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Contemporary LVADs – From Device to Outcome

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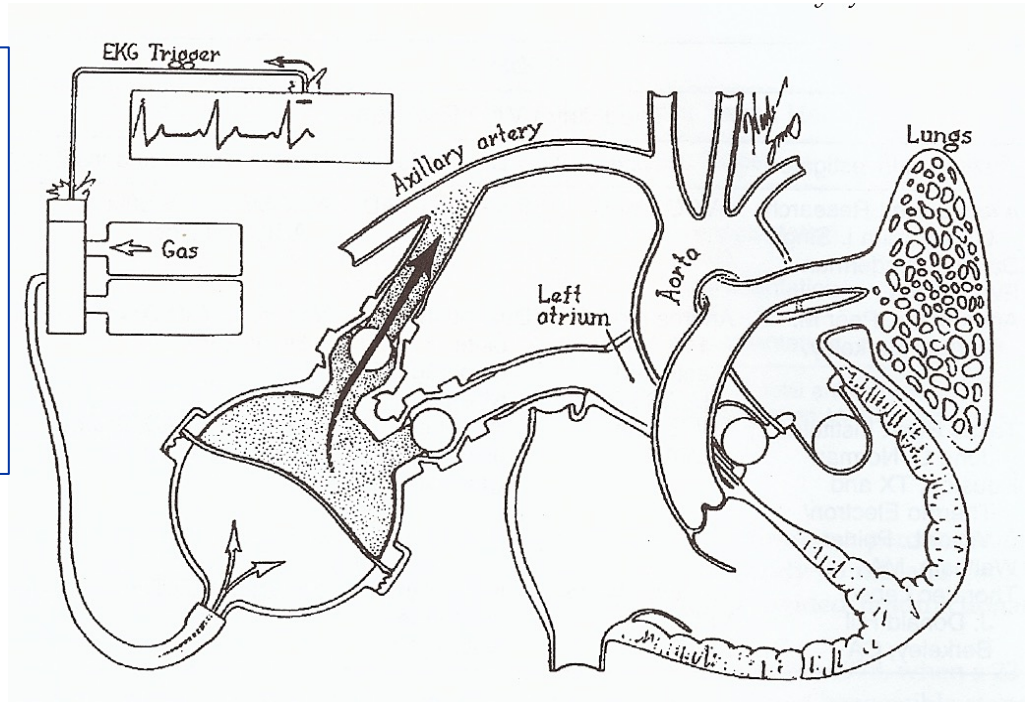
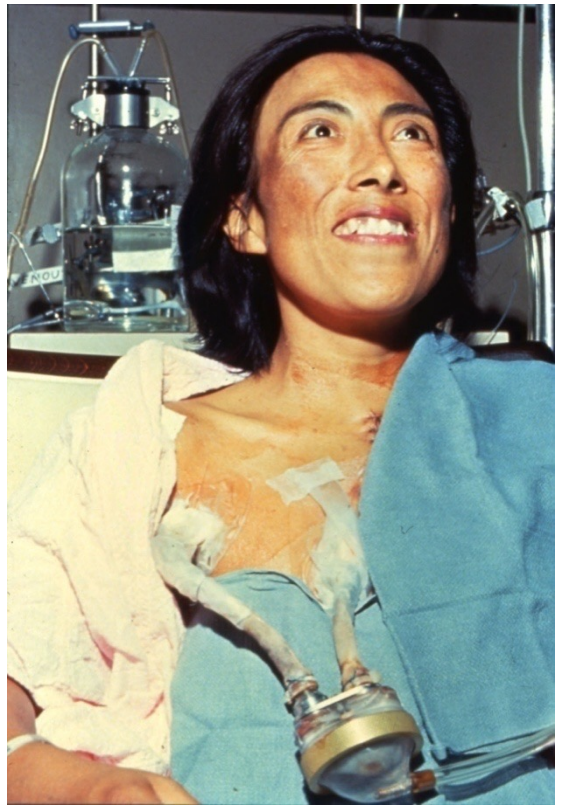
FIRST SUCCESSFUL LVAD

1966 – Dr. Debakey
37 y/o, post-cardiotomy failure
Implant of Paracorporeal, pneumatically operated LVAD
Bridge-to-recovery





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DEVICES – COMMERCIALLY APPROVED

1st Generation Device

HM VE/XVE

Volume Displaced

Vented & Electric actuation

Approved for BTT & DT

1st Generation Device

PVAD

Right/Left/BiV Support

Electric & Pneumatic

Approved for BTT indication

1st Generation Device

Novacor

Electric

Approved for BTT indication, not approved DT

2nd Generation Device

HM II

Axial Flow

Approved for BTT and DT

3rd Generation Device

HVAD

Centrifugal Flow

Hydrodynamic /Magnetic Technology

Was approved for BTT & DT

3rd Generation Device

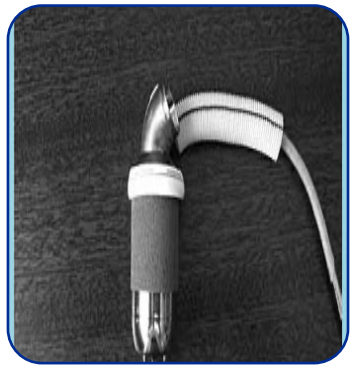
HM3

Centrifugal Flow

Full Mag-Lev Technology

Approved for BTT & DT

DEVICES - INVESTIGATIONAL



2nd Generation Device

Jarvik 2000

Axial Flow

Clinical trial ongoing

2nd Generation Device

HeartAssist 5 (Reliant Heart)

Axial Flow

Clinical trial terminated

3rd Generation Device

VentrAssist (Ventracor)

Centrifugal

Hydrodynamic /Mag Technology

Did not get commercial approval

3rd Generation Device

DuraHeart (Terumo)

Centrifugal

Full Mag/Lev Technology

Clinical trial terminated

3rd Generation Device

Levacor (WorldHeart)

Centrifugal

Full Mag/Lev Technology

Clinical trial terminated

3rd Generation Device

EvaHeart 2

Centrifugal

Hydraulically Levitated Technology

Tipless Inflow

Clinical trial ongoing

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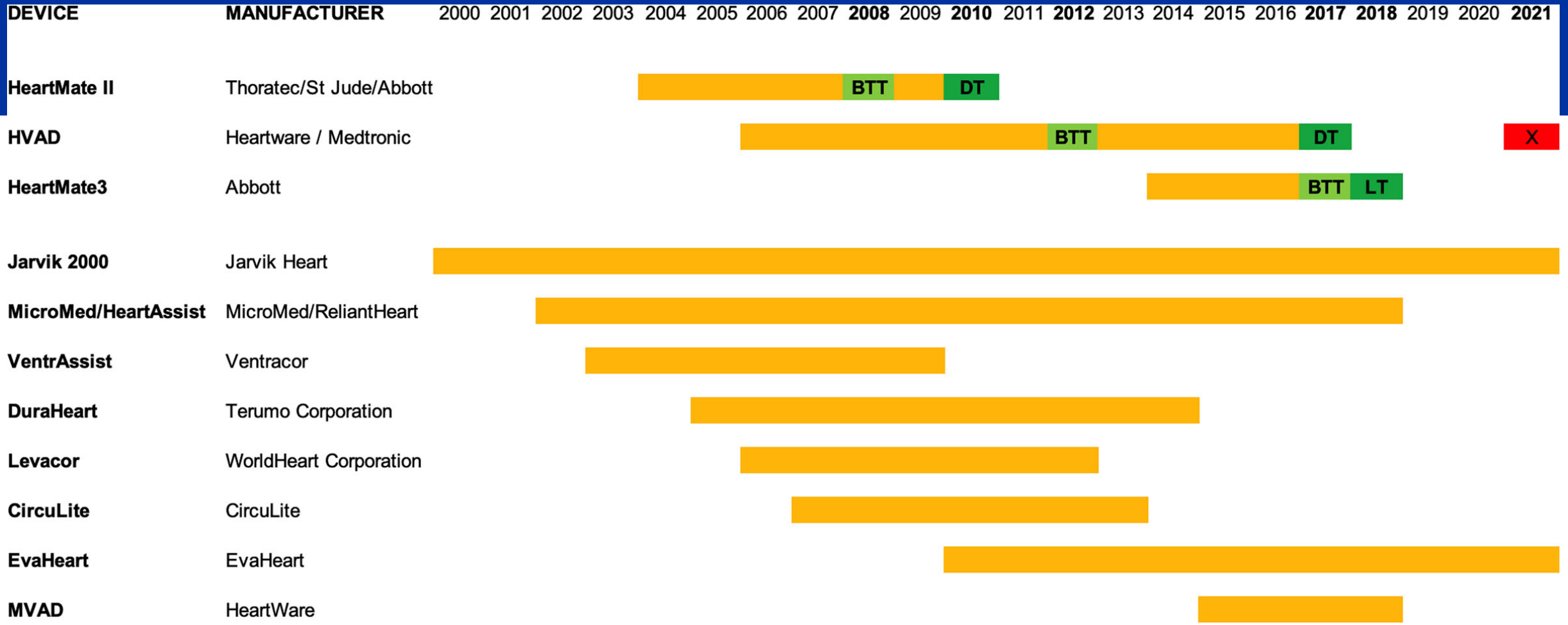

Josef Stehlik. Circulation. The Long and Winding Road to an Effective Left Ventricular Assist Device: The Demise of Medtronic's HVAD, Volume: 144, Issue: 7, Pages: 509-511, DOI: (10.1161/CIRCULATIONAHA.121.056027)

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LANDMARK TRIALS

REMATCH (2001): Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure

HM XVE (n68) vs OMT (n61)

Randomized; non-eligible for transplantation

1 year survival (p .002)

52% LVAD

25% OMT

2 year survival (p .09)

23% LVAD

8% OMT

INTrEPID: Investigation of Non-transplant Eligible Patients who are Inotrope Dependent

Novacor LVAD (n37) vs OMT (n18)

Non-randomized

6 month survival (p .03)

46% LVAD

22% OMT

1 year survival (p .02)

23% LVAD

11% OMT

HeartMate II (2007): Non-randomized, implant in high priority listed pts

HeartMate II (n133)

6 month safety and efficacy

75% enrolled achieved outcome at 6 months:

Transplant, explant or stable on support

Survival with LVAD:

89% 1 month

75% 6 months

68% 12 months

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LANDMARK TRIALS

HeartMate II (2009): Randomized, multicenter; implant in non-transplant eligible pts

HeartMate II (n134) vs HeartMate XVE (n66) 2:1 Randomization

Survival free from Stroke or reoperation at 2 years: (p .0001)

46% HMII

11% HM XVE

1 & 2 year survival:

68% & 58% HM II

55% & 24% HM XVE

ROADMAP (2015): Risk Assessment & Comparative Effectiveness of Left Ventricular Assist Device & Medical Management in Ambulatory Heart Failure Patients

HeartMate II (n97) vs OMT (n103)

Non-randomized, observational

Included ambulatory, non-inotrope dependent pts

Survival & improved 6MWD at 12 months based on as treated therapy:

80% HMII

65% OMT

ROADMAP 2: Evaluation of 2 year results in original ROADMAP population

Survival & improved 6MWD at 2 years based on as treated therapy:

70% HMII

41% OMT

In pts with delayed LVAD implant:

No deaths at 30 days

90% survival at 1 year

No sig disadvantage to delayed implant

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LANDMARK TRIALS

ADVANCE Trial (2012): comparison of HeartWare LVAD (HVAD) vs. pts supported on FDA approved devices as derived from INTERMACS

HVAD (n140) vs. Control (n499)

Survival at 6 months on original device, transplant or explant:

90.7% HVAD

90.1% Control device

Survival 30, 60, 180 & 360 days:

HVAD: 99%, 96%, 94%, 86%

Control: 97%, 95%, 90%, 85%

ADVANCE Continued Access Protocol (CAP) (2013): Additional 193 pts enrolled, implanted with HVAD

Survival at 60 days:

97%

Survival at 6 months:

91%

Survival at 1 year:

84%

26.4% of pts originally enrolled in ADVANCE trial remained on support > 2 years

ENDURANCE (2017): HeartWare Ventricular Assist System as Destination Therapy of Advanced Heart Failure

HVAD (n297) vs. HMII (n148) 2:1 randomization, non-transplant eligible pts

Survival at 2 years free from stroke (p .0103):

HVAD 55%

HMII 57.4%

Stroke rate (ischemic & hemorrhagic) higher in HVAD vs HMII

29.7 % vs 12.1%

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LANDMARK TRIALS

ENDURANCE Supplemental Trial (2018): assessed impact of BP management on stroke rates in pts receiving HVAD

HVAD (n308) vs. HMII (n157); 2:1 randomization

BP goals standardized for HVAD

Neurologic injury (primary end-point):

HVAD 14.7%

HMII 12.1%

Neurologic event profile was improved with comparison of original ENDURANCE pts vs. those enrolled in supplemental trial, reduction of 50.5%

HeartMate 3 CE Mark Clinical Trial Investigation (2015):

HM 3 (n50)

Outcome/end-point compared with HMII historical data from INTERMACS

Survival 30 & 60 days:

98% & 92%

2 year follow-up:

Survival 6 months, 1&2 years:

92%, 81%, 74%

MOMENTUM 3 (2019): Multicenter Study of MagLev Technology in Patients undergoing MCS with HM3

HM3 (n515) vs. HMII (n505) 1:1 randomized, pts enrolled met indications for either BTT or DT

Survival at 2 years, free of stroke or re-operation for device malfunction ($p < .0001$):

HM3 76.9%/73.2%

HMII 63.7%58.7%

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SECONDARY OUTCOMES

- Improvement in QOL and NYHA class
  - LVAD vs OMT groups
- Incidence of pump replacement due to malfunction/failure/thrombosis
  - HMII(16.2%) vs HVAD (8.8%) – ENDURANCE
  - HMII (11.3%) vs HM3 (2.3%) – MOMENTUM 3
- Incidence of pump thrombosis
  - HMII (14%) vs HM3 (1%) – MOMENTUM 3
- 2011-2014: Increased incidence of Pump thrombosis in HMII
  - 2.2% to 8.4% in 180 period (Starling, et. al. 2014)
  - Resulted on PRE VENT trial

CONSIDERATIONS

- Clinical trial outcomes reflective of outcomes in patients in clinical practice?
  - Patients implanted post-device approval meet clinical trial characteristics – would your patient be excluded?
  - What are the implications for your patients?
- Should clinical trial inclusion/exclusion criteria change to be more reflective of those patients in clinical practices?


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Thank you!

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