How to prevent and treat catheter-related thrombosis

Sergio Bertoglio, M.D.
Department of Surgery
UNIVERSITY OF GENOVA - ITALY
Lecturer and/or Consultancy agreements:

Baxter
B. Braun
Becton Dickinson - Bard
BMR - Brazil
DEKRA
Innova Medica
Polymed P1Health
PREVENTION OF CR-VTE

RIGHT CATHETER FOR RIGHT PATIENT

- PERIPHERAL OR CENTRAL
- EXTERNAL OR TOTALLY IMPLANTABLE

ASSESSMENT OF RIGHT VENOUS SITE AND SIZE

FOR PERIPHERAL INSERTED CVCs, MIDLINES OR SIMILAR RESPECT C/V RATIO RANGE \( \leq 0.3 \)

RIGHT TECHNIQUE OF IMPLANT AND MANAGEMENT

- PERCUTANEOUS US GUIDED
- MSI AND ANTT
- APPROPRIATE TIP LOCATION
- MANAGEMENT PROTOCOLS
RISK FACTORS FOR CR-VTE

PATIENT FACTORS
• Previous history of VTE
• Cancer and stage of cancer
• Acquired factors (Caprini risk score or similar)
• Congenital factors (AT def., Leiden V, PS/PC def., APC res., other)

FACTORS RELATED TO MATERIALS
• Catheter size and multilumen larger devices
• Catheter materials (Thermoplastic PUR or SIL)
• Fixation and stabilization methods for external catheters (PICCs, Midline)

IMPLANTATION TECHNIQUE
• Extensive use of US
• Venous and site access evaluation
• Reduction of number of tentatives and less parietal damage
• Choice of the vein with a catheter/vein ratio (0.45 0.33)
FACTS AND FIGURES ABOUT CR-VTE

MODERATE INCIDENCE
- Variable rates depending on the type of catheter and patient medical history (0.5-35%)
- Less than 1/3 of CR-T are symptomatic

VERY LOW MORTALITY RATES
- Estimated fatal events attributable to CR-VTE are less than 0.05% (1/5000 events)

ELEVATED CLINICAL IMPACT
- Medical treatment and monitoring
- Patient’s fear especially for PE
- Increased economic resources
CR-VTE

OBJECTIVE OF TREATMENT

- Reduce symptoms
- Prevent extension of the thrombus
- Prevent chronic venous occlusion
- Prevent VTE recurrence and/or PE
- Maintain the catheter unless no longer needed, non functional, dislodged or infected
Maintain the catheter unless no longer needed, non functional, dislodged or infected

- Even if the catheter is removed anticoagulation is still required to prevent recurrent VTE or PE

- A reinsertion of another catheter is usually needed

- There is no evidence that removal of the catheter improves outcome (ISTH 2013 and ACCP 2016 Guidelines and Recommendations)
CR-VTE TREATMENT
simple, highly successful and safe

Therapeutic landscape is similar to that of VTE mainly based on anticoagulation obtained by

1. UFH (only patients with severe renal failure)
2. LWMH/ FUNDAPARINUX
3. VK antagonists
4. DOACs (anti-Xa or thrombin inhibitors)
5. Thrombolysis (Urokinase / r-TPA)
THE DIFFERENT PHASES FOR A CR-VTE TREATMENT

INITIAL PHASE

EXTENDED PHASE
PATIENT RELATED SCENARIOS FOR CR-VTE TREATMENT

NON CANCER PATIENTS

CANCER PATIENTS

SYMPTOMATIC OR INCIDENTAL ASYMPTOMATIC CR-THROMBOSIS

SIMILAR APPROACH
ALGORITHM FOR THE MANAGEMENT OF CR-VTE

INITIAL PHASE: from 5 -10 days to 3 months or resolution of symptoms

NON CANCER PATIENTS

ANTICOAGULATION WITH LWMH OR FUNDAPARINUX AT THERAPEUTIC DOSAGE
NCCN, ASCO, ACCP, ESMO.ISTH Guidelines

CANCER PATIENTS
INITIAL PHASE: There is a marginal role for thrombolysis

- SVC Syndrome
- Acute limb threat
- Severe symptoms progression

Consider r-TPA or urokinase for low bleed risk patients

CONTINUE ANTICOAGULATION
**INITIAL PHASE: Therapeutic options**

<table>
<thead>
<tr>
<th>Drug</th>
<th>DOSE SUGGESTED</th>
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<tbody>
<tr>
<td>ENOXAPAIN</td>
<td>1mg/kg b.i.d. 1.5 mg/kg o.d.</td>
</tr>
<tr>
<td>DALTEPARIN</td>
<td>100 U/kg b.i.d. 200 U/kg o.d.</td>
</tr>
<tr>
<td>NADROPARIN</td>
<td>2850-7600 IU b.i.d. Body weight adjusted</td>
</tr>
<tr>
<td>TINZAPARIN</td>
<td>175 U/Kg o.d.</td>
</tr>
<tr>
<td>FUNDAPARINUX</td>
<td>5-10 mg o.d. Body weight</td>
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ALGORITHM FOR THE MANAGEMENT OF CR-VTE

EXTENDED PHASE OF TREATMENT

NON CANCER PATIENTS
(ACCP 2016)
For a minimum of 3 months
Extension > 3 months only for elevated risk patients

• VKA (INR2-3) superior to LWMH (Grade 2c)

• DOACs superior to VKA (Grade 2B)
ALGORITHM FOR THE MANAGEMENT OF CRT

EXTENDED TREATMENT

CANCER PATIENTS
(NCCN, ASCO, ESMO, ACCP Guidelines)
Indefinite anticoagulation as long as the CVC is in place, active cancer and CT

• LWMH or Fundaparinux at prophylactic dosage
• Overlap to VKA (INR value target 2-3) can be considered beyond 3-6 months for non advanced/metastatic patients and not active CT
• Few data on extended treatment with DOACs for cancer patients
OVERLAP FROM LWMH TO ORAL VKA (dose-adjusted to INR) FOR EXTENDED TREATMENT

• OVERLAPPING FROM LWMH TO VKA IS FEASIBLE AND SAFE

• NOT INCREASED RISK OF MAJOR BLEEDING

• A SLIGHT LOWER RISK OF RECURRENT VTE AND THE NEED FOR REPEATED INR MONITORING FAVORS LWMH

• THE USE OF VKA (dose-adjusted to INR from 2 to 3) IS NOT INDICATED FOR CANCER PATIENTS WITH ADVANCED OR METASTATIC DISEASE AND ACTIVE CHEMOTHERAPY
Can we use DOACs for extended treatment of CR-VTE in cancer patients?

EDOXABAN FOR THE TREATMENT OF CANCER ASSOCIATED VTE PROBE TRIAL
from HOKUSAI VTE Cancer Investigators
G.E. Raskob, N. van Es, P. Verhamme, et al., N ENGL J MED 2018: 378;615-24

HOKUSAI TRIAL

RECURRENT VTE

MAJOR BLEEDING

MAJOR BLEEDING EVENTS OCCURRED MAINLY IN PATIENTS WITH GI TRACT CANCER
Can we use DOACs for extended treatment of CR-VTE in cancer patients?

SELECT-D Trial

**RECURRENT VTE**

<table>
<thead>
<tr>
<th>Time Since Trial Entry (months)</th>
<th>Recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Dalteparin: 5, 20, 35, 40</td>
</tr>
<tr>
<td></td>
<td>Rivaroxaban: 5, 20, 35, 40</td>
</tr>
</tbody>
</table>

**MAJOR BLEEDING**

<table>
<thead>
<tr>
<th>Time Since Trial Entry (months)</th>
<th>Major Bleed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Dalteparin: 5, 10, 15, 20</td>
</tr>
<tr>
<td></td>
<td>Rivaroxaban: 5, 10, 15, 20</td>
</tr>
</tbody>
</table>

**OVERALL SURVIVAL**

<table>
<thead>
<tr>
<th>Time Since Trial Entry (months)</th>
<th>OS (%)</th>
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<tbody>
<tr>
<td>0</td>
<td>Dalteparin: 75, 50, 25, 10</td>
</tr>
<tr>
<td></td>
<td>Rivaroxaban: 75, 50, 25, 10</td>
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Can we use DOACs for extended treatment of CR-VTE in cancer patients?

YES AT LEAST FOR EDOXABAN AND RIVAROXABAN

SAFETY AND EFFICACY

PATIENT COMPLIANCE

SUPERIOR COSTS FOR EXTENDED TREATMENT

WE NEED RCTs FOR PATIENTS WITH CR-VTE
THE NEED FOR EXTENDED TREATMENT IN CASE CR-VTE APPEARS AN OPEN CONTROVERSY

- REDUCE PERSISTENT OR RECURRENT CR-VTE
- PREVENT PE AND RELATED MORTALITY
Cumulative rates of recurrent thromboembolism in patients with catheter related thrombosis

(RIETE TRIAL  Registry 2015)

J VASC SURGERY VENOUS AND LYMPHATIC DISORDERS, July 2015

12 months recurrent DVT/PE and related mortality

GLOBAL RECURRENT DVT 2.58%
GLOBAL RECURRENT PE 1.97%
MORTALITY FOR RECURRENT PE 0.89%

ESTIMATED GLOBAL RISK OF MORTALITY FOR CR-VTE = 1/5.000 THROMBOTIC EVENTS
Catheter-related thrombosis natural history in adult patients: a tale of controversies, misconceptions, and fears

Fulvio Pinelli and Paolo Balsorano

- CRT represents an unavoidable event following vessel wall trauma, and it typically occurs within 2 weeks from venous catheter insertion.
- Asymptomatic PICC- and CICC-related thrombosis does not require treatment, and it is not associated with significant risk of sequelae in non-high-risk patients (PE and PTS).
- Symptomatic PICC- and CICC-related thrombosis requires prompt treatment and is not associated with significant risk of sequelae in non-high-risk patients.
POSITION BASED ON EBM AND GUIDELINES

**PRESENCE OF RISK FACTORS AND PERSISTENCE OF SYMPTOMS**

- **CANCER PATIENT IN ACTIVE TREATMENT**
  - **STAY ON EXTENDED ANTICOAGULATION**

- **NO CANCER PATIENT IN ACTIVE TREATMENT**
- **ABSENCE OF RISK FACTORS**
- **CLINICAL RESOLUTION OF THROMBUS AND SYMPTOMS**

**STOP EXTENDED ANTICOAGULATION**

FOR OTHER CLINICAL SCENARIOS FURTHER TRIALS ARE NEEDED
CAHALLENGING SCENARIOS FOR THE CRT TREATMENT

ALGORITHM FOR CVC REMOVAL (if indicated)
ACCP, ASCO, ISTH, Positions

1. CRT DIAGNOSIS
2. 3-10 DAYS LWMH ANTICOAGULATION
3. CATHETER REMOVAL
4. EXTEND ANTICOAGULATION FOR 3 MONTHS (prophylactic dosages)
   - LWMH / Fondaparinux
   - VKA
   - NOA
Thank you!