Disclosures

- No disclosures to report

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Update on MOMENTUM 3 Trial: The Final Word?

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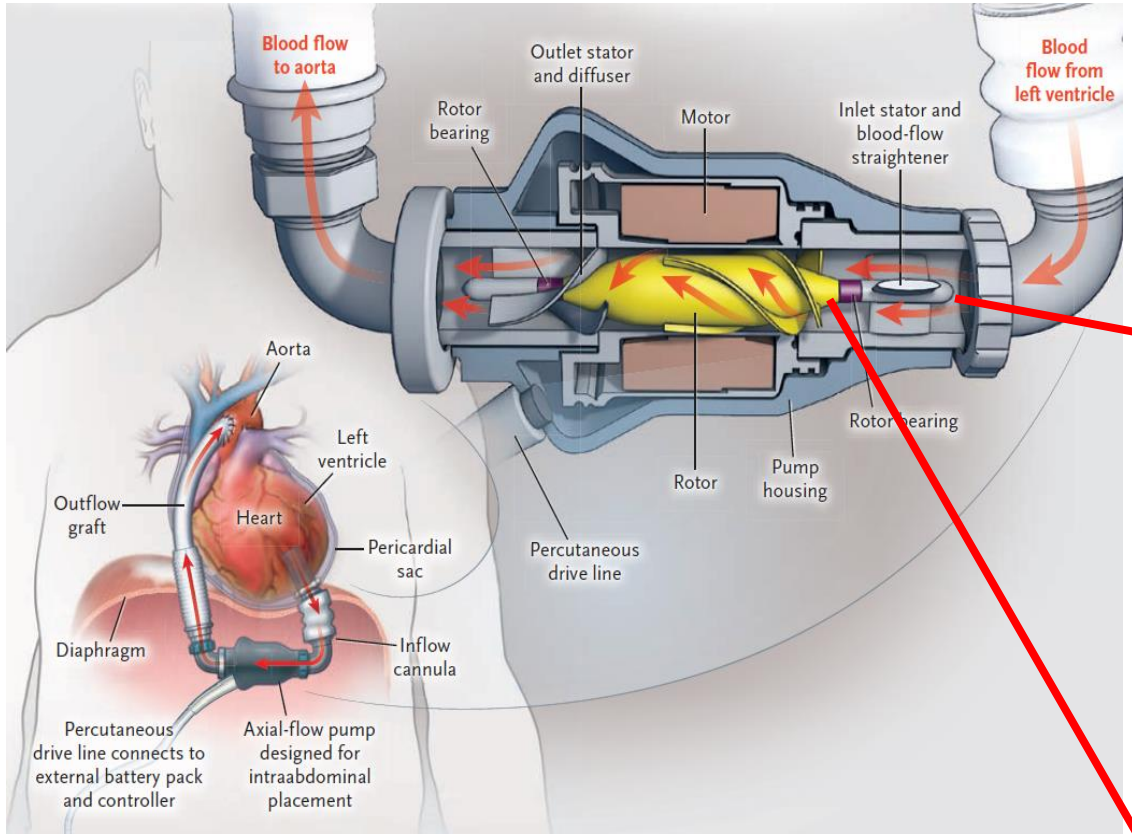
LVAD Therapy

- LVAD demonstrated to have significant survival and quality of life benefits
- Now exceeds heart transplantation in number of procedures
- Further adoption into less ill patients is limited by significant adverse events related to device hemocompatibility
  - Stroke
  - Device thrombosis
  - Bleeding

HeartMate II Pump Design

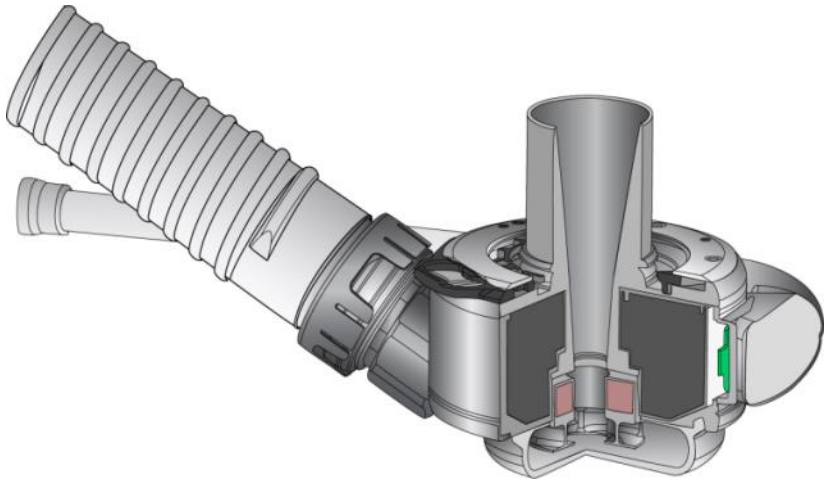


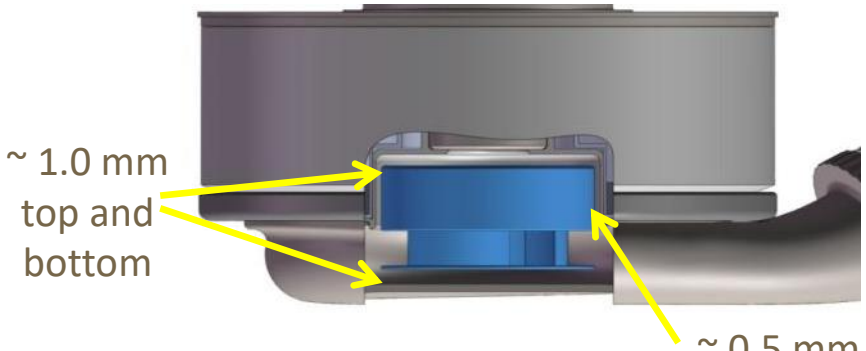
- Mechanical pivot design
- Associated with pump thrombosis
- Small gaps – high shear stresses and blood trauma

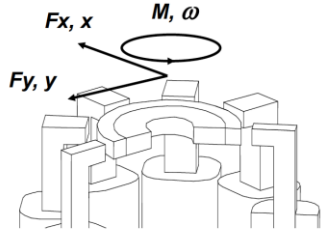
HeartMate III: Full MagLev Technology

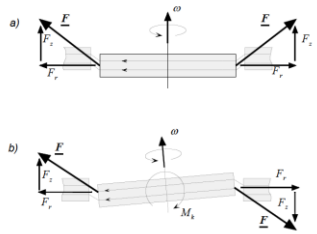
Key Design Benefits: Optimized Geometry

- HeartMate III secondary flow paths are ~0.5 mm along the side, and ~1.0 mm pump above and below the rotor.
- HeartMate III pump surfaces are flat and flow is undisturbed.



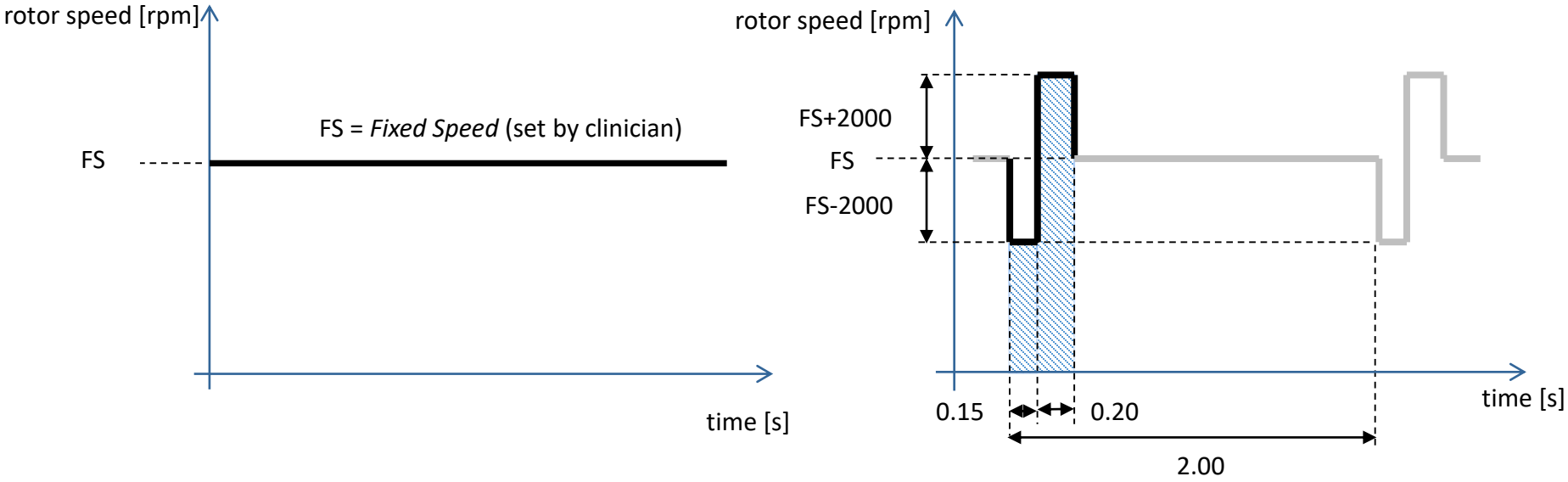






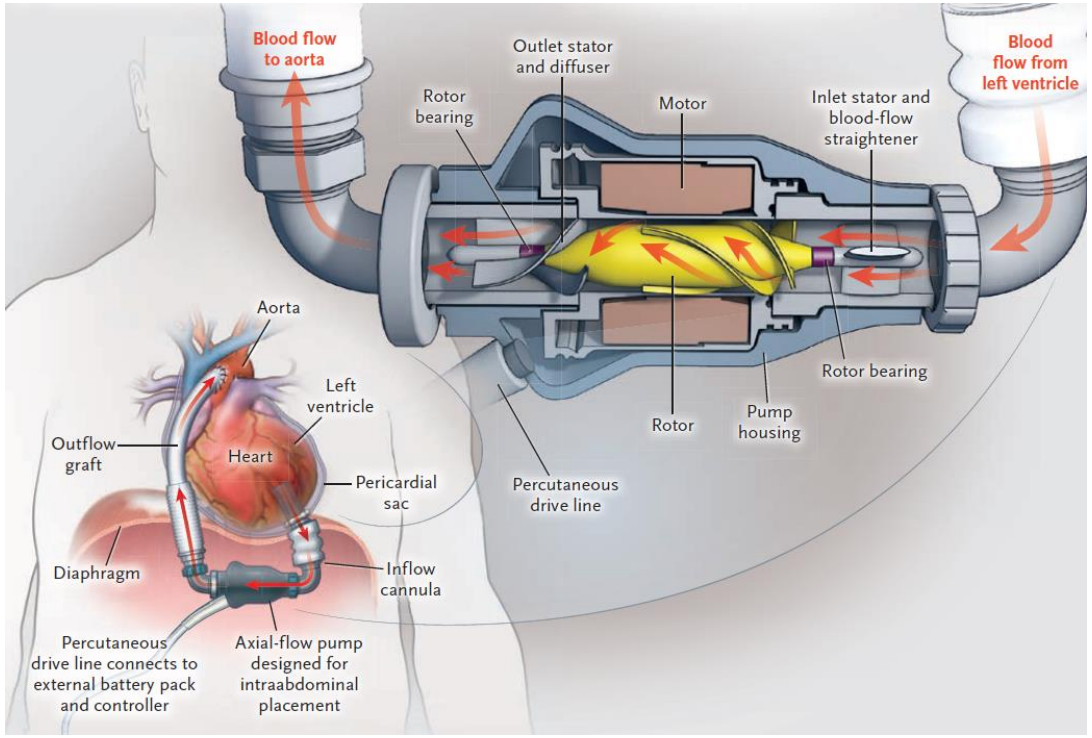
Artificial Pulse

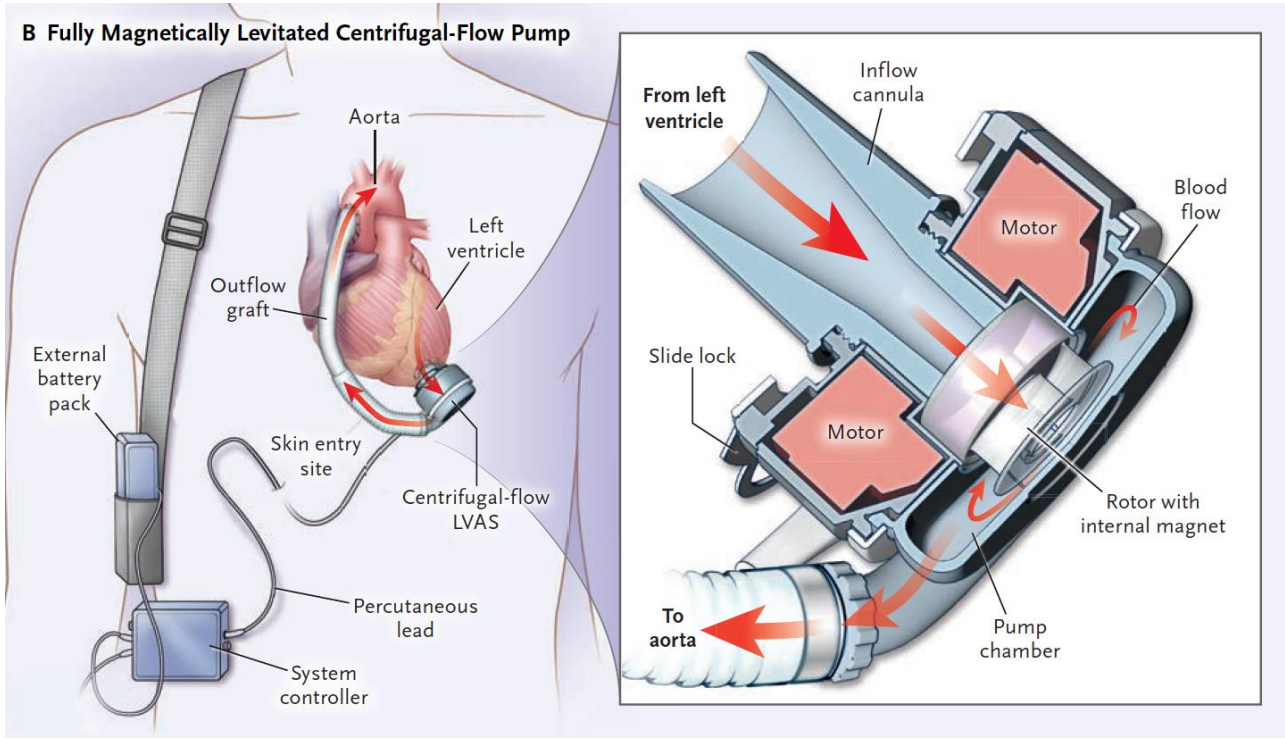
- Functions to promoting better washing of blood pump and prevent areas of statsis
- While unproven, augmenting the pulsatility that is generally diminished in rotary pump patients may have benefit for some patients or in certain circumstances, perhaps in part addressing adverse events such as; aortic insufficiency, bleeding and thrombogenesis



MOMENTUM 3

HeartMate II versus HeartMate 3

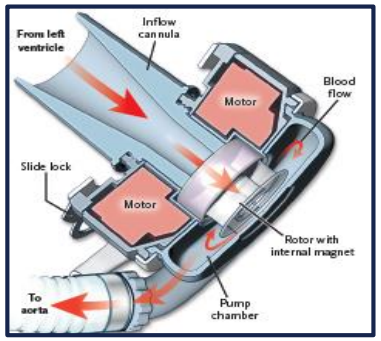




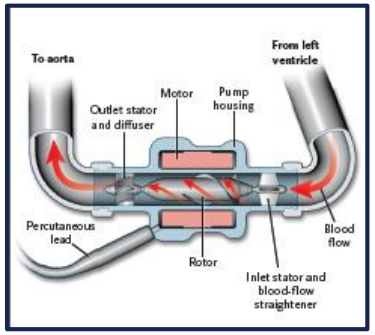
Mehra MR, et al; for the MOMENTUM 3 investigators. *N Engl J Med*. 2018.

MOMENTUM Long Term Cohort 2-Year Followup

HeartMate 3



HeartMate II



Patient meets MOMENTUM 3 eligibility criteria?

Randomization 1:1

Short Term (ST) Cohort[1]
N=294
6-month follow-up

Additional 72 patients enrolled

Long Term (LT) Cohort
N=366
2-year follow-up

Full Cohort
N=1028
2-year follow-up

Intent-to-Treat (ITT) Population
N=366

HeartMate 3 Pump
N=190

HeartMate II Pump
N=176

Withdrawn before implant
N = 4
No LVAD implant: 1
Withdrawal of consent: 1
Transplant: 1
Implanted with non-study LVAD: 1

Withdrawn before implant
N = 1
Death: 1

Per Protocol Population
N=361

Implanted with HeartMate 3
N=189

Implanted with HeartMate II
N=172

[1]Mehra et al. A Fully Magnetically Levitated Circulatory Pump for Advanced Heart Failure. *N Engl J Med* 2017;376(5):440-50.

Study Aim and Primary Endpoint

Study Aim

- The long-term (2-year) study is designed to ascertain success to optimally support patients who wait for extended periods for heart transplantation or are ineligible for heart transplantation (e.g., destination therapy)

Primary Endpoint

- Survival at 2 years free of disabling stroke (>3 modified Rankin Score) or reoperation to replace or remove a malfunctioning device

Mehra MR, et al; for the MOMENTUM 3 investigators. *N Engl J Med*. 2018.

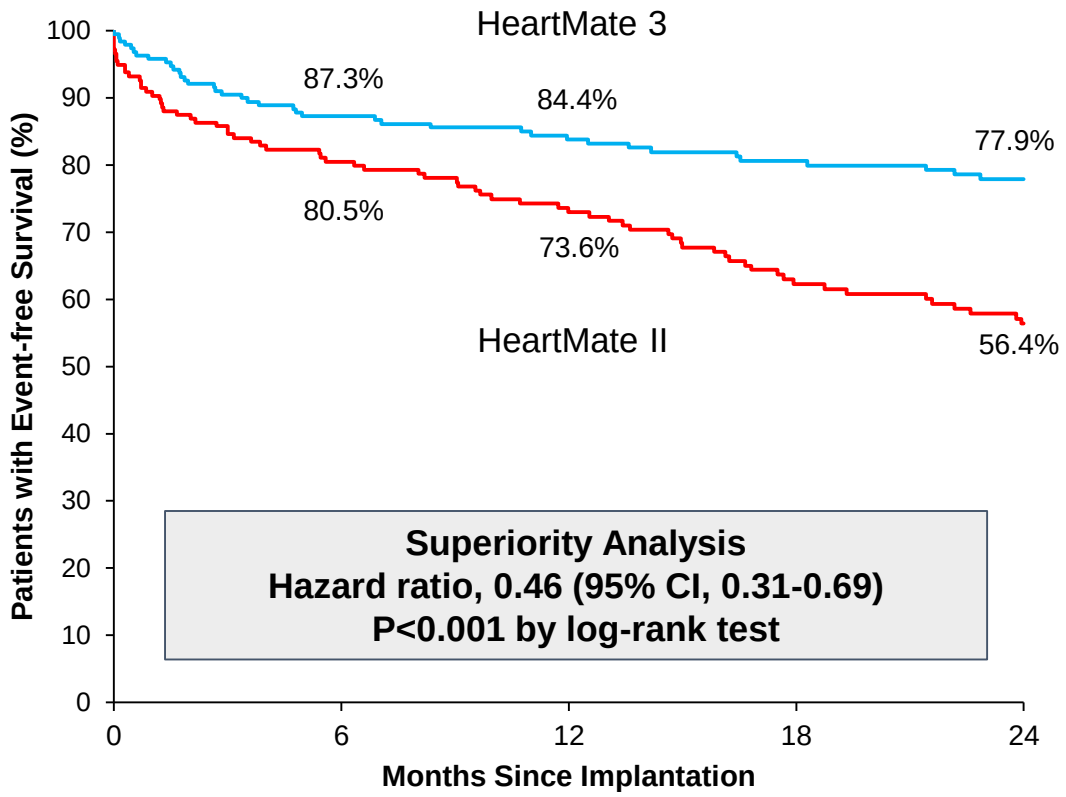
MOMENTUM 3 Baseline Characteristics

Characteristic	HeartMate 3 (n=190)	HeartMate II (n=176)
Age - years		
Mean	61 ± 12	59 ± 12
Median (range)	65 (19-81)	61 (24-84)
Male sex - no. (%)	150 (78.9)	143 (81.2)
Race or ethnic group - no. (%)		
White	127 (66.8)	131 (74.4)
Black or African American	52 (27.4)	32 (18.2)
Other*	11 (5.8)	13 (7.4)
Body surface area - m^2	2.1 ± 0.3	2.1 ± 0.3
Ischemic cause of heart failure - no. (%)	80 (42.1)	88 (50.0)
History of atrial fibrillation - no. (%)	81 (42.6)	83 (47.2)
History of stroke - no. (%)	16 (8.4)	20 (11.4)
Previous cardiac surgical procedure - no. (%)		
Coronary-artery bypass	44 (23.2)	41 (23.3)
History of valve replacement or repair	18 (9.5)	7 (4.0)
Concomitant medication or intervention - no (%)		
Intravenous inotropic agents	167 (87.9)	152 (86.4)
Diuretic	166 (87.4)	165 (93.8)
ACE inhibitor or Angiotensin II-receptor antagonist	58 (30.5)	66 (37.5)
Beta-blocker	111 (58.4)	98 (55.7)
CRT/CRT-D	75 (39.5)	62 (35.2)
ICD/CRT-D	122 (64.2)	123 (69.9)
IABP	25 (13.2)	26 (14.8)

There were significant differences between groups for history of valve replacement or repair (P=0.04) and diuretic use (P=0.05).
*Includes Asian, Native Hawaiian or Pacific Islanders, and other. CRT(-D) denotes cardiac resynchronization therapy with or without defibrillator; ICD, implantable cardioverter-defibrillator; IABP, intraaortic balloon pump.

Primary End Point Analysis (ITT)

Survival at 2 years free of disabling stroke (>3 mRS) or reoperation to replace or remove a malfunctioning device

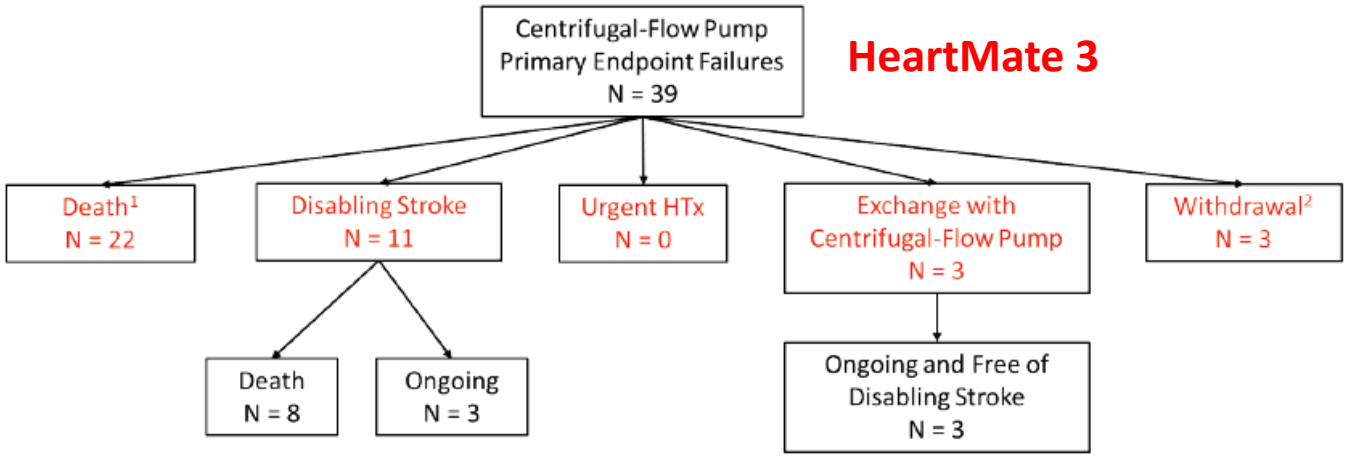


No. at Risk					
HeartMate 3	190	161	141	122	111
HeartMate II	176	134	114	90	75

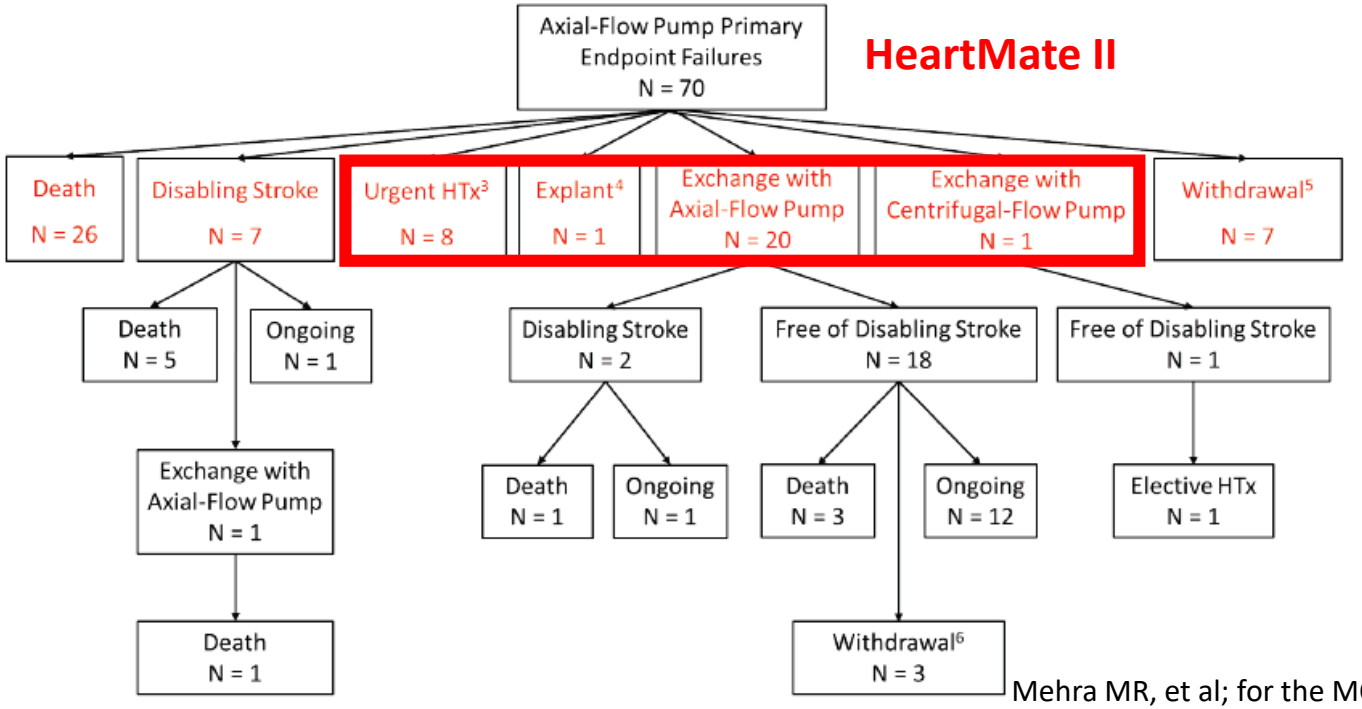
Mehra MR, et al; for the MOMENTUM 3 investigators. *N Engl J Med*. 2018.

mRS denotes modified Rankin Score; CI, confidence interval

Primary Endpoints



[1]Two subjects experienced disabling stroke but did not survive to 60 days post stroke for modified Rankin Score evaluation. [2]Includes withdrawal prior to implant (1), for noncompliance (1), and explant to total artificial heart (1).



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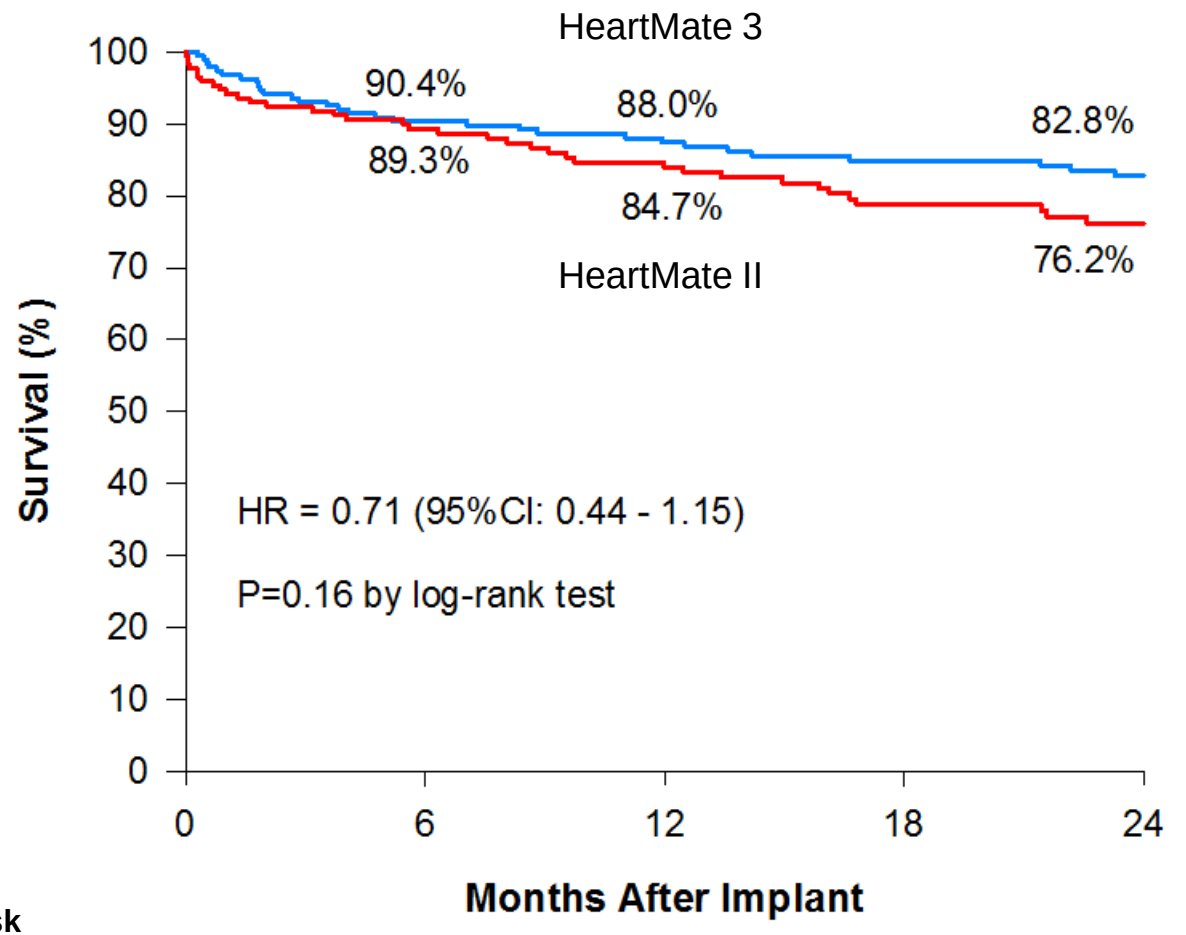
Primary Endpoint Component 1

Overall Survival



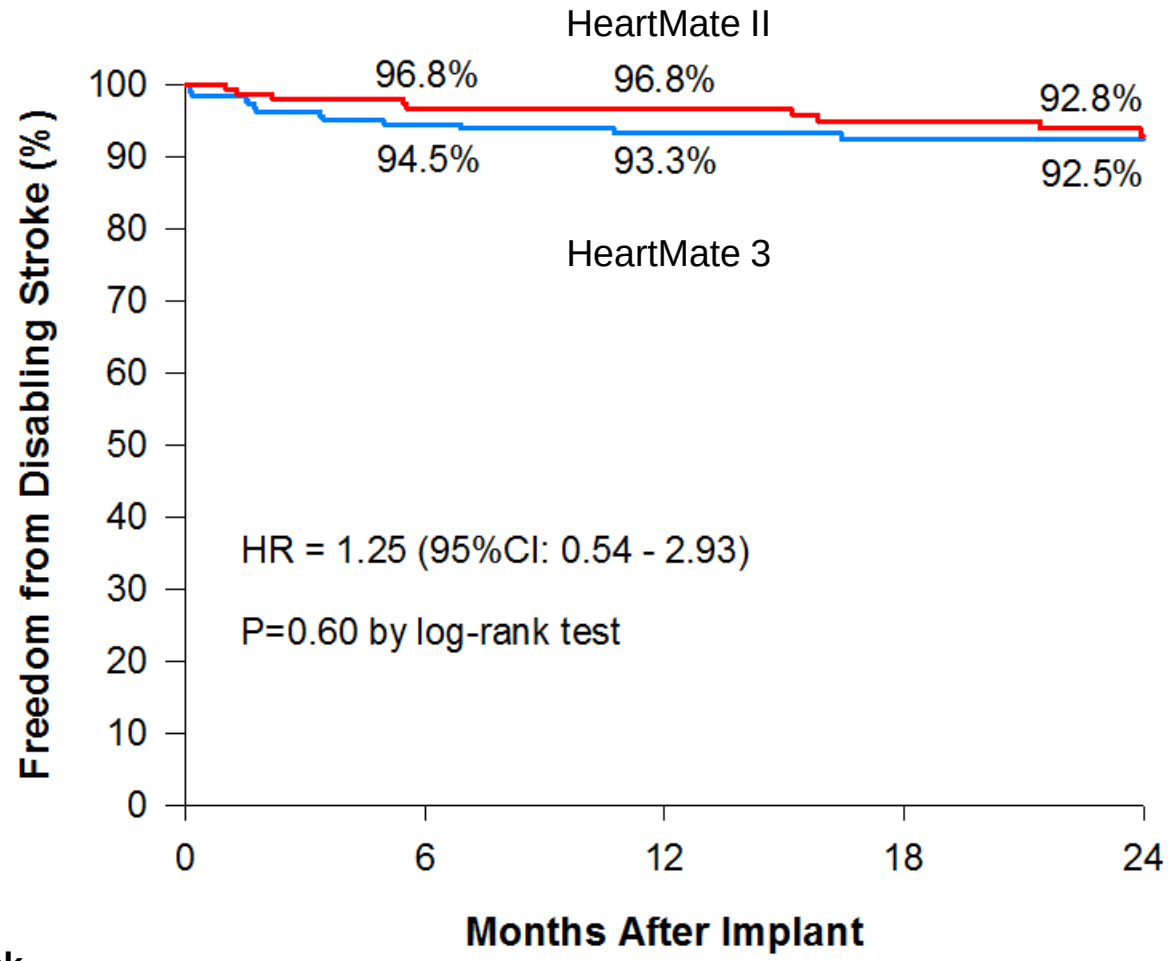
No. at Risk					
HeartMate 3	189	165	146	127	117
HeartMate II	172	141	121	98	86

HR denotes hazard ratio; CI, confidence interval

Mehra MR, et al; for the MOMENTUM 3 investigators. *N Engl J Med*. 2018.

Primary Endpoint Component 2

Freedom from Disabling Stroke (mRS > 3)



No. at Risk

HeartMate 3	189	162	142	123	114
HeartMate II	172	139	121	97	84

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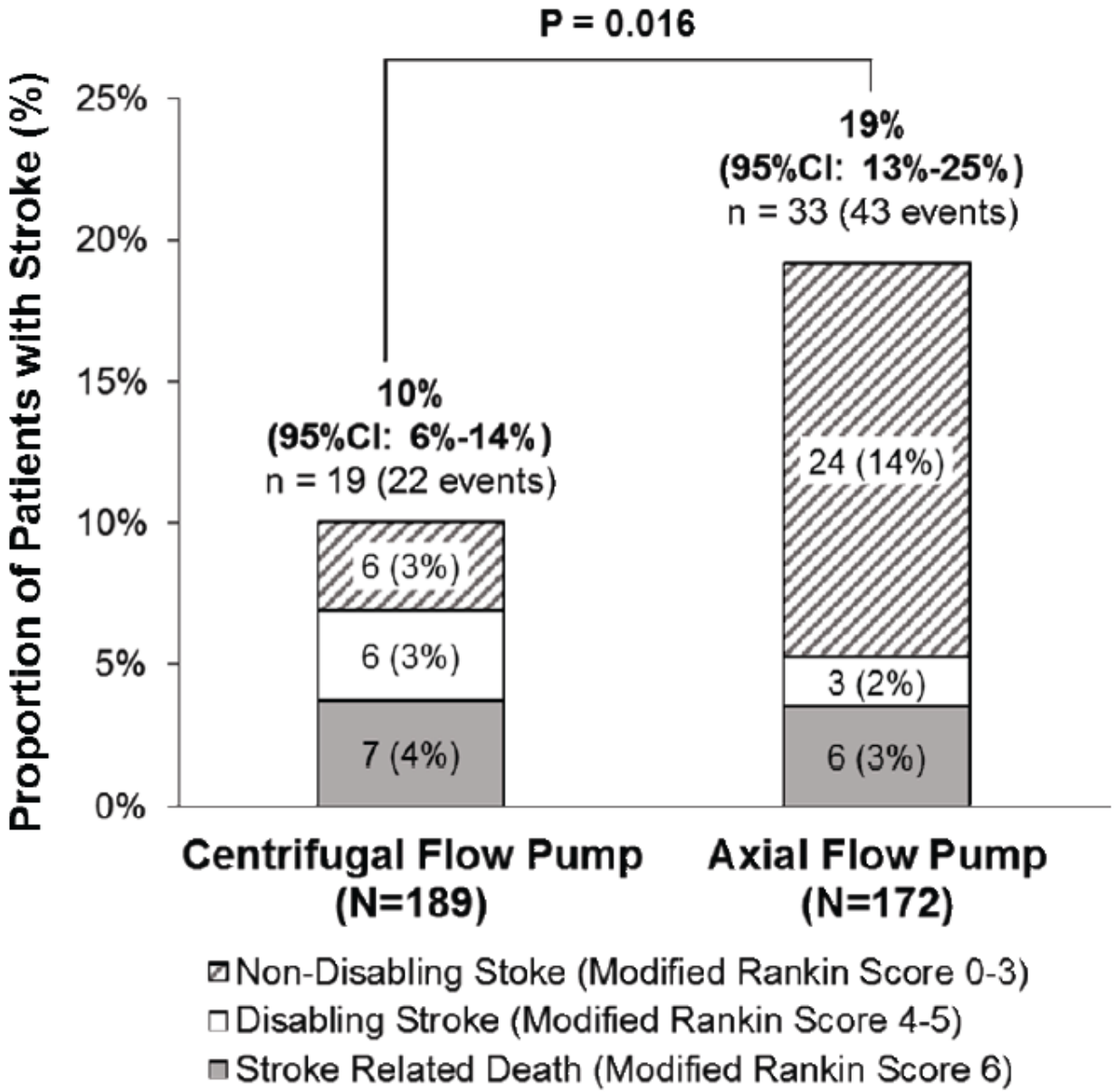
HR denotes hazard ratio; CI, confidence interval

All Stroke Events and Severity



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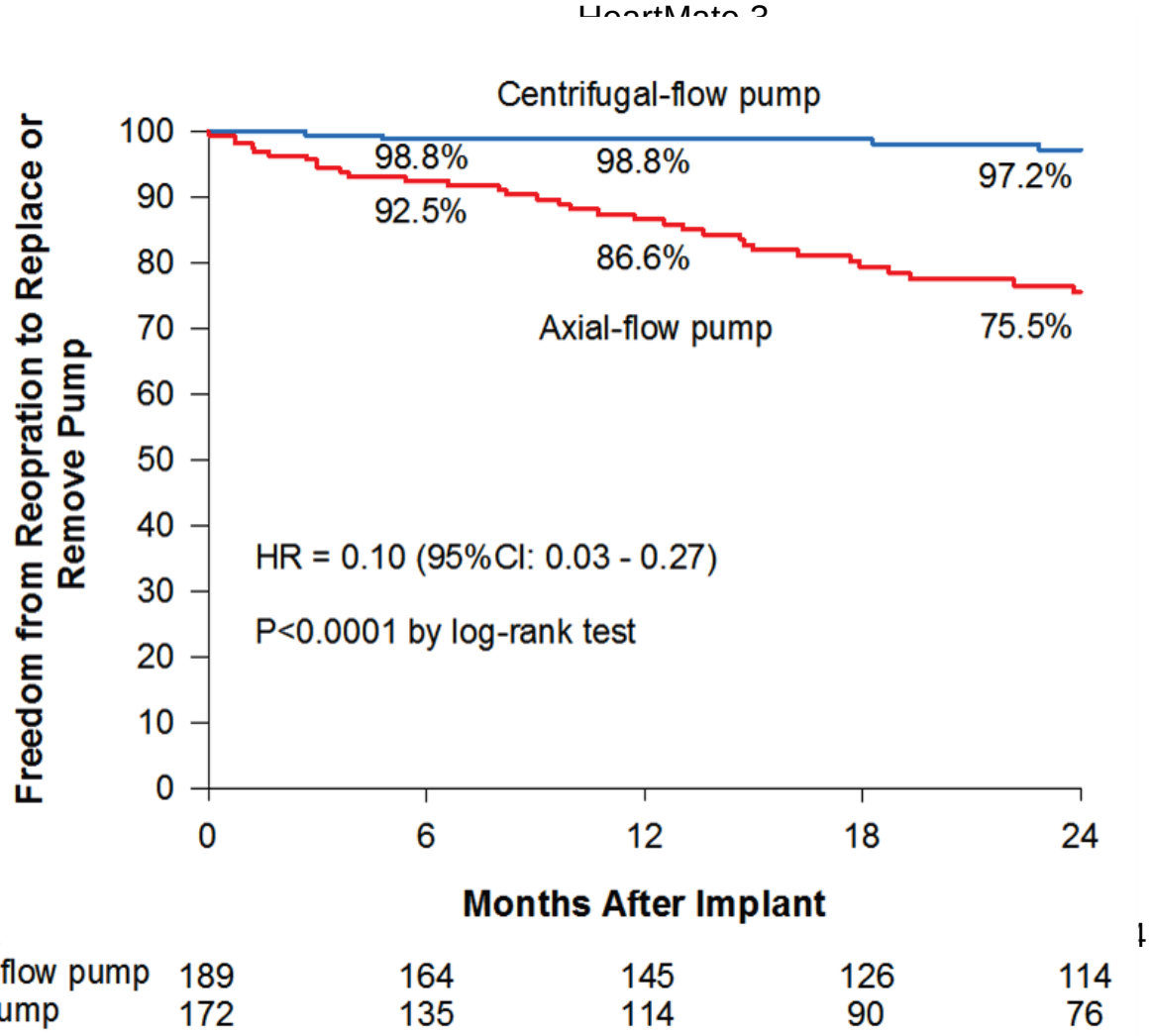
Primary Endpoint Component 3

Freedom from Reoperation to Replace or Remove Pump

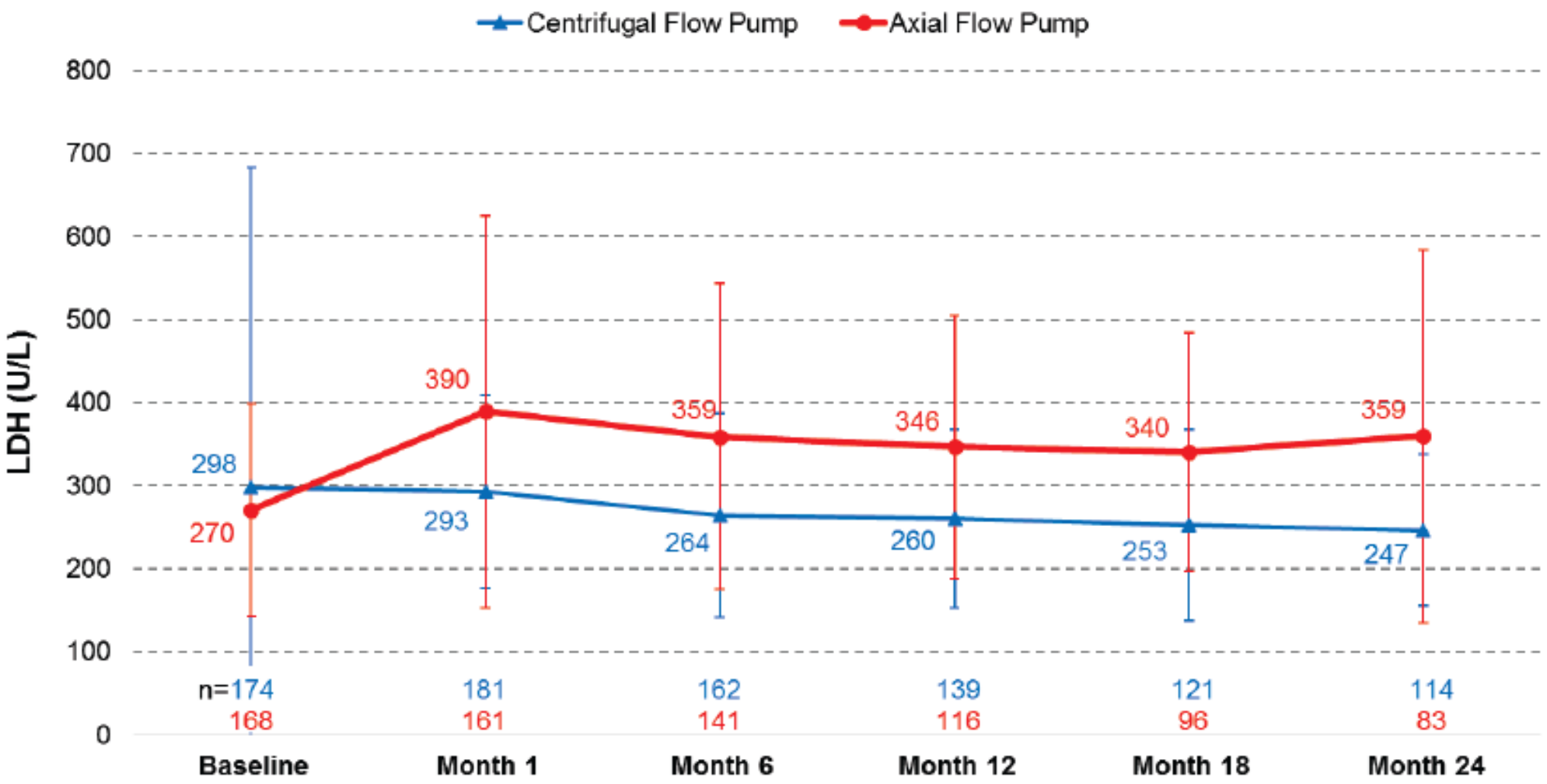


- There was a **ten-fold** difference in the reoperation rate between HeartMate II and HeartMate 3
- HeartMate 3 reoperations were due to infection (1), electrical fault (1), and outflow-graft twist (1)
- **2/3rd** of HeartMate II reoperations were due to “pump thrombosis or severe hemolysis”

Mehra MR, et al; for the MOMENTUM 3 investigators. *N Engl J Med*. 2018.

HR denotes hazard ratio, CI, confidence interval

Lactate Dehydrogenase (LDH) Levels over Time



Key Adverse Events

Pump Thrombosis, Neurological Events, Bleeding

	HeartMate 3 (n=189)		HeartMate II (n=172)			
	n (%)	no. of Events	n (%)	no. of Events	HR (95% CI)	P Value*
Suspected or confirmed pump thrombosis	2 (1.1)	2	27 (15.7)	33	0.06 (0.01-0.26)	<0.001
Resulting in reoperation	0 (0)	0	21 (12.2)	25	NA	<0.001
Any stroke	19 (10.1)	22	33 (19.2)	43	0.47 (0.27-0.84)	0.02
Ischemic stroke	12 (6.3)	14	23 (13.4)	26	0.44 (0.22-0.88)	0.03
Hemorrhagic stroke	8 (4.2)	8	16 (9.3)	17	0.42 (0.18-0.98)	0.06
Other neurologic event⁺	22 (11.6)	25	15 (8.7)	16	1.27 (0.66-2.45)	0.39
Bleeding	81 (42.9)	187	90 (52.3)	206	0.71 (0.53-0.96)	0.07
Bleeding that led to surgery	23 (12.2)	29	30 (17.4)	34	0.66 (0.38-1.13)	0.18
Gastrointestinal bleeding	51 (27.0)	107	47 (27.3)	100	0.92 (0.62-1.37)	1.00

Mehra MR, et al; for the MOMENTUM 3 investigators. *N Engl J Med*. 2018.

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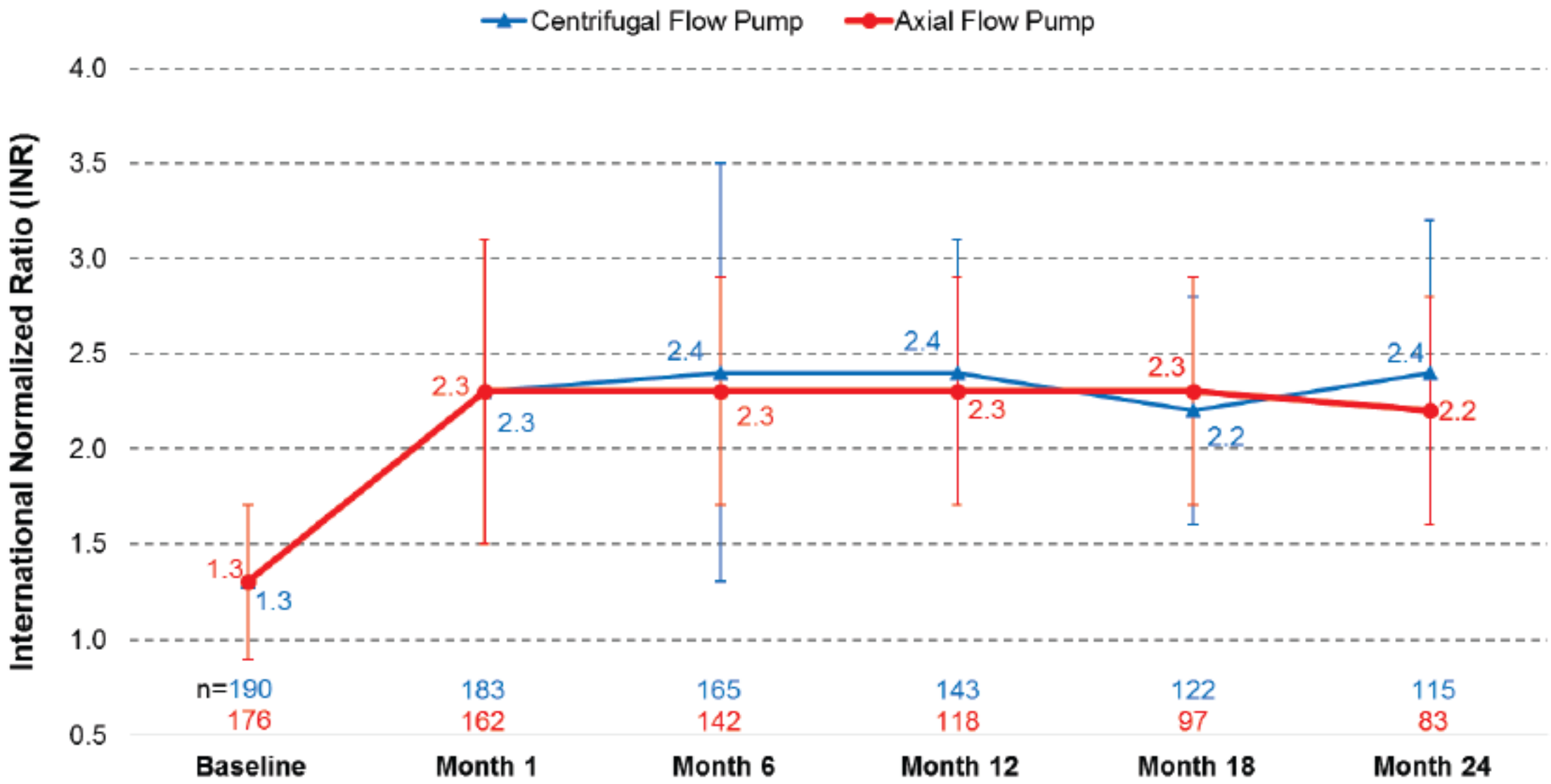
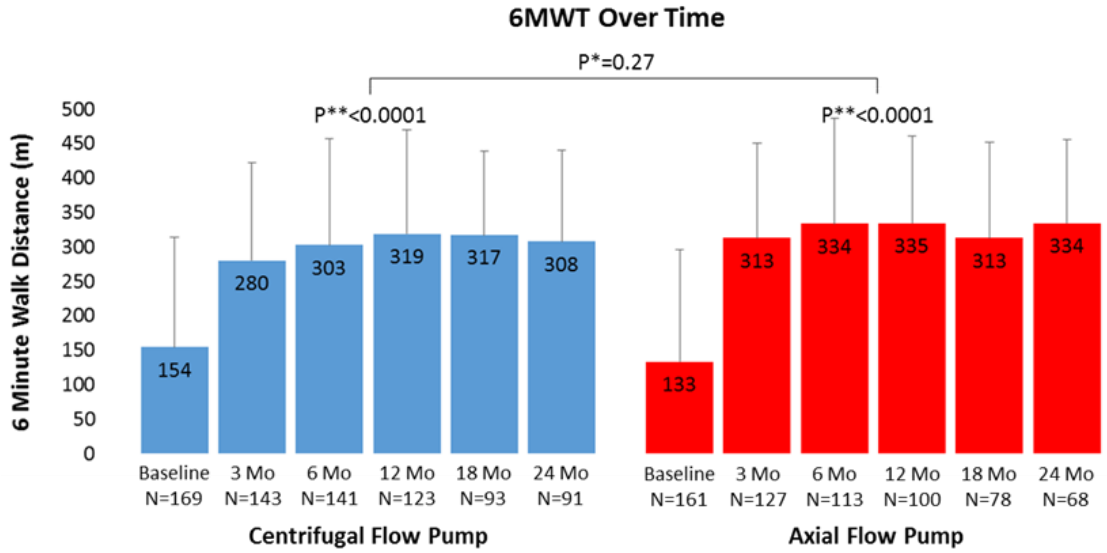
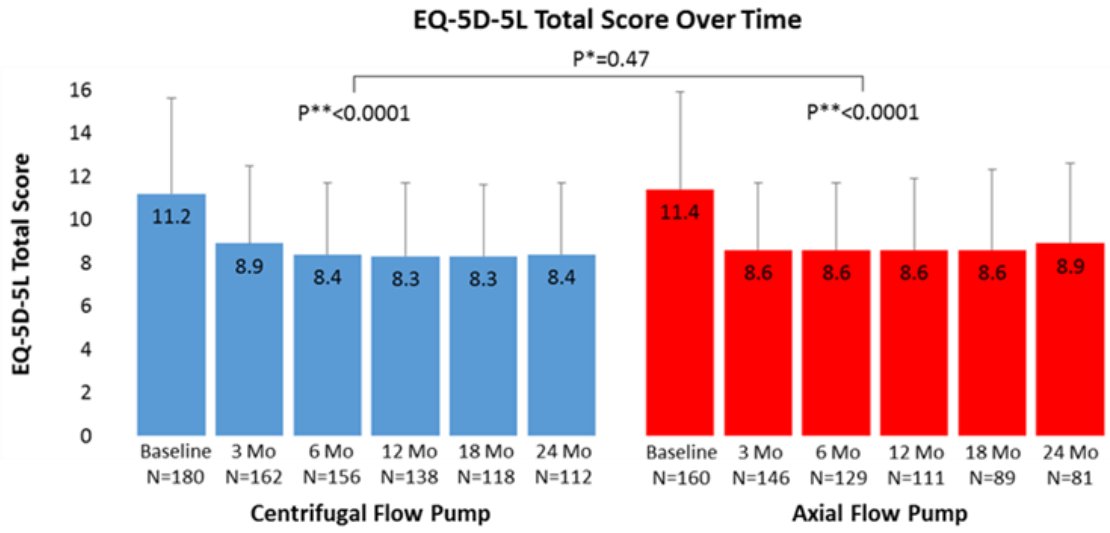
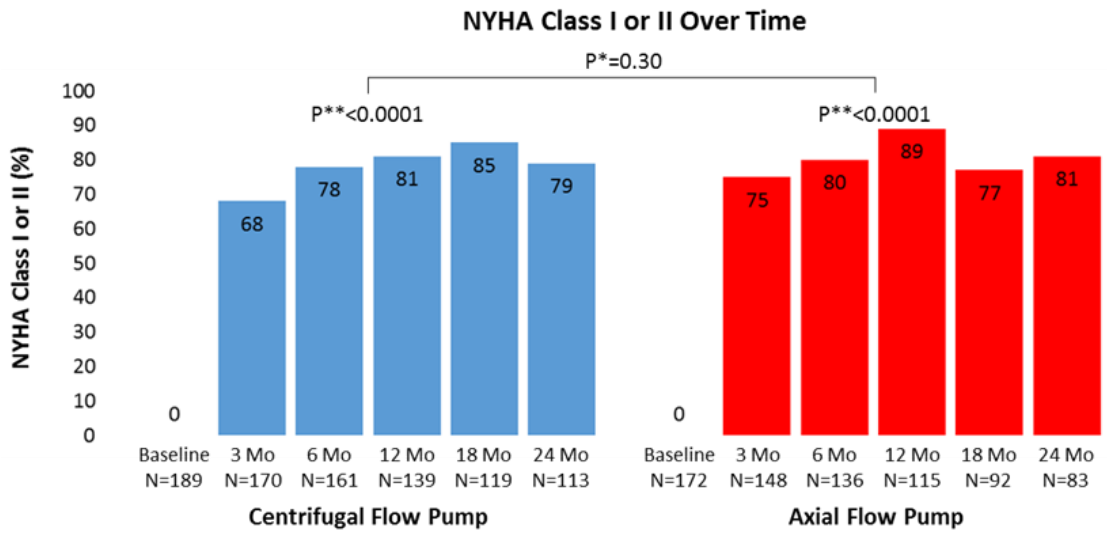
*P values were calculated with the use of Fisher's exact test. ⁺Includes transient ischemic attacks and neurologic events other than stroke

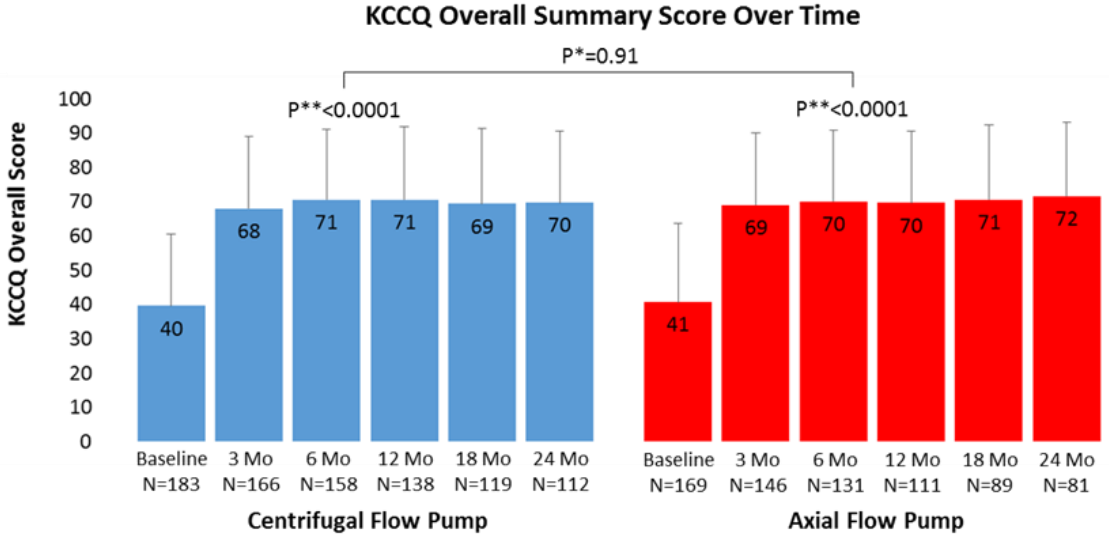

Centrifugal Flow Pump
Axial Flow Pump
International Normalized Ratio (INR)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.3
1.3
2.3
2.3
2.4
2.3
2.4
2.3
2.3
2.2
2.4
2.2
n=190
176
183
162
165
142
143
118
122
97
115
83
Baseline
Month 1
Month 6
Month 12
Month 18
Month 24

Functional Status and Quality of Life









*P-value between treatment arms over time

**P-value for treatment over time

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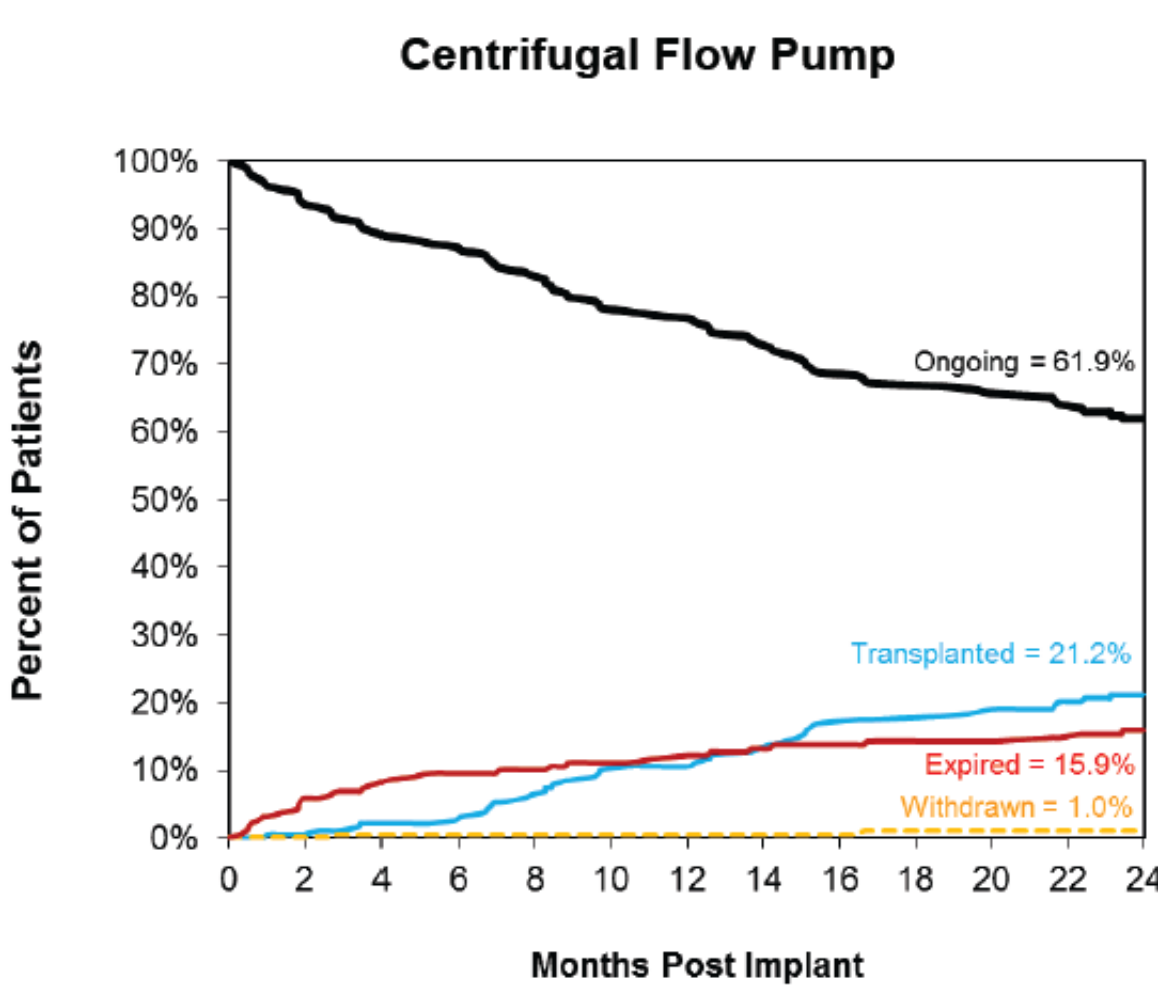
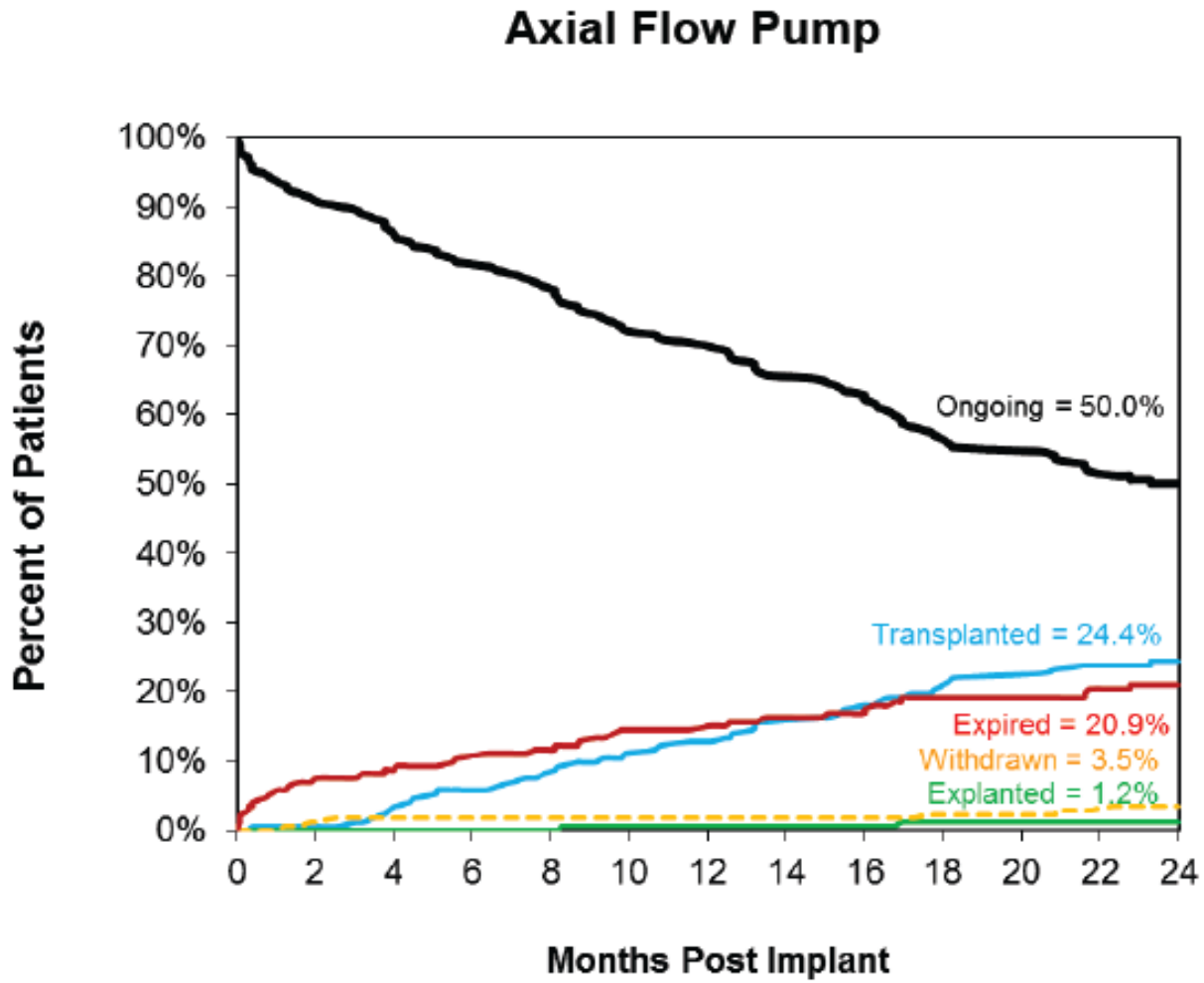
Competing Outcomes





Conclusions

- The HeartMate 3 LVAS is clinically superior when compared to the HeartMate II axial-flow pump, at 2-years
- These benefits were primarily driven by a lower reoperation rate in the HeartMate 3 arm
  - largely due to excess device malfunctions resulting from **pump thrombosis** in the HeartMate II LVAS
- A markedly lower rate of stroke was observed with the HeartMate 3 LVAS
- Same clinical benefit/ outcomes derived for patients identified as BTT, BTC, and DT

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