EXPAND Heart Trial

- **POPULATION:** Heart transplant candidates
- **PI:** Karol Mudy, MD & Daniel DiBardino, MD
- **CONTACT INFO:** Kelly Wilson | Kelly.Wilson@allina.com | 612-863-6288
- **DESCRIPTION:** International Trial to Evaluate the Safety and Effectiveness of the Portable Organ Care System (OCS™) Heart for Recruiting, Preserving and Assessing Expanded Criteria Donor Hearts for Transplantation
- **CRITERIA LIST/QUALIFICATIONS (RECIPIENTS):**
  - Registered adult male or female primary heart transplant candidate
  - No prior solid organ or bone marrow transplant
  - No chronic use of hemodialysis or diagnosis of chronic renal insufficiency
  - No multi-organ transplant candidates
- **SPONSORS:** TransMedics, Inc.
MCS Potpourri in 3 "Straightforward" Cases

Conflict of Interest

- Nothing to disclose
- I love to operate…
Case 1

- 47 y.o. female with a past medical history of ulcerative colitis, on chronic immunosuppression; tobacco abuse and polysubstance abuse many years ago
- Upper respiratory symptoms, cough, sinus congestion for 7-10 days.
- Prescribed course of Bactrim.

- No improvement, started to develop progressive chest pressure
- On the day of admission had acute onset N/V, followed by severe pain in the neck and between shoulder blades with some radiation to the jaw.
- Presented to the local ED, hypotensive
- Started on neo-sinephrine infusion and transferred to ANW.
Case 1

- Upon admission to ANW was minimally responsive, had diffuse skin mottling and poor peripheral pulses.
- Hypotensive, with MAPS in the low 50s, HR 140s
- Intubated with escalating doses of vasopressors.

WBC 17K
Hgb 10
Plt 80K
Creat 3.3
HCO3 12
Lactate 12
Case 1

- Sepsis?
- Aortic dissection?
- MI?

- EKG – sinus tachycardia, no STT changes
- CTA → negative for dissection
- 2D echo→
Case 1

- Cardiogenic shock
- Transferred to CV lab for VA ECMO and IABP placement.
Case 1

VA ECMO/IABP placed in the cath lab (15F,25F)
- Coronary angiogram normal
- Very low regional sats on both LE
- No dopplerable pulses

• Vascular surgery called and placed distal perfusion catheters in both LE with almost immediate improvement
What’s the etiology of her CM?

Septic cardiomyopathy

- Myocardial cell shortening is reduced by exposure to the serum of septic patients
- Role of tumor necrosis factor and interleukin-1b
- Increase in intracellular cGMP and nitric oxide production
- Increased phosphorylation of troponin I that reduces myofilament response to Ca2+
Septic cardiomyopathy

- It is acute and reversible, provided the patient recovers.
- Depressed LV systolic function is associated with normal or low LV filling pressure, unlike the “classic” pattern of cardiogenic shock.
- Common RV dysfunction.
- Worse survival?

Case 1

- Transferred to the CCU
- Relatively stable, weaning pressors
No significant LV ejection (Pulse Pressure < 20)
LV unloading

- 207 articles published between 1993 and 2016
- Adult series 67%, pediatric 29%, mixed population 4%
- Percutaneous approach in 84% of the cases
- Direct unloading (LA) in 31%
- IABP (27%), trans-aortic (27%), LV (11%), and PA (4%)
- Percutaneous trans-septal approach in 22%
- Surgically in 16%, (open chest surgery in 71%, and minimally invasive surgery in 29%)

Consequences of minimal/no LV ejection

- LV pressure overload, LV dilatation, increase in left atrial pressure, and pulmonary edema.
- Increase in wall stress and myocardial oxygen consumption, jeopardizing ventricular recovery
- Closure of aortic valve leading to stasis and thrombosis
- Mortality > 90%
Does an IABP work?

Effects of Additional Intra-aortic Balloon Counter-Pulsation Therapy to Cardiogenic Shock Patients Supported by Extra-corporeal Membranous Oxygenation

Lian-Yu Lin1,2,*, Chen-Wei Liao2,*, Chih-Hsien Wang3, Nai-Hsin Chi3, Hsi-Yu Yu3, Nai-Kuan Chou3, Juey-Jen Hwang3, Jiong-Lee Lin3, Fu-Tien Chiou3, & Yih-Sheng Chen3

Extra-corporeal membranous oxygenation (ECMO) has been applied in patients with cardiopulmonary failure. One critical drawback of peripheral ECMO is an increase in left ventricular (LV) afterload which could be counterbalanced by the combination of intra-aortic balloon counter-pulsation (IABP) therapy. We hypothesised that an add-on therapy with IABP could improve outcomes in patients receiving ECMO support. We included patients (>18 years old) from 2002 to 2013 requiring ECMO support due to cardiogenic shock in a medical center. A total of 523 patients (222 ECMO alone and 310 combined IABP plus ECMO) were included. The mortality rates at 2 weeks (44.5% vs. 47.7%) after ECMO implantation were not different between the two groups (ECMO vs. combined group). After adjustment for propensity score and potential confounders, the odds ratios of outcomes within 14 days (combined group vs. ECMO) for poor LV systolic function, high preload, multi-organ failure and mortality were not different. The results remained similar for subgroup analysis. Compared with ECMO alone, combined IABP and ECMO treatment did not improve outcomes in patients with circulatory failure.
Case 1

- Underwent LV vent placement given severely depressed EF and lack of meaningful ejection.
Case 1

- Influenza B positive
- Tox screen positive for methamphetamine
- Aneuric/acidotic → CRRT started
- Rising CK
Case 1 Days 1-9

- Overall stable on VA ECMO
- Pressors weaned
- Opening eyes and following simple commands
- Unsuccessful multiple weans of ECMO

Case 1

- Myocardial biopsy showed normal heart muscle; most likely etiology stress-induced/toxic/metabolic
Case 1

- Continue?
- LVAD?
- Withdrawal of care?
MHIF CV Grand Rounds – Oct. 16, 2017

MHI/ANW Data
LVAD 1 year survival

LVAD 81.7%
ECMO→LVAD 75%

MHI/ANW Data
LVAD 1 year survival

LVAD 81.7%
ECMO→LVAD 75%

MHI/ANW Data
LVAD 1 year survival

LVAD 81.7%
ECMO→LVAD 75%
Case 1

• Uneventful postoperative course
• Weaning pressors
• Weaning RVAD daily, tolerating well
• Successfully decannulated on POD #10

RVAD explant
RVAD explant

RVAD explant
Case 1

- Stable on HVAD support
- Recovery of kidney function
- Rehab, walking, tracheostomy decannulated
- Follow up echoes
Case 1

• Plan to DC home and explant in 2-3 months to avoid significant bleeding complications during surgery.
Case 1

- Acute onset slurred speech, NIHSS of 8 with some hemineglect
- Stroke code was called and CTA identified the thrombus in the right M3 territory

Transarterial mechanical thrombectomy: Right M3 segment embolus.
Case 1

- Initial plan- decommissioning of the LVAD
- 2 days later- another TIA
Case 1

- Successful LVAD explant
- Discharged home after 7
- LVEF remains normal with mildly depressed RV systolic function by MRI
- ICD placed

Case 1 - “circle of life”

ECMO

LVAD explant

ECMO-LV vent

Vent / CRRT

RVAD explant

LVAD-RVAD
Case 2

- 51 yo M, transfer from OSH presented with ?STEMI with subtotal LM
- PEA cardiac arrest then CPR in the cath lab, LVEF 10% on LV-gram. LVEDP 40.
- Ongoing cardiogenic shock despite salvage PCI to LM/LCx
Case 2

- Emergent CABG x2 with LIMA to LAD, SVG to OM1
- PCS, unable to separate from CPB
- Peripheral VA ECMO
- Transferred to ANW
Case 2- ANW

• Poor peripheral perfusion
• No ejection

?
Case 2- OR

- Central cannulation for CPB
- Apical LV vent
- …and…
- …SURPRISE…

Case 2- OR

- Normal size ascending aorta, no IMH
- Upon opening the aortic lumen for anastomosis of the return cannula- flap
- Systemic cooling to 18 Celsius
• Ascending aortic replacement with hemi-arch replacement in DHCA

Case 2- OR

• Open chest for severe coagulopathy-modified vacuum dressing placed
• Return to ICU- HD stable
Case 2- OR

- Good ECMO flows- 4-5 liters
- Low flow on LV vent- 28 Fr R angle cannula
- ???
- No pulsatility on S-G catheter
Case 2- immediate return to OR

- BiVAD configuration:
  - LV vent apex → LVAD inflow
  - ascending aortic cannula → LVAD outflow
  - RA drainage → RVAD inflow
  - PA cannula → RVAD outflow
Case 2

• Good flow through LVAD and RVAD
• Chest closed POD #3
Case 2

- Good flow through LVAD and RVAD
- Chest closed POD #3
- CT head - L ischemic stroke
Case 2

- Care continued
- Extubated; right hemiparesis, sensory aphasia
Case 2

- FFWD 4 weeks- started making urine/ CRRT
- “...Over the last 3 weeks, he has made significant gains in language and functional abilities. He currently has moderate receptive aphasia and right hemiparesis. He will continue to make gains and speech therapy will certainly help with his aphasia...”
Case 2

- Heartmate 3 planned for Tuesday
- RVAD will remain - reconfiguration to “explantable at the bedside” - avoiding re-opening the chest
INTERMACS

- Interagency Registry for Mechanically Assisted Circulatory Support

| INTERMACS 1 | "Crash and burn" | Hemodynamic instability in spite of increasing doses of catecholamines and/or mechanical circulatory support with critical hypoperfusion of target organs (severe cardiogenic shock) |
| INTERMACS 2 | "Sliding on isoropines" | Intravenous inotropic support with acceptable blood pressure but rapid deterioration of kidney function, nutritional state, or signs of congestion |
| INTERMACS 3 | "Dependent stability" | Hemodynamic stability with low or intermediate, but necessary due to hypotension, doses of inotropics, worsening of symptoms, or progressive kidney failure |
| INTERMACS 4 | "Frequent flyer" | Temporary cessation of inotropic treatment is possible, but the patient presents frequent symptom recurrences and typically with fluid overload |
| INTERMACS 5 | "Nursehound" | Complete cessation of physical activity, stable at rest, but frequently with moderate water retention and some level of kidney dysfunction |
| INTERMACS 6 | "Walking wounded" | Minimal irritation on physical activity and absence of congestion while at rest. Easily fatigued by light activity |
| INTERMACS 7 | "Placeholder" | Patient in NYHA functional class II or III with no current or recent unstable water balance |
Case 3

• 55 yo M, ICM, NYHA class IV, INTERMACS 4
• LVEF 20-25%, normal valves
• CLINIC
Case 3

- BRIEF HOSPITAL COURSE:
- Mr. (…) is 55 with end-stage ischemic cardiomyopathy (EF 20-25%, LVEDd 5.5 cm) and stage D heart failure. He was admitted for HeartMate 3 LVAD implantation. He had post-operative RV dysfunction, temporarily supported with dobutamine which was then weaned off over several days.
- ADMISSION- 6/14/2017  DISCHARGE- 6/28/2017
- PROCEDURES PERFORMED DURING HOSPITALIZATION:
  - LVAD HeartMate 3 6/18/17
  - RHC 6/14/17
- COMPLICATIONS IN HOSPITAL: None

Original Article

INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) Profiling Identifies Ambulatory Patients at High Risk on Medical Therapy After Hospitalizations for Heart Failure

Garrick C. Stewart, MD, MPH; Michelle M. Kittleson, MD; Parag C. Patel, MD; Jennifer A. Cowger, MD; Chetan B. Patel, MD; Maria M. Mountis, DO; Frances L. Johnson, MD; Maya E. Guglin, MD; J. Eduardo Rame, MD, MPhil; Jeffrey J. Teuteberg, MD; Lynne W. Stevenson, MD
Methods and Results—This prospective, observational study enrolled 166 patients with chronic New York Heart Association class III-IV HF, ejection fraction ≤30%, and ≥1 HF hospitalization in the previous year, excluding patients listed for transplant or receiving chronic intravenous inotropic therapy. Subjects were followed for at least 12 months or until death, mechanical support, or transplant. Baseline features, quality of life, and outcomes were compared according to INTERMACS profile. Mean age was 57 years, ejection fraction 18%, and 57% had HF >5 years, whereas 23% of subjects were INTERMACS profile 4, 32% profile 5, and 45% profile 6/7. At 1 year, only 47% of this ambulatory advanced HF cohort remained alive on medical therapy. Patients in INTERMACS profile 4 were more likely to die or require mechanical support, with only 52% of these patients alive without support after the first 6 months. Profile 6/7 patients had 1-year survival of 84%, similar to outcomes for contemporary destination left ventricular assist device recipients. Quality of life using the indexed EuroQol score was poor across profiles 4 to 7, although severe limitation was less common than for ambulatory patients enrolled in INTERMACS before ventricular assist device implantation.

Figure 1. Competing events. Mutually exclusive end points of death, ventricular assist device (VAD), or transplant (Tx) were tracked through 1 year, with the cumulative percentage of events at any given time point equal to 100%.
Figure 2. Survival according to INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) profile. Estimated survival was modeled through 1 year using the Kaplan-Meier method with censoring at either ventricular assist device (VAD) or transplant. Survival was significantly different between patient profile groups (P=0.039).

Figure 3. Survival free of ventricular assist device (VAD) rescue according to INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) profile. Estimated survival or VAD was modeled through 1 year using the Kaplan-Meier method with censoring at transplant. Survival free of VAD rescue was significantly different according to INTERMACS profile (P<0.001).
In conclusion, ambulatory patients with chronic systolic HF, a heavy symptom burden, and at least 1 recent HF hospitalization are at high risk of death or progression to advanced cardiac therapies, despite optimal contemporary medical therapy. INTERMACS profiles are a useful shorthand for describing disease severity in patients with ambulatory advanced HF. Survival in patients who are INTERMACS profile 4 is lower than with contemporary LVADs, confirming the appropriateness of MCS use under existing indications and suggesting an opportunity for expanded deployment in appropriately selected patients.

Summary

- Variety of MCS
- Not “one fits all”
- Early implantation improves survival
“Saving world...
...one centrifugal pump at a time...”[1]

[1] K. Mudy

PCS

- Incidence 05-1.5% [1]
- Mortality 60% [2]

PCS

- Group of conditions resulting in “failure to separate from cardiopulmonary bypass requiring MCS” or “the need for MCS within 48h after index procedure”

Fukuhara et al GTCS 2016

Etiology

- PRESERVATION
  - Ischemia
  - Myocardial stunning
  - PGD
- Preoperative comorbidities
Devices

- ECMO
- VAD
  - LVAD
  - RVAD
  - BiVAD

ECMO

- Readily available
- Complete cardio-pulmonary support
- “Known entity”
ECMO- cannulation strategy

ECMO- cannulation strategy
ECMO

- Bleeding - anticoagulation and surgical sites
- Limb ischemia
- Stroke
- LV distention

LV distention and venting

- Increased afterload - central cannulation doesn’t protect from LV distention
LV distention and venting

External VAD surgical
External VAD surgical

BiVAD configuration
BiVAD configuration

- Central cannulation - potential for ambulation
- Conversion to uni-ventricular support
- Robust flow and potential for avoiding hemolysis
PCS - Results

• Incidence 05-1.5% [1]
• Mortality 60% [2]

Results

• Incidence 0.38 - 11.4%
• Survival to hospital discharge
  24\textsuperscript{[3]} - 92\textsuperscript{[4]}% (!!)

Results

- No clear definition of PCS
- Selection bias

Results

- Is it only going to be 50%?
- PCS patients characteristics:
  - older
  - high BMI
  - higher doses of pressors
  - CPB inflammatory response
Results

• Is it only going to be 50%?
• Technical complexity of surgery
  - myocardial ischemia/ stunning
  - coronary graft/ valve dysfunction
  - sternotomy

Results

• Perioperative risk factors
  - age >70 (OR 1.6)
  - diabetes (OR 2.5)
  - preoperative renal failure (OR 2.1)
  - obesity (OR 1.8)
  - EUROSCORE> 20% (OR 1.8)
  - operative lactate>4 (OR 2.2)

Results

• “When was last time you regretted putting someone on ECMO too early?”* 

*Robert Bartlett

Results

• Retrospective review of 3462 patients undergoing heart surgery
• Mortality post CPB:
  - no inotropes 2.0%
  - low dose 3.0%
  - moderate dose 7.5%
  - high dose 21%
  - 2 inotropes high dose 42%
  - 3 high dose 80%

Case

- 58 yo Female, presented with NSTEMI
- Coronary angiogram- 2 vessel CAD- LAD plus Cx
- Normal LVEF, normal RV
- Remote history of smoking
- Referred for CABG

- Straightforward 😊

Case - OR

- Upon exposure of OM1- large tear in LAA- repaired through atriotomy
- LAD- poor target- lumen below 1 mm
- LIMA- LAD performed, Cx ungrafted
- Upon weaning CPB- V fibrillation
- Discussed with cardiology- percutaneous peripheral ECMO placement- US guided, fluoroscopy/ Chest closed- CVICU
Case

- Take-back for bleeding POD#1 (chest opened 2nd time, muscle bleeder, closed)
- Stented coronaries
- Wean off ECMO- POD#3

- OR- ECMO explant
- Vascular complication- bleeding- massive transfusion → TRALI

Case

- TRALI- hemodynamic instability- lack of peripheral access
- Central VA ECMO (chest open 3rd time)
- ECMO weaned POD #2- explantation (chest opened 4th time, closed with plates, advancement flaps)

- 1 week later- mediastinitis
Case

- Multiple debridements - alive doing well
- Wound healed with VAC

Future

- Clear definition of PCS
- Preoperative consideration/ planning for MCS in high risk cases
- Early initiation of MCS for PCS
Summary

- PCS happens and mortality is high
- Patients are high risk preoperatively
- MCS often initiated late
- Early MCS improves survival

Minneapolis Heart Institute

- 1200 open heart cases
- 70+ VA ECMOs
- 40+ LVADs
- 20 heart transplants per year
- Heartmate II, Heartmate 3, HVAD
## Results

### Fukuhara et al. GTCS 2016

#### Table 1. Representative studies describing postcardiomyotomy cardiogenic shock and mechanical circulatory support device therapy

<table>
<thead>
<tr>
<th>References</th>
<th>No. of patients</th>
<th>Incidence of PCS (%)</th>
<th>Initial MCS</th>
<th>Duration of support</th>
<th>Survival to hospital discharge</th>
<th>Mid-term outcomes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balabani et al. [59]</td>
<td>322</td>
<td>11.4%</td>
<td>IABP</td>
<td>N/A</td>
<td>52%</td>
<td>N/A</td>
<td>Only patients who were unable to wean off CPR. No delayed PCS included</td>
</tr>
<tr>
<td>Amla et al. [54]</td>
<td>344</td>
<td>5.9%</td>
<td>IABP</td>
<td>Survivors: 80 ± 78 h</td>
<td>42% (3 mo)</td>
<td>40% (1 y)</td>
<td>Preoperative IABP (15%) included in the analysis</td>
</tr>
<tr>
<td>Magwood and Simpson [110]</td>
<td>34</td>
<td>7</td>
<td>VA-ECMO</td>
<td>97 ± 74</td>
<td>N/A</td>
<td>N/A</td>
<td>High incidence of intraoperative ischemia (48%)</td>
</tr>
<tr>
<td>Wang et al. [53]</td>
<td>18</td>
<td>3</td>
<td>VA-ECMO</td>
<td>7-496 h</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Musial et al. [50]</td>
<td>23</td>
<td>6.3%</td>
<td>VA-ECMO</td>
<td>0.5-144 h</td>
<td>50%</td>
<td>N/A</td>
<td>High rate of bleeding (52%), IABP ischemia, and renal failure</td>
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<tr>
<td>Grayson et al. [64]</td>
<td>31</td>
<td>NA</td>
<td>ABEMED</td>
<td>8.7 ± 9.4 h</td>
<td>29%</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Köte et al. [57]</td>
<td>55</td>
<td>NA</td>
<td>ABEMED</td>
<td>5.7 ± 6.9 h</td>
<td>49%</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Hoy et al. [50]</td>
<td>60</td>
<td>0.5</td>
<td>BioMedics centrifugal</td>
<td>1-19 days</td>
<td>44%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Fukuhara et al GTCS 2016**

#### Table 2. Evaluation of LVAD support outcomes

<table>
<thead>
<tr>
<th>References</th>
<th>No. of patients</th>
<th>Device used</th>
<th>Malfunction (%)</th>
<th>Survival to hospital discharge</th>
<th>Mid-term outcomes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pinna et al. [46]</td>
<td>11</td>
<td>Thoratec HeartMate</td>
<td>0.5</td>
<td>N/A</td>
<td>55%</td>
<td>46% (1 y)</td>
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<tr>
<td>Peng et al. [59]</td>
<td>173</td>
<td>N/A</td>
<td>Short-term VADs</td>
<td>N/A</td>
<td>41%</td>
<td>N/A</td>
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<tr>
<td>Hou et al. [49]</td>
<td>53</td>
<td>2.9</td>
<td>VA-ECMO</td>
<td>7.5 ± 6.7 h</td>
<td>33%</td>
<td>N/A</td>
</tr>
<tr>
<td>Elshahawy et al. [81]</td>
<td>233</td>
<td>0.6</td>
<td>VA-ECMO</td>
<td>N/A</td>
<td>36%</td>
<td>N/A</td>
</tr>
<tr>
<td>Wu et al. [62]</td>
<td>110</td>
<td>2.6</td>
<td>VA-ECMO</td>
<td>143.3 ± 111.1 h</td>
<td>42%</td>
<td>N/A</td>
</tr>
<tr>
<td>Rutter et al. [47]</td>
<td>517</td>
<td>1.3</td>
<td>CentriMag</td>
<td>3.3 ± 2.9 h</td>
<td>25%</td>
<td>N/A</td>
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<tr>
<td>Akay et al. [55]</td>
<td>22</td>
<td>N/A</td>
<td>Centrimag</td>
<td>5 days</td>
<td>97%</td>
<td>N/A</td>
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<tr>
<td>Goff et al. [13]</td>
<td>16</td>
<td>N/A</td>
<td>Impella 5.0</td>
<td>3.7 ± 2.9 h</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Lofforte et al. [59]</td>
<td>47</td>
<td>1.5</td>
<td>VA-ECMO</td>
<td>9.8 ± 8.6 h</td>
<td>92%</td>
<td>N/A</td>
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<td>Lerman et al. [17]</td>
<td>32</td>
<td>N/A</td>
<td>Impella 5.0</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Takeyama et al. [10]</td>
<td>37</td>
<td>N/A</td>
<td>Centrimag</td>
<td>14 days</td>
<td>32</td>
<td>N/A</td>
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<tr>
<td>Fletcher et al. [5]</td>
<td>80</td>
<td>N/A</td>
<td>VA-ECMO</td>
<td>7 ± 6</td>
<td>34%</td>
<td>N/A</td>
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</tbody>
</table>
Percutaneous VAD

- Impella- microaxial
  1. 2.5
  2. CP
  3. RP
  4. 5.0- requires cutdown
  5. LD- ascending aorta
Percutaneous/ External VAD

Conversion rate (percutaneous to open) at ANW – 4/10 (inadequate flows)