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A multidisciplinary team-based process improves outpatient anticoagulation quality with continuous-flow left-ventricular assist devices

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While continuous-flow left-ventricular assist devices (CF-LVAD) prolong survival in patients with heart failure who are refractory to medical therapy [1], contemporary devices expose patients to a superposed risk of both thromboembolic and bleeding events [2,3]. Precise anticoagulation management is therefore essential in mitigating these potentially catastrophic complications. Historically at the Miami Transplant Institute (MTI), anticoagulation was managed by specialized personnel, including LVAD coordinators, heart failure cardiologists, and cardiothoracic surgeons. In November 2014, a multidisciplinary quality improvement initiative at the MTI was devised with the aim of optimizing anticoagulation practice in ambulatory CF-LVAD patients. This initiative consisted of establishing an anticoagulation management protocol, standardizing INR target ranges, and integrating a clinical pharmacist as a consultant into the care team. The objective of this report is to evaluate the ability of the initiative to improve anticoagulation control in CF-LVAD patients compared to a historical control cohort.

This study enrolled all CF-LVAD patients whose anticoagulation was managed at our center between May 2014 and April 2015. Anticoagulation quality and clinical outcomes were compared between the preintervention group (PRE) (05/01/2014–10/30/2014) and post-intervention group (POST) (11/1/2014–04/30/2015) phases. The primary endpoint was the time within the therapeutic international normalized ratio (INR) range time in therapeutic range (TTR) as calculated using the Roosendaal Linear interpolation method [4]. Bleeding and thromboembolic events were defined according to the INTERMACS criteria [5]. Each patient had to be included in both the PRE and POST phase in order to serve as their own control. Differences in TTR and bleeding/thromboembolic events between the PRE and POST cohorts were analyzed with a paired t-test or chi-square test, respectively using SPSS version 22.0 (IBM Corporation). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a prior approval by our institution’s human research committee with waiver of informed consent (given the retrospective nature of the work).

Thirty-three patients (age 51 years, male 84.8%, BTT 45.5%, HeartMate II [HMII] 72.7%) from May 2014 to April 2015 yielded 1675 INR values with 10,618 days of follow-up (5419 days, PRE group; 5199 days, POST group). The average TTR in the PRE group was 29.7 ± 11.1%, which increased to 60 ± 21.4% in the POST group (p < 0.001) (Table 1). TTR in the POST patients was numerically higher in those with the HMII device relative to HeartWare HVAD (64 ± 19.9% vs 49.8 ± 23.1%, respectively; p = 0.092). Rates of bleeding and thromboembolic complications were similar between the PRE and POST groups (Table 1).

Previous data have established the benefit of a pharmacist-driven clinic for managing ambulatory non-LVAD patients receiving warfarin-based anticoagulation [6]. Bishop et al. demonstrated a significant improvement in TTR after the implementation of a pharmacist-managed anticoagulation clinic coupled with patient INR self-testing in a small cohort of CF-LVAD patients [7]. While these findings are certainly positive, not all LVAD centers have the resources to deploy full-time pharmacist-managed anticoagulation services, and the availability of patient INR testing can be limited by insurance coverage. Our study...
was able to show that marked improvement in TTR is possible in LVAD patients without the use of a dedicated anticoagulation clinic. The average TTR in our POST group (60%) was actually higher than previous LVAD cohorts managed by these traditional models, including those reported by Bishop et al.[7] (44%) and Jennings et al.[8] (51%).

This noteworthy improvement was likely due to the multifaceted nature of our intervention, which included deployment of standardized target INR ranges, use of warfarin dosing algorithms, less frequent INR monitoring in stable patients, enhanced drug–drug interaction screening, and clinical pharmacist consultation for out-of-range values. Despite improving TTR, there was no difference in the rate of clinical endpoints between the PRE and POST groups in our study. These findings are likely due to the small sample size and the low rate of bleeding and thrombotic complications during the study period. Despite these limitations, recent literature has demonstrated that poor INR control (TTR less than 50%) in CF-LVAD patients is associated with a nearly 3 fold increased risk of thromboembolic complications [9], which suggests that TTR may be a valid surrogate endpoint for anticoagulation quality in this patient population.

Our findings must be viewed in the context of a single center retrospective analysis with a relatively small sample size and follow-up period. Despite these limitations, this study demonstrated that an outpatient multidisciplinary anticoagulation quality improvement initiative can be successfully implemented in a CF-LVAD population without the establishment of a traditional anticoagulation clinic. This model is desirable particularly in institutions where patients are geographically dispersed and resources may be limited. Future studies are warranted to determine the reproducibility of these findings in a larger patient population.

**Conflict of interest**

None declared.

**Funding**

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**References**


**Table 1**

Anticoagulation quality and clinical outcomes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticoagulation control</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time in therapeutic range (%)</td>
<td>29.7 ± 11.1</td>
<td>60.0 ± 21.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time INR 1.5 (days)</td>
<td>5.3 ± 8.6</td>
<td>3.0 ± 6.0</td>
<td>0.138</td>
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<td>Time INR ≥ 4.0 (days)</td>
<td>5.4 ± 6.8</td>
<td>5.0 ± 7.8</td>
<td>0.766</td>
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<tr>
<td><strong>Clinical outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with bleeding event</td>
<td>4 (12.1)</td>
<td>3 (9.1)</td>
<td>0.689</td>
</tr>
<tr>
<td>Number of bleeding events</td>
<td>7</td>
<td>4</td>
<td>0.52</td>
</tr>
<tr>
<td>(all gastrointestinal bleeding)</td>
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<td></td>
<td></td>
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<tr>
<td>Average INR at time of bleed</td>
<td>3.26</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>Patients with TE events</td>
<td>3* (9.1)</td>
<td>4* (12.1)</td>
<td>0.689</td>
</tr>
<tr>
<td>Number of TE events</td>
<td>6</td>
<td>5</td>
<td>1.00</td>
</tr>
<tr>
<td>Stroke</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pump thrombosis</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Minor hemolysis</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Major hemolysis</td>
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</tr>
<tr>
<td>Pump exchange</td>
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<td>0</td>
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</tr>
<tr>
<td>Other</td>
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<tr>
<td><strong>Average INR at time of TE</strong></td>
<td>2.826</td>
<td>2.76</td>
<td></td>
</tr>
</tbody>
</table>

INR = international normalized ratio; TE = thromboembolic.

* One patient had a transient ischemic attack (TIA) and two major hemolysis events, one patient had a stroke and a ventricular thrombus, and one patient had a minor hemolysis event.

* One patient had one minor and one major hemolysis event, one patient had a stroke and two patients each had a major hemolysis event.

Ventricular thrombus.