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Research Article

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Feasibility of Conducting a 6-Months Long Home-based Exercise Program with Protein Supplementation in Elderly Community-dwelling Individuals with Heart Failure

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Abstract

Objective: Cardiac cachexia is a condition associated with heart failure, particularly in the elderly, and is characterized by loss of muscle mass with or without the loss of fat mass. Approximately 15% of elderly heart failure patients will eventually develop cardiac cachexia; such a diagnosis is closely associated with high morbidity and increased mortality. While the mechanism(s) involved in the progression of cardiac cachexia is incompletely established, certain factors appear to be contributory. Dietary deficiencies, impaired bowel perfusion, and metabolic dysfunction all contribute to reduced muscle mass, increased muscle wasting, increased protein degradation, and reduced protein synthesis. Thus slowing or preventing the progression of cardiac cachexia relies heavily on dietary and exercise-based interventions in addition to standard heart failure treatments and medications.

Methods: The aim of the present study was to test the feasibility of an at-home exercise and nutrition intervention program in a population of elderly with heart failure, in an effort to determine whether dietary protein supplementation and increased physical activity may slow the progression, or prevent the onset, of cardiac cachexia. Frail elderly patients over the age of 55 with symptoms of heart failure from UAMS were enrolled in one of two groups, intervention or control. To assess the effect of protein supplementation and exercise on the development of cardiac cachexia, data on various measures of muscle quality, cardiovascular health, mental status, and quality of life were collected and analyzed from the two groups at the beginning and end of the study period.

Results: More than 50% of those who were initially enrolled actually completed the 6-month study. While both groups showed some improvement in their study measures, the protein and exercise group showed a greater tendency to improve than the control group by the end of the six months.

Conclusion: These findings suggest that with a larger cohort, this intervention may show significant positive effects for elderly patients who are at risk of developing cardiac cachexia.

Keywords: Exercise; Protein supplementation; Heart failure; Cardiac cachexia; Aging; Weakness; Physical function

Introduction

Age-associated changes occur at different rates in various systems of the body over decades with an ultimate reduction of physical strength and function [1-4]. Often, the problems experienced by geriatric patients are due to a combination of physiological changes and age-associated diseases that further accelerate the decline, resulting in an increased health-burden on the individual and ultimately the society.

A common aging change that occurs in the skeletal muscles is termed sarcopenia and is characterized by loss of skeletal muscle mass that occurs at a rate of approximately 1% per year after age forty and can be exacerbated by sedentary behavior, poor nutritional intake, and pathological conditions [1,5-10]. Loss of skeletal muscle fibers is replaced by adipose tissue with subsequent reduction in strength [4,8].

Cachexia is a complex, clinical syndrome characterized by rapid involuntary weight loss, sarcopenia and weakness, and occurs in approximately 15-40% of patients with HF [11-16]. A diagnosis of cachexia is associated with high morbidity with increased risk of falls, frequent hospitalizations, nursing home placement, as well as increased mortality [15]. While the mechanism(s) involved in the progression of cardiac cachexia are incompletely established, certain factors appear to contribute to its development (Figure 1). Dietary deficiencies, especially of protein, and impaired bowel perfusion contribute to reduced muscle mass and increased muscle wasting, possibly due to reduced digestive abilities and increased protein loss from the gut [6,17,18]. Metabolic dysfunction may also contribute to cardiac cachexia through increased muscle metabolic rate, increased protein degradation, reduced protein synthesis, and increased proinflammatory cytokines and neuroendocrine factors [6,17]. Thus, slowing or preventing the progression of cardiac cachexia likely relies heavily on dietary and exercise-based interventions in addition to HF therapies and medications. Such interventions typically include not only an increase in the total number of calories consumed each day, but a pointed effort to increase the protein intake of the individual to 1.5-2.2 g/kg body weight per day [7,19-22]. Additionally, increased physical activity, both aerobic and resistance exercise, has been demonstrated to reduce sarcopenia, improve muscle strength and cardiovascular function and reduce metabolic dysfunction [20,23,24].

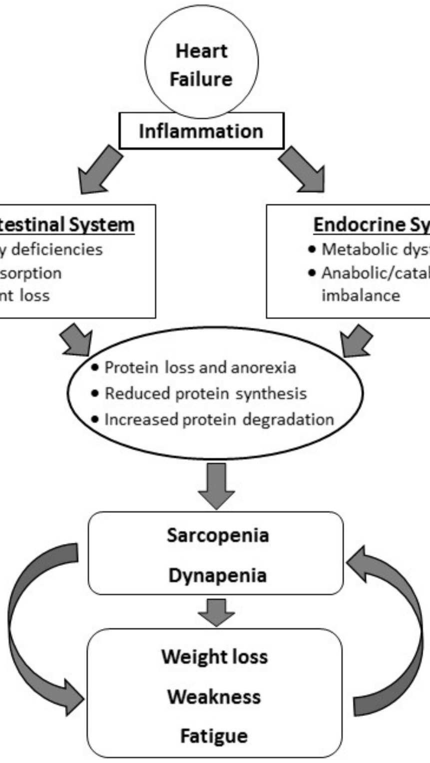

Figure 1: Schematic illustrating the progression of heart failure to cardiac cachexia. Heart failure induces a state of systemic inflammation, inciting dysregulation and imbalances in the gastrointestinal and neuroendocrine systems. This leads to progressive muscle degradation both in terms of muscle quantity and muscle quality.

In our study described in this paper we tested the feasibility of a home-based exercise and protein supplementation program in non-obese elderly with HF at risk for cardiac cachexia. We chose to address dietary protein intake as it has been demonstrated by Wolfe et al and other investigators that older adults often become deficient in certain amino acids, specifically leucine, which is vital for growth and maintenance of muscle [21,22,25-27].

In addition, the elderly also suffer from anabolic resistance which limits their ability to synthesis muscle as compared to younger adults using the same dose of protein [7,22].

While exercise is known to help ameliorate muscle wasting, many elderly people do not participate in regular physical activity due to a great variety of barriers including disability or difficulty in performing exercises, safety concerns, lack of instruction, inability to participate in group exercises or travel to a fitness center [28,29]. Our hypothesis was that a home-based, light exercise program plus protein supplementation might improve the function and quality of life of elderly patients with HF.

Methods

The University of Arkansas for Medical Sciences Institutional Review Board reviewed and approved this prospective pilot study (IRB protocol # 136344). This was a six month long randomized, controlled study. Eleven frail elderly patients from the Reynolds Institute on Aging at UAMS were enrolled in one of two groups, intervention or control, to assess the effect of exercise and protein supplementation on functional outcomes and quality of life (Figure 2, Table 1).

All enrollees were over the age of 55 with BMIs between 19-30 and symptoms of HF, New York Heart Association (NYHA) categories 2-3 (Table 1). HF diagnoses included all subtypes of chronic HF, including systolic, diastolic, heart failure with preserved ejection fraction (HFPEF), right, left, or combined heart failure.

Data on various measures of muscle strength, cardiovascular health, mental status, and quality of life were collected and analyzed from the two groups at the beginning and end of the study period.

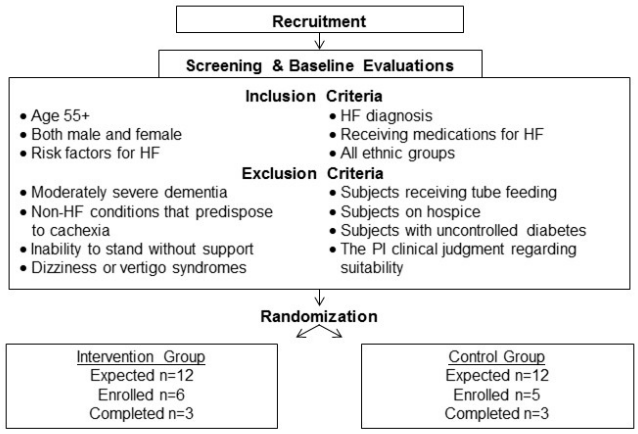

Figure 2: Flow diagram of study design and subject enrollment. UAMS patients 55 years and older with heart failure were invited to participate in this study.

We developed an exercise DVD customized for the elderly with varying degrees of disability so that subjects would find the exercises safe and easy to follow. The DVD was based on the guidelines from the National Institute on Aging (NIA) and developed under the instruction of an exercise physiologist, an experienced fitness trainer and a team of geriatricians who also provided consultation.

The exercises (aerobic and resistance), targeted the core muscle group, especially, the key muscles groups of the upper and lower extremities involved in ambulation, balance, lifting and functional independence.

In addition, four elderly attendees (2 men and 2 women) of the Ottenheimer Fitness and Rehabilitation Center volunteered to assist in the development of the DVD. In this real-life DVD, the study physician performed the exercises in front of the subjects and they followed at their own pace.

In addition to the program being recorded on DVDs, all exercises were provided in a pamphlet version for those study subjects who did not have a DVD player at home. When the pamphlet was given to the subjects, all exercises were demonstrated by the study physician to ensure that subjects understood how to perform all of the exercises in the program.

Group	Control	Exercise+Protein	All
Gender (n) All enrolled subjects			
Male	2	3	5
Female	3	3	6
Race/Ethnicity (n) All enrolled subjects			
African American	2	2	4
White, Non-Hispanic	3	4	7
Study Status (n) All enrolled subjects			
Enrolled	5	6	11
Completed	3	3	6
Age (SE)*	75 (3.79)	84 (0.58)	80 (2.64)
BMI (SE)*			
Baseline (SE)	26.78 (1.35)	23.58 (1.66)	25.18 (1.19)
End of study (SE)	27.04 (1.31)	23.70 (2.07)	25.37 (1.33)
Approximately 45% of enrollees were male, and approximately 57% were African American. The average age of subjects who completed the study differed by 9 years from the control to the protein and exercise group. Additionally, the BMI of those who completed the study differed by over 3 units from the control to the exercise/protein group. *BMI and Age for subjects who completed the study (n=6).			

Table 1: Study subject demographics.

Screening examination and evaluations

A medical examination by the study physician was performed in all subjects at baseline and at 6 months. Those in the intervention group also received routine examinations at 2 and 4 months. The examination lasted 30 minutes and was comprised of questions pertinent to signs and symptoms of HF, with a focused physical examination of the cardiac and musculoskeletal system. Vital signs (pre- and post-functional evaluations) consisted of the following: pulse Ox, respiratory rate, pulse rate, and blood pressure (BP).

Functional evaluations consisted of following: get-up and go, grip strength, leg extension, and 6 minute walking test (6MWT). Cognitive testing was measured using the Saint Louis University Mental (SLUMs) Exam and assessed the following: Attention and Working Memory; Cognition; Executive Function; Language; Mental Health; Reasoning and Problem Solving [30]. All evaluations and measures were performed by trained research staff. Instructions for each evaluation were given in both verbal and written formats.

Intervention group: Exercise + protein

Each subject in the intervention group received an exercise DVD, and a commercially available nutritional supplement Premier 100% whey isolate powder (Premier Nutrition Inc, San Francisco, CA). Subjects were provided with a log book to record their diet and exercise routines. All study supplies, including the DVD and protein supplementation were provided free of charge to all subjects for the entire length of the study. The subjects were asked to perform 20 minutes of exercise 6 days per week, with a warm up and cool down routines, by following the instructions on the exercise DVD.

Aerobic and resistance exercises were performed on alternating days with allowance for one rest day per week. Protein supplementation was optimized for each subject after analyses of their normal diet by a research dietician. Each patient was provided written instructions on how to achieve the target protein consumption of 1.5 g/kg per day. Patients also received weekly phone calls from the PI to check for compliance with the exercise program and protein supplementation.

Baseline and end-study evaluations on the patients included functional tests, signs and symptoms of HF, cognitive test and SF36.

Control group: Usual care

The control group received usual care from their PCPs. At the end of the study after six months, the subjects in the control group were provided nutritional consultation by the study dietician and an exercise DVD and/or written exercise material was provided to them.

The Control group received the same baseline and end-study evaluations as the intervention group.

Statistical analysis

The mean (±SE) of the baseline study measures, the end of study measures, and their difference (post-study minus pre-study) were calculated by treatment group. For calculations by treatment group, the difference for each measure was calculated as differenc=post-pre. These differences were then compared between treatment groups to determine if the change from pre to post differed in individuals in control group or the protein group.

The Wilcoxon Rank Sum Test that was used to evaluate if treatment groups showed significant differences. The Mann-Whitney U was also used with a p-value <0.05 considered statistically significant. All statistical analyses were carried out in R (Vienna, Austria), version 3.1.0. A p-value <0.05 was considered statistically significant [https://www.r-project.org/.].

Results

More than half of subjects who signed up for the study completed the study (Figure 2). Four subjects completed the baseline procedures and removed themselves from the study at a later date, citing reasons including: too far to travel for follow-up study visits, study activities take more time than expected and unexpected family health issues. One subject signed up for the study, but did not return for baseline study procedures and was lost to follow-up. Of those who completed the study, half were women, and 4 of the 6 were African American. The average age of those in the control group was 73 ± years, while the average age for those in the protein and exercise group was 80 ± years (Table 1). For those participants who completed the study, the average ages for the control and protein/exercise groups were 75 ± and 84 ± respectively.

The mean baseline BMI for the control group was 24.3, and for the intervention group was 25.4. For those participants who completed the study, the mean baseline BMI for the control and protein/exercise groups were 26.8 and 23.6, respectively (Table 1).

Measure	Differences from pre and post by groups			
	Control		Exercise+Protein	
	Mean	SE	Mean	SE
Get up and go (seconds)	2.83	1.42	1.82	0.91
Grip strength, Right (lbs)	5.21	2.6	3.87	1.93
Grip strength, Left (lbs)	5.38	2.69	1.27	0.63
Quadriceps Strength (lbs)	22.58	11.29	2.5	1.25
6 Minute Walk (ft)	-141.82	70.91	-161.07	80.53
Pulse rate (Before 6 MWT)	3	1.5	0.33	0.17
Pulse rate (After 6 MWT)	3.67	1.83	-0.33	0.17
Respiration rate (Before 6 MWT)	0.5	0.25	0	0
Respiration rate (After 6 MWT)	-0.5	0.25	1.6	0.8
*Systolic BP (Before 6 MWT)	14.67	7.33	-2.17	1.08
*Systolic BP (After 6 MWT)	-3.17	25.25	-14.5	7.25
*Disatolic BP (Before 6 MWT)	9.75	28.54	-6.83	3.42
*Diastolic BP (After 6 MWT)	1.5	0.75	-15.33	7.67
Pulse Ox (Before 6 MWT)	-0.58	0.29	0.17	0.08
Pulse OX (After 6 MWT)	1.42	0.71	-1.33	0.67

Note: The small sample size and a mean age difference of nine years between the groups could have affected the results. In spite of this the protein group tended to improve in some of the cardiovascular test items (*). All results were NS.

Table 2A: Changes in health outcomes; physical measures.

There were 28 measures that were collected on all subjects at the beginning and end of the study (Tables 2A and 2B). Both the control and protein groups appeared to improve in a number of the functional activities by the end of the study period, but there were no significant differences in the measures of physical function, cardiovascular function or signs and symptoms of heart failure between the groups. However, the patients in the protein group appeared to perceive less fatigue, an improved overall general health, and reduced limitation of physical function at the end of six months. The patients in the control group did not improve in the SF 36 scores (Table 2B).

Measure	Differences from pre and post by groups			
	Control		Exercise+Protein	
	Mean	SE	Mean	SE
Heart failure symptoms				
*Fatigue (0-3)	0.5	0.25	0.2	0.1
*Shortness of breath (0-3)	0.25	0.13	-0.47	0.23
*Chest pain (0-10)	3.5	1.75	0	0
Palpitations (0-3)	-0.75	0.38	0.13	0.07
SLUMS	-3	1.5	-1.83	0.92
SF-36 results				
Physical functioning	-5	2.5	-28.33	14.17
*Energy/Fatigue	-4.17	2.08	12.83	6.42
*Emotional well-being	-14.33	7.17	-4.27	2.13
Social functioning	-10.42	5.21	-33.75	16.88
Pain	5.21	2.6	-6.67	3.33
*General health	-17.08	8.54	8.33	4.17
*Limits/Physical health	-6.25	3.13	25	12.5
Limits/Emotional problems	-22.22	11.11	-44.44	22.22

Heart failure symptoms: Higher values=increased severity. SF-36 results: lower value=increased impairment. The small sample size and a mean age difference of nine years between the groups could have affected the results. In spite of this the protein group tended to improve in some of test items (*). All results were NS.

Table 2B: Changes in health outcomes; self-reported and cognitive measures.

Discussion

The purpose of this pilot study was to test the feasibility of a home-based exercise and protein supplementation program for elderly at risk of developing cardiac cachexia. While enrollment numbers were low, more than 50% of enrolled subjects completed the 6 month long study. For those in the exercise and protein group, even participants who could not complete the study stated that they had enjoyed the program, and reported numerous positive feelings regarding strength, self-esteem and greater health awareness. The intervention group also showed a tendency towards greater overall improvement compared to the control group by the end of the six month period, suggesting that a larger cohort might demonstrate significant effects for elderly who are at risk of developing cardiac cachexia.

It is well known that exercise may improve both systolic and diastolic BP in the elderly, as both an acute and chronic effect [31,32]. Furthermore, exercise has been shown to improve HF symptoms [33]. However, elderly patients frequently have several barriers for starting an exercise program and continuing it on a regular basis. This is partly due to limitations of transportation to an exercise facility, limited guidance regarding the type and frequency of exercise needed for optimal benefit, and physical limitations such as arthritis and/or other disabilities [34]. Our exercise program helped to address these issues by enabling the elderly to exercise in the comfort of their own home, using a program that was developed to be safe and suitable for elderly HF patients. Additionally, giving the participants' better access to an in-home exercise program, as well as following up with regular phone calls from the study physician, may have led to the increase in the positivity of their perceived physical and mental health, as indicated by the change in SF-36 scores. Participating in an exercise routine has been shown to be a positive driving force in an elderly individual's perception of their health status [35]. Socially engaging those who are following an exercise routine serves to enforce the positive effects of the participation, and may encourage them to feel well enough physically and emotionally to pursue social relationships beyond their normal activities [35,36]. This increase in positive health perception might have led to the perception of increased energy, reduced fatigue, increased health, and a reduction in the limitations their physical issues placed on their normal life activities in the intervention group. Generating a positive relationship with an exercise routine may encourage elderly with HF and those at risk of developing cardiac cachexia to work toward preventing and slowing cachexia progression.

Additionally, higher protein intake could be beneficial for cardiovascular function and thereby reduce HF symptoms [7,24,37-39]. However, with the various digestive issues that HF patients may encounter as the disease progresses, normal levels of protein may not suffice. Branched-chain amino acids (BCAAs) have shown promise in improving the health of the elderly [24,25,37,40]. Treatment with BCAAs supplementation has been shown to decrease heart rate, preserve body weight, delay the deterioration of cardiac function, and extend the life span in various animal models [41-43]. It was suggested that the mechanism for this benefit lies in the enhancement of innate antioxidant defense genes and a reduction in the production of reactive oxygen species [41,42]. Additionally, protein supplementation may serve to provide a general state of improved health just due to improved nutrition. Many elderly are at risk for nutritional deficiencies due to several factors including changes in oral health, malabsorption, changes in taste perception, and even social factors such as decreased ability to afford nutritious food items, decreased ability to prepare food and decreased opportunity for shopping [2]. Protein supplementation offers the opportunity for the elderly HF patient to conveniently enhance their normal dietary intake and optimize their nutrition to delay age-related sarcopenia and ameliorate or prevent cardiac cachexia.

Limitations

Our study had several limitations including a rather small sample size. However, this was only a pilot study with an objective to test the feasibility of the study design and patient compliance of the frail, elderly patients over six months. Additionally, of the patients who completed the study, the control groups were on average nine years younger and had a higher BMI than the protein group. This might have led to the smaller declines in function in the control group versus the protein and exercise. A younger cohort with better health may also, in part, have contributed to the greater improved scores for grip strength and quadriceps strength in the control group over the protein and exercise group. For elderly people with ongoing health issues, 6 months is typically a very long time to commit to a study and more frequent communication with the subjects between visits might ensure better compliance. Furthermore, the intervention was not placebo controlled or blinded.

However, some of the strengths of the study included the design of the in-home exercise program by an interdisciplinary team with input and participation by the elderly subjects. In collaborating with exercise specialists trained to work with elderly patients, we were able to develop a DVD suitable for home use by the frail elderly individuals. This was evidenced by the positive feedback received by several subjects.

Conclusion

This pilot study showed that a home-based exercise and protein supplementation program might be a feasible method for studying interventions to slow and stabilize the progression of HF as well as possibly prevent cardiac cachexia. Larger sample sizes, slightly shorter study duration will be helpful in studying the usefulness of this intervention to improve the lives of elderly HF patients and prevent the development or progression of cardiac cachexia.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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