HeartMate II Pump Thrombosis

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From Bedside Observation....

- How it began
- What evolved
- What is the data
- What was our responsibility
- What comes next
Initial Cleveland Clinic Awareness to Action

Mid-2011

• Concern about possible increasing incidence of pump thrombosis
• Formation of a “Thrombosis” group lead by Thoratec
• Last meeting of this group in Atlanta (2/15/2013) several implanting institutions report similar concern

2/22/2013

• Chair requests thorough investigation of CCF experience
Definition

Confirmed

- Thrombus within blood contacting surfaces of device inflow cannulae or outflow conduit or grafts

Suspected

- Suggestive pump-related malfunction
  - Hemolysis, Unexplained “heart” failure, Abnormal pump parameters
- All cases with anatomic reason excluded
Pump Thrombosis

8 Confirmed
16 Suspected

Timing

• 8 before 4\textsuperscript{th} quarter 2011
  5 months to 3.4 years post-implant
• 16 since then
  10 within 3 months post-implant
Question

Is there a relation between risk of pump thrombosis and date of implant?

Confounding factors

- Surgeons
- Anticoagulation protocol
Parallel Approach

Random Survival Forest
• Non-parametric assumption-free method
• Machine learning

Temporal Decomposition Model
• Parametric
• Machine learning
Free of Thrombosis at 3 Mo.

HeartMate II Implant Date

%
Free of Thrombosis

Months after HeartMate II Implant

0 6 12 18 24 30 36 42

% 100 80 60 40 20

10/04 – 09/11

09/11 – 02/13
Risk of Pump Thrombosis

%/y

Months after HeartMate II Implant
LDH

Before 9/11

Thrombosis

Since 9/11

mg/dL

Months after Implant
AC: 21,122 measurements, 296 devices

INR

Before 9/11

Thrombosis

Since 9/11

Months after Implant
The principal shortcoming of your study is that it is based on the experience of a single center. All of the reviewers of your manuscript raised this issue in their comments to the editors. In order to publish your work, we will need solid confirmation of your findings from the experience of other centers, registries, or data bases. There is concern that center-specific characteristics or practices at Cleveland Clinic may be at play, and it is essential that your study include a much broader dataset in order to provide confirmation/validation of the findings at your center. The editors believe that your findings are interesting and potentially quite important. With that said, we do not want to take a chance on misleading the medical community without convincing validation of your findings.

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Statistical Reviewer
Comments for the Author:
This paper reports a dramatic and alarming increase in Heartmate II pump thrombosis after September, 2011 at the Cleveland Clinic. This is important information that should be shared widely.
CDWP Cooperative Consortium

- Centers combined data of all HM II device implants and reported CONFIRMED PUMP THROMBOSIS

- 1058 Devices from 4 centers
- *Non-uniform closing dates
Occurrence and Incidence of Confirmed Pump Thrombosis Stratified According to Implantation Date.

CONFIRMED Pump Thrombosis at 3 Months after HeartMate II Implantation.

Overall Occurrence of **CONFIRMED** Pump Thrombosis after HeartMate II Implantation.

Percentage of Devices with Confirmed Pump Thrombosis at 3 Months after HeartMate II Implantation.


No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>HeartMate II support without thrombosis</th>
<th>Thrombosis with transplantation or replacement</th>
<th>Thrombosis with neither transplantation nor replacement</th>
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<tbody>
<tr>
<td>Months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
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<td>6</td>
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</table>

Elevated Lactate Dehydrogenase (LDH) Levels within 3 Months after HeartMate II Implantation.

INTERMACS Registry Analysis Pump Thrombosis
LDH
Kirklin J. JHLT 2013

Fig 13

INTERMACS: HeartMate II Pump Analysis
Implants: April 2008 – December 2012, n=6910
Follow-up: Through June 2013

By LDH Groups

% Freedom from Device Exchange or Death due to Thrombus

<table>
<thead>
<tr>
<th>LDH group</th>
<th>n</th>
<th>Events</th>
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<tbody>
<tr>
<td>Missing</td>
<td>4581</td>
<td>223</td>
</tr>
<tr>
<td>0-400</td>
<td>1318</td>
<td>52</td>
</tr>
<tr>
<td>401-1000</td>
<td>819</td>
<td>66</td>
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<tr>
<td>&gt;1000</td>
<td>192</td>
<td>41</td>
</tr>
<tr>
<td>Totals</td>
<td>6910</td>
<td>382</td>
</tr>
</tbody>
</table>

p(overall) < .0001

Event: Device Exchange due to Thrombus**
(censored at death, transplant and recovery)

Months post implant

** Thrombus events include 'probable' thrombus
LDH, lactate dehydrogenase

66% missing LDH
8.2% Events (192/2329)
21.4% Events LDH >1000 (41/192)
Early HM 2 Pump Thrombosis has Increased. Why?

- Four EXPERIENCED centers with consistent observations—not only isolated to these 4 centers
  - Are patients different? Is reporting different? Is management different?
- Is the device different?
  - >17,000 implants worldwide (50-100/wk)
  - Pump thrombosis seen with previous mechanical pivot-based bearing devices
  - Pathological reports show 60-70% laminated thrombus at inlet (front-loaded) bearing
  - Do some pumps have a lower tolerance to sub therapeutic anticoagulation, INR<2?
PUMP POWER ELEVATION

Group 1
N=9

Group 2
N=8

Group 3
N=2
What is Next For Us?

• Collaborative data collection: Cleveland Clinic, Wash Univ, Duke, Penn, Columbia
• All HM II implants through Dec 31, 2013
• 90 Days follow up: common closing date March 31, 2014
• Thoratec invited to collaborate to provide all device related variable
• Extensive patient level variables from INTERMACS and site data collection
• Pump measurements via xrays
• Data analysis team led by Eugene Blackstone MD
• IRB approvals in progress