High-sensitivity cardiac troponin and the under diagnosis of myocardial infarction in women: a prospective cohort study

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Table S1. Diagnosis of myocardial infarction using contemporary and high-sensitivity assays

	Contemporary assay [a]	High-sensitivity assay (single threshold) [b]	High-sensitivity assay (sex-specific threshold) [c]	P-value [d]	P-value [e]
All patients (n=1,126)					
Type 1 myocardial infarction	**172 (15%)**	**222 (20%)**	**242 (21%)**	**<0.001**	**0.003**
Type 2 myocardial infarction	47 (4%)	55 (5%)	56 (5%)	0.012	0.999
Myocardial injury	27 (2%)	38 (3%)	40 (4%)	<0.001	0.727
Unstable angina	38 (3%)	28 (2%)	28 (2%)	0.004	0.999
Other	842 (75%)	783 (70%)	760 (68%)	<0.001	0.004
Men (n=622)					
Type 1 myocardial infarction	**117 (19%)**	**142 (23%)**	**131 (21%)**	**0.001**	**0.002**
Type 2 myocardial infarction	27 (4%)	30 (5%)	28 (5%)	0.999	0.999
Myocardial injury	12 (2%)	15 (2%)	12 (2%)	0.999	0.999
Unstable angina	27 (4%)	20 (3%)	22 (4%)	0.074	0.480
Other	439 (71%)	415 (67%)	429 (69%)	0.035	0.035
Women (n=504)					
Type 1 myocardial infarction	**55 (11%)**	**80 (16%)**	**111 (22%)**	**<0.001**	**<0.001**
Type 2 myocardial infarction	20 (4%)	25 (5%)	28 (6%)	0.008	0.250
Myocardial injury	15 (3%)	23 (5%)	28 (6%)	<0.001	0.250
Unstable angina	11 (2%)	8 (2%)	6 (1%)	0.073	0.480
Other	403 (80%)	368 (73%)	331 (66%)	<0.001	<0.001

a. Contemporary assay single threshold 50 ng/L
b. High-sensitivity assay single threshold 26 ng/L
c. High-sensitivity assay sex-specific thresholds: women 16 ng/L and men 34 ng/L
d. McNemar's test comparing diagnosis based on high-sensitivity troponin assay using sex-specific thresholds to the contemporary assay using a single threshold
e. McNemar's test comparing diagnosis based on high-sensitivity troponin assay using sex-specific thresholds to the high-sensitivity assay using a single threshold

Table S2. Baseline characteristics of women with and without myocardial infarction where assays were concordant (groups 3 and 1 respectively) and those only identified using the high-sensitivity assay with sex-specific thresholds (group 2)*

	Group 1 n=337	Group 2 n=56	Group 3 n=55
Age	65 (16)	76 (12)	75 (15)
Chest pain	264 (79)	42 (75)	48 (87)
Risk Factors			
Smoker	57 (19)	10 (20)	8 (15)
Hypertension	165 (49)	36 (64)	31 (56)
Hyperlipidaemia	135 (40)	28 (50)	20 (36)
Diabetes mellitus	43 (13)	11 (20)	9 (16)
Past medical history			
Ischaemic heart disease	124 (37)	34 (61)	17 (31)
Myocardial infarction	56 (17)	23 (41)	13 (24)
Ischaemic stroke	15 (4)	7 (12)	5 (9)
Transient ischaemic attack	21 (6)	1 (2)	3 (5)
Peripheral vascular disease	2 (1)	0 (0)	3 (5)
Revascularisation			
Previous PCI	32 (10)	7 (12)	7 (13)
Previous CABG	12 (4)	5 (9)	2 (4)
Haemodynamics			
Systolic pressure, mmHg	137 (25)	137 (30)	138 (30)
Diastolic pressure, mmHg	71 (14)	71 (17)	75 (18)
Heart rate, beats per minute	77 (18)	83 (21)	84 (18)
Clinical chemistry			
Haemoglobin, g/dL	130 (56)	127 (15)	125 (17)
Creatinine, mg/dL	72 (23)	90 (38)	95 (49)
Urea, mg/dL	6 (6)	9 (8)	7 (4)
Cholesterol, mmol/L	5 (1)	5 (1)	5 (1)
Electrocardiography			
ST elevation	9 (3)	5 (9)	16 (30)
ST depression	23 (7)	11 (20)	13 (24)
T wave inversion	63 (20)	15 (27)	12 (22)
Admission drugs			
Aspirin, n (%)	109 (33)	29 (54)	20 (36)
Clopidogrel, n (%)	37 (11)	9 (17)	4 (7)
B-blockers, n (%)	83 (25)	22 (41)	14 (25)
ACE inhibitors, n (%)	89 (27)	21 (39)	23 (42)
Statins, n (%)	123 (37)	30 (56)	20 (36)
Warfarin, n (%)	15 (5)	7 (13)	3 (5)
Proton pump inhibitor, n (%)	119 (36)	26 (48)	20 (36)

*Excludes patients adjudicated as type 2 myocardial infarction or myocardial injury

Table S3. Baseline characteristics of men with and without myocardial infarction where assays were concordant (groups 3 and 1 respectively) and those only identified using the high-sensitivity assay with sex-specific thresholds (group 2)*

	Group 1 n=451	Group 2 n=14	Group 3 n=117
Age	61 (15)	64 (17)	67 (14)
Chest pain, n (%)	383 (85)	14 (100)	99 (85)
Risk Factors			
Smoker, n (%)	145 (34)	6 (46)	38 (34)
Hypertension, n (%)	227 (50)	7 (50)	61 (53)
Hyperlipidaemia, n (%)	210 (47)	9 (64)	54 (47)
Diabetes mellitus, n (%)	69 (15)	3 (21)	25 (22)
Past medical history			
Ischaemic heart disease, n (%)	193 (43)	9 (64)	54 (47)
Myocardial infarction, n (%)	135 (30)	8 (57)	33 (28)
Ischaemic stroke, n (%)	38 (8)	3 (21)	8 (7)
Transient ischaemic attack, n (%)	20 (4)	0 (0)	3 (3)
Peripheral vascular disease, n (%)	12 (3)	1 (7)	8 (7)
Revascularisation			
Previous PCI, n (%)	93 (21)	4 (29)	18 (16)
Previous CABG, n (%)	40 (9)	2 (14)	14 (12)
Haemodynamics			
Systolic pressure, mmHg	133 (22)	141 (23)	131 (22)
Diastolic pressure, mmHg	73 (15)	75 (14)	74 (14)
Heart rate, beats per minute	78 (18)	78 (15)	81 (22)
Clinical chemistry			
Haemoglobin, g/dL	141 (17)	142 (24)	138 (21)
Creatinine, mg/dL	82 (24)	133 (197)	104 (57)
Urea, mg/dL	6 (3)	7 (6)	7 (4)
Cholesterol, mmol/L	4 (1)	5 (1)	5 (1)
Electrocardiography			
ST elevation, n (%)	36 (8)	1 (8)	42 (36)
ST depression, n (%)	13 (3)	1 (8)	29 (25)
T wave inversion, n (%)	75 (17)	3 (23)	34 (29)
Admission drugs			
Aspirin, n (%)	178 (40)	9 (64)	46 (40)
Clopidogrel, n (%)	55 (12)	5 (36)	12 (11)
Beta-blockers, n (%)	119 (27)	8 (57)	34 (30)
ACE inhibitors / ARB, n (%)	149 (34)	5 (36)	38 (33)
Statin, n (%)	194 (44)	8 (57)	52 (45)
Warfarin, n (%)	28 (6)	1 (7)	6 (5)
Proton pump inhibitor, n (%)	139 (31)	6 (43)	31 (27)

*Excludes patients adjudicated as type 2 myocardial infarction or myocardial injury

Figure S1. Distribution of troponin and upper reference limits (99th percentile) in 4,590 samples from healthy men and women
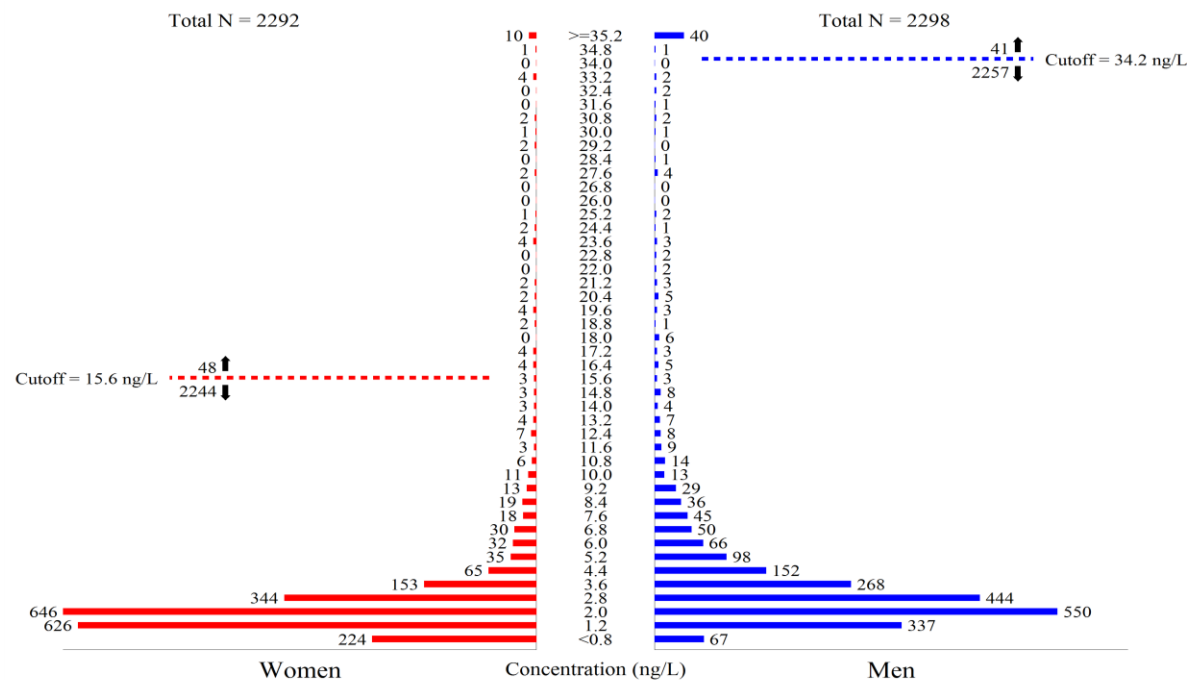
Reference population consists of 1,531 persons with an equal number of men and women. Inclusion criteria were age 21 to 75 years, no previous medical illness, normal renal function (eGFR >60 mL/min), glycated haemoglobin (HbA1c) ≤ 6% and normal B-type naturetic peptide concentrations (male ≤ 25 pg/mL and female ≤ 40 pg/mL) (Rogers et al *Clin Chem*; 2013 (10) A225).