Antithrombotic therapy following stent reconstruction for PTS

Real world practice and the planned ARIVA trial

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Disclosure

Speaker name: Tim Sebastian

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

I do not have any potential conflict of interest
Real World Practise

Case Scenario

• 40 y male
• 2 DVTs in last 10 years
• Now left venous leg ulcer (PTS)
• Dx: Left iliac vein obstruction
• Undergoes venous stent recanalization

Antithrombotic therapy?
Current Practise

32%: VKA (life-long)
25%: VKA (limited duration)

19%: DOAC (life-long)
15%: DOAC (limited duration)

45%: Antiplatelet therapy

25%: After AC was stopped
13%: In combination with AC
7%: Single use without AC

% refers to the proportion of physicians currently practising the particular antithrombotic regimen
No recommendation on antithrombotic therapy for patients with venous stent implants available

Consider use of balloon angioplasty and stent for selected patients, but no recommendation on antithrombotic management
“Continuous anticoagulation with warfarin … is strongly recommended, although there is no evidence from controlled studies on this issue.”

“The relative importance of antiplatelet agents versus anticoagulants has never been evaluated in clinical trials.”
Swiss Venous Stent Registry

Subgroup of 121 patients treated for postthrombotic syndrome

- 35 (29%) with IVC stents
- 119 (98%) with iliac stents
- 86 (71%) stent below the inguinal ligament
- 36 (30%) bilateral interventions

Mean follow-up 796 days

Continued vs. discontinued anticoagulation therapy?

VKA vs. DOACs?
<table>
<thead>
<tr>
<th>Baseline</th>
<th>Continued AC (82)</th>
<th>Discontinued (39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>46 years</td>
<td>39 years</td>
</tr>
<tr>
<td>Women</td>
<td>29 (35%)</td>
<td>29 (74%)</td>
</tr>
<tr>
<td>Recurrent VTE</td>
<td>34 (42%)</td>
<td>8 (21%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>34 (42%)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>May Thurner Anatomy</td>
<td>19 (23%)</td>
<td>24 (62%)</td>
</tr>
</tbody>
</table>
## Swiss Venous Stent Registry

<table>
<thead>
<tr>
<th>Antithrombotic therapy</th>
<th>Continued AC (82)</th>
<th>Discontinued (39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin K</td>
<td>23 (28%)</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>DOAC</td>
<td>46 (56%)</td>
<td>30 (77%)</td>
</tr>
<tr>
<td>Switch (VKA, DOAC)</td>
<td>11 (13%)</td>
<td>0</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>2 (2%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Initial therapy with antiplatelet agent</td>
<td>15 (18%)</td>
<td>5 (13%)</td>
</tr>
<tr>
<td>Mean duration of therapy, days</td>
<td>723 days</td>
<td>393 days</td>
</tr>
</tbody>
</table>
Discontinued vs. continued AC

Primary Patency Rate

Discontinued Anticoagulation (39) 
Continued Anticoagulation (82)

Follow-up, months

65% 59%

Secondary Patency Rate

Discontinued Anticoagulation (39) 
Continued Anticoagulation (82)

Follow-up, months

94% 86%

Long Rank (Mantel-Cox): p = 0.61

Long Rank (Mantel-Cox): p = 0.26

VTE EVENTS in DISCONTINUED GROUP
• 3 patients stent thrombosis before cessation
• 5 patients with stent thrombosis after cessation
• 1 patients with PE, 1 patients with contralateral DVT after cessation
Vitamin K antagonist vs. DOAC

Primary Patency Rate

- Vitamin K Antagonist (34)
- Direct Oral Anticoagulant (73)

Secondary Patency Rate

- Vitamin K Antagonist (34)
- Direct Oral Anticoagulant (73)

Long Rank (Mantel-Cox): $p = 0.57$

Long Rank (Mantel-Cox): $p = 0.95$
May Thurner Anatomy

Stenting below Inguinal Lig.

May Thurner Anatomy

Stent end above inguinal ligament

Stent end below inguinal ligament

Long Rank (Mantel-Cox): $p = 0.03$

Long Rank (Mantel-Cox): $p = 0.77$

PERMANENT STENT FAILURE

- 5/10 patients with stents below CVF
Benefit of Additional Antiplatelet Agents?

Retrospective, 62 patients with iliocaval stent procedures, 38P treated with antiplatelet agents. Antiplatelet medication predicted a significant decreased risk of stent malfunction (HR 0.23, p=0.007)
Use of AP in VTE disease

WARFASA: 403 patients
- Pat. with first unprovoked DVT and completed anticoagulation therapy
- Randomized to aspirin or placebo

ASPIRE: 822 patients

Recurrence rate per year

6.6% aspirin vs 11.2% placebo
HR 0.58 (95% CI: 0.36-0.93)
p = 0.02

4.8% aspirin vs 6.5% placebo
HR 0.74 (95% CI: 0.52-1.05)
p = 0.09
Swiss Venous Stent Registry
Patients with venous stent implants

Primary Patency Rate

Secondary Patency Rate

Postthrombotic Syndrome (n=121)
Acute iliofemoral DVT (n=122)

74%
95% CI 66-82%
p = 0.003

61%
95% CI 52-70

95%
95% CI 91-99%
p = 0.256

89%
95% CI 83-95

Need for more aggressive treatment in PTS patients in the early phase?
Is there a place for antiplatelet therapy in addition to oral anticoagulation?
Aspirin plus rivaroxaban

versus

rivaroxaban alone

for the prevention of venous stent thrombosis in patients with post-thrombotic syndrome
Study design

• Multi-center
• International (Austria, Germany, Switzerland)
• Randomized
• Open-label (aspirin on top of rivaroxaban)
• Controlled (rivaroxaban alone)
Study design

Main inclusion criteria
› Confirmed diagnosis of PTS (Villalta score > 4 pts)
› Patients scheduled for stent recanalization IVC, iliac veins, common femoral vein
› Patients either on active treatment with rivaroxaban or patients planned for treatment with rivaroxaban after procedure

Main exclusion criteria
› Previous procedures in target vessel
› Ongoing antiplatelet therapy, or antiplatelet therapy within the previous 7 d
› Acute thrombosis (< 3 mo prior to procedure)
› Pre-existing coagulopathy
› Malignant growth (relapse free >5 y)
Study design

**Primary Endpoint**
- Primary patency rate after 6 mo

**Main Secondary Endpoint**
- Assisted primary and secondary patency rate after 6 mo
- Primary sustained clinical success after 6 mo (def. Villalta < 5 pts and absence of repeated procedures)
- Difference of limb circumference of affected leg in comparison to contralateral leg at 6 mo CTB
- CIVIQ-20 (quality of life) at 6 mo CTB
- Villalta / rVCSS scores at 6 mo CTB
- Adverse events: stent thrombosis, recurrent VTE any site, stent compression/ fracture, bleeding

CTB = compared to baseline
Schedule

284 patients planned to be included
First Patient IN: Q2 2019
Last Patient OUT: Q4 2021

Centers in with more than 20 PTS interventions per year are invited to participate in this trial
Summary

• Currently, antithrombotic management of PTS patients with stents is experienced-based rather than evidenced-based.

• We see a shift from the use of VKA to DOACs, but no evidence on efficacy available.

• It might be safe to withdraw selected patients from anticoagulation therapy. Those need to be followed-up to detect late events.

• The ARIVA trials might be able to provide insight whether anticoagulation therapy combined with aspirin is beneficial to prevent early stent failure.
Thank you for your attention!

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