

# Pump Thrombosis



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**Professor and Vice Chair**

*Dept Cardiothoracic Surgery*

# Disclosures



- Thoratec Inc. medical advisory board
- Heartware Inc. medical advisory board and surgical proctor
- Terumo Inc., Chair, AEC DuraHeart BTT Trial
- Sunshine Heart Inc DSMB
- Medtronic consultant

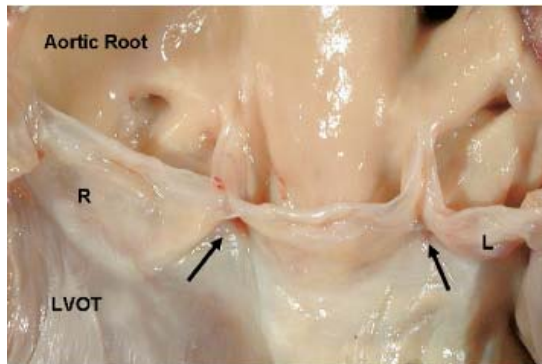
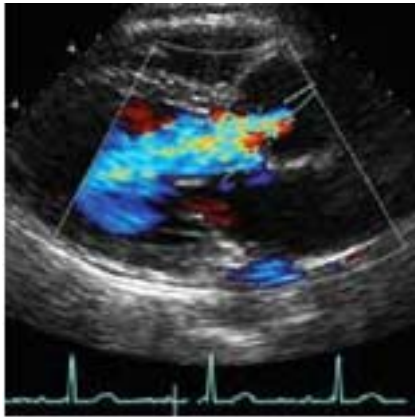
# Successes



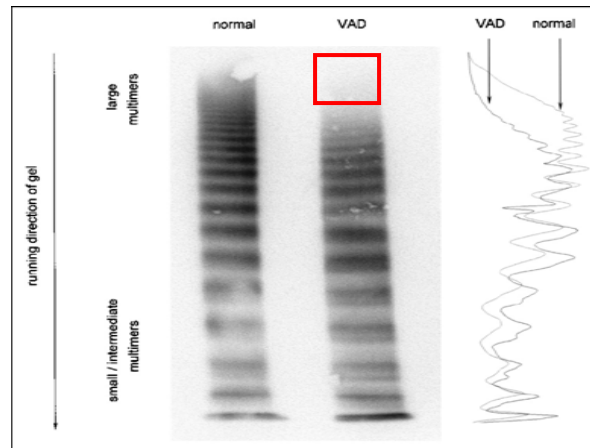
- Transition from pulsatile technology to CF:
  - Improved survival
  - Improved quality of life
  - Reduced event rates for infection, organ dysfunction, RHF
  - Drastic improvement in device reliability
  - Smaller, faster operation
  - Enhanced applicability

# New Challenges in CFLVAD Era

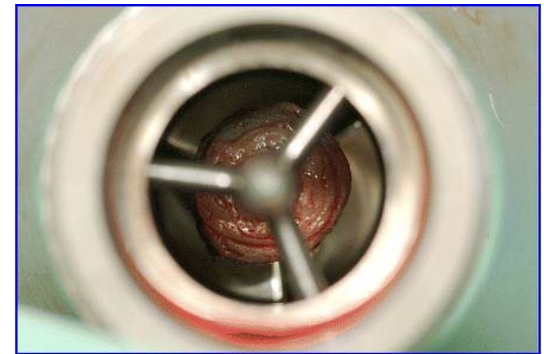
## De Novo Aortic Insufficiency




## GIB/AVM/aVWS



## Pump Thrombosis



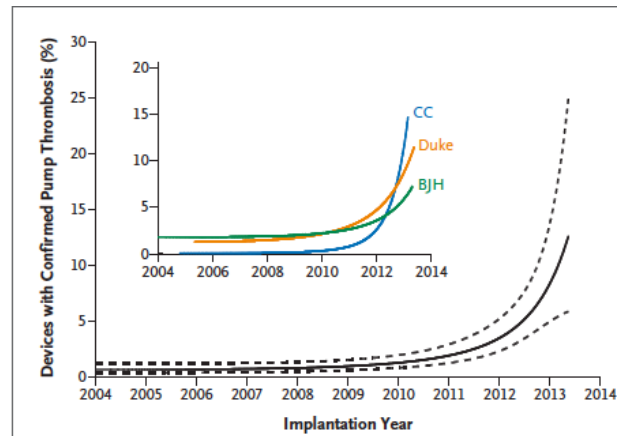
# Why Talk About Pump Thrombus?

- 
- Known and potentially fatal complication
  - Death knell of MicroMed-DeBakey VAD
  - Increasing “noise” among clinicians and VAD coordinators starting in early 2011
  - (<http://healthgroups.yahoo.com/group/mcscollaboration>)
  - Described for both available CF LVADs
  - Implications as LVADs are being considered for the lesser sick

ORIGINAL ARTICLE

# Unexpected Abrupt Increase in Left Ventricular Assist Device Thrombosis

Randall C. Starling, M.D., M.P.H., Nader Moazami, M.D., Scott C. Silvestry, M.D., Gregory Ewald, M.D., Joseph G. Rogers, M.D., Carmelo A. Milano, M.D., J. Eduardo Rame, M.D., Michael A. Acker, M.D., Eugene H. Blackstone, M.D., John Ehrlinger, Ph.D., Lucy Thuita, M.S., Maria M. Mountis, D.O., Edward G. Soltesz, M.D., M.P.H., Bruce W. Lytle, M.D., and Nicholas G. Smedira, M.D.



**Figure 1. Overall Occurrence of Confirmed Pump Thrombosis at 3 Months after HeartMate II Implantation.**

Dashed lines represent the 95% confidence interval. There was a steep increase in the occurrence of thrombosis starting in early 2011. The inset shows the changing occurrence of confirmed pump thrombosis according to study site (Cleveland Clinic [CC], Barnes-Jewish Hospital [BJH], and Duke University Medical Center [Duke]).

# Pump Thrombus

## *Definition*

### Device Malfunction

Device malfunction denotes a failure of one or more of the components of the MCS system which either directly causes or could potentially induce a state of inadequate circulatory support (low cardiac output state) or death. A failure that was iatrogenic or recipient-induced will be classified as an Iatrogenic/Recipient-Induced Failure.

Device failure should be classified according to which components fails as follows:

1) **Pump failure** (blood contacting components of pump and any motor or other pump actuating mechanism that is housed with the blood contacting components). In the special situation of pump thrombosis, thrombus is documented to be present within the device or its conduits that result in or could potentially induce circulatory failure.

2) **Non-pump failure** (e.g., external pneumatic drive unit, electric power supply unit, batteries, controller, interconnect cable, compliance chamber)

# Hemocompatibility & Rheology of CF LVADs



- Hemocompatibility: max blood flow; reduce stasis/hemolysis/turbulence/retrograde flow
- LVADs activate coagulation and endothelial systems
- Blood contacting surfaces play role in thrombotic complications and mandate anti-plt and anti-coag Rxs
- Both HMII and HW induce aVWS
- Glycoprotein Ib disturbance in platelets
- “Maintenance” LDH : HMII > HW
- Fibrin split products: HW > HMII



# Pump Thrombosis

## Predisposing Factors



- **Patient Related** - individual conditions that render patient more likely to have thrombotic complications, including pump thrombus
- **Device Related** - inherent to the technology itself
- **Management Related** - implantation technique, anticoagulation, pump speed

# Predisposing Factors

## *Patient Related*



- CHF is a prothrombotic state
- Atrial fibrillation
- Pre-existent LV thrombus/trabeculation
- Mechanical prostheses
- Infection
- Malignancy
- Hypercoagulable state:
  - Protein C/S def, Factor V Leyden, antiphospholipid Ab, asa insensitivity, MTHFR C667T mutation, HIT, antithrombin def, plasminogen def

# Predisposing Factors

## *VAD Related*

- Heat generated by pump rotors
- Outflow graft kink/compression
  - Disconnected graft protector w impingement (HMII)
  - Positional



# Predisposing Factors

## *Management Related*



- Inadequate anticoagulation:
  - No heparin bridging
  - Subtherapeutic INR
  - Ongoing/recurrent GIB/epistaxis
- Absence of antiplatelet agent
- Inflow cannula malposition
- Low pump flow due to:
  - Low speed setting to manage AI, GIB or assess/induce recovery
  - Suboptimal HTN management

# Pump Thrombus:

## Signs/Symptoms



- Asymptomatic:
  - Transient or sustained power elevations
  - Early or late post implant
- Symptomatic:
  - Hemolysis (pfhgb, bilis, LDH, dark urine)
  - CHF (left- ± right-sided)

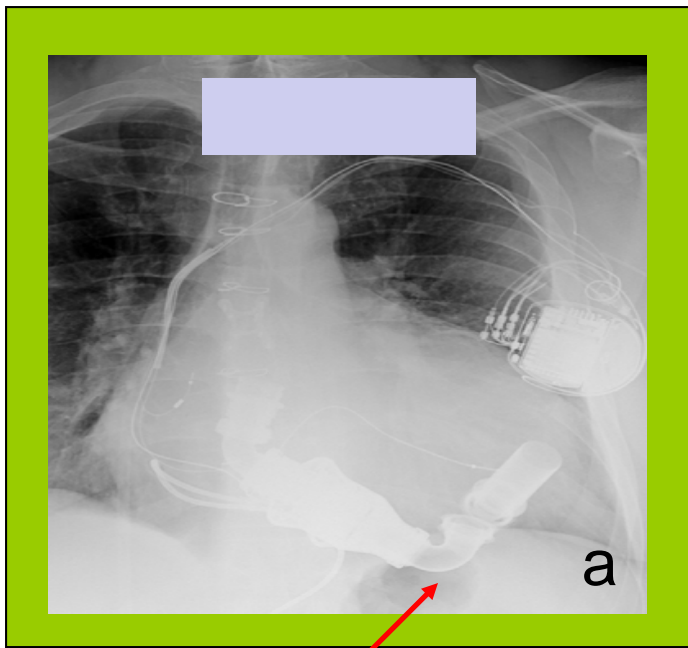
# Diagnostic Evaluation



- Imaging
  - CXR
  - CTA
  - Echo
    - Usual windows
    - Ramp studies
  - LHC: V-gram, Outflow-gram
- Hemodynamics: RHC

# Imaging - X Ray

- Assess Inflow and Outflow (HMII)



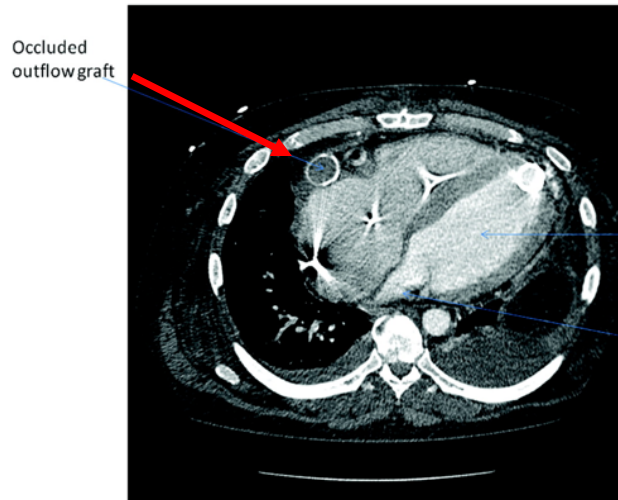
Suboptimal inflow angle



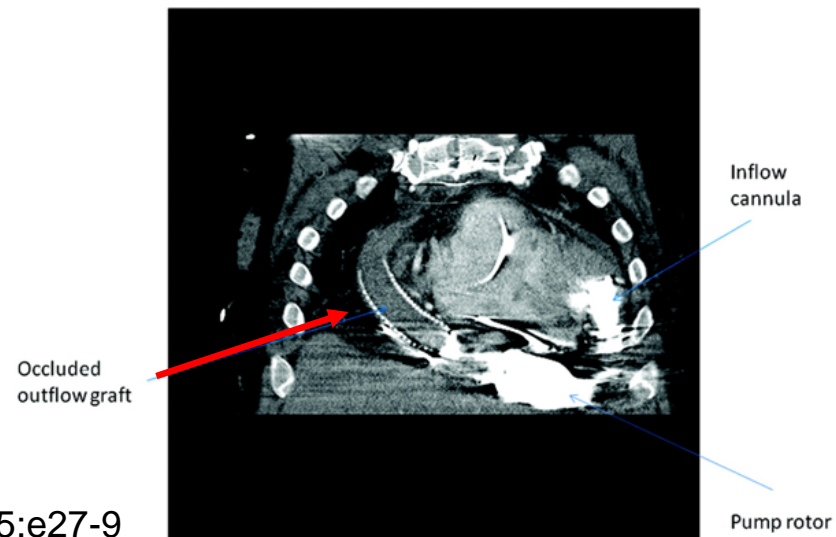
Detached outflow protector

a, courtesy V Jeevanandam; b, courtesy Thoratec Inc

# Imaging - CT(A)

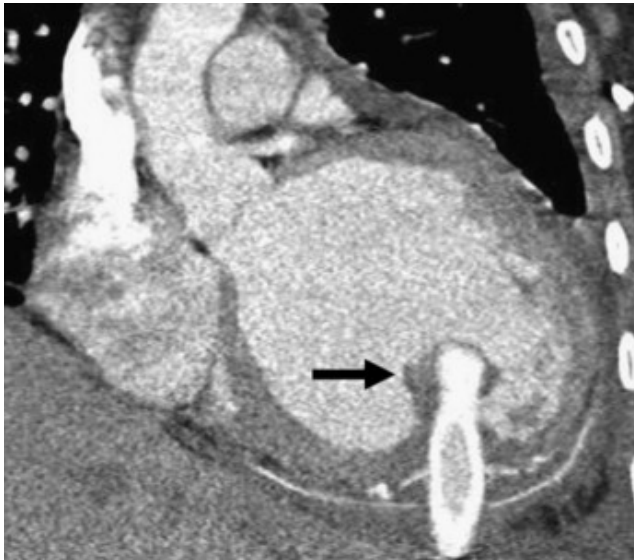


Reflux of contrast into outflow graft

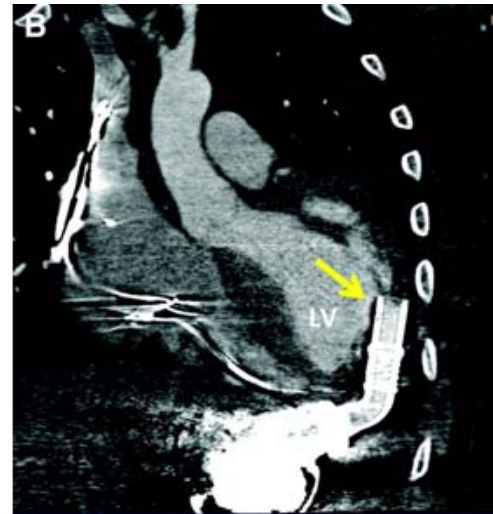




# Imaging - CT(A)



**Inflow Thrombus**



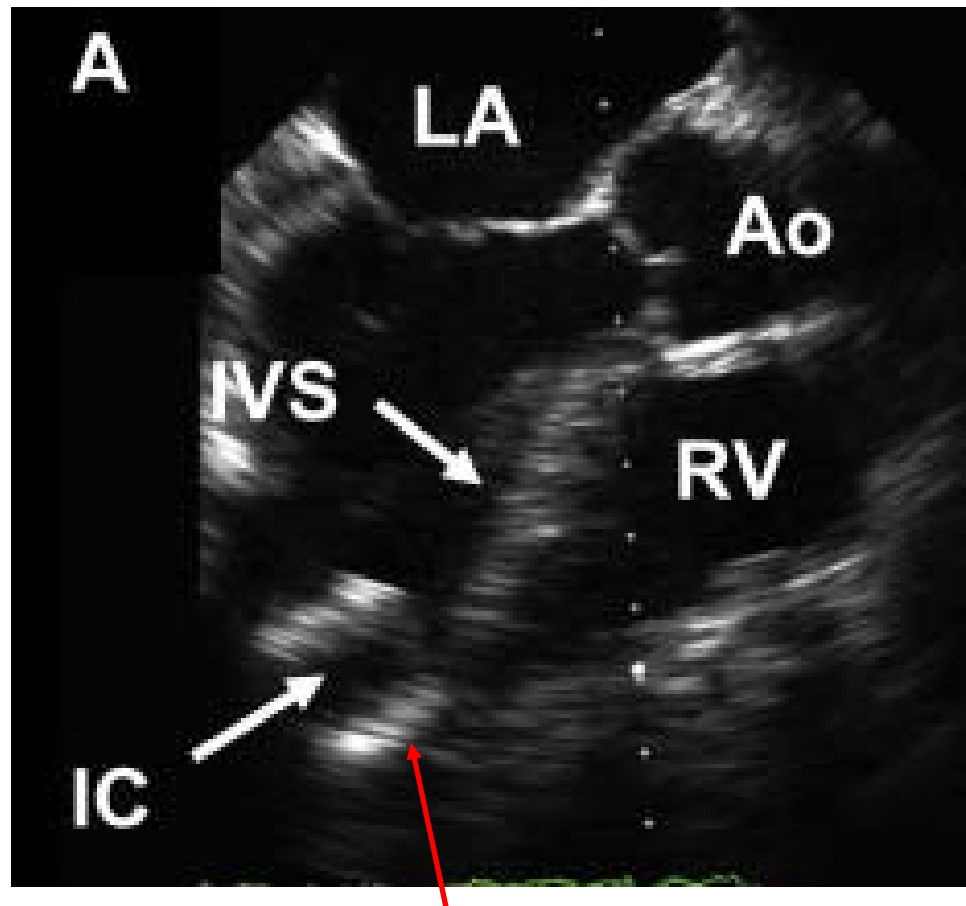
**Malpositioned Inflow**

# Imaging - Echo



- LV thrombus
- Dilated LV
- Mitral regurgitation
- Aortic valve opening
- Failure to reduce LVEDD with increase RPMs - Ramp study

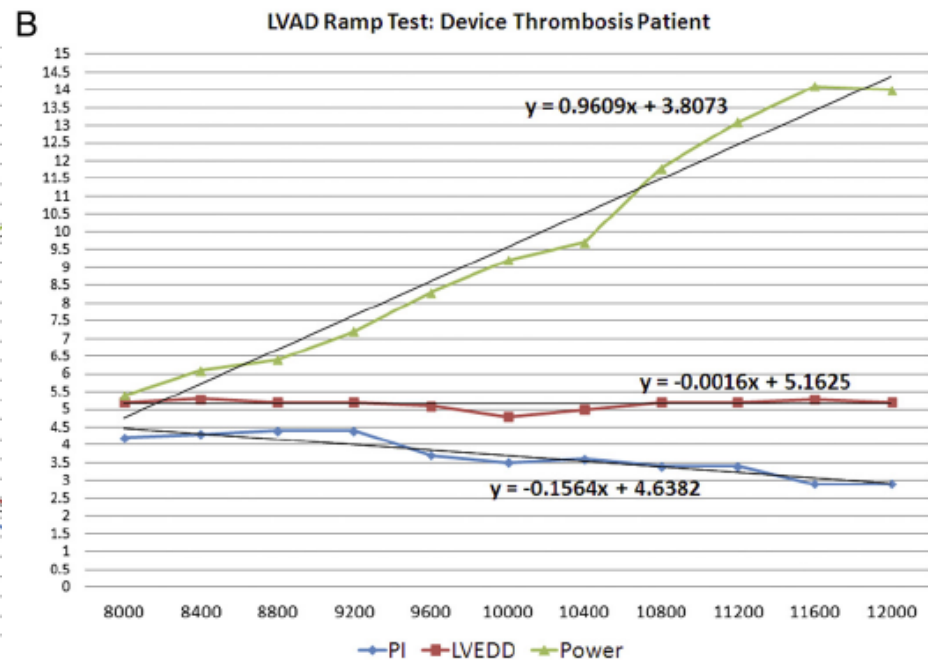
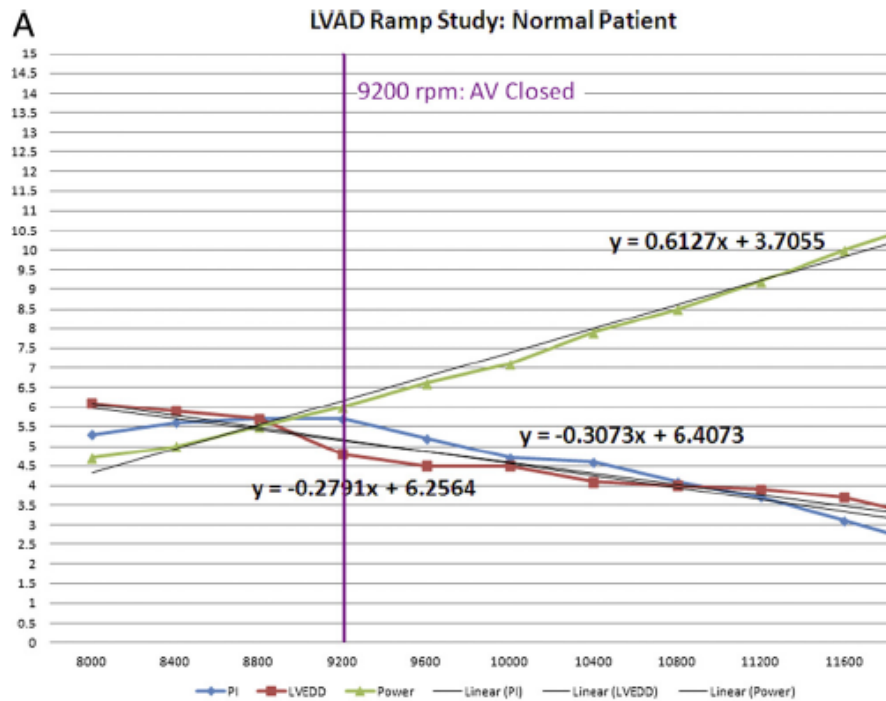
# Imaging - Echo



Medially displaced inflow

# Echo - Ramp Study

Stepwise increase in LVAD speed with Echo monitoring of LVEDD, PI, power, MR, AI and RVSP)



Uriel N, et al. JACC 2012

# RHC/LHC



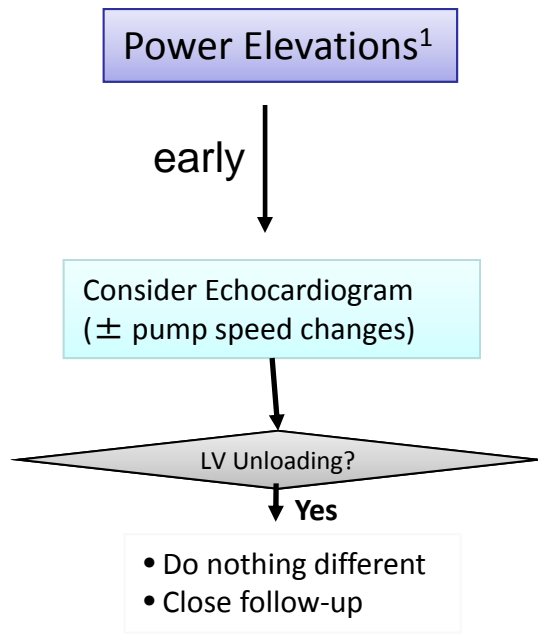
- RHC: elevated PCWP and right sided pressures
- LHC: dye into LV cavity to assess outflow graft filling or direct dye into outflow via retrograde catheter

# Thrombosis Workgroup



- Clinicians interested in addressing pump thrombus/power spikes seen in last 12 mo among recipients of HMII
- Facilitated by Thoratec Inc.
- Goal: algorithm for pump thrombus evaluation and management

# Workgroup Proposed Management of Suspected Pump Thrombosis

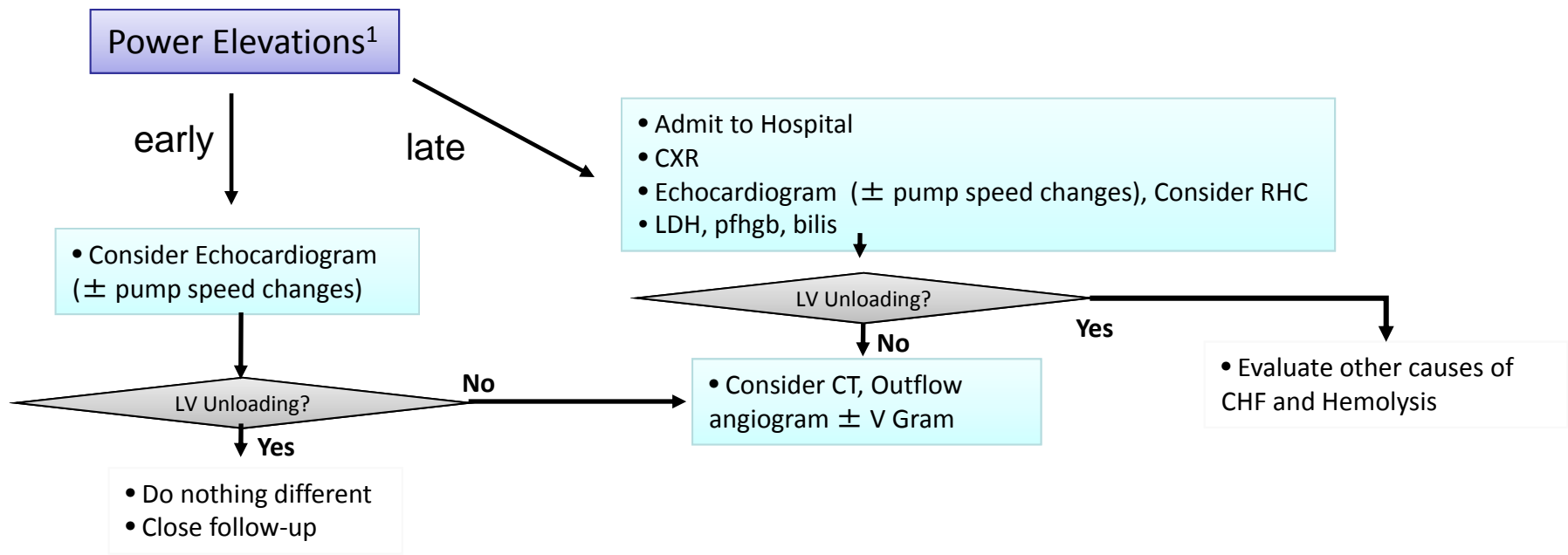


## **Definitions:**

### **<sup>1</sup>Power Elevations:**

- a) Sustained (>24hrs) Power > 10W; or
- b) Sustained (> 24hrs) Power Increase > 2W from Baseline

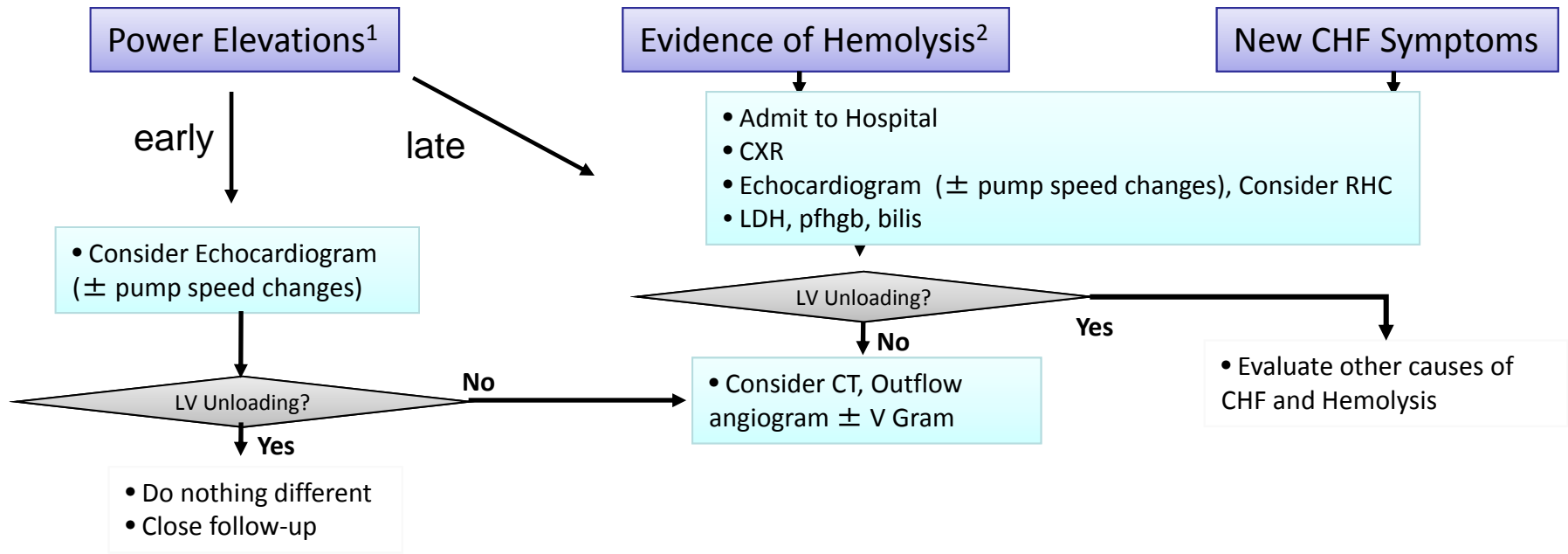
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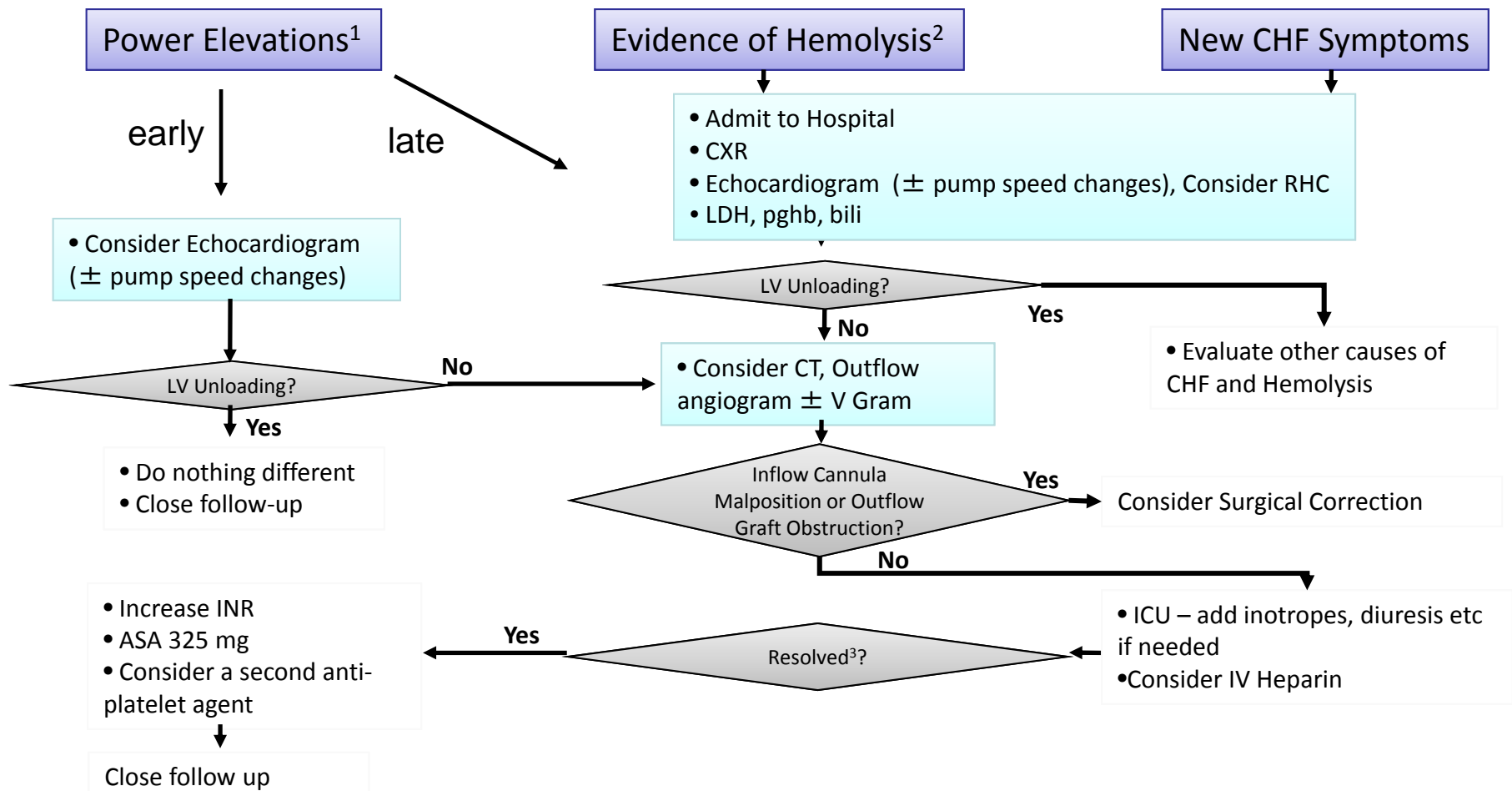


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<sup>2</sup>**Hemolysis:**  
 a) Clinical Diagnosis; or  
 b) LDH > 2.5x discharge value and PHGB > 20 and/or Low haptoglobin levels

# Workgroup Proposed Management of Suspected Pump Thrombosis



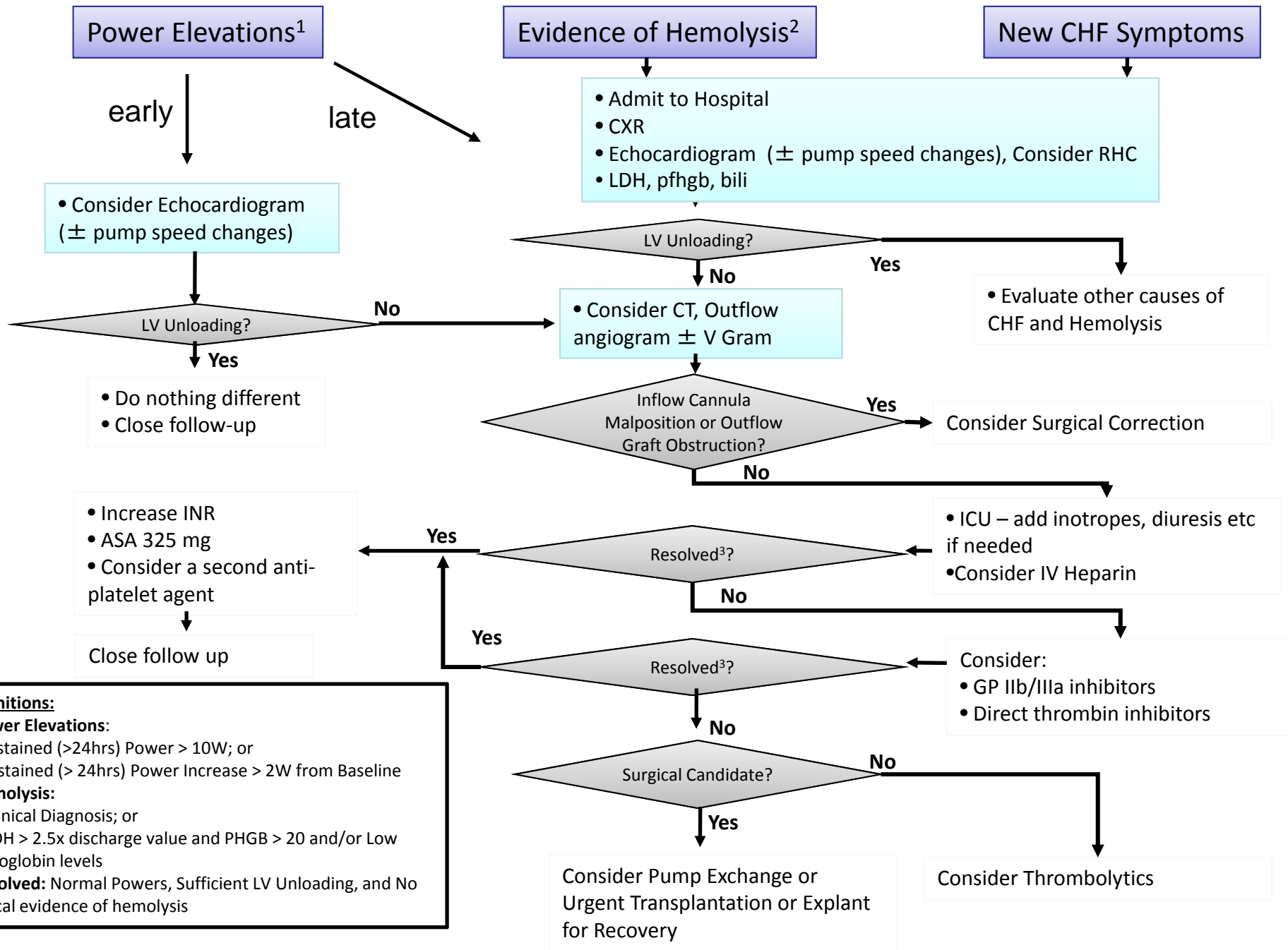
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<sup>3</sup>**Resolved:** Normal Powers, Sufficient LV Unloading, and No clinical evidence of hemolysis

# Workgroup Proposed Management of Suspected Pump Thrombosis



# Pump Exchange

## Subcostal approach

- Avoids re sternotomy morbidity
- Direct access to pump
- Groin cannulation or off pump
- Reserved for pump thrombus limited to pump housing.
- Shorter CPB, less bleeding
- Shorter LOS

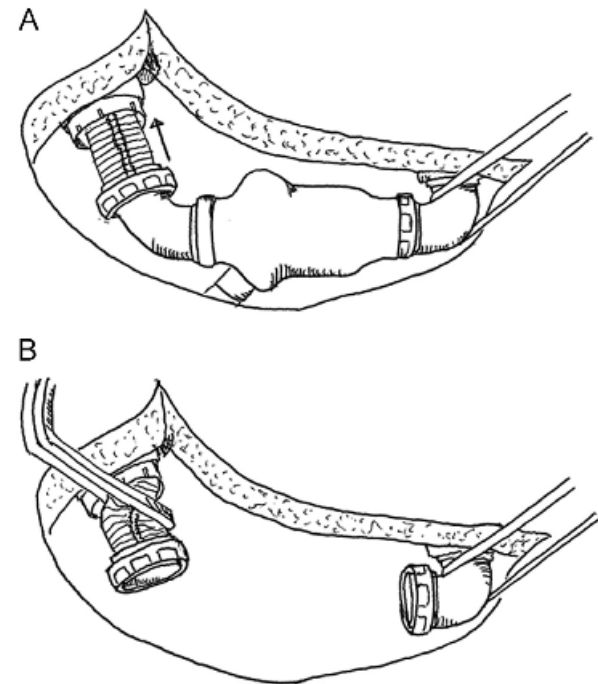
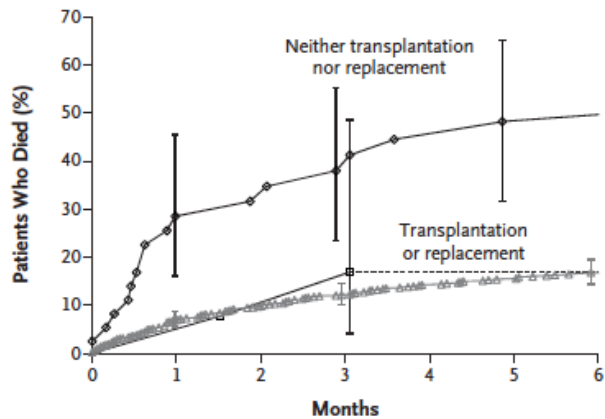


Figure from Ota et al JHLT 2014

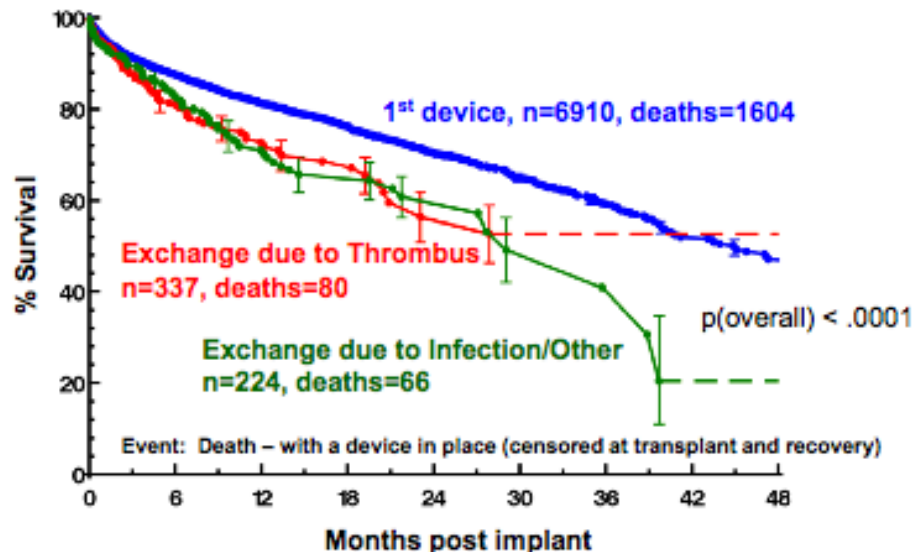


No. at Risk	0	1	2	3	4	5	6
HeartMate II support without thrombosis	895	790	709	652	612	576	531
Thrombosis with transplantation or replacement	32	13	13	13	10	10	10
Thrombosis with neither transplantation nor replacement	40	25	23	20	18	15	15

**Figure 5. Mortality According to Management Strategy after Confirmed Pump Thrombosis.**

Squares indicate deaths after heart transplantation or pump replacement, and diamonds indicate deaths of patients who did not undergo heart transplantation or pump replacement, with the horizontal axis truncated at 6 months. For reference, triangles indicate deaths without confirmed pump thrombosis during HeartMate II support from the time of implantation (gray). Symbols represent nonparametric estimates, and I bars 95% confidence intervals. The dashed line represents patients for whom follow-up data were available and who remained alive.

## Survival after Exchange

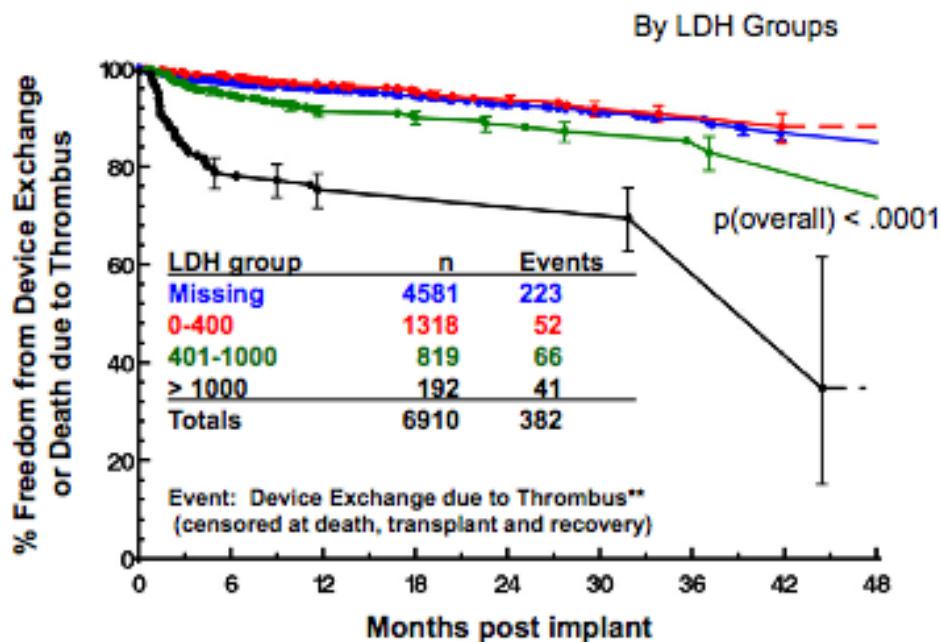


NEJM 2014;370:33-40

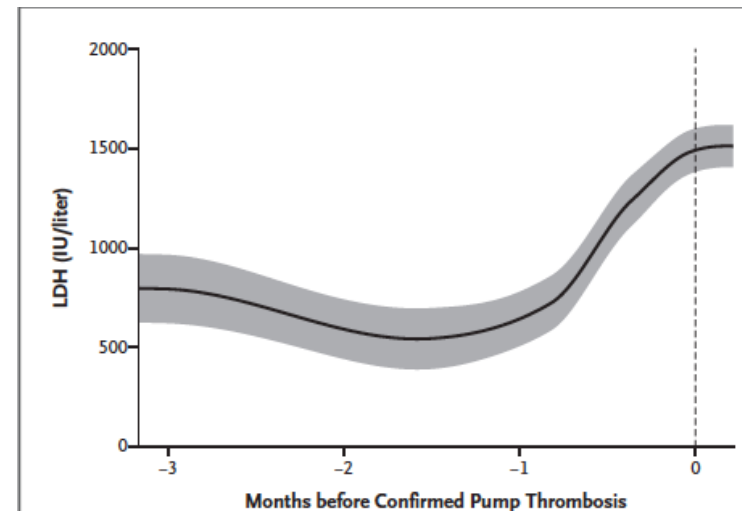
JHLT 2014;370:33-40

# LDH

- Preferred serological marker of hemolysis
- Earlier marker than pfHgb
- 2.5 x ULN is highly suggestive



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



**Figure 4.** LDH Values before Confirmed Pump Thrombosis.

The time of pump thrombosis (time zero) is shown at the right side of the graph, and LDH values up to 3 months before confirmed thrombosis are shown. The solid line represents the estimate of the LDH level, as generated by the locally estimated scatterplot smoother (loess), and the gray band represents the bootstrapped 95% confidence interval.

# Thrombus in Literature

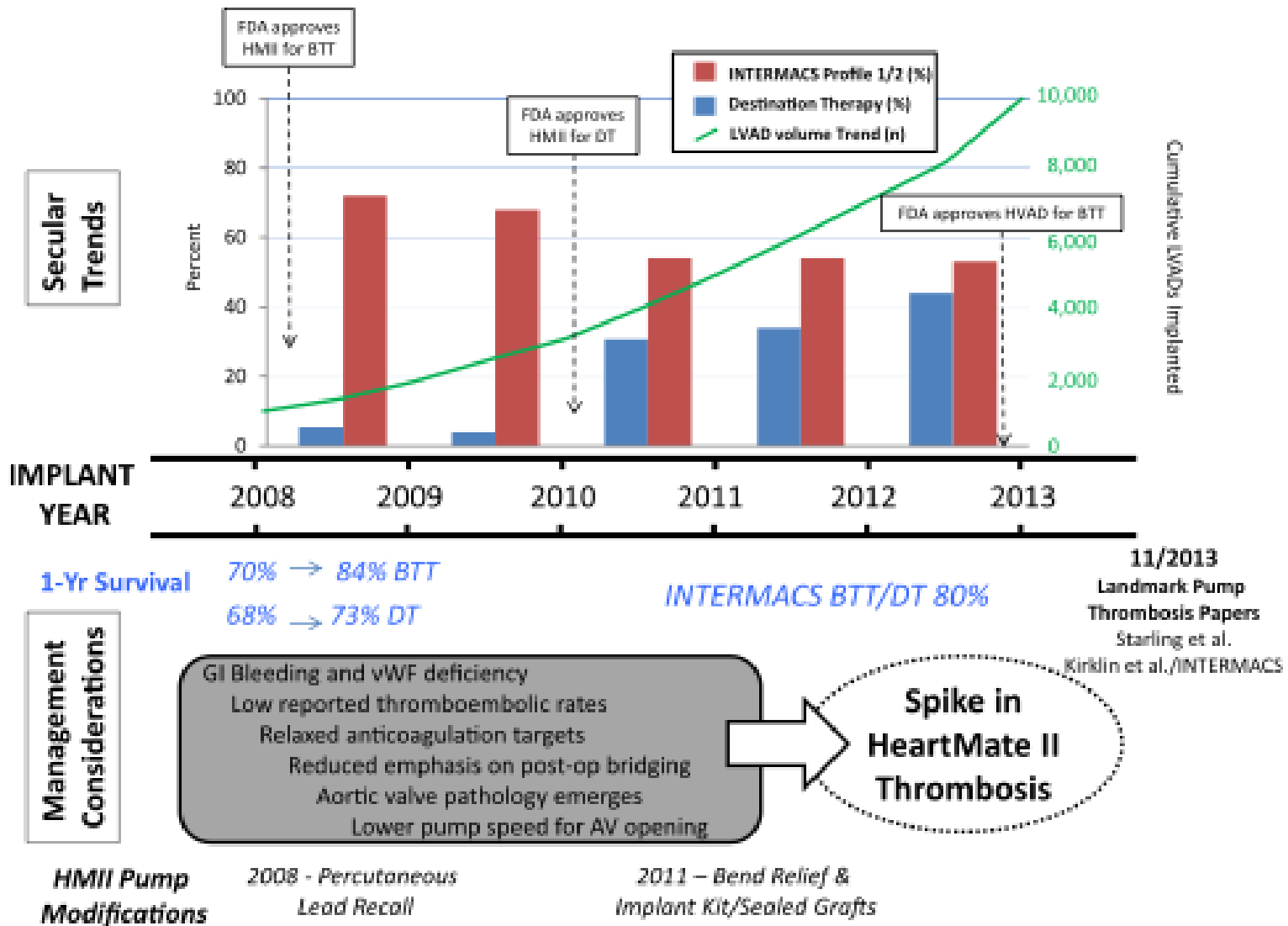
Author	Year	Device	# Pts	POD	Treatment	Outcome
Rothenburger	2002	MicroMed	8	53-430d	rTPA, 100mg IV	Full resolution, minor epistaxis, no bleeding complication
Delgado	2005	Jarvik 2000	2	9d, 116d	Intracavitary rTPA 1mg/min	1 died from complications on pump thrombosis
Studer	2006	DeBakey Child	1	1 month	Plavix 150 mg	Recurrent thrombus successfully treated with plavix 150mg
Tschirkov	2007	INCOR	1	155d	Intracavitary reteplase	Full resolution
Jahanyar	2007	MicroMed	1	110d	TPA IV	3 recurrent episodes, all resolved with TPA
Hayes	2007	Jarvik 2000	1	39d	IV tenecteplase	Full resolution
Blais	2008	HMII	1	196d	Integrellin, Heparin	Recurrence successfully treated with argatroban
Thomas	2008	HVAD	1	140d	Hep/Plavix/Tirofiban	Full resolution
Meyer	2008	HMII	1	2 months	Hirudin	Recurrence/transplantation
Bhamidipati	2010	HMII	1	18d	Pump exchange	Full resolution
Kiernan	2011	HVAD	1	5 months	Intracavitary alteplase	Full resolution
Paluszkiewicz	2011	HMII	1	1 month	Thrombolysis	Full resolution
Bashir	2011	HMII	1	3d	Pump exchange	Full resolution
Aissaoui	2012	Heartware	6	ND	Pump exchange (6)	Full resolution
Mishkin	2012	HMII	1	2 months	Disconnected pump	Awaiting transplant
Al-Quthami	2012	HMII	2	33, 42 days	Hep/Eptifibatide	Full resolution

# Incidence & Rate

Incidence Event ppy

HMII BTT, NEJM 2007, n=133	2%	0.03
HMII DT, NEJM 2009, n=134	4%	0.024
HMII DT CAP, Circ HF 2009, n=281	6%	0.038
HW BTT, Circulation 2012, n=137	2.1%	0.03
HW BTT + CAP, JHLT 2014, n=382	8.1%	0.08
INTERMACS HMII, JHLT 2014, n=6910	5.5%	NA
HMII, NEJM 2014 n=837	8.4%	NA





# Summary



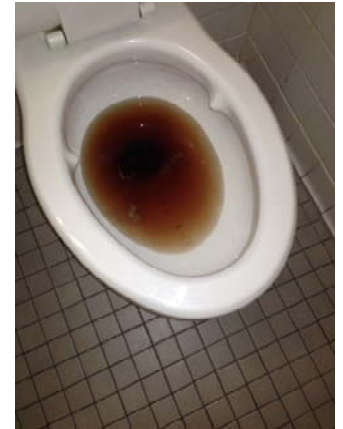
- Pump thrombus is dreaded complication of CF LVAD technology
- Assessment of modifiable risk factors essential (afib, mech valve, etc)
- Imaging and functional studies (ramp) can confirm diagnosis
- The proposed algorithm can serve as a launching point when confronted with suspected pump thrombus

# Summary



- Etiology of pump thrombus is likely **MULTIFACTORIAL**
- Recommendations:
  - High vigilance w LDH screening
  - Pathology evaluation of all explants
  - Accurate reporting of suspicious and confirmed events to INTERMACS
  - Further large cohort studies to ascertain risk factors

# Pearls



- Hemolysis = pump thrombus
- Serial LDH monitoring best method for early diagnosis
- If urine is black, exchange the pump
- If CHF/pump malfxn (high PCWP), exchange pump
- For HMII, thrombus is typically a chronic fibrin deposition - don't give thrombolytics
- Pump exchange via subcostal approach best option in HMII.
- Thrombolytics may be considered for HW thrombosis if log file suggests recent event

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Thank you