SUPPLEMENTAL MATERIAL

Title: Sex Differences in Long-term Mortality after Myocardial Infarction: A Systematic Review
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Supplemental Tables: 3
Supplemental Figures: 1

Supplemental Table S1. Characteristics of excluded studies

Author, Year	Study Name, Years of Inclusion	Same Study Population	Reason for Exclusion
Crowley, 2003[S1]	Worcester Heart Attack Study, 1975-1999	Goldberg, 1993	- Limited to diabetics only - Shorter follow-up of 5 years
Donahue, 1993[S2]	Worcester Heart Attack Study, 1974-1986	Goldberg, 1993	- Older study - Results are stratified by diabetes
Eliasson, 2011[S3]	Northern Sweden MONICA Registry, 1989-2006	Isaksson 2011	- No adjusted gender estimates reported
Galatius, 1998[S4]	Danish Verapamil Infarction Trial, 1979-1981	Galatius-Jensen, 1996	- Includes probable and no infarction patients - Primary outcome reinfarction
Grundtvig, 2012[S5]		Grundtvig, 2011	- No adjusted gender estimates
Herlitz 1996 (*Clinical Cardiology)*[S6]	Sahlgrenska University Hospital, 1986-1987	Welin, 2000	- No adjusted gender estimates reported
Herlitz 1996 (*Amer J Hypertens*)[S7]	Sahlgrenska University Hospital, 1986-1987	Welin, 2000	- No adjusted gender estimates reported - Shorter follow-up of 5 years
Herlitz 1997[S8]	Sahlgrenska University Hospital, 1986-1987	Welin, 2000	- No adjusted gender estimates reported - Strong suspicion and vague suspicion of AMI included - Shorter follow-up of 5 years
Koek 2007[S9]	Dutch National Hospital Discharge Register, 1995	Koek, 2006	- Results stratified by diabetes
Launbjerg 1994 (*BMJ)*[S10]	Danish Verapamil Infarction Trial, 1979-1981	Galatius-Jensen, 1996	- Includes probable and no infarction - No adjusted gender estimates reported
Launbjerg 1994 (*Cardiology*)[S11]	Danish Verapamil Infarction Trial, 1979-1981	Galatius-Jensen, 1996	- Includes AMI and non-AMI patients - No adjusted gender estimates reported
Norhammar 2008[S12]	RIKS-HIA, 1995-2002	Lawesson 2012	- Smaller sample size - Results stratified by diabetes
Peltonen 2000[S13]	Northern Swedish MONICA Study, 1985-1994	Isaksson 2011	- No age-adjustment - Shorter follow-up

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S2. Donahue RP, Goldberg RJ, Chen Z, Gore JM, Alpert JS. The influence of sex and diabetes mellitus on survival following acute myocardial infarction: a community-wide perspective. J Clin Epidemiol. 1993;46:245-52.

S3. Eliasson M, Jansson JH, Lundblad D, Naslund U. The disparity between long-term survival in patients with and without diabetes following a first myocardial infarction did not change between 1989 and 2006: an analysis of 6,776 patients in the Northern Sweden MONICA Study. Diabetologia. 2011;54:2538-43.

S4. Galatius S, Launbjerg J, Mortensen LS, Hansen JF. 5993 survivors of suspected myocardial infarction. 10 year incidence of later myocardial infarction and subsequent mortality. Eur Heart J. 1998;19:564-9.

S5. Grundtvig M, Hagen TP, Amrud ES, Reikvam A. Reduced life expectancy after an incident hospital diagnosis of acute myocardial infarction - Effects of smoking in women and men. Int J Cardiol. 2013;167:2792-7.

S6. Herlitz J, Bang A, Hartford M, Karlson BW. Influence of gender on survival, mode of death, reinfarction, use of medication, and aspects of well being during a period of five years after onset of acute myocardial infarction. Clin Cardiol. 1996;19:555-61.

S7. Herlitz J, Bang A, Karlson BW. Five-year prognosis after acute myocardial infarction in relation to a history of hypertension. Am J Hypertens. 1996;9:70-6.

S8. Herlitz J, Karlson BW, Lindqvist J, Sjolin M. Long-term prognosis in men and women coming to the emergency department with chest pain or other symptoms suggestive of acute myocardial infarction. Eur J Emerg Med. 1997;4:196-203.

S9. Koek HL, Soedamah-Muthu SS, Kardaun JW, Gevers E, de Bruin A, Reitsma JB, Bots ML, Grobbee DE. Short- and long-term mortality after acute myocardial infarction: comparison of patients with and without diabetes mellitus. Eur J Epidemiol. 2007;22:883-8.

S10. Launbjerg J, Fruergaard P, Madsen JK, Mortensen LS, Hansen JF. Ten year mortality in patients with suspected acute myocardial infarction. BMJ. 1994;308:1196-9.

S11. Launbjerg J, Fruergaard P, Madsen JK, Mortensen LS, Hansen JF. Ten-year mortality of patients admitted to coronary care units with and without myocardial infarction. Risk factors from medical history and diagnosis at discharge. DAVIT-Study Group. Danish Verapamil Infarction Trial. Cardiology. 1994;85:259-66.

S12. Norhammar A, Stenestrand U, Lindback J, Wallentin L. Women younger than 65 years with diabetes mellitus are a high-risk group after myocardial infarction: a report from the Swedish Register of Information and Knowledge about Swedish Heart Intensive Care Admission (RIKS-HIA). Heart. 2008;94:1565-70.

S13. Peltonen M, Lundberg V, Huhtasaari F, Asplund K. Marked improvement in survival after acute myocardial infarction in middle-aged men but not in women. The Northern Sweden MONICA study 1985-94. J Intern Med. 2000;247:579-87.

Supplemental Table S2. Study quality characteristics

Study Characteristic	Reference
Study Design	
Source of data	
Registries	6,9,11,12,14,16,17,18,20,21,26,27,30,31,35,36,41,42,44
Randomized clinical trials	19,33,37,38
Hospital/community cohort	7,8,10,13,15,22,23,24,28,29,32,34,39,40,43,45
Retrospective study design	6,14
Diagnosis of AMI	
2 of 3 established criteria*	8,9,11,12,13,15,17,18,20,21,22,24,28,30,31,33,35,36,37,38, 39,40,41,42,43,44,45
1 of 3 established criteria*	10,19,29
Discharge diagnosis/ICD-9 codes	6,14,16,26,27,34
Did not specify criteria	7,23,32
Inclusion Criteria	
Specific conditions	
Heart failure	31
Cardiac arrest	29
Ventricular fibrillation	43
Age criteria	11,18,20,21,28,36,38,40,41
Treatment	
PCI only	13,29,30
Streptokinase only	22
Follow-Up	
Start-point	
Admission	8,9,10,11‡,12,13,14,17,20,21,22,23,24,26,27,29,32,35,39,42,45
Discharge	6,10,16,19,30,34,41,43,44
15 days	22,38
30 days	7,11,12,13,15,18,21,23,28,33,35,36
3 months	40
After onset of heart failure†	31
After randomization§	37
Multiple start points analyzed	10,11,12,13,21,22,23,35
Length of follow-up	
<10 years	6,7,8,9,10,11,12,13,16,18,24,26,27,28,29,30,31,32,33,34,35,36,37
≥10 years	14,15,17,19,20,21,22,23,38,39,40,41,42,43,44,45

Source of follow-up data	
Population registries/death certificates	11,14,16,17,18,19,20,24,27,28,29,33,34,35,38,40,42,45 7,9,10,13,21,31,39,43
Medical records/patient contact	6,26,32
Administrative claims data	8,12,15,23,30,36,37,41,44
Population registries and medical records	22
Not specified	
Provided information on losses to follow-up	8,9,10,13,15,16,18,19,20,21,27,28,30,33,35,36,39,40,41,45

[*] Criteria for diagnosis of AMI included: 1) ischemic symptoms, 2) ECG changes, and 3) elevations in cardiac enzymes

[†] In study by Hellerman et al, 59% of heart failure episodes occurred within 30 days of MI and 68% within 1 year post-MI

[‡] In study by Lowel et al, survival was calculated only among patients who survived first 24 hours of admission.

[§] In study by Reynolds et al, median (IQR) time from MI to randomization was 8.5 (5.0, 17.0) in women and 8.0 (5.0, 16.0) in men.

Supplementary Table S3. Distribution of risk factors, clinical presentation, and treatment in men vs. women across studies

Characteristic	Higher Percentage in Women	No Difference Between Genders	Lower Percentage in Women
Risk Factors/Comorbid Conditions			
Diabetes Mellitus	6, 11, 12, 13, 16, 18, 19, 20, 21, 24, 26, 27, 32, 34, 37, 39, 40, 42, 44, 45	9, 35, 41	
History of CHF	6, 9, 16, 24, 26, 37, 42	32	
Hypertension	6, 9, 11, 12, 16, 18, 19, 20, 21, 24, 32, 34, 37, 39, 41, 42, 44, 45	13, 15, 35	
Smoking			9, 11, 12, 13, 15, 18, 19, 32, 34, 35, 37, 39, 41, 42, 45
Prior MI		13	6, 19, 22, 32, 34, 37, 42, 45
Obesity	9, 32		35
Angina	34, 41	12, 15, 19, 21, 37	
Depression/Psychiatric History	24, 32, 40, 41	35	
Renal Dysfunction	6, 26, 32, 45	16, 42	
Hypercholesterolemia	9	12, 13, 37, 45	6
Clinical Presentation			
Killip Class 3 or 4	12, 21, 42	15	
Anterior MI	37, 44	12, 13, 15, 19, 21	
Cardiac Arrest		11, 19	
CHF/Pulmonary Edema	15, 24, 37, 44	11, 19	
Cardiogenic Shock	11, 44	13, 15, 19	
Heart block	15	19, 44	
Arrhythmias		9, 12, 15, 21, 32, 44	19
Treatment			
Coronary angiography		21	6, 11, 16, 24, 42
CABG		12, 21, 32, 44	6, 9, 11, 16
PCI		9, 11, 32, 45	6, 12, 16, 44
Fibrinolytics		32, 45	11, 34, 44
In-Hospital Medications			
Aspirin	42		34
Beta-blockers	42		11, 12, 34, 44
Calcium-channel blockers	42	11, 44	
Diuretics	11, 34, 42, 44		
ACE inhibitors	11, 12, 42		
Statins		11	42
Nitrates	42	11	34, 44

Discharge Medications			
Aspirin		9, 16, 37, 45	42
Beta-blockers		9, 16, 32, 37	11, 12, 24, 34, 42, 45
Calcium-channel blockers	16, 24, 37, 45	9, 11	
Diuretics	9, 11, 16, 34, 37, 45		
ACE inhibitors	11, 24	12, 32, 34, 37	16, 42, 45
Statins	11	32, 37	24, 34, 42, 45
Nitrates	16, 37, 45	9, 11, 24	

Abbreviations: ACE, angiotensin-converting enzyme; CABG, coronary artery bypass grafting; CHF, congestive heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention.