Title: Comparison of Self-Reported Physical Activity between Survivors of Out-of-Hospital Cardiac Arrest and Patients with Myocardial Infarction without cardiac arrest: a case-control study

Short title: Physical Activity in Cardiac Arrest Survivors and Patients with Myocardial Infarction

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Abstract

Aims: To investigate whether out-of-hospital cardiac arrest (OHCA) survivors had lower levels of self-reported physical activity compared to a non-cardiac arrest control group with myocardial infarction (MI), and to explore if symptoms of anxiety, depression, kinesiophobia (fear of movement) and fatigue were associated with a low level of physical activity.

Methods: Predefined case–control sub-study within the international Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest (TTM2) trial. OHCA survivors at 8 of 61 TTM2 sites in Sweden, Denmark and the United Kingdom were invited.

Participants were matched 1:1 to MI controls. Both OHCA survivors and MI controls answered two questions on self-reported physical activity, categorized as a low, moderate, or high level of physical activity, and questionnaires on anxiety and depression symptoms, kinesiophobia, and fatigue 7 months after the cardiac event.

Results: Overall, 106 of 184 (58%) eligible OHCA survivors were included and matched to 91 MI controls. In total, 25% of OHCA survivors and 20% of MI controls reported a low level of physical activity, with no significant difference (p=0.13). Symptoms of kinesiophobia and fatigue were significantly associated with a low level of physical activity in both groups. OHCA survivors had significantly more kinesiophobia compared to MI controls (18% versus 9%, p=0.04), while levels of anxiety and depression symptoms and fatigue were similar.

Conclusion: OHCA survivors had similar levels of physical activity compared to matched MI controls. High level of kinesiophobia and fatigue were associated with a low level of physical activity in both groups.

Trial registration: Registered at ClinicalTrials.gov: NCT03543332, date of registration June 1, 2018.

1:1 **Introduction**

One third of the out-of-hospital cardiac arrest (OHCA) survivors in the Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest (TTM2) trial reported a low level of physical activity equal to or below the recommended threshold for primary prevention.[1] Primary prevention of cardiovascular events according to the World Health Organization and the European Society of Cardiology involves undertaking regular physical activity, at a level of

moderate intensity ≥150 min/week, vigorous intensity ≥75 min/week, or a combination of both, to decrease all-cause mortality and morbidity.[2-4]

The most common cause of OHCA is ischaemic heart disease including myocardial infarction (MI).[5, 6] Following MI, the European Association of Preventive Cardiology encourages patients, including survivors of cardiac arrest (CA) caused by MI, to engage in physical activity to prevent future cardiac events.[7] Adherence to physical activity guidelines[2, 7] can increase survival after MI and reduce the risk of rehospitalization.[8-10] Participation in supervised, exercise-based cardiac rehabilitation during the initial months following the cardiac event, at least three days per week, at moderate to high intensity, for a minimum of 20 minutes per session, aims to enhance participants' physical activity levels.[7] Similarly to patients suffering from MI, OHCA survivors of non-MI cause are also likely to benefit from physical activity,[1] but whether they have different frequency and intensity of physical activity has not been explored.

OHCA survivors often experience additional physical,[11] cognitive,[12] emotional problems[13] and fatigue[14] related to brain injury secondary to the circulatory arrest.[15] The European Resuscitation Council and European Society of Intensive Care Medicine recommend follow-up for all cardiac arrest survivors, including screening for cognitive impairment, emotional problems and fatigue.[16] OHCA survivors may therefore have higher risk of a low level of physical activity, compared to MI patients, for whom current exercise-based cardiac rehabilitation programs have been designed.[7] In the TTM2 trial, OHCA survivors with obesity and problems with mobility and processing speed had a lower level of physical activity, while no associations were found between age, sex, and

general physical and cognitive function.[1] There are however other potential risk factors that may be associated with a low level of physical activity in OHCA survivors and MI controls, such as symptoms of anxiety, depression,[11, 17] fatigue[18] and kinesiophobia[19] which have not yet been investigated. Kinesiophobia is defined as an excessive, irrational, and debilitating fear of physical movement.[20] It is vital to identify patients with low physical activity who have suffered cardiac events with or without cardiac arrest, as they may have an increased risk of suffering new cardiac events.[9, 10]

The primary aim of this sub-study, performed in conjunction with the TTM2 trial, was to investigate whether OHCA survivors had lower levels of self-reported physical activity, compared to a non-cardiac arrest MI control group, 7 months after the cardiac event. The secondary aim was to explore if symptoms of anxiety, depression, kinesiophobia and fatigue were associated with a low level of physical activity in both groups 7 months after the cardiac event.

Our pre-defined hypotheses[21] were:

1. OHCA survivors have lower levels of self-reported physical activity compared to the MI control group.
2. Symptoms of anxiety, depression, kinesiophobia and fatigue are associated with a low level of physical activity in both OHCA survivors and MI controls.

2 Methods

2:1 Procedure and study design

This was a predefined case–control explorative sub-study of the TTM2 trial. The TTM2 trial investigated if targeted temperature management at 33°C was superior to early treatment of fever (≥37.8°C).[22, 23] There were no differences between the two temperature groups in primary (death), secondary (poor functional outcome)[23] or exploratory (cognition and societal participation)[24, 25] outcomes. Therefore, we regarded the OHCA survivors as one group for this sub-study.

In the TTM2 trial, all survivors (n=939) were invited to a face-to-face follow-up at 6 months after the OHCA. By the end of the follow-up, eligible survivors at 8 of 61 TTM2 sites (Table A) in Sweden, Denmark and the United Kingdom were invited to the present sub-study and provided verbal as well as written information about its focus on physical activity (ClinicalTrials.gov: NCT03543332). The sub-study was performed at sites declaring a special interest in the field, and with relevant resources and infrastructures. For those who consented, an additional follow-up meeting was scheduled within 4 weeks. Questionnaires were distributed by mail before or during the additional meeting. If the participant had not filled out the questionnaires, there was the option to fill them in after the meeting and send them back in a pre-paid envelope.[21]

OHCA survivors in the sub-study were matched to MI controls at an intended 1:1 ratio. The MI controls were invited to a similar follow-up approximately 7 months after their cardiac event and received the same questionnaires as the OHCA survivors before, during or after the visit.

Participants were enrolled between July 2018 and January 2021. This sub-study was coordinated with another TTM2 sub-study investigating neuropsychological function.[26, 27]

2:2 Participants

The TTM2 trial included comatose adults who suffered an OHCA of presumed cardiac or unknown cause. The main exclusion criteria were an interval from return of spontaneous circulation to screening of more than 180 minutes, unwitnessed cardiac arrest with asystole as the initial rhythm, and if there were limitations in care.[23] Additional exclusion criteria for this sub-study were >80 years of age, a Clinical Frailty Scale[28] score >7 before the OHCA, a pre-arrest dementia diagnosis, inability to speak the local language well enough to complete the assessments without assistance from an interpreter, active drug abuse, and being a wheel-chair user.[21]

The control group consisted of participants with a recent history of acute MI and emergency percutaneous coronary intervention but without cardiac arrest. The controls were matched for country, time point of hospitalization (± 4 weeks), sex and age (best match). MI controls were recruited at one site in Sweden, Denmark, and United Kingdom respectively and were only part of the two sub-studies on physical activity[21] and neuropsychological functioning.[26] The rationale for selecting participants with a history of MI as controls was based on the presumption that they had experienced a traumatic cardiac event and cardiac ischaemia, with the same potential pre-event cardiovascular risk factors, but without the risk for hypoxic/ischemic brain injury.

In local cardiac registry data (Lund, Sweden), 20% of the MI patients had a low level of physical activity, 52% a moderate and 28% a high level.[29] As described in the study protocol, we made an assumption that 30% of the OHCA survivors would have a low level of physical activity, 58% a moderate and 12% a high level of physical activity.[21] Based on this, a priori sample size and power calculation, with a power of >80% and a significance level of p=0.05, showed that 105 participants in each group were needed to demonstrate statistical differences in levels of physical activity (low, moderate and high) between OHCA survivors and MI controls.[21]

2:3 Ethics

The TTM2 trial was undertaken according to the Code of Ethics of the World Medical Association (Declaration of Helsinki).[30] Ethical review boards of all participating sites in Sweden, Denmark and the United Kingdom approved the TTM2 trial sub-study protocol. Written informed consent to participate in the sub-study was obtained before the follow-up for both OHCA survivors and MI controls.

2:4 Outcome and outcome assessments

A protocol for outcome reporting in the sub-study has been published.[21] Changes from the original study protocol are presented in the Supplemental material. They were all minor and non-critical changes.

2:4:1 Self-reported physical activity

The primary outcome self-reported physical activity was assessed by two questions asking how many days in the past week the participant completed physical activity of moderate intensity (30 minutes or more) and of vigorous intensity (20 minutes or more) (Table 1). The questions were followed by examples of moderate and vigorous intensity physical activities. Alternative answers ranged from 0 to 7 days for both moderate and vigorous intensity physical activities.[31] These answers were categorized into three groups: low, moderate, and high level of physical activity (Table 2, Supplement Table B). A low level of physical activity corresponds to a physical activity level below the recommended threshold for primary prevention.[2] A moderate level achieves the recommended threshold. A high level includes both moderate and vigorous intensity physical activity in accordance to secondary prevention during exercise based cardiac rehabilitation.[7] Responses to these questions have been shown to correspond to objective assessments of physical activity in both OHCA survivors and MI patients.[32, 33] Self-reports could be used to identify OHCA survivors with low levels of physical activity.[32]

2:4:2 Variables of anxiety, depression, kinesiophobia and *fatigue*

Information on symptoms of anxiety, depression, kinesiophobia and fatigue were obtained by self-reported questionnaires. For symptoms of anxiety and depression, the Hospital Anxiety and Depression Scale (HADS) is recommended post cardiac arrest[16] and shown evidence to be a valid instrument in a cardiac population.[34] It ranges from 0 to 21, with a score >7 indicating clinically significant difficulties.[35] The Tampa Scale for Kinesiophobia Heart (TSK-Heart) is a 17-item questionnaire used to detect kinesiophobia, with a total score ranging from 17 to 68. Values >37

represent a high level of kinesiophobia.[36] TSK-Heart has adequate reliability and validity for patients with coronary artery disease.[36] It is recommended to screen for fatigue post cardiac arrest[16] and post MI.[37] The Multidimensional Fatigue Inventory (MFI-20) is a 20-item questionnaire assessing fatigue severity in five dimensions; General fatigue, Physical fatigue, Mental fatigue, Reduced motivation and Reduced activity. Total scores are calculated for each dimension separately with higher scores indicating a higher level of fatigue.[38]

Socio-demographical and medical characteristics for the OHCA survivors including age and sex, OHCA and in-hospital variables were obtained from the TTM2 trial database, and for MI controls from their medical records and at the sub-study follow-up meeting.

3: Statistical analysis

Descriptive statistics of the variables are presented with numbers and percentages for binary and categorical variables, and for continuous variables as mean and standard deviation (SD) when normally distributed, or median and quartiles [Q1, Q3] when non-normally distributed. Potential differences between OHCA survivors and MI controls were investigated with the non-parametric Mann-Whitney U-test for continuous data and the Chi-square test for categorical data.

Since the primary goal was to identify and compare the OHCA survivors and MI controls with a low physical activity, potentially running an increased risk of suffering a new cardiac event, [9, 10] the results of the two questions on physical activity were dichotomized into a low versus a moderate/high level as the dependent outcome variable. Univariable logistic regressions models

were then used to identify risk factors associated with a low level of physical activity for OHCA survivors and MI controls separately. Due to too small groups, multivariable logistic regressions models were performed with only 3 of the 8 scales reflecting the 3 different questionnaires: HADS-A, TSK-Heart and Physical fatigue. The Variance Inflation Factor was for the model in OHCA survivors 1.35-1.37 and in MI controls 1.17-1.24 indicating no problems with multicollinearity. Effect sizes are reported as odds ratios (OR) with 95% confidence intervals (CI). P-values <0.05 were used to indicate statistically significant differences. Data was computerized and analyzed by the IBM® Statistical Package for Social Sciences (SPSS) 29.

4: Results

Overall, 106 of 184 (58%) eligible OHCA survivors were included in this sub-study (Sweden n=55, United Kingdom n=32 and Denmark n=19) together with 91 matched MI controls (Sweden n=52, the United Kingdom n=27 and Denmark n=12). A flow-chart of inclusion is presented in Figure 1.

The OHCA survivors and the MI controls were matched for age and were similar in educational attainment. In total, 58% of the OHCA survivors had MI as cause of their OHCA. The OHCA survivors had less chronic hypertension compared to MI controls (64% versus 80%). Further demographic and clinical characteristics are reported in Table 3 and Supplement Table C.

There was no significant difference in levels of physical activity between OHCA survivors and MI controls (p=0.13). Of the OHCA survivors, 25% (n=27/106) reported a low level of physical

activity compared to 20% (n=18/91) of the MI controls. A moderate level of physical activity was reported by 49% of OHCA survivors (n=52/106) and 44% of MI controls (n=40/91), and a high level of physical activity was reported by 26% (n=28/106) and 36% (n=33/91), respectively.

There were no significant differences in symptoms of anxiety (median 3 [Q1:1, Q3:6] versus 4 [Q1:2, Q3:7], p=0.18) or depression (median 2 [Q1:1, Q3:4] versus 2 [Q1:1, Q3:6], p=0.18) between OHCA survivors and MI controls , with 16% versus 18%, reporting anxiety symptoms and 13% versus 9% reporting depressive symptoms. Kinesiophobia was, however, significantly more common in OHCA survivors compared to MI controls (median 29 [Q1:24, Q3:36] versus 27 [Q1:23, Q3:32], p=0.04), and reported by 18% versus 9%. In addition, there were no significant differences in general fatigue (median 10 [Q1:8, Q3:13] versus 11 [Q1:8, Q3:15], p=0.17), physical fatigue (median 11 [Q1:7, Q3:14] versus 10 [Q1:8, Q3:4], p=0.84), mental fatigue (median 8 [Q1:4, Q3:10] versus 8 [Q1:4, Q3:11], p=0.51), reduced activity (median 10 [Q1:6, Q3:13] versus 9 [Q1:7, Q3:13], p=0.71) or reduced motivation (median 7 [Q1:5, Q3:10] versus 9 [Q1:6, Q3:12], p=0.54) between OHCA survivors and MI controls (Table 4).

The univariable logistic regression models showed that neither symptoms of anxiety nor depression were significantly associated with a low level of physical activity in OHCA survivors or MI controls. However, symptoms of kinesiophobia were associated with a low level of physical activity in both OHCA survivors (TSK-Heart: OR=1.09, 95% CI 1.02–1.16, p=0.01) and MI controls (TSK-Heart: OR= 1.09, 95% CI 1.02–1.18, p=0.01). For OHCA survivors, all five

dimensions of fatigue were associated with a low level of physical activity. For MI controls, four dimensions of fatigue were associated with a low level of physical activity (Table 5).

The multivariable logistic regression models showed that HADS-A, TSK-Heart and Physical fatigue were significantly associated with a low level of physical activity in OHCA survivors but none in MI controls (Table 6).

5: Discussion

Contrary to our first hypothesis[21], there was no statistically significant difference in the proportions of OHCA survivors and MI controls reporting a low level of physical activity. A possible explanation may be that OHCA survivors and MI controls share many characteristics, such as age, sex and pre-event cardiovascular risk. The additional risk of hypoxic brain injury caused by the cardiac arrest did not increase the risk in our sample for a low level of physical activity.

Among the general population, one in four adults worldwide and one in three adults in Europe do not meet the recommendation of physical activity per week.[2, 39, 40] These numbers are difficult to compare directly to a specific population. We assumed that 30% of the OHCA survivors and 20% of the MI controls would have a low level of physical activity as presented in the study protocol.[21] Our results confirmed this assumption for the MI controls, while less OHCA survivors in our study had a low level of physical activity. It should however be noted that fewer OHCA survivors in this sub-study reported a low level of physical activity compared to all survivors in the main TTM2 trial (25% versus 34%)[1] due to a possible selection bias (Supplement Table A).

Our results exhibited that Kinesiophobia and Fatigue were associated with a low level of physical activity among both OHCA survivors and MI controls, although we had expected a stronger association based on clinical experience and knowledge from other studies.[18, 41] Furthermore, our second hypothesis was only partly accepted,[21] since symptoms of anxiety and depression were not associated with a low physical activity level. This could be due to a selected sample included in the sub-study and the sample may not be representative of the entire OHCA and MI population. Contrary to our pre-defined hypothesis, anxiety symptoms increased the physical activity level in the multivariable model among OHCA survivors and needs to be further investigated. This could be due to cardiac anxiety in OHCA survivors[42] which needs to be further investigated.

A Swedish study reported kinesiophobia amongst 20% of coronary artery disease patients, mostly MI patients, 6 months after the cardiac event.[43] Those who reported a high level of kinesiophobia had significantly lower degree of physical activity.[41] We found less kinesiophobia among our MI controls using the same questionnaire (9%) and may be due to better awareness of kinesiophobia today or a selection bias in the study sample. Numerically, the two groups were similar. Interestingly, we found a significant difference with more kinesiophobia in the OHCA survivors compared to the MI controls. Cardiac events such as OHCA and MI may both be terrifying and painful, causing existential threat[44, 45] and fear of movement.

Fatigue after a cardiac arrest has previously only been examined in a small study population, indicating that fatigue was associated with decreased physical activity.[18] However, in a previous study individuals reporting fatigue after a MI were almost four times more likely to report a low

level of physical activity compared to those without fatigue.[46] An interesting finding of the present study was that there were no significant differences in any of the five sub-scales of the MFI-20 between OHCA survivors and MI controls. A damaged myocardium after a MI, coupled with decreased heart rate and blood pressure due to medication, may significantly decrease the cardiac function and contribute to fatigue.[46] In this study, 73% of the participating OHCA survivors had reduced left ventricular ejection fraction of the heart. In addition, 64% of OHCA survivors and 80% of MI controls had chronic hypertension and current pharmaceutical treatment for high blood pressure, possible contributing to the fatigue reported by both groups.

A strength of this study was that it was performed in conjunction with a large well-designed randomized clinical trial according to a specified protocol.[21] In addition, the main outcome was obtained by using two questions of physical activity[31] that have shown significant agreement with objective physical activity assessment after both OHCA[32] and MI.[33] Another strength is that we were able to obtain detailed information about symptoms of anxiety, depression, kinesiophobia and fatigue in both OHCA survivors and matched MI controls. To our knowledge, this is the first study investigating kinesiophobia in OHCA survivors.

There are numbers of limitations. First, the results may not be generalizable to all cardiac arrest populations since we only included survivors of OHCA from cardiac or unknown cause unconscious at time point of randomization. Second, survivors included in this sub-study had a higher level of physical activity compared to the entire group of survivors in the TTM2 trial.[1] This may be due to selection bias and differences between countries, since only 3 of 14 countries participated in the sub-study. Another possible reason is that only the most motivated and

physically active OHCA survivors participated. Third, we did not meet our goal to include 105 MI controls.[21] This was mainly related to the Covid-19 pandemic that transiently halted clinical research at all study sites. Furthermore, 58% of the OHCA survivors had MI as cause of their arrest, producing a discrepancy in our background variables with the MI controls who all had suffered from an acute MI. Somewhat fewer OHCA survivors with MI as cardiac arrest cause than non-MI OHCA survivors had a low level of physical activity (23% versus 30%) (Supplement Table D). Finally, we have no details about the content of the rehabilitation interventions, for example frequency, intensity, duration or type of activities, which theoretically may have influenced the results.

The European Association of Preventive Cardiology recommends physical activity according to primary prevention after the initial cardiac rehabilitation period.[7] Individuals with a low level of physical activity and symptoms of kinesiophobia and/or fatigue should be identified, preferably within 3 months after the cardiac event,[16] as they may benefit from targeted support. Our suggestion is then to provide the identified patients with support and redo the assessment, preferably 6-9 months after the cardiac event. The two questions about physical activity could be useful to screen for a low level of physical activity in clinical practice and research settings.[32]

Possible treatment of kinesiophobia and fatigue may include a structured plan for regular physical activity.[47,15] Coping with kinesiophobia after a cardiac event is a dynamic process that requires support[45] and needs to be further investigated. A systematic review and meta-analysis showed that physical exercise programmes reported significant reduction in fatigue in individuals with chronic conditions.[48] Another potential intervention may be fatigue self-management. However, there is

currently no evidence-based treatment for fatigue after OHCA or MI. Development of new treatment strategies aimed to increase physical activity and reduce kinesiophobia and fatigue after a cardiac event are needed.[45]

7: Conclusion

OHCA survivors had similar levels of physical activity compared to MI controls, matched for country, sex, age and time point of hospitalization, with the same potential pre-event cardiovascular risk factors. High level of kinesiophobia and fatigue were associated with a low level of physical activity in both groups.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author (KH).

Conflicts of interest

Katarina Heimburg, Erik Blennow Nordström, Hans Friberg, Lisa G. Oestergaard, Anders M. Grejs, Thomas R. Keeble, Hans Kirkegaard, Marco Mion, Niklas Nielsen, Christian Rylander, Magnus Segerström, Åsa B. Tornberg, Susann Ullén, Johan Undén, Matt P. Wise, Tobias Cronberg and Gisela Lilja report conflicts of interest: None.

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CRediT author contributions

Katarina Heimburg: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization, Project administration. **Erik Blennow Nordström**: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing - Review & Editing, Visualization, Project administration. **Hans Friberg**: Writing - Review & Editing, Funding acquisition. **Lisa G. Oestergaard**: Investigation, Writing - Review & Editing, Project administration. **Anders M. Grejs**: Resources, Writing - Review & Editing, Project administration. **Thomas R. Keeble**: Methodology, Resources, Writing - Review & Editing, Project administration. **Hans Kirkegaard**: Methodology, Resources, Writing - Review & Editing, Project administration. **Marco Mion**; Methodology, Investigation, Data Curation, Writing - Review & Editing, Project administration. **Niklas Nielsen**: Writing - Review & Editing, Funding acquisition. **Christian Rylander**: Resources, Writing - Review & Editing, Project administration. **Magnus Segerström**: Investigation, Data Curation, Writing - Review & Editing, Project administration. **Åsa B. Tornberg**: Methodology, Writing - Review & Editing, Supervision. **Susann Ullén**: Conceptualization, Methodology, Validation, Writing - Review & Editing. **Johan Undén**: Resources**,** Writing - Review & Editing. **Matt P. Wise**: Resources, Writing - Review & Editing, Project administration. **Tobias Cronberg**: Conceptualization, Methodology, Investigation, Resources, Data Curation, Writing - Review & Editing, Supervision, Project administration, Funding acquisition**. Gisela Lilja**: Conceptualization, Methodology, Investigation, Resources,

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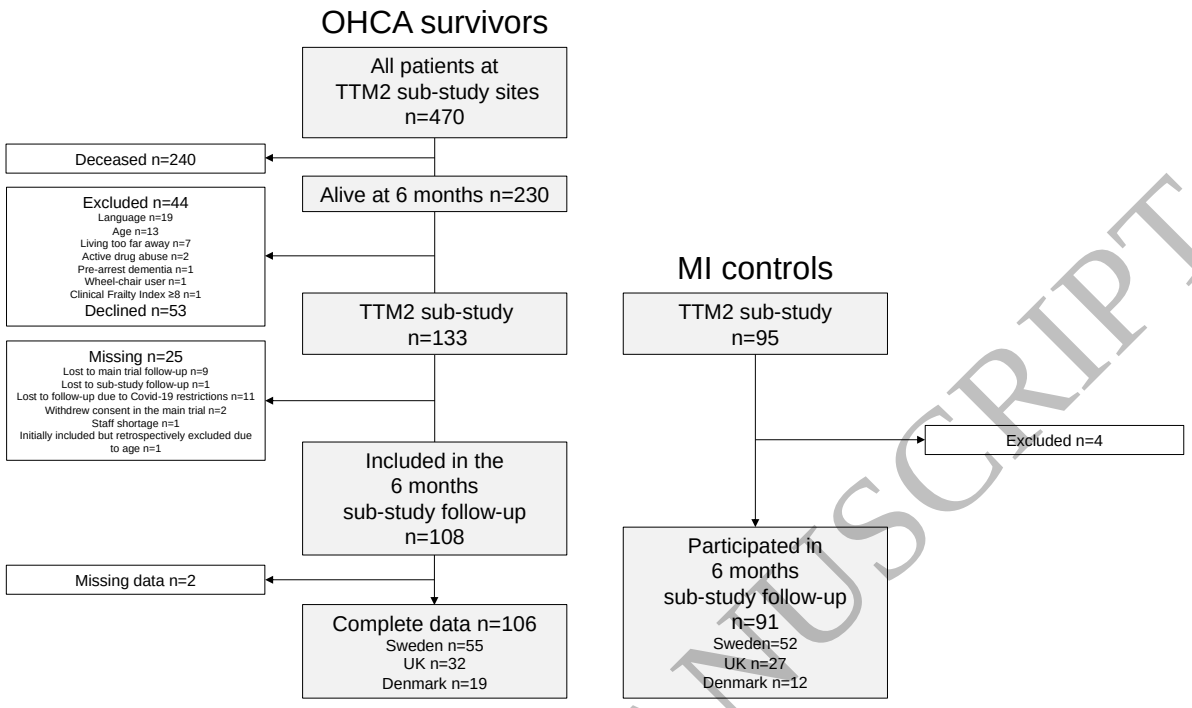


Figure 1: Flow chart of out-of-hospital cardiac arrest (OHCA) survivors in the physical activity sub-study with matched myocardial infarction (MI) controls in the Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest (TTM2) trial in Sweden, the United Kingdom (UK) and Denmark.

Table 1: The two questions on self-reported moderate and vigorous intensity physical activity during the last week used in out-of-hospital cardiac arrest survivors included in the physical activity sub-study performed in conjunction with the Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest (TTM2) trial and in matched myocardial infarction controls.

	Questions on physical activity	**Examples given to participants**
Question 1 Moderate intensity physical activity	In the last week, how many days have you engaged in moderate intensity physical activities for at least 30 minutes a day? (could be performed in blocks that last for at least 10 minutes adding up to a total of 30 minutes or more)	Moderate intensity physical activities denote activities performed for at least 10 minutes that leads to a moderate level of effort and a noticeably accelerate of heart rate. Examples of activities on this level include a brisk walk, heavy cleaning, washing windows, cleaning the car, carpentry, bicycling with light effort, golf, swimming leisurely or similar. For more examples, see Haskell [31].
Question 2 Vigorous intensity physical activity	In the last week, how many days have you engaged in vigorous intensity physical activities for at least 20 minutes (in one block)?	Vigorous intensity physical activities are an activity that leads to a substantial increase in heart rate and e.g. causes rapid breathing. Examples of activities at this level includes jogging, running, walking very very brisk, shoveling/digging, bicycling with a moderate

		effort/fast, swimming moderate/hard, tennis or similar. For more examples, see Haskell [31]

Table 2: Categorization in three ordered groups based on number of days of self-reported 30 minutes in total of moderate and/or 20 minutes of vigorous intensity physical activity a day during the last week [21] in the Targeted Hypothermia versus Targeted Normothermia after Out-of-hospital Cardiac Arrest trial (TTM2) sub-study.

Physical activity level	**Self-reported moderate intensity and vigorous intensity physical activity in days the last week**
A low level of physical activity	<5 days of moderate intensity physical activity at least 30 minutes in total per day/ <3 days of vigorous intensity physical activity at least 20 minutes per day
A moderate level of physical activity	≥ 5 days of moderate intensity physical activity at least 30 minutes in total per day/ ≥3 days vigorous intensity physical activity at least 20 minutes per day
A high level of physical activity	≥2 days of moderate intensity physical activity at least 30 minutes in total per day and ≥3 days vigorous intensity physical activity at least 20 minutes per day

Table 3: Characteristics of all OHCA survivors, all MI controls and OHCA survivors and MI controls categorized into a low or moderate/high level of self-reported physical activity in the Targeted Hypothermia versus Targeted Normothermia after Out-of-hospital Cardiac Arrest trial (TTM2) sub-study.

Variables	All OHCA survivors included in the sub-study	OHCA survivors: low level physical activity	OHCA survivors: moderate/ high level physical activity	All MI controls included in the sub-study	MI controls: low level physical activity	MI controls: moderate/ high level physical activity
Numbers (%)	106	27/106 (25)	79/106 (75)	91	18/91 (20)	73/91 (80)
Socio-demographic characteristics						
Age years median [Q1:Q3]	63 [57:71]	62 [58:72]	62 [56:70]	65 [57:71]	65 [55:70]	64 [57:72]
Male sex n (%)	94 (89)	24 (89)	71 (90)	81 (89)	17 (94)	64 (88)
Education University level n (%)	42 (40)	16 (59)	26 (33)	26 (29)	1 (6)	25 (34)
Living situation home n (%)	105 (99)	26 (96)	79 (100)	91 (100)	18 (100)	73 (100)
Working before OHCA/MI n (%)	63 (59)	14 (52)	49 (62)	56 (62)	13 (72)	43 (59)
Cardiac arrest						
Location of OHCA at home n (%)	52 (49)	12 (45)	40 (51)	n/a	n/a	n/a
Bystander witness n (%)	97 (92)	24 (89)	73 (92)	n/a	n/a	n/a
BP CPR n (%)	92 (87)	23 (85)	69 (87)	n/a	n/a	n/a
Shockable rhythms n (%)	94 (89)	22 (81)	72 (91)	n/a	n/a	n/a

OHCA to ROSC min median [Q1:Q3]	20 [13:30]	20 [13:30]	21 [13:31]	n/a	n/a	n/a
In-hospital						
ICU LOS days median [Q1:Q3]	4 [3:6]	3 [2:6]	4 [3:6]	n/a	n/a	n/a
Hospital LOS days median [Q1:Q3]	15 [12:26]	14 [11:26]	15 [12:26]	4 [4:6]	5 [3:8]	4 [4:6]
MI cause to CA n (%)	62 (58)	14 (52)	48 (61)	n/a	n/a	n/a
LVEF n (%):	102/106	27/27	73/79			
Normal ≥55%	28 (27)	6 (22)	21 (29)	n/a	n/a	n/a
Mildly reduced 45-54%	37 (36)	10 (37)	26 (36)			
Moderately reduced 30-44%	24 (24)	9 (33)	15 (20)			
Severely reduced <30%	13 (13)	2 (8)	11 (15)			
6-7 months follow-up						
CR n (%)	24 (23)	4 (15)	20 (25)	57 (63)	13 (72)	44 (60)
Exercise based CR n (%)	39 (37)	9 (33)	30 (38)	4 (4)	0 (0)	4 (6)
Smoking n (%)	13 (12)	6 (22)	7 (9)	11 (12)	5 (28)	6 (8)
Diabetes n (%)	13 (12)	4 (15)	9 (12)	17 (19)	5 (28)	12 (16)
Hypertension n (%)	68 (64)	19 (70)	49 (63)	70 (80)	11 (69)	59 (81)
BMI median [Q1:Q3]	27 [24:29]	27 [24:32]	26 [23:29]	26 [24:29]	26 [24:30]	26 [24:29]
Working n (%)	48 (45)	11 (41)	37 (47)	45 (50)	10 (56)	35 (48)
Poor mRS 4-5 n (%)	3 (3)	3 (11)	0 (0)	n/a	n/a	n/a

Abbreviations denote OHCA = Out-of-Hospital Cardiac Arrest, MI = Myocardial Infarction, BP CPR = By standard Performed Cardiopulmonary Resuscitation, ROSC = Return of Spontaneous Circulation, LOS = Length of Stay, ICU = Intensive Care Unit, LVEF = Left Ventricular Ejection Fraction, CR = Cardiac Rehabilitation, BMI = Body Mass Index, mRS = modified Rankin Scale.

Table 4: Results from all OHCA survivors, all MI controls and OHCA survivors and MI controls categorized into a low or moderate/high level of self-reported physical activity in the Targeted Hypothermia versus Targeted Normothermia after Out-of-hospital Cardiac Arrest trial (TTM2) sub-study. A HADS score of > 7 indicates clinical difficulties. A TSK-Heart score of > 37 represents a high level of kinesiophobia. Higher scores on the MFI-20 indicate more problem.

Variables: 7-months follow-up	All OHCA survivors included in the sub-study	OHCA survivors: low level physical activity	OHCA survivors: moderate/ high level physical activity	All MI controls included in the sub-study	MI controls: low level physical activity	MI controls: moderate/ high level physical activity
Numbers (%)	106	27/106 (25)	79/106 (75)	91	18/91 (20)	73/91 (80)
HADS-A median [Q1:Q3]	3 [1:6]	2 [1:5]	3 [1:6]	4 [2:7]	6 [3:10]	4 [1:6]
HADS-D median [Q1:Q3]	2 [1:4]	2 [1:4]	2 [1:4]	2 [1:6]	5 [1:8]	2 [1:5]
TSK-Heart median [Q1:Q3]	29 [24:36]	33 [27:38]	28 [23:35]	27 [23:32]	32 [25:35]	26 [22:30]
MFI-20 median [Q1:Q3] General fatigue	10 [8:13]	11 [10:16]	10 [6:12]	11 [8:15]	13 [11:17]	11 [7:14]

Physical fatigue	11 [7:14]	13 [10:17]	11 [6:13]	10 [8:14]	13 [10:16]	9 [7:13]
Mental fatigue	8 [4:10]	9 [5:13]	7 [4:10]	8 [4:11]	10 [7:15]	8 [4:11]
Reduced activity	10 [6:13]	12 [9:15]	9 [5:12]	9 [7:13]	13 [8:15]	9 [7:13]
Reduced motivation	7 [5:10]	9 [7:12]	7 [4:10]	9 [6:12]	9 [8:11]	8 [4:11]

Abbreviations denote OHCA = Out-of-Hospital Cardiac Arrest, MI = Myocardial Infarction, HADS = Hospital Anxiety and Depression Scale, TSK-Heart = Tampa Scale for Kinesiophobia Heart, MFI-20 = Multidimensional Fatigue Inventory.

Table 5: Univariable analysis of potential risk factors associated with a low level of physical activity expressed as odds ratios for the event among OHCA survivors and match MI controls separately in the physical activity sub-study of the Targeted Hypothermia versus Targeted Normothermia after Out-of-hospital Cardiac Arrest (TTM2) trial. A HADS score of > 7 indicates clinical difficulties. A TSK-Heart score of > 37 represents a high level of kinesiophobia. Higher scores on the MFI-20 indicate more problem.

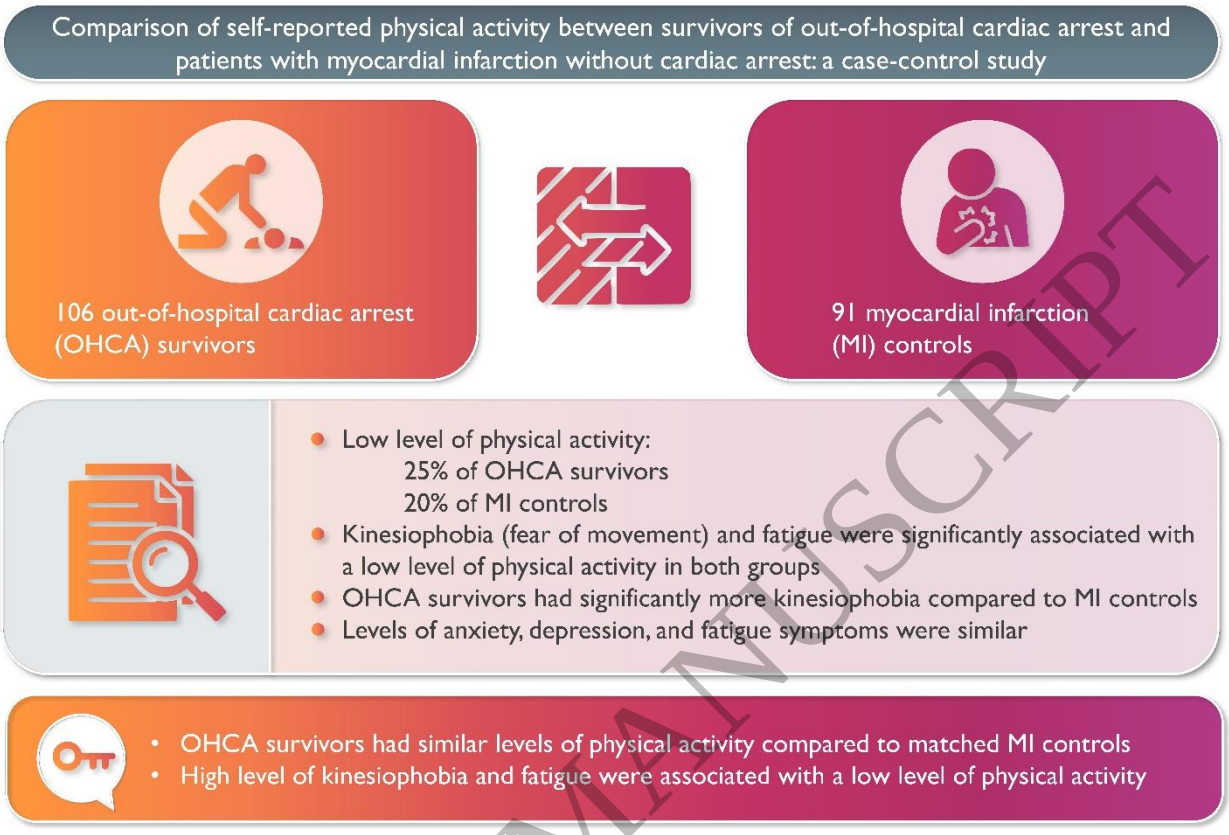
Potential risk factors of a low level of physical activity	OHCA survivors univariable model OR (95% CI)	p-value	MI controls univariable model OR (95% CI)	p-value
Anxiety symptoms by HADS-A	0.98 (0.86, 1.11)	0.73	1.14 (1.00, 1.29)	0.05
Depression symptoms by HADS-D	1.07 (0.93, 1.23)	0.32	1.17 (1.00, 1.36)	0.05
Kinesiophobia by TSK-Heart	1.09 (1.02, 1.16)	**0.01***	1.09 (1.02, 1.18)	**0.01***
General fatigue by MFI-20	1.17 (1.04, 1.31)	**0.007***	1.16 (1.02, 1.33)	**0.03***
Physical fatigue by MFI-20	1.15 (1.03, 1.28)	**0.01***	1.18 (1.04, 1.33)	**0.01***
Mental fatigue by MFI-20	1.12 (1.00, 1.25)	**0.04***	1.18 (1.03, 1.35)	**0.02***
Reduced activity by MFI-20	1.18 (1.06, 1.31)	**0.003***	1.14 (1.01, 1.30)	**0.04***
Reduced motivation by MFI-20	1.14 (1.01, 1.29)	**0.03***	1.10 (0.95, 1.27)	0.22

Abbreviations denote OHCA= Out-of-Hospital Cardiac Arrest, MI = Myocardial Infarction, OR = Odds Ratio, CI = Confidence Interval, HADS = Hospital Anxiety and Depression Scale, TSK-Heart = Tampa Scale for Kinesiophobia Heart, MFI-20 = Multidimensional Fatigue Inventory. *= significant p <0.05.

Table 6: Multivariable analysis of potential risk factors associated with a low level of physical activity expressed as odds ratios for the event among OHCA survivors and matched MI controls separately in the physical activity sub-study of the Targeted Hypothermia versus Targeted Normothermia after Out-of-hospital Cardiac Arrest (TTM2) trial. A HADS score of > 7 indicates clinical difficulties. A TSK-Heart score of > 37 represents a high level of kinesiophobia. Higher scores on the MFI-20 indicate more problem.

Potential risk factors of a low level of physical activity	OHCA survivors multivariable model OR (95% CI)	p-value	MI controls multivariable model OR (95% CI)	p-value
Anxiety symptoms by HADS-A	0.83 (0.70, 0.98)	**0.03***	1.07 (0.92, 1.24)	0.37
Kinesiophobia by TSK-Heart	1.09 (1.00, 1.17)	**0.04***	1.07 (0.99, 1.15)	0.11
Physical fatigue by MFI-20	1.18 (1.03, 1.34)	**0.02***	1.08 (0.93, 1.24)	0.31

Abbreviations denote OHCA= Out-of-Hospital Cardiac Arrest, MI = Myocardial Infarction, OR = Odds Ratio, CI = Confidence Interval, HADS = Hospital Anxiety and Depression Scale, TSK-Heart = Tampa Scale for Kinesiophobia Heart, MFI-20 = Multidimensional Fatigue Inventory. *= significant p <0.05.



Graphical Abstract
559x381 mm (x DPI)

Novelty box

- 25% of the cardiac arrest survivors and 20% of the myocardial infarction controls reported a low level of physical activity.
- Symptoms of kinesiophobia (fear of movement) and fatigue were significantly associated with a low level of physical activity in both groups.
- Cardiac arrest survivors had significantly more kinesiophobia compared to myocardial infarction controls.