Impact of Heart Failure Management Using Thoracic Fluid Monitoring From A Novel Wearable Sensor: Results of the Benefits of Microcor (µCor™) in Ambulatory Heart Failure (BMAD) Trial

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Background

- Heart failure (HF) is a major public health problem afflicting over 26 million people globally.
- Annually, in the United States, more than 1 million patients are hospitalized with a primary diagnosis of heart failure; and by 2030 it is expected that over 8 million people will be affected.
- Although significant developments have occurred to advance heart failure medical therapy, hospital readmission rates remain high at ≥ 50% within the first 6 months with 24% occurring within the first 30 days (Desai 2012).
- Strategies and approaches aimed to reduce hospital readmissions have potential to improve patient care as well as ease the burden on the healthcare system.

Purpose

- In this study, we evaluate a strategy of using data from a novel RF sensor to manage heart failure and compare it to a concurrent control group.

Study Design

- This investigation is a multicenter, multinational, prospective, concurrent control clinical trial consisting of 2 arms
  - BMAD HF (Benefit of Microcor in Acute Decompensated Heart Failure; control arm)
  - BMAD Tx (Benefit of Microcor in Acute Decompensated Heart Failure with radar directed Therapy; intervention arm)
- The study was powered for a primary endpoint of the comparison of heart failure hospitalization by time to first event between the two study arms.
- The study was IRB and ethics committee approved (NCT03476187, NCT04096040). Informed consent was obtained from all subjects.

Key Inclusion and Exclusion Criteria

Inclusion Criteria

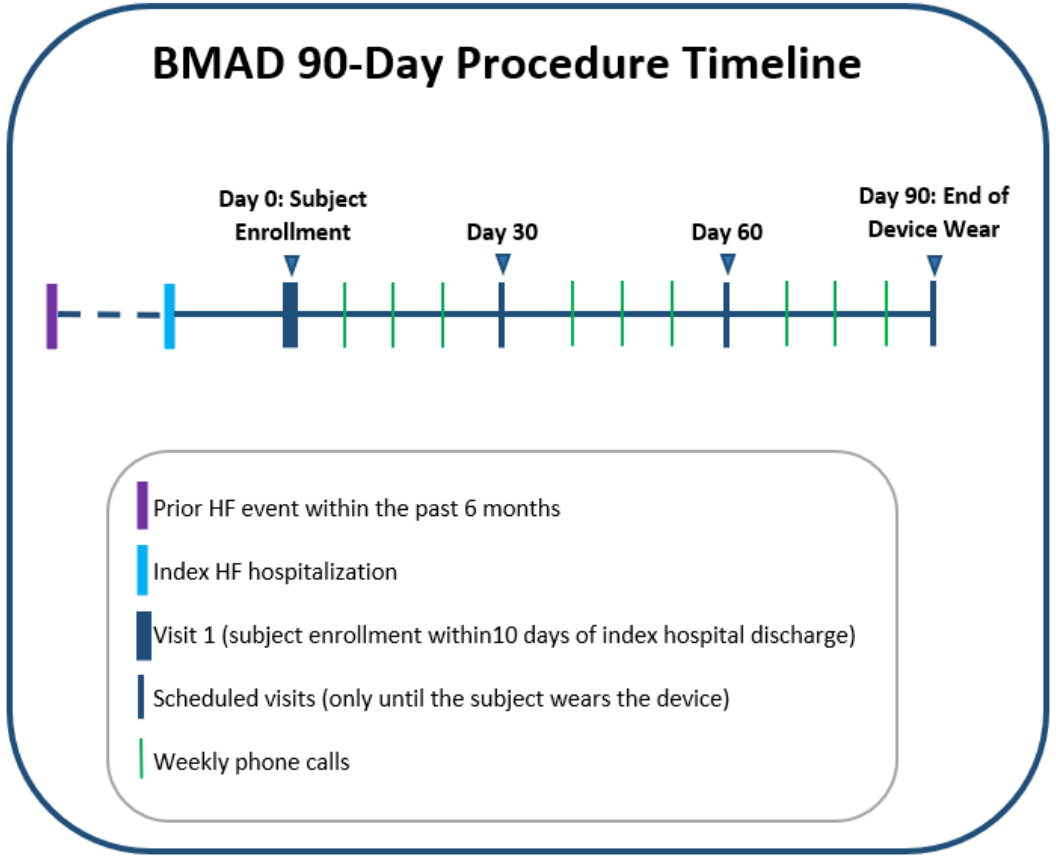
- Patients discharged from the hospital for heart failure in the previous 10 days were eligible for enrollment in the study
- Heart failure event within the previous 6 months was required defined as a hospitalization, emergency room visit, observation unit visit, or unplanned clinic visit where medical management or treatment for HF related pulmonary congestion was administered
- No LVEF criteria required

Exclusion Criteria

- Wearable cardiac defibrillator (WCD)
- Subcutaneous implantable cardioverter defibrillator
- Left ventricular assist device (LVAD)
- Life expectancy of less than a year due to a non-cardiac disease
- Skin sensitivity to medical adhesives
- Anticipated to start dialysis within 90 days
- Received a percutaneous coronary intervention (PCI) less than 24 hours after onset of HF-related symptoms during index hospitalization

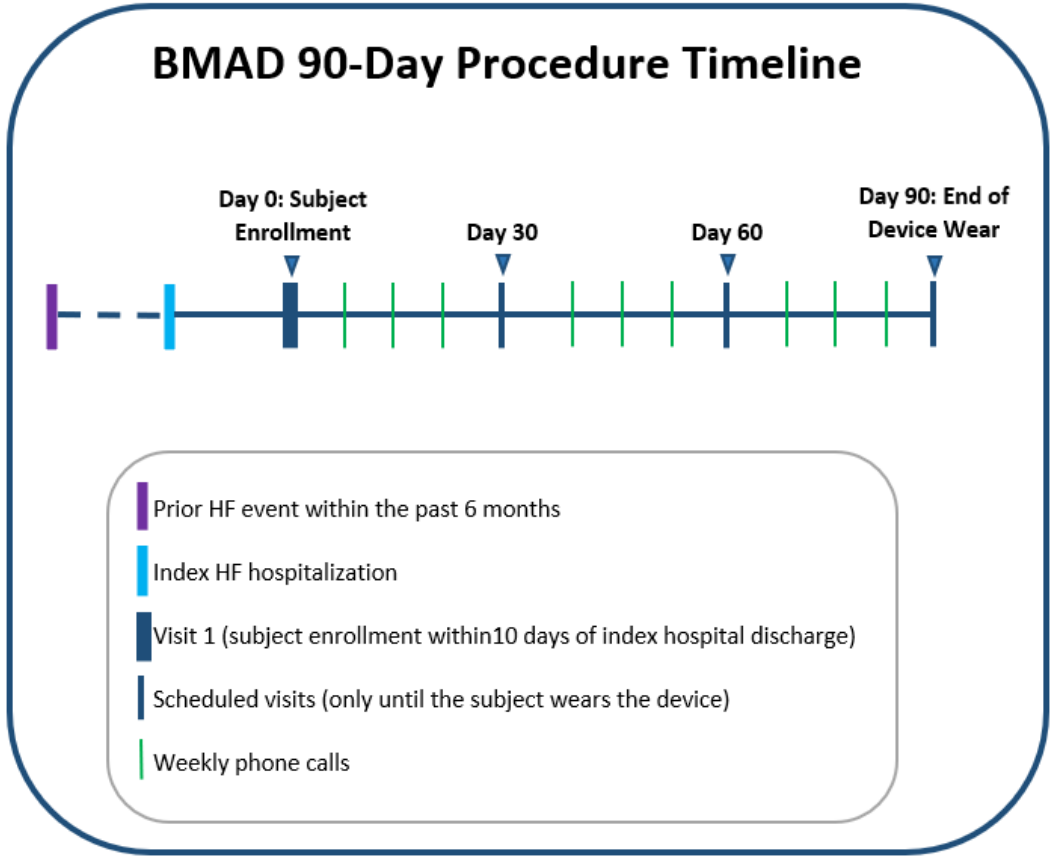
Study Procedures

- Subjects were asked to wear the HFMS for up to 90 days
- Subjects participated in weekly phone calls, monthly office visits, and 6 month and 1 year follow-up phone calls
- Quality of life was assessed via the Kansas City Heart Failure Questionnaire (KCCQ-12)
- Control arm (BMAD-HF) the investigators and subjects were blinded to the device data
- Intervention arm (BMAD-TX) device data was shared with the investigator through a secure website
- The control arm began prior to the intervention arm and the data collection in the two arms overlapped.



Study Procedures

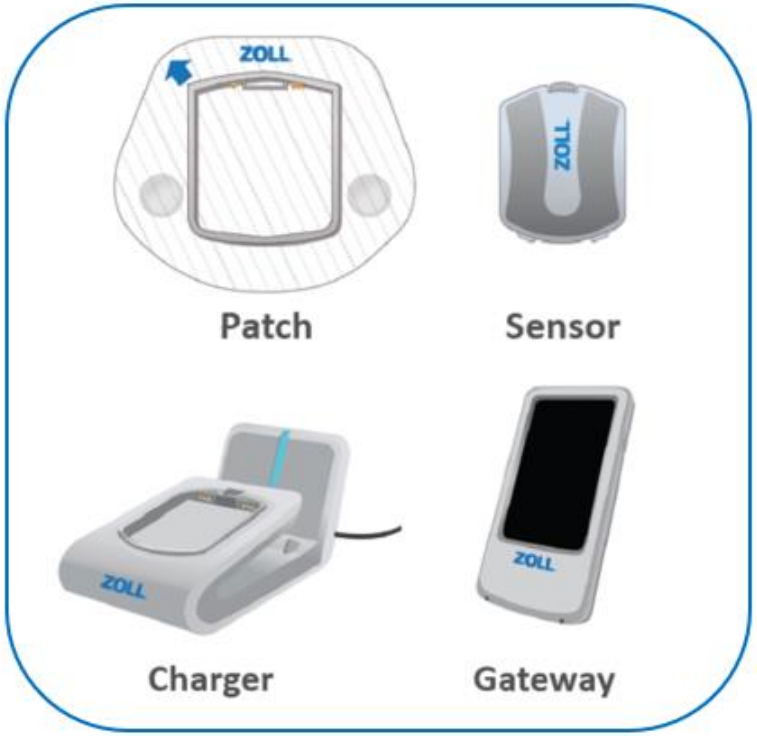
- Thoracic fluid index (TFI) is a unitless metric derived from RF data. This device uses a threshold of higher than 1.2 as representing 3 standard deviations from the population mean being associated with an increased risk of worsening HF.
- Data update reports were sent only to the investigator when a subject's TFI remained higher than the threshold value for 3 consecutive days or more.
- After receiving a data update report, the investigator contacted the subject for a structured interview. Based on the device report and the structured interview, the investigator decided on a course of action which could be medication changes, a lifestyle or diet change, an office/hospital visit, or no change at all.

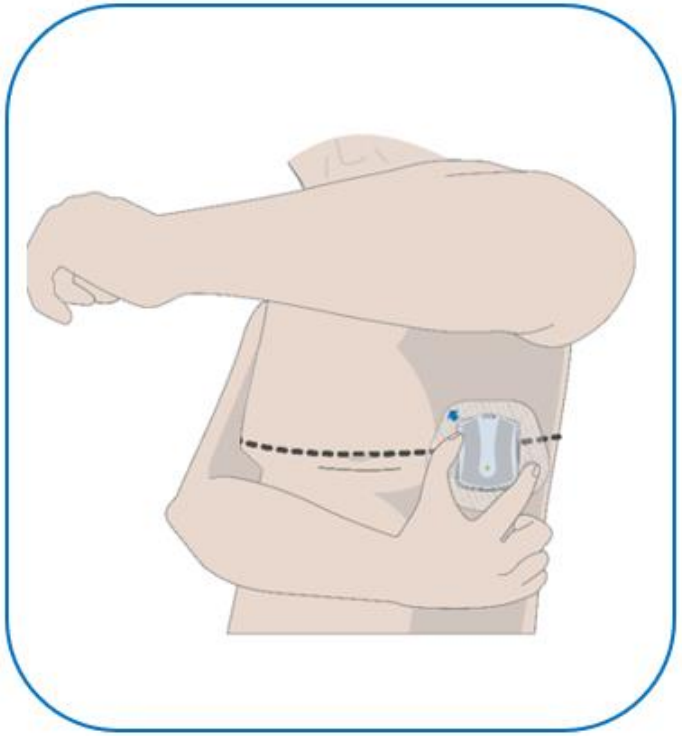


Statistical Analysis

- The analysis was performed as intention to treat (ITT).
- Time-to-event analysis was performed on hospitalizations that were adjudicated as primarily due to HF
- Kaplan-Meier curves were generated to compare the time to first event between the two studies
- Other HF events including emergency room visits and deaths were included in supplemental analyses
- The quality of life subscale of the KCCQ-12 was used to measure quality of life. Scores were calculated for each patient at baseline and at day 90. The mean difference in baseline scores were compared between the two study arms. To assess the change in quality of life over time, change scores were calculated for each patient. A two-sample t-test was used to evaluate differences in the change of quality of life between patients in the BMAD-HF and BMAD-TX arms.
- An adjudication committee of 3 cardiologists adjudicated all study events (hospitalizations, ER visits, and deaths).

Device

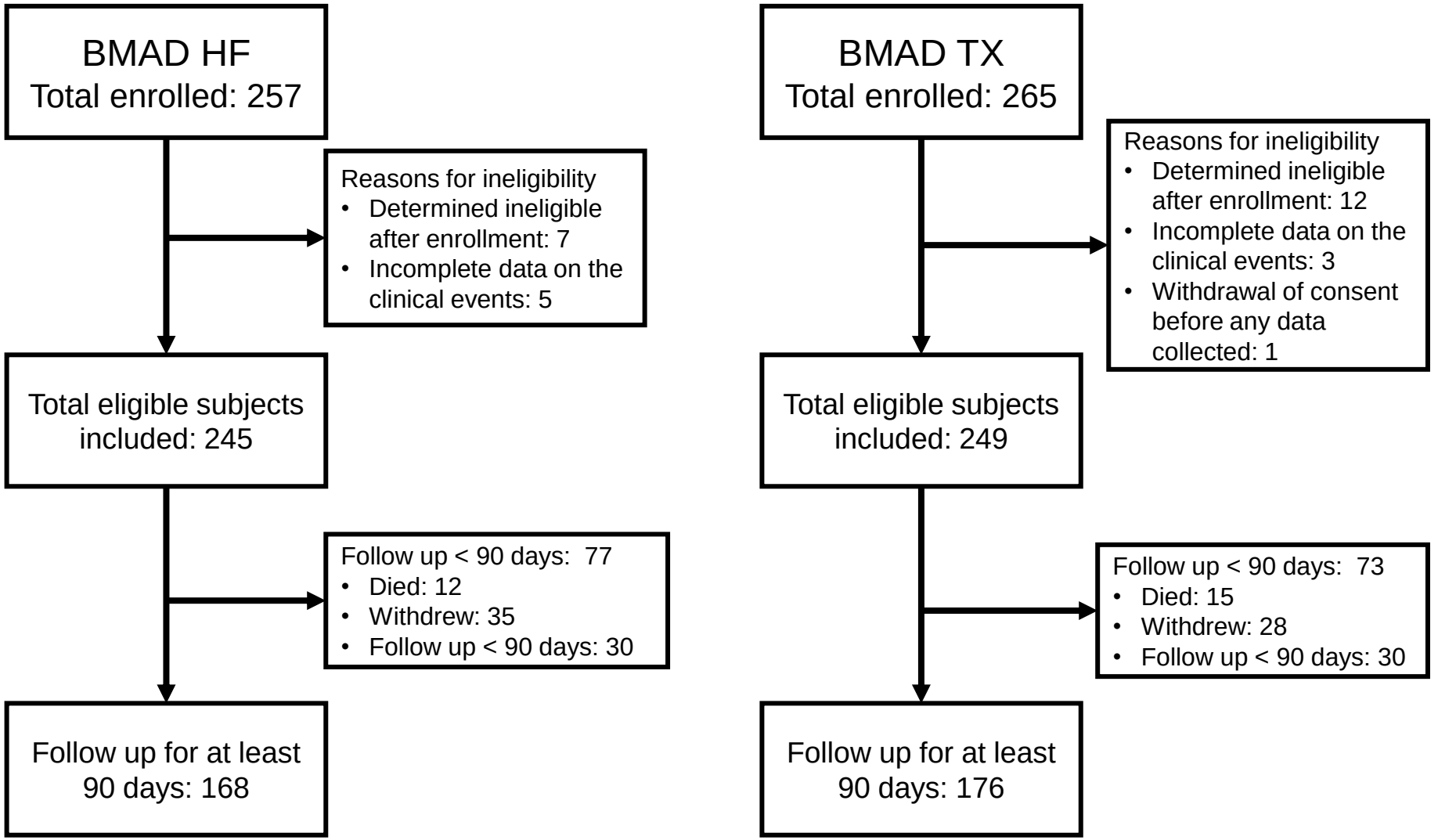




ZOLL Heart Failure Monitoring System (HFMS)

- Detects ECG and heart rate through 2 electrodes, and respiration rate, activity, and posture through a tri-axial accelerometer.
- A measure of lung fluid, is estimated using low-power electromagnetic pulses in the RF wavelength range between 0.5-2.5 GHz.

Results

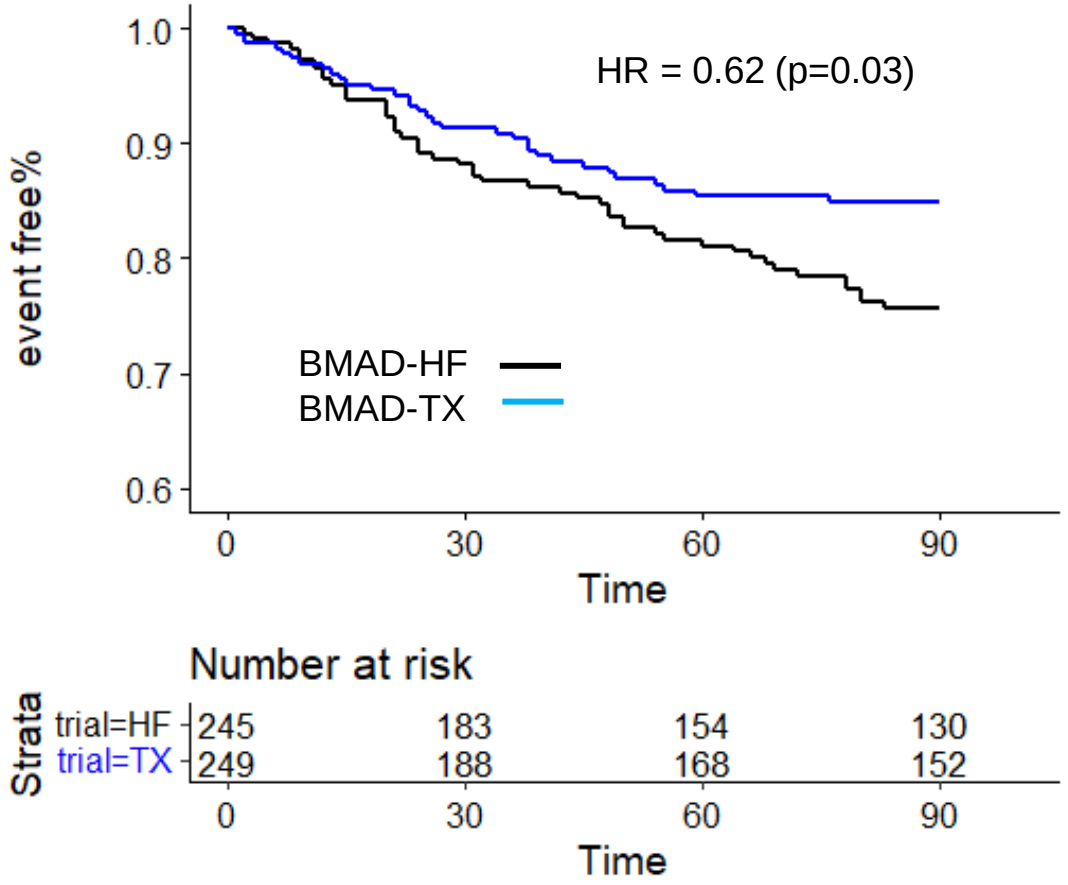

BMAD HF
Total enrolled: 257
Reasons for ineligibility
• Determined ineligible after enrollment: 7
• Incomplete data on the clinical events: 5
Total eligible subjects included: 245
Follow up < 90 days: 77
• Died: 12
• Withdrew: 35
• Follow up < 90 days: 30
Follow up for at least 90 days: 168
BMAD TX
Total enrolled: 265
Reasons for ineligibility
• Determined ineligible after enrollment: 12
• Incomplete data on the clinical events: 3
• Withdrawal of consent before any data collected: 1
Total eligible subjects included: 249
Follow up < 90 days: 73
• Died: 15
• Withdrew: 28
• Follow up < 90 days: 30
Follow up for at least 90 days: 176

Baseline Characteristics

Variable	Category	BMAD HF (n = 245)	BMAD TX (n = 249)	p-value
Age	≤65	116 (47.3%)	99 (39.8%)	0.11
	>65	129 (52.7%)	150 (60.2%)	
Sex	Female	101 (41.2%)	105 (42.2%)	0.9
	Male	144 (58.8%)	144 (57.8%)	
Ethnic	black	64 (26.1%)	63 (25.3%)	0.92
	others	181 (73.9%)	186 (74.7%)	
NYHA	I/II	34 (13.9%)	43 (17.3%)	0.06
	III	115 (46.9%)	90 (36.1%)	
	IV	28 (11.4%)	43 (17.3%)	
	NA	68 (27.8%)	73 (29.3%)	

Variable	Category	BMAD HF (n = 245)	BMAD TX (n = 249)	p-value
CKD	N	134 (54.7%)	128 (51.4%)	0.48
	U	4 (1.6%)	3 (1.2%)	
	Y	107 (43.7%)	118 (47.4%)	
Etiology	Ischemic	109 (44.5%)	115 (46.2%)	0.12
	Non-ischemic	136 (55.5%)	130 (52.2%)	
	NA	0 (0%)	4 (1.6%)	
LVEF	≤40	127 (51.8%)	105 (42.2%)	0.07
	>40	116 (47.3%)	136 (54.6%)	
	NA	2 (0.8%)	8 (3.2%)	
BP Sys	≤123	134 (54.7%)	114 (45.8%)	0.053
	>123	110 (44.9%)	135 (54.2%)	

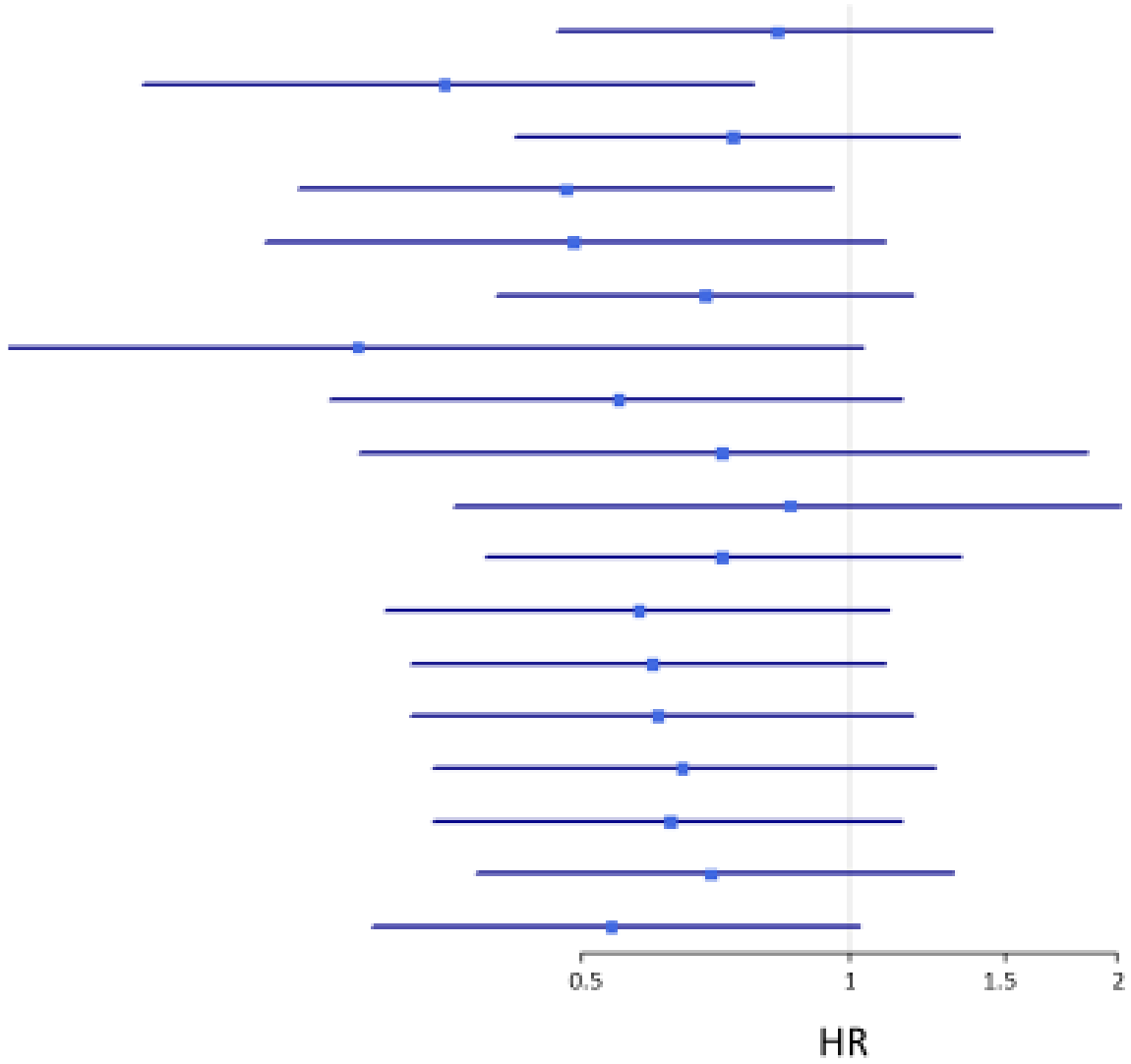
Kaplan-Meier Analysis of Time to First Event for HF Hospitalization



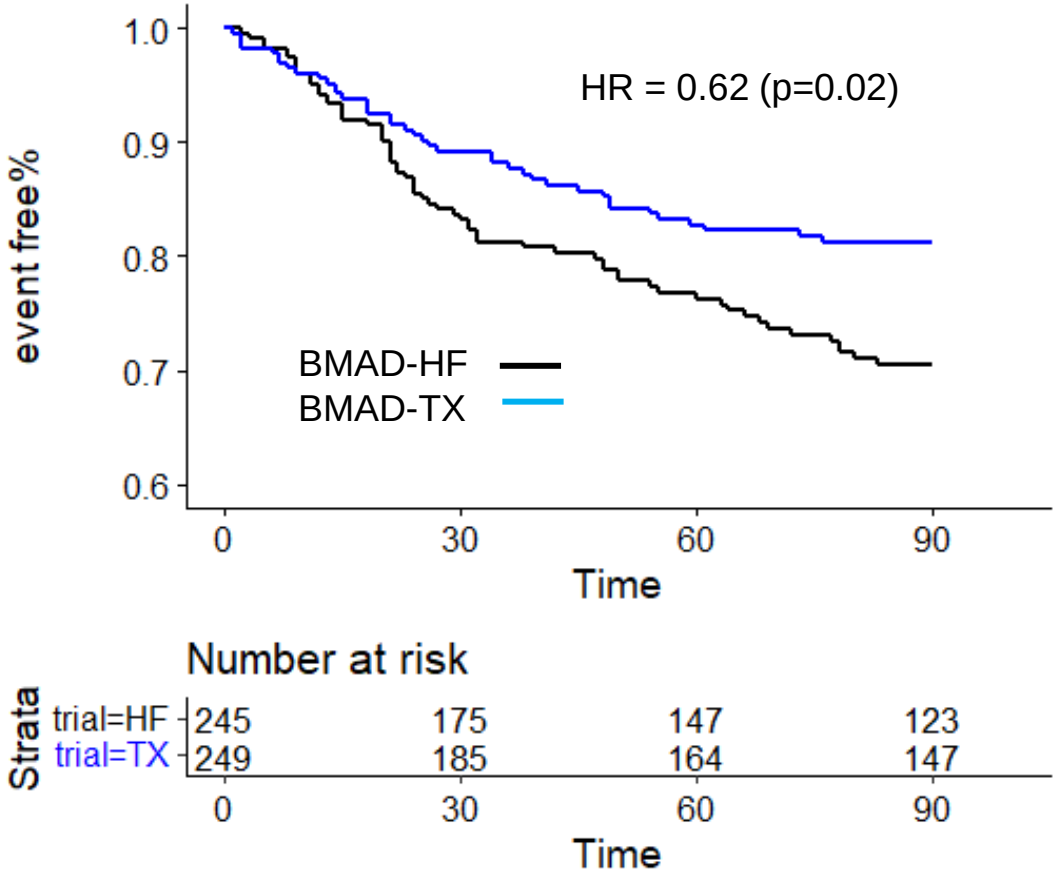
- 38% relative risk reduction
- 7% absolute risk reduction at 90 days
- NNT = 14.3

Subgroup Analysis for HF Hospitalizations

	Group	N	HR	p-value
Age	>65 yrs	279	0.83	0.52
	≤65 yrs	215	0.35	0.01
Sex	Male	288	0.74	0.32
	Female	206	0.48	0.04
Ethnic	Black	127	0.49	0.08
	Others	367	0.69	0.17
NYHA	I & II	77	0.28	0.06
	III	205	0.55	0.11
	IV	71	0.72	0.50
CKD	Yes	225	0.72	0.30
	No	262	0.58	0.10
Etiology	Ischemic	224	0.60	0.10
	Non-ischemic	226	0.61	0.14
LVEF	≥ 40%	232	0.65	0.19
	< 40%	252	0.63	0.13
Sys BP	≥ 123 mmHg	248	0.7	0.27
	< 123 mmHg	245	0.54	0.06

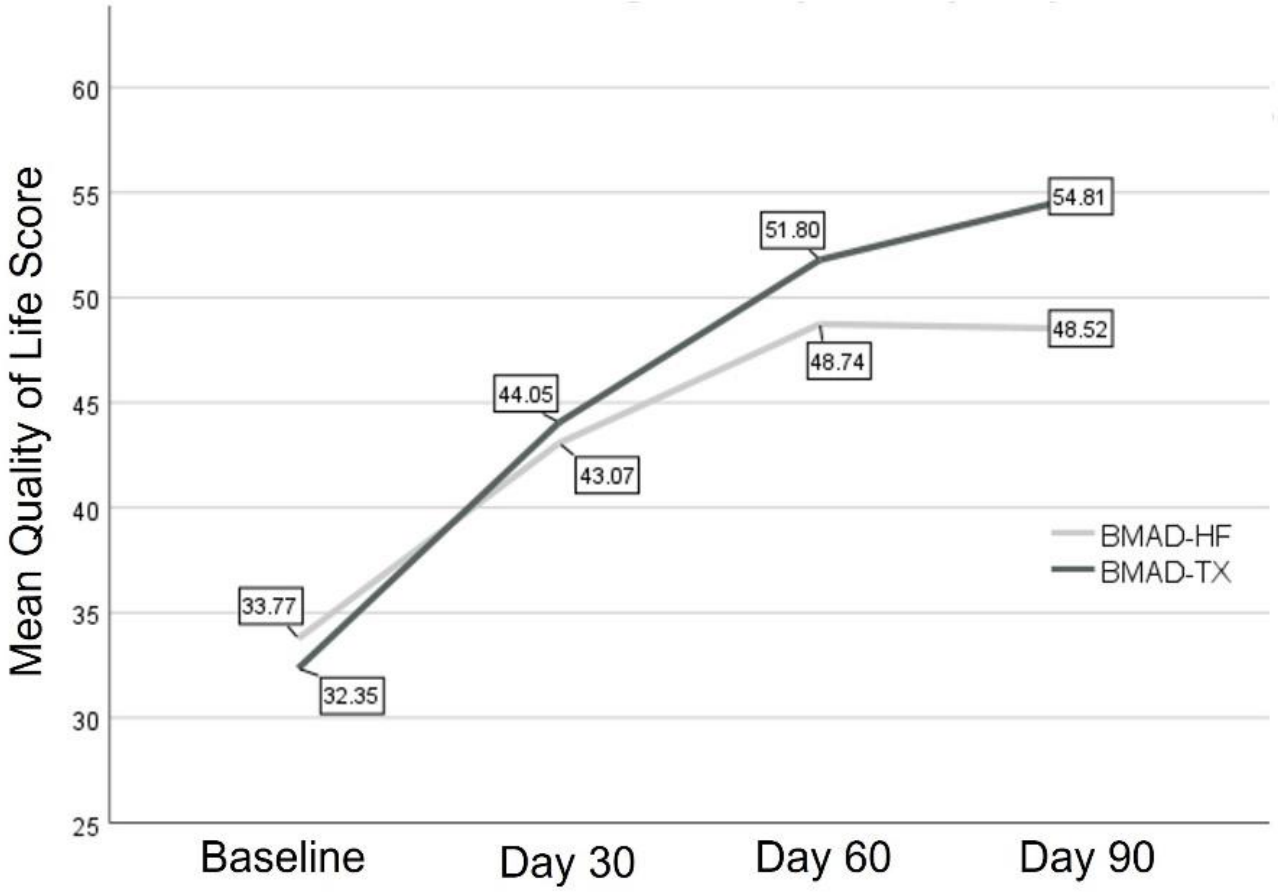


Kaplan-Meier Analysis of Time to First Event for HF Hospitalization, ER visit or Death



- 38% relative risk reduction

Change in Quality of Life - KCCQ



- Both arms experienced an average improvement in quality of life
- BMAD-TX arm reported an average increase in quality of life that was 12-points higher than patients in the BMAD-HF arm (p=.004)
- Responder analysis revealed that nearly 70% of patients in the BMAD-TX arm reported a clinically meaningful improvement in quality of life (90 of 137 patients) compared to 50% of patients in the BMAD-HF arm (67 of 133 patients)

Limitations

- This is a concurrent control clinical, and not a randomized clinical trial.
  - Differences in baseline characteristics or site practice may influence the outcome of the trial.
  - There were no differences between the 2 studies in inclusion or exclusion criteria.
- As the studies started before COVID, any effect the pandemic might have had on the study results during the course of the studies is unclear.

Conclusions

- This study demonstrates that a strategy of managing heart failure using a threshold alert from the HFMS system results in a 38% relative risk reduction in HF readmissions following a HF hospitalization
- The percentage of patients who suffer a HF readmission is reduced by an absolute value of 7%, or an NNT of 14.3 patients to prevent a patient from having a HF readmission.
- A composite endpoint including HF hospitalization, HF ED visits and death was included as a secondary analysis and also demonstrated a 38% relative risk reduction.
- Quality of life, as measured by the KCCQ questionnaire, was improved more in the intervention arm, and the magnitude of benefit, 12 points greater improvement than the control arm, is clinically meaningful.