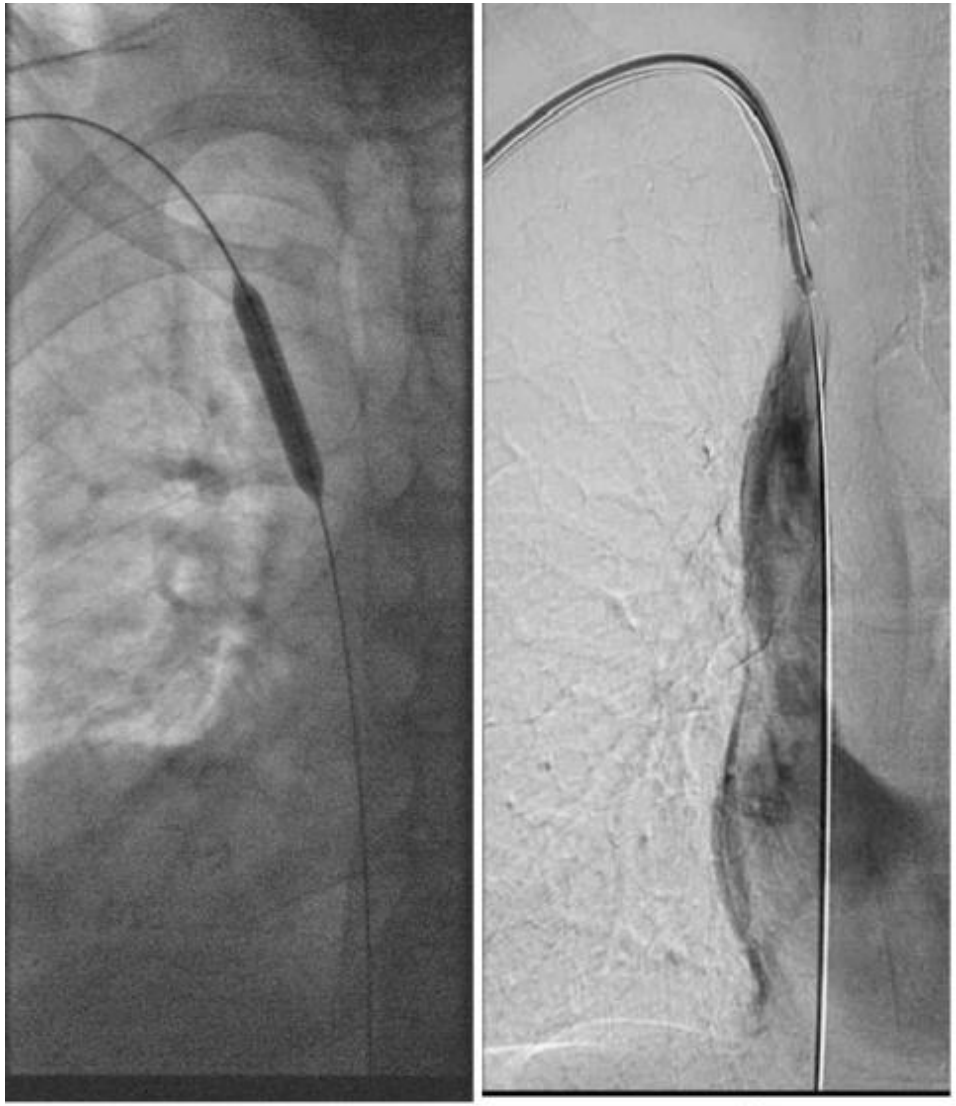
**Fibrin sheath removal from central venous catheters: an internal snare manoeuvre**

Arra S. Reddy, Elvira V. Lang, Jennifer Cutts, Shaun Loh and Max P. Rosen



# *Dilatazione con palloncino*





(a) (b)

# Fibrin Sleeve Stripping for Salvage of Failing Hemodialysis Catheters: Technique and Initial Results[1]

Martin R. Crain, MD • Mark W. Mewissen, MD • Gregory J. Ostrowski, DO
Ricardo Paz-Fumagalli, MD • Robert A. Beres, MD[2] • Richard A. Wertz, MD

Radiology 1996; 198:41–44

*CONCLUSION:* Multiple PFSS procedures can prolong patency in hemodialysis catheters with a fibrin sleeve.

# Percutaneous Fibrin Sheath Stripping versus Transcatheter Urokinase Infusion for Malfunctioning Well-positioned Tunneled Central Venous Dialysis Catheters: A Prospective, Randomized Trial[1]

Richard J. Gray, MD
Abraham Levitin, MD[2]
David Buck, MD
Lisa C. Brown, RN
Yvonne H. Sparling, MS
Kathleen A. Jablonski, PhD
Amanuel Fessahaye, MD[3]
Atul K. Gupta, MD

JVIR 2000; 11:1121–1129

**CONCLUSION: There is no significant difference in time to primary patency between the two methods. Both allow temporary catheter salvage in most patients.**

# Fibrin Sheath Stripping versus Catheter Exchange for the Treatment of Failed Tunneled Hemodialysis Catheters: Randomized Clinical Trial[1]

Michael Merport, MD
Timothy P. Murphy, MD
Thomas K. Egglin, MD
Gregory J. Dubel, MD

JVIR 2000; 11:1115–1120

**CONCLUSIONS: Malfunctioning tunneled hemodialysis catheters treated by means of EX are significantly more likely to remain patent for up to 4 months than are those treated by means of PFSS. According to the results of this trial, PFSS should not be performed as a routine therapy for catheter malfunction.**

# Sleeve sintomatico: trattamento trombolitico


- Gray et (2000): nessuna differenza di outcome tra infusione di urokinasi (250.000 U / 4 ore) e PCRSS
- Low dose (5000 to 9000 U) lock: risultati molto disomogenei (success rate 14 – 95%)
- High dose (25,000 to 100000 IU) lock: successo fino al 100% (Donati et al, 2011)
- IPOTESI DI EFFICACIA: AZIONE SULLA COMPONENTE TROMBOTICA/FIBRINOSA DELLO SLEEVE (TERAPIA PRECOCE)

# Sleeve: quale futuro?


Intervento sui fattori di rischio:

- Posizione punta
- Frizione sui segmenti curvi dell'asse venoso (cateteri lunghi e flessibili)

Per analogia con gli stent medicati: cateteri con superfici trattate (chimico-fisicamente) con sostanze citostatiche o citotossiche SPECIFICHE

# Sleeve: quale futuro?


## JOURNAL OF VASCULAR ACCESS

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

--Manuscript Draft--

| | |
|---|---|
| **Manuscript Number:** | JVA-D-17-00147R1 |
| **Full Title:** | Chlorhexidine coated peripherally inserted central catheters reduce fibroblastic sleeve formation in an in vivo ovine model. |
| **Short Title:** | Chlorhexidine catheter coating reduce fibroblastic sleeve formation in vivo |
| **Article Type:** | Original Research Article |
| **Section/Category:** | Intensive care |
| **Keywords:** | fibroblastic sleeve, sheep, chlorhexidine, catheter, coatings, PICC |
| **Manuscript Region of Origin:** | UNITED STATES |

European Journal of Haematology

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Volume 98, Issue 4
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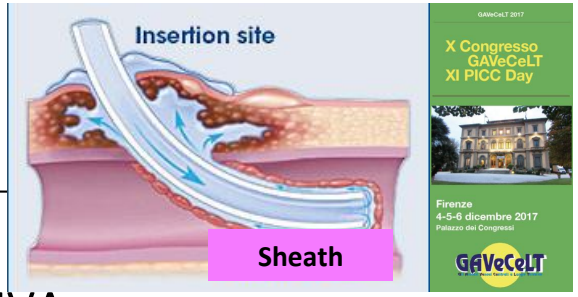
Pages 318–319


**Editorial**

# Central venous catheter thrombosis and the fibrin sleeve: unraveling the mystery

Katherine A. Hajjar

# Conclusioni (1)




Patogenesi comune alla trombosi

Evento a insorgenza PRECOCE anche se a manifestazione clinica TARDIVA

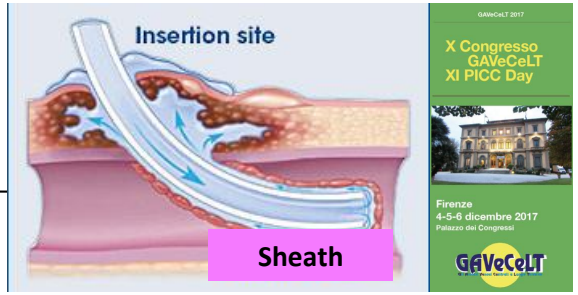
Ancora non chiaro perché alcuni traumi endoteliali evolvano in trombosi e altri in sleeve; di fatto i due eventi non si associano se non in proporzione minima

Necessaria chiarezza definitoria: “trombo pericatetere” (eco) = SLEEVE!!!

Significato clinico:

- Bassa incidenza generale, alta in popolaz. specifiche, rilevante SE SINTOMATICO
- Rilevante per i pazienti destinati al cateterismo cronico (dialisi in fallimento fistola, nutrizione parenterale totale cronica) − SALVARE IL CATETERE
- Meno rilevante negli altri casi: rimozione e nuovo impianto (su guida vs de novo)

# Conclusioni (1)




Rapporto trombosi/sleeve?

Non disponibili trattamenti farmacologici efficaci

Trattamenti invasivi efficaci ma alto rischio di recidiva

Prevenzione: fattori legati all'impianto

- posizione punta
- lunghezza del device

Ricerca diretta su materiali anti-sleeve

# GRAZIE !!!