IN VENA VITA

Le vene: un tesoro da difendere.

L'accesso vascolare appropriato come parte integrante del percorso terapeutico.

La trombosi catetere correlata.

29-30 Gennaio 2015 -Roma

Aula Magna, Pontificia Università Urbaniana

Utilizzo o rimozione?

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20TH ANNUAL AVA CONFERENCE
Changing Paradigms: Patient Safety and Quality Improvement
Association for Vascular Access

Catheter related central venous thrombosis: the development of a nationwide Consensus Paper in Italy

Mauro PITTIRUTI, Roberto BIFFI, Costantino CAMPISI, and the GAVeCeLT Committee for the Consensus Paper about catheter-related central venous thrombosis

GAVeCeLT
Gli Accessi Venosi Centrali a Lungo Termine

Eight Questions to be answered - 2

5 Which is the role of the position of the catheter tip?

6 In case of thrombosis, when should the catheter be removed?

7 Which is the best pharmacologic intervention?

8 Can we prevent catheter-related central venous thrombosis?

WoCoVA
World Congress Vascular Access

GAVeCeLT
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Q 6a - In case of thrombosis, when should the catheter be removed?

No randomised trial addresses this specific issue.
Most data come from retrospective studies.

Catheter removal or maintainance do not influence the outcome*.

Though,
(a) local thrombolitic treatment may require the presence of the catheter;
(b) a poor peripheral veins status could represent a major limiting factor for most therapies, if the catheter has been removed.

WoCoVA
World Congress Vascular Access

Thrombosis resolved in only 25% (6 of 24) when the catheter was not removed (P < .05).

About 50% of the symptomatic patients have documented resolution of thrombus on follow-up study, following therapy.

Of the patients who had thrombus resolution, 75% resolved by 100 days.

New-site UEDVT developed in 86% of patients with thrombosis who underwent catheter removal and immediate catheter placement in a new site.

(Jones M, 2010).

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Q 6b - In case of thrombosis, when should the catheter be removed?

Catheter should be removed in case of :

- infected thrombus
- malposition of the tip
- irreversible occlusion of the lumen.

Strength B Recommendation

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SOR 2008

Based on the literature review and the well-argued judgment of French experts, the 2008 SOR (Standard, Options, Recommendations) guidelines* for the prevention and treatment of CVC-associated thrombosis in patients with cancer are as follows.

**** Ann Oncol 2009; 20: 1459 -71***

Primary prevention of CVC-associated thrombosis in patients with cancer

Standards:

1. The distal tip of CVC should be placed at the junction between the superior vena cava and the right atrium.

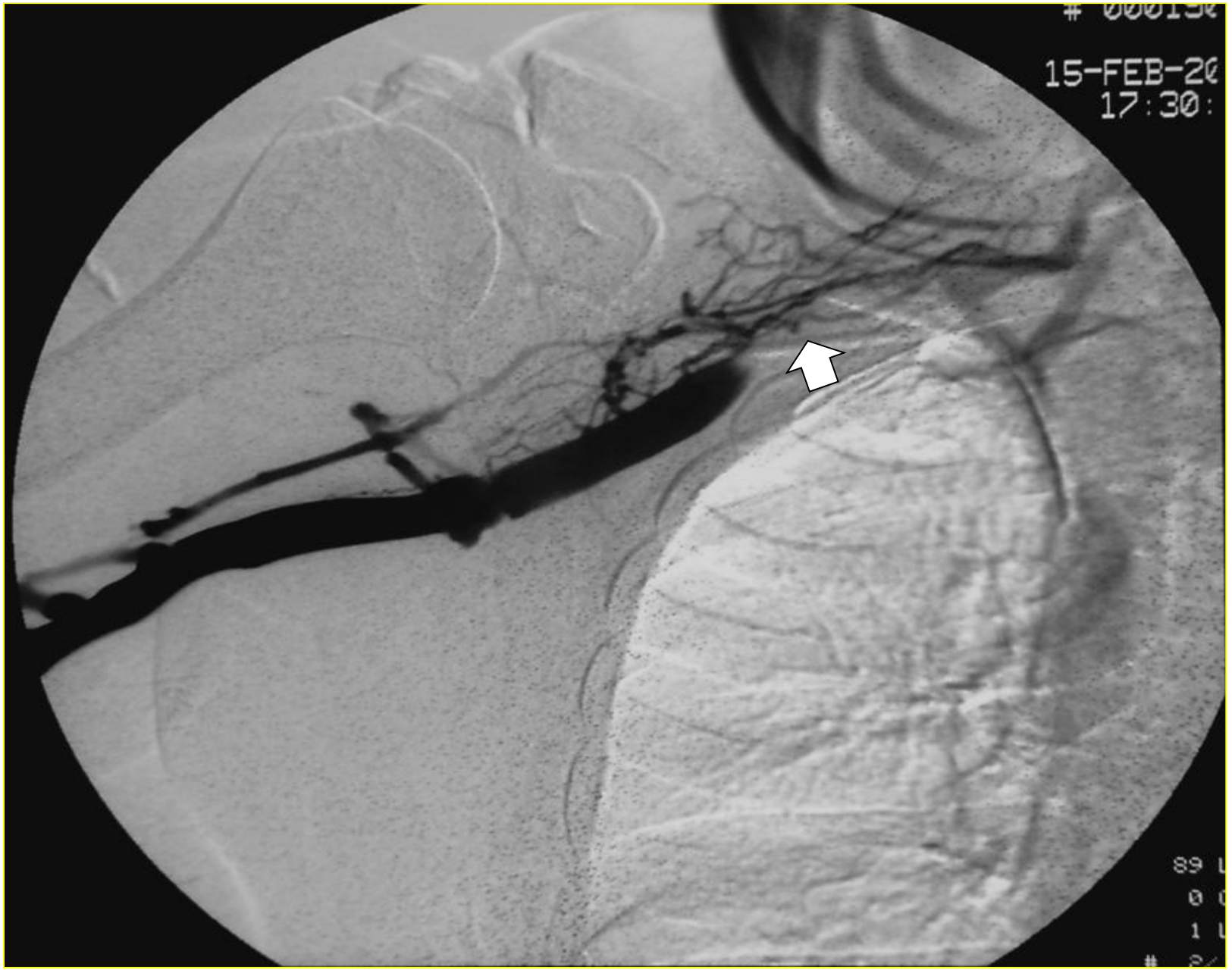
2 . The primary prevention of CVC-associated thrombosis with anticoagulant drugs is not recommended in patients with cancer.

SOR 2008
Treatment of CVC-associated thrombosis in patients with cancer

Standards:

1. The treatment of CVC-associated thrombosis should be based on the prolonged use of LMWH.

2. In the event of severe renal impairment, the treatment should be based on the use of UFH, rapidly followed (possibly as early as the first day) by VKA.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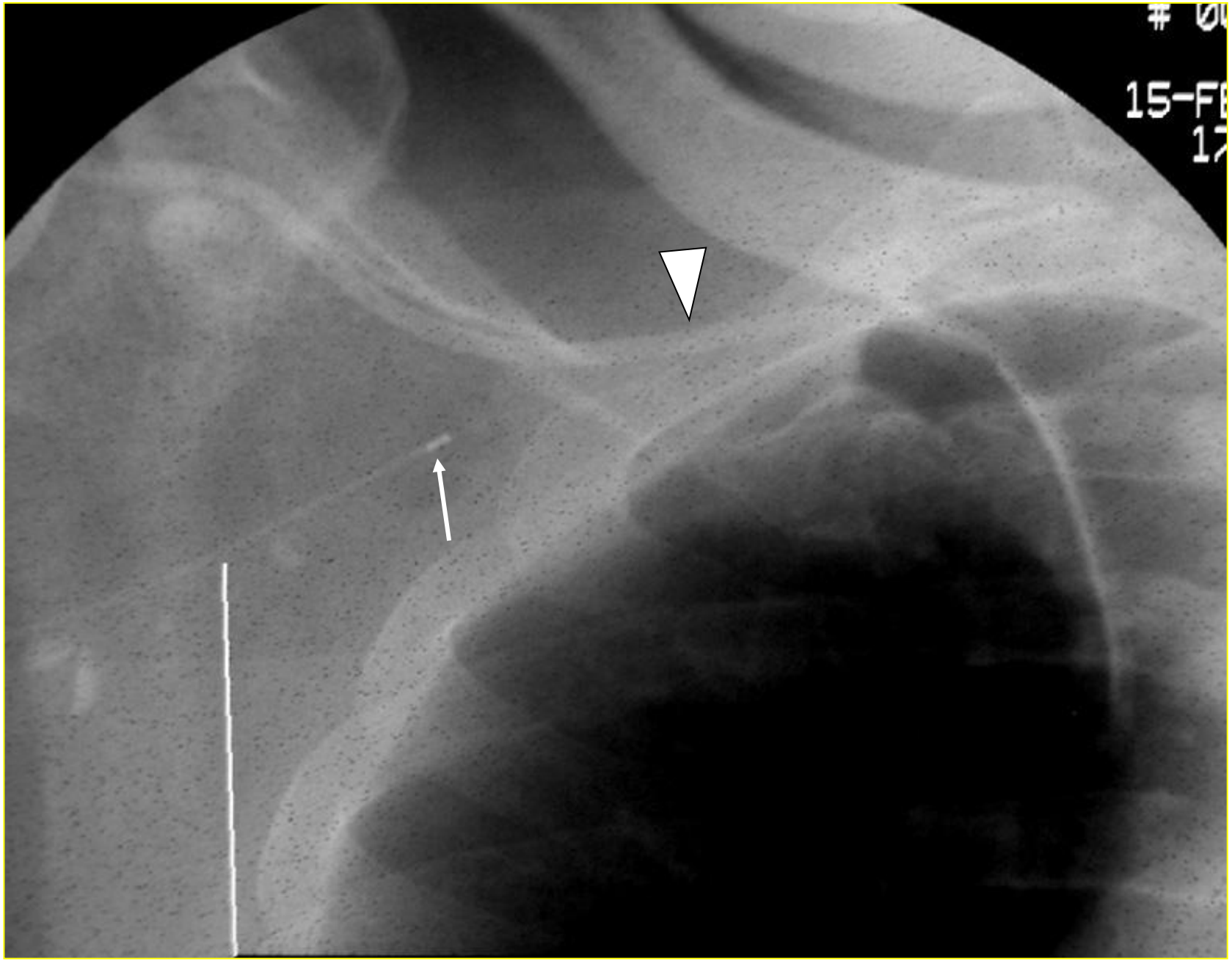

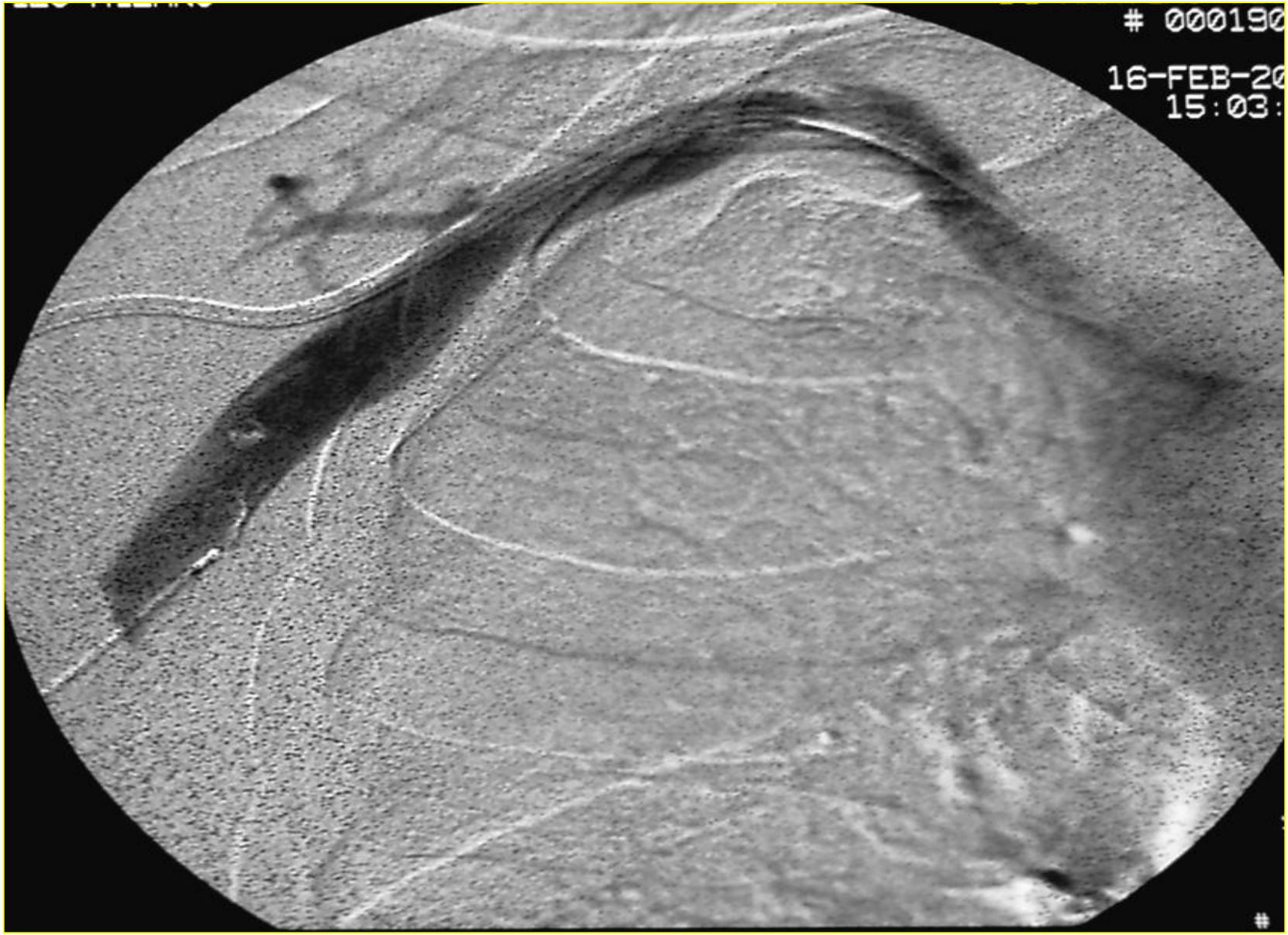
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SOR 2008
Treatment of CVC-associated thrombosis in patients with cancer

Standards (cont'd)

3. Maintenance of the catheter is justified in the event that the catheter is mandatory, functional, in the right position, and not infected, with a favorable clinical evolution under close monitoring. In this case, an anticoagulant treatment should be maintained as long as the catheter is present.

Risk factors for catheter-related thrombosis (CRT) in cancer patients: a patient -level data (IPD) meta-analysis of clinical trials and prospective studies.

W Saber*, T Moua, EC Williams, M Verso, G Agnelli, S Couban, A Young, M De Cicco, R Biffi, CJ Van Rooden, MV Huisman, D Fagnani, C. Cimminiello, M Moia, M Magagnoli, SP Povoski, SF Malak and AY Lee.

J Thromb Haemost 2010, 9: 312-9.

*University of Wisconsin School of Medicine and Public Health, Madison, WI-USA

Risk factors for catheter-related thrombosis (CRT) in cancer patients: a patient -level data (IPD) meta-analysis of clinical trials and prospective studies.

Background

Knowledge of independent, baseline risk factors for Catheter-Related-Thrombosis (CRT) may help select adult cancer patients who are at high risk to receive prophylaxis.

MM

Multivariate logistic regression analysis of 17 prespecified baseline characteristics was conducted in 5636 subjects from 5 RCTs and 7 prospective studies.

Results

425 events CRT were observed. Main findings:

Past history of DVT vs no history increased risk (OR: 2.03; 95% CI: 1,05-3,92)
Improper vs proper tip location increased risk (OR: 1.92; 95% CI: 1,22-3,02)

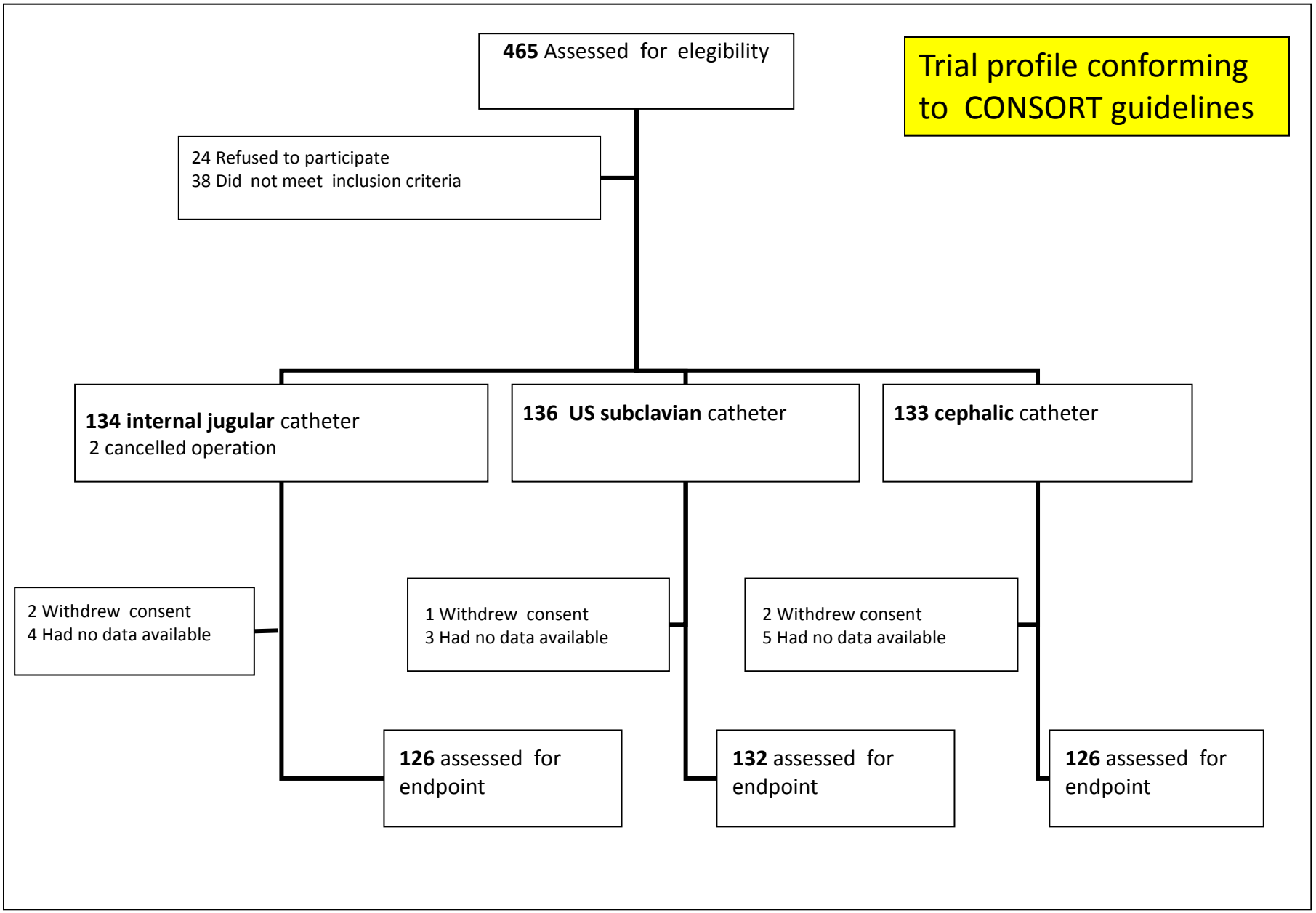
Risk factors for catheter-related thrombosis (CRT) in cancer patients: a patient -level data (IPD) meta-analysis of clinical trials and prospective studies.

Limitations

- No data about different use of prothrombotic antineoplastic drugs
- No data about schedules (bolus, c.i.) and type of tumours treated
- No data about mutation of Factor V Leiden or prothrombin gene
- Variable duration of Follow up
- Not all eligible studies provided primary data

Conclusions

All these findings should be viewed as exploratory and require validation by prospective studies.



R Biffi, *Ann Oncol 2009*

Diagnosis of catheter-related central venous thrombosis:

Power and color Doppler ultrasonography of internal jugular and subclavian veins was carried out at regular intervals
(1 and 4 months after implant)

OR

anytime when clinically suggested by the appearance of arm or facial swelling and/or pain.

Patients with positive or dubious ultrasound (US) scans underwent a neck–chest computerized tomography scan (CT), with i.v. contrast medium administration.

R Biffi, *Ann Oncol 2009*

Characteristics of the patients - 1

CHARACTERISTIC	INTERNAL JUGULAR	SUBCLAVIAN	CEPHALIC	TOTAL
No. of patients	134 (33.2%)	136 (33.7%)	133 (33.0%)	403
Patient gender				
Female	104 (77.6%)	108 (79.4%)	101 (76.0%)	313 (77.6%)
Male	30 (22.4%)	28 (20.6%)	32 (24.0%)	90 (22.4%)
Age (yrs.)				
Mean ± Stdev	53.4 ± 12.2	50.5 ± 12.0	52.1 ± 11.4	52.0 ± 11.9
Pathology				
Breast cancer	80 (59.7%)	88 (64.7%)	70 (52.6%)	238 (60%)
Others	54 (40.3%)	48 (35.3%)	63 (47.4%)	165 (40%)

R Biffi, *Ann Oncol 2009*

Characteristics of the patients - 2

CHARACTERISTIC	INTERNAL JUGULAR	SUBCLAVIAN	CEPHALIC	TOTAL
No. of patients	134 (33.2%)	136 (33.7%)	133 (33.0%)	403
Right side	95 (67.6%)	95 (70.9%)	90 (68.8%)	280 (69.5%)
Median duration of implant (range, days)	863 (0 - 988)	490 (0– 666)	551 (0– 1087)	596 (0– 1087)
Alive at the end of the study	113 (84.3%)	116 (85.3%)	109 (81.9%)	338 (83.9%)
Patients with at least 6 months follow up	117 (87.3%)	123 (90.4%)	120 (90.2 %)	360 (89.3%)
Patients who died within 6 month follow up	9 (6.7%)	9 (6.7%)	8 (6.9%)	26 (6.4%)

R Biffi, *Ann Oncol 2009*

Ann Oncol. 2009 May;20(5):935-40. doi: 10.1093/annonc/mdn701. Epub 2009 Jan 29.

Best choice of central venous insertion site for the prevention of catheter-related complications in adult patients who need cancer therapy: a randomized trial.

Biffi R, Orsi F, Pozzi S, Pace U, Bonomo G, Monfardini L, Della Vigna P, Rotmensz N, Radice D, Zampino MG, Fazio N, de Braud F, Andreoni B, Goldhirsch A

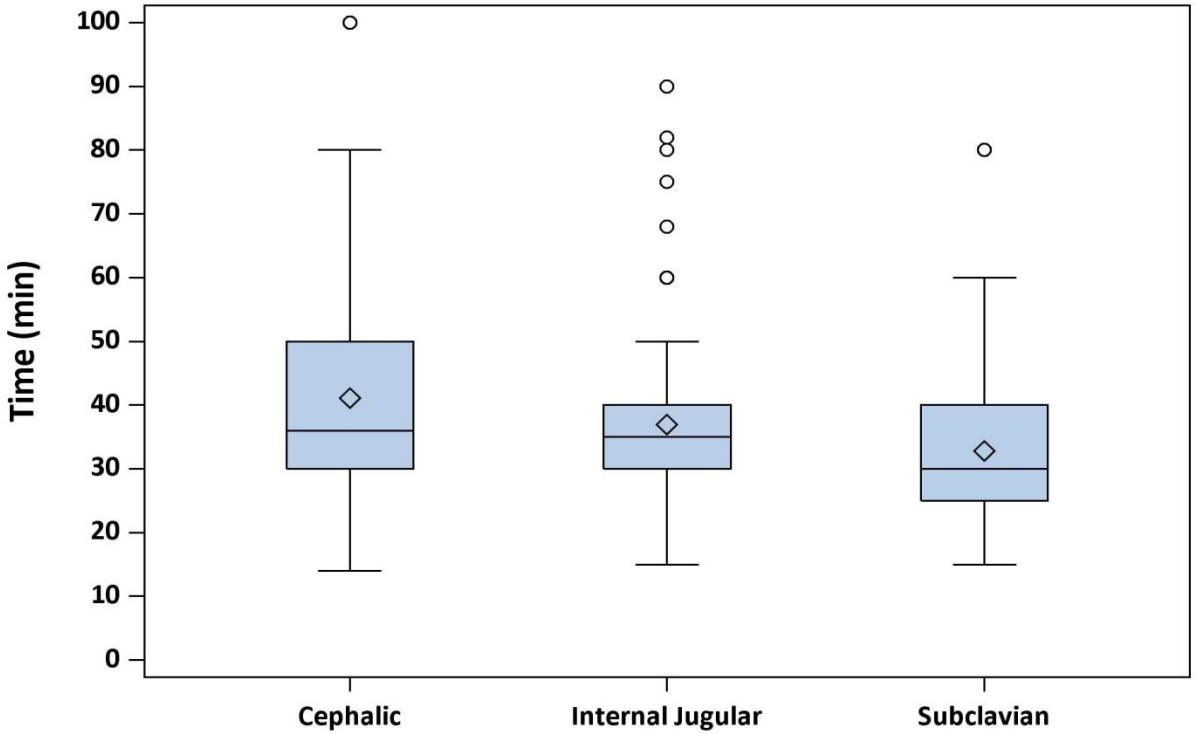
RESULTS:

Infections occurred in one, three and one patients (internal jugular, subclavian and cephalic access, respectively, P = 0.464), whereas venous thrombosis was observed in 15, 8 and 11 patients (P = 0.272).

R Biffi, *Ann Oncol 2009*

IMPACT OF ULTRASOUND (US) GUIDANCE ON PROCEDURAL TIME - 1

Procedural time: analysis by Intention-to-treat



Comparisons (Wilcoxon test) :
Cephalic vs. Internal Jugular P = 0.227;
Cephalic vs. US Subclavian ***P = .0003***;
Internal Jugular vs. US Subclavian ***P = .009***;

R Biffi, *Ann Surg Oncol 2014*

Cost of purchase and implantation of a TIVAD in this RCT by implantation site

Parameter	Internal jugular	Subclavian	Cephalic
Device	287.00	287.00	287.00
Supplies Fluoroscopy Local anesthesia Monitoring Operating Room costs (including medical and nursing staff)	1460.00	1368.00	1481.00
US device and personnel training	n.a.	32	n.a.
Laboratory tests	45.00	45.00	45.00
Total	**1792,00**	**1732,00**	**1813,00**

R Biffi, *Ann Surg Oncol 2014*

Cost of diagnosis and management of the complications observed in this clinical series (Euro)

Pneumothorax (1 case) – Management: observation (a)	**Internal Jugular**	**Subclavian**	**Cephalic**
Chest X-ray: 1 (postoperative) + 1 (six Hours) + 1 (48 hours)			165.00
Day Hospital stay			500.00
Total			**665.00**

Port-related bacteraemia (7 cases:1+3+3) - Management: proper course of antibiotic therapy w/wo removal of the device (b)	**Internal Jugular (1)**	**Subclavian (3)**	**Cephalic (3)**
Blood culture and susceptibility test	60.00	180.00	180.00
Antibiotic treatment	400.00	1200.00	1200.00
Removal of the device	326.00	326.00	652.00
Day Hospital stay	500.00	1500.00	1500.00
Total	**1286.00**	**3206.00**	**3532.00**

R Biffi, *Ann Surg Oncol 2014*

Cost of diagnosis and management of the complications observed in this clinical series (Euro)

Central venous thrombosis 34 cases: 15+8+11) – Management: Low molecular weight heparin 100 IU/kg bid for 3 months w/wo removal of the device	**Internal Jugular (15)**	**Subclavian (8)**	**Cephalic (11)**
Real-time US scan (at diagnosis and four weeks later)	7560.00	4032.00	5544.00
Low molecular weight heparin s.c. 100 IU/kg bid for 3 months	21870.00	11664.00	16038.00
Removal of the device			652.00
Laboratory test	1350.00	720.00	990.00
Day Hospital stay	15000.00	8000.00	11000.00
Total	**45780.00**	**24416.00**	**34224.00**
Global cost of complications' diagnosis and treatment	**47066.00**	**27622.00**	**38411.00**

R Biffi, *Ann Surg Oncol 2014*

Global cost of purchase, implantation and maintenance of a TIVAD in this RCT (Euro).
[R Biffi et al, *Ann Surg Oncol 2014*]

Experimental Group	Internal Jugular	Subclavian	Cephalic
Cost of single port purchase and implantation	1792.00	1732.00	1813.00
Number of implanted ports, as per intent-to-treat	133	136	134
Global cost of devices' purchase and implantation	238366.00	235552.00	242942.00
Cost of treatment of early complications	-	-	665.00
Cost of treatment of late complications	47066.00	27622.00	37756.00
Global cost of complications' diagnosis and treatment	47066.00	27622.00	38411.00
Global cost of devices' purchase, implantation and complications'treatment	285432.00	263174.00	281353.00
Device maintenance cost (six months)	31654.00	31654.00	31654.00
Global cost for each patient treated	2384.10	2167.85 *	2335.87

* Wilcoxon test, P: .0001

Conclusions and take-home messages

Thrombosis remains the most frequent and costly complication, although it is not the most frequent cause of TIVAD removal.
Clinical data derived from our study should be matched with the indication not to routinely use prophylactic anticoagulants in patients bearing a TIVAD.

Costs of prophylaxis vs costs of the proper treatment of venous thromboses complicating the post-implant course (extended up to six months), without taking into account the possible costs related to diagnosis and treatment of the side effects of anticoagulants.

Interestingly, there was a trend of the thrombosis rate in favor of US-guided subclavian access, possibly through a reduction of the vessel trauma caused by US guidance. This could be matter of future investigation, aiming at detection of an inner superiority of US-guided access in thrombotic events >>> RCT comparing US guided TIVAD w/wo prophylaxis.

Thank you for your attention !

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