BMJ Open

Rockwood Clinical Frailty Scale as a predictor of adverse outcomes among older adults undergoing aortic valve replacement: a protocol for a systematic review

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To cite: Prendiville T, Leahy A, Quinlan L, *et al*. Rockwood Clinical Frailty Scale as a predictor of adverse outcomes among older adults undergoing aortic valve replacement: a protocol for a systematic review. *BMJ Open* 2022;**12**:e049216. doi:10.1136/bmjopen-2021-049216

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-049216).

Received 18 January 2021
Accepted 02 December 2021

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ABSTRACT

Introduction Frailty is associated with adverse outcomes relating to cardiac procedures. It has been proposed that frailty scoring should be included in the preoperative assessment of patients undergoing aortic valve replacement. We aim to examine the Rockwood Clinical Frailty Scale (CFS), as a predictor of adverse outcomes following aortic valve replacement.

Methods and analysis Prospective and retrospective cohort studies and randomised controlled trials assessing both the preoperative frailty status (as per the CFS) and incidence of adverse outcomes among older adults undergoing either surgical aortic valve replacement or transcatheter aortic valve replacement will be included. Adverse outcomes will include mortality and periprocedural complications, as well as a composite of 30-day complications. A search will be conducted from 2005 to present using a prespecified search strategy. Studies will be screened for inclusion by two reviewers, with methodological quality assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. Relative risk ratios with 95% CIs will be generated for each outcome of interest, comparing frail with non-frail groups. Data will be plotted on forest plots where applicable. The quality of the evidence will be determined using the Grading of Recommendations, Assessment, Development and Evaluation tool.

Ethics and dissemination Ethical approval is not required for this study as no primary data will be collected. We will publish the review in a peer-reviewed journal on completion.

PROSPERO registration number CRD42020213757.

Strengths and limitations of this study

- This study will synthesise the totality of evidence with respect to the association of Clinical Frailty Scale-defined frailty with adverse outcomes after surgical and transcatheter aortic valve replacement in older people and inform evidence-based practice on the utility of such an instrument.
- The review will employ rigorous methods to identify, select, appraise and synthesise the findings, adhering to standardised reporting guidelines to standardise the conduct and reporting of the review.
- Limitations of the review may include a low number of suitable studies, low-quality evidence of included studies and heterogeneity in the conduct and reporting of study outcomes and duration of follow-up.

INTRODUCTION

Surgical (SAVR) or transcatheter aortic valve replacement (TAVR) remains the mainstay of treatment for severe aortic stenosis, with the latter originally developed to facilitate intervention in the older, more frail and higher risk population.[1] TAVR has more recently been shown to be equivalent to SAVR in the intermediate and low-risk groups,[2 3] leading to its wider use as a valve replacement strategy, particularly in older people.[4–6]

Frailty is common in older people and is associated with poorer outcomes following either TAVR or open cardiac surgery.[7 8] It is characterised by decreased physiological reserve, making an individual vulnerable to increased dependency and/or mortality when exposed to a stressor.[9] The prevalence of frailty is expected to increase as life expectancy continues to rise.[10 11]

The Rockwood Clinical Frailty Scale (CFS),[12] first described in 2005, is a semi-quantitative tool used to estimate an individual's degree of frailty on a scale of 1 (very fit) to 9 (terminally ill). Patients who score a 5 or higher are considered frail. The main advantage of the CFS is its ease of application, as a score can be derived through a brief interview with a patient or family member without the need for further objective data such as grip

strength or gait speed. Interobserver variability has been reported however,[13] which may affect the applicability of the scale, particularly among non-geriatricians.

It has been recommended that a measure of frailty be included in the preoperative risk assessment of older patients undergoing aortic valve replacement.[14] We aim to examine the data on the association of frailty (as defined by the CFS) with adverse outcomes following either TAVR or SAVR.

METHODS

Study design

We will conduct a systematic review to identify research studies which reported the incidence of adverse outcomes following either SAVR or TAVR, in which patients had their frailty status measured preoperatively using the CFS. Our study will use the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy principles and will reference the Preferred Reporting Items for Systematic Reviews and Meta-Analyses standardised reporting guidelines.[15]

Search identification

Using a predefined search strategy, a systematic search will be conducted using the MEDLINE (Ovid), PubMed, CINAHL, Scopus, Embase, PsycINFO, Science Direct, Academic Search Complete, WHOLIS by Virtual Health Library, Web of Science and Cochrane Library databases. Studies published after 2005 (when the CFS was first published) will be included. There will be no language restriction. Search results will be imported into Endnote and duplicates removed. All abstracts will be screened independently by two reviewers (TP and LQ/MOC) regarding suitability for inclusion, with disputes resolved by a third independent reviewer (RG).

A sample search strategy for PubMed is included in the online supplemental data 1.

Eligibility criteria

Studies will be selected for inclusion if they examine the incidence of adverse outcomes following SAVR or TAVR in older adults and include a preoperative frailty assessment using the CFS. Both the 7-item and 9-item CFS will be examined, with a score of >4 indicating a frail patient.[12] Prospective and retrospective cohort studies and randomised controlled trials will be included. Our population of interest will be patients greater than 65 years of age undergoing these interventions.

Primary and secondary outcomes

The primary outcome for this study will be 12-month mortality post-aortic valve replacement. Data on a number of secondary outcomes (as defined by the Valve Academic Research Consortium) will be collected,[16] as well as rates of functional decline or rehospitalisation and length of stay in hospital or the intensive care unit (ICU). All secondary outcomes are listed in the online supplemental data 2.

Meta-analysis will be undertaken where data are available on a similar outcome across two or more studies. Data relating to TAVR and SAVR will be reported separately.

Study quality

The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool will be used to assess the methodological quality of included studies by examining the risk of bias as well as the generalisability of the studies to our population of interest.[17] Each primary/secondary outcome will be taken as a 'reference standard' and will be reported separately, while the CFS will be taken as the index test—in practice we will use this to ensure that rates of adverse outcomes were not interpreted prior to application of the CFS. Each paper will be independently assessed by two reviewers (TP and AS). Disagreements regarding study quality will be resolved by discussion with a third reviewer (CP). The Grading of Recommendations, Assessment, Development and Evaluation tool will be used to determine the strength of the body of evidence collected.

Data extraction

Data extraction will be completed independently by two separate authors (TP and AL). A data extraction form will be used to compile relevant data. Data will be extracted including authors and year of publication, country, population studied, sample size, baseline demographics, baseline CFS Score, characteristics of the person scoring the CFS (research, cardiology or geriatric clinician), valve procedure undertaken, reported outcomes and length of follow-up. Relevant authors will be contacted if additional data are required.

Statistical analysis

Stata V.12 and Review Manager V.5.4.1 will be used to analyse data. Relative risk ratios with 95% CIs will be calculated for each dichotomous outcome of interest (comparing frail with non-frail patient groups). Continuous variables will be presented as mean±SD or median with IQR (for non-parametric data) and compared using independent sample T-testing (parametric data) or Mann Whitney U testing (non-parametric data).

Data on similar outcomes across two or more studies will be presented on forest plots. Meta-analysis will be undertaken where applicable.

Data statement

Dataset will be made available from the Open Science Framework repository, doi: 10.17605/OSF.IO/7HPVE.

Patient and public involvement

The writing of this review protocol did not include input from patients or the general public. The outcomes we are looking to measure were determined from clinical observation of older adults and the AVR (ie, SAVR/TAVR) process. The dissemination of our review will include

patient and public involvement. The Ageing Research Centre at the University of Limerick has established a stakeholder group of older adults to support patient and public involvement and input in study designs from the outset. We will engage with this group, who will provide important input to inform the discussion around our review findings.

Ethics and dissemination

No primary data are to be collected for this review, so ethical approval is not required. We will aim to publish our study in a peer-reviewed journal on completion.

DISCUSSION

This systematic review aims to examine the totality of evidence regarding the strength of association of frailty (as measured by the CFS) with adverse outcomes after aortic valve replacement among hospitalised older adults.

The incorporation of TAVR has expanded the treatment of aortic valve disease in a frail older cohort where surgery would not otherwise have been considered,[1] though contemporary data show increasing usage in the intermediate and lower risk populations.[4 18] The risks of TAVR are outlined in the literature, with overall 30-day mortality rates of 2.3%, 5.4% and 4.2% according to recent data from the US, French and German registries, respectively.[4 6 19] Furthermore, data from the UK suggest that approximately 40% of patients undergoing TAVR are frail, while in the USA at least 60% of patients had at least one marker of frailty noted. Both of these cohorts demonstrated increased mortality following the procedure.[20 21] Other frailty-associated factors, such as low body mass index or age greater than 90 years, have also been associated with poorer outcomes.[22 23]

Current widely used risk scores for aortic valve procedures include the Society of Thoracic Surgeons (STS) risk score and the European System for Cardiac Operative Risk Evaluation (EuroSCORE),[24 25] both of which were developed in the SAVR population. These appear to correlate poorly with mortality following TAVR,[26 27] giving rise to the development of newer, more specific TAVR risk scores.[28–30] Neither the STS Score nor the EuroSCORE include an objective measurement of frailty though assessing frailty has the potential to improve their predictive performance, particularly in older adults. There is a lack of consensus on how frailty is best measured.[31] Frailty tools specific to TAVR such as the Essential Frailty Toolset (EFT) have been developed in recent years and have shown statistical significance in predicting mortality.

The role of frailty scores is twofold—not only to predict which patients are at high risk of complications but also in which patients the procedure may be clinically futile (despite being technically successful). Both the CFS and EFT were consistently predictive of mortality and futility for older patients with severe frailty undergoing TAVR.[31]

The CFS is a commonly used and well-validated measure of frailty, taking into account a patient's level of mobility and ability to perform activities of daily living.[32–35] A key advantage of the CFS is obviating the need for an independent dedicated mobility and cognitive assessment to inform test scoring. Other scores such as the Geriatric Assessment Frailty Score by Skaar *et al* are labour intensive, requiring a mini-mental state exam (MMSE), weight, height, Hospital Anxiety and Depression Scale Score, Charlson Comorbidity Index and Nottingham Activities of Daily Living Scale Score to be calculated.[36] Therefore, it would be difficult to translate this process from research into clinical practice on a wider scale. The EFT involves a cognitive assessment using the MMSE or mini-Cog and a prespecified mobility assessment along with laboratory testing.

While the CFS was initially designed for geriatricians as a means of summarising the findings of a comprehensive geriatric assessment,[12] due to its relative brevity of application it may be more accessible to other non-geriatric trained clinicians as a means of assessing frailty.[37] Better understanding of the influence of the background expertise of the rating clinician (eg, cardiology or geriatric trained) will inform on the validity of the CFS. Significant inter-rater variability in the application of the CFS was reported by Surkan *et al* across intensive care and geriatric medicine specialists, although the score remained prognostically significant.[13] In contrast, other studies have reported good inter-rater agreement: one comparing trained research assistants with geriatric experts[34] and another comparing primary care physicians, community nurses, internal medicine doctors and intensivists.[38]

Understanding the ability of the CFS to predict outcomes following aortic valve replacement will inform clinical practice.

Contributors TP: Principal author of protocol and review paper. AL: Coauthor of protocol and review paper and was involved in data extraction. LQ: Screening research studies regarding suitability for inclusion. AS: Assessing quality of included studies. ES: Paper review and editing. AG: Statistical analysis. CP: Paper review and editing and resolving disputes regarding study quality. IC: Paper review and editing. MOC: Conceptualisation, paper review and editing and screening research studies regarding suitability for inclusion. RG: Methodology, paper review and editing, statistical analysis and resolving disputes regarding study inclusion.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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Sample Search Strategy (MEDLINE via Pubmed)

("transcatheter aortic valve replacement"[MeSH Terms] OR "cardiac surgical procedures"[MeSH Terms] OR "aortic valve stenosis"[MeSH Terms] OR "aortic valve replacement"[Title/Abstract] OR "aortic valve implantation"[Title/Abstract] OR "cardiac surgery"[Title/Abstract] OR "cardiovascular surgery"[Title/Abstract] OR "cardiothoracic surgery"[Title/Abstract] OR "TAVR"[Text Word] OR "TAVI"[Text Word] OR "PAVR"[Text Word] OR "PAVI"[Text Word] OR "SAVR"[Text Word]) AND ("frailty"[MeSH Terms] OR "frail elderly"[MeSH Terms] OR "frailty"[Title/Abstract] OR "clinical frailty scale"[Text Word] OR "CFS"[Text Word] OR ("canadian study of health"[Text Word] AND "aging"[Text Word]) OR "CSHA"[Text Word])

Limits: from 2005

Secondary Outcomes

1. In-hospital mortality
2. 30-day mortality
3. 3-month mortality
4. 6-month mortality
5. Early safety (at 30 days)
6. Periprocedural myocardial infarction
7. Coronary obstruction
8. Stroke
9. Acute kidney injury
10. Major vascular complications
11. Minor vascular complications
12. Life-threatening bleeding
13. Major bleeding
14. Minor bleeding
15. Permanent pacemaker implantation
16. Valve-in-valve deployment
17. Cardiac tamponade
18. Conversion to open surgery
19. Functional decline
20. Readmission at 30 days
21. Readmission at 3 months
22. Readmission at 6 months
23. Readmission at 12 months
24. Length of stay in hospital
25. Length of stay in ICU

Events 5-18 are defined in the VARC-2 consensus document.