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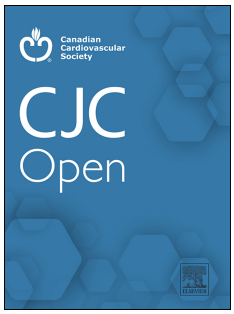

Young Women with Acute Myocardial Infarction: Risk Prediction Model for 1-Year Readmission

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Young Women with Acute Myocardial Infarction: Risk Prediction Model for 1-Year Readmission

Short Title: Readmission Risk Model in Young Women with AMI

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BRIEF SUMMARY

We created a risk prediction model of 1-year post-AMI readmission among young women. The predictors retained in the final model included any in-hospital complication, baseline perceived physical health, obstructive coronary artery disease, diabetes, history of congestive heart failure (CHF), low income (<30,000 USD), depression, length of hospital stay, and race (White versus Non-White). Several of the predictors in the final model were gender-related, though the determinants of readmission with the largest positive coefficients were history of CHF and diabetes.

Word Count: 79

ABSTRACT

Background: Although young women (≤55 years) are at higher risk than similarly aged men for readmission within one-year after an acute myocardial infarction (AMI), there are no risk prediction models for them. The present study developed and internally validated a risk prediction model of 1-year post-AMI readmission among young women that considered demographic, clinical, and gender-related variables.

Methods: We used data from the US VIRGO study (n=2,007 women), a prospective observational study of young patients hospitalized with AMI. Bayesian Model Averaging was used for model selection and bootstrapping for internal validation. Model calibration and discrimination were respectively assessed with calibration plots and area under the curve (AUC).

Results: Within 1-year post-AMI, 684 (34.1%) women were readmitted at least once. The final model predictors included: any in-hospital complication, baseline perceived physical health, obstructive coronary artery disease (CAD), diabetes, history of congestive heart failure (CHF), low income (<30,000 USD), depressive symptoms, length of hospital stay, and race (White versus non-White). Of the 9 retained predictors, 3 were gender-related. The model was well calibrated and exhibited modest discrimination (AUC=0.66).

Conclusion: Our female-specific risk model was developed and internally validated in a cohort of young females hospitalized with AMI and can be used to predict risk of readmission. Whereas clinical factors were the strongest predictors, the model included several gender-related variables (i.e. perceived physical health, depression, income level). However, discrimination was modest, indicating that other unmeasured factors contribute to variability in readmission risk among younger women.

Word Count: 243

Non-standard Abbreviations and Acronyms:

AMI: Acute Myocardial Infarction

BMA: Bayesian model averaging

CI: Confidence Interval

CAD: Coronary Artery Disease

ESSI: ENRICHD Social Support Instrument

OR: Odds ratio

PHQ-9: Patient Health Questionnaire-9

PSS-14: Perceived Stress Scale

SAQ: Seattle Angina Questionnaire

SES: Socioeconomic status

TRIPOD: Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis

US: United States

VIRGO: Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients

INTRODUCTION

Young women (≤55 years) hospitalized for acute myocardial infarction (AMI) are more frequently readmitted than young men during the first year after discharge[1-3], reflecting poorer outcomes[4,5]. Beyond sex-related (i.e. biological) factors, gender-related factors (i.e., psycho-socio-cultural) of young women are associated with worse outcomes after a first AMI[5-7]. Gender is a complex construct consisting of various domains including gender identity (e.g. level of stress as a personality trait); gender roles (e.g. household primary earner, employment, household chores); gender relations (e.g. marital status, social support); and institutionalized gender (e.g socio-economic status)[8,9].

Prior research has revealed that women of all ages have a higher risk of 1-year post-AMI readmission after adjustment for demographics and clinical factors[2]. However, after further adjustment for health status and gender-related factors, this association with female sex is attenuated[2]. These results suggest that gender-related factors (e.g., stress, social support, etc.) may better explain the differences in likelihood of readmission between young women and men than sex-related factors alone.

A major obstacle to the development of risk prediction models and effective interventions for young women with AMI is that gender-related factors have not been routinely collected in existing cohort studies. In fact, risk models for post-AMI readmission have historically failed to incorporate these factors[10]. In addition, existing AMI-specific readmission risk models do not measure risk separately in men and women, have unclear generalizability, and are often derived from older populations[10]. A recent study developed a prediction model for risk of 1-year readmission among young adults hospitalized for AMI that highlighted female sex as a predictor.[3] Because interventions for reducing readmission have previously failed in mitigating traditional risk factors, a step forward would be the development of a female-specific risk model

that facilitates intervention on nontraditional modifiable factors for improving outcomes in this population[11,12].

To address this gap in knowledge, our main objective was to develop and internally validate a risk prediction model of 1-year post-AMI readmission among young women that considers both sex- and gender-related variables[13-15]. We used data from the VIRGO study (Variation In Recovery: Role of Gender on Outcomes of Young AMI Patients)[16]; the largest prospective multicenter longitudinal study of young patients (≤55 years) hospitalized for AMI. In addition to traditional variables (from prior AMI risk models), VIRGO has a broad range of gender-related factors as well as rigorously adjudicated readmissions[16]. Because we suspect that gender-related factors may have a larger effect on females than in males, we see the need to develop this model in a female-only cohort. We hypothesize that the consideration of gender-related factors in a female cohort may yield a risk prediction model that includes such gender-related factors in addition to the traditional clinical factors.

METHODS

Our study uses data gathered through the VIRGO study, which was designed to investigate factors associated with higher rates of adverse clinical outcomes in young women (≤55 years) with AMI. The VIRGO study design has been previously described[16]. In brief, participants aged between 18-55 years were prospectively recruited across 103 sites in the US, between August 2008 and May 2012 and using a 2:1 enrollment ratio for women versus men. A total of 2,985 US adults (67.2% women) hospitalized for AMI were enrolled. After excluding in-hospital deaths (N=6), this resulted in a final cohort of 2,979 participants. Of those participants, the sub-cohort of 2007 women was used to develop and internally validate our risk prediction model of 1-year readmission. Institutional Review Board approval was obtained at each

participating institution, and patients provided informed consent for their study participation, including baseline hospitalization and interviews.

All-cause readmission was the primary outcome, defined as any hospital or observation stay lasting more than 24 hours within 1-year of post-AMI discharge. The readmission adjudication process has been previously described[3]. Based on prior work in post-AMI readmission and interest in gender-related indicators, we initially selected 63 candidate variables for the risk prediction model **(Supplemental Table S1)**[2,3,10,17]. A combination of medical record abstraction and standardized in-person interviews administered by trained personnel was used to collect information at baseline and before discharge regarding demographics, baseline cardiac risk factors and comorbidities, clinical and laboratory variables. We also considered additional care-related variables during index hospitalization including receipt of percutaneous coronary intervention (PCI) and late presentation to a hospital. Late presentation was defined as presenting more than 6 hours after symptom onset based on the American Heart Association/American College of Cardiology (AHA/ACC) guidelines.[18] In terms of gender-related variables (i.e., psycho-socio-cultural), we used a framework to identify variables across the four domains of gender defined by the Canadian Institutes of Health Research (CIHR) which included: *gender roles* (household primary earner status, current employment/working status, support for household chores and current presence of health insurance); *gender identity* (e.g. level of depression, stress, quality of life); *gender relations* (e.g. marital status, social support); and *institutionalized gender* (low income [personal income ≤30,000 USD] which is a marker of low socio-economic status) **(Supplemental Figure S1)**. These variables capture elements of the psycho-social construct of gender, which is separate from the conceptualization of sex as a biological factor. Depression, stress, quality of life and social support were assessed using

validated patient reported outcome measures in cardiac populations, including: the Patient Health Questionnaire-9 (PHQ-9) to measure depression[17], the 14-item global Perceived Stress Scale (PSS-14)[19] to measure perceived stress, the Seattle Angina Questionnaire (SAQ) to measure disease specific quality of life[20,21] and the Short Form-12 (SF-12) to measure general health-related quality of life[22]. For the purposes of this study, the SAQ angina frequency, physical limitation, treatment satisfaction and quality of life domains were used as well as the physical (PCS) and mental component (MCS) scores of the SF-12. Lastly, we used the ENRICHD Social Support ESSI-5 Instrument to measure perceived social support[23]. For this study we also used a question from the full length 7-item scale to measure the burden of household chores.

STATISTICAL METHODS

We generated descriptive statistics for the overall population and reported frequencies for categorical variables and means (standard deviations) or medians (interquartile ranges) for continuous and count variables. Differences in baseline characteristics between readmitted and non-readmitted women were evaluated with $\chi 2$ tests, t tests, and Wilcoxon rank-sum tests as appropriate. Of the initial 63 candidate variables, 16 variables were ineligible based on the criteria outlined in **(Supplemental Figure S2**), which included high levels of missingness, very high or very low prevalence, and unreliable inter-hospital assessment. For example, systolic and diastolic blood pressure exhibited 48% missingness and could not therefore be considered as candidate variables. This resulted in 47 candidate variables with missingness generally <3%. Data from angiograms at baseline exhibited the highest level of missingness at 10.1%, implying that presence of coronary artery disease (CAD) (obstructive versus non-obstructive) could not be determined for those women. PSS-14 data were missing for 6.5%. Ejection fraction, SF-12 PCS and MCS were missing <5% and there was no missingness in the outcome. Under the

assumption that the data were missing-at-random, and based on maximum missingness from the angiograms, we generated 10 imputations using fully conditional specifications as implemented in the SAS procedure MI[24].

Our development and validation processes followed the practices outlined in the TRIPOD statement (Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis)[25]. Selection for the multivariable model used Bayesian model averaging (BMA), a selection approach used in the SILVER-AMI study and described elsewhere[3,26]. Because BMA was used for selection rather than the corresponding P values, some terms retained in the model may not exhibit P-values below 0.05. Finally, we separately fit logistic regression of readmission to each of the 10 imputations and used Firth penalized maximum likelihood to estimate the associations within each imputation-specific model[27]. The coefficients from the imputation-specific models were subsequently combined using Rubin's rules[24]. The performance of the model was evaluated by assessing area under the curve (AUC) and calibration of the predicted risk. We considered good fit in each imputation as an AUC ≥65% and plots of the mean observed probabilities with confidence intervals that overlap with the diagonal line representing perfect agreement as recommended in the TRIPOD directives. Internal validation based on bootstrapping was employed to iteratively apply the coefficients derived from 100 bootstrapped samples to the full sample to estimate the optimism of the model's AUC. Optimism indicates how much model fit can be expected to decrease when applied to external datasets drawn from the same population. With the exception of BMA, as implemented in the R package 'BMA'[28], all analyses were conducted using SAS Version 9.4 with SAS/STAT 14.3. Cary, NC: SAS Institute Inc; 2014[29]. Statistical significance was defined as a two-sided p-value <0.05.

Finally, we constructed an integrated predictiveness curve (IPC) to identify meaningful intervention thresholds to aid in clinical decision-making and understanding of women's predicted risk of readmission[30]. The IPC is a graphical representation of the distribution of predicted readmission risk. We plotted the average predicted risk of 1-year readmission within each decile of predicted risk in the development cohort using GraphPad Prism 9 (GraphPad Software, Inc. 2020). Using the observed rate of readmission as a reference, we calculated and plotted the average predicted risk of readmission among women with key protective and deleterious predictors in the model. The average predicted risk refers to the model-predicted 1-year risk of readmission among women sharing a particular risk factor in the sample.

RESULTS

Baseline characteristics for the overall sample (N=2,007) and stratified by readmission status are presented in **Table 1**. The mean age of women was 47.2 ± 6.3 years and 26.0% were Black. Women who were readmitted within 1-year post-AMI were more likely to be older, Black, unmarried and not living with a partner, and with lower income. They were also less likely to be employed or to be the primary earner in the household, and tended to work fewer hours. They also had a more adverse clustering of cardiac risk factors and co-morbidities, longer hospital length of stay (LOS), were less likely to be discharged to another institution, and more likely to experience in-hospital complications. Lastly, women who were readmitted tended to have lower social support, a higher burden of stress and depression, poorer physical/mental health and worse disease-specific quality of life (i.e., greater angina frequency, more physical limitations, and lower treatment satisfaction).

There were a total of 1,293 readmissions within 1 year of discharge with AMI and approximately 34.1% of women were readmitted at least once. The median time to first

readmission was 71.5 days (IQR 20.0 – 188.0). The majority of readmissions were for cardiac reasons, most commonly for stable or unstable angina (33.4%). Approximately 42.2% were non-cardiac while 97 readmissions (7.5%) were for recurrent AMI **(Supplemental Table S2)**. Of the 2,007 women, up to 418 (20.8%) were readmitted once, 128 (6.4%) were readmitted twice, and 138 (6.9%) were readmitted three or more times. Women who were readmitted three or more times were younger (46.6 years), more likely to be White (62.3%), and presented with primarily cardiac complaints (53.3%).

A total of 9 predictors were selected using BMA **(Figure 1)**: CHF (OR = 1.65, 95% CI 1.10 – 2.49), diabetes (OR = 1.29, 95% CI 1.05 – 1.58), experiencing any in-hospital complication (OR = 1.25, 95% CI 0.98 – 1.60), increasing length of hospital stay (OR = 1.03, 95% CI 1.01 – 1.06), obstructive CAD (OR = 1.30, 95% CI 0.96 – 1.78), low income (OR = 1.17, 95% CI 0.95 – 1.43), depressive symptoms at baseline (OR = 1.03, 95% CI 1.01 – 1.04), white race (OR = 0.76, 95% CI 0.61 – 0.95), and better physical health at baseline (OR = 0.98, 95% CI 0.97 – 0.99). With regard to magnitude of the model coefficients, the strongest predictors of readmission within 1-year were CHF and obstructive CAD. Of the 9 predictors, 3 were gender-related: physical health, low income, and depressive symptoms. Only two predictors, specifically better physical health and White race, were protective. The final model had excellent calibration and modest discrimination (AUC (95% CI) = 0.655 (0.641 – 0.669)) across the 10 imputed datasets **(Figure 2)**. Internal validation via bootstrapping calculated an optimism (95% confidence interval for the AUC of 1.2% (0.08% – 1.22%), suggesting comparable model performance in external datasets drawn from the same population. An individual's probability of readmission within one year is easily calculated using the model coefficients and that patient's predictor values as illustrated in Supplemental Figure S3.

The 1-year observed rate of readmission in the derivation cohort was 34%. For the IPC we calculated the average predicted risk of 1-year readmission among subgroups of the women with the two most deleterious predictors and the most protective predictor **(Supplemental Figure S4)**. The average predicted risks among the women with these deleterious and protective factors can be compared to the observed rate. The 1-year average predicted risks of readmission among women with CHF and among women with any in-hospital complications were 58% and 41%, respectively. Notably, the average predicted risk among women with CHF corresponds to the highest decile. Further, the 1-year average predicted risk of readmission among women in the top quartile of the SF-12 physical component score was 23%.

DISCUSSION

In this study of U.S young women hospitalized for AMI, over a third experienced at least one readmission within 1-year of follow-up. Clinical factors, including history of CHF and diabetes, were the strongest predictors of readmission. Further, women with obstructive CAD and longer hospital stays, the latter an indicator of poor overall health, were more likely to be readmitted. In contrast, white race was associated with lower odds of readmission. Several of the predictors were gender-related (i.e. better physical health, low income, and depression), indicating that those factors were important complements to the dominant clinical and acute care factors. This is distinct from traditional prediction models, which tend to primarily include indicators of AMI severity[10]. The model demonstrated excellent calibration and modest discrimination in a cohort of young women hospitalized with AMI in the US and can be used to evaluate the risk of readmission during the first year of recovery.

This study provides several novel contributions to the field. This is the first study that considers gender-related variables in its development of a risk prediction model for 1-year

readmission specific to young women hospitalized for AMI. Apart from a recently published study[3] most of the existing AMI-specific readmission risk models have been developed in older populations[10]. The few studies with participants aged <50 years did not conduct age-based sub-analyses to identify predictors of readmission specific to younger adults.[3,10] Moreover, prior models did not stratify analyses based on sex[10], generally relied on single-center study designs, and were developed using data from administrative, electronic medical record and clinical databases that did not benefit from the expertly-adjudicated readmissions characteristic of VIRGO. Lastly, previous studies have largely focused on readmission within 30-days.

Our group recently published a study focused on the development and validation of a 1-year readmission risk model in the complete VIRGO cohort (women and men).[3] Compared to the model derived from the complete VIRGO cohort, the female-only model included three unique predictors: history of CHF, obstructive CAD, and race. Notably, the strongest predictor of increased readmission risk in the women-only model, history of CHF, was not retained in the model derived in the complete VIRGO cohort. The calibration and discrimination of the models were nearly identical when validated in their respective study samples. Our findings suggest that relative to men, factors related to pre-event cardiac conditions such as CHF and obstructive CAD may be particularly important predictors of post-AMI readmission among younger women. Previous studies have shown that participating in either in-hospital or home-based cardiac rehab programs that focused on physical activity, diet, and other lifestyle factors was associated with reduced risk of readmission among patients with CHF.[31,32] Further, one study using data from TriNetX found that exercise-based cardiac rehab was associated with lower odds of 18-month readmission among patients with chronic coronary syndrome compared to patients who underwent percutaneous coronary intervention.[33] Cardiac rehab has been shown to be

underutilized in women and interventions to improve access and uptake, such as improving physician referrals, offering home-based programs or transportation to in-hospital programs, and creating programs tailored to young women, may be especially important to reduce post-AMI readmissions in this population.[34]

Our model also included race, which is distinct from the model derived from the mixed-sex VIRGO cohort. Specifically, white race was a strong protective predictor of readmission. A systematic review of post-AMI risk prediction models found that the addition of race improved indicators of model performance in one model that was derived using Centers for Medicare and Medicare Services (CMS) administrative data.[10] Another single-center study developed three separate 30-day readmission risk prediction models among patients hospitalized for AMI, CHF, and pneumonia. Race (White versus Non-White) was only retained as a final predictor in the model derived in patients who were initially hospitalized for AMI.[35] The inclusion of race in our women-only model is consistent with previous risk prediction models of post-AMI readmission. Further, young women represent a notably underrepresented group, as a majority of risk prediction models of post-AMI readmission are developed in middle-aged and older adults. Women with multiple socially disadvantaged identities (i.e. non-White race) have been shown to be at increased risk for post-AMI readmission.[36,37] Previous studies posit that race serves as a marker for several indicators of health affected by socioeconomic measures, which may explain why factors such as employment and health insurance status were not retained in the model.[38] Interventions that address structural barriers such as improving the utilization of readmission-reduction strategies in under-resourced hospitals and implementing care coordination may reduce racial disparities in post-AMI readmission.[39]

It is emerging that gender-related factors (i.e., social norms and expectations assigned to women)[8,9] can differentially impact health behaviors and disease burden[6]. Notably, our model includes several gender-related factors and relatively few clinical factors.[6] This suggests that even after adjustment for clinical confounders, factors associated with gender identity, roles, relations and institutionalized gender may be important predictors of readmission among younger women with AMI. Distinct from previous studies, measures of disease severity and presentation characteristics were considered, but not retained in our final model[10]. Of note, depressive symptoms and low income were predictors of readmission. Depression is an independent risk factor for cardiac morbidity and mortality[40], and has also been shown to be associated with increased risk of readmission[41]. It is hypothesized that depression negatively impacts care-seeking behavior, medication adherence, and health behaviors[40]. Very few prior risk prediction models for post-AMI readmission have included patient-level indicators of income.[42] Young adults are more likely to have unmet medical needs compared to older adults and previous studies suggest that the lack of financial resources serves as a barrier to accessing healthcare.[43] A previous study among non-elderly adults (age 18 – 64 years) with CAD found that women were more likely to report financial hardship from medical bills than men.[44] This suggests that the uneven distribution of wealth and of access to health-promoting resources may serve to perpetuate sex-related disparities in AMI recovery.

Furthermore, experiencing any in-hospital complication and having a longer hospital stay, both proxies of overall health status, were associated with increased risk of readmission. Women have been found to be more prone to complications during hospitalization than men [5], predominantly CHF[10]. Suboptimal AMI care may explain some of the variation in risk for in-hospital events and subsequent readmission. Indeed, patients who were less likely to receive

recommended diagnostic imaging and percutaneous coronary intervention were at higher risk for 30-day readmission post-AMI[45]. While diabetes, cerebrovascular disease, and cardiac dysrhythmia have been associated with an extended hospital LOS in patients with AMI[46,47], the LOS was not associated with 7- or 30-day readmission[47]. In contrast, our findings indicate that longer LOS is an important predictor of longer-term readmission among young women.

LIMITATIONS

Some limitations should be considered in the interpretation of our findings. First, important measures of baseline risk and disease severity (e.g. GRACE score and Killip class) were excluded from analysis based on inconsistencies in how they were measured and reported at different study sites. Second, important gender-related variables such as caregiver burden, personality traits, and social roles were not available. The presence of feminine traits and social norms are important determinants of health-behaviors[6]. Given the importance of these additional gender-related factors, their availability in a composite measure of gender[7,48], might have led to a deeper insight in factors associated with readmission. Third, our findings may not be generalizable to women of some racial minority groups (i.e. American Indian, Alaska Native, Asian, Pacific Islander, East Indian) or Hispanic women who were under-represented in the study. Nevertheless, it is important to note that the VIRGO cohort is the largest and most racially diverse cohort of young AMI survivors in the U.S. Perhaps the primary limitation is that the AUC of our model indicated only modest discrimination at 0.66. Notwithstanding, this value is in the upper range of existing risk prediction models (0.53 – 0.79)[3,10]. Further, we only considered patient-level predictors as candidate variables for the model. The modest discrimination of our final model indicated that healthcare system-level factors may also

contribute to variation in readmission risk. Readmission as an outcome is challenging to predict because it is influenced by complex interactions between individual- and system-level factors as well as by individualized decision making among providers of healthcare. Lastly, we acknowledge that because this model is based on data from women only and was not validated in an external dataset, it may have limited generalizability.

CONCLUSION

Congestive heart failure, diabetes, and obstructive coronary artery disease were the strongest positively predictors of 1-year readmission among younger women hospitalized for AMI. However, gender-related factors including income level, depressive symptoms, and patient-reported physical health were important complements. This model demonstrated excellent calibration and modest discrimination and can be used to predict the risk of 1-year readmission following hospitalization for AMI among younger women.

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Table 1. Baseline characteristics of young women hospitalized for AMI who were readmitted and not readmitted within 1-year (comparison of 45 variables that passed 1st stage selection including missingness).

	All patients (N=2007)	All patients (Missing)	Not Readmitted (N=1323)	Not Readmitted (Missing)	Readmitted within 1 year (N=684)	Readmitted within 1 year (Missing)	P-value
Socio-Demographics/SES							
Ethnicity White / Caucasian	1485 (74.0%)	0 (0.0%)	1009 (76.3%)	0 (0.0%)	476 (69.6%)	0 (0.0%)	0.0012
Married or Living with spouse	1053 (52.5%)	0 (0.0%)	725 (54.8%)	0 (0.0%)	328 (48.0%)	0 (0.0%)	0.0036
Primary earner	1484 (73.9%)	0 (0.0%)	1002 (75.7%)	0 (0.0%)	482 (70.5%)	0 (0.0%)	0.0108
Low Income	956 (47.6%)	0 (0.0%)	573 (43.3%)	0 (0.0%)	383 (56.0%)	0 (0.0%)	<0.0001
Working	1128 (56.2%)	0 (0.0%)	804 (60.8%)	0 (0.0%)	324 (47.4%)	0 (0.0%)	<0.0001
Mean work hours per week	21.7 (21.62)	13 (0.6%)	23.6 (21.62)	10 (0.8%)	18.0 (21.16)	3 (0.4%)	<0.0001
ESSI 7 – Help with daily chore	1255 (62.5%)	0 (0.0%)	834 (63.0%)	0 (0.0%)	421 (61.5%)	0 (0.0%)	0.6278
Cardiac risk factors							
Diabetes	799 (39.8%)	0 (0.0%)	468 (35.4%)	0 (0.0%)	331 (48.4%)	0 (0.0%)	<0.0001
Obesity (BMI≥30 kg/m^2)	1107 (55.2%)	0 (0.0%)	704 (53.2%)	0 (0.0%)	403 (58.9%)	0 (0.0%)	0.0171
Hypertension	1347 (67.1%)	0 (0.0%)	847 (64.0%)	0 (0.0%)	500 (73.1%)	0 (0.0%)	<0.0001
Dyslipidemia	1679 (83.7%)	0 (0.0%)	1085 (82.0%)	0 (0.0%)	594 (86.8%)	0 (0.0%)	0.0055
Currently Smoking	601 (29.9%)	0 (0.0%)	394 (29.8%)	0 (0.0%)	207 (30.3%)	0 (0.0%)	0.8230
Family History of CVD	1350 (67.3%)	0 (0.0%)	882 (66.7%)	0 (0.0%)	468 (68.4%)	0 (0.0%)	0.5112
Inactivity	751 (37.4%)	0 (0.0%)	454 (34.3%)	0 (0.0%)	297 (43.4%)	0 (0.0%)	<0.0001
Medical History							
Previous MI	413 (20.6%)	0 (0.0%)	231 (17.5%)	0 (0.0%)	182 (26.6%)	0 (0.0%)	<0.0001

History of Renal Disease	254 (12.7%)	0 (0.0%)	144 (10.9%)	0 (0.0%)	110 (16.1%)	0 (0.0%)	0.0009
History of COPD	284 (14.2%)	0 (0.0%)	159 (12.0%)	0 (0.0%)	125 (18.3%)	0 (0.0%)	0.0001
History of heart failure	115 (5.7%)	0 (0.0%)	48 (3.6%)	0 (0.0%)	67 (9.8%)	0 (0.0%)	<0.0001
Presentation Characteristics							
Ejection Fraction < 40 percent	211 (10.5%)	0 (0.0%)	133 (10.1%)	0 (0.0%)	78 (11.4%)	0 (0.0%)	0.3442
Angiogram		203 (10.1%)		126 (9.5%)		77 (11.3%)	0.0028
Non-obstructive CAD <50%	232 (11.6%)		174 (13.2%)		58 (8.5%)		
Obstructive CAD ≥ 50%	1572 (78.3%)		1023 (77.3%)		549 (80.3%)		
Peak Troponin, Median (IQR)	5.9 (1.3 – 23.0)	26 (1.3%)	5.9 (1.4 – 23.6)	18 (1.4%)	5.8 (1.3 – 22.1)	8 (1.2%)	0.4146
Estimated Glomerular Filtration Rate (eGFR)	88.1 (25.74)	8 (0.4%)	89.2 (23.84)	6 (0.5%)	86.0 (28.96)	2 (0.3%)	0.0143
First White Blood Cell Count	10.8 (3.89)	8 (0.4%)	10.7 (3.74)	4 (0.3%)	10.8 (4.16)	4 (0.6%)	0.7522
First Hematocrit	39.7 (4.95)	9 (0.4%)	39.9 (4.64)	5 (0.4%)	39.2 (5.47)	4 (0.6%)	0.0015
Chest pain as primary symptom	1733 (86.3%)	0 (0.0%)	1149 (86.8%)	0 (0.0%)	584 (85.4%)	0 (0.0%)	0.3640
Type of Myocardial Infarction		0 (0.0%)		0 (0.0%)		0 (0.0%)	0.2358
STEMI	920 (45.8%)		619 (46.8%)		301 (44.0%)		
NSTEMI	1087 (54.2%)		704 (53.2%)		383 (56.0%)		
Total length of stay in Days, Median (IQR)	3.0 (2.0 – 5.0)	10 (0.5%)	3.0 (2.0 – 4.0)	6 (0.5%)	3.0 (2.0 – 6.0)	4 (0.6%)	<0.0001
Discharge Counseling							
Recommended Counselling (Cardiac+Diet+Smoking)	631 (31.4%)	0 (0.0%)	418 (31.6%)	0 (0.0%)	213 (31.1%)	0 (0.0%)	0.8353
Exercise Counselling	1845 (91.9%)	0 (0.0%)	1215 (91.8%)	0 (0.0%)	630 (92.1%)	0 (0.0%)	0.8342
Discharge Medication							

Clopidogrel/Thienopyridines	1355 (67.5%)	0 (0.0%)	889 (67.2%)	0 (0.0%)	466 (68.1%)	0 (0.0%)	0.6723
Statins	1814 (90.4%)	0 (0.0%)	1188 (89.8%)	0 (0.0%)	626 (91.5%)	0 (0.0%)	0.2142
Dual Antiplatelet Therapy (DAPT)	1289 (64.2%)	0 (0.0%)	848 (64.1%)	0 (0.0%)	441 (64.5%)	0 (0.0%)	0.8674
ACEI/ARBs	1229 (61.2%)	0 (0.0%)	797 (60.2%)	0 (0.0%)	432 (63.2%)	0 (0.0%)	0.2038
Beta Blockers	1798 (89.6%)	0 (0.0%)	1188 (89.8%)	0 (0.0%)	610 (89.2%)	0 (0.0%)	0.6692
Calcium Channel Blocker	122 (6.1%)	0 (0.0%)	77 (5.8%)	0 (0.0%)	45 (6.6%)	0 (0.0%)	0.5001
Gender Psychosocial factors, Mean (SD)							
Social Support (ESSI 5), Median (IQR)	27.0 (23.0 – 30.0)	39 (1.9%)	27.0 (23.0 – 30.0)	19 (1.4%)	27.0 (22.0 – 30.0)	20 (2.9%)	0.1396
Depression (PHQ-9), Median (IQR)	8.0 (3.0 – 13.0)	82 (4.1%)	7.0 (3.0 – 12.0)	44 (3.3%)	9.0 (4.0 – 15.0)	38 (5.6%)	<0.0001
Stress (PSS-14), Median (IQR)	27.0 (21.0 – 33.0)	131 (6.5%)	27.0 (20.0 – 33.0)	75 (5.7%)	28.5 (22.0 – 35.0)	56 (8.2%)	<0.0001
Physical Limitation (SAQ), Median (IQR)	91.7 (58.3 – 100.0)	56 (2.8%)	94.4 (66.7 – 100.0)	32 (2.4%)	80.6 (47.2 – 100.0)	24 (3.5%)	<0.0001
Anginal Frequency (SAQ), Median (IQR)	90.0 (70.0 – 100.0)	7 (0.3%)	90.0 (70.0 – 100.0)	5 (0.4%)	90.0 (60.0 – 100.0)	2 (0.3%)	<0.0001
Treatment satisfaction (SAQ), Median (IQR)	100.0 (87.5 – 100.0)	18 (0.9%)	100.0 (87.5 – 100.0)	13 (1.0%)	100.0 (81.25 – 100.0)	5 (0.7%)	0.0056
Quality of life (SAQ), Median (IQR)	58.3 (41.7 – 75.0)	14 (0.7%)	58.3 (41.7 – 75.0)	10 (0.8%)	50.0 (33.3 – 66.7)	4 (0.6%)	<0.0001
General Health, PCS (SF-12), Median (IQR)	42.9 (32.5 – 42.9)	92 (4.6%)	45.1 (35.2 – 53.5)	58 (4.4%)	38.8 (28.6 – 48.4)	34 (5.0%)	<0.0001
General Health, MCS (SF-12), Median (IQR)	44.9 (34.9 – 54.4)	92 (4.6%)	46.4 (36.2 – 54.7)	58 (4.4%)	43.2 (32.7 – 53.4)	34 (5.0%)	0.0003

Abbreviations: BMI (body mass index); CVD (cardiovascular disease); MI (myocardial infarction); COPD (chronic obstructive pulmonary disease); CAD (coronary artery disease); STEMI (ST-Elevation MI); ACEI/ARBs (angiotensin-converting enzyme inhibitors/angiotensin receptor blockers); NSTEMI (Non-ST Elevation MI); ESSI-5 (ENRICHD Social Support instrument); PHQ-9 (Patient Health Questionnaire-9); PSS-14 (Perceived Stress Scale), SAQ (Seattle Angina Questionnaire); SF-12 PCS (Short Form-12 physical component score); SF-12 MCS (Short Form-12 mental component score)

FIGURE LEGENDS

Figure 1. Forest plot for risk model for 1-year readmission among young women (<= 55 years) hospitalized for acute myocardial infarction (AMI). Associations between model predictors and readmission displayed as odds ratios **(black squares)** with 95% confidence intervals **(horizontal lines)**. PHQ-9 = Patient Health Questionnaire – 9; SF-12 = 12-item Short Form Health Survey

Figure 2. Calibration Plot of Observed versus Predicted Risk from the 9-Predictor Risk Model of All-cause Readmission within 1-year of Hospitalization for acute myocardial infarction (AMI) among young women. This calibration plot demonstrates how well the deciles of observed and predicted probabilities of 1-year readmission **(blue circles)** agree over the entire range of predicted risk with 95% confidence intervals **(vertical red lines)**. The **diagonal blue line** represents perfect agreement. AUC = area under the curve.