The Reliability and Prognosis of In-Hospital Diagnosis of Metabolic Syndrome in the Setting of Acute Myocardial Infarction

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Objectives
This study sought to examine the reliability and prognostic importance of an in-hospital diagnosis of metabolic syndrome (MetS) in the setting of acute myocardial infarction (AMI).

Background
Because the factors that comprise MetS are believed to be altered in the setting of AMI, the diagnosis of MetS during AMI hospitalization and its prognostic significance have not been studied.

Methods
We assessed patients within a multicenter registry for metabolic factors at baseline and 1 month post-AMI and followed them for mortality and rehospitalizations. The accuracy of an inpatient diagnosis of MetS was calculated using a 1-month follow-up as the gold standard. Patients were categorized based on MetS diagnosis at baseline and 1 month, and the combined endpoint of death or rehospitalization over 12 months was compared between groups.

Results
Of the 1,129 patients hospitalized for AMI, diagnostic criteria for MetS were met by 69% during AMI hospitalization and 63% at 1 month. Inpatient MetS diagnosis had a sensitivity and specificity for outpatient diagnosis of 87% and 61%, respectively, and was associated with an 11 times increased odds of an outpatient diagnosis (C-index 0.74). Compared with patients without MetS during hospitalization and follow-up, patients classified as MetS during AMI but not follow-up had worse outcomes, whereas those classified MetS at follow-up had the worst outcomes (rates for combined endpoint 27% vs. 37% vs. 38%; log-rank p = 0.01).

Conclusions
In a large cohort of patients with AMI, the diagnosis of MetS is common and can be made with reasonable accuracy during AMI. MetS is associated with poor outcomes, regardless of whether the diagnosis is confirmed during subsequent outpatient visit, and identifies a high-risk cohort of patients that may benefit from more aggressive risk factor modification. (J Am Coll Cardiol 2013;62:704–8) © 2013 by the American College of Cardiology Foundation

Although typically thought of as a risk factor for developing incident diabetes and cardiovascular disease, metabolic syndrome (MetS) has been shown to be associated with increased mortality and recurrent ischemic events among patients with stable coronary artery disease (CAD), independent of its associations with diabetes and obesity (1). However, it is not known whether MetS carries the same prognostic importance in the setting of an acute ischemic event. Furthermore, it is unclear if the same diagnostic criteria used in the outpatient setting can be used during acute myocardial infarction (AMI). The adrenergic surge that occurs with an AMI is thought to be associated with substantial variability in many of the factors that comprise MetS, particularly blood pressure, glucose, and lipid values.
However, an earlier diagnosis of MetS may allow for better risk stratification and initiation of aggressive risk factor modification before discharge, when changes have the greatest likelihood of being implemented by the patient (2,3).

Methods

Study population and protocol. Details of the TRIUMPH (Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status) prospective cohort study have been previously published (4). Briefly, 4,340 patients from 24 U.S. hospitals were enrolled into the TRIUMPH registry (2005 to 2008). All patients had biomarker evidence of myocardial necrosis and additional clinical evidence supporting the diagnosis of AMI. Baseline data were obtained through chart abstraction and detailed interviews. Consenting patients had their waist circumference measured and fasting blood specimens collected before discharge. Blood was analyzed at a core laboratory (Clinical Reference Laboratory, Lenexa, Kansas) for glucose and lipid levels. Laboratory values determined for clinical purposes were recorded and used if core data were unavailable. Patients could opt for 1-month follow-up by telephone or in-home visit, which allowed for collection of additional clinical and laboratory data. The final blood pressure recorded in the chart was used for baseline assessment.

MetS was determined using Adult Treatment Panel III criteria (Online Exhibit A) (5). Although antihypertensive medications are typically included in this definition, we excluded beta blockers (all patients) and angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (patients with ventricular dysfunction) because these may have been used for purposes other than blood pressure control. Only patients with baseline and 1-month assessments sufficient to determine the presence or absence of MetS were included (Fig. 1). Patients were interviewed 6 and 12 months post-AMI, and charts from patients reporting interim rehospitalizations were requested and adjudicated (4). Mortality was assessed by the Social Security Death Masterfile. Each participating hospital obtained institutional research board approval, and all patients provided written informed consent.

Statistical analysis. Patients were categorized into 4 groups: 1) no MetS baseline and no MetS 1-month (MetS−/MetS−); 2) MetS baseline and no MetS 1-month (MetS+/MetS−); 3) no MetS baseline and MetS 1-month (MetS−/MetS+); and 4) MetS baseline and 1-month (MetS+/MetS+). Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for MetS diagnosis at baseline as a predictor of outpatient MetS and for the 5 individual MetS components. Logistic regression was used to evaluate the ability of baseline MetS diagnosis to predict follow-up MetS diagnosis.

Kaplan-Meier curves were used to compare time to all-cause death or rehospitalization from 1 to 12 months post-AMI across the MetS groups, and Cox proportional hazards were used to estimate hazard ratios (HRs), adjusted for the GRACE (Global Registry of Acute Coronary Events) discharge score (6). Because the outpatient diagnosis of MetS is the gold standard, we combined MetS−/MetS+ and MetS+/MetS+ groups into “true MetS” for the outcomes analysis (for 4-group sensitivity analysis, see Online Fig. 1). Finally, we explored whether the association between MetS and prognosis was attributable solely to the presence or absence of diabetes.

All analyses were conducted using SAS version 9.2 (SAS Institute, Inc., Cary, North Carolina), and statistical significance was determined by a 2-sided p value of < 0.05.

Results

Patient population. Of the 4,266 patients enrolled in the TRIUMPH study who survived 1 month after AMI, 1,303 agreed to an in-home assessment with blood draw. Among those, 1,129 patients (87%) had sufficient metabolic data at baseline and after 1 month to determine the presence or absence of MetS (Fig. 1; for generalizability analysis, see Online Exhibit B). Overall, participants had an average age of 59.7 years, 34% were women, and the average body mass index was 29.9 kg/m². Diabetes was present in 29.4%, and 20.4% had a prior AMI.

![Flow Chart of Patients in Study Cohort](image-url)
Sensitivity, specificity, positive predictive value, and negative predictive value. Diagnostic criteria for MetS were met by 69% of patients during AMI hospitalization and 63% at 1-month follow-up (Fig. 2). The percentage meeting each criterion of MetS was similar between assessments (±5%) with the exception of impaired fasting blood glucose (66% at baseline vs. 54% at 1 month). In terms of individual patients, the MetS classification was changed for 22% from baseline to 1 month. The sensitivity and specificity of MetS diagnosis at baseline for the diagnosis at 1 month were 87% and 61%, respectively (Table 1). The most stable individual component was abdominal obesity, and the 3 laboratory assessments were more unstable from baseline to 1 month. MetS diagnosis during hospitalization was associated with a 10.8 times increased odds (95% confidence interval [CI]: 8.0 to 14.5) of outpatient MetS diagnosis (C-index 0.742).

Patient characteristics of different metabolic groups. The demographics and clinical characteristics of the 4 metabolic groups, based on the diagnosis of MetS during index hospitalization and at 1 month post-AMI, are shown in Table 2. Patients categorized as MetS+ during index hospitalization were more likely to have diabetes and to have multivessel disease on angiogram. Patients identified as MetS+ during index hospitalization had worse metabolic values across the spectrum of measured factors compared with patients categorized as MetS–, including higher body mass index, higher triglyceride levels, lower high-density lipoprotein cholesterol (HDL) levels, and higher glucose and insulin levels (Online Table 1).

Outcomes of different metabolic groups. Patients with no MetS at baseline and follow-up had the best outcomes over the year following AMI (mortality 2.0%; rehospitalization 25.6%). Patients classified as MetS+ during the AMI but not follow-up had worse outcomes (mortality 2.5%; rehospitalization 33.7%). True MetS patients (MetS+/MetS+ and MetS+/MetS–; see the Online Appendix for 4-group analysis) had the worst outcomes (mortality 4.1%; rehospitalization 36.2%), with rates of combined endpoints: 27% versus 37% versus 38%, respectively (log-rank p = 0.01) (Fig. 3). In analyses adjusted for GRACE score (a measure of AMI severity), MetS+/MetS– was associated with a nonsignificant trend toward increased hazard of death or rehospitalization (HR: 1.39; 95% CI: 0.96 to 2.01; p = 0.082), and true MetS was associated with a significantly increased hazard (HR: 1.56; 95% CI: 1.19 to 2.06; p = 0.002) (reference MetS–/MetS–).

To examine whether the association between MetS and prognosis was driven by a concurrent diagnosis of diabetes, we additionally adjusted for diabetes and the interaction of diabetes × MetS. The interaction terms were not statistically significant (p > 0.1), indicating that the association of the MetS group with poor outcomes did not vary according to diabetes status. Furthermore, among patients without diabetes, the association between MetS group and poor outcome remained consistent (Online Fig. 2).

### Discussion

In this large, multicenter prospective AMI cohort study, the diagnosis of MetS was exceedingly common both at the time of AMI and at 1 month after the acute event. Although many of the individual components may have been altered during the AMI, the diagnosis of MetS—as a constellation of factors—has reasonable accuracy at the time of AMI hospitalization. Furthermore, patients identified as MetS during the AMI were at high risk for poor outcomes, regardless of the MetS diagnosis at the 1-month follow-up. Therefore, identifying these patients at the time of an

### Table 1. Accuracy of Baseline Assessment of MetS and Its Components for 1-Month Post-AMI Assessment

<table>
<thead>
<tr>
<th>Component</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic syndrome</td>
<td>87.2%</td>
<td>61.2%</td>
<td>79.3%</td>
<td>73.8%</td>
</tr>
<tr>
<td>Abdominal obesity</td>
<td>92.7%</td>
<td>87.8%</td>
<td>91.6%</td>
<td>89.3%</td>
</tr>
<tr>
<td>High triglycerides</td>
<td>64.4%</td>
<td>77.0%</td>
<td>66.3%</td>
<td>75.5%</td>
</tr>
<tr>
<td>Low HDL-C</td>
<td>82.4%</td>
<td>60.2%</td>
<td>76.1%</td>
<td>69.1%</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>93.5%</td>
<td>61.1%</td>
<td>89.7%</td>
<td>72.3%</td>
</tr>
<tr>
<td>Impaired fasting glucose/diabetes</td>
<td>85.7%</td>
<td>57.6%</td>
<td>70.0%</td>
<td>77.7%</td>
</tr>
</tbody>
</table>

HDL-C = high-density lipoprotein cholesterol; NPV = negative predictive value; PPV = positive predictive value.
AMI—when therapeutic and lifestyle changes are most likely to occur (2,3)—is not only feasible but may also be optimal from a patient care perspective. Importantly, the components of MetS are all measures routinely collected as part of clinical care; therefore, these patients can be easily “flagged” as MetS (and high risk) to the treating physician. These patients could then be targeted for more intensive lifestyle changes, closer follow-up, and reassessment during the subsequent outpatient physician visit.

Prior studies. MetS is generally considered a constellation of factors that increases an individual’s risk for developing diabetes or a primary cardiac event, and its prognostic importance has been demonstrated most often in this capacity (7,8). Therefore, it is not surprising that the prevalence of MetS among patients with AMI in our study was much higher than that in the general American adult population (approximately 25% [9]) or among patients with stable CAD (approximately 40% to 50% [10]). Importantly, MetS in our study was associated with adverse prognosis after an AMI, even after adjustment for the GRACE score.

Study limitations. First, many patients declined participation in the metabolic substudy of the TRIUMPH trial. However, because the baseline characteristics of nonparticipants were similar to those of participants, the analytic population remained fairly representative of a general AMI population who survives to 1 month after AMI. Second, because of a low number of events, we were limited in our ability to adjust for a large number of covariates in our outcomes models. Nevertheless, we adjusted for the GRACE score, which integrates many prognostically important variables and has excellent predictive value for long-term post-AMI mortality (6). Finally, although we demonstrated an association of MetS with poor outcomes and thus provided an additional tool for risk stratification after AMI, we do not yet know whether early recognition of these patients as MetS will mitigate this excessive risk. We also do not know if more aggressive lifestyle interventions beyond those routinely prescribed to patients with AMI provide additional benefit in these high-risk patients. Future studies are needed to determine whether identifying patients as MetS during their AMI will improve outcomes.

### Table 2

Baseline Characteristics of 4 Groups Based on Baseline and 1-Month Diagnoses of MetS

<table>
<thead>
<tr>
<th>No MetS</th>
<th>MetS</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MetS−/MetS− (n = 256)</td>
<td>MetS+/MetS− (n = 162)</td>
<td>MetS−/MetS+ (n = 91)</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>61.6 ± 12.0</td>
<td>58.2 ± 11.4</td>
</tr>
<tr>
<td>Female</td>
<td>27.0%</td>
<td>29.0%</td>
</tr>
<tr>
<td>White</td>
<td>74.5%</td>
<td>79.0%</td>
</tr>
<tr>
<td>Current smoker</td>
<td>40.9%</td>
<td>44.7%</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>15.2%</td>
<td>15.4%</td>
</tr>
<tr>
<td>Prior angoplasty</td>
<td>11.7%</td>
<td>18.5%</td>
</tr>
<tr>
<td>Prior bypass surgery</td>
<td>8.6%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>51.6%</td>
<td>52.5%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5.9%</td>
<td>13.0%</td>
</tr>
<tr>
<td>ST-segment elevations</td>
<td>54.3%</td>
<td>47.5%</td>
</tr>
<tr>
<td>Multivessel disease (≥2 vessels)</td>
<td>42.5%</td>
<td>48.4%</td>
</tr>
<tr>
<td>LV dysfunction</td>
<td>46.7%</td>
<td>40.7%</td>
</tr>
<tr>
<td>GRACE score</td>
<td>102.4 ± 28.2</td>
<td>94.8 ± 26.3</td>
</tr>
</tbody>
</table>

Values are mean ± SD or %.

GRACE = Global Registry of Acute Coronary Events; LV = left ventricular; MetS = metabolic syndrome.

### Figure 3

Survival Free From Death or Rehospitalization Across Metabolic Groups

MetS−/MetS− = no metabolic syndrome (MetS) at baseline and after 1 month (n = 256). MetS+/MetS− = MetS at baseline but not at 1 month (n = 162).
MetS−/MetS+ and MetS+/MetS− = true MetS patients (i.e., MetS diagnosed as an outpatient; n = 711).
In this multicenter registry of patients with AMI, we found that MetS was exceedingly common, could be diagnosed with reasonable accuracy during hospitalization, and was associated with increased risk of death or rehospitalization over the 12 months following AMI. Patients who were classified as MetS during the acute event but did not qualify at follow-up still represented a high-risk group, underscoring the importance of identifying these patients during their initial hospitalization. Further work that seeks to identify patients with MetS prospectively during AMI and institute more aggressive lifestyle changes may help reduce the excess risk for poor long-term outcomes in this population.

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REFERENCES


Key Words: long-term outcomes ● metabolic syndrome ● myocardial infarction.

APPENDIX

For an expanded methods section and supplemental figures and a table, please see the online version of this article.