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REVIEW

Prevention and Reversal of Frailty in Heart Failure
— A Systematic Review —

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Background: Frailty is prevalent in patients with heart failure (HF) and associated with increased morbidity and mortality. Hence, there has been increased interest in the reversibility of frailty following treatment with medication or surgery. This systematic review aimed to assess the reversibility of frailty in patients with HF before and after surgical interventions aimed at treating the underlying cause of HF. It also aimed to assess the efficacy of cardiac rehabilitation and prehabilitation in reversing or preventing frailty in patients with HF.

Methods and Results: Searches of PubMed, MEDLINE and Academic Search Ultimate identified studies with HF patients undergoing interventions to reverse frailty. Titles, abstracts and full texts were screened for eligibility based on the PRISMA guidelines and using predefined inclusion/exclusion criteria in relation to participants, intervention, control, outcome and study design. In total, 14 studies were included: 3 assessed the effect of surgery, 7 assessed the effect of rehabilitation programs, 2 assessed the effect of a prehabilitation program and 2 assessed the effect of program interruptions on HF patients.

Conclusions: Overall, it was found that frailty is at least partially reversible and potentially preventable in patients with HF. Interruption of rehabilitation programs resulted in deterioration of the frailty status. Future research should focus on the role of prehabilitation in mitigating frailty prior to surgical intervention.

Key Words: Frailty; Heart failure; Prehabilitation; Rehabilitation

Frailty has been defined as a "medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death".[1] Despite this consensus definition, opinions on what constitutes frailty and how it should be measured vary widely, as reflected by the various instruments that have been developed to assess and quantify frailty.[2,3] The two most widely cited frailty instruments are the Physical Frailty Phenotype[4] (or a modification of it), which is based on the concept that frailty is a physical syndrome with 5 physical domains, and the deficit accumulation index (or frailty index [FI]), which is based on the concept that frailty constitutes an accumulation of deficits across multiple (up to 70) physical, functional, medical and psychosocial domains.[5]

Regardless of which frailty instrument is utilized, multiple reviews have concluded that frailty is prevalent in patients with heart failure (HF) and associated with multiple adverse outcomes.[6–8] These include increased morbidity and mortality in medically treated patients,[3,9,10] following surgical interventions including elective cardiac surgery,[11] ventricular assist device (VAD) implantation,[12–14] and heart transplantation.[15] Frail patients who survive these procedures typically spend longer in the intensive care unit (ICU) and hospital in general during their recovery. Although most studies of frailty have been conducted in aged populations, studies of frailty in HF indicate that the presence of frailty is associated more with disease severity rather than the chronological age of the patient.[3,9,10] This raises the question of whether HF-associated frailty is reversible following successful treatment with medication, device implantation or surgery, including heart transplantation. Moreover, given the increased procedural morbidity and mortality that frail HF patients experience following major interventions, prehabilitation has been proposed as an approach that may prevent or reverse frailty prior to high-risk interventions. The aim of this systematic review was twofold: first, to assess the reversibility of frailty in patients with HF following major surgical interventions aimed at treating the underlying

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cause of the HF and second, to assess the efficacy of cardiac rehabilitation (CR) and prehabilitation in reversing or preventing frailty before or after high-risk interventions in patients with HF.

Methods

Study Selection Criteria

The Participants, Intervention, Control, Outcomes and Study Type (PICOS) criteria are outlined in **Table 1**. Randomized controlled trials (RCT) and cohort studies were included if the intervention involved a procedure, exercise program or a halt in a program in frail patients with HF. Acceptable comparator groups included patients who were assigned to standard care.

Studies were excluded if they were not in English, were systematic reviews or if they did not include an intervention.

Table 1. PICOS Criteria for Included Studies

	Criterion
Participants	Heart failure patients with either preserved or reduced ejection fraction with frailty
Intervention	Prehabilitation, rehabilitation or procedure
Control	Standard medical care
Outcomes	Reduction in frailty score or other measurement of strength – e.g., 6-min walk test, grip strength, short physical performance battery
Study types	Randomized control trial or cohort study

Search Strategy

A search of PubMed, MEDLINE and Academic Search Ultimate (ASU) from the years 2010–2021 was conducted. The search terms were "heart failure AND frailty AND Rehabilitation OR Prehabilitation". The reference lists of manuscripts that met our inclusion criteria were screened for additional articles that met our inclusion criteria.

Study Selection

After the search was complete, the titles and abstracts were independently screened in accordance with the inclusion and exclusion criteria. Duplicates were also removed. Subsequently, the full-text manuscripts of the abstracts that met our inclusion criteria were assessed for inclusion. Studies were excluded if they were not in English, were systematic reviews or if they did not involve an intervention.

Risk-of-Bias Assessment

There were various study types included in this review, and so several risk-of-bias assessment tools were utilized. Single-arm, uncontrolled, interrupted time-series studies, and cohort studies were assessed using the Risk of Bias In Non-randomised Studies of Interventions (ROBINS-I).[16] Randomized trials were assessing using version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2).[17,18]

Data Extraction

The information extracted from the articles included the number of subjects, median age, sex, population, frailty and quality of life (QoL) measure (e.g., hand grip strength [HGS], short physical performance battery [SPPB]), type of intervention (LVAD, valvuloplasty, rehabilitation, prehabilitation), duration of intervention, and the primary and secondary endpoints. Due to the heterogeneity in population, endpoints, duration and QoL measures, we were unable to perform a meta-analysis; therefore, the data is presented as a qualitative systematic review.

Results

The database searches identified a total of 219 results (PubMed: 138, MEDLINE: 51 and ASU: 30), from which 194 were excluded after assessment of the titles and 9 excluded as duplicates. The remaining 16 full-text papers were assessed, resulting in the exclusion of another 6. Records searched manually resulted in 5 additional studies being identified, from which 1 was excluded, which brought the total number of studies included in this study to 14. A PRISMA flow diagram depicting these results is shown in the **Figure**.[19]

Risk-of-Bias and Quality of Evidence

The risk-of-bias assessments are shown in **Supplementary Tables 1–3**, for single-arm, uncontrolled interrupted time-series studies, cohort studies and randomized trials, respectively. By definition, the quality of evidence that uncontrolled, interrupted time-series studies provide is generally poor. In further detail, 2/7 of these studies showed low level risk-of-bias, 4/7 showed moderate risk-of-bias and 1 had serious risk-of-bias especially, due to its retrospective approach, with serious risk of deviations from the intended intervention. All 4 randomized trials were of moderate quality with moderate overall risk-of-bias, especially given the inability for these trials to blind participants from receiving rehabilitation or standard-of-care.

Frailty Assessment Before and After Major Procedures

We identified 3 studies that assessed frailty before and after major procedural or surgical interventions aimed at treating the underlying cause of the HF[12,14,20] (**Table 2**). Two studies reassessed frailty after LVAD implantation. Chung et al[12] studied 72 patients undergoing LVAD implantation for advanced HF. They reported that reduced HGS prior to LVAD implantation was associated with increased procedural death. In LVAD recipients who survived the operation, they reported significant improvement in HGS by 3 months post-LVAD implantation with further improvement by 6 months. Maurer et al[20] assessed the Fried Frailty Phenotype (FFP) in 29 patients before and after LVAD implantation. They observed a significant improvement in the FFP score, although the improvement was only observed after 3 months. Furthermore, despite an overall improvement in mean frailty score, 53% of their study population were rated as frail at 6 months' follow-up. Jha et al[14] reported significant improvements in FFP and HGS in 13 frail patients 4 months after LVAD implantation and in another 13 frail patients 6 months after heart transplantation. Despite improvements in the group as a whole, 3 of the 13 LVAD supported patients remained frail at follow-up. None of the 13 frail patients who underwent heart transplantation were frail at follow-up.

CR Programs

Seven studies evaluated CR programs in chronic heart disease, including patients with HF (**Table 3**):[21–28] 3 were retrospective studies,[21,22,28] and 4 were prospective randomized trials.[23–27] All 3 retrospective studies recruited elderly

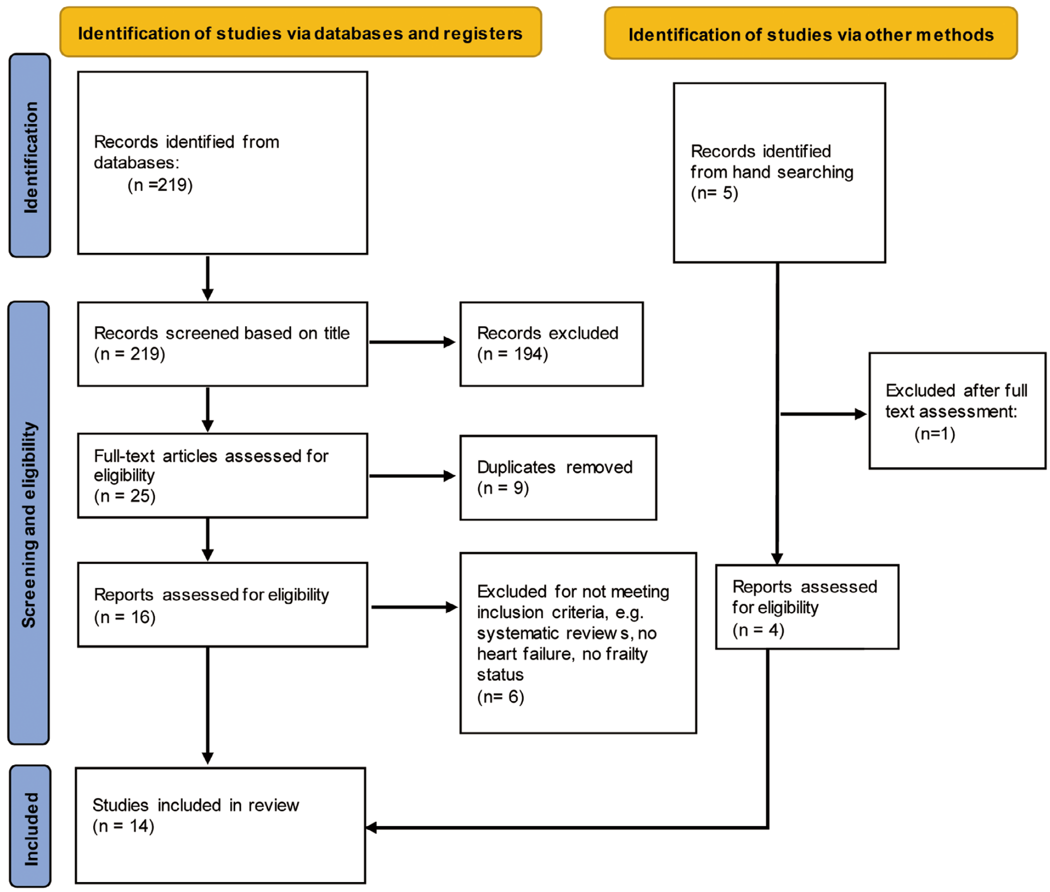

Figure. PRISMA flow chart (adapted from Page MJ, et al[19]).

inpatients with cardiovascular disease. The proportions of the study populations with a diagnosis of HF in these studies were 23%, 53% and 100% respectively. In 2 of the retrospective studies, the authors reported a significant improvement in a range of frailty measures, including HGS, gait speed and Barthel Index following a comprehensive exercise rehabilitation program.[21,28] In addition, Harada et al reported that CR significantly improved nutritional intake and skeletal muscle mass in patients with and without sarcopenia.[21] In another large retrospective study involving 3,277 patients recruited from 15 hospitals across Japan, Kamiya et al reported that patients who participated in a CR program after an admission with acute decompensated HF (ADHF) experienced fewer deaths and HF rehospitalization over a median 2.4 years' follow-up.[22] When stratified by frailty status, CR was found to improve the outcome of patients classified as fit, mildly frail or moderately frail, but there was no benefit observed in those classified as severely frail (FI ≥0.42).[22]

Of the 4 prospective randomized studies, 1 involving patients admitted with ADHF was a small pilot randomized study aimed at assessing the safety and feasibility of conducting CR in these vulnerable patient populations.[26] Reeves et al reported a significantly greater improvement in the SPPB at 6 months in ADHF patients randomized to a 12-week multidomain physical rehabilitation program compared with control patients receiving usual care.[26] In a single-center study from Bulgaria, Papathanasiou[25] randomized 120 frail patients with HF to either high-intensity aerobic interval training (HIAIT) or moderate intensity continuous exercise for 12 weeks. After 6 months, significant improvements were reported in both groups, with the HIAIT group demonstrating significantly greater improvements in 6-min walk distance and QoL. A major limitation of that study, however, was the lack of a validated frailty instrument applied to the study population.[25]

Two prospective multicenter randomized trials compared the effect of a structured exercise training program on top of standard multidisciplinary management in patients recently admitted with ADHF.[23,24] In both trials, the intervention involved a 3-month center-based exercise training program followed by 3 months of home-based exercise. The primary endpoint of both trials was the effect of the intervention on death and rehospitalization; however, both trials also assessed frailty in both the intervention and control groups at baseline and follow-up. Although neither trial found that the intervention reduced the primary endpoint, both trials reported that frailty improved over 6 months.[23,24] In the EJECTION-HF trial, Mudge et al[24] assessed the FI at baseline and 6 months in 256 subjects with a mean age of 62 years. At baseline, 110 (43%) were not-frail (FI ≤0.2), 119 (46%) were frail (FI

Table 2. Characteristics of Included Studies That Assessed the Effect of Procedures on Heart Failure Patient Outcomes

Study	No. of subjects Age (years) % male	Population	Frailty/ QoL measure	Intervention	Primary endpoint	Secondary endpoints	Study type/comments
Chung et al (2014)[12]	72 59±2 89%	CHF LVAD	HGS	LVAD	Significant improvement in HGS at 3 months (18%, P<0.05) and 6 months (46%, P<0.005)		Prospective, single-center, uncontrolled, single-arm interrupted time-series study Low baseline HGS (<25% of body weight) associated with increased operative death
Maurer et al (2017)[20]	29 71±5 72%	>60 years old Destination LVAD All frail	FFP	LVAD	Improved FFP at 6 months from 3.9 to 2.8 (P<0.005)	10% mortality at 6 months	Prospective, multicenter, uncontrolled, single-arm interrupted time-series study Despite overall improvement in the frailty score, 53% still rated as frail at follow-up
Jha et al (2017)[14]	100 51±10 54%	CHF VAD (21 not-frail and 19 frail pre-VAD) HTx (43 not-frail and 17 frail pre-Htx)	FFP HGS	VAD (n=40) HTx (n=60)	Improved FFP at 4 months post-VAD from 4.0 to 1.4 (P<0.001) in 13 frail patients pre-VAD Improved FFP at 6 months post-HTx from 3.3 to 0.8 (P<0.001) in 13 frail patients pre-HTx	Improved HGS in both cohorts	Prospective, single-center, cohort study design Pre-VAD and pre-HTx frailty associated with increased operative death risk

CHF, chronic heart failure; FFP, Fried Frailty Phenotype; GS, gait speed; HGS, handgrip strength; HTx, heart transplantation; LVAD, left ventricular assist device; QoL, quality of life.

>0.2–0.39), and 27 (11%) were very frail (FI ≥0.4). Frailty was more common with older age, female sex, ADHF, worse HF symptoms, and preserved ejection fraction (HFpEF). Mean FI improved significantly by 0.03 units over 6 months, with greater improvements observed in the frail cohorts and a trend towards greater improvement in the intervention group.[24] In the Rehab-HF trial,[23] the authors randomized 349 subjects recently admitted with ADHF to a center-based rehabilitation intervention that included multiple physical-function domains or usual care; 55% were frail and 41% were pre-frail at baseline. After 3 months, both groups demonstrated improvements in a range of frailty measures, with the intervention group having significantly greater improvement in the SPPB score and QoL as assessed by the Kansas City Quality of life Questionnaire compared with the usual care group.[23]

Cardiac Prehabilitation Programs

We identified only 2 published studies of prehabilitation, 1 in frail patients awaiting elective cardiac surgery[29] and 1 in patients with advanced HF awaiting heart transplantation[30] (**Table 4**). Both were small pilot studies. Waite et al[30] evaluated a 6-week home-based exercise program in 22 frail patients awaiting elective cardiac surgery or TAVR. In the 15 patients who underwent reassessment after 6 weeks, the authors reported significant improvement in the clinical frail scale, SPPB score and 6-min walk distance. No adverse events were observed. Gimeno-Santos et al[29] evaluated a hospital-based individually tailored exercise program in 19 patients awaiting heart transplantation. They reported a significant increase in functional capacity, exercise capacity, QoL and emotional well-being in 11 patients who underwent re-evaluation prior to heart transplantation; however, no formal frailty assessment at baseline or follow-up was undertaken in their study population.

Interruption of CR

Finally, 2 observational studies examined the effect of unintended interruption of CR due to the COVID-19 pandemic (**Table 5**). Kato et al[31] followed 15 elderly patients (mean age 80 years) with HF who ceased attending a CR clinic for 7 weeks when the Government of Japan declared a state of emergency during the COVID-19 pandemic, then resumed CR following a lifting of the state of emergency. The authors conducted a range of frailty measures at 3 time points: before and after the state of emergency and 3 months after resuming CR. They observed an increase in the proportion of patients who were classified as frail between the beginning and end of the state of emergency, which was only partially reversed 3 months after resumption of CR. In another study, Taylor et al[32] monitored physical activity from implanted cardiac devices in 317 cardiac patients (mean age 69 years) over an 8-week period spanning 4 weeks prior to and 4 weeks after the announcement of a COVID-19 enforced lockdown; 92% had a previous diagnosis of HF and 56% were classified as frail. The authors reported a precipitous fall in daily physical activity over the first 2 weeks of the lockdown with little improvement in the 3rd and 4th weeks.

Discussion

The major findings of this review are that frailty is at least partially reversible and potentially preventable in patients with HF. The review also found limited evidence and use of prehabilitation in patients with advanced HF.

Effect of Intervention

Although frailty has been associated with increased procedural and surgical deaths in patients with HF undergoing LVAD implantation or heart transplantation, frail patients who survive these procedures generally demonstrate significant reversibility in the frailty phenotype.[12,14,20] In 3 of the studies included in this review, improvement in measures of frailty was only observed at ≥3 months following the surgery.[12,14,20] Despite the overall improvement in frailty status, not all patients who were frail preoperatively became non-frail postoperatively.[14,20] Although the num-

Table 3. Characteristics of Included Studies That Assessed the Effect of Rehabilitation Programs on Heart Failure Patients

Study	No. of subjects Age (years) % male	Population	Frailty/QoL measure	Intervention	Duration
Reeves et al (2017)[26]	27 60–98 39%	≥60 years old ADHF >50% frail 80% cognitive impairment	SPPB	Tailored, progressive, multidomain physical rehabilitation intervention starting in hospital and continuing post-discharge	12 weeks
Harada et al (2017)[21]	322 72±12 58%	Inpatients with cardiovascular disease 28% with sarcopenia	Muscle mass, GS, HGS LWBI Nutritional intake	CR incorporating exercise training, nutrition and medication	NR
van Dam van Isselt et al (2018)[28]	58 79±10 43%	Inpatients with cardiovascular disease 53% CHF	Barthel Index 6-min walk MLWHQ	GR-cardio program	4–6 weeks
Kamiya et al (2020)[22]	3,277 75±15 60%	ADHF	Frailty Index	Exercise-based CR within 3 months of discharge	Up to 5 months
Papathanasiou et al (2020)[25]	120 64±7 58%	Frail, CHF	6-min walk MvO2 MLWHFQ	HIAIT vs. MICT	12 weeks
Mudge et al (2021)[24] EJECTION HF	256 62±14 (36% >70 years old) 76%	Recent (<6 weeks) ADHF stratified by frailty 43% non-frail	Frailty Index	Center-based CR for 3 months followed by home-based CR for 3 months	3 months intervention plus 3 months maintenance
Kitzman et al (2021)[23] Rehab-HF	349 73±8 48%	>60 years old Recent ADHF 55% frail and 41% pre-frail at baseline	SPPB FFP MOCA KCQQ	Exercise rehabilitation (strength, endurance, balance, mobility) vs. control	3 months intervention plus 3 months maintenance

ADHF, acute decompensated heart failure; CFS, clinical frail scale; CHF, chronic heart failure; CR, cardiac rehabilitation; FFP, Fried Frailty Phenotype; GR, geriatric rehabilitation; HIAIT, high-intensity aerobic interval training; HR, hazard ratio; IG, intervention group; KCQQ, Kansas City Quality of life Questionnaire; LOS, length of stay; LWBI, leg weight bearing index; MICT, moderate intensity continuous training; MLWHFQ, Minnesota Living With Heart Failure Questionnaire; MOCA, Montreal Cognitive Assessment; MvO2, myocardial oxygen consumption; NR, not recorded; QoL, quality of life; SMI, skeletal muscle index; SPPB, short physical performance battery.

(**Table 3** continued the next page.)

bers of patients included in these single-center studies were small, it is noteworthy that the proportion of patients who remained frail postoperatively was higher in the study with the oldest study population.[20] Similar findings with regard to reversal of frailty have been reported in patients undergoing kidney, liver, or lung transplantation.[33–35] In a study of 349 patients undergoing kidney transplantation, McAdams-DeMarco et al reported that for the study population as a whole, frailty status worsened over the 1st month post-transplant, returned to baseline in the 2nd month and improved 3 months post-transplant.[34] In 2017, Lai et al reported that frailty status deteriorated in liver transplant recipients over the 3 months post-transplant before improving modestly by 12 months.[33] Montgomery et al reported that pretransplant frailty was largely reversed in patients who undertook a 3-month rehabilitation program after lung transplantation.[35] Collectively, these reports suggest that following any major surgical intervention, frailty is likely to worsen in the first few months and that improvement of frailty status is unlikely to be observed within the first 3 months post-intervention. Although not directly addressed in this review, it is likely that other patient characteristics interact with frailty to contribute to postoperative morbidity and mortality. For example, a frail patient undergoing heart transplantation with a redo sternotomy is likely to have longer ICU and hospital length of stay when compared with a frail patient undergoing primary heart transplant.[36,37] These findings provide a strong rationale for the role of CR in preparing patients (especially those who are frail) who are being assessed for major surgi-

Study	Primary endpoint	Secondary endpoints	Study type/comments
Reeves et al (2017)[26]	Greater improvement in SPPB score (by +1.1) in the intervention group	Reduced all-cause rehospitalization rate in the intervention group correlated with improvement in SPPB	Multicenter, unblinded, randomized control trial 1 : 1 randomization using computer generated list and stratified by enrolling site and heart failure category Control being standard treatment No safety issues
Harada et al (2017)[21]	GS, HGS, LWBI and nutritional intake all increased after exercise training in patients with and without sarcopenia	SMI associated with protein intake and statin use	Retrospective, single-center, cohort study design Sarcopenia associated with older age, female sex and CHF
van Dam van Isselt et al (2018)[28]	Change in frailty/QoL at end of program and at 6 months Significant improvement in all measures	Cardiovascular hospitalization and death at 6 months 10 readmissions and 4 deaths during the program 10/31 CHF patients died	Retrospective, single-center, uncontrolled, single-arm interrupted time-series study Feasibility study
Kamiya et al (2020)[22]	CR associated with significant reduction in both HF hospitalization and death after propensity matching HR 0.77 (95% CI 0.65–0.92)	CR associated with improved mortality and HF hospitalization with mild-moderate frailty but no benefit in severe frailty	Multicenter, retrospective cohort study 26% participated in CR
Papathanasiou et al (2020)[25]	Significant improvement with both exercise programs but greater improvement with HIAIT	No safety concerns	Single-center, randomized controlled trial Block randomization stratified by sex, age, NYHA Class and cause of CHF As part of large-sized single-center, prospective randomized controlled trial No validated frailty instrument used in the recruitment of patients to the trial
Mudge et al (2021)[24] EJECTION HF	Improved Frailty Index from 0.23 to 0.20 at 6 months (P<0.001) with greater improvement in the frail groups	No significant difference in hospitalization or death at 12 months	Post-hoc analysis of a prospective, randomized trial of single-center-based exercise training in addition to multidisciplinary management (MDM) vs. MDM alone
Kitzman et al (2021)[23] Rehab-HF	Improved SPPB score in intervention group	No significant difference in hospitalization or death at 6 months	Multicenter, randomized controlled trial 82% retention and 67% adherence to the intervention Greater improvement in frail group

cal interventions.

Effect of CR in Frail HF Patients

Recent systematic reviews of CR in patients with HF have concluded that CR reduces HF-associated and all-cause rehospitalization and improves exercise performance and QoL.[38,39] However, these studies have been conducted predominantly in young, male subjects with HF with reduced EF and stable mildly symptomatic (NYHA Class I–II) HF. In contrast, 4 studies of CR in frail HF patients included in this review recruited patients during or shortly after a hospital admission for ADHF with more symptomatic HF (NYHA Class II–IV), and included a higher proportion of women and patients with HFpEF.[22–24,26] In most studies, CR entailed a 3-month program incorporating exercise training components aimed at increasing mobility, endurance and muscle strength. Inclusion of other program elements such as nutritional supplementation/advice and psychosocial support was more variable. All programs were hospital-based with direct supervision of the participants by trained staff. Most studies concluded that CR improved frailty, although the response was variable depending on the frailty instrument used.

Effect of Cardiac Prehabilitation on Frail HF Patients

Prehabilitation is an attractive concept for frail heart transplant patients being assessed for advanced HF therapies; however, we were only able to find 2 published studies that addressed this issue.[29,30] Both studies reported that exercise training was safe, improved exercise performance and also improved frailty status in the study that measured this.[30] These findings suggest a role for prehabilitation in both reversing and preventing frailty in this high-risk population. There are 2 prospective randomized trials examining the role of prehabilitation prior to LVAD or heart transplantation currently listed on the US National Library of Medicine clinical trials.gov website as complete: PREHAB-HTx (NCT02957955) and PREHAB-HF (NCT03580759). One trial states that only 2 subjects were enrolled while the other enrolled 6 subjects prior to completion. The reason for low enrolment is unclear, but a possible contributor is that many patients listed for LVAD or heart transplanta-

Table 4. Characteristics of Included Studies That Assessed the Effect of Prehabilitation Programs on Heart Failure Patient Outcomes

Study	No. of subjects Age (years) % male	Population	Frailty/ QoL measure	Intervention	Duration	Primary endpoint	Study type/ comments
Kato et al (2021)[31]	15 80±6 27%	≥65 years old, CHF patients attending cardiac rehabilitation	Kihon CL SPPB HGS GS STS	Covid-induced lockdown Combined endurance and resistance training	Pre- and post-interruption and 3 months post resumption of cardiac rehabilitation	Significant deterioration in frailty status post-interruption with trend to improvement 3 months after resumption	Prospective, single-center, uncontrolled, single-arm interrupted time-series study
Taylor et al (2021)[32]	311 69 77%	Patients with implanted devices 92% CHF 56% frail (PRISMA-7 ≥3)	Device PA monitor	Covid-induced lockdown	4 weeks post lockdown	Abrupt decrease in PA during 1st 2 weeks of lockdown	Prospective, multicenter, uncontrolled, single-arm interrupted time-series study

CHF, chronic heart failure; Kihon CL, Kihon checklist; GS, gait speed; HGS, handgrip strength; PA, physical activity; PRISMA-7, Program of Research on Integration of Services for the Maintenance of Autonomy Questionnaire; QoL, quality of life; SPPB, short physical performance battery; STS, sit-to-stand test.

Table 5. Characteristics of Included Studies That Assessed the Effect of Exercise Programs Interruptions on Heart Failure Patient Outcomes

Study	No. of subjects Age (years) % male	Population	Frailty/ QoL measure	Intervention	Duration	Primary endpoint	Secondary endpoints	Study type/ comments
Waite et al (2017)[30]	22 NR NR	≥65 years old Frail patients awaiting elective heart surgery	CFS 6 min SPPB	Home-based Prehab exercise program with balance and strength training	≥6 weeks	Significant Improvement in CFS, 6-min walk distance, GS, SPPB	Change in 6-min walk distance associated with hospital LOS	Prospective, single-center, uncontrolled, single-arm interrupted time-series study No safety issues
Gimeno-Santos et al (2020)[29]	11 55±11 82%	Stable CHF Awaiting heart transplant	6-min walk MvO2 MLWHFQ	Hospital-based Prehab exercise endurance and resistance training + nutritional support	8 weeks	Improved 6-min walk (P=0.06), MvO2 MLWHFQ		Prospective, single-center, uncontrolled, single-arm interrupted time-series study Main aim was preventing deterioration in physical condition while awaiting heart transplant

CFS, clinical frail scale; GS, gait speed; LOS, length of stay; MLWHFQ, Minnesota Living With Heart Failure Questionnaire; MvO2, myocardial oxygen consumption; NR, not recorded; QoL, quality of life; SPPB, short physical performance battery.

tion live remotely from the transplant center, making center-based rehabilitation impractical. Other potentially important variables include poor patient motivation,[40] and safety concerns, particularly for home-based programs.[41] Despite these concerns, Singer et al recently reported the safety and efficacy of a home-based, mobile health technology-facilitated intervention to treat frailty in patients listed for lung transplantation.[42]

Effect of Interruption of CR on Frailty in HF Patients

Two studies reported the effect of an interruption of CR caused by the COVID-19 pandemic on physical activity and frailty. Both highlighted that the benefits of CR can rapidly degrade when physical activity is restricted.

Review Limitations

We did not assess the role of nutritional supplementation; however, this has been the subject of a recent systematic review by Nichols et al[43] who assessed the effect of protein and essential amino acid supplementation on muscle strength and performance in people with chronic HF. Interestingly, they found that it did not improve strength, but may increase 6-min walk distance, muscle mass and QoL. They concluded that further studies are needed to confirm this finding, as only 5 RCTs and 1 cohort study met their inclusion criteria. This suggests that a tailored prehabilitation program for HF patients should aim to combine muscle strength training as well as protein supplementation to achieve the best outcomes possible for the patient.

Conclusions

Frailty is associated with increased morbidity and mortality in patients with advanced HF undergoing LVAD implantation and heart transplantation. Despite the increase in procedural risk, frailty is largely reversible in most patients following these procedures. CR is safe and effective at improving frailty and QoL in patients with advanced HF; however, interruption of CR can lead to rapid deconditioning. Cardiac prehabilitation is a promising approach to reversing and preventing frailty prior to major surgical interventions. However, further research is required to establish its safety and efficacy.

Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Files

Please find supplementary file(s);
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