ORIGINAL RESEARCH

Impact of Marital Status on the Outcome of Acute Coronary Syndrome: Results From the Acute Coronary Syndrome Israeli Survey

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***Background*—**Marriage is one of the common forms of social support. Conflicting evidence exists about the impact of marital status on the outcomes of patients with acute coronary syndrome (ACS). It is further not clear if sex disparity exists in the outcome of married and nonmarried patients with ACS.

***Methods and Results*—**Data from the ACS Israeli Survey, collected between 2004 and 2016, were used to compare baseline characteristics, clinical indexes, and outcomes of married and nonmarried patients with ACS. Cox regression analysis and propensity score matching were used to explore if marital status was independently associated with long-term outcome. Of 7233 patients included with reported marital status, 5643 (78%) were married. Married patients were younger (62.69±12.07 versus 68.47±14.84 years; $P<0.001$), more frequently men (83.1% versus 54.8%; $P<0.001$), and less likely to be hypertensive (61.1% versus 69.3%; $P<0.001$). All-cause mortality incidence at 30 days and at 1 year was lower in married patients (3.1% versus 7.6% [$P<0.001$]; and 7.1% versus 15.3% [$P<0.001$], respectively). After adjusting for multiple covariates, the hazard ratio for 5-year all-cause mortality for married patients was 0.74 (95% CI, 0.62–0.88). Similar results were observed after propensity score matching. Kaplan-Meier estimates for all-cause mortality at 5 years demonstrated the best prognosis for married men and the worst for nonmarried women.

***Conclusions*—**Marriage is independently associated with better short- and long-term outcomes across the spectrum of ACS. Attempts to intensify secondary prevention measures should focus on nonmarried patients and especially nonmarried women.
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Key Words: acute coronary syndrome • disparities • marital status • outcome

Social support is a well-established determinant of outcome in patients with coronary artery disease (CAD).[1–4] Ample literature demonstrates a lower risk for morbidity and mortality in patients with CAD with solid social support, across various subpopulations. Marriage is one of the closest and most intimate social support environments, but nevertheless, conflicting evidence exists about the association between marital status and outcomes of patients with CAD.[5–13] These and other reports prompt the question whether marriage is independently associated with a better outcome or, perhaps, married patients represent a biased subpopulation of patients with better health and lower inherent risk for depression and, thus, are less prone to a dire outcome.[14] Furthermore, it is not clear if sex disparities exist when the impact of marriage on the outcome of patients with acute coronary syndrome (ACS) is studied. Most of the existing data emerged from studies including stable patients undergoing percutaneous coronary artery intervention, those undergoing coronary artery bypass surgery, or patients with acute myocardial infarction.[8,10,15] The impact of marriage on the outcome of patients along the full spectrum of ACS is less robust.[6,12] We, thus, aimed to explore the association between marital status and outcomes of patients with ACS along the full spectrum of ACS. We also aimed to explore if sex disparities exist in the outcomes of married and nonmarried patients.

Methods

Study design

Data for the present analysis were drawn from the ACS Israeli Survey, collected between 2004 and 2016. Because of the

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Accompanying Figures S1 and S2 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.011664

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Clinical Perspective

What Is New?

- Marriage is associated with better short- and long-term outcomes across the spectrum of acute coronary syndrome.
- This association differs between sexes, with married men having the best outcomes, whereas poorest outcomes were recorded in nonmarried women.

What Are the Clinical Implications?

- Marital status may indicate a supportive social environment of the patient with acute coronary syndrome, with the lack of this support associated with poor outcome.
- Close postdischarge follow-up and intensification of secondary prevention means should be considered for nonmarried patients, especially for nonmarried women.

sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to The Israeli Center for Cardiovascular Research at ICCR@sheba.gov.il.

Briefly, the ACS Israeli Survey is a biennial nationwide survey of all patients with ACS admitted at 26 public Israeli medical centers, collecting data prospectively for over a decade. These data include demographic, laboratory, and clinical information. Follow-up for outcomes was performed at 30 days by a clinic visit or a telephone call reporting length of admission, readmission, and major adverse cardiovascular events (defined as death/myocardial infarction/unstable angina/cerebrovascular accident/stent thrombosis/urgent revascularization), whereas all-cause mortality incidence at 1 and at 5 years was extracted from the ministry of interior affairs database. The survey was approved by each of the local Institutional Review Boards as an observational study, and each participant gave informed consent.

Patients were grouped on the basis of self-reported marital status as either "married" (including married or attached) or "nonmarried" (including single, divorced, and widowed). Comparative analyses of clinical, demographic, and outcome indexes were performed between married and nonmarried patients.

Statistical Analysis

Continuous variables were compared using Student *t* test or ANOVA and are expressed as a mean±SD for variables with normal distribution. The groups were tested with χ^2 for categorical variables and with *t* test or Mann-Whitney test, as appropriate, for normal/nonnormal distributed continues variables.

Table 1. Baseline Characteristic of Married and Nonmarried Patients

Characteristics	Married Patients (n=5643)	Nonmarried Patients (n=1590)	*P* Value
Age, mean±SD, y	62.69±12.07	68.47±14.84	<0.001
Sex (male), n (%)	4691 (83.1)	871 (54.8)	<0.001
Dyslipidemia, n (%)	3835 (68.2)	1053 (66.3)	0.154
Hypertension, n (%)	3443 (61.1)	1099 (69.3)	<0.001
Current smokers, n (%)	2196 (39.1)	528 (33.4)	<0.001
Diabetes mellitus, n (%)	2099 (37.2)	610 (38.4)	0.404
Family history of coronary artery disease, n (%)	1470 (28.7)	323 (23.1)	<0.001
Prior myocardial infarction, n (%)	1786 (31.7)	491 (31.0)	0.584
Prior coronary artery bypass surgery, n (%)	558 (9.9)	145 (9.1)	0.388
Prior percutaneous coronary intervention, n (%)	1761 (31.3)	432 (27.3)	0.003
Chronic renal failure, n (%)	597 (10.6)	226 (14.2)	<0.001
Peripheral vascular disease, n (%)	385 (6.8)	127 (8.0)	0.122
Prior cerebrovascular accident/transient ischemic event, n (%)	433 (7.7)	164 (10.3)	0.001
Congestive heart failure, n (%)	377 (6.7)	181 (11.4)	<0.001

Survival analysis comparing the groups was completed by the Kaplan-Meier method, followed by the log-rank test. To explore the effect of study groups on survival, Cox models were performed, adjusting for other explanatory covariates. Indexes were chosen to be included in the models if a significant difference ($P<0.1$) was found between the study groups, as presented in Table 1.

To minimize heterogeneity between the 2 study groups, propensity score matching was performed. The propensity score evaluated the chance to be in the nonmarried group by using a logistic regression, including the following covariates: age, sex, hypertension, current smokers, family history of CAD, chronic renal failure, history of cerebrovascular accident/transient ischemic attack, history of congestive heart failure, past percutaneous coronary intervention, and dyslipidemia. The area under the curve was 0.67. The propensity score matching was performed with a caliper of 0.024 and a 1:3 matching. The cumulative probabilities for 5-year all-cause mortality for the matched groups are displayed by the Kaplan-Meier curve, with a comparison of cumulative events using the log-rank test.

Table 2. Clinical and Outcome Indexes of Married and Nonmarried Patients

Indexes	Married Patients (n=5643)	Nonmarried Patients (n=1590)	*P* Value
Clinical indexes			
STEMI at presentation	2457 (43.5)	707 (44.5)	0.53
GRACE score >140	666 (15.9)	390 (31.8)	<0.001
Killip class III/IV at presentation	269 (4.86)	153 (9.82)	<0.001
Outcome indexes			
In-hospital mortality	141 (2.5)	92 (5.8)	<0.001
Readmission at 30 d	893 (17.8)	257 (19.1)	0.28
MACE at 30 d	559 (9.9)	248 (15.6)	<0.001
All-cause mortality at 30 d	172 (3.1)	120 (7.6)	<0.001
All-cause mortality at 1 y	394 (7.1)	241 (15.3)	<0.001

Data are given as number (percentage) of patients. GRACE indicates Global Registry of Acute Coronary Events; MACE, major adverse cardiac event (all-cause mortality, unstable angina, myocardial infarction, stent thrombosis, or urgent revascularization); STEMI, ST-segment–elevation myocardial infarction.

Statistics were performed using R (R core team [version 3.4.4]; March 2018).

Results

A total of 7233 patients with reported marital status were included between 2004 and 2016, of whom 5643 (78%) reported to be married or attached. Baseline characteristics are presented in Table 1. Compared with nonmarried patients, married patients were younger (62.69±12.07 versus 68.47±14.84 years; $P<0.001$), more frequently men (83.1% versus 54.8%; $P<0.001$), and less likely to be hypertensive (61.1% versus 69.3%; $P<0.001$). Although the incidence of ST-segment–elevation myocardial infarction as their presenting syndrome did not differ between the 2 groups (43.5% versus 44.5%; $P=0.53$), married patients had higher rates of primary reperfusion compared with nonmarried patients (74.2% versus 68.2%; $P=0.002$). Better outcomes (in-hospital mortality, major adverse cardiovascular events, and all-cause mortality, as presented in Table 2) were recorded in married patients compared with nonmarried patients. When the differences in all-cause mortality were explored at 5 years, Kaplan-Meier curve (Figure 1A) demonstrated a significantly better outcome for married patients. Multivariate Cox regression analysis (Figure S1) for all-cause mortality at 5 years yielded a hazard ratio of 0.74 (95% CI, 0.62–0.88) for married patients. Propensity score matching enabled adjustment for the intergroup differences. After matching, 2997 patients were included in the married group, and those patients were compared with 999 patients in the nonmarried group. Similar to the former analyses, after propensity matching, Kaplan-Meier survival estimates yielded results indicating lower all-cause mortality at 5 years for married patients (Figure 1B; $P<0.001$ for log rank).

As shown in Table 3, exploring sex differences within the 2 groups demonstrates that overall, compared with nonmarried women, married women had a lower risk profile (eg, younger age [67.34±10.78 versus 74.62±12.49 years; $P<0.001$], lower incidence of ST-segment–elevation myocardial infarction at presentation [36.1% versus 42.7%; $P=0.005$], and lower rates of GRACE (Global Registry of Acute Coronary Events) score >140 [21.5% versus 43.0%; $P<0.001$]). Opposed to women, married men had similar baseline characteristics compared with nonmarried men, save for older age and a higher incidence of a GRACE score >140 in nonmarried patients. As in the general cohort, married patients had better outcomes compared with nonmarried patients for most indexes. Analysis of the differences in all-cause mortality over 5 years, stratified by sex (Figure 2), shows that the best outcome was recorded in married men, followed by married women, then nonmarried men; and the worst outcome was recorded in nonmarried women. Furthermore, sex-specific multivariate Cox regression analysis for all-cause mortality at 5 years (Figure S2) demonstrates that within married individuals, men, but not women, had a statistically significant survival benefit, with a hazard ratio of 0.78 (95% CI, 0.63–0.97). No statistically significant interaction between marital status was found ($P=0.87$ for interaction).

Discussion

The main findings of this analysis demonstrate the following: (1) Compared with nonmarried patients, marriage is independently associated with better outcomes across the full spectrum of ACS. The hazard ratio for 5-year all-cause mortality for married patients was 0.74 (95% CI, 0.62–0.88). (2) Sex differences exist in the long-term prognosis after ACS, with married men having the best long-term prognosis, whereas nonmarried women have the worst long-term prognosis.

CAD is one of the leading causes of morbidity and mortality; thus, risk stratification strategies are constantly implemented, attempting to identify patients at higher risk for poor prognosis. Although daily practice tends to focus mainly on established biological risk factors for CAD (ie, hyperlipidemia, diabetes mellitus, and hypertension), it is clear that psychosocial parameters impact both the risk and the outcome of CAD. Solid social support is one of the main psychosocial parameters known to be associated with better health and outcome.[16–18] It is thought that by modifying behavioral patterns, social support

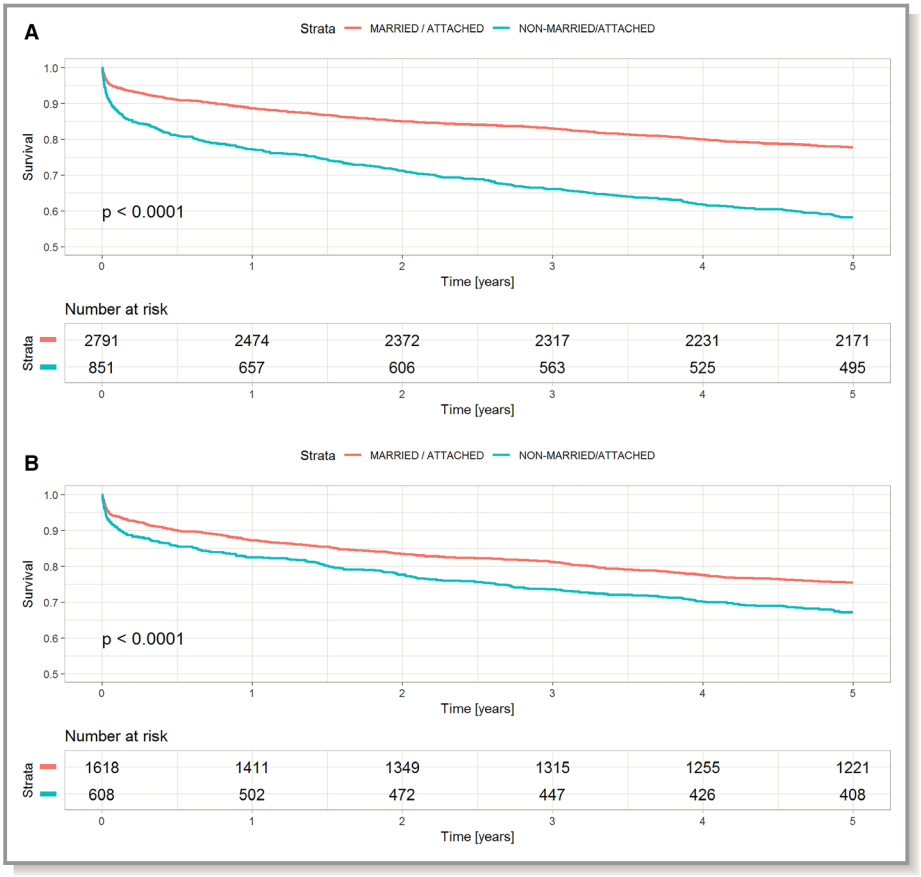

Figure 1. **A**, Kaplan-Meier 5-year survival estimate for married and nonmarried patients (unadjusted). **B**, Kaplan-Meier 5-year survival estimate for married and nonmarried patients after propensity matching.

assists in promoting a healthier lifestyle and, thus, the risk for disease decreases.[19,20]

The merits of marriage, one of the common forms of social support, were established in numerous studies in the context of CAD, including patients with acute myocardial infarction, those undergoing coronary bypass surgery, and even in patients sustaining sudden cardiac death.[7–9,21] Although these and other studies were able to associate between marital status and outcome, a few other reports have failed to demonstrate that. For example, Consuegra-Sánchez et al reported that the best prognosis after acute myocardial infarction was demonstrated for divorced patients, the worst prognosis for widowed patients, and similar prognosis for married and single patients.[10] Similar disparities were reported by Venters et al.[11] Thus, the question of whether marital status is independently associated with outcomes is still unsettled.

By using both multivariate analysis and propensity matching techniques, the present study adds to the accumulating knowledge that marriage is independently associated with better short- and long-term outcomes. Several explanations were suggested for underscoring this association: First, marriage may be seen as a "selection bias" in which healthier patients are more frequently married.[22] This was only partially evident in our study, in which the baseline characteristics of the population do not indicate a clear higher a priori risk profile for nonmarried patients. Another theory may relate to "social causation," which suggests that marriage promotes health by combining social support alongside with other, nonpsychological factors, such as financial security, acting together as behavior modifiers toward a healthy lifestyle. This may be associated with better adherence to medications, prompt care seeking, and participation in rehabilitation programs; all are well-established factors associated with improved outcomes.[23–26] Last, living alone is more frequently associated with depression, which, in turn, is associated with poor outcomes after acute myocardial infarction.[5,16,17,27] This association may have a plausible physiological cause; Carney et al demonstrated decreased heart rate variability in depressed

Table 3. Baseline Characteristics and Outcome Comparison Between Married and Nonmarried Patents, Stratified by Sex

	Women			Men		
Index	Married (n=952)	Nonmarried (n=719)	*P* Value	Married (n=4691)	Nonmarried (n=871)	*P* Value
Baseline characteristics						
Age, mean±SD, y	67.34±10.78	74.62±12.49	<0.001	61.75±12.10	63.40±14.72	<0.001
Dyslipidemia, n (%)	692 (73.0)	487 (67.7)	0.022	3143 (67.2)	566 (65.1)	0.226
Hypertension, n (%)	689 (72.5)	576 (80.1)	<0.001	2754 (58.8)	523 (60.3)	0.453
Current smokers, n (%)	200 (21.1)	122 (17.1)	0.047	1996 (42.7)	406 (46.8)	0.028
Diabetes mellitus, n (%)	426 (44.8)	321 (44.8)	1.000	1673 (35.7)	289 (33.2)	0.170
Family history of CAD, n (%)	206 (23.9)	108 (17.3)	0.003	1264 (29.6)	215 (27.7)	0.295
Prior MI, n (%)	234 (24.6)	200 (27.8)	0.154	1552 (33.2)	291 (33.6)	0.851
Prior CABG, n (%)	68 (7.1)	62 (8.6)	0.305	490 (10.4)	83 (9.5)	0.453
Prior PCI, n (%)	243 (25.6)	152 (21.2)	0.043	1518 (32.4)	280 (32.4)	0.995
Chronic renal failure, n (%)	116 (12.2)	101 (14.1)	0.293	481 (10.3)	125 (14.4)	<0.001
PVD, n (%)	58 (6.1)	56 (7.8)	0.204	327 (7.0)	71 (8.2)	0.243
Prior CVA/TIA, n (%)	83 (8.7)	85 (11.8)	0.045	350 (7.5)	79 (9.1)	0.118
CHF, n (%)	75 (7.9)	87 (12.1)	0.005	302 (6.4)	94 (10.8)	<0.001
STEMI at presentation, n (%)	344 (36.1)	307 (42.7)	0.008	2113 (45.0)	400 (45.9)	0.658
GRACE score >140, n (%)	147 (21.5)	234 (43.0)	<0.001	519 (14.8)	156 (22.8)	<0.001
Outcome indexes						
Readmission at 30 d, n (%)	158 (18.7)	126 (20.9)	0.313	735 (17.6)	131 (17.6)	1.000
MACE at 30 d, n (%)	115 (12.1)	145 (20.2)	<0.001	444 (9.5)	103 (11.8)	0.037
In-hospital mortality, n (%)	29 (3.0)	52 (7.2)	<0.001	112 (2.4)	40 (4.6)	<0.001
All-cause mortality at 30 d, n (%)	41 (4.3)	73 (10.2)	<0.001	131 (2.8)	47 (5.4)	<0.001
All-cause mortality at 1 y, n (%)	87 (9.2)	136 (19.3)	<0.001	307 (6.6)	105 (12.1)	<0.001

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; CHF, congestive heart failure; CVA, cerebrovascular accident; GRACE, Global Registry of Acute Coronary Events; MACE, major adverse cardiac event (all-cause mortality, unstable angina, myocardial infarction, stent thrombosis, or urgent revascularization); MI, myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; STEMI, ST-segment–elevation MI; TIA, transient ischemic attack.

patients, as a potential link between depression and increased mortality after myocardial infarction.[28]

The present study adds another important observation about sex disparities in outcomes after ACS. Conflicting evidence emerges from the literature about this issue.[7,9,12] The present and other previous studies claim for a poor prognosis for nonmarried women compared with men. This was evident in our study by both the Kaplan-Meier curve and the Cox regression model, with the latter demonstrating that both marital status and sex were independently associated with poor long-term outcome. Furthermore, marriage was associated with survival benefit, mainly for men. These disparities might result from a higher incidence of depression among women, especially if nonmarried.[18,29] Other social explanations for these differences include the fact that women had a longer delay in seeking care, they were less likely to involve their spouses in the recovery process, and, in general, they were believed to have less support and lack of belief in their cardiac conditions.[30]

The current study has several limitations: First, because our focus was on the married population, we included all nonmarried patients as one group. It is plausible that this heterogeneous population, which includes those never married, divorced, and widowed, should be explored in a separate study as they each may have a different outcome. Second, this was a retrospective analysis of a cohort with data collected biennially, and as such, these data may include unknown confounders. Last, data about marital status were self-reported and, thus, may be subject to reporting bias.

In conclusion, this study adds to the accumulated knowledge highlighting the association between marital status and outcomes after ACS. Because marital status can be viewed as a risk-stratifying index, it is suggested that caregivers focus on secondary prevention measures in the nonmarried patients, especially nonmarried women, probably reflecting a more vulnerable population.

Figure 2. Kaplan-Meier 5-year survival estimate for married and nonmarried patients, stratified by sex ($P<0.001$).

Disclosures

None.

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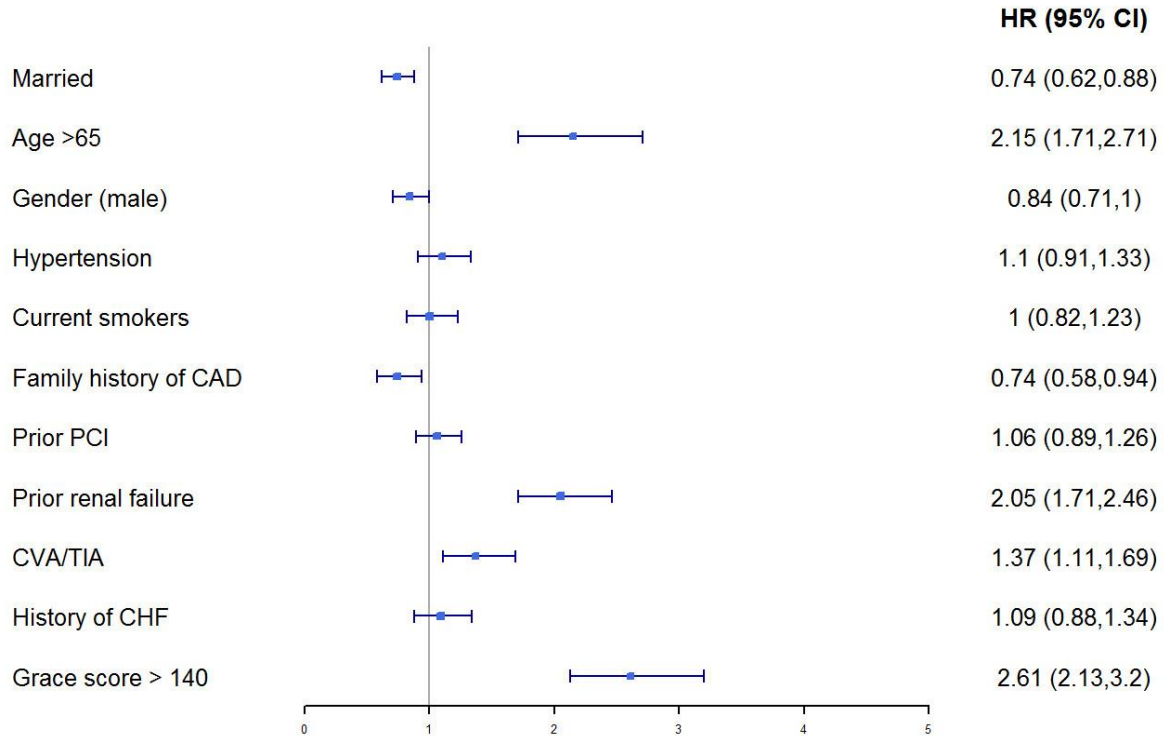
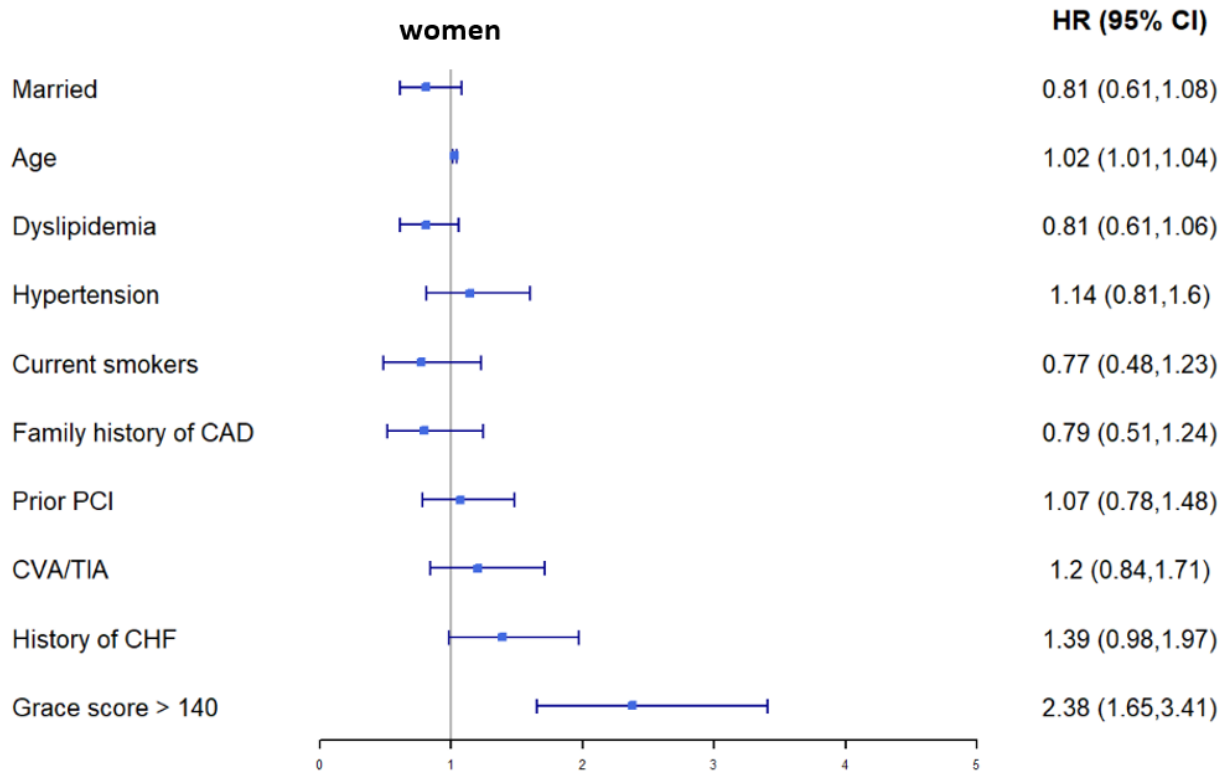
Supplemental Material

Figure S1. Hazard ratio (95% CI) for indices associated with 5-year all-cause mortality.



CAD- coronary artery disease; PCI- percutaneous coronary interventions; CVA- cerebrovascular vascular accident; TIA- transient ischemic accident; CHF- congestive heart failure.

Figure S2. Hazard ratio (95% CI) for indices associated with 5-year all-cause mortality – by sex (first panel -women; second panel -men).



CAD- coronary artery disease; PCI- percutaneous coronary interventions; CVA- cerebrovascular vascular accident; TIA- transient ischemic accident; CHF- congestive heart failure.