Anticoagulation Therapy for Left Ventricular Thrombus

Thursday | October 22, 2020 | 12:00 – 1:00PM ET

**Presenter**
Arthur Allen, PharmD, CACP

**Guest Speaker**
Ann Marie Navar, MD, PhD

**AC Forum Moderators**
Geoffrey Barnes, MD, MSc
Tracy Minichiello, MD
Diane Wirth, ANP-BC, CACP
Presenters

Arthur Allen, PharmD, CACP
• Anticoagulation Program Manager, VA Salt Lake City Health Care System

Geoffrey Barnes, MD, MSc
• Assistant Professor of Internal Medicine, Vascular and Cardiovascular Medicine, University of Michigan

Tracy Minichiello, MD
• Professor of Medicine, University of California, San Francisco
• Chief of Anticoagulation and Thrombosis Services, San Francisco VA Medical Center

Ann Marie Navar, MD, PhD
• Associate Professor of Medicine in the Division of Cardiology, University of Texas Southwestern Medical Center

Diane Wirth, ANP-BC, CACP
• Adult Nurse Practitioner, Grady Memorial Hospital
• Manager Heart Failure Program, Grady Memorial Hospital
Disclosures

The following speaker disclosures have the following relevant financial relationships with commercial interests:

Arthur L. Allen, PharmD, CACP
  • Janssen, Portola (Speakers Bureau), BMS/Pfizer Alliance, Boehringer-Ingelheim, Roche (Consultant)

Geoffrey Barnes, MD, MSc
  • Pfizer/Bristol-Myers Squibb, Janssen, Acelis Connected Health (Consultant)

Ann Marie Navar, MD, PhD
  • Received funding for research to her institution from Amgen, Janssen, Amarin, Sanofi, Regeneron, and honoraria and consulting fees from Amarin, Amgen, Astra Zeneca, BI, Esperion, Janssen, Lilly, Sanofi, Regeneron, NovoNordisk, Novartis, The Medicines Company, New Amsterdam, Cerner, 89Bio, and Pfizer

Diane Wirth, ANP-BC, CACP
  • Janssen Pharmaceuticals (Consultant / Speaker Bureau)
Objectives

• Discuss LV thrombus and its treatment

• Discuss off-label DOAC use for LV thrombus

• Discuss the RED VELVT trial

• Participate in open discussion with expert panelists
LVT - Background

• Most commonly associated with Anterior STEMI & dilated cardiomyopathy

• Virchow’s Triad in LVT
  • **Stasis:** Reduced ventricular contractility
  • **Injury:** Local myocardial injury
  • **Hypercoagulability:** Inflammatory response to acute tissue injury

• Complications: Stroke/Systemic Embolism


[Image source](https://www.flickr.com/photos/gandhiji40/395241000)
LVT - Incidence

- Less common in the current era of reperfusion therapy/PCI
- Reported LVT rates vary in studies
  - Pre-PCI – Average 33%
  - PCI Era – Average 10%

*Figure 1. (a) Temporal trends in incidence of LV thrombus (LVT) in patients presenting with anterior myocardial infarction. (b) Cumulative incidence of LVT in studies reported in the pre-PCI era compared to PCI era (before and after 1995).*

LVT - Complications

- LVT-related thromboembolism rates also reduced in the PCI-era
- Reported rates vary in studies
  - Pre-PCI – Average 22.3%
  - PCI Era – Average 5.5%
- Risk highest within the first 1-2 weeks

Figure 4.  (a) Incidence of thromboembolism in left ventricular thrombus (LVT). (b) Cumulative incidence of thromboembolism with LVT in studies reported before and after 1995.

Diagnosis

- **Echocardiography**
  - Most common test
  - ECHO contrast may be necessary
    - When LV apex poorly visualized
    - To r/o residual thrombus after treatment course

- **Cardiac CT**

- **Cardiovascular Magnetic Resonance (CMR)**
  - Considered gold standard
  - Can determine old vs. new thrombosis

![Transthoracic ECHO](https://upload.wikimedia.org/wikipedia/commons/2/24/Thrombus_in_the_apex_of_left_ventricle_E00757_%28CardioNetworks_ECHOpedia%29.jpg)
LVT Treatment Guidelines

• Overall existing guidelines:
  • Are dated (Best available guidance from 2012 – 2014)
  • Contain mostly low-grade recommendations (2c, IIb, etc.)
  • Focus primarily on LV thrombus occurring in the setting of anterior MI
  • Favor warfarin unless intolerant
  • Favor a fixed course of AC therapy (Primarily 3 months)
    • No focus on repeat imaging for thrombus clearance

Limitations of the Guidelines

• Most of the LVT studies date back to 1980s
  • Before reperfusion/PCI era & before routine DAPT

• Lack of clarity on:
  • Expected timeline for LVT resolution
  • Best course of action for LVT due to non-ischemic causes/incidental LVT
  • Cessation vs. maintenance of anticoagulation in patients with persistent LVT or persistent wall motion abnormality
DOACs for LVT

• Historically no RCTs comparing warfarin with DOACs
• Evidence with DOAC limited to case reports and series
  • ~250 patients in total
  • Primarily focused on the outcome of thrombus resolution
  • Lack standardized dosing and durations
  • Mixed results (mostly favorable)

Off-label Use of Direct Oral Anticoagulants Compared With Warfarin for Left Ventricular Thrombi

Retrospective Evaluation of DOACs and Vascular Endpoints of Left Ventricular Thrombi (RED VELVT) observational study.

JAMA Cardiol. 2020;5(6):685-692
RED-VELVT Study - Overview

• Design: Retrospective cohort study evaluating treatment patterns and outcomes at 3 tertiary care academic medical centers

• Patients: 514 eligible patients with LV thrombi (by Echo) between October 1, 2013, and March 31, 2019
  • Data Captured
    • Baseline clinical & demographic information
    • Echo data including size, morphology & mobility
    • Embolic events

• Median f/u 351 days (Range – 51-866)

• Outcomes: Stroke and systemic embolism (SSE)

JAMA Cardiol. 2020;5(6):685-692
Treatment during different time periods were treated as a time-dependent covariate.
Patients & Therapies

93 pts received no oral AC therapy

43 pts received no AC therapy at all

Warfarin

- Any = 300
- Only = 236

DOAC

- Any = 185
- Only = 121

Of the 514 patients with left ventricular thrombi, 421 were treated with an oral anticoagulant. Three hundred were treated with warfarin at any point during the follow-up period (any warfarin) and 185 were treated with a direct oral anticoagulant (DOAC; any DOAC). These groups included a mixed cohort of 64 patients (therapy change), who switched treatment, such that there were 236 patients treated exclusively with warfarin (warfarin only), and 121 patients treated exclusively with a DOAC (DOAC only). Among the patients treated with a DOAC, 150 were treated with apixaban, 51 with rivaroxaban, and 9 with dabigatran. No patients were treated with edoxaban.

JAMA Cardiol. 2020;5(6):685-692
Baseline Characteristics

- Groups relatively well matched overall
- DOAC patients had significantly more:
  - Whites
  - H/o VTE
  - H/o AF
- Nearly twice as many patients with protruding/pedunculated thrombus in DOAC arm
  - Did not meet statistical significance

*JAMA Cardiol. 2020;5(6):685-692*
Results, cont.

Figure 2. Survival Curves for Freedom From Stroke and Systemic Embolism

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>Warfarin</th>
<th>DOAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of days</td>
<td>87</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>193</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>138</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>99</td>
<td>37</td>
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<tr>
<td></td>
<td>73</td>
<td>22</td>
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<tr>
<td></td>
<td>59</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>33</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>2</td>
</tr>
</tbody>
</table>

- 54 SSE events
- 36 strokes
- 18 systemic emboli

Survival curves are shown for freedom from stroke and systemic embolism (SSE) in patients with left ventricular thrombus after index echocardiogram, Mantel-Byar P < .001. DOAC indicates direct oral anticoagulant.

*JAMA Cardiol. 2020;5(6):685-692*
Results, cont.

- Only DOAC use and prior SSE were associated with a difference in SSE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable HR (95% CI)</th>
<th>P value</th>
<th>Multivariable HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOAC use (vs warfarin)</td>
<td>2.71 (1.31-5.57)</td>
<td>.01</td>
<td>2.64 (1.28-5.43)</td>
<td>.01</td>
</tr>
<tr>
<td>Prior SSE</td>
<td>2.13 (1.22-3.72)</td>
<td>.01</td>
<td>2.07 (1.17-3.66)</td>
<td>.01</td>
</tr>
<tr>
<td>Thrombus mobility</td>
<td>1.80 (0.96-3.38)</td>
<td>.07</td>
<td>1.52 (0.80-2.87)</td>
<td>.20</td>
</tr>
<tr>
<td>Patient age</td>
<td>0.99 (0.97-1.01)</td>
<td>.19</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>White ethnicity (vs other)</td>
<td>1.57 (0.91-2.70)</td>
<td>.10</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy (vs nonischemic)</td>
<td>0.89 (0.51-1.55)</td>
<td>.69</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.02 (0.99-1.06)</td>
<td>.16</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Estimated GFR</td>
<td>1.00 (0.99-1.01)</td>
<td>.61</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>History</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Atrial fibrillation</td>
<td>0.94 (0.49-1.79)</td>
<td>.85</td>
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<td>Venous thromboembolism</td>
<td>1.03 (0.52-2.06)</td>
<td>.93</td>
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<td>Antiplatelet therapy</td>
<td>0.98 (0.70-1.36)</td>
<td>.90</td>
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<td>Bridging anticoagulation</td>
<td>0.96 (0.45-2.00)</td>
<td>.90</td>
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<td>Presenting embolism</td>
<td>1.46 (0.73-2.91)</td>
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<td>Left ventricular ejection fraction</td>
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<td>Thrombus size</td>
<td>1.05 (0.95-1.18)</td>
<td>.35</td>
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<td>Pedunculated or protruding thrombus morphologic characteristics</td>
<td>1.00 (0.31-3.22)</td>
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*JAMA Cardiol. 2020;5(6):685-692*
Author’s Conclusions

• 43.9% of patients treated with off-label DOAC

• DOAC use associated w/ more SSE events vs. warfarin even after adjustment for other factors

• ... off-label use of DOACs for LV thrombi should be undertaken with caution

JAMA Cardiol. 2020;5(6):685-692
These findings should be interpreted with caution. The signal for excess stroke emerged late, long after the generally accepted window of time needed for anticoagulation. ... this study begs for better understanding of the off-label use of DOACS and prompts a call for larger studies ...

JAMA Cardiol. 2020;5(6):692-693
Panel Discussion
Significant findings from RED VELVT

• ~1/3 had no echo to confirm resolution
• 8.7% of patients with confirmed resolution suffered SSE w/in 30 days of the echo confirming resolution
• 9 SSE occurred among patients being treated w/ OAC w/in the first 3 months of therapy
  • 3-months to end of the study, another 22 SSE
• OAC use was not associated with thrombus resolution

*JAMA Cardiol. 2020;5(6):685-692*
Findings NOT associated with difference in SSE

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*Please note that the full table and its context are not fully visible in the image provided.*
Panel Discussion
Anticoagulation Centers of Excellence (ACE) Rapid Resource

• Original ACE content
• Developed from the field
• Vetted through the ACE committee

Join us for our next webinar highlighting

2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation

Wednesday | November 18, 2020 | 12:00 - 1:00 PM ET

**Guest Speaker**  
Dr. Gregory Y H Lip

**Presenter**  
Tracy Minichiello, MD

**AC Forum Moderators**  
Arthur Allen, PharmD, CACP  
Geoffrey Barnes, MD, MSc  
Diane Wirth, ANP-BC, CACP

Access the guideline here:

• 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)
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