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RESUSCITATION

#### **Clinical paper**

### Subjective factors of depressive symptoms, ambulation, pain, and fatigue are associated with physical activity participation in cardiac arrest survivors with fatigue

#### Young Joo Kim<sup>a, \*</sup>, Vicky Joshi<sup>b</sup>, Qiang Wu<sup>c</sup>

<sup>a</sup> 600 Moye Blvd, MS668, HSB3305, Department of Occupational Therapy, College of Allied Health Sciences, East Carolina University, Greenville, NC, 27834, USA

<sup>b</sup> Danish Knowledge Centre for Rehabilitation and Palliative Care (REHPA), University of Southern Denmark, and Odense University Hospital, Denmark

<sup>c</sup> 600 Moye Blvd, 2209 East Carolina Heart Institute, Department of Biostatistics, College of Allied Health Sciences, East Carolina University, Greenville, NC, 27834, USA

#### Abstract

Aim: This study aimed to examine the associations between participation in physical activities and objective and subjective factors modifiable by rehabilitation in cardiac arrest survivors with fatigue.

**Methods:** Participants in a clinical feasibility study (N=19) completed several subjective (patient-reported) and objective outcome measures on one occasion only. The associations between an individual's level of participation in physical activities (Participation Objective Participation Subjective) and their levels of cognition (Computer Assessment of Mild Cognitive Impairment), body movement (Keitel Functional Test), depressive symptoms (Center for Epidemiologic Studies Depression Scale), ambulation and pain (Health Utilities Index Mark 3), and fatigue impact (Modified Fatigue Impact Scale) were explored. Pearson's correlation coefficientr was calculated for all associations, except for body movement (Spearman's correlation coefficient  $r_s$ ). **Results:** As hypothesized, we found weak-to-moderate, positive factor of ambulation ability (r=0.501). We found moderate, negative associations between participation in physical activities and subjective factors of cognition in physical activities and subjective factors of depressive symptoms (r=-0.590), pain (r=-0.495), physical fatigue impact (r=-0.591), and psychosocial fatigue impact (r=-0.557).

**Conclusion:** The moderate, negative and positive associations between participation in physical activities and subjective factors suggest that subjective complaints of depressive symptoms, ambulation ability, pain, and fatigue impact may be important factors when seeking to improve participation in physical activities. In particular, addressing physical and cognitive endurance as well as perceptions of fatigue may hold the key to increasing physical activity in cardiac arrest survivors with fatigue.

Keywords: Cardiac arrest, Fatigue, Participation, Physical activity, Subjective factors, Rehabilitation

\* Corresponding author at: 600 Moye Blvd, MS668, HSB3305, Department of Occupational Therapy, College of Allied Health Sciences, East Carolina University, Greenville, NC, 27834, USA.

E-mail address: kimyo15@ecu.edu (Y.J. Kim).

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#### Introduction

The American Heart Association recently stated the need for a coordinated plan for long-term rehabilitation to improve participation in daily activities among cardiac arrest (CA) survivors affected by physical, cognitive, and emotional problems after CA.<sup>1</sup> Improving participation in physical activities can bring positive long-term health benefits including decreased mortality, chronic disease prevention, and improved quality of life.<sup>2</sup> Cardiac rehabilitation is effective in increasing the steps per day and the proportion of participants categorized as physically active in people with heart disease.<sup>3</sup> However, despite these positive effects, cardiac rehabilitation graduates have still shown long hours of sedentary behavior which is associated with increased triglycerides and body mass index.<sup>4</sup> Interventions aimed at increasing activity levels at workstations or during television viewing for office workers or people with obesity have shown to be effective in reducing sitting time or increasing energy expenditure.<sup>5</sup> However, none of the interventions were targeted specifically at people with cardiac problems, and these interventions are not applicable to those who are unemployed or do not have high television viewing time.

Considering the positive effects of physical activity and the negative effects of sedentary time, addressing participation at all levels of physical activity during post-CA rehabilitation would be beneficial for CA survivors' health and well-being. To do so, it is imperative to understand the factors related to physical activity in CA survivors. For example, studies have shown that higher functional classification level and physical and cognitive function are positively associated with physical activity in people with heart failure.<sup>6–8</sup> More than half of CA survivors experience fatigue that negatively impacts their performance and participation in daily activities.<sup>9,10</sup> The concept of fatigue has been described as including both an individual's perceptions of fatigue and performance fatigability.<sup>11</sup> Fatigability is the inability to sustain physical and mental activity due to fatigue, whereas perceptions of fatigue refers to the feeling of tiredness that individuals feel during physical and mental activities.<sup>12</sup> It is possible that CA survivors are at risk of experiencing limited participation in physical activities due to both types of fatigue.9

The purpose of this study was to examine the association between participation in physical activities by CA survivors with fatigue and a range of both objective and subjective factors that were considered as modifiable by post-CA rehabilitation. In the study, physical activity is defined as "any bodily movement produced by skeletal muscles that requires energy expenditure" according to the World Health Organization (WHO),<sup>13</sup> therefore, all activities are included except sedentary behavior. It was hypothesized that participation in physical

activities would be positively associated with cognition, body movement, and ambulation ability and negatively associated with presence of depressive symptoms, pain, and fatigue in CA survivors with fatigue.<sup>14,15</sup>

#### **Methods**

#### Study design

We conducted a cross-sectional analysis using data from a singlegroup feasibility study on the effectiveness of a fatigue intervention for CA survivors with fatigue.<sup>16</sup> Nineteen participants completed a range of outcome measures one week before commencing the intervention. The original feasibility study was approved by the Institutional Review Board of the University of Pittsburgh (PRO09110375).

#### Participants

Participants were 19 adults who had a CA at least three months prior to the study, reported moderate-to-severe fatigue (4 or greater out of a possible range of 1–7) according to the Fatigue Severity Scale (FSS), <sup>17</sup> had access to a phone, lived within 150 miles of the research center, could comprehend and speak English, demonstrated intact cognition, <sup>16</sup> and lived in the community. The rationale for the study eligibility criteria is available elsewhere.<sup>16</sup> The median FSS score of 19 participants was 5.56 with IQR of 4.67–6.67. Informed consent was obtained from all participants. One participant did not complete the feasibility study, but her pretest data was available for this cross-sectional analysis.

#### Measures

Demographic and medical information was collected using the studyspecific forms. Objective factors were measured by performance tests, and subjective factors by self-report, reflecting participants' perception of their status. A trained occupational therapist administered all measures on the same day. The chosen factors are constructs that can be modified by rehabilitation professionals,<sup>18,19</sup> hence, demographic or medical factors were not included. The *a priori* hypothesized associations between participation in physical activities and objective and subjective factors are provided in Table 1.<sup>20</sup>

#### Participation in physical activities

The Participation Objective scale and the Participation Subjective scale of the Participation Objective Participation Subjective (POPS) measure objective and subjective participation in 26 activities in five

Table 1 – A pr	iori associations	between partic	ipation in physica	al activities and	objective and	subjective facto	rs.

	Participation in physical activities - Participation Objective Scale
Cognition - CAMCI	A weak, positive (r=0.10-0.39) association
Body movement - KFT	A moderate, positive ( $r_s$ =0.40–0.69) association
Depressive symptoms - CES-D	A moderate, negative (r = $-0.69$ to $-0.40$ ) association
Ambulation ability - HUI-3 Ambulation	A moderate, positive (r=0.40-0.69) association
Pain - HUI-3 Pain	A moderate, negative (r = $-0.69$ to $-0.40$ ) association
Fatigue - MFIS Physical, Cognitive, and Psychosocial subscales	A moderate, negative (r = $-0.69$ to $-0.40$ ) association
CAMCI: Computer Assessment of Mild Cognitive Impairment. KFT: Keitel Function	nal Test. CES-D: Center for Epidemiologic Studies Depression Scale. HUI-3:

Health Utilities Index Mark 3. MFIS: Modified Fatigue Impact Scale.

areas: domestic life, interpersonal interactions and relationships, major life, transportation, and community, recreational, and civic life. These 26 activities were considered as physical activity according to the WHO definition.<sup>21</sup> In our study, the Participation Objective scale was used to measure participation in physical activities by asking participants to self-report on the amount of activity the participant was undertaking. Both Participation Objective and Subjective scales have shown good test-retest reliability and were strongly correlated with another participation measure involving complex physical activities.<sup>22,23</sup> In addition, the Participation Subjective scale was more strongly correlated with self-reported quality of life and depression measures than the Participation Objective scale in people with traumatic brain injury. This indicates the Participation Objective and Subjective scales measure different constructs, demonstrating their construct validity.<sup>22</sup> A higher score indicates greater participation.

#### **Objective factors**

Computer Assessment of Mild Cognitive Impairment (CAMCI) is a self-administered, computer-based assessment designed to detect mild cognitive impairment and consists of seven subtests. Subtests assess verbal, visual, and working memory, and executive function as well as cognitive abilities related to everyday functioning. CAMCI has been found to be highly reliable, sensitive, and specific for mild cognitive impairment detection in older adults without known neurological diseases.<sup>20,24</sup> A higher score indicates better cognitive ability.

Keitel Functional Test (KFT) is a performance-based assessment measuring body movement involving upper and lower extremities and the spinal column using 24 items. A trained observer administers fifteen items on each side of the body separately and nine items on both sides together. KFT showed good reliability and construct validity of moderate to good correlations with pain and activity difficulty measures in people with rheumatoid arthritis.<sup>25</sup> A higher score indicates more restricted range of motion and limited strength.

#### Subjective factors

Center of Epidemiology Study Depression Scale (CES-D) is a selfreported, 20-item scale that measures the presence and severity of depressive symptoms during the past week. It has demonstrated robust psychometric properties in middle-aged US population.<sup>26</sup> A higher score indicates more depressive symptoms.

Health Utilities Index Mark 3 (HUI-3) is a generic, preferencebased utility,<sup>27</sup> health-related quality of life assessment measuring multi-attributes of health status. In our study, we used the singleattribute scores for seven ambulation items and two pain items to represent the self-reported ability of ambulation and self-reported pain severity affecting the ability to perform activities in the past 4 weeks.<sup>28</sup> HUI-3 has shown convergent validity with other quality of life measures in people with cardiovascular diseases.<sup>29</sup> A higher score indicates better ambulation ability and lower pain interference.

Modified Fatigue Impact Scale (MFIS) measures the impact of fatigue on daily function using 21 questions divided over three subscales: physical, cognitive, and psychosocial. Participants rated their perceptions of fatigue in the past 4 weeks on a scale 0–4 (never to almost always). MFIS has been used to study various conditions, including heart failure, traumatic brain injury, and multiple sclerosis.<sup>30–32</sup> Psychometric properties for MFIS show excellent test-retest reliability and excellent concurrent validity with the Expanded Disability Status Scale and Fatigue Severity Scale.<sup>33,34</sup> A higher score indicates greater fatigue impact.

#### Statistical analyses

Data for all assessments but KFT were normally distributed when examined visually and by Kolmogorov-Smirnov test. Therefore, we calculated Spearman's correlation coefficient  $r_s$  to examine the association between Participation Objective scale of POPS and KFT and Pearson's correlation coefficient *r* for all other associations. For all analyses, an alpha level of 0.05 was used, and 95% confidence intervals for correlation coefficient were calculated. In addition, scatter plots of the correlations were created for visual representation. All analyses and plots were completed using IBM SPSS 26 Statistics.

#### Results

Participant demographic and medical information is provided in Table 2. Mean age was 53.84 years (SD=11.34), and all participants were white. Half the participants had greater than high school education and only four were engaged in paid-work at the time of study participation. The median (range) days since CA was 113.5 (96–2518). The majority of participants had suffered an out-of-hospital CA, and half had received bystander cardiopulmonary resuscitation and therapeutic hypothermia.

Weak to moderate, positive associations between Participation Objective scale of POPS and CAMCI (r=0.370, P=.12), KFT ( $r_s$ =0.414, P=.08), and HUI-3 ambulation (r=0.501, P=.03) were found. In addition, moderate, negative associations were found between Participation Objective scale of POPS and HUI-3 pain (r=-0.495, P=.03), MFIS psychosocial subscale (r=-0.557, P=.01), CES-D (r=-0.59, P=.008), MFIS cognitive subscale (r=-0.591, P=.008), and MFIS physical subscale (r=-0.629, P=.004) (Table 3).

The scatter plots (Figs. 1 and 2) show that, as Participation Objective scale of POPS increased (better physical activity), CAMCI total percentile (better cognition) and HUI-3 ambulation and pain (better ambulation ability and pain) increased. In addition, as Participation Objective scale of POPS decreased (worse physical activity), KFT total scores (worse body movement), CES-D (worse depressive symptoms), and MFIS physical, cognitive, and psychosocial subscales (worse fatigue impact) increased.

#### Discussion

In this study, we examined the associations between participation in physical activities and rehabilitation-modifiable objective and subjective factors in CA survivors with fatigue. A weak, positive association was found between participation in physical activities and cognition. In addition, participation in physical activities was moderately, positively associated with body movement and ambulation ability, and moderately, negatively associated with subjective reports of depressive symptoms, pain, and physical, cognitive, and psychosocial fatigue impacts. Therefore, all *a priori* hypotheses were met.

The prevalence of cognitive impairments after CA ranges from 13% to 100%.<sup>35</sup> Cognitive impairment in people with cardiac conditions can negatively affect their exercise capacity and participation in physical activities, particularly complex activities that are cognitively demanding.<sup>14,36</sup> Conversely, physical activity can improve cognition in older adults.<sup>37</sup> Therefore, it is not surprising that we found a positive association between participation in complex activities and cognition.

	Range	Participants
Age. vears. M (SD)	35 – 73	53.84 (11.34)
White (%)	_	19 (100)
Male (%)	_	10 (52.6)
Highest education completed (%)		· · ·
Less than high school	_	1 (5.3)
High school	_	9 (47.4)
Partial college	_	4 (21.1)
Full college	_	3 (15.8)
Graduate/professional training	_	2 (10.5)
Engaged in paid-work		
Before CA (%)	_	9 (47.4)
After CA (%)	_	4 (21.1)
Married (%)	_	9 (47.4)
Living alone (%)	_	4 (21.1)
Living environment		
House (%)	_	15 (78.9)
Apartment or condominium (%)	_	3 (15.8)
Mobile home (%)	-	1 (5.3)
Out-of-hospital CA (%) (N=18)	_	12 (66.7)
Cardiac etiology (%) (N=18)	_	16 (88.9)
Days since CA (median) (N=18)	96 – 2518	113.5
Witnessed CA (%) (N=18)	-	11 (61.1)
Bystander CPR (%) (N=18)	-	9 (50.0)
Ventricular fibrillation/tachycardia rhythm (%) (N=18)	-	17(94.4)
Hypothermia achieved (%) (N=18)	-	9 (50.0)
Duration of coma, days, $M$ (SD) (N = 9)	1 – 5	2.89 (1.17)
Duration of intubation, days, $M(SD)$ (N = 13)	2 – 26	5.31 (6.52)
Length of stay (N=18)		
Intensive care unit, days, M (SD)	1 – 17	5.22 (3.72)
Total inpatient, days, M (SD)	2 – 28	10.50 (5.81)

# Participation in physical activity and body movement showed a moderate, positive association. In a study involving older adults, no associations were found between shoulder and hip range of motion and self-reported physical activity.<sup>38</sup> However, the relationships between the flexibility-focused interventions and functional performance, mostly including gait and balance, may have been inconclusive due to the variability of the intervention protocols and outcome

## Table 3 – Correlations between ParticipationObjective Scale score and objective and subjectivefactors (N = 19).

	Participation Objective Scale		
	r or r <sub>s</sub>	P (95% CI)	
CAMCI	0.370	.12 (10–.70)	
KFT	0.414 <sup>a</sup>	.08 (72–.05)	
CES-D	-0.590	.008 (-82 to18)	
HUI-3 Ambulation	0.501	.03 (.06–.77)	
HUI-3 Pain	-0.495	.03 (.05–.77)	
MFIS Physical	-0.629	.004 (84 to24)	
MFIS Cognitive	-0.591	.008 (82 to18)	
MFIS Psychosocial	-0.557	.013 (80 to13)	

CAMCI: Computer Assessment of Mild Cognitive Impairment. KFT: Keitel Functional Test. CES-D: Center for Epidemiologic Studies Depression Scale. HUI-3: Health Utilities Index Mark 3. MFIS: Modified Fatigue Impact Scale. <sup>a</sup>  $r_{\rm fs}$ . measures.<sup>39</sup> Unlike range of motion measurements on single or multiple movements, KFT assesses the overall body movement using functional tasks, such as supine to long sit. Therefore, body movement examined by KFT may have more closely resembled the movement required for physical activities in POPS, resulting in the moderate, positive association. As participation in complex activities typically involves whole body movement, functional ranges of motion of the whole body may be more important to consider in the rehabilitation of physical activities in CA survivors with fatigue.

In our study, self-reported depressive symptoms were moderately and negatively associated with participation in physical activities. Depressive symptoms include many factors that can lead to physical inactivity, such as lack of energy and motivation; therefore, this result was expected and has been observed in various populations including older adults with heart failure and primary care patients.<sup>8,40</sup> Considering that approximately 13% of CA survivors experience depression,<sup>41</sup> this moderate, negative association is important to note during the rehabilitation process.

Self-reported ambulation ability was moderately and positively associated with participation in physical activities. This indicates CA survivors with limited ambulation ability may have the disadvantage of decreased physical activity participation. In older adults with cardiac conditions in an inpatient setting, gait speed has been shown to be significantly and positively associated with average steps and energy expenditure per day.<sup>42</sup> Two further studies involving healthy young and older women, and community dwelling older adults found significant and positive associations between gait speed and their level of physical activity.<sup>43,44</sup> Many POPS activities require standing



Fig. 1 – Scatter plots with trend lines for correlations between Participation Objective Scale score and objective factors. A. Computer Assessment of Mild Cognitive Impairment. B. Keitel Functional Test.

and walking, as do the physical activities we engage in every day, for example, shopping for groceries. To minimize the impact of ambulation difficulty on participation in physical activities, rehabilitation programs for CA survivors should consider including screening and assessment, and remediation and compensation of ambulation problems, such as Timed Up and Go test and Dynamic Gait Index, and gait training using meaningful activities and environmental modification.

We found a moderate, negative association between pain interference and participation in physical activities. Although pain is one of the most frequent symptoms individuals experience prior to CA,<sup>45</sup> pain post CA has been sparsely explored and reported in this population.<sup>1</sup> However, considering that 29% of the general population describe chronic pain that lasts longer than 6 months,<sup>46</sup> it would not be surprising to find a higher prevalence of pain in CA survivors. In a meta-analysis study on people with low back pain, decreased risk of low back pain was significantly associated with overall participation in physical activities.<sup>47</sup> In addition, in people with heart failure, pain intensity, discomfort, and interference were significantly and negatively associated with functional performance and functional capacity.<sup>48</sup> Exercise has been shown to be effective for pain management in various health conditions.<sup>11</sup> Although it would be difficult to determine the effect of pain on physical activity level,<sup>11</sup> it is hypothesized that pain may also negatively affects physical activity levels in CA survivors based on significant associations shown in other populations.47,48

In our study, we found moderate, negative associations between participation in physical activities and fatigue impacts. Similar associations have been shown in multiple populations. In individuals with heart failure, fatigue distress and fatigue interference were the strongest predictors of energy expenditure on physical activities.<sup>15</sup> In older adults, self-reported fatigue severity was associated with 12 mins per day less physical activity level compared to those without fatigue.<sup>49</sup> In our study, physical fatigue impact showed the highest negative association with physical activities, followed by cognitive and psychosocial fatigue impact. Considering that many of the POPS activities are related to physical ability and social participation, this was an expected result. However, cognitive fatigue impact was also associated with participation in physical activities. Cognitive fatigue impact in MFIS reflects the fatigue impact on cognitive ability such as attention, memory, and thinking speed. Therefore, this association may be better understood in regards to the association between cognition and participation in physical activities we found. Our finding also indicates the importance of cognitive endurance in increasing participation in physical activities in addition to physical endurance. It is understandable for healthcare professionals to focus on improving physical endurance or minimizing perceptions of physical fatigue; however, addressing cognitive endurance and perceptions of cognitive fatigue could be as important as physical impact in effectively increasing physical activity participation.

Survival after CA is increasing, as is the number of CA survivors needing rehabilitation due to physical and cognitive deficits. The factors examined in our study can be addressed by rehabilitation professionals through remediation and/or compensatory approaches. Both rehabilitation approaches can reduce the impact of those factors to increase physical activity participation. Depressive symptoms may not be completely eliminated; however, their impact can be reduced through the use of mindfulness therapy or cognitive behavioral therapy techniques.<sup>50</sup> In addition, there are few treatment strategies to reduce fatigue severity, but the impact of fatigue on daily activities may be reduced by incorporating energy saving or compensatory strategies.<sup>16</sup>

While our study findings address important aspects for CA survivors living with fatigue, there are several limitations. We used a convenient sampling method to target a very specific population of CA survivors with a relatively wide range of time since CA and with no information available on time to return of spontaneous circulation. The study sample size was also small. Hence, our results may not be generalizable to the general CA survivor population. In addition, the outcome measure POPS focuses on participation in complex activities and does not include physical exercise itself. Therefore, readers should not interpret the results in relation to participation in only exercise. However, we would argue that these complex physical activities are more relevant to the daily life of CA survivors living in the community because they occupy a greater proportion of the day compared to only moderate-to-vigorous intensity physical activity. The factors examined were self-reported or objectively measured through instrumentation or observation. It may have been a more equivalent and comprehensive comparison if ambulation was objectively measured through observation or cognition was measured both objectively and subjectively: however, this was not possible for the many factors that are inherently subjective, such as pain and fatique.



Fig. 2 - Scatter plots with trend lines for correlations between Participation Objective Scale score and subjective factors. A. Center for Epidemiologic Studies Depression Scale. B. Health Utilities Index Mark 3 - Ambulation. C. Health Utilities Index Mark 3 - Pain. D. Modified Fatigue Impact Scale – Physical Scale. E. Modified Fatigue Impact Scale – Cognitive Scale. F. Modified Fatigue Impact Scale – Psychosocial Scale.

#### Conclusion

As hypothesized, participation in physical activities was moderately, positively associated with the objective report of body movement and the subjective report of ambulation ability, and moderately, negatively associated with the subjective reports of depressive symptoms, pain, and fatigue impact in CA survivors with fatigue. A smaller, positive association between participation in physical activities and cognition was found. Subjective complaints of depressive symptoms, ambulation ability, pain, and fatigue impact may be important factors to improve participation in physical activities. In particular, addressing physical and cognitive endurance as well as perceptions of fatigue may hold a key to increasing physical activity in CA survivors with fatigue. Future research should investigate these associations among a broader group of CA survivors. These modifiable factors should also be included in rehabilitation interventions targeted at improving participation for CA survivors with fatigue.

#### **Conflict of interest**

The authors have no conflict of interest.

#### **CRediT authorship contribution statement**

Young Joo Kim: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration, Funding acquisition. Vicky Joshi: Conceptualization, Writing original draft, Writing - review & editing. Qiang Wu: Conceptualization, Writing - original draft, Writing - review & editing.

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#### **Appendix A. Supplementary data**

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resplu.2020.100057.

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