PICC and venous thrombosis

Mauro Pittiruti
Catholic University Hospital, Rome - Italy
Catheter-related thrombosis

What are we talking about?

... a pathophysiological phenomenon with several obscure issues...
Catheter-related thrombosis

Definition is often unclear
The pathogenesis is multifactorial and controversial
Diagnosis may be difficult
The epidemiology is not well known
Treatment is somehow controversial
Preventive measures are often neglected
Definition of CRT
Definition of CRT

1) THROMBOSIS IS NOT CLOTTING OF THE CATHETER LUMEN
Definition of CRT

1) THROMBOSIS IS NOT CLOTTING OF THE CATHETER LUMEN

The blood-derived material which may occlude the catheter lumen is NOT a thrombus, but a clot (a ‘coagulum’) and very often a clot mixed with non-blood derived substances (biofilm, drug precipitates, etc.)
Definition of CRT

1) **THROMBOSIS IS NOT CLOTTING OF THE CATHETER LUMEN**

By definition, a thrombus occurs secondary to an endothelial injury and – as such – can occur exclusively INSIDE A VESSEL.
Definition of CRT

1) 

THROMBOSIS IS NOT CLOTTING OF THE CATHETER LUMEN

Both the ‘tissue factor’ (extrinsic) pathway and the ‘contact activation’ (intrinsic) pathway are secondary to a damage of the vessel wall.
Definition of CRT

1) THROMBOSIS IS NOT CLOTTING OF THE CATHETER LUMEN

Lumen occlusion is a complication which can be 100% prevented by an appropriate policy of catheter care; CRT is a complication which can be minimized but not eliminated.
Confusion will be my epitaph ...
(King Crimson, 1969)

Management of occlusion and thrombosis associated with long-term indwelling central venous catheters

Jacquelyn L. Baskin, MD, Ching-Hon Pui, MD, Ulrike Reiss, MD, Judith A. Willimas, MD, Monika L. Metzger, MD, MSc, Raul C. Ribeiro, MD, and Scott C. Howard, MD, MSc

Conclusion

Long-term CVCs are important for the medical care of children and adults with chronic illness, but can lead to various complications such as CVC occlusions and CRT. The etiology of a catheter occlusion determines the appropriate treatment, but most occlusions are thrombotic and should be treated with thrombolytic therapy. Alteplase is most commonly used in North America but new agents have shown promising improvements in efficacy and onset of action. Further studies are required to compare new thrombolytics to those currently available.

**Thrombotic CVC occlusions can cause CRT**, which can lead to post-thrombotic syndrome, pulmonary embolism, and an increased risk for catheter infections. Although prevention of
Obviously...

An occluded catheter can NEVER cause a venous thrombosis.

Though, on the contrary, a venous thrombosis at the tip of the VAD may occlude the catheter....
Definition of CRT

2) THROMBOSIS IS NOT THE FIBROBLASTIC SLEEVE WHICH SURROUNDS THE CATHETER
Definition of CRT

2) THROMBOSIS IS NOT THE FIBROBLASTIC SLEEVE WHICH SURROUND THE CATHETER

The fibroblastic sleeve (erroneously named ‘fibrin sleeve’ or ‘fibrin sheath’) is a physiological phenomenon which occurs every time a foreign body is in prolonged contact with the blood inside the vessels.
Definition of CRT

2) THROMBOSIS IS NOT THE FIBROBLASTIC SLEEVE WHICH SURROUNDS THE CATHETER

The fibroblastic sleeve starts with the deposition of circulating fibronectin over the catheter, while thrombosis starts from tissue factors released by endothelial injury.
Definition of CRT

2) THROMBOSIS IS NOT THE FIBROBLASTIC SLEEVE WHICH SURROUNDS THE CATHETER

The fibroblastic sleeve is a tissue made of mostly of fibroblastic cells; the thrombus is a tissue made of aggregated platelets mixed with a mesh of fibrin protein.

Experimental evidence in rats favors the hypothesis of a migration of smooth muscle cells from the endothelium and collagen deposition (Stas M, J Vasc Surg 1998).
Definition of CRT

CRT = Appearance of a thrombus on the vascular wall, most frequently where the endothelium is damaged by the catheter introduction site and/or where the contact between vein wall and catheter is maximal.

PARIETAL THROMBUS is the typical expression of CRT; it may have different extension and clinical relevance:

- < 50% of the lumen - almost always asymptomatic
- > 50% of the lumen - with or without collateral circulation - symptomatic or not
- 100% of the lumen (obstructive thrombosis) - usually with collateral circulation and usually symptomatic (edema, pain).
Pathogenesis of CRT

CRT may occur (1) from endothelial damage at the site of venipuncture, or (2) as the effect of a mechanical trauma of the catheter (and specially the catheter tip) against the venous wall, or (3) as the result of a chemical injury to the endothelium.
Pathogenesis of CRT

(1) endothelial damage at the site of venipuncture
   - Upper limb CRT after PICC insertion
   - Jugular/subclavian CRT after CICC insertion
   - Femoral/Iliac CRT after FICC insertion

(2) mechanical trauma or chemical injury of the vein wall
   - central venous thrombosis (brachiocephalic/SVC)
     due to CICC or PICC with inappropriate tip position
Diagnosis of CRT

As regards the diagnosis of CRT, the widespread use of ultrasound in the field of venous access devices has changed everything.
Diagnosis of CRT

Widespread use of US:

- Has increased the possibility of diagnosis of asymptomatic thrombosis
- Has increased the possibility of early diagnosis
- Has reduced the role of angiography and CT
Diagnosis of CRT

Particularly easy with PICCs, since arm veins are easy to explore:
Diagnosis of CRT

Current practice:

- If CRT is suspected, first step is doppler US
- If the whole thrombus is visualized (‘head to tail’), no further exam is needed
- If the thrombus extends to the brachiocephalic or further, a CT scan with i.v. contrast is needed
Diagnosis of CRT

Pitfalls of US:

- Extensive use of US may lead to diagnosis of asymptomatic CRT and to over-treatment

- Operators with poor experience may confuse fibroblastic sleeve with CRT (which may lead to over-treatment, too)

- Even with a normal US finding, a malfunctioning VAD may have a thrombus on its tip (typically, if malpositioned)
Classification of CRT

According to the extension of the thrombus inside the vein:

- **Mural thrombosis** (non-obstructive)
  - Either asymptomatic or symptomatic
  - With or without collateral circulation

- **Complete venous thrombosis** (obstructive)
  - Mostly symptomatic
  - With collateral circulation
Classification of CRT

According to the location of the thrombus inside the venous system:

- **Upper limb thrombosis** (PICCs)
  - basilic, brachial, cephalic, axillary

- **Central thrombosis** (PICCs and CICCs)
  - Axillary, subclavian, jugular, brachiocephalic, SVC

- **Lower limb thrombosis** (FICCs)
  - Femoral, iliac, IVC
Classification of CRT

According to the presumed pathogenesis:

- CRT due to endothelial damage on the site of venipuncture (mechanical injury)
  - Typically associated with ‘traumatic’ insertion

- CRT due to endothelial damage at the tip of the catheter (mechanical and/or chemical injury)
  - Typically associated with tip malposition
Epidemiology of CRT

As any VAD is associated with some degree of endothelial injury, any VAD is potentially associated with CRT.

Symptomatic: 0-28% (?)

Asymptomatic: 12-66% (?)

(The Oncologist, 2008)

(‘%’ is more appropriate than ‘episodes/1000 VAD days’)
CVC RELATED THROMBOSIS (CRT)

**SYMPTOMATIC**
Range from 0 to 28%

**ASYMPTOMATIC**
Range from 12 to 66%


**SYMPTOMS vs US vs CT vs ANGIOGRAPHY**
Which are the risk factors?

A confused problem:

- Underpowered studies
- Multiple confounding variables and disomogeneity in patients recruitment
- Unclear definition of CRT itself
Risk factors for CRT

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

By Melina Verso and Giancarlo Agnelli

Table 4. Risk Factors for Development of CVC-Related DVT

<table>
<thead>
<tr>
<th>CVC Features</th>
<th>Patient Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical structure</td>
<td>High platelet count</td>
</tr>
<tr>
<td>Catheter diameter</td>
<td>Cancer-related activation of coagulation cascade</td>
</tr>
<tr>
<td>Numbers of lumens</td>
<td>CVC-related activation of coagulation cascade</td>
</tr>
<tr>
<td>Catheter tip positions</td>
<td>Chemotherapy-related activation of coagulation cascade</td>
</tr>
<tr>
<td>Side of insertion</td>
<td>Thrombophilic molecular abnormalities</td>
</tr>
<tr>
<td>Insertion techniques</td>
<td></td>
</tr>
<tr>
<td>Previous CVC insertion</td>
<td></td>
</tr>
<tr>
<td>CVC-related infections</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CVC, central venous catheter; DVT, deep venous thrombosis.
The conventional risk factors for thrombosis are summarized in the Virchow’s triad: vascular injury, stasis and hypercoagulability. On this basis, factors involved in the pathogenesis of catheter-related thrombosis include vessel wall injury as a result of the needle insertion; venous stasis or occlusion as a result of the catheter placement; the central position of the tip; the material of the catheter; the nature of substances being infused.
Risk factors for CRT

1 – the patient
2 – the disease
3 – the VAD
4 – the insertion technique
Risk factors for CRT

1 - the patient
Which are the patients’ risk factors?

In prospective studies, mutations of Factor V Leiden and/or prothrombin gene have been found to be related to an higher incidence of central venous thrombosis in cancer patients bearing a central venous catheter.

Screening procedures have not been proven to be cost-effective.
Risk factors for CRT

2 – the disease
Risk is increased in ICU patients

In particular:
- FICC
- Aged patients
- Prolonged immobilization
- VAD inserted in emergency
- Septic patients
Risk is increased in cancer patients
TUMOR CELL-DEPENDENT MECHANISMS OF BLOOD CLOTTING ACTIVATION

Production of procoagulant and fibrinolytic activities

Direct blood clotting activation

Expression of Adhesion Receptors

Release of cytokines and angiogenic factors

Activation of host cell (endothelial cells, platelets, leukocytes) procoagulant and proadhesive properties

Thrombin and Fibrin formation

Hypercoagulable State of the Host
Neoplastic disease and chemotherapy are recognised risk factors for development of deep vein thrombosis in patients bearing a central venous catheter.

Pathophysiology is known: it includes direct release of thrombogenic factors by neoplastic cells, decrease of antithrombotic natural factors induced by tumour, and the procoagulant activity of many antitumour drugs.
<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Risk score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Site of cancer</strong></td>
<td></td>
</tr>
<tr>
<td>Very high risk (stomach, pancreas)</td>
<td>2</td>
</tr>
<tr>
<td>High risk (lung, <em>lymphoma</em>, gynecologic, bladder, testicula)</td>
<td>1</td>
</tr>
<tr>
<td>Pre-CT platelet count &gt; 350,000/ml</td>
<td>1</td>
</tr>
<tr>
<td>Hemoglobin level &gt;10 g/dL or use of erythropoietin stimulating agents</td>
<td>1</td>
</tr>
<tr>
<td>Pre-CT leukocyte count &gt; 11*10⁹/L</td>
<td>1</td>
</tr>
<tr>
<td>BMI &gt; 35 Kg/m²</td>
<td>1</td>
</tr>
</tbody>
</table>

*Not all cancer patients have the same risk*

*Khorana A et al, Blood 2008*
7.0.3. For cancer patients with indwelling central venous catheters, we recommend that clinicians not use either prophylactic doses of LMWH (Grade 1B) or mini-dose warfarin (Grade 1B) to try to prevent catheter-related thrombosis.
Should we use routine pharmacological prophylaxis in some patients with VAD?

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

38 | JAVA | Vol 12 No 1 | 2007
Should we use routine pharmacological prophylaxis in some patients with VAD?

Conclusions of the Consensus

- Although some open-label, early trials suggested a benefit of oral, low-dose daily warfarin or daily subcutaneous dose of LMWHs, more recent randomized, double-blind, placebo-controlled, and sufficiently powered trials did not find any advantages for either of these prevention strategies.
- The choice to start a prophylaxis of venous thromboembolic events in all oncology patients bearing a CVC, either with LMWHs or with minidose warfarin, remains unsupported by evidence-based medicine.
- GAVeCeLT suggests considering prophylaxis with a daily single dose of LMWH 100 IU/kg only in high-risk population (including those who have a family history or previously suffered from idiopathic venous thrombotic events of the upper or lower vena cava district).
Risk factors for CRT

3 – the VAD
Q3

Is there any device or material which may intrinsically reduce the risk?

- Silicon and polyurethane catheters are less thrombogenic than polyethylene or PVC ones.
- A lower diameter of the catheter might be protective against the risk of central venous thrombosis.

Strength B Recommendation
Risk factors for CRT

Is there any clinical evidence that some material – specifically treated with antithrombotic substances – may actually reduce the risk of CRT?

NO

(or: ‘not yet’ ?)
Are dialysis-VAD particularly at risk of CRT?

Of course they are, mainly because of the necessity of inserting catheters of very large caliber.

Still, the rate of CRT can be minimized by puncturing the biggest vein available (right brachio-cephalic vein).
Are pediatric VAD particularly at risk of CRT?

Of course they are, mainly because of the necessity of inserting catheters in very small veins.

Still, the rate of CRT can be minimized by carefully matching the catheter caliber with the vein caliber (e.g.: brachio-cephalic vein in neonates)
Are FICC particularly at risk of CRT?

- Yes

- Much evidence shows that Femorally Inserted Central Catheters are at increased risk of CRT (in adult patients)

- Lower limb CRT is also associated with a four fold increase of risk of PE (Minet 2015)
Are FICC particularly at risk of CRT?

ESPEN Guidelines on Parenteral Nutrition: Central Venous Catheters
(access, care, diagnosis and therapy of complications)

Mauro Pittiruti a, Helen Hamilton b, Roberto Biffi c, John MacFie d, Marek Pertkiewicz e

The use of the femoral vein for PN is relatively contraindicated, since this is associated with a high risk of contamination at the exit site in the groin, and a high risk of venous thrombosis.
Are PICC particularly at risk of CRT?

The contention that PICC may have a prohibitive risk of CRT has been discussed in four recent reviews:

- Pikwer et al (Anaesthesia, 2012)
- Chopra et al (The Lancet, 2013)
- Fallouh et al. (Am J Med 2015)
- Zochios (JVA 2015)
Are PICC particularly at risk of CRT?

Pikwer A, Åkeson J, Lindgren S.

Complications associated with peripheral or central routes for central venous cannulation.

Are PICC particularly at risk of CRT?

In this review by Pilker et al., the authors included in their analysis for PICC-related thrombosis, at least five studies dealing with PICCs inserted without US.

One of the studies used the same size of PICCs regardless of the vein’s diameter.

Only three of the studies had declared diagnostic criteria used for thrombosis.

No study was prospective and/or randomized.
Are PICC particularly at risk of CRT?

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

Summary

Background Peripherally inserted central catheters (PICCs) are associated with an increased risk of venous thromboembolism. However, the size of this risk relative to that associated with other central venous catheters (CVCs) is unknown. We did a systematic review and meta-analysis to compare the risk of venous thromboembolism associated with PICCs versus that associated with other CVCs.

Methods We searched several databases, including Medline, Embase, Biosis, Cochrane Central Register of Controlled Trials, Conference Papers Index, and Scopus. Additional studies were identified through hand searches of bibliographies and internet searches, and we contacted study authors to obtain unpublished data. All human studies published in full text, abstract, or poster form were eligible for inclusion. All studies were of adult patients aged at least 18 years who underwent insertion of a PICC. Studies were assessed with In studies without a comparison group, the pooled frequency of venous thromboembolism receiving PICCs. In studies comparing PICCs with other CVCs, summary of random effects meta-analysis.

Findings Of the 533 citations identified, 64 studies (12 with a comparison group) with 29,503 patients met the eligibility criteria. In the non-comparison studies, the deep vein thrombosis was highest in patients who were critically ill (13.91%, 95% CI 6.67%, 4.69–8.64). Our meta-analysis of 11 studies comparing the PICCs with that related to CVCs showed that PICCs were associated with an (OR 2.55, 1.54–4.23, p<0.0001) but not pulmonary embolism (no events). We reported a thrombosis rate of 2.7% and pooled OR of 2.55, the number needed to harm relative to CVCs was 26 (95% CI 13–71).

Interpretation PICCs are associated with a higher risk of deep vein thrombosis than are CVCs, especially in patients who are critically ill or those with a malignancy. The decision to insert PICCs should be guided by weighing the risk of thrombosis against the benefit provided by these devices.

Chopra V, Anand S, Hickner A, Buist M, Rogers MA, Saint S, Flanders SA.
Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis.
Lancet. 2013;382:311-25
Are PICC particularly at risk of CRT?

Is this meta-analysis really valid?

- Meta-analyses should be preferably performed on prospective randomized clinical trials (PRCT) published on peer-reviewed journals

- On the contrary, this ‘meta-analysis’ included any type of clinical papers (retrospective, non-randomized, etc.) and even abstracts and papers published on non-peer-reviewed journals
Are PICC particularly at risk of CRT?

- Though, risk of bias was assessed independently by two researchers and 11 studies were finally included in a meta-analysis.

- Unfortunately, some of these 11 studies did not have thromboembolic risk as their main outcome; some were performed without the use of ultrasound; in some studies the same catheter size was used in all patients, regardless of the vein caliber; many were retrospective.
Are PICC particularly at risk of CRT?

Overall, the 64 studies collected by Chopra et al. are extremely heterogeneous:

- Asymptomatic vs symptomatic thrombosis
- Old fashioned PICC at the antecubital fusa (no US) vs. US-guided PICC at midarm
- Oncological vs. non-oncological patients
- Most studies give little or no information about tip position
- Some studies included PICCs inserted in patients with obvious contraindication to PICC insertion
- ..................
Are PICC particularly at risk of CRT?

Is this systematic review really valid?

At least 6 of the 64 studies report asymptomatic CRT (with obviously high %)

- Cortelezzi 2003  25 %
- Abdullah 2005  38.5 %
- Paauw 2008  33 %
- Trerotola 2010  52 %
- Bonizzoli 2011  27 %
- Catalano 2011  6.8 %
Are PICC particularly at risk of CRT?

Is this systematic review really valid?

At least 1 of the 64 studies confuses CRT with lumen occlusion (Worth 2009)

At least 1 study deals with CRT in pediatric patients (Vidal 2008)

At least 1 study reports a high rate of not acceptable tip positions (Lobo 2009)

At least 1 of the 64 studies deals exclusively with CRBSI and does not mention CRT (Mollee 2011)

At least 2 studies on neurological patients (from the same center) include also PICCs inserted in paretic arms (Wilson 2012, Fletcher 2011)
Are PICC particularly at risk of CRT?

Is this systematic review really valid?

At least 14 of the 64 studies report experience with old-fashioned PICCs inserted without microintroducer and without US, at the antecubital fissa.


- CRT : 0.5 % - 14.9 %
Are PICC particularly at risk of CRT?

Is this systematic review really valid?

In summary, out of 64 studies ‘analyzed’ in this review, only 9 can be taken seriously into consideration:

- 8 in non-oncological patients
- 1 in oncological patients
Are PICC particularly at risk of CRT?

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>King 2006</td>
<td>2.1 %</td>
</tr>
<tr>
<td>Al Raay 2010 (ICU pts)</td>
<td>0.9 %</td>
</tr>
<tr>
<td>Evans 2010</td>
<td>3.0 %</td>
</tr>
<tr>
<td>Fearonce 2010 (burns)</td>
<td>2.7 %</td>
</tr>
<tr>
<td>DeLemos 2011 (neuro)</td>
<td>3.0 %</td>
</tr>
<tr>
<td>Pittiruti 2012 (ICU pts)</td>
<td>3.0 %</td>
</tr>
<tr>
<td>Sperry 2012</td>
<td>1.3 %</td>
</tr>
<tr>
<td>Liem 2012</td>
<td>3.0 %</td>
</tr>
<tr>
<td>1 study in oncological patients</td>
<td></td>
</tr>
<tr>
<td>Aw 2012</td>
<td>5.6 %</td>
</tr>
</tbody>
</table>
Are PICC particularly at risk of CRT?

The best conclusion we can draw from this ‘systematic review and meta-analysis’ is that the expected risk of symptomatic PICC-related thrombosis is about 1-3% in non-oncological patients and slightly higher (5-6%) in oncological patients.

Which we already knew.
Are PICC particularly at risk of CRT?

Peripherally inserted central catheter (PICC)-related thrombosis in critically ill patients

Vasileios Zochios¹, Imraan Umar², Nicola Simpson³, Nicola Jones¹

¹ Cardiothoracic Intensive Care Unit, Critical Care Area, Papworth Hospital NHS Foundation Trust, Papworth Everard Cambridge - UK
² Department of Surgery, University Hospitals of Leicester NHS Trust, Leicester Royal Infirmary, Leicester - UK
³ Intensive Care Unit, Department of Anesthesia and Critical Care, Kettering General Hospital NHS Foundation Trust, Kettering, Northamptonshire - UK
Are PICC particularly at risk of CRT?

This review by Zochios et al. is carried out without any systematic methodology. It describes a few studies about PICC-related thrombosis. Moreover, most of the studies quoted in this review are affected by bias related to the insertion technique, to the type of device used (inappropriate caliber) and to the retrospective design.
Are PICC particularly at risk of CRT?

Fallouh N, McGuirk HM, Flanders SA, Chopra V.

Peripherally Inserted Central Catheter-Associated Deep Vein Thrombosis: A Narrative Review.

Are PICC particularly at risk of CRT?

In this paper, Fallouh et al. have not conducted any systematic assessment of the studies: they just discuss some studies from the literature, trying to define a clinical approach on how to detect patients with increased risk of PICC-related thrombosis.
Are PICC particularly at risk of CRT?

And what about the studies published in 2013-2015?

Let us consider only fully published studies on peer-reviewed journals, reporting symptomatic CRT secondary to US-guided PICCs.
Are PICC particularly at risk of CRT?

<table>
<thead>
<tr>
<th>13 studies in non-oncological patients</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Botella-Carretero 2013 (HPN)</td>
<td>0 %</td>
</tr>
<tr>
<td>- Evans 2013</td>
<td>1.9 %</td>
</tr>
<tr>
<td>- Pan 2014</td>
<td>0.5 %</td>
</tr>
<tr>
<td>- Itkin 2014</td>
<td>4.3 %</td>
</tr>
<tr>
<td>- non-tapered</td>
<td>4.3 %</td>
</tr>
<tr>
<td>- tapered</td>
<td>3.6 %</td>
</tr>
<tr>
<td>- Mermis 2014</td>
<td>7.6 %</td>
</tr>
<tr>
<td>- 5-6Fr PICCs</td>
<td>0 %</td>
</tr>
<tr>
<td>- 4Fr PICCs</td>
<td></td>
</tr>
<tr>
<td>- Wilson 2014</td>
<td>1.6 %</td>
</tr>
<tr>
<td>- Haglund 2014</td>
<td>3.1 %</td>
</tr>
<tr>
<td>- Valbousquet 2015 (surgery)</td>
<td>0 %</td>
</tr>
<tr>
<td>- Greene 2015</td>
<td>5.4 %</td>
</tr>
<tr>
<td>- Lisova 2015</td>
<td>4 %</td>
</tr>
<tr>
<td>- Austin 2015 (burns)</td>
<td>5.5 %</td>
</tr>
<tr>
<td>- Dupont 2015</td>
<td>2 %</td>
</tr>
<tr>
<td>- Toure 2015</td>
<td>1.4 %</td>
</tr>
</tbody>
</table>
Are PICC particularly at risk of CRT?

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moraza-Dulanto 2012</td>
<td>5 %</td>
</tr>
<tr>
<td>Gong 2012</td>
<td>0 %</td>
</tr>
<tr>
<td>Cotogni 2013</td>
<td>0 %</td>
</tr>
<tr>
<td>Bellesi 2013 (hemato)</td>
<td>5 %</td>
</tr>
<tr>
<td>Pittiruti 2014</td>
<td>0.5 %</td>
</tr>
<tr>
<td>Li 2014</td>
<td>0 %</td>
</tr>
<tr>
<td>Mitrovic 2014 (hemato)</td>
<td>3.8 %</td>
</tr>
<tr>
<td>Martella 2015 (hemato)</td>
<td>0 %</td>
</tr>
<tr>
<td>Kang 2015</td>
<td>5.2 %</td>
</tr>
<tr>
<td>Sriskanadarajah 2015 (hemato)</td>
<td>5.6 %</td>
</tr>
<tr>
<td>Morano 2015 (hemato)</td>
<td>7.7 %</td>
</tr>
<tr>
<td>Cotogni 2015</td>
<td>1.1 %</td>
</tr>
</tbody>
</table>
Are PICC particularly at risk of CRT?

Though there is a wide variation between centers, it is still evident that the expected rate of CRT with PICCs is not really different from the expected rate of CRT with CICCs:

- **0 - 3 %** in non-oncological patients

- **0 - 6 %** in oncological patients (and particularly in hematological patients)
Are PICC particularly at risk of CRT?

But WHY this wide variation between centers?

Let us consider 3 studies on PICCs in neurological patients, all from the same center (Michigan University):

Fletcher 2011  8.1 %
Wilson 2012  8.4 %
Wilson 2013  8.4 %

In all three studies, PICCs were also inserted in paretic arms (!).
Are PICC particularly at risk of CRT?

On the other hand, let us consider studies including PICCs inserted with specific attention to the catheter caliber and/or with a proper insertion bundle for preventing thrombosis:
In conclusion:

- PICCs are **theoretically** more prone to CRT (small veins; extended interaction between catheter and vein wall; high risk of tip malposition)

- Still, there is **no convincing clinical evidence** that the rate of CRT associated with PICCs is definitely higher than with CICCs

- Also: a wise choice of catheter size and a proper insertion technique may reduce CRT effectively
In other words:

- If PICCs are inserted respecting the proper indications/contraindications and paying attention to the catheter/vein caliber and to the tip position, the expected rate of CRT is 3% or less

That’s why we need an insertion bundle
Thank you for your attention!

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