

Physical Activity and Survival After an Acute Coronary Syndrome: Data From the ERICO Study

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Background: Due to enhancements in health care, the number of individuals who survive an acute coronary syndrome (ACS) event is rising. In this population, the impact of physical activity on long-term survival is still a matter of debate. We aimed to analyze the association between the level of physical activity during the first 4 years of follow-up and survival. **Methods:** We analyzed data from 692 patients admitted due to an ACS event in a community hospital in Brazil. Physical activity was assessed using the long version of the International Physical Activity Questionnaire at 30 days, 180 days, and yearly after the first event. Mortality data were obtained using phone contacts, medical records, and official death documents. We built time-dependent Cox proportional hazard models to analyze whether physical activity levels during follow-up were associated with survival. **Results:** Our main sample had 280 (40.5%) women and a mean age of 62.6 (12.5) years. In all assessments, 50.8% to 74.9% of study participants had physical activity levels below recommendations for healthy individuals. Physical inactivity increased the risk of death (hazard ratio [HR], 1.82; 95% confidence interval, 1.13–2.92). There was no statistically significant survival difference between insufficiently active and active participants. **Conclusions:** Many individuals who survive an ACS event have poor physical activity levels. Physical inactivity after an ACS event significantly increases the risk of death. Our findings provide additional support to reinforce, in clinical practice, the benefits of physical activity in individuals who survive an ACS event.

Keywords: epidemiology, cohort, motor activity, mortality, long-term prognosis, risk factors

Key Points

- We analyzed long-term physical activity data after discharge among 692 individuals admitted due to an acute coronary syndrome event in a community hospital in Brazil.
- In all assessments, 50.8% to 74.9% of study participants had physical activity levels below recommendations for healthy individuals.
- Physical inactivity was associated with an increased risk of all-cause mortality in this cohort.

Cardiovascular diseases (CVD) are the leading cause of death in many countries, including Brazil.^{1,2} In the past decades, however, mortality rates due to CVD have been steadily declining.² This is partly due to higher survival after an acute coronary syndrome (ACS) event. Improvements in symptom recognition,³ systems of care,⁴ in-hospital treatment,³ and secondary prevention^{4,5} are essential drivers for increased survival.^{3,4}

This scenario reinforces the importance of studying factors associated with long-term outcomes in individuals who survive an ACS event. Among these variables, physical activity is of particular interest. The benefits of physical activity on the cardiovascular

health of individuals without previous coronary artery disease (CAD) are extensively documented. However, even in this group, excessive physical activity may result in a ceiling effect or adverse outcomes.^{6,7} Whether these benefits extend to individuals who survive an ACS event is a subject of debate. Pitsavos et al⁸ evaluated the in-hospital prognosis of 2172 patients diagnosed with myocardial infarction (MI) or unstable angina (UA) in Greece. Physically active individuals had lower in-hospital and 30-day mortality than physically inactive individuals. A 10-year follow-up of the same cohort by Papataxiarchis et al⁹ observed a long-term association between physical activity levels measured at enrollment and CVD mortality but only among participants without ACS episodes before baseline. Wannamethee et al¹⁰ evaluated 772 men aged between 40 and 59 years with diagnosed CAD and showed that participants who performed light or moderate physical activity had a decreased risk of death after 5 years of follow-up compared with inactive ones. Ku et al¹¹ evaluated data from 2370 individuals with CAD in Taiwan and found that those who engaged in physical activity equivalent to or higher than 1000 kcal/week had an approximately 40% lower mortality risk than inactive patients

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during a 7-year follow-up. Recently, a systematic review by Gonzalez-Jaramillo et al¹² including 33,576 patients with CAD acknowledged a beneficial effect of physical activity on survival, with a hazard ratio (HR) for all-cause mortality of 0.49 (95% CI, 0.39–0.62) associated with physical activity. These last 3 articles, however, included individuals with CAD regardless of the occurrence of an acute event. On the other hand, Wang et al¹³ conducted a prospective study with 1010 individuals with CAD and found that physical activity during follow-up was not associated with the 10-year risk of cardiovascular death.

The Strategy of Registry of Acute Coronary Syndrome (ERICO) study is a cohort study of individuals who were treated for an acute coronary event in a community hospital in Brazil. ERICO is focused on prognostic factors for long-term survival after an ACS event. In this article, we analyze association between the level of physical activity and long-term survival in ERICO.

Methods

Study Design and Setting

ERICO study^{14,15} recruitment occurred between February 2009 and December 2013. Individuals with an ACS event diagnosis (UA or MI) in the Hospital Universitário da Universidade de São Paulo were invited to participate in the study. Hospital Universitário da Universidade de São Paulo is a teaching community hospital with 260 beds located in the neighborhood of Butantã, São Paulo. The estimated population of the Butantã district in 2019 was approximately 450,000 inhabitants, with a mean human development index of 0.928 and a population density of 37.24 inhabitants/km². About 16.2% of its population lives in deprived areas (*favelas*), contrasting with areas of high purchasing power in the same region.¹⁶

Participants should meet previously published criteria to be included in the ERICO study.¹⁷ Individuals with UA, ST-segment elevation myocardial infarction, or non-ST-segment elevation myocardial infarction were included in the cohort. For a diagnosis of MI, both of the following criteria must be present: (1) symptoms consistent with cardiac ischemia within 24 hours of presenting at the hospital and (2) troponin I levels above the 99th percentile with a test-specific coefficient of variation <10%. ST-segment elevation myocardial infarction diagnosis requires both of the following criteria: (1) criteria for MI diagnosis and (2) one of the following: (1) persistent ST-segment elevation of ≥ 1 mm in 2 contiguous electrocardiographic leads or (2) presence of a new or presumably new left bundle branch block. For non-ST-segment elevation myocardial infarction diagnosis, participants must present (1) criteria for MI diagnosis and (2) absence of criteria for ST-segment elevation myocardial infarction diagnosis. For UA diagnosis, all of the following 3 criteria must be fulfilled: (1) symptoms consistent with cardiac ischemia 24 hours before hospital admission; (2) absence of MI criteria; and (3) at least one of the following: (1) history of CAD; (2) positive CAD stratification test (invasive or noninvasive); (3) transient ST segment changes ≥ 0.5 mm in 2 contiguous leads, new *T*-wave inversion of ≥ 1 mm, and/or pseudonormalization of previously inverted *T* waves; (4) troponin I > 0.4 ng/mL; or (5) diagnostic concordance of 2 independent physicians.

Sociodemographics, cardiovascular risk factors, and previous medication data were retrieved by trained staff. ERICO medical researchers reviewed all cases to verify whether the inclusion criteria were met. These researchers retrieved clinical, laboratory, and electrocardiographic data from medical charts. Due to its observational design, treatment decisions for participants of the ERICO

cohort were defined by the hospital staff without influence from the study protocol.

Thirty days after the index event, participants were invited for an onsite reevaluation. Clinical and laboratory data were retrieved during this assessment, and questionnaires about physical activity and symptoms of depression were applied. After 6 months and yearly, participants were contacted to verify their vital status. In these contacts, physical activity and depression symptoms questionnaires were used again by trained staff.

ERICO study protocol was approved by the Institutional Review Board of the Hospital Universitário da Universidade de São Paulo (approval number 866/08).

Study Sample

From the 1085 ERICO participants, we excluded 49 participants who died within 30 days after the index event. Of the 1036 eligible ERICO participants, 344 were excluded because (1) they did not answer phone contacts at 30 days, (2) they were unable to complete the physical activity questionnaire at the 30-day follow-up, or (3) they refused to complete the physical activity questionnaire at the 30-day follow-up. Individuals with medical-oriented restrictions for physical activity (if any) were not excluded from the study. Therefore, our sample consisted of 692 ERICO participants.

Time-Dependent Physical Activity Variable

Physical activity in ERICO was assessed using the long version of the International Physical Activity Questionnaire (IPAQ). IPAQ addresses 4 domains of physical activity (leisure, transport, occupational, and domestic). There are questions regarding each activity's intensity, duration, and frequency. For main analyses, participants were classified as active (≥ 150 min of moderate and/or vigorous physical activity per week or ≥ 75 min of vigorous physical activity per week), partially active (presence of moderate and/or vigorous physical activity without reaching active levels), and inactive (no moderate and/or vigorous physical activity per week) in all the aforementioned domains mentioned. The time-dependent physical activity variable used information from the first 4 years of follow-up (30 d, 180 d, and yearly thereafter).

Mortality Data

As mentioned before, vital status was verified at each telephone interview. These interviews were performed 30 days, 180 days, and yearly after the index event. We searched official death records for information about all participants whether (1) we had information that they had died or (2) we could not contact them at the time. Vital status during follow-up was updated through medical registries and death certificates in collaboration with the municipal and state health offices. Protocols for the cause of death definition were also published in earlier articles.^{15,18} Two medical doctors reviewed these data and classified the cause of death for deceased participants according to the information from death certificates. If necessary, a third doctor analyzed the death certificate, followed by a consensus meeting. Vital status data collection ended in December 2016, corresponding to a maximum follow-up of 7.6 years.

Other Variables

Age, sex, educational level, race, and smoking status were self-reported. Information about hypertension, diabetes, dyslipidemia, previous CAD, heart and kidney failures, and stroke diagnoses before

the index event were also self-reported. Echocardiography determined the left ventricle ejection fraction during the index event. Body mass index was defined as weight divided by squared height.

Statistical Analysis

Categorical variables are presented as absolute counts and proportions and compared among groups using chi-squared tests. Continuous variables following normal distributions are presented as means and standard deviations and compared across groups using analysis of variance. Continuous variables following nonnormal distributions are presented as medians and interquartile ranges and compared across groups using Kruskal–Wallis tests.

For all survival analyses, the start of follow-up (T_0) was defined as the 30th day after the index event as this was when the first application of the physical activity questionnaire was performed. We present Kaplan–Meier curves for the sample according to physical activity level and compare survival probabilities using log-rank tests. We built time-dependent Cox proportional hazard models¹⁹ to analyze whether physical activity levels were associated with survival. Physical activity was included in the model as a time-dependent variable. The initial set of covariates was selected aiming for clinically relevant conditions with potential implications on long-term survival after an ACS (age, sex, educational level, race and smoking status, hypertension, diabetes, dyslipidemia, body mass index, previous CAD, heart and kidney failures and stroke diagnoses, and left ventricle ejection fraction). We acknowledge correlations among these factors are different from those found in the general population, and associations with long-term survival are influenced by the impact of risk factors and comorbidities in pre- or in-hospital survival during an ACS event. Due to this rationale and to avoid including unnecessary covariates

in the main model, covariates in adjusted Cox models were further selected using a backward stepwise approach, using an exclusion threshold at $P = .10$. The exceptions were age, sex, and physical activity, which were maintained in the model irrespective of statistical significance. If there were independent variables with a $P > .10$, the variable with the highest P value was excluded from the model. This procedure was repeated until no variables were associated with a P value above the exclusion threshold.

We adopted an imputation procedure for missing values in physical activity levels due to loss of information (ie, the participant was alive at the 180-d/1-y follow-up time point but did not answer the IPAQ questionnaire). In this procedure, we eliminated missing values by carrying forward the physical activity level value registered in the previous assessment. Due to potentially heterogeneous associations between physical activity and mortality according to sex, we also present Cox models for men and women separately. We also used a multiple imputation method as a sensitivity analysis. In this case, we estimated missing physical activity levels at each time point using a multinomial regression model including age, sex, ACS subtype, educational level, hypertension, and diabetes as physical activity level predictors. The significance level was set at 0.05. All analyses were conducted using R software.²⁰

Results

Our main sample had 280 (40.5%) women and a mean age of 62.6 (12.5) years. Table 1 shows the characteristics of study participants according to their physical activity level 30 days after the index event. We found that younger age ($P < .001$) and current smoking at baseline ($P = .001$) were positively associated with physical activity. On the other hand, individuals with previous hypertension ($P = .006$), diabetes ($P < .001$), dyslipidemia ($P = .007$), or self-classified as sedentary

Table 1 Characteristics of Study Participants According to the Level of Physical Activity 30 Days After the Index Event

	Active (n = 249)	Insufficiently active (n = 130)	Inactive (n = 313)	Total (N = 692)
Female sex, N (%)	115 (46.2%)	115 (36.7%)	50 (38.5%)	280 (40.5%)
Age, y, mean (SD)	58.1 (10.9)	62.2 (11.1)	66.4 (13.0)	62.6 (12.5)
ACS diagnosis				
STEMI, N (%)	78 (31.3%)	31 (23.8%)	86 (27.5%)	195 (28.2%)
NSTEMI, N (%)	100 (40.2%)	67 (51.5%)	126 (40.3%)	293 (42.3%)
UA, N (%)	71 (28.5%)	32 (24.6%)	101 (32.3%)	204 (29.5%)
Smoking status at baseline, N (%)				
Never	55 (22.4%)	37 (28.9%)	113 (36.8%)	205 (30.1%)
Past	98 (39.8%)	49 (38.3%)	121 (39.4%)	268 (39.4%)
Current	93 (37.8%)	42 (32.8%)	73 (23.8%)	208 (30.5%)
Hypertension, N (%)	171 (69.8%)	103 (79.8%)	248 (80.8%)	522 (76.7%)
Diabetes, N (%)	67 (27.6%)	56 (44.4%)	131 (42.8%)	254 (37.6%)
Dyslipidemia, N (%)	98 (45.0%)	72 (59.0%)	163 (57.6%)	333 (53.5%)
Self-perceived sedentarism, N (%)	154 (63.6%)	90 (71.4%)	234 (78.3%)	478 (71.7%)
Previous CAD, N (%)	54 (22.6%)	43 (34.1%)	75 (25.4%)	172 (26.1%)
Previous heart failure, N (%)	36 (15.9%)	27 (22.5%)	64 (22.6%)	127 (20.2%)
Previous stroke, N (%)	14 (6.0%)	20 (16.0%)	36 (12.1%)	70 (10.7%)
BMI, mean (SD)	27.3 (4.7)	27.0 (4.4)	27.0 (5.1)	27.1 (4.8)
LVEF < 50%, N (%)	43 (24.6%)	32 (35.6%)	74 (34.7%)	149 (31.2%)

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; NSTEMI, non ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

(through a yes or no questionnaire) before the index event ($P = .001$) were less likely to be physically active 30 days after the index event.

Table 2 shows the level of physical activity at all assessments for men and women. Physical inactivity was common in the sample during the entire follow-up. Importantly, physical activity levels decreased during the first year of follow-up, recovering from 2 years on. Supplementary Figure S1 in [Supplementary Material S2](#) (available online) shows physical activity level trajectories over time in more detail, further highlighting these dynamics. Considering that physical activity assessments occurred between sequential time points during the first year of follow-up (between 30 and 180 d or between 180 d and 1 y), 18.0% and 22.0% showed increasing and decreasing physical activity levels, respectively. On the other hand, physical activity assessments occurred between sequential time points after the first year of follow-up (between 1 and 2 y, between 2 and 3 y, and between 3 and 4 y); 24.0% and 10.2% showed increasing and decreasing physical activity levels, respectively. In all time points evaluated, adequate physical activity levels were more common among women than men. The difference in physical activity levels according to sex had borderline significance at 30 days ($P = .067$). It was statistically significant at 180 days ($P < .001$), 1 year ($P < .001$), 2 years ($P = .007$), 3 years ($P = .022$), and 4 years ($P < .001$).

Median follow-up in the sample was 4.1 years (1510 d; interquartile range: 1115–1911 d), and 18.5% of the sample died during follow-up. Survival probability (Kaplan–Meier) curves according to the level of physical activity 30 days after the index event are presented in Figure 1. Active participants had a higher probability of long-term survival compared with inactive participants. Table 3 shows the results from Cox models for overall survival using time-dependent physical activity variables. Considering the models with value imputation for missing physical activity data, inactive participants had a higher risk of death during follow-up compared with active ones (HR, 1.82; 95% confidence interval [CI], 1.13–2.92). In this model, survival among active and insufficiently active participants was not statistically different. However, point estimates suggested a greater risk of mortality among those who did not achieve adequate levels of physical activity (HR: 1.17; 95% CI, 0.67–2.06).

Supplementary Tables S1 and S2 in [Supplementary Material S1](#) (available online) show sex-stratified Cox models. A trend toward higher mortality was observed in women (HR: 1.86; 95% CI, 0.91–3.84) and men (HR: 1.80; 95% CI, 0.94–3.42). For both sexes, point HR estimates were close to those found for the entire sample, suggesting that the lack of statistical significance was mostly due to small subsample sizes. Sensitivity analyses using multiple imputations for missing physical activity data during

follow-up led to similar conclusions (see Supplementary Tables S3–S5 in [Supplementary Material S1](#) [available online]).

Discussion

Our study shows high prevalence of poor physical activity in individuals who survive an ACS event. Physical activity during the first 4 years of follow-up positively impacted survival rates. The risk of death was more than 2 times higher in physically inactive participants compared with active ones in adjusted models.

Secondary prevention after an ACS event in Brazil is challenging, as Birck et al⁵ demonstrated using data from the Brazilian Longitudinal Study of Adult Health–Brasil (ELSA–Brasil) study. In that cohort, only 35% of the participants reporting coronary heart disease diagnosis at baseline received drug treatment as recommended by clinical guidelines. In this scenario, our findings of high prevalence of physical inactivity must be highlighted. ERICO study protocol included using the long version of the IPAQ questionnaire.²¹ Although concerns with the precision of estimating physical activity using questionnaires apply,²² there is evidence from South American populations²³ that the IPAQ mostly overestimates, rather than underestimates, the level of physical activity. Therefore, the actual prevalence of physical inactivity in our setting may be even higher than that disclosed in our analyses. Physical inactivity after an ACS event may be a typical scenario, as the results from other studies suggest. Ter Hoeve et al²⁴ analyzed ActiGraphy data during waking hours from 114 individuals who participated in an outpatient cardiac rehabilitation program after an ACS event. One year after the end of the rehabilitation program, 62.3% of the time was related to sedentary behavior. Moderate to vigorous activity, defined as that corresponding to ≥ 672.5 counts, occurred only 6.7% of the time, and a small subset of that (0.49% of waking hours) was dedicated to moderate to vigorous activity lasting 10 or more minutes. Long-term physical inactivity was also described in the mentioned cohort of 772 individuals with coronary heart disease by Wannamethee et al.¹⁰ In that sample, 323 (41.8%) were physically inactive or reported only occasional physical activity.

Previous studies complement and contextualize the significance of our findings of a protective effect associated with physical activity. Pitsavos et al⁸ showed that physical activity levels before the onset of an ACS event influence the survival of individuals who suffer an ACS event. In that study, individuals who were at least minimally active had an odds ratio for death within the first 30 days after an ACS event of 0.60. Our study analyzed data from ERICO

Table 2 Physical Activity Levels During the First 4 Years After an Acute Coronary Event

	30 d	180 d	1 y	2 y	3 y	4 y
Men						
Active, N (%)	134 (32.5%)	41 (16.0%)	50 (21.5%)	107 (44.4%)	88 (43.3%)	65 (42.5%)
Insufficiently active, N (%)	80 (19.4%)	59 (23.0%)	57 (24.5%)	70 (29.0%)	72 (35.5%)	59 (38.6%)
Inactive, N (%)	198 (48.1%)	156 (60.9%)	126 (54.1%)	64 (26.6%)	43 (21.2%)	29 (19.0%)
Total	412	256	233	241	203	153
Women						
Active, N (%)	115 (41.1%)	66 (38.8%)	70 (45.2%)	86 (56.6%)	73 (54.1%)	66 (58.4%)
Insufficiently active, N (%)	50 (17.9%)	47 (27.6%)	41 (26.5%)	24 (15.8%)	29 (21.5%)	17 (15.0%)
Inactive, N (%)	115 (41.1%)	57 (33.5%)	44 (28.4%)	42 (27.6%)	33 (24.4%)	30 (26.5%)
Total	280	170	155	152	135	113

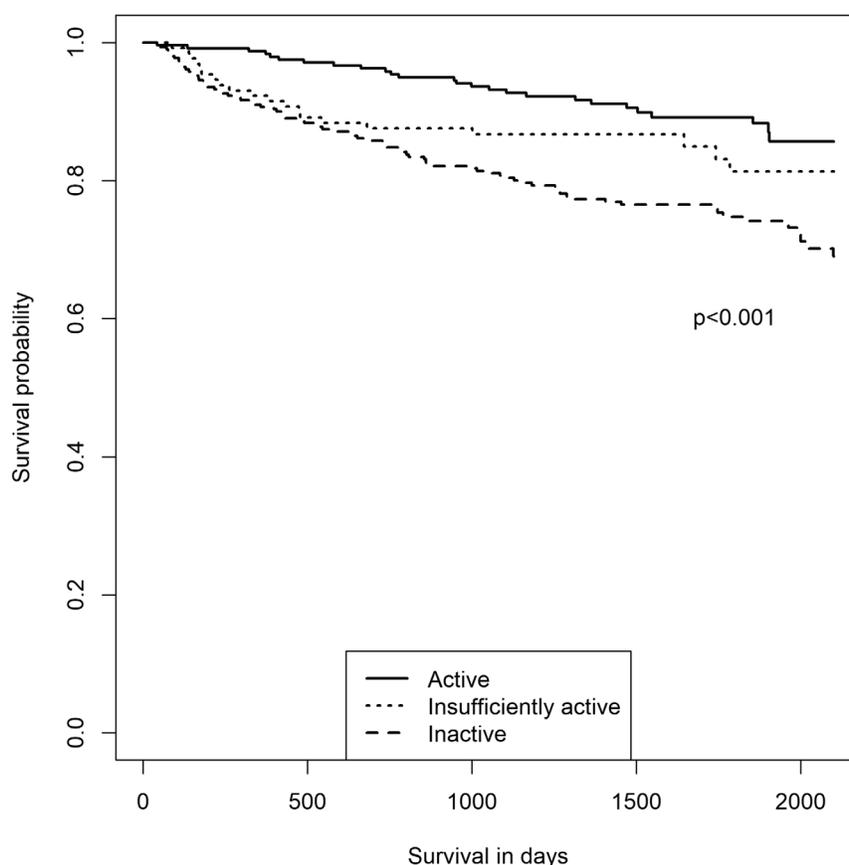


Figure 1 — Survival probability according to the level of physical activity 30 days after the index event.

Table 3 HRs (95% CI) for Overall Survival in Models Considering Physical Activity as a Time-Dependent Variable

Variable	HR (95% CI)
Physical activity	
Active	Reference
Insufficiently active	1.17 (0.67–2.06)
Inactive	1.82 (1.13–2.92)
Age (1-y increase)	1.05 (1.04–1.07)
Male sex	0.82 (0.63–1.08)
ACS subtype	
STEMI	0.52 (0.31–0.86)
NSTEMI	Reference
UA	0.58 (0.38–0.90)
Previous heart failure	1.88 (1.16–3.06)
Previous stroke	2.21 (1.54–3.18)
Body mass index	
Normal	Reference
Overweight	0.65 (0.42–0.99)
Obesity	0.76 (0.46–1.24)
LVEF < 50%	1.82 (1.17–2.81)

Abbreviations: ACS, acute coronary syndrome; CI, confidence interval; HR, hazard ratio; LVEF, left ventricular ejection fraction; NSTEMI, non ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina. Note: HRs significant at the 0.05 level are in bold.

participants who survived the first 30 days after the index event. Based on Pitsavos et al's⁸ findings, it is reasonable to consider that our sample is subject to some bias due to a reduced representation of individuals who were inactive after hospitalization. However, this bias would probably weaken the association between physical activity and long-term post-ACS mortality. Therefore, the finding of a positive association in our study is strong evidence for this putative association. Recently, Kim et al²⁵ analyzed data from 23,871 individuals with CVD (MI, stroke, heart failure, and peripheral artery disease) covered by the Korean National Health Insurance Service. They observed a benefit of physical activity on long-term survival (median follow-up, 42 mo) when analyzing the entire sample or stratified by CVD diagnosis. Al-Shaar et al²² analyzed data from 1651 individuals who survived an MI in the Health Professionals Follow-up Study cohort (all male, median follow-up 14 y) and described a 39% reduction in the risk of death among those physically active before and after the MI. A substantial (27%) reduction in the risk of death was also observed among those who increased their level of physical activity after the MI compared with those who remained physically inactive. On the other hand, the analyses from Wang et al¹³ in the Heart and Soul Study did not find a significant association between physical activity and 10-year mortality (either cardiovascular or noncardiovascular) among individuals with stable CAD in adjusted models. Their result, however, can be partially explained by the covariates included in adjusted models. Although physical activity was not associated with survival, exercise capacity (in metabolic equivalents) was protective for noncardiovascular death in their analyses. In addition, inducible ischemia was a risk factor for cardiovascular

and noncardiovascular death. Low exercise capacity and/or inducible ischemia may be closely correlated with physical activity, and including these covariates in models may weaken the association between physical activity and mortality.

Our study expands the previous findings of the protective role of physical activity on long-term survival after an ACS event to a sample of individuals treated in a public community hospital from a middle-income country where marked economic inequalities exist. In this setting, patients frequently live in places characterized by a high population density, poorly organized urban settlements, and the lack of well-conserved public areas destined for leisure.²⁶ These features make continued physical activity increasingly challenging. However, our results suggest that these limitations do not nullify the positive effects of physical activity on survival after an ACS event.

The current body of evidence (including our study) suggests that moderate physical activity before and after an ACS episode yields an important survival benefit. On the other hand, it is essential to note that the adequate level of exercise during the first days after an ACS event was not evaluated in these studies, and we must acknowledge that it was beyond the objectives of the present study to determine the best moment to initiate a physical activity program for patients who survive an ACS event. However, our results support that beginning moderate physical activity after 30 days is safe (at least in individuals recovering from an ACS event without further complications), and advocating against long-term physical inactivity after an ACS event is reasonable. Decreasing physical activity levels during the first year of follow-up also warrants further investigation as this may be an important opportunity to stimulate healthy lifestyle changes in this population. Further studies are also needed to determine the safety of moderate physical activity for individuals who were not sufficiently represented in the ERICO study sample.

Our study has some strengths. We could analyze a sample from a community hospital in Brazil, a middle-income country. Both scenarios are usually underrepresented in post-ACS studies. Individuals were assessed using a validated questionnaire at multiple time points, and mortality data were checked against official death records. We applied a statistical approach to incorporate physical activity information during long-term follow-up. Some limitations must be pointed out as well. As previously considered, IPAQ is known to overestimate an individual's physical activity, and we do not have objective physical activity data using Acti-Graphy. However, this characteristic of the questionnaire also highlights the high prevalence of physical inactivity described in this study. We could not retrieve physical activity information at 30 days for 344 participants. Reasons include incomplete IPAQ information, loss to follow-up, or inability to complete the questionnaires due to health issues or personal circumstances. Although we do not believe this resulted in biased analyses, we acknowledge that this lack of information increases the uncertainty of our findings. Another source of bias could come from missing physical activity data during follow-up. In the main analyses, we adopted a carry-forward imputation method, and in sensitivity analyses, we used a multiple imputation technique based on sociodemographic and clinical data. Results from both models were very similar, which strongly supports the consistency of our findings. At the final evaluations (3 and 4 y after the index event), the number of participants who answered the IPAQ questionnaire in ERICO declined. Although we do not expect physical activity's effect on mortality to change 3–4 years after an acute event, generalizations of our findings for longer periods must be

made with caution. Follow-up from 180 days on was made by phone contact, which did not allow for updating information on time-varying covariates, such as body mass index and ventricular function. Finally, the observational nature of a cohort study does not allow definite conclusions about the effectiveness of stimulating physical activity on the survival of patients who survive an ACS event. Physically active individuals may also engage in other healthy behaviors and have more access to health care or enhanced adherence to medical treatment, all potentially impacting survival. In the same direction, physical activity prescriptions were not assessed, and individuals under restrictions for physical activity may also be under high mortality risk due to their underlying clinical conditions. However, the proportion of individuals with clinical restrictions for moderate physical activity is probably low. Also, the association between physical inactivity and mortality remained significant after controlling for important clinical confounders, such as previous stroke, previous heart failure diagnosis, and left ventricle ejection fraction. Therefore, we may advocate that physical inactivity in this setting identifies a high-risk subgroup of individuals for whom it is reasonable to consider the stimulus to physical activity as part of a comprehensive health care plan.

In conclusion, we found a high prevalence of physical inactivity in our sample of individuals who have experienced an ACS event. Being physically inactive after an ACS event significantly increases the risk of death. Our findings provide additional support for reinforcing, in clinical practice, the benefits of physical activity for patients who survive an ACS event.

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