

The FRAilty MEasurement in Heart Failure (FRAME-HF) Project

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degree of

Doctor of Philosophy

Under the supervision of Professor Jane Phillips,
Associate Professor Caleb Ferguson, and Adjunct
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Certificate of Original Authorship

I, **Julee McDonagh** declare that this thesis, is submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Faculty of Health at the University of Technology Sydney. This thesis is wholly my own work unless otherwise reference or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis. This document has not been submitted for qualifications at any other academic institution.

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“I can do all things through Christ who strengthens me”, Philippians 4:13 NKJV.

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3. Jha SR, **McDonagh J**, Prichard R, Newton PJ, Hickman LD, Fung E, et al. #Frailty: A snapshot Twitter report on frailty knowledge translation. *Australasian Journal on Ageing*. *Australasian Journal on Ageing*. 2018;37(4):309–12.
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Book Chapters

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Abstract

Background

Frailty is a complex, multifaceted syndrome frequently experienced by older people and those living with chronic disease, such as heart failure. The presence of frailty is a robust predictive indicator of worse outcomes in people with heart failure, including rehospitalisation and mortality. Despite increasing interest in assessing frailty over the last decade, there is an absence of consensus regarding the universal definition of frailty and the optimal means of assessment for this population. Consequently, the clinical recommendations surrounding frailty assessment in patients with heart failure are ambiguous. Given this reality, there is an urgent need to identify the optimal way to assess frailty in a heart failure population.

Aim

The 'FRaIly MEasurement in Heart Failure' (FRAME-HF) project aims to determine the most suitable and clinically relevant frailty instrument(s) for use in adults living with heart failure.

Methods

Setting and participants: The FRAME-HF project was undertaken at St Vincent's Hospital, a global leader in specialised cardiovascular care, located in Sydney, Australia. This project involved two groups of participants: 1) Individuals aged 18 years and older with a confirmed diagnosis of heart failure currently admitted to the cardiology ward or attending the outpatient heart failure clinic, and 2) Cardiovascular clinicians (i.e., registered nurses, physicians, and allied health professionals) providing treatment to patients admitted to the cardiology ward and/or attending the outpatient heart failure clinic.

Design: Deductive sequential mixed methods project comprising three interrelated yet discrete studies: a systematic review (Study 1) explores how frailty has been assessed in heart failure research and elucidates which frailty domains are the most frequently assessed; a cross-sectional study (Study 2) examines the correlation and inter-rater agreement between subjective clinician estimates of frailty and a formal frailty assessment, using a modified version of the Frailty Phenotype in adults with heart failure; and a prospective cohort study (Study 3). The prospective cohort study is the core data

component. It comprises two parts: Part A, which evaluates the validity of three commonly used physical frailty instruments, the Frailty Phenotype, the St Vincent's Frailty instrument and the SHARE-FI; and Part B, which compares the ability of six frailty instruments (the three physical frailty instruments above, as well as, three multi-domain instruments, the Deficit Accumulation Index, the St Vincent's Frailty instrument plus cognition and mood domains, and the FRAIL scale) to predict composite rehospitalisation and mortality at 12 months. Data integration of the three FRAME-HF studies, using narrative and joint display approaches, generated a series of clinical recommendations for future practice and research which can help clinicians implement routine frailty assessment in the heart failure clinical setting.

Results

Study 1: A systematic review identified seven different frailty instruments used to identify frailty in heart failure studies to date, none of which were validated for use in patients living with heart failure. The Frailty Phenotype, a 'physical frailty instrument', was the most commonly used instrument, and physical function the most frequently assessed frailty domain. There is also a lack of consensus and robust evidence regarding which frailty assessment method is most suitable and clinically relevant for adults with heart failure.

Study 2: A cross-sectional study of the association between subjective clinician estimates of frailty and a formal frailty assessment using a modified version of the Frailty Phenotype. Thirty-nine clinicians (nurses, physicians and allied health professionals) completed frailty estimates, and 75 patients had their frailty assessed using the modified Frailty Phenotype, producing 194 paired frailty assessments. This study revealed that correlation and inter-rater agreement between pooled clinician-estimated frailty and the formal frailty assessment was fair ($r_s = 0.52$; $\kappa = 0.33$, CI: 0.23 – 0.43). Correlation and agreement were highest between allied-health estimated and formal frailty ($r_s = 0.71$; $\kappa = 0.45$, CI: 0.22 – 0.68), though this was only moderate. These results confirm that subjective clinician estimates of frailty are not a reliable replacement for formal frailty assessment in adults living with heart failure, emphasising the need for assessment with a valid and reliable frailty instrument.

Study 3: Part A evaluated the convergent and discriminant validity of three physical frailty instruments. Of the three instruments compared, the SHARE-FI and the St Vincent's Frailty instrument displayed stronger validity than the Frailty Phenotype in this cohort. Part B

showed that the six frailty instruments potentially relevant for use in adults living with heart failure displayed adequate predictive performance with C-statistic values between 0.71-0.73 and sensitivity between 88-92%. The SHARE-FI and the Deficit Accumulation Index reported the highest odds for rehospitalisation and mortality at 12 months (OR 2.43 [0.81 -7.24] and 1.66 [0.74 – 3.72], respectively). These results suggest that all six instruments are suitable for risk-stratification and research purposes. However, their applicability for routine clinical care and as part of a frailty management plan is yet to be determined. Data integration revealed that, of the frailty assessment instruments compared in this project, the SHARE-FI might be the most suitable and clinically relevant frailty instrument for use in adults living with heart failure, but these results need confirmation in a larger cohort.

Conclusion

The FRAME-HF project provides important novel information regarding the assessment of frailty in heart failure and has identified several critical areas for future research. Most importantly, a validated frailty instrument for use in people living with heart failure, one that is quick and easy to use in a resource-restricted clinical environment, is required. Further work regarding the preferred setting and time-point in the illness trajectory to assess frailty (i.e., inpatient vs. outpatient) and consensus regarding the definition of frailty and the optimal instrument for use in a heart failure population is needed. The applicability of the instruments evaluated in this project for use in routine clinical care and a frailty management plan is also a high priority for future research. Finally, frailty assessment needs to be incorporated into cardiovascular clinicians' daily practice and universally accepted as an integral part of heart failure clinical management.

Abbreviations

AKPS	Australian-modified Karnofsky Performance scale: a measure used to determine functional capacity, primarily used in palliative care (1).
CGA	Comprehensive geriatric assessment
CSANZ	Cardiac Society of Australia and New Zealand
DMI-10	Depression in Medical illness-10 questionnaire: used to determine the presence of depression in those who are medically ill, with a score of ≥ 9 (out of 30) indicative of possible or probable depression (2).
eGFR	Estimated glomerular filtration rate
EQ5D-5L	The EuroQoL 5D- 5l questionnaire: used to measure health-related quality of life (3).
FRAIL scale	The Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight scale: a short multi-domain frailty instrument that assesses five domains of frailty to determine the degree of frailty in an individual (frail, pre-frail, or robust) (4).
HF-PEF	Heart Failure with Preserved Ejection Fraction: the heart's inability to fill with blood effectively (5).
HF-REF	Heart Failure with Reduced Ejection Fraction: the heart's inability to pump blood effectively (5).
IMPACCT	Improving Palliative, Aged and Chronic Care through Clinical trials and Translation: a research centre in Sydney, Australia.
LVEF	Left Ventricular Ejection Fraction: a measure obtained from echocardiogram often used to diagnose the type of heart failure (i.e., pumping or filling problem)
MDT	Multidisciplinary team: is a term used to describe various health care professionals from different specialities working together to provide supportive care and case management to individuals, particularly older adults (6).
MoCA	Montreal Cognitive Assessment: a questionnaire delivered to individuals to

	determine the presence of mild cognitive impairment, with a score of ≥ 26 (out of 30) indicative of mild cognitive impairment (7).
NHFA	The National Heart Foundation of Australia
NYHA	New York Heart Association
PICF	Participant Information and Consent Form
ROC curve	Receiver Operating Characteristic curve
SHARE-FI	Survey of Health Ageing and Retirement in Europe Frailty Index: a physical frailty instrument that assesses five physical domains of frailty to determine the degree of frailty in an individual (frail, pre-frail, or non-frail) (8).
SVF	St Vincent's Frailty instrument: a physical frailty instrument that assesses five physical domains of frailty to determine the degree of frailty in an individual (frail, pre-frail, or non-frail) (9).
SVF+	St Vincent's Frailty Instrument plus cognitive and mood domains: a multi-domain frailty instrument that assesses seven domains of frailty to determine the degree of frailty in an individual (frail, pre-frail, or non-frail) (10, 11).

Glossary

Data integration	The process of combining data from multiple research methods and studies to generate knowledge of insight unavailable to single method studies (12).
Deficit Accumulation Index	Deficit Accumulation Index: a multi-domain frailty instrument that assesses frailty according to the number of functional, medical, or social deficits an individual has (13, 14).
Frailty syndrome	A clinically recognisable syndrome of vulnerability to acute stressors, characterised by physical weakness and muscle wastage (15).
The Frailty Phenotype	A physical frailty instrument that assesses five physical domains of frailty to determine the degree of frailty in an individual (frail, pre-frail, or non-frail) (16).
Heart Failure	The heart's inability to fill and/or pump blood effectively due to structural or functional disease (5).
Inpatient	A person who is currently receiving treatment in an acute care facility.
Meta-inference	The overall conclusions, explanations, or understanding developed through combining the inferences obtained from missed methods study (17, 18).
Outpatient	A person who is currently receiving care in the community or clinic setting.
Pre-habilitation	The process of enhancing an individual's functional capacity to enable them to withstand major surgery (19).

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