Acute Ischemic Heart Disease

Comparison of the performances of cardiac troponins, including sensitive assays, and copeptin in the diagnostic of acute myocardial infarction and long-term prognosis between women and men

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Background Concerns have been raised about possible gender disparities in cardiac investigations and/or outcome. This study sought to examine and compare the diagnostic and prognostic performance of selected cardiac biomarkers in women versus men.

Methods In a prospective, multicenter cohort of patients with acute chest pain cardiac troponin T (cTnT) (fourth-generation Roche assay), high-sensitivity cTnT (hs-cTnT), and copeptin were measured at presentation.

Results Of 1,247 patients, 420 were women and 827 were men. Although the rate of acute myocardial infarction was similar in women (14.5%) and men (16.6%, $P = .351$), women more frequently had cardiac but noncoronary causes of chest pain (17.4% vs 10.8%, $P = .001$) and less frequently had unstable angina (8.8% vs 16.6%, $P = .002$) than men. Diagnostic accuracy as quantified by the area under the receiver operating characteristic curve (AUC) for acute myocardial infarction in women was 0.90 (95% CI 0.84-0.95) for cTnT, which was lower than the AUC for hs-cTnT alone (0.94, 95% CI [0.91-0.98]), the combination of cTnT with copeptin (0.96, 95% CI [0.94-0.98]) or the combination of hs-cTnT with copeptin (0.96, 95% CI [0.93-0.98]) ($P = .008$, $P = .006$, and $P = .002$, respectively). Prognostic accuracy as quantified by the AUCs for 1-year mortality was 0.69 (0.56-0.83), 0.86 (0.79-0.93), 0.87 (0.81-0.94), and 0.87 (0.80-0.94), respectively. No relevant gender differences in AUCs were observed.

Conclusion The diagnostic and prognostic performance of cTnT, hs-cTnT, and copeptin is as good in women as in men. High-sensitivity cTnT and the combination of cTnT and copeptin outperform cTnT alone, both in women and men. (Am Heart J 2013;166:30-7.)

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The management of patients with acute chest pain who present to the emergency department (ED) remains a clinical challenge. During the last decades, concerns have been raised about possible gender disparities in cardiac procedures and/or outcome.[1–3] Indeed, several studies have reported higher crude in-hospital mortality as well as short-term mortality in women with acute myocardial infarction (AMI) than in men[3–6]; the difference seemed at least partly attributable to less diagnostic and therapeutic cardiac procedures and reperfusion therapy.[2,6–10] Several hypotheses may be generated to explain these gender differences including the global perception that women have less often coronary artery disease than men,[11]

the atypical nature of symptoms often reported by women, which may have led clinicians to consider differential diagnosis.[4]

To date, clinical assessment, electrocardiogram (ECG), and measurement of markers quantifying cardiomyocyte necrosis, mainly cardiac troponins (cTn), form the cornerstones of the diagnosis of AMI.[12] Recently, high-sensitive assays of cTn (hs-cTn) and copeptin, the c-terminal part of the vasopressin prohormone, demonstrated their incremental value when used instead of or in combination with conventional assay of cTn in cohorts predominately recruiting men.[13–15] A gender difference in the diagnostic accuracy of cTn or copeptin, if existed, should be considered of major clinical importance and could contribute to gender differences in outcome. In a cohort of patients with AMI, maximal cTnT concentrations were lower in women than in men, both in ST-elevation and non–ST-elevation AMI.[16] In addition, the 99th percentile of hs-cTn seems to be lower in women than in men[17] as well as the concentration of copeptin in healthy women versus men.[14,18]

Methods

Study design and population

The Advantageous Predictors of Acute Coronary Syndrome Evaluation is an ongoing prospective international multicenter study designed and coordinated by the University Hospital Basel, Switzerland.[13] Briefly, consecutive patients presenting to the ED with symptoms suggestive of AMI of <12 hours have been included, after informed consent, and were followed up at regular intervals. Patients with terminal kidney failure requiring dialysis were excluded. The objective of the present study was to examine if cTn and copeptin perform equally well in women than in men. The study was carried out according to the principles of the Declaration of Helsinki and approved by the local ethics committee.

Routine clinical assessment

All patients underwent a clinical assessment that included medical history, physical examination, 12-lead ECG, continuous ECG monitoring, pulse oximetry, standard blood tests, and chest radiography. Cardiac troponins were measured at presentation and after 6 to 9 hours or as long as clinically indicated. The following cTn assays were used for the clinical care of the patients at the participating hospitals: Abbott Axsym-cTnI ADV (Abbott Park, IL), Beckmann Coulter Accu-cTnI (Marseille' France), and Roche cTnT 4th generation. Treatment of patients was left at discretion of the attending physician.

Adjudicated final diagnosis

Final diagnoses were adjudicated 2 times: first, using standard cTn levels and, second, using hs-cTnT levels for adjudication. The main diagnostic analysis is based on the first adjudication. The second adjudication was added for a confirmatory analysis to demonstrate that the findings also apply with the detection of small AMIs that would have been missed by the use of standard cTn only. To determine the final diagnosis for each patient, 2 independent cardiologists reviewed all available medical records and results of laboratory tests (including cTn values obtained at the participating hospitals), radiologic testing, ECG, echocardiography, cardiac exercise test, and coronary angiography from the time of the patient's arrival to the ED to the end of the 60-day follow-up period. Acute myocardial infarction was diagnosed when there was evidence of myocardial necrosis in association with clinical signs of myocardial ischemia. Necrosis was diagnosed by a rising and/or falling pattern of the local cTn level (or the hs-cTnT level for the second adjudication) with at least 1 value above the 99th percentile [or the 10% coefficient of variation (CV) level for those assays with a CV >10% at the 99th percentile].[19]

Investigational assays

Plasma samples (and serum samples for the core laboratory measurement of cTnT and hs-cTnT in the first 800 patients) for measuring the concentration of cTnT, hs-cTnT, and copeptin were collected in plastic tubes. After centrifugation, samples were frozen at −80°C until assayed in a blinded fashion in a dedicated core laboratory (median delay from collection to measurement was 12 months). Cardiac troponin T was measured using a commercially available electrochemiluminescence immunoassay (4th generation cTnT; Roche Diagnostics, Mannheim, Germany); the limit of detection is of 0.01 μg/L, and a coefficient of variation of <10% is achieved at 0.035 μg/L. High-sensitivity cTnT was measured using a commercially available electrochemiluminescence immunoassay (Roche Diagnostics); the 99th percentile cutoff point is of 14 ng/L, and a coefficient of variation of <10% is achieved at 13 ng/L.[13] Copeptin was measured using a commercial sandwich immunoluminometric assay (B.R.A.H.M.S LUMItest CT-proAVP; BRAHMS AG, Hennigsdorf/Berlin, Germany).[20] Since the initial publication, the capture antibody was replaced by a murine monoclonal antibody directed to amino acids 137 to 144 (GPAGAL) of pro-Arginin-Vasopressin to improve the accuracy of the assay. The lower detection limit was 0.4 pmol/L, and the functional assay sensitivity (<20% inter assay CV) was <1 pmol/L.[21]

Follow-up and clinical end points

After hospital discharge, patients were followed up at 30, 90, and 360 days by telephone calls using a standardized form. If unsuccessful, the primary care physicians were contacted, and both the medical records of the hospitals and the death certificates were consulted. If the patient reported any symptoms, visit, or was readmitted to hospital, the physician was contacted, and all medical documents were examined.

The coprimary diagnostic end points were the accurate detection of patients with AMI and non–ST-segment elevation AMI (NSTEMI).

The primary prognostic end point was all-cause mortality within 360 days. Secondary prognostic endpoints was the combined of death/AMI within 360 days.

Statistical analysis

Values are expressed as means ± SD, medians with interquartile range, or counts and percentages, as appropriate.

Table I. Baseline characteristics according to gender

	All patients (n = 1247)	Women (n = 420)	Men (n = 827)	*P*
Age, y	64 (51-76)	72 (59-70)	60 (48-73)	<.001
Risk factors, n (%)				
Hypertension	793 (63.6)	274 (65.2)	519 (62.8)	.389
Hypercholesterolemia	557 (44.7)	162 (38.6)	395 (47.8)	.002
Diabetes	257 (20.6)	74 (17.6)	183 (22.1)	.063
Current smoking	304 (24.4)	100 (23.8)	204 (24.7)	.739
Body mass index	26.4 (24-30)	25.7 (22.3-29.5)	26.8 (24.4-29.7)	.008
History, n (%)				
Coronary artery disease	458 (36.7)	119 (28.3)	339 (41.0)	<.001
Previous myocardial infarction	306 (24.5)	66 (15.7)	240 (29.0)	<.001
Renal failure	128 (10.3)	50 (11.9)	78 (9.4)	.174
Previous treatment, n (%)				
Aspirin	488 (39.1)	140 (33.3)	348 (42.1)	.003
β-Blocker	471 (37.8)	149 (35.5)	322 (38.9)	.234
ACE inhibitor/AT-2-blocker	510 (40.9)	166 (39.5)	354 (41.6)	.482
Statin	499 (36.0)	126 (30.0)	323 (39.1)	.002
Time from onset of symptoms to presentation, h	3 (2-6)	4 (2-6)	3 (2-6)	.254
Clinical findings				
Heart rate, beat/min	76 (66-89)	78 (68-92)	74 (65-88)	.003
Systolic blood pressure, mm Hg	142 (127-160)	144 (130-164)	141 (126-158)	.081
Diastolic blood pressure, mm Hg	84 (74-93)	82 (72-92)	85 (76-94)	.002
Time from maximum of chest pain, h	4 (2-6)	4 (2-7)	4 (2-6)	.264
ECG findings, n (%)				
ST deviation	253 (20.3)	79 (18.8)	174 (21.0)	.355
T-wave inversion	167 (13.4)	58 (13.8)	109 (13.2)	.758
Laboratory findings				
Hemoglobin level, g/L	143 (132-153)	134 (125-142)	148 (138-156)	<.001
Creatinine, μmol/L	76 (65-92)	66 (56-80)	80 (70-94)	<.001
Glomerular filtration rate, mL/min/1.73 m^2	88.8 (61-116.8)	83.5 (54.9-112)	91.6 (64.6-118.6)	<.001
cTnT fourth generation, μg/L	0.01 (0.01-0.01)	0.01 (0.01-0.01)	0.01 (0.01-0.01)	.245
Patients with cTn above the cutoff value	170 (13.8)	52 (12.6)	118 (14.4)	.379
hs-cTnT, ng/L	9 (4-24)	10(4-24)	9 (5-23)	.492
Copeptin, pmol/L	6.8 (3.5-15.8)	5.1 (2.9-15.7)	7.7 (4.1-15.9)	.001
Coronary angiogram performed	330 (26.5)	96 (22.9)	234 (28.3)	.040

Continuous Gaussian variables are presented as means ± SD; non-Gaussian variables, as medians with interquartile range. Comparisons between independent groups were made using the χ^2 method and Mann-Whitney U test, respectively. The cutoff value for cTn is set at the 99th percentile or the 10% CV level for those assays with a CV >10% at the 99th percentile. *ACE*, Angiotensin-converting enzyme.

Receiver operating characteristic curves were constructed to assess the sensitivities and specificities of cTnT, hs-cTnT, and copeptin for both diagnostic and prognostic purposes; their accuracy was compared in women versus men.[22]

Time to event at 360 days is presented as Kaplan-Meier curves for all prognostic end points; comparisons between groups were performed with log-rank test.

To evaluate the possible impact of different cutoff values, risk ratios for all prognostic end points were compared between women and men using first the recommended cutoff values and then the different 99th percentile observed in women and men.

All statistical analyses were performed with the STATA statistical software version 10.1 (StataCorp LP, College Station, TX) and MedCalc software (Ostend, Belgium) (version 11.2.1.0) ($P < .05$ for significance).

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The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents

Results

Study population

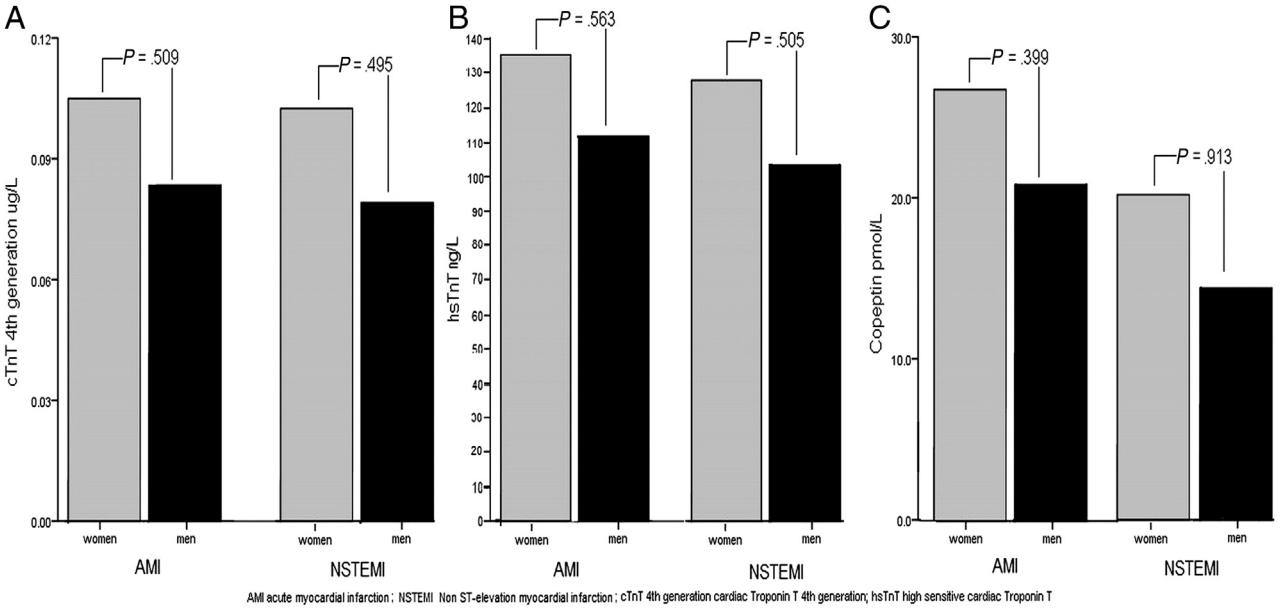
A total of 1,247 patients were included in the present analysis, comprising 420 women (34%) and 827 men (66%). Baseline characteristics according to gender are listed in Table I. The adjudicated final diagnosis was AMI in 198 patients (15.9%) (14.5% in women vs 16.6% in men, $P = .351$), including NSTEMI in 148 patients (11.9%) (10.7% in women vs 12.4% in men, $P = .369$). Other diagnosis included unstable angina in 174 patients (14.0%) (8.8% in women vs 16.6% in men, $P = .002$), cardiac but noncoronary cause in 162 patients (13.0%) (17.4% vs 10.8%, respectively, $P =$

Table II. Diagnostic accuracy of cTnT, hs-cTnT, copeptin alone, and in combination with cTnT/hs-cTnT in the detection of AMI and NSTEMI

		AUC in women (95% CI)	AUC in men (95% CI)	P*
AMI	cTnT	0.90 (0.84-0.95)	0.88 (0.84-0.92)	.633
	hs-cTnT	0.94 (0.91-0.98)	0.95 (0.93-0.97)	.702
	Copeptin	0.79 (0.73-0.85)	0.73 (0.68-0.78)	.120
	cTnT and copeptin	0.96 (0.94-0.98)	0.96 (0.94-0.97)	.742
	hs-cTnT and copeptin	0.95 (0.93-0.98)	0.96 (0.94-0.97	.879
NSTEMI	cTnT	0.91 (0.86-0.97)	0.90 (0.86-0.94)	.624
	hs-cTnT	0.95 (0.91-0.99)	0.96 (0.94-0.97)	.815
	Copeptin	0.75 (0.68-0.83)	0.70 (0.64-0.76)	.250
	cTnT and copeptin	0.96 (0.93-0.99)	0.96 (0.94-0.97)	.864
	hs-cTnT and copeptin	0.96 (0.92-0.99)	0.96 (0.94-0.98)	.941

Final diagnosis adjudicated using conventional assay of cTn levels.
*The *P* value compares the AUC curve of women and men.

Figure 1



Concentration of biomarkers at presentation in men and women with AMI and NSTEMI. **A**, Cardiac troponin T. **B**, High-sensitivity cTnT. **C**, Copeptin.

.001), noncardiac cause of chest pain in 60 patients3 (48.4%) (50.0% vs 47.5%, respectively, *P* = .408), and remained of unknown origin in 110x patients3 (48.4%) (9.3% vs 8.6%, *P* = .680).

Concentrations of cTnT, hs-cTnT, and copeptin

Cardiac troponin T was measured at presentation in 1,185 patients (95% of the total cohort), hs-cTnT in 1,181 patients (95%), and copeptin in 1,201 patients (96%). Among the total cohort, there was no significant gender difference in cTnT or hs-cTnT levels, whereas copeptin levels were lower in women versus men (5.1 [2.9-15.8] pmol/L vs 7.7 [4.1-16.0] pmol/L, respectively, *P* = .001) (Table I); no gender differences existed in the subgroup of patients with AMI (Figure 1).

Diagnostic accuracy of cTnT, hs-cTnT, and copeptin in women and men

Table II shows the accuracy of cTnT, hs-cTnT, copeptin alone, and in combination to diagnose AMI and NSTEMI.

Regarding the diagnosis of AMI in women, the area under the receiver operating characteristic curve (AUC) was 0.90 (95% CI 0.84-0.95) for cTnT, which was lower than the AUC for hs-cTnT alone (0.94, 95% CI [0.91-0.98], *P* = .008), the combination of cTnT with copeptin (0.96, 95% CI [0.94-0.98], *P* = .006), and the combination of hs-

Table III. Diagnostic accuracy of cTnT, hs-cTnT, copeptin alone, and in combination with cTnT/hs-cTnT in the detection of AMI and NSTEMI, based on hs-cTnT assay

		AUC in women (95% CI)	AUC in men (95% CI)	P*
AMI	cTnT	0.84 (0.78-0.89)	0.83 (0.79-0.87)	.910
	hs-cTnT	0.92 (0.89-0.96)	0.93 (0.91-0.95)	.717
	Copeptin	0.77 (0.71-0.84)	0.71 (0.66-0.75)	.085
	cTnT and copeptin	0.91 (0.86-0.96)	0.905 (0.86-0.93)	.716
	hs-cTnT and copeptin	0.93 (0.90-0.96)	0.93 (0.91-0.95)	.843
NSTEMI	cTnT	0.83 (0.77-0.90)	0.83 (0.79-0.87)	.934
	hs-cTnT	0.92 (0.88-0.96)	0.93 (0.90-0.95)	.827
	Copeptin	0.74 (0.66-0.81)	0.68 (0.62-0.73)	.177
	cTnT and copeptin	0.89 (0.83-0.95)	0.88 (0.84-0.92)	.802
	hs-cTnT and copeptin	0.92 (0.88-0.96)	0.93 (0.90-0.95)	.910

*The *P* value compares the AUC curve of women and men.

cTnT with copeptin (0.96, 95%CI [0.93-0.98], $P = .002$); in addition, the combination of copeptin with hs-cTnT tended to outperform hs-cTnT alone ($P = .092$). Overall, there was no gender difference in the diagnostic accuracy of AMI for cTnT ($P = .633$), hs-cTnT ($P = .702$), the combination of copeptin with cTnT ($P = .743$), or the combination of copeptin with hs-cTnT ($P = .879$).

These findings were confirmed after exclusion of patients with ST-segment elevation AMI (Table II) and when the final diagnosis was readjudicated using hs-cTnT levels (Table III).

No gender differences existed in the subgroups of patients <50 years and >50 years for cTnT ($P = .235$ and $P = .116$, respectively) and hs-cTnT ($P = .155$ and $P = .276$). Diagnostic accuracy of copeptin was higher in women versus men <50 years, whereas there was no gender difference for patients >50 years ($P < .001$ and $P = .308$).

Prognostic accuracy of cTnT, hs-cTnT, and copeptin in women and men

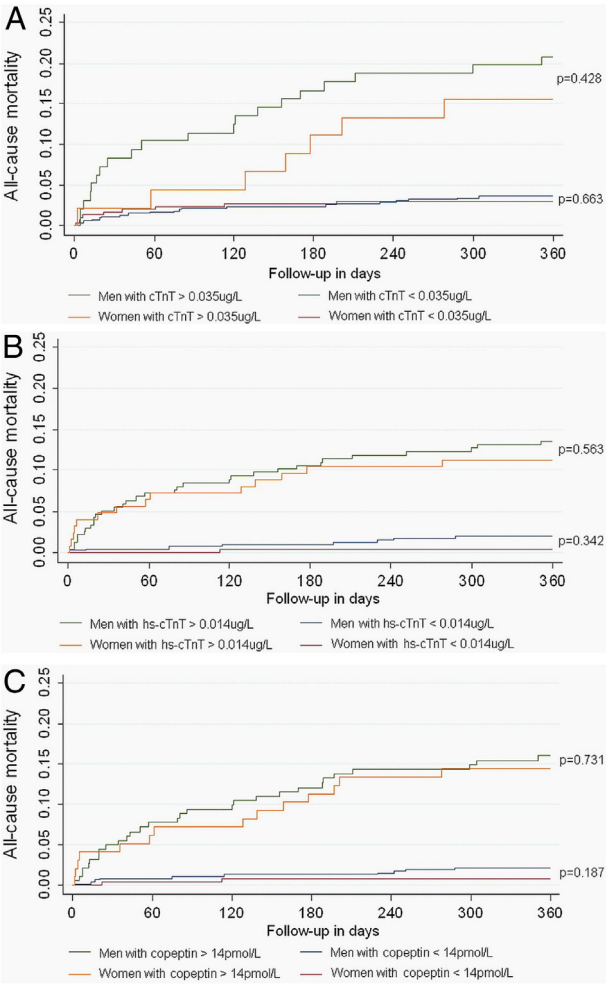
No patient was lost to follow-up. Of the 1,247 enrolled patients, 1,009 (81%) completed the 360-day period of follow-up. Sixty patients (6.0%) died within 360 days, and 83 (8.2%) patients reached the combined endpoint of death/AMI.

Cardiac troponin T, hs-cTnT, and copeptin concentrations at presentation were increased in patients who died versus survivors (0.03 [0.01-0.19] μg/L vs 0.01 [0.01-0.01] μg/L, $P < .001$, 60 [20-200] ng/L versus 10 [0-20] ng/L, $P < .001$, and 42.2 [19.3-99.4] pmol/L vs 6.4 [3.4-14.1] pmol/L, $P < .001$, respectively). There was no gender difference in survival rates in patients with elevated or normal cTnT, hs-cTnT, and copeptin concentrations (Figure 2).

Both copeptin and hs-cTnT outperformed the prediction of 1-year mortality and 1-year death/AMI offered by cTnT in women ($P = .003$ and $P = .002$ for 1-year mortality and $P = .004$ and $P < .001$ for the combined 1-year death/AMI, respectively) (Table IV).

When applying gender-specific cutoff values for hs-cTnT and copeptin, again, no significant differences

Figure 2



Kaplan-Meier curves for all-cause mortality occurrence within 360 days according to gender and elevated versus normal concentrations of cTnT (**A**), hs-cTnT (**B**), and copeptin (**C**).

Table IV. Prognostic accuracy of cTnT, hs-cTnT, copeptin alone, and in combination with cTnT/hs-cTnT

		AUC in women (95% CI)	AUC in men (95% CI)	P*
360-d mortality	cTnT	0.69 (0.56-0.83)	0.73 (0.65-0.81)	.628
	hs-cTnT	0.86 (0.79-0.93)	0.79 (0.72-0.86)	.172
	Copeptin	0.88 (0.82-0.94)	0.81 (0.74-0.89)	.160
	cTnT and copeptin	0.87 (0.81-0.94)	0.82 (0.75-0.89)	.283
	hs-cTnT and copeptin	0.87 (0.80-0.94)	0.82 (0.75-0.89)	.283
360-d mortality/AMI	cTnT fourth generation	0.63 (0.52-0.75)	0.65 (0.59-0.72)	.768
	hs-cTnT	0.81 (0.74-0.88)	0.71 (0.64-0.78)	.053
	Copeptin	0.80 (0.70-0.90)	0.71 (0.63-0.78)	.129
	cTnT and copeptin	0.80 (0.69-0.90)	0.70 (0.62-0.78)	.161
	hs-cTnT and copeptin	0.79 (0.68-0.89)	0.71 (0.62-0.79)	.229

*The *P* value compares the AUC curve of women and men.

Table V. Prognostic significance of increased cTnT, hs-cTnT, and copeptin measurements according to the applied cutoff value

		Applying the recommended cutoff value*			Applying a different cutoff value in women and men†		
		Hazard ratios (95% CI) in women	Hazard ratios (95% CI) in men	P	Hazard ratios (95% CI) in women	Hazard ratios (95% CI) in men	P
360-d mortality	cTnT	6.78 (2.47-18.64)	7.05 (3.68-13.52)	.949			
	hs-cTnT	27.95 (3.64-214.43)	8.25 (3.75-18.15)	.274	16.92 (2.21-129.69)	6.63 (3.92-18.99)	.5454
	Copeptin	14.23 (4.48-45.14)	13.40 (6.39-18.14)	.932	21.10 (4.73-94.19)	13.85 (6.60-29.09)	.621
360-d mortality/AMI	cTnT	4.00 (1.59-10.06)	4.13 (2.31-7.38)	.954			
	hs-cTnT	11.38 (3.28-39.51)	4.31 (2.41-7.71)	.166	23.36 (3.10-176.18)	4.14 (2.33-7.35)	.106
	Copeptin	7.67 (3.08-19.11)	6.13 (3.49-10.74)	.681	7.47 (2.83-19.70)	5.84 (3.34-10.22)	.667

*The recommended cutoff point is of 0.035 μg/L for cTnT (fourth-generation assay), 14 ng/L for hs-cTnT, and 18.9 pmol/L for copeptin.
† The reported 99th percentiles in women and men are 10 ng/L and 14.5 ng/L, respectively, for hs-cTnT[17] and 12.9 pmol/L and 19.5 pmol/L, respectively, for copeptin (data from the manufacturer).

between the utility in women and men were found (Table V).

Discussion

We report 4 major findings. First, we found important gender differences regarding the final diagnoses underlying acute chest pain. Although women had similar rates of AMI, including NSTEMI, they more frequently had cardiac but noncoronary causes of chest pain and less frequently had unstable angina than men. Second, there was no significant difference in the diagnostic accuracy of cTnT, hs-cTnT, and copeptin, alone or in combination, in women versus men; hs-cTnT and the combination of cTn and copeptin outperformed the diagnostic accuracy of cTn alone. This finding was validated in a second analysis in which the final diagnoses were readjudicated using hs-cTnT levels to also identify very small AMIs. Third, the risk of death is increased to a similar extent in both women and men having elevated versus normal concentration of cTnT, hs-cTnT, or copeptin. Fourth, the prognostic accuracy offered by cTnT, hs-cTnT, and copeptin was similar in women and men, even when a different cutoff value based on the 99th percentile value in women and men was applied.

These findings have important clinical implications and extend previous work on gender differences.[3-10,16,23] The role of cardiac biomarkers may be even more prominent in women because they more likely than men report atypical symptoms, such as dyspnea, weakness, nausea, and backpain[1]; these unspecific complaints may delay accurate diagnosis or even lead to misdiagnosis of AMI or acute coronary syndrome.

The recognition of gender disparities in cardiac diagnosis dates back to 1991 when Ayanian and Epstein[8] reported that women were less likely to undergo coronary angiograms as well as revascularization. Since then, numerous studies have investigated the existence of possible gender disparities in diagnosis and prognosis of patients with AMI. Although initial reports of higher mortality in women have been not confirmed in recent studies that adjusted for baseline characteristics (ie, age, risk factors and comorbidities) as well as the cardiac procedures performed,[2,6,16,23] there are more consistent reports of less cardiac diagnostic procedures performed in women.[3,8,9] Although this was not the aim of our study, we did not find any gender

differences in the rates of all-cause mortality and in the combined end point of death/AMI, a finding consistent with most recent studies.[5,9,16,23]

Previous work had nurtured the concern of gender disparity in the diagnostic and prognostic accuracy of cardiac biomarkers as they reported lower levels of copeptin and hs-cTnT in healthy women than in men.[17,18] Second, the much higher incidence of takotsubo cardiomyopathy in women suggested gender-specific response to acute stress conditions that might affect the diagnostic utility of copeptin.[24] In our study of unselected patients with acute chest pain in the ED, we observed lower copeptin levels in women than in men among the total cohort but similar levels in women and men with a final adjudicated diagnosis of AMI or acute coronary syndrome. This is supported by previous studies.[14,18] More importantly, we found that the diagnostic and prognostic accuracies of cTn, hs-cTnT, and copeptin are similar in women and men. The similarly high diagnostic accuracy of the novel biomarkers hs-cTnT and copeptin observed in women should help in the early diagnosis of AMI in women. This has important clinical implications as it should ensure the rapid initiation of evidence-based therapies in women.[25,26] Further studies are needed to further explore the possible benefits and/or risks of using gender-specific 99th percentiles as clinical decision values; however, no gender prognostic difference exists even after application of these specific cutoff values.[17]

In a previous study that was aimed at comparing the accuracy of relative versus absolute changes in hs-cTn concentrations in the diagnosis of AMI, we observed no relevant gender differences.[27] The present report is consistent with and extends the previous report to a larger population, the subgroups of patients with NSTEMI and prognostic assessment.

Our study should be interpreted within its limitations. First, we enrolled patients in whom chest pain was the predominate symptom. Although patients with shortness of breath as an accompanying symptom were included as well, we did not include patients presenting with dyspnea only. We acknowledge that dyspnea might be considered as "an anginal symptom" that seems to be more prevalent in women than in men.[4] Second, we examined 3 important biomarkers in the early diagnosis of AMI: cTnT, hs-cTnT, and copeptin. We think that one should not prematurely extrapolate our findings to other cardiac biomarkers.

In conclusion, the diagnostic and prognostic performance of cTnT, hs-cTnT, and copeptin is as good in women as in men. High-sensitivity cTnT and the combination of cTnT and copeptin outperform cTnT alone, both in women and men.

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