Quality of Life and Functional Capacity In the Multicenter Study of MAGLEV Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (MOMENTUM 3) Pivotal Trial

Jennifer A. Cowger, Yoshifumi Naka, Keith Aaronson, Douglas Horstmanshof, Sanjeev Gulati, Deborah Rinde-Hoffman, Sean Pinney, Sirtaz Adatya, David J. Farrar, Ulrich P. Jorde

on Behalf of the MOMENTUM 3 Investigators

MOMENTUM 3

#Drs. Mehra, Uriel, Goldstein, Cleveland served as Study Oversight Committee and contributed equally to the trial conduct and oversight

Relevant Financial Relationship Disclosure Statement

Jennifer Cowger, MD

discuss off label use and/or investigational use of the following drugs/devices: HeartMate 3 LVAD

tMate 3 is an investigation device not available for commercial use in the United States

following relevant financial relationships exist related to this presentation:

wger: Funding for research related travel (Abbott) & institutional research funds (Abbott, Medtronic); Y
: Consultant (Abbott); K Aaronson: None; D. Horstmanshoff: None; S. Gulati: Speaker's Bureau (Abbott,
tronic, Novartis); D. Rinde-Hoffman: None; S. Pinney: None; S. Adatya: None; D. Farrar: Employee of Abb
rde: Consultant (Abbott).

MOMENTUM

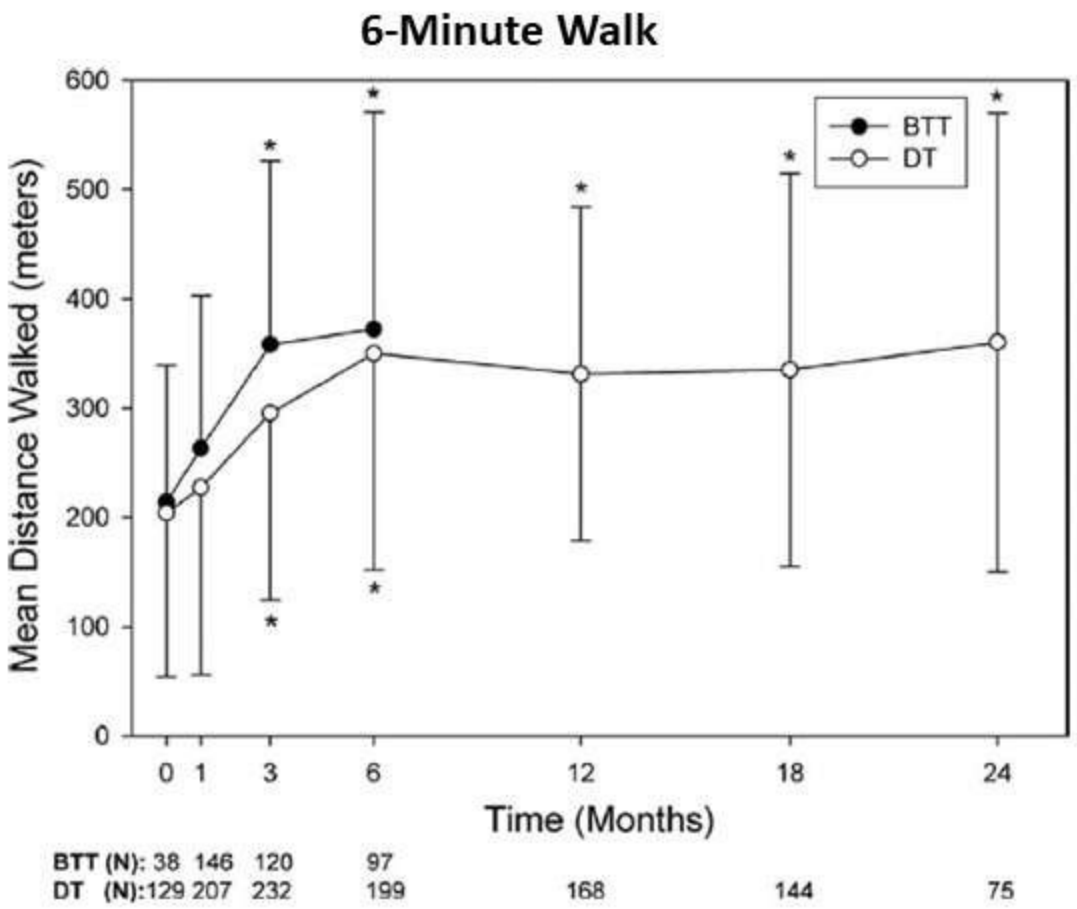
Introduction

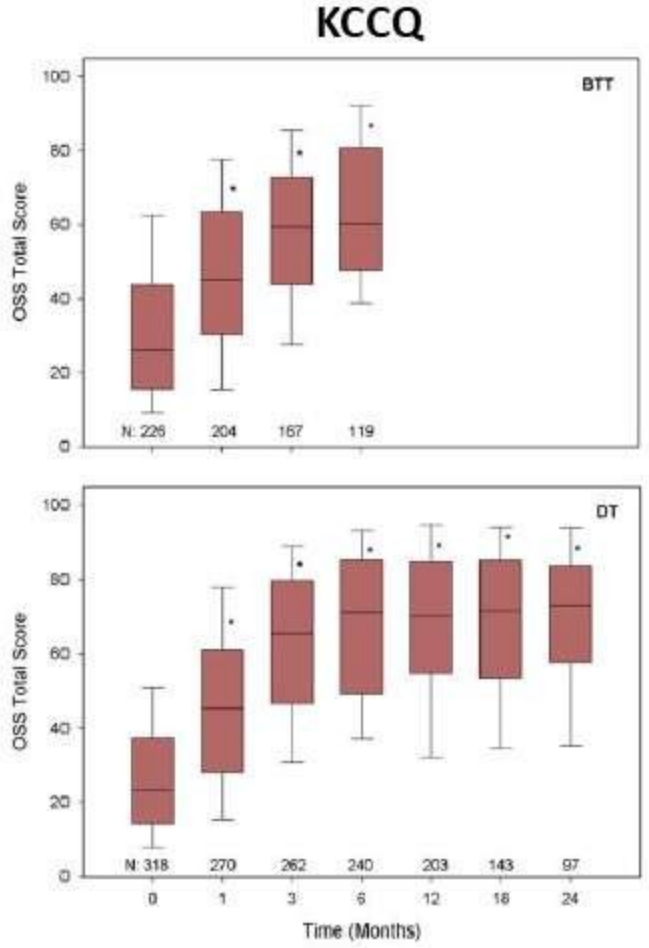
Clinical trials and registry studies have shown improvements in both **functional capacity (FC)** and **health related quality of life** (Hr-QOL) after LVAD

	Study Cohort	N	Measures
Rogers et al. J Am Coll Cardiol 2010; 55:1826	HMII BTT and DT	655	6MWT, NYHA, KCCQ, MLWHF
Grady et al JHLT 2014;33:412	INTERMACS	1559	EQ5D
Arnold et al Circ HF 2016;9:epub	INTERMACS	1638	KCCQ
Grady et al JHLT 2016;35:777-88.	INTERMACS	5640	EQ5D
Estep et al JACC 2015;66:1747	ROADMAP (LVAD and OMM)	200	6MWT, EQ5D

MOMENTUM

HMII BTT and DT Functional Capacity and Hr-QOL



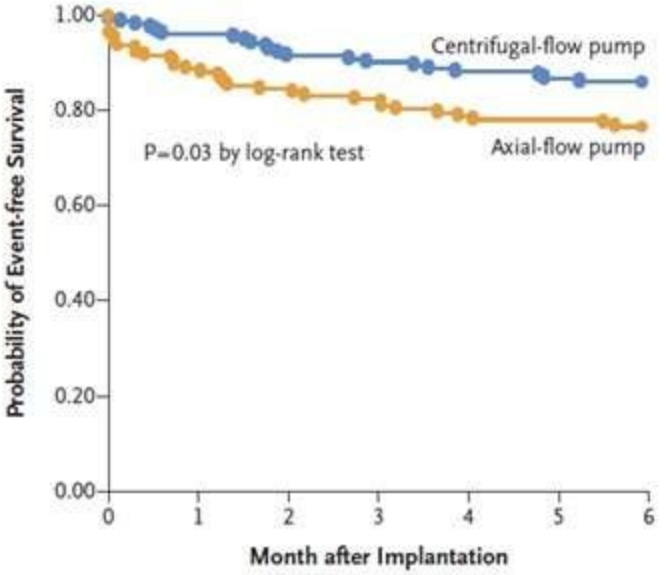


Rogers, J Am Coll Cardiol 2010;55:1826-34

MOMENTUM 3 Clinical Trial

mproved event-free survival at 6 months with the HeartMate 3 (HM3) vs. th
HeartMate II (HMII)[1]

Survival free of Stroke and Device Replacement



No. at Risk							
Centrifugal-flow pump	152	146	138	135	130	128	127
Axial-flow pump	142	125	119	116	110	106	103

a MR, et al. *N Engl J Med. 2017 Feb 2;376(5):440-450*

MOMENTUM

Primary Objectives

Quantify the change in Health-related Quality of Life (Hr-QOL) and Functional Capacity (FC) in both HM3 and HMII subjects

Assess the impact of serious adverse events on Hr-QOL and FC at 6 months

Determine factors contributing to patients "**Living Well on an LVAD"** at 6 months

MOMENTUM

Target Population

OMENTUM3 key inclusion criteria:

- Advanced systolic heart failure (LVEF ≤25%)
- Severe functional limitations (NYHA IIIB or IV) refractory to standard medical therapy

ey exclusion criteria:

- Planned biventricular support
- Irreversible end-organ dysfunction
- Active infection

l randomization to the HM3 or HMII LVAD

6 months of follow-up (short term cohort)

al. Clinical trial design and rationale of the multicenter study of MagLev technology in Patients undergoing mechanical support therapy with the HeartMate 3 (MOMENTUM 3) IDE clinical study protocol. *J Heart Lung Transplant.* 2016;35:528-36.

MOMENTUM

Quality of Life and Functional Capacity Metrics

re-specified Endpoints:

Health-related Quality of Life was assessed using standard nstruments:

- Kansas City Cardiomyopathy Questionnaire
- EuroQOL-5D

Functional Capacity assessed using:

- Six Minute Walk Distance (6MWD)
- New York Heart Association Functional Class

Data collected at baseline, 3 and 6 months

MOMENTUM

Quality of Life and Functional Capacity Metrics

re-specified Endpoints:

Health-related Quality of Life was assessed using standard nstruments:

- Kansas City Cardiomyopathy Questionnaire
- EuroQOL-5D

Functional Capacity assessed using:

- Six Minute Walk Distance (6MWD)
- New York Heart Association Functional Class

Data collected at baseline, 3 and 6 months

MOMENTUM

Quality of Life and Functional Capacity Metrics

re-specified Endpoints:

Health-related Quality of Life was assessed using standard
nstruments:

- Kansas City Card
- EuroQOL-5D

Functional Cap

- Six Minute Walk
- New York Heart Association Functional Class

Data collected at baseline, 3 and 6 months

At each follow-up:

- **Patients unable to complete 6MWT due to CHF symptoms = 0 meters**
- **Patients unable to complete 6MWT due to all other causes = excluded**

MOMENTUM

Study Endpoints

Endpoint 1: Hr-QOL and FC at 6 months in subjects supported with a HM3 vs. HMII LVAD

Endpoint 2: Hr-QOL and FC at 6 months in subjects with vs. without serious adverse events (SAE) at 3 months

- SAE: bleeding, stroke, pump thrombosis, right heart failure, major infection, or cardiac arrhythmias

Endpoint 3: "Living well on an LVAD" at 6 months

- defined as satisfactory Hr-QOL (KCCQ > 50) and FC (NYHA Class I/II *or* 6MWT >300 meters)

MOMENTUM

Data Analysis

Continuous variables are presented as mean ± standard deviation or media

[Q1,Q3]

- Linear Mixed-Effects Modeling was performed to assess changes in QOL and FC over time
- Takes into account paired patient data and is less sensitive to missing data

Categorical variables compared with Fisher's Exact Test

Correlates of "Living Well on an LVAD" assessed with Cox multivariable

regression (hazard ratio [95% CI])

MOMENTUM

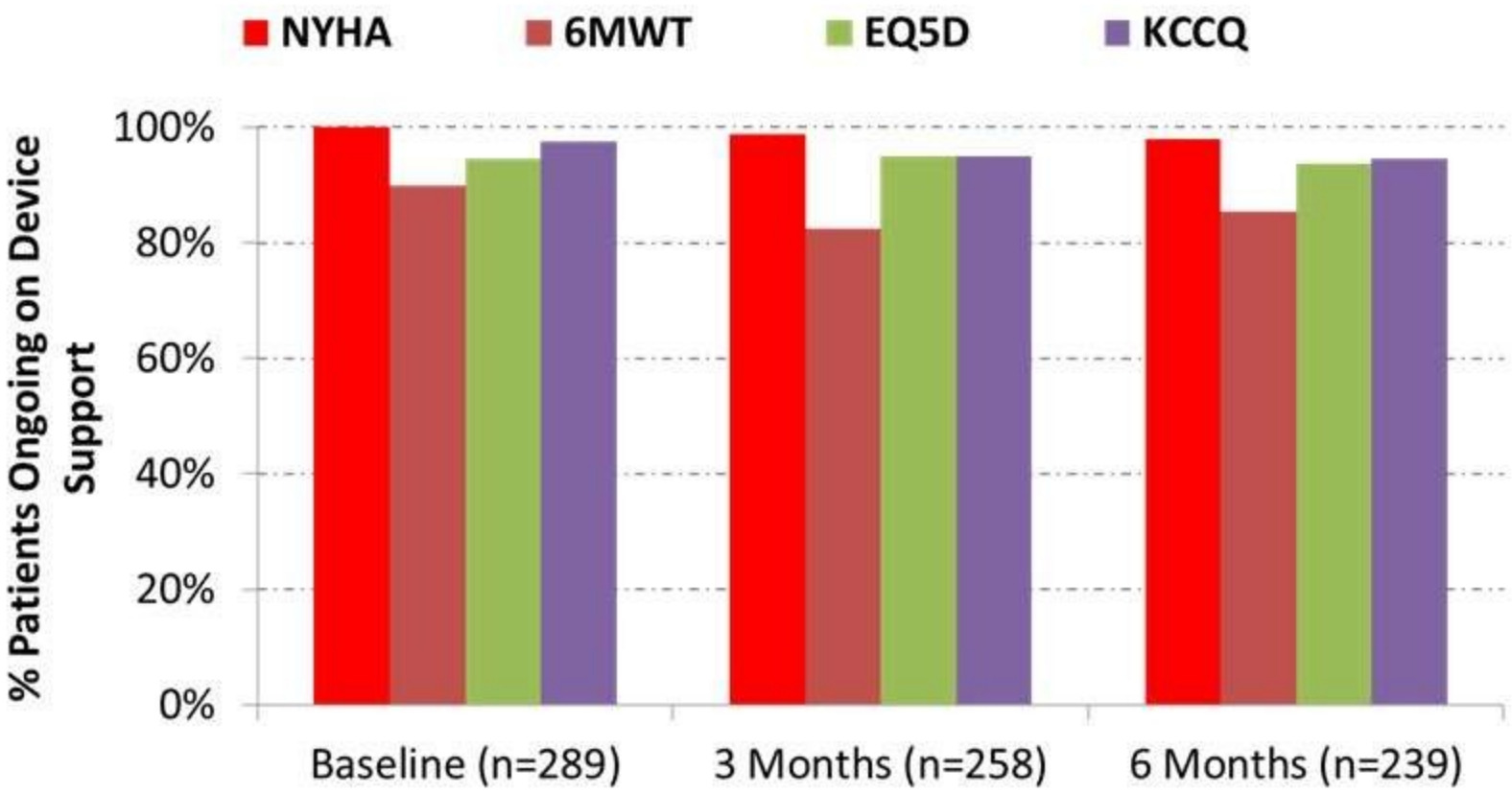
Results

MOMENTUM

Results: Baseline Characteristics (As-Treated)

Characteristic	HeartMate 3 (n=151)	HeartMate II (n=138)
Age - years		
Mean	60 ± 12	59 ± 12
Median (*range*)	64 (19 - 81)	61 (24 - 78)
Male sex - n(%)	120 (79%)	111 (80%)
Caucasian Race – n(%)	103 (68%)	105 (76%)
Body surface area - m^2	2.1 ± 0.3	2.1 ± 0.3
Ischemic cause of heart failure - n(%)	68 (45%)	68 (49%)
History of stroke - n(%)	12 (8%)	14 (10%)
INTERMACS Profile – n(%)		
1	1 (1%)	2 (1%)
2	50 (33%)	43 (31%)
3	76 (50%)	69 (50%)
4	22 (15%)	22 (16%)
5-7	2 (1%)	2 (1%)
Bridge to Transplant (BTT)- n(%)	40 (26%)	36 (26%)
Serum sodium - mmol/L	135.6 ± 3.9	135.0 ± 4.2
Serum creatinine - mg/ml	1.4 ± 0.4	1.4 ± 0.4

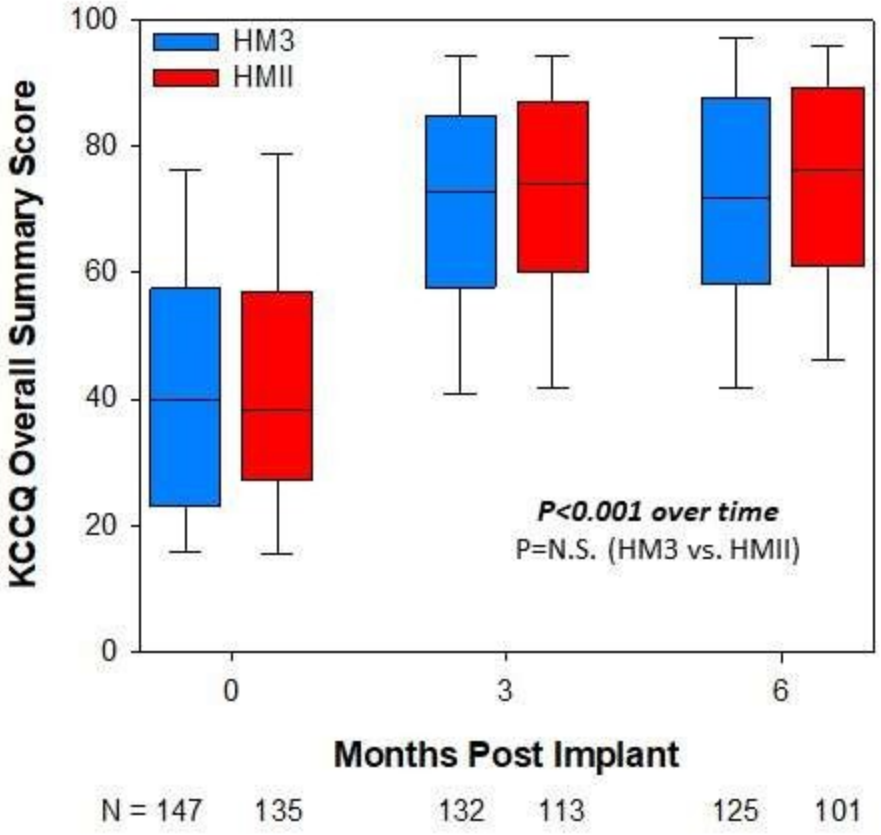
Percent of Available Patients Completing the Hr-QOL and FC tests



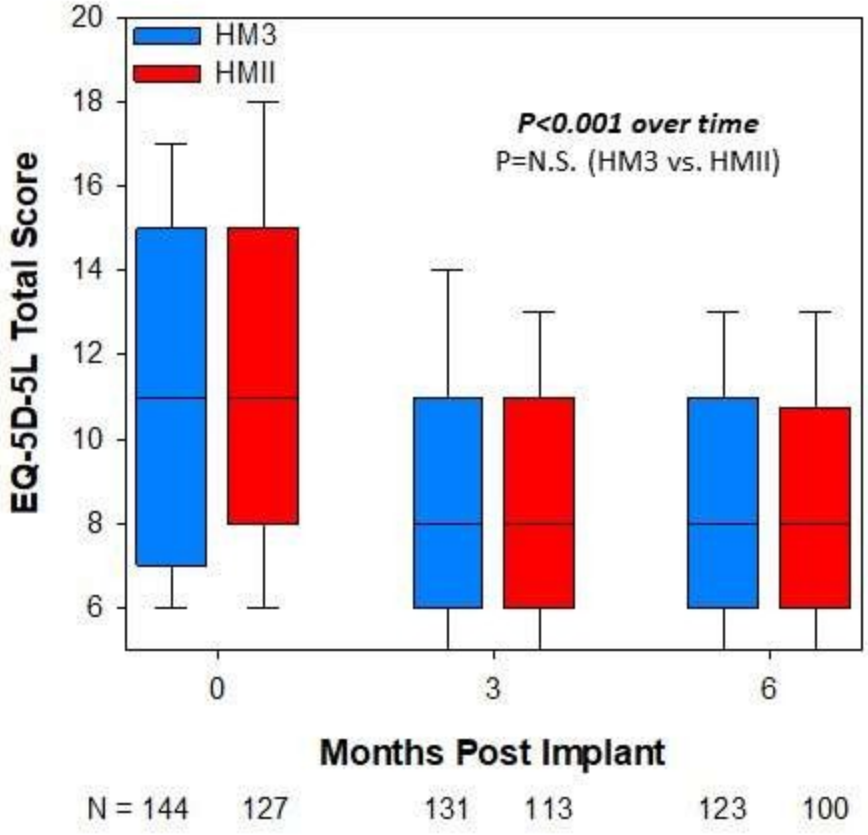
MOMENTUM

Comparison of Hr-QOL

KCCQ



EQ-5D

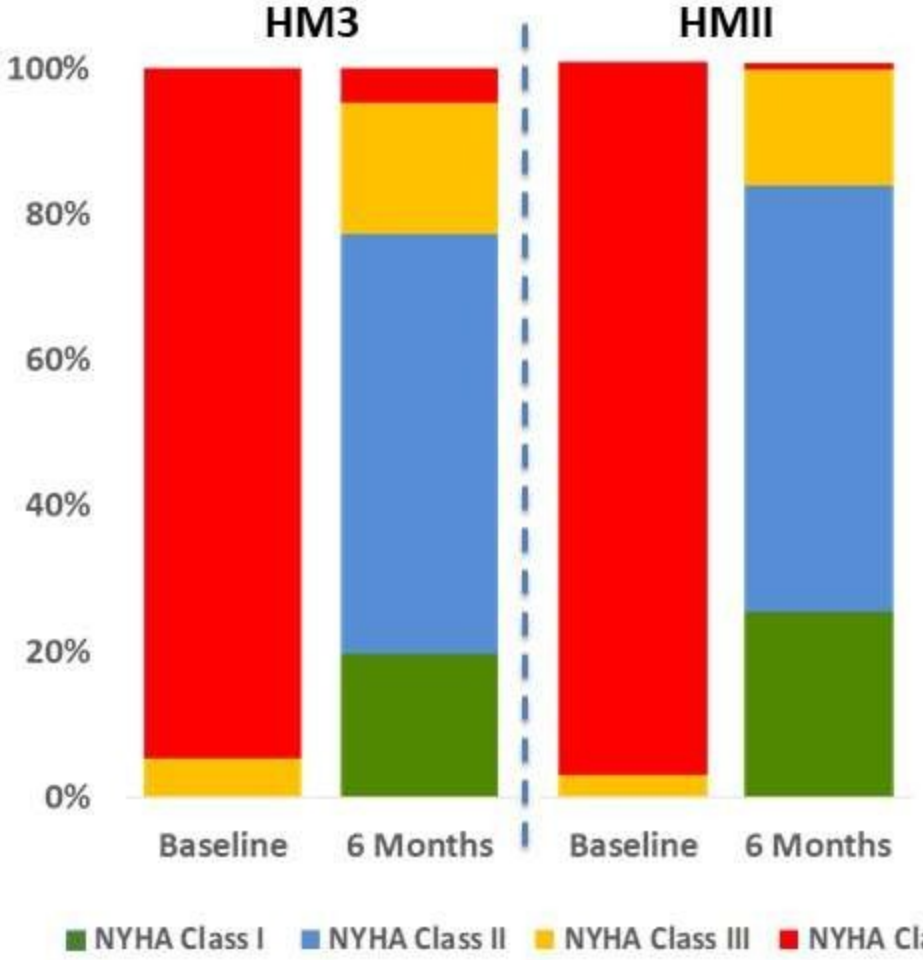


MOMENTUM

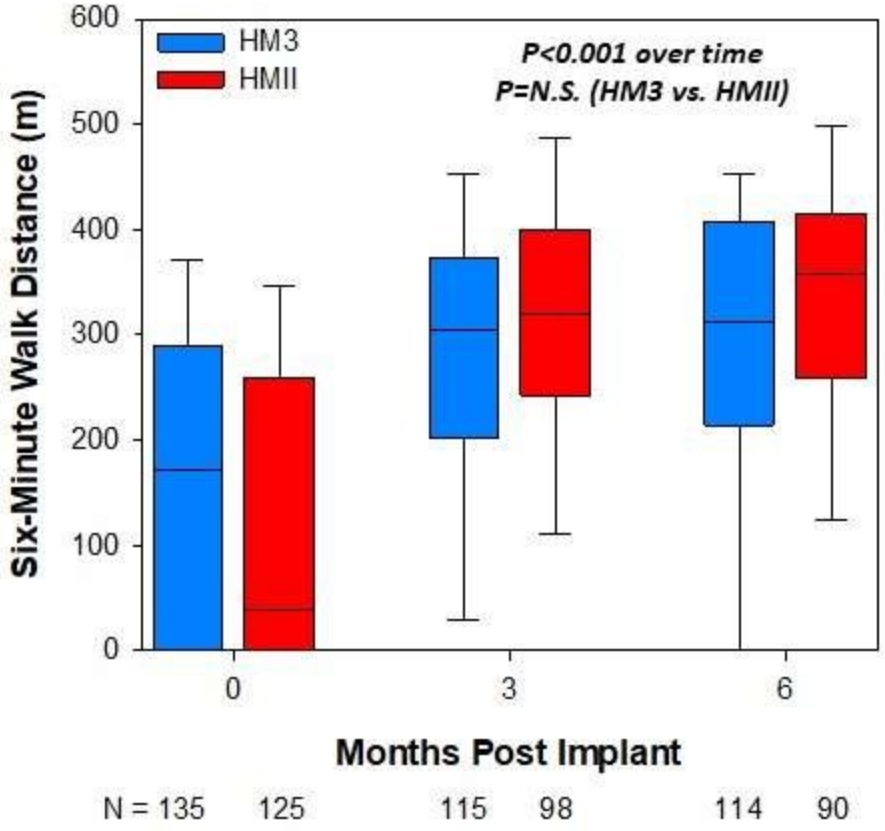
Comparison of FC

NYHA Class

P<0.001 over time
P=N.S. (HM3 vs. HMII)

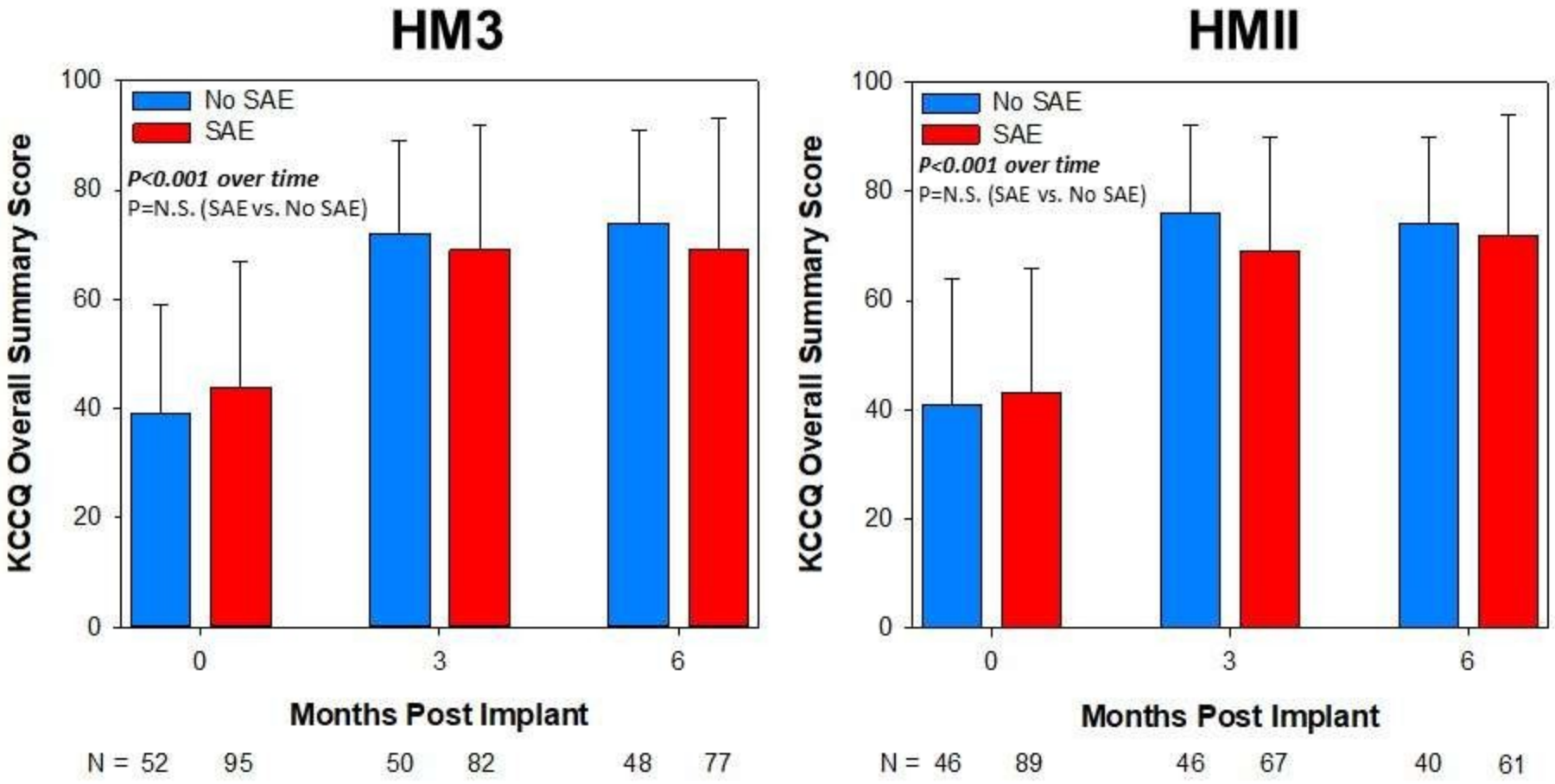


6 MWT



MOMENTUM

KCCQ in Subjects With and Without SAE



KCCQ overall summary scores increase over time in <u>both</u> patients with and without an SAE

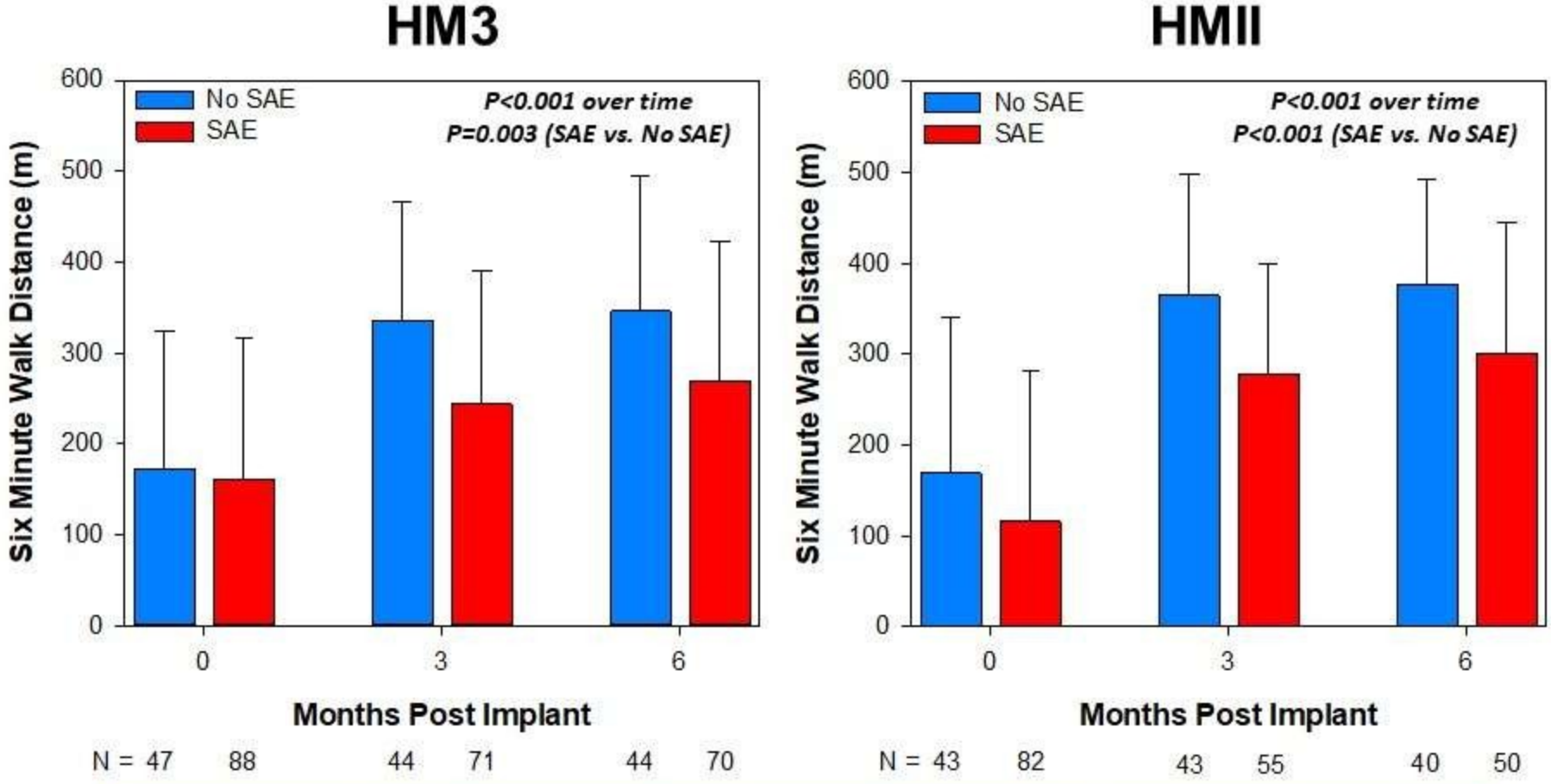
MOMENTUM

EQ-5D in Subjects With and Without SAE

EQ-5D total scores improves over time in <u>both</u> patients with and without an SAE

MOMENTUM

6MWT in Subjects With and Without SAE



- **6MWT improves significantly more in patients who do <u>not</u> experience a serious adverse event**

MOMENTUM

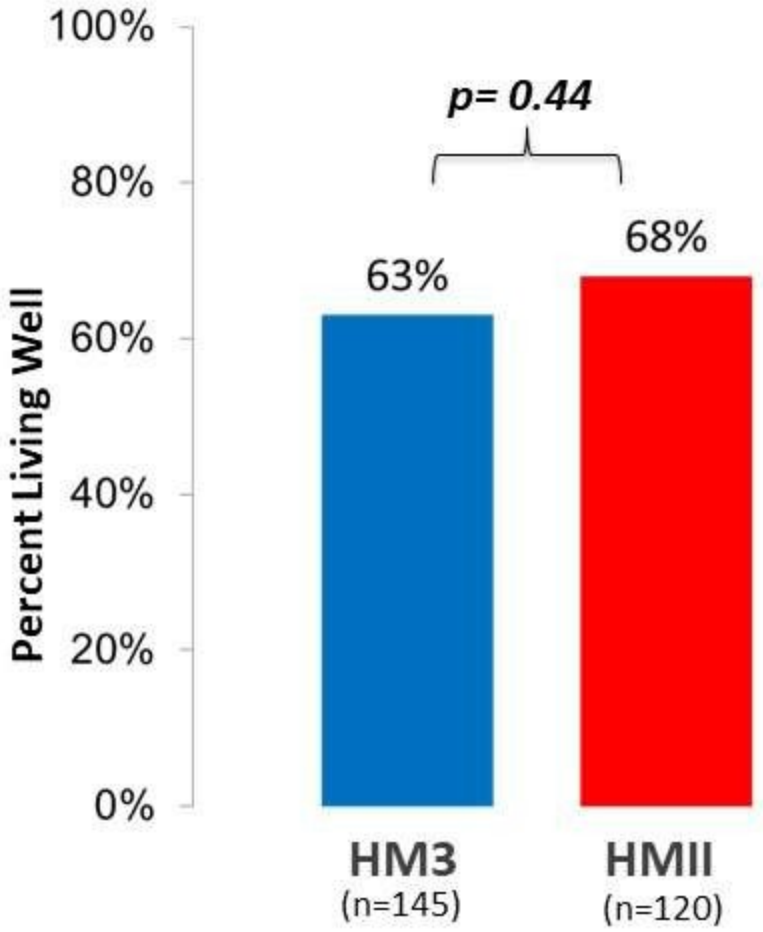
Patients "Living Well on an LVAD" at 6 months

Living Well on an LVAD:

1) KCCQ overall score >50 at 6 months

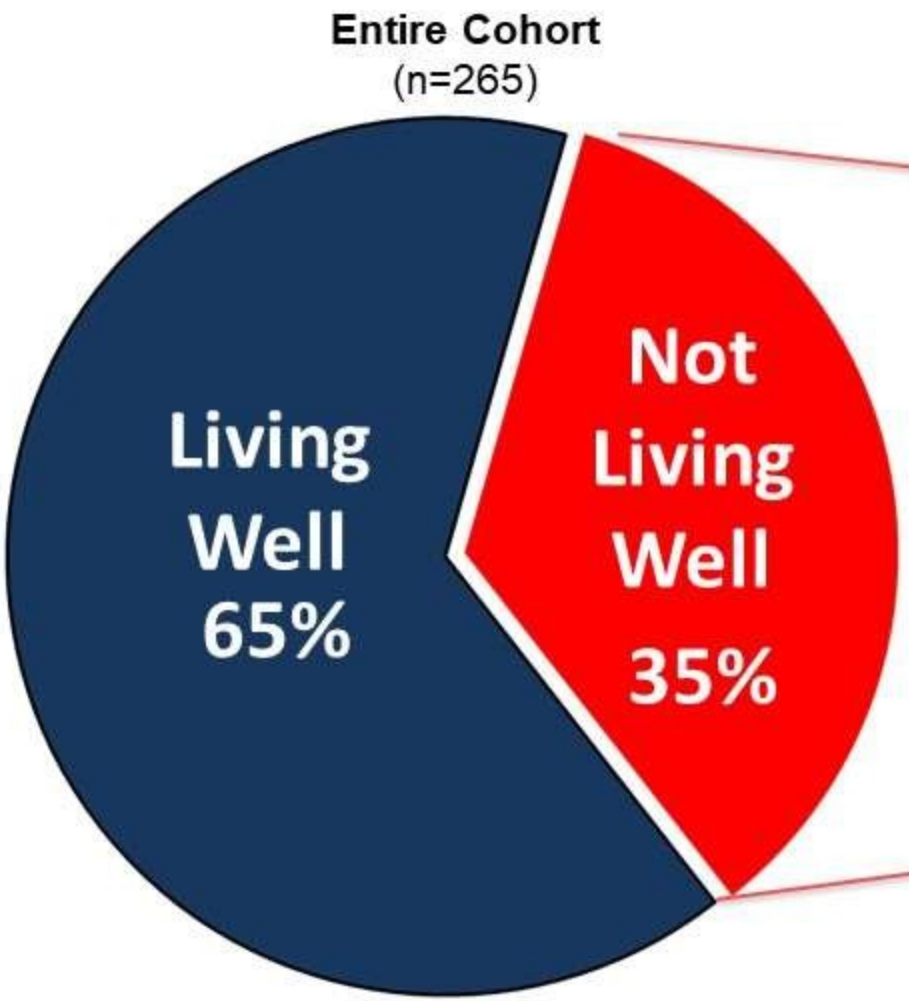
AND

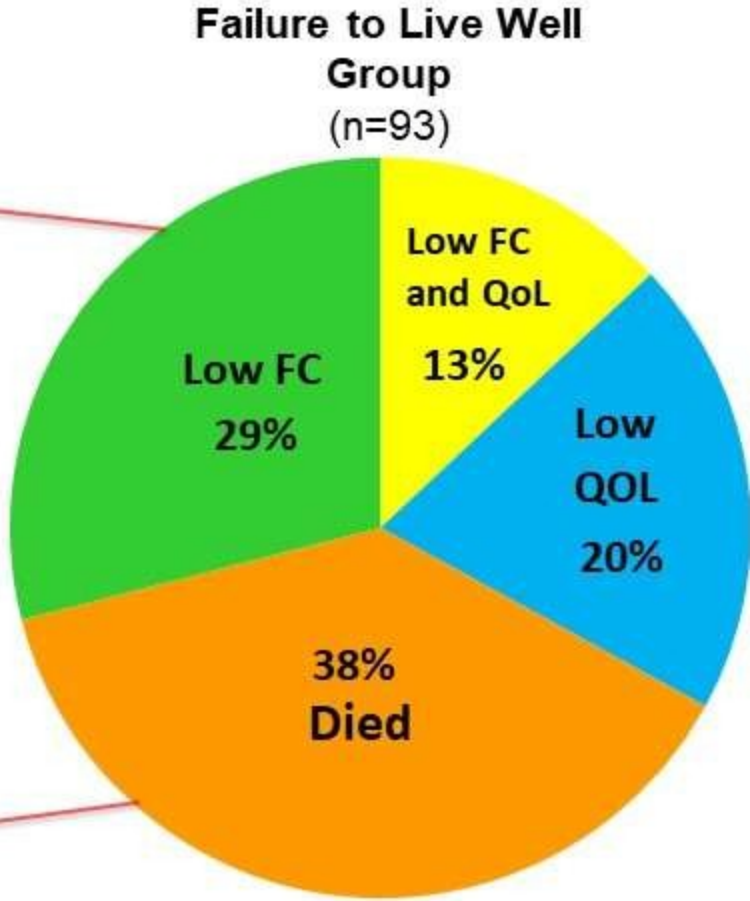
2) NYHA class I/II *or* 6MWT >300 meters at 6 months



MOMENTUM

Failure to Live Well at 6 months:
Breakdown of Endpoint





MOMENTUM

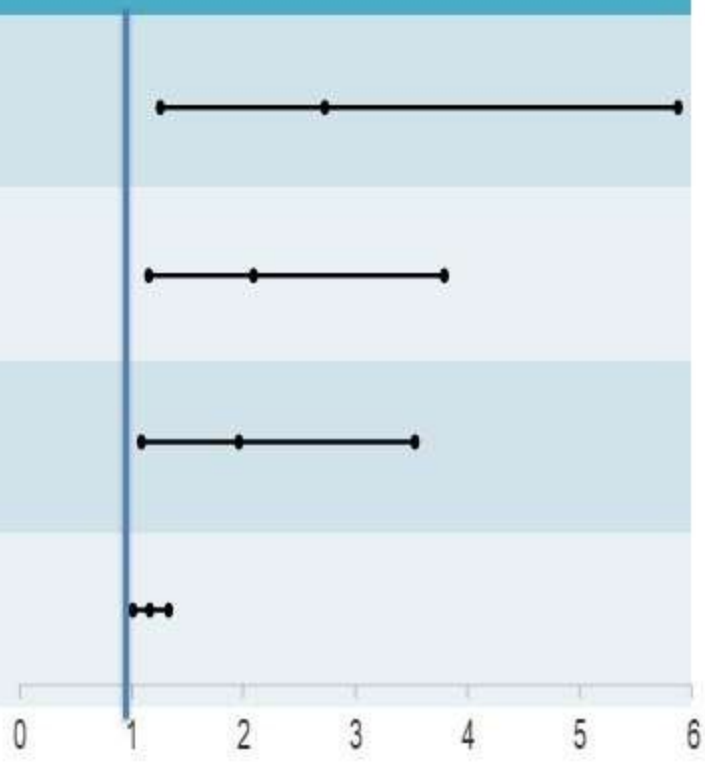
Correlates of "Living Well on an LVAD"

	Met Living Well Endpoint (n = 172)	Failed Living Well Endpoint (n = 93)	P*
Pump Type - HM3	91 (53%)	54 (58%)	0.44
Age (years)	***59 ± 12***	***62 ± 13***	***0.02***
Age > 65 years (n = 106)	***59 (34%)***	***47 (51%)***	***0.01***
Male (n = 212)	137 (80%)	75 (81%)	0.87
BMI (kg/m^2)	28 ± 6	29 ± 5	0.11
Destination therapy (n = 153)	93 (54%)	60 (65%)	0.12
INTERMACS Profile 1-3 (n = 222)	148 (86%)	74 (80%)	0.29
History of diabetes (n = 111)	71 (41%)	40 (43%)	0.80
History of cancer (n = 38)	24 (14%)	14 (15%)	0.86
Baseline Hgb >10 g/dL (n = 225)	***156 (91%)***	***69 (74%)***	***<0.001***
Baseline 6MWD (m)	***167 ± 156 (n = 156)***	***115 ± 167 (n = 84)***	***0.003***
Non-ambulatory (n = 106)	***59 (38%)***	***47 (56%)***	***0.010***
Baseline KCCQ OSS	***45 ± 22 (n = 169)***	***37 ± 20 (n = 90)***	***0.004***
SAE within first 3 months (n = 171)	***99 (58%)***	***72 (77%)***	***0.001***
Hemocompatibility Score	***0.5 ± 0.9 (n = 172)***	***1.4 ± 2.2 (n = 93)***	***<0.001***

TUM

Multivariable Correlates of "Living Well on an LVAD"

Baseline Variable		OR [95% CI]
Preop Hgb	>10 g/dL	2.73 [1.26-5.88] p = 0.01
Age	< 65 years	2.09 [1.15-3.79] p = 0.02
Able to perform 6MWT preop	Yes	1.96 [1.09-3.53] p = 0.02
KCCQ preop	Per 10-unit increase	1.16 [1.01-1.33] p = 0.04



MOMENTUM

Limitations

tudy findings should be viewed as hypothesis generating
nd exploratory since:

- This short term cohort (294/1028) represents the first U.S. experience and is only a limited proportion of the total MOMENTUM 3 IDE trial
- Follow-up was limited to 6 months post implant
- Non-blinded outcomes are subject to bias

MOMENTUM

Conclusions

Hr-Quality of Life and Functional Capacity improved significantly MOMENTUM 3 patients, independent of device use

2/3 of patients met the endpoint of "Living Well on an LVAD" at 6 months

Independent predictors of "Living Well on an LVAD"

- Younger age (<65 years)
- Ability to ambulate preoperatively
- Absence of preoperative anemia
- Higher preoperative Hr-QOL scores

MOMENTUM

Conclusions

The occurrence of a Serious Adverse Event did not influence Hr-QOL measures; However, functional capacity was adversely affected

- The divergence may support the need for development of new Hr-QOL instruments to allow for better characterization of the LVAD patient's experience.

MOMENTUM

On behalf of MOMENTUM 3 Investigators:

Thank you!

MOMENTUM 3

eridge Dr., Pleasanton, CA 94588 USA, Tel: 1 925 847 8600
cular.Abbott/HeartMate3

mary: Prior to using these devices, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, s, potential adverse events and directions for use.

e 3™ LVAS Indications: The HeartMate 3™ Left Ventricular Assist System is indicated for providing short- and long-term mechanical circulatory .g., as bridge to transplant or myocardial recovery, or destination therapy) in adult and pediatric patients with advanced refractory left ventricular re and with an appropriate body surface area.

e 3™ LVAS Contraindications: The HeartMate 3 Left Ventricular Assist System is contraindicated for patients who cannot tolerate, or who are anticoagulation therapy.

e 3™ LVAS Adverse Events: Adverse events that may be associated with the use of the HeartMate 3 Left Ventricular Assist System are: death, cardiac arrhythmia, localized infection, right heart failure, respiratory failure, device malfunctions, driveline infection, renal dysfunction, sepsis, her neurological event (not stroke-related), hepatic dysfunction, psychiatric episode, venous thromboembolism, hypertension, arterial non-central ystem (CNS) thromboembolism, pericardial fluid collection, pump pocket or pseudo pocket infection, myocardial infarction, wound dehiscence, (not associated with suspected device thrombosis) or pump thrombosis.

MOMENTUM