# About OMICS Group

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# About OMICS Group Conferences

OMICS Group International is a pioneer and leading science event organizer, which publishes around 400 open access journals and conducts over 300 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

# Gastrointestinal Bleed in Left Ventricular Assist Devices

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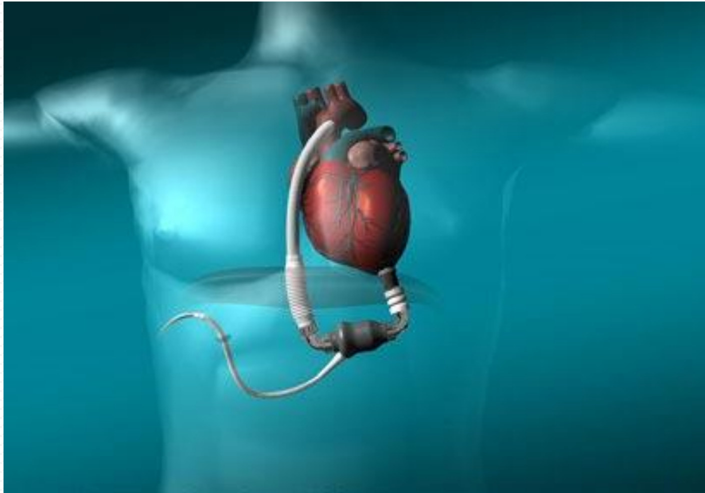
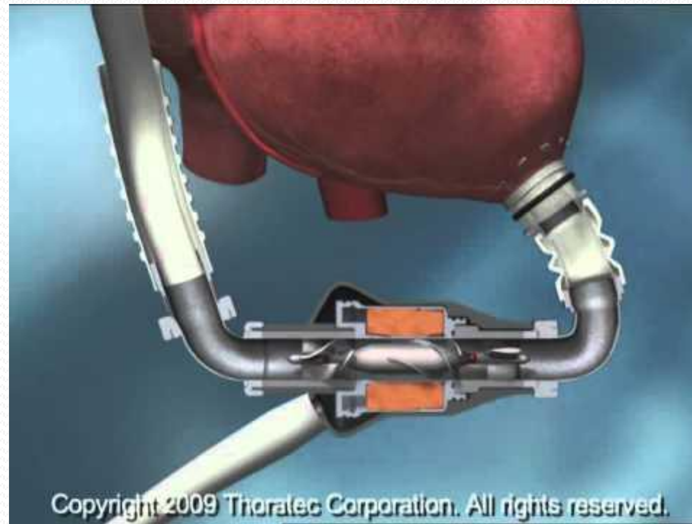
# No Disclosures

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# GI Bleeding Facts

- Common and significant medical problem
- Mortality UGIB: 3.5-13%
- Mortality LGIB: 1 - 5%
- Morbidities and costs associated with:
  - Readmission
  - Transfusion
  - Diagnostic imaging/Rx
  - Risks of re-bleed after reinstitution of coumadin/anti-platelet
- ASA and coumadin independent risk factors for both UGIB and LGIB

# GI Bleeding Sites
## *Anticoagulated Patients*

- Data retrospective, small or single-center studies
- Site identified in 80% cases
- GDU and erosions 50%
- LGI source 25-33%
- <u>Unknown in 17-29%</u>

"…I have seen at least 10 patients with calcific aortic stenosis who had massive gastrointestinal bleeding for which I could discover no cause, ….hoping that a letter to a prominent journal might elicit some response about the matter"

Dr. Edward Heyde, 1937

*The* NEW ENGLAND JOURNAL *of* MEDICINE

CLINICAL IMPLICATIONS OF BASIC RESEARCH

*The* Clinical Implications of Basic Research *series has focused on highlighting laboratory research that could lead to advances in clinical therapeutics. However, the path between the laboratory and the bedside runs both ways: clinical observations often pose new questions for laboratory investigations that then lead back to the clinic. One of a series of occasional articles drawing attention to the bedside-to-bench flow of information is presented here, under the* Basic Implications of Clinical Observations *rubric. We hope our readers will enjoy these stories of discovery, and we invite them to submit their own examples of clinical findings that have led to insights in basic science.*

**BASIC IMPLICATIONS OF CLINICAL OBSERVATIONS**

# From Clinical Observation to Mechanism — Heyde's Syndrome

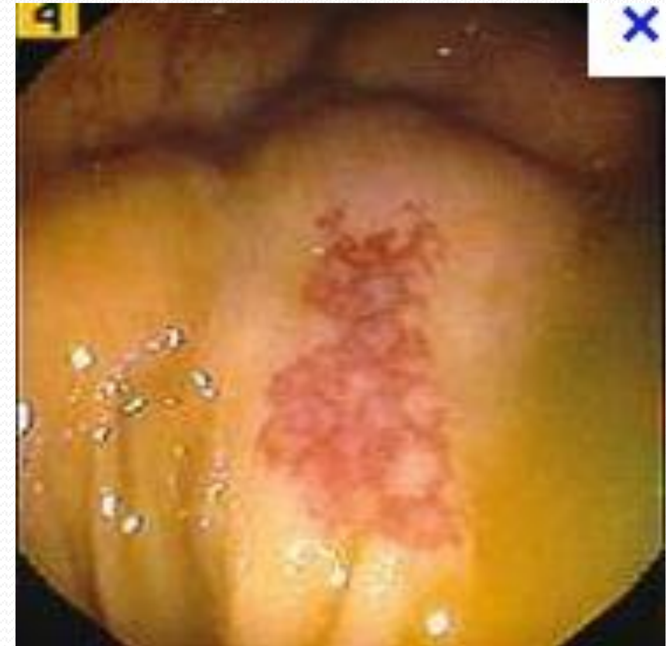
Joseph Loscalzo, M.D., Ph.D.

In 1958, E.C. Heyde, a general practitioner from Vancouver, Washington, sent to the *Journal* the following letter to the editor, in which he reported an association between calcific aortic-valve

of the statistical strength of the association between these two disorders, let alone inadequate in offering a potential mechanism to account for such an association.[3]

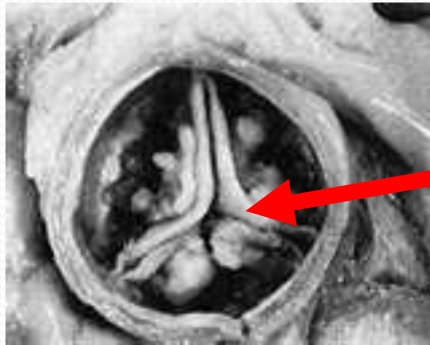
# Heyde’s Syndrome

Aortic Stenosis



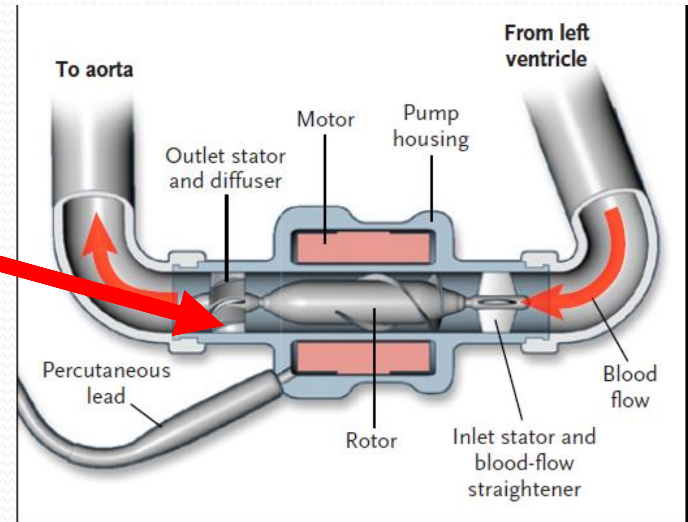
Bowel AVM

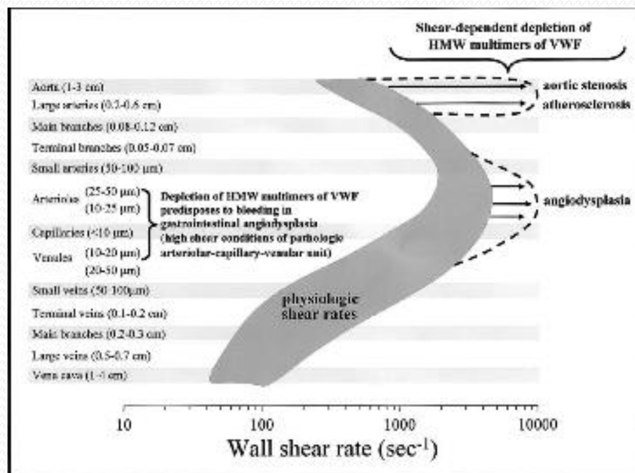
# Heyde's Syndrome ≈ CF LVAD Physiology

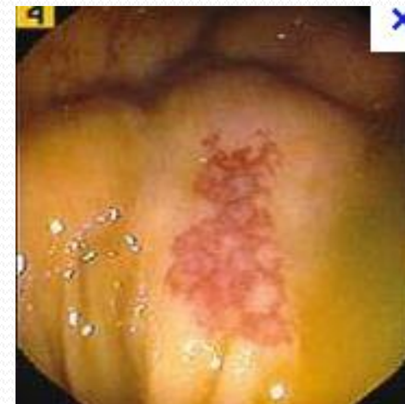


Aortic Stenosis

- Reduced Pulse Pressure
- Shear Stress



Small Bowel AVM

Von Willebrand multimer

Decreased production of thyroid hormone → Decreased synthesis of von Willebrand factor

ADAMTS 13

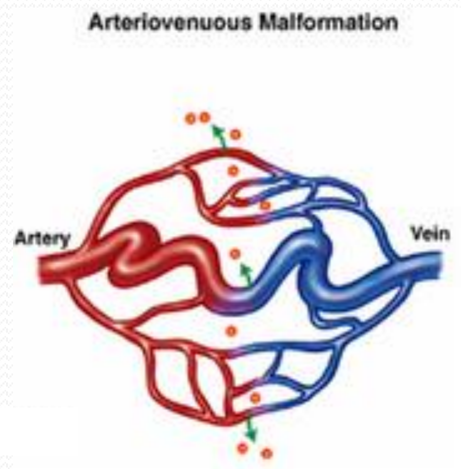
Coiled von Willebrand

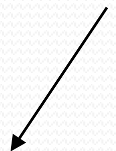
Mechanical stress

Uncoiling

Proteolysis

Mediates plt adhesion under high shear stress conditions



Impaired thrombus generation

# AS, GIB, aVWD and reversal with AVR

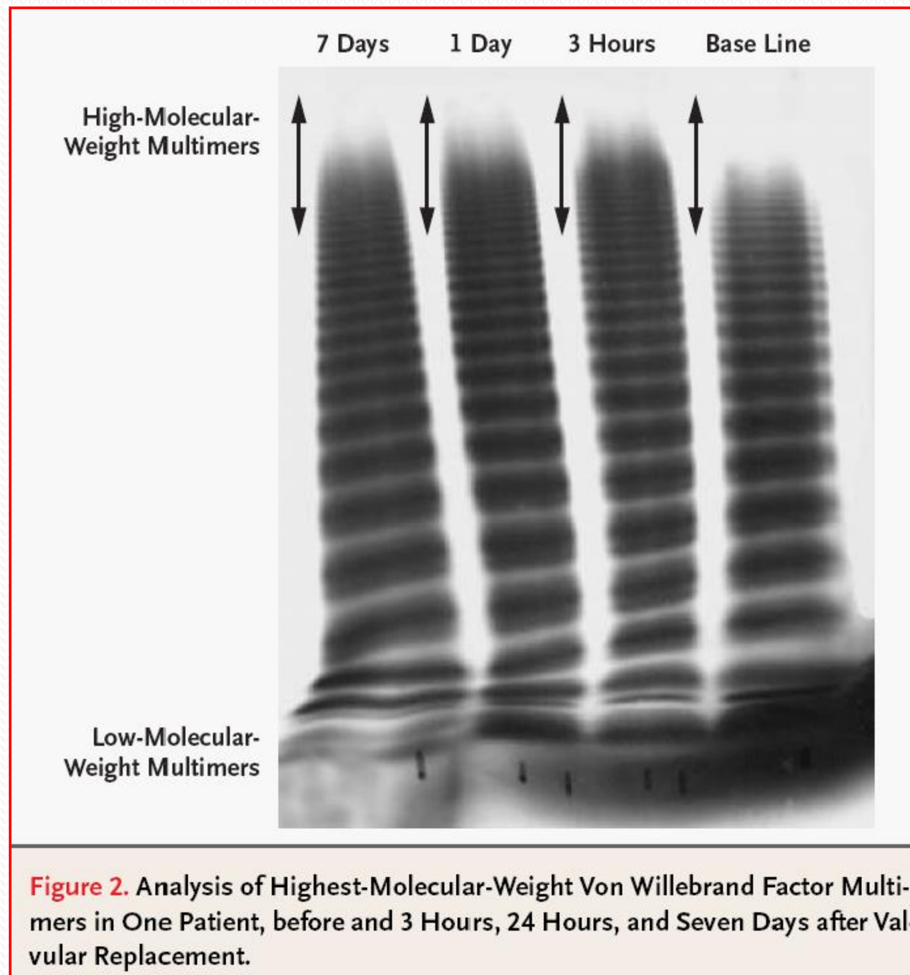



Figure 2. Analysis of Highest-Molecular-Weight Von Willebrand Factor Multimers in One Patient, before and 3 Hours, 24 Hours, and Seven Days after Valvular Replacement.

*Vincentelli et al. NEJM 2003;349:343-9*

# LVADs and GIB

## Gastrointestinal Bleeding From Arteriovenous Malformations in Patients Supported by the Jarvik 2000 Axial-Flow Left Ventricular Assist Device

George V. Letsou, MD,[a] Nyma Shah, BS,[b] Igor D. Gregoric, MD,[b] Timothy J. Myers, BS,[b] Reynolds Delgado, MD,[c] and O. H. Frazier, MD[b,d]

- First description, 3 pts
- 2 patients resolved after OHT
- 1 patient died MSOF

# LVADs and GIB

- GIB was not an important adverse event in pulsatile VAD experience
- Concern for thromboembolism led to manufacturer recommendation for antiplatelet & anticoagulation in CF LVADs
- Unquestionable increase GIB in recipients of CF LVAD technologies….is it due to antithrombotic regimen alone?

# Use of a Continuous-Flow Device in Patients Awaiting Heart Transplantation

Leslie W. Miller, M.D., Francis D. Pagani, M.D., Ph.D., Stuart D. Russell, M.D.,
Ranjit John, M.D., Andrew J. Boyle, M.D., Keith D. Aaronson, M.D.,
John V. Conte, M.D., Yoshifumi Naka, M.D., Donna Mancini, M.D.,
Reynolds M. Delgado, M.D., Thomas E. MacGillivray, M.D.,
David J. Farrar, Ph.D., and O.H. Frazier, M.D.,
for the HeartMate II Clinical Investigators*

Heart Failure

# Extended Mechanical Circulatory Support With a Continuous-Flow Rotary Left Ventricular Assist Device

Francis D. Pagani, MD, PHD,* Leslie W. Miller, MD,† Stuart D. Russell, MD,‡
Keith D. Aaronson, MD,* Ranjit John, MD,§ Andrew J. Boyle, MD,§ John V. Conte, MD,‡
Roberta C. Bogaev, MD,|| Thomas E. MacGillivray, MD,¶ Yoshifumi Naka, MD,#
Donna Mancini, MD,# H. Todd Massey, MD,** Leway Chen, MD,** Charles T. Klodell, MD,††
Juan M. Aranda, MD,†† Nader Moazami, MD,‡‡ Gregory A. Ewald, MD,‡‡ David J. Farrar, PHD,§§
O. Howard Frazier, MD,|| for the HeartMate II Investigators†

*Ann Arbor, Michigan; Washington, DC; Baltimore, Maryland; Minneapolis, Minnesota; Houston, Texas; Boston, Massachusetts; New York and Rochester, New York; Gainesville, Florida; St. Louis, Missouri; and Pleasanton, California*

# Advanced Heart Failure Treated with Continuous-Flow Left Ventricular Assist Device

Mark S. Slaughter, M.D., Joseph G. Rogers, M.D., Carmelo A. Milano, M.D.,
Stuart D. Russell, M.D., John V. Conte, M.D., David Feldman, M.D., Ph.D.,
Benjamin Sun, M.D., Antone J. Tatooles, M.D., Reynolds M. Delgado, III, M.D.,
James W. Long, M.D., Ph.D., Thomas C. Wozniak, M.D.,
Waqas Ghumman, M.D., David J. Farrar, Ph.D., and O. Howard Frazier, M.D.,
for the HeartMate II Investigators*

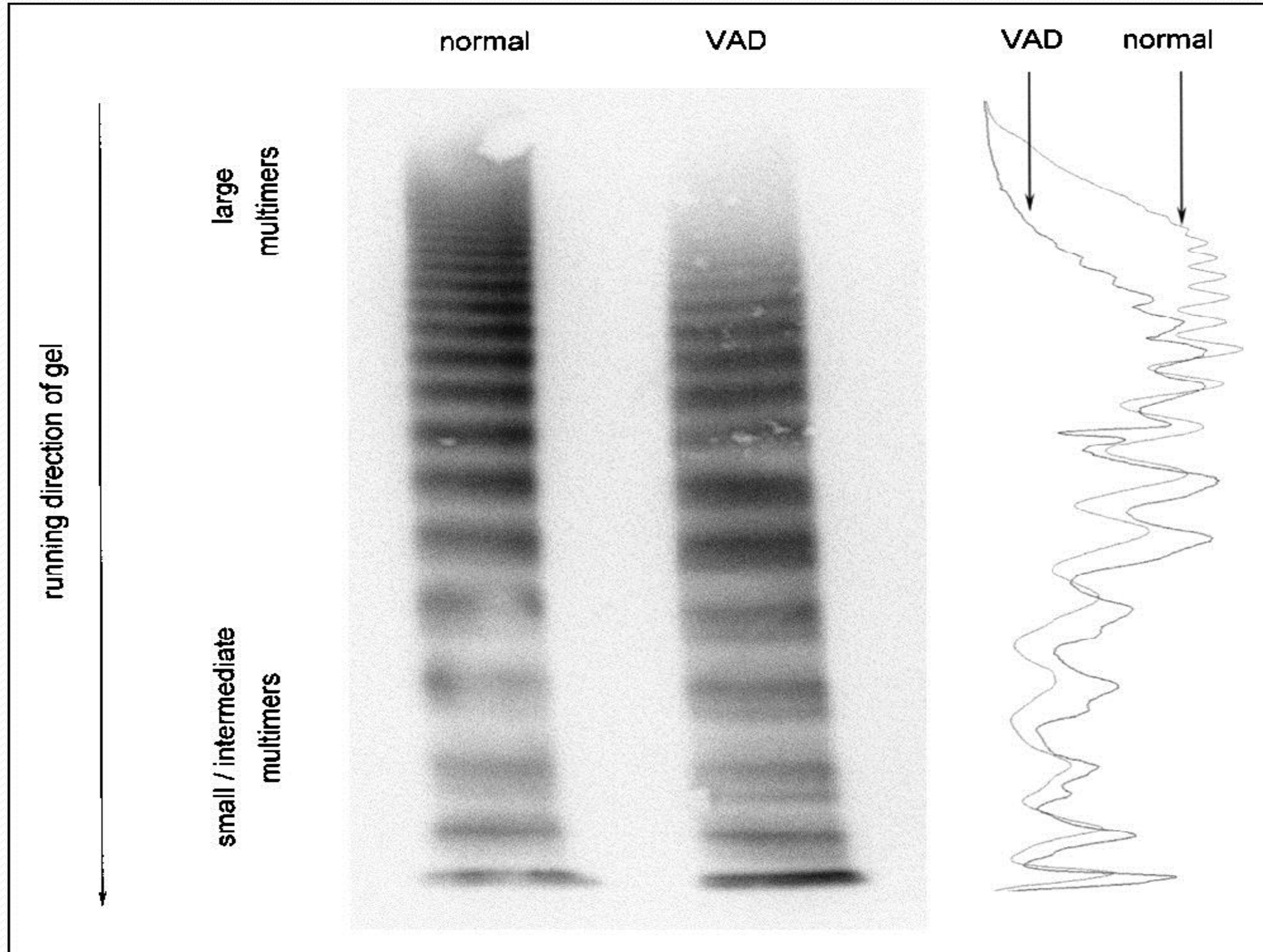
No mention of GIB !!!!

# LVADs and GIB

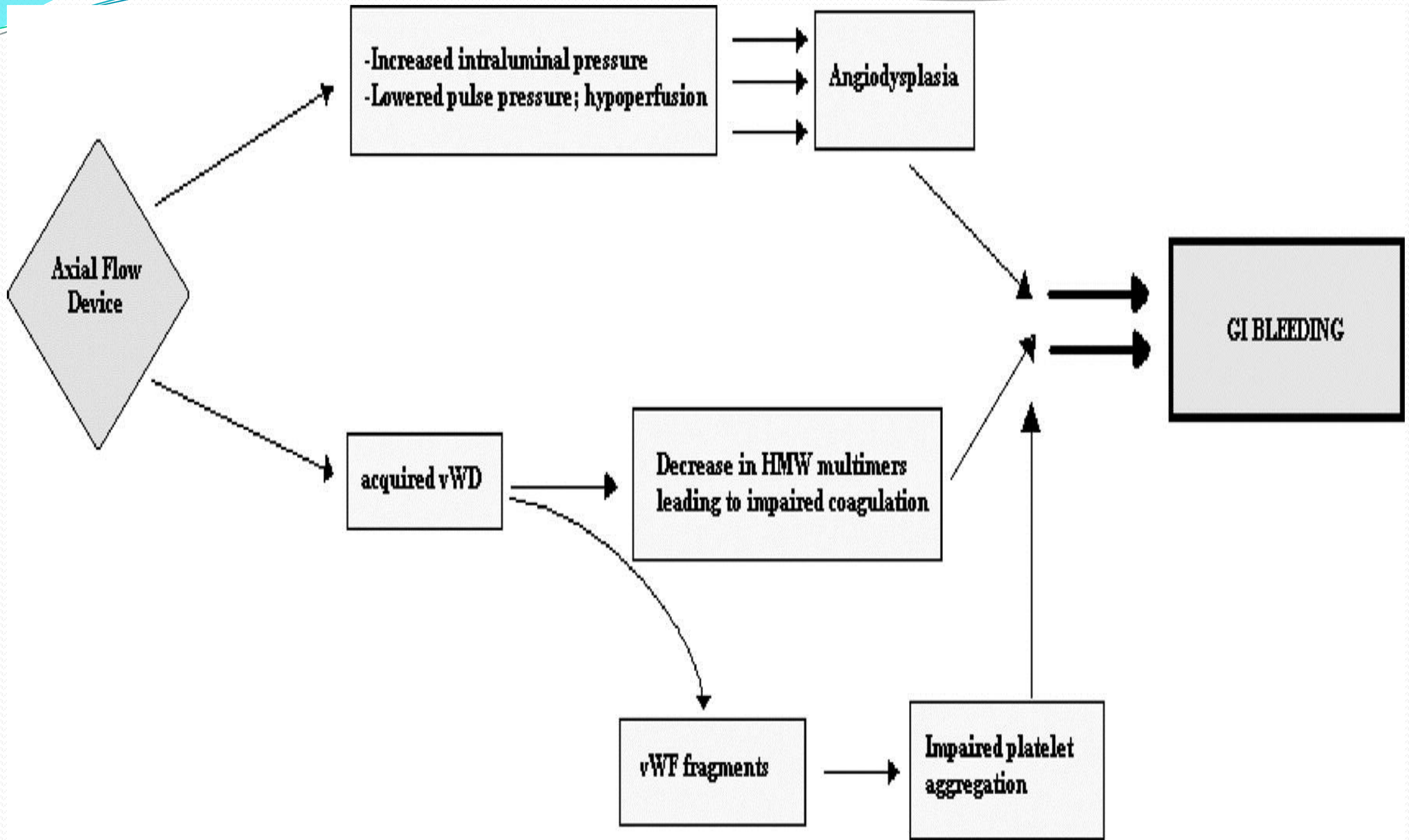
*Single Ctr Experience*

| Author | Year | N | LVAD | Incidence | Site of GIB |
|---|---|---|---|---|---|
| Crow | 2009 | 101 | XVE | 6.8 per 100 pt-yrs | ? |
| | | | HMII, VA, MM | 63 per 100 pt-yrs | |
| Stern | 2010 | 33 | HMII | 40%, 2yrs f/up | 65% unk site |
| Meyer | 2010 | 26 | HMII | 11%, 1-25 mo | all sb avm |
| Crow | 2010 | 37 | HMII | 13.5%, 10 mo | ? |
| Uriel | 2010 | 79 | HMII | 33% mean 370d f/up | ? |
| Hayes | 2010 | 36 | VA, J, HW | 14% | most avms |
| Demirozu | 2011 | 172 | HMII | 19% | 31% avm |
| Schaffer | 2011 | 86 | HMII | 28% at one year | ? |
| John | 2011 | 102 | HMII | 17.6% | ? |

# Can Axial Flow Pumps Cause Acquired vWF?




EJCTS 2008, 33; 4: 679-684




Suarez J et al. Circ Heart Fail 2011;4:779-784

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# Not the Whole Story…

- All CFVAD pts develop aVWS
- Most CFVAD recipients do not have GIB !!
- Many CFVADs pts that bleed have conventional GIB sites…
- Clearly, other factors must explain the high incidence
- avWD likely contributor
- Elevated INR, Blood Type O and excessive fibrinolysis other potential players

Incidence and Management of Gastrointestinal Bleeding With Continuous Flow Assist Devices

Ashim Aggarwal, MD, MRCP, Rojina Pant, MD, Shivani Kumar, Priya Sharma, BA, Colleen Gallagher, BSN, Antone J. Tatooles, MD, Pat S. Pappas, MD, and Geetha Bhat, MD, PhD

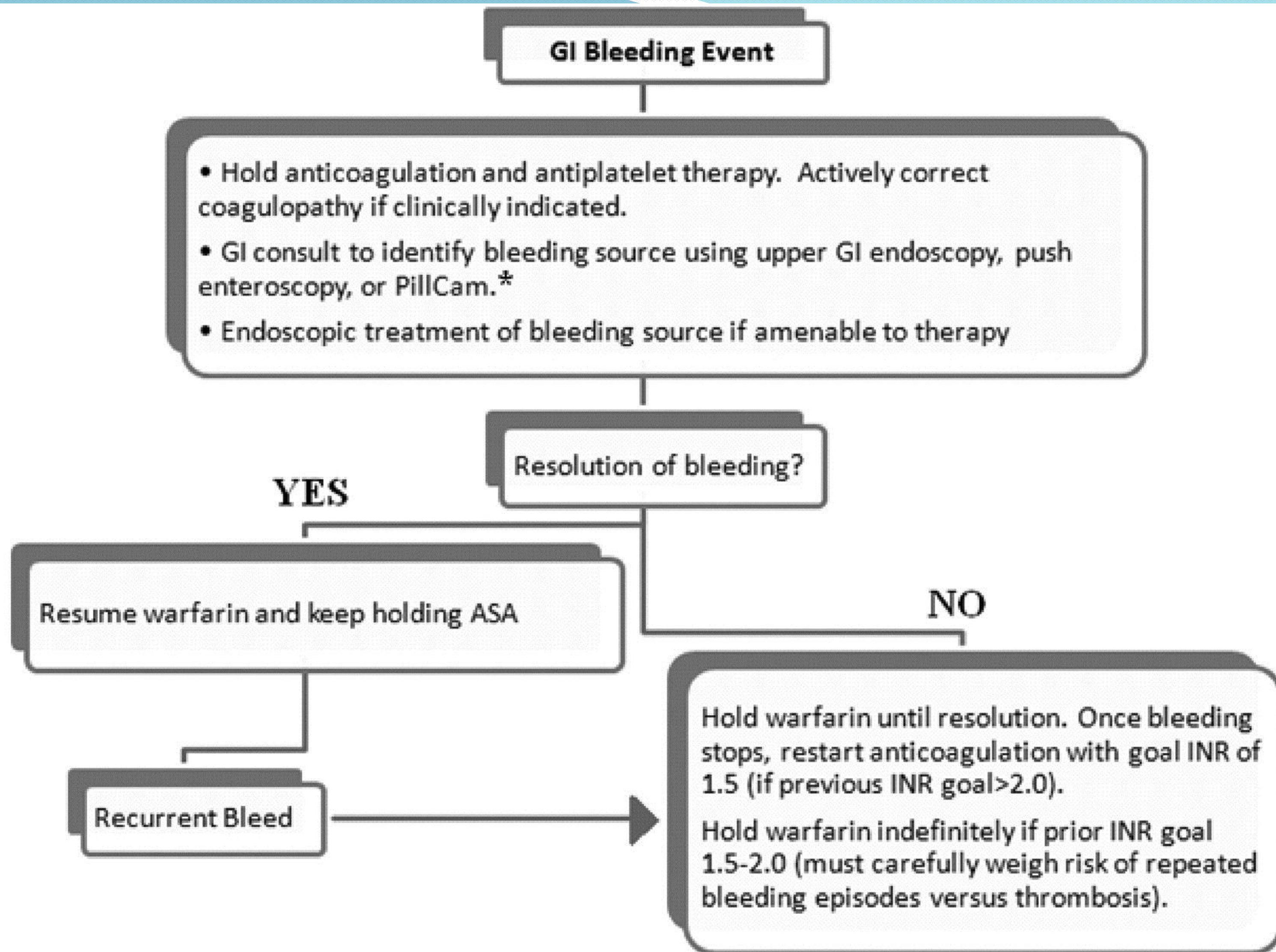
Center for Heart Transplant and Assist Devices and Department of Cardiothoracic Surgery, Advocate Christ Medical Center, Oak Lawn, Illinois

- 23% gastrointestinal bleed (GIB) in 101 patients
- Previous history of GIB, increased INR, low platelets and age were predictors

Ann Thorac Surg. 2012; 93:1534-40

# So You have a GIB Event..

- Admit
- Hold ASA/warfarin
- Reverse Vit K antagonism (FFP) PRN
- Transfuse platelets PRN
- GI consult
- Upper and lower GI endoscopy....




*There are no data indicating that endoscopy or the PillCam are beneficial in management of GI bleeding early after LVAD implantation when pre-LVAD endoscopy showed no bleeding source.

**Suarez J et al. Circ Heart Fail 2011;4:779-784**

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# UGI & LGI Endoscopy are Unrevealing….Now What?

- Capsule endoscopy and/or push enteroscopy for Dx ± Rx
- If bleeding stops, and hct stabilizes, restart coumadin first; ASA later
- If bleeding persists:
  - Transfuse as necessary
  - Reduce speed - AoV open, pulsatility, less shear stress
  - Others: octreotide (splanchnic vasoconstrictor), estrogens, Humate-P, FVIII concentrates
  - Listing for transplantation
  - Hold coumadin/ASA indefinitely

# Summary

- GIB (and other mucosal bleeding) is a significant AE following CFLVAD support
- Loss of HMW vWF is universal
- AVM frequent etiology of GIB
- Other factors must play a role in the genesis of GIB
- Dx may require unconventional imaging (Pillcam, DBPE)
- Reinitiation of anticoag/antiplt is done cautiously
- Role of speed reduction and adjunctive Rxs like estrogen, octreotide unclear - thrombotic potential (pump thrombus)
- More data needed to elucidate age, blood type, fibrinolysis, pulsatility as potential factors

# Thank You

Any Questions??

# Thanks' for your kind attention!!!!!!

# Let Us Meet Again

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