

Supplementary Online Content

Dahabreh IJ, Paulus JK. Association of episodic physical and sexual activity with triggering of acute cardiac events: systematic review and meta-analysis. *JAMA*. 2011;305(12):1225-1233.

eAppendix. Search Strategies for Bibliographic Databases

eTable 1. Detailed Characteristics of Eligible Studies

eTable 2. Quality Assessment of Eligible Studies

eTable 3. Effect of Physical Exertion on Serious Cardiac Events by Groups of Usual Physical Activity

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix: Search Strategies for Bibliographic Databases

MEDLINE (4914 citations, no language restrictions)

- #4 #1 AND #2 AND #3
- #3 exercise OR exertion OR ((physical OR sexual) AND (activity OR activities))
- #2 cross-over OR cross over OR crossing over OR crossover* OR trigger*
- #1 myocardial OR cardiovascular OR cardiac OR (sudden AND death) OR unstable angina OR cardiogenic OR coronary OR "myocardial infarction"[MeSH Terms] OR "death, sudden, cardiac"[MeSH Terms] OR "coronary disease"[MeSH Terms] OR "coronary artery disease"[MeSH Terms] OR "acute coronary syndrome"[MeSH Terms]

EMBASE (717 citations, no language restrictions)

- #12 #10 AND #11 (717 citations)
- #11 #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
- #10 #1 AND #2
- #9 coronary AND ('disease'/exp OR disease)
- #8 'cardiovascular disease'/exp OR 'cardiovascular disease'
- #7 'coronary artery disease'/exp OR 'coronary artery disease'
- #6 'sudden death'/exp OR 'sudden death'
- #5 'sudden cardiac death'/exp OR 'sudden cardiac death'
- #4 'heart infarct'/exp OR 'heart infarct'
- #3 'myocardial infarction'/exp OR 'myocardial infarction'
- #2 'crossover' OR 'cross over' OR 'cross-over'
- #1 case

Web of Science (1017 citations)

Forward citation search for all studies considered eligible after full text screening, across “All years” and no language restriction, including the following databases: Science Citation Index Expanded, Social Sciences Citation Index, Arts & Humanities Citation Index, Conference Proceedings Citation Index- Science, Conference Proceedings Citation Index- Social Science & Humanities.

eTable 1: Detailed Characteristics of Eligible Studies

Author, year (country)	Study setting and participant selection	Recruitment period	Number of cases	Definition of cases	Mean age [SD] (% male)	Activity type and intensity	Hazard period	Control exposure and control period(s) ^a
<i>Episodic physical activity - Myocardial infarction</i>								
Mittleman, 1993 (USA) ¹²	Determinants of Myocardial Infarction Onset Study (22 community hospitals and 23 tertiary care centers). Included cases of acute MI among patients identified by reviewing coronary care unit medical records. 43 of 1271 eligible cases were unable to complete the interview.	1989-1992	1228	Elevated CK, with MB isoenzymes; identifiable onset of pain or other symptoms typical of MI	62 [13] (68)	Peak exertion of ≥ 6 METs	1 hour	-Usual frequency of physical activity in the past year -Physical activity during the same 1 hour period of the previous day
Willich, 1993 (Berlin, Germany) ¹³	Klinikum Steglitz coronary care unit Patients with a primary diagnosis of acute MI from a single center. Excluded were those with poor health, inability to communicate with investigators or who died before interview.	1989-1991	224	Chest pain lasting 20 minutes or more not relieved by nitrates, ECG changes suggestive of evolving MI, and subsequent increase in at least one of three cardiac enzymes (CK, AS, or LDH)	63 [13] (64)	Exertion of ≥ 6 METs	1 hour	-Usual frequency of physical exertion over the past year
Willich, 1993 (Augsburg, Germany) ¹³	Triggers and Mechanisms of Myocardial Infarction Study Routine monitoring of myocardial infarction hospitalizations in the central hospital, 12 hospitals within the study area, and 13 hospitals adjacent to the study area. Excluded were those with poor health, inability to communicate with investigators or who died before interview.	1989-1991	970	Chest pain lasting 20 minutes or more not relieved by nitrates, ECG changes suggestive of evolving MI, and subsequent increase in at least one of three cardiac enzymes (CK, AS, or LDH)	60 [8] (77)	Exertion of ≥ 6 METs	1 hour	-Usual frequency of physical exertion over the past year
Giri, 1999 (USA) ³²	Hartford Hospital Acute MI Study Patients with MI hospitalized within 12 hours of symptom onset. 408 of the 1048 patients meeting these criteria were excluded due to thrombolysis treatment (225), transfer to another hospital for rescue angioplasty (112), vein graft occlusion (42), declined participation (5) or other factors (24).	1995-1998	640	MI treated with primary angioplasty	61 [14] (70)	Exertion of > 6 METs	1 hour	-Usual frequency of heavy exertion (> 6 METs) over the past year
Hallqvist, 2000 (Sweden) ³³	Stockholm Heart Epidemiology Program Patients with a first MI recruited from 10 emergency hospitals in Stockholm county. Of 1489 cases identified, 790 were not interviewed due to death/severity of illness (495), not identified or recruited (210) lack of consent (64). 39 interviewed cases excluded due to poor response quality.	1993-1994	660	First event of MI, diagnosed according to symptoms, ECG and enzyme levels.	NR [45-70] ^b (57)	Exertion of ≥ 6 METs	1 hour	-Usual annual frequency of heavy physical activity -Physical activity during the same 1 hour period of the previous day
Baylin, 2007 (Costa Rica) ³⁴	Three recruitment hospitals in Central Valley, Costa Rica. 530 incident cases of non-fatal acute first MI identified. 10 cases declined to participate, 10 died before data collection complete.	1995-1998	480	WHO criteria	57 [11] (74) ^c	Exertion of > 6 METs	1 hour	-Habitual frequency of heavy physical activity in the last year
von Klot, 2008 (Germany) ³⁵	Cases drawn from population-based KORA Myocardial Infarction registry in Augsburg who were 24 hour survivors of acute MI aged 25-74 years. Among 2089 eligible cases, 476 did not consent or were not able to be interviewed and 312 could not identify timing or AMI onset or exposure in day before AMI	1999-2003	1301	Symptoms, enzyme elevation and ECG findings (MONICA framework)	61 [25-74] ^d (77)	Exertion of ≥ 5 METs	2 hours	-Two control periods, 24 and 48 hours before onset of AMI symptoms

eTable 1 (continued): Detailed Characteristics of Eligible Studies

Author, year (country)	Study setting and participant selection	Recruitment period	Number of cases	Definition of cases	Mean age [SD] (% male)	Activity type and intensity	Hazard period	Control exposure and control period(s)
<i>Episodic physical activity – Sudden cardiac death</i>								
Whang, 2006 (USA) ³⁶	Cases were 288 cases of sudden cardiac death arising from the prospective Nurses Health Study (cohort of female registered nurses aged 30-35 years followed up every 2 years)	1980-2004	288	Death or cardiac arrest that precipitated death within 1 hour of symptom onset as documented by medical records or reports from next of kin	NR [NR] (0)	Exertion of ≥ 5 METs	"at the time of sudden cardiac death"	-Usual amount of exertion over the past year, as reported on the most recent questionnaire ^e
Albert, 2000 (USA) ³⁷	Cases were sudden deaths from cardiac causes drawn from the prospective Physicians Health Study (cohort of male physicians aged 40-84 years based on a randomized controlled trial of aspirin and beta-carotene). 590 men in the cohort with angina, prior coronary revascularization or missing physical activity data excluded.	1982-1994	122	Deaths for which there was evidence of coronary heart disease at or before death and no evidence of a non-coronary cause were classified as due to cardiac causes. Sudden death was defined as death within one hour after the onset of symptoms or death after a witnessed cardiac arrest or abrupt collapse that was not preceded by symptoms lasting more than one hour.	61 [10] (100)	Exertion of ≥ 6 METs	1 hour	-Usual annual frequency of exertion, derived from baseline questionnaire -Sensitivity analysis on the usual duration of physical exercise
Selb Semerl, 2003 (Slovenia) ³⁸	Cases were residents of the republic of Slovenia aged between 20 and 65 years old with sudden cardiac death occurring outside the hospital ascertained through the Death Register of Slovenia. Only married individuals were included in the study to ensure the availability of data on physical activity during the hazard and control periods.	2000-2001	206	Sudden death was defined as instantaneous death or death within an hour after the onset of cardiac symptoms.	NR [NR] (81)	Exertion of ≥ 6 METs	1 hour	-Usual frequency and duration of physical activity in the year preceding sudden cardiac death
<i>Episodic physical activity – Acute coronary syndromes</i>								
Strike, 2006 (UK) ³⁹	Eligible cases were patients aged 18-90 with acute coronary syndromes admitted to 4 hospitals in the London area. Excluded were those with co-morbid conditions, or an inability to recall time of symptom onset or to complete the interview in English.	2001-2004	295	Chest pain plus verification by diagnostic ECG changes, or troponin T measurement or CK increase.	60 [12] (78)	Exertion of ≥ 6 METs	1 hour	-24 hours before symptom onset -Usual frequency and duration of exertion over the previous 6 months

eTable 1 (continued): Detailed Characteristics of Eligible Studies

Author, year (country)	Study setting and participant selection	Recruitment period	Number of cases	Definition of cases	Mean age [SD] (% male)	Activity type and intensity	Hazard period	Control exposure and control period(s)
<i>Sexual activity – Myocardial infarction</i>								
Muller, 1996 (USA) ¹⁴	Determinants of Myocardial Infarction Onset Study (22 community hospitals and 23 tertiary care centers) Included cases of nonfatal MI among patients with prior coronary artery disease identified by reviewing coronary care unit medical records. Inclusion relied on ability to complete a structured interview. 141 of 1774 interviewed declined to answer questions about sexual activity.	1989-1993	1633	Elevated CK, with MB isoenzymes; identifiable onset of pain or other symptoms typical of MI	63 [12] (70)	Sexual activity	2 hours	-Average sexual activity over the past year - Sexual activity in the comparable 2-hour period at the same time on the day before the MI.
Moller, 2001 (Sweden) ⁴⁰	Stockholm Heart Epidemiology Program Cases were those with a first non-fatal MI, admitted to coronary care units of Stockholm County's hospitals. Among 1489 identified, 699 were interviewed and 790 were not, mostly due to death/illness (495). 40 interviewed cases excluded due to missing/unreliable information.	1993-1994	659 ^f	Swedish Society of Cardiology, 1991	NR [45-70 - range] (50)	Sexual activity	2 hours ^g	-Usual annual frequency of sexual activity
Baylin, 2007 (Costa Rica) ³⁴	Three recruitment hospitals in Central Valley, Costa Rica 530 incident cases of non-fatal acute first MI identified. 10 cases declined to participate. 10 died before data collection complete	1995-1998	470	WHO criteria	57 [11] (74)	Sexual activity	2 hours	-Usual frequency of sexual activity in the last year
Masoomi, 2010 (Iran) ⁴¹	Shafa hospital (single center) in Kerman, Iran 200 eligible cases with a first acute MI identified upon admission to the coronary care unit.	Jan – July 2009	198	ESC and ACC joint guidelines	60 [12] (62)	Sexual activity	12 hours	NR

ACC = American College of Cardiology; AST = aspartate aminotransferase; CK = creatine kinase; KORA = Cooperative Health Research in the Region of Augsburg; EKG = LDH = lactate dehydrogenase; ESC = European Society of Cardiology; Mets = metabolic equivalents; MI = myocardial infarction; NR = not reported; SD = standard deviation; WHO = World Health Organization. Numbers have been rounded to the nearest integer.

^aSome studies used multiple control periods.

^bRange.

^cData extracted for the total study population (n=520). Only 480 individuals had information on exposure to “heavy physical exposure”.

^dMedian [range].

^eDifferent questionnaires were administered between 1980 and 2004. All questionnaires asked about usual exertion over the previous year.

^fOf 699 interviewed patients 40 were excluded because of missing, unreliable, or inaccurate information regarding time of disease onset or exposure.

^gThe study reported results for multiple hazard periods. For consistency with the other studies investigating the sexual activity-MI association, we used the results of analyses based on a 2 hour hazard period.

eTable 2: Quality Assessment of Eligible Studies

Reporting items	Study population	Participation rate	Definition of the outcome explicitly reported	Hazard period defined	Hazard period duration justified or sensitivity analysis to different period lengths reported	Assessment of exposure	Control period defined	Control period selection subjected to sensitivity analysis (i.e. assessment of multiple control periods)
Mittleman, 1993	Hospital-based multicenter study	97%	Yes	Yes	Sensitivity analysis performed with hazard periods between 1 to 5 hours pre-MI.	Interviews by specially trained personnel a median of 4 days after MI (range: 0-30 d). 1/3 of the interviews were randomly audiotaped for QC. Interviewers were not informed of the duration of the hypothesized hazard period.	Yes	Yes
Willich, 1993 (Berlin)	Hospital-based single center study	75%	Yes	Yes	No	Standardized interviews by study nurses with clinical experience in cardiovascular disease specially trained for the study. Interviews followed patient transfer from coronary care unit to general ward.	Yes	No
Willich, 1993 (Augsburg)	Hospital-based multicenter study	75%	Yes	Yes	No	Standardized interviews by study nurses with clinical experience in cardiovascular disease specially trained for the study. Interviews followed patient transfer from coronary care unit to general ward.	Yes	No
Giri, 1999	Hospital-based single center study	78% ^a	Yes	Yes	No	Interview by study physician using standardized forms during hospital admission. 4% of interviews were conducted with the spouse/cohabitating partner and 9.7% by telephone with patients.	Yes	No
Hallqvist, 2000	Nested within SHEEP, a population based case-referent study	70% ^b	Yes	Yes	Sensitivity analysis performed for hazard periods up to 4 hours pre-MI.	Interviews by specially trained nurses during hospital stay or shortly afterwards. Median duration between MI onset and interview was 15 days. Interviewers were not informed of assumptions about the length of the induction period.	Yes	Yes
Baylin, 2007	Hospital-based multicenter study	97%	Yes	Yes	Selected based on previous studies.	Interviews by trained personnel following a standardized protocol and using a questionnaire with close-ended questions.	Yes	No
Von Klot, 2008	Nested within the population-based KORA Myocardial Infarction Registry	83%	Yes	Yes	Sensitivity analysis for hazard periods of 2-4 hours and >4 hours pre-MI.	Standardized data collection form (diary interview) by trained research nurses on the ward (median 9 days after MI)	Yes	Yes
Whang, 2006	Nested within the Nurses; Health Study, a prospective cohort study	NR	Yes	Not adequately	No	Ascertained from medical records or reports from next of kin (cases were deceased).	Yes	No

eTable 2 (continued): Quality Assessment of Eligible Studies

Reporting items	Study population	Participation rate	Definition of the outcome explicitly reported	Hazard period defined	Hazard period duration justified or sensitivity analysis to different period lengths reported	Assessment of exposure	Control period defined	Control period selection subjected to sensitivity analysis (i.e. assessment of multiple control periods)
Albert, 2000	Nested within the Physicians' Health Study, a randomized controlled trial	80%	Yes	Yes	Sensitivity analysis performed based on a hazard period of 30 minutes	Based on medical records or reports from next of kin (cases were deceased).	Yes	Yes
Selb Semerl, 2003	Population-based study based on the Death Register of Slovenia	87% ^c	Yes	Yes	No	Data were obtained through mailed questionnaires sent to the spouses and attending physicians of patients experience sudden cardiac death within 1 to 3 months of the event.	Yes	No
Strike, 2006	Hospital-based multicenter study	79%	Yes	Yes	Predefined based on previous studies.	Structured interviews conducted on average 2.5 days after admission, with 95% complete within 5 days.	Yes	Yes
Muller, 1996	Hospital-based multicenter study	92%	Yes	Yes	Sensitivity analysis performed for hazard periods between 1 to 4 hours pre-MI.	Structured interviews by specially trained personnel a median of 4 days after MI. Approximately 1/3 of the interviews were randomly audiotaped for QC.	Yes	Yes
Moller, 2001	Nested within SHEEP, a population based case-referent study	91%	Yes	Yes	Sensitivity analysis performed for hazard periods up to 4 hours pre-MI.	Interviews by specially trained nurses during admission or after discharge. Interviewers kept notes on whether questions regarding sexual activity "seemed to embarrass the patient".	Yes	No
Masoomi, 2010	Hospital-based single center study	99%	Yes	Yes	No	Interviews by a trained physician and a self-administered questionnaire on the first day of admission.	No	No

^aPatients not undergoing catheterization were excluded.

^bThe participation rate is based on the number of patients interviewed among all MI cases in the study base, excluding those that were dead or too sick to participate.

^cFrom a total of 376 mailed questionnaires 276 (73%) responses were received. Of those 238 (86%) cases fulfilled the definition of sudden cardiac death and 206 (87%) provided data on the physical activity and were included in the analyses.

eTable 3: Effect of Physical Exertion on Serious Cardiac Events by Groups of Usual Physical Activity

Author, year ^a	Classification of habitual activity	Habitual activity levels	Number of cases	RR (95% CI)
<i>Episodic physical activity – Myocardial infarction</i>				
Mittleman, 1993	Weekly frequency of physical exertion.	<1 time/week	1027	107 (67-171)
		1-2 times/week	68	19.4 (9.9-38.1)
		3-4 times/week	40	8.6 (3.6-20.5)
		≥5 times/week	93	2.4 (1.5-3.7)
Willich, 1993	Weekly frequency of physical exertion.	<4 times/week	125	6.9 (4.1-12.2)
		≥4 times/week	145	1.3 (0.8-2.2)
Giri, 1999	Patients graded their level of physical activity relative to their peers at work and leisure (modified scoring scheme of the LRC PAQ). ^b	Very low activity	27	30.5 (4.4-209.9)
		Low activity	123	20.9 (3.1-142.1)
		Moderate activity	45	2.9 (0.5-15.9)
		High activity	5	1.2 (0.3-5.2)
Hallqvist, 2000 (Sweden)	Weekly frequency of heavy physical exposure.	<1 times/ week	284	100.7 (52.7-192.4)
		1-2 times/week	49	6.9 (2.5-18.5)
		3-4 times/week	22	3.7 (0.9-14.9)
		≥5 times/week	44	3.3 (1.9-6.2)
Baylin, 2007	Usual energy expenditure ratio in moderate to vigorous activities; individuals spending less than 10% of their daily energy in the performance of moderate to vigorous activities are considered “sedentary”.	<10%	NR	27.49 (18.64-40.54)
		10%-20%		9.78 (4.55-21.04)
		20%-50%		2.42 (1.21-4.85)
		≥50%		1.33 (0.63-2.85)
von Klot, 2008 ^c	Duration of physical exertion (≥5 MET) during three control days.	<1 h/day	NR	4.47 (2.69-7.42)
		1-3 h/day		1.73 (1.12-2.65)
		>3 h/day		0.86 (0.56-1.33)
<i>Episodic physical activity – Sudden cardiac death</i>				
Albert, 2000	Weekly frequency of vigorous exertion.	<1 time/week	32	74.1 (22.0-249)
		1-4 times/week	67	18.9 (10.2-35.1)
		≥5 times/week	23	10.9 (4.5-26.2)
Whang, 2006	Duration of moderate to vigorous exertion per week.	<2 hours/week	NR	8.98 (3.32-24.30)
		≥2 hours/week		1.49 (0.61-3.61)
Selb Semerl, 2003	Weekly frequency of physical activity	<1 time/week	73 ^d	51.44 (19.31-137.06)
		1-2 times/week	40	6.93 (2.24-21.49)
		3-4 times/week	38	5.62 (2.68-11.79)
		7 times/week	64	1.70 (0.99-6.70)

eTable 3 (continued): Effect of Physical Exertion on Serious Cardiac Events by Groups of Usual Physical Activity

Author, year ^a	Classification of habitual activity	Habitual activity levels	Number of cases	RR (95% CI)
<i>Sexual activity – Myocardial infarction</i>				
Muller, 1996	Weekly frequency of strenuous (≥ 6 MET) physical exertion.	≤ 1 time/week	679	3.0 (2.0-4.5)
		2 times/week	33	1.9 (0.2-17.1)
		≥ 3 times/week	146	1.2 (0.4-3.7)
Moller, 2001	"Physical fitness"	"patients who normally get very little exercise"	NR	4.4 (1.5-12.9)
		"patients with a more active exercise pattern"		0.7 (0.1-5.1)
Baylin, 2007	Usual energy expenditure ratio in moderate to vigorous activities;. See also the same study for myocardial infarction.	$< 10\%$	NR	6.06 (2.49-14.74)
		$\geq 10\%$		5.07 (1.62-15.88)

CI = confidence interval; RR = relative risk; NR = not reported.

^aThe studies by Strike et al. and Masoomi et al. did not present data on how the influence of habitual activity levels on the triggering effects of exercise.

^bAmong patients who reported strenuous physical activity, those grading themselves as more active or equally active than their peers were classified as highly active and moderately active, respectively. Among patients who reported no strenuous physical activity, those grading themselves as equally or less active than their peers were classified as low active and very low active, respectively.

^cEstimates are from fixed effects meta-analysis for two groups of patients acutely exposed to physical activity of 5 and ≥ 6 metabolic equivalents.

^dNumbers of patients as provided in the publication.