Optimal In-Hospital and Discharge Medical Therapy in Acute Coronary Syndromes in Kerala

Results From the Kerala Acute Coronary Syndrome Registry

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Background—In-hospital and postdischarge treatment rates for acute coronary syndrome (ACS) remain low in India. However, little is known about the prevalence and associations of the package of optimal ACS medical care in India. Our objective was to define the prevalence, associations, and impact of optimal in-hospital and discharge medical therapy in the Kerala ACS Registry of 25718 admissions.

Methods and Results—We defined optimal in-hospital ACS medical therapy as receiving the following 5 medications: aspirin, clopidogrel, heparin, β-blocker, and statin. We defined optimal discharge ACS medical therapy as receiving all of the above therapies except heparin. Comparisons by optimal versus nonoptimal ACS care were made via Student t test for continuous variables and χ² test for categorical variables. We created random effects logistic regression models to evaluate the association between Global Registry of Acute Coronary Events risk score variables and optimal in-hospital or discharge medical therapy. Optimal in-hospital and discharge medical care were delivered in 40% and 46% of admissions, respectively. Wide variability in both in-hospital and discharge medical care was present, with few hospitals reaching consistently high (>90%) levels. Patients receiving optimal in-hospital medical therapy had an adjusted odds ratio (95% confidence interval) = 0.93 (0.71, 1.22) for in-hospital death and an adjusted odds ratio (95% confidence interval) = 0.79 (0.63, 0.99) for major adverse cardiovascular event rates. Patients who received optimal in-hospital medical care were far more likely to receive optimal discharge care (adjusted odds ratio [95% confidence interval] = 10.48 [9.37, 11.72]).

Conclusions—Strategies to improve in-hospital and discharge medical therapy are needed to improve local process-of-care measures and ACS outcomes in Kerala. (Circ Cardiovasc Qual Outcomes. 2013;6:00-00.)

Key Words: acute coronary syndrome ■ health policy and outcome research ■ registries

In-hospital and discharge medical therapies for acute coronary syndrome (ACS) have been demonstrated to be highly effective and cost effective, including in middle-income countries such as India.1 Despite substantial reductions in ACS-related morbidity and mortality with the combination of antiplatelet agents, β-blockers, statins, and anticoagulants for patients with ACS, treatment rates of individual drug classes remain low in both inpatient2,3 and postdischarge settings4 in India. Quality improvement studies have demonstrated stepwise improvements in outcomes with increases in guideline-based or optimal ACS in-hospital care.5 However, little is known about the prevalence and predictors of the package of optimal in-hospital or discharge medical therapy for patients with ACS in India.

Our objective was to define the prevalence, association, and effect of optimal in-hospital and discharge medical therapy in the Kerala ACS Registry of 25718 admissions as part of an ongoing ACS quality improvement project in Kerala.

Methods

Details of the Kerala ACS Registry have been previously described.2 Briefly, representatives from 185 hospitals that treat patient with ACS in Kerala were approached to participate in the Kerala ACS Registry. One hundred and forty hospitals responded, and 125 hospitals agreed to participate. We prospectively collected data on 25748 consecutive ACS admissions from 2007 to 2009. Patients were included if they were ≥18 years of age, presented with chest pain, and had 1 of the following: (1) ST-segment elevations in 2 contiguous leads, (2) ST depressions or T wave inversion
WHAT IS KNOWN

- Antiplatelet agents, anticoagulants, statins, and β-blockers have been shown to reduce the risk of death and other major adverse cardiovascular events when given to patients with acute coronary syndromes (ACS).
- Optimal quality of care for ACS includes the provision of these medications. To date, data are limited on the frequency of optimal in-hospital and discharge medical care for patients with ACS in India.

WHAT THE STUDY ADDS

- Using data from the state of Kerala ACS Registry of 25718 ACS admissions, optimal in-hospital and discharge medical care were delivered in only 40% and 46% of ACS admissions, respectively. Wide variability occurred across the 125 participating hospitals.
- Optimal in-hospital and discharge medical care for ACS were more common in academic, nonrural hospitals.
- The provision of optimal in-hospital medical care was associated with a 21% lower risk of in-hospital major adverse cardiovascular events (odds ratio [95% confidence interval], 0.79 [0.63, 0.99]). The provision of optimal discharge medical care was most strongly associated with optimal in-hospital care (odds ratio [95% confidence interval], 10.48 [9.37, 11.72]), suggesting that strategies to improve overall ACS care in Kerala should focus on in-hospital process-of-care measures as a first step.

Results

The participant flowchart is provided in Figure I in the online-only Data Supplement. The mean (SD) age of presentation was 60 (12) years, and the majority (77%) of participants were men (Table 1). Unemployed patients were less likely to receive optimal in-hospital (37% versus 39%; P<0.001) and discharge (38% versus 39%; P<0.001) medical care. Patients with prior hypertension, diabetes mellitus, and smoking were more likely to receive optimal in-hospital and discharge medical care, but patients with prior myocardial infarction were less likely to receive optimal in-hospital (12% versus 16%; P<0.001) and discharge (13% versus 16%; P<0.001) medical care. Patients with prior myocardial infarction were less likely to receive optimal medical care (13% versus 17%; P<0.001).

Table 2 demonstrates the prevalence of optimal in-hospital and discharge medical care by hospital-level characteristics. Rural hospitals were less likely to provide optimal in-hospital (33% versus 42%; P<0.001) and discharge (35% versus 50%; P<0.001) medical care. However, academically affiliated hospitals were more likely to provide optimal in-hospital (64% versus 39%; P<0.001) and discharge (65% versus 45%; P<0.001) medical care. There appeared to be no difference in rates of optimal in-hospital (40% versus 41%; P=0.14) and discharge (46% versus 46%; P=0.23) medical care among hospitals with or without a cardiologist on staff, respectively.

Hospitals with cardiac catheterization laboratories had lower rates of optimal in-hospital medical care (36% versus 42%; P<0.001) than hospitals without cardiac catheterization laboratories, but the former hospitals had somewhat higher rates of optimal discharge medical care (48% versus 45%; P<0.001). When we explored the relationship between optimal care and academic status among hospitals with cardiac catheterization...
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In hospitals with cardiac catheterization laboratories, we found that optimal in-hospital care was delivered in 31% and 64% (P < 0.001) of nonacademic (n = 120) and academic (n = 5) hospitals, respectively. A similar pattern was seen for optimal discharge medical care (45% versus 65%; P < 0.001).

We found weak correlations between most in-hospital and discharge medications, and correlation coefficients among discharge medications were higher (Table 3). The correlation coefficients were highest between clopidogrel and β-blockers for both in-hospital (correlation coefficient, 0.44) and discharge (correlation coefficient, 0.74) medical care. Figure 1 demonstrates the proportion of each possible in-hospital and discharge medication combination. Single and dual antiplatelet medical therapies were the most common in-hospital and discharge therapies (individually and in combination), and β-blockers (both individually and in combination) were the least common. Discharge medication rates were lower than in-hospital medication rates for all combinations. Figures II and III in the online-only Data Supplement demonstrate the variability across hospitals in delivering optimal in-hospital and discharge medical care, respectively.

Patients receiving optimal in-hospital therapy had lower in-hospital death rates (3.6% versus 4.1%; unadjusted odds ratio [OR; 95% confidence interval (CI)], 0.86 [0.76, 0.98]) and lower MACE rates (5.2% versus 6.1%; unadjusted OR [95% CI], 0.84 [0.75, 0.94]; Table 4). These estimates were attenuated with adjustment. Patients receiving optimal in-hospital medical therapy had an adjusted OR (95% CI) = 0.93 (0.71, 1.22) for in-hospital death and an adjusted OR (95% CI) = 0.79 (0.63, 0.99) for MACE.

Patients presenting with Killip class >1 were less likely to receive optimal in-hospital medical therapy (OR [95% CI], 0.56 [0.50, 0.63]) and discharge medical therapy (OR [95% CI], 0.67 [0.59, 0.75]) even after adjustment (Table 5). Patients presenting with STEMI were less likely to receive optimal in-hospital medical care (adjusted OR [95% CI], 0.51 [0.42, 0.62]) compared with patients presenting with unstable angina, but patients presenting with STEMI were more likely

Table 1. Patient-Level Characteristics by Presence or Absence of Optimal In-Hospital and Discharge Medical Therapy

<table>
<thead>
<tr>
<th></th>
<th>Optimal In-Hospital Medical Therapy</th>
<th>Nonoptimal In-Hospital Medical Therapy</th>
<th>P Value</th>
<th>Optimal Discharge Medical Therapy</th>
<th>Nonoptimal Discharge Medical Therapy</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>10,307 (40)</td>
<td>15,411 (60)</td>
<td></td>
<td>11,397 (46)</td>
<td>13,353 (54)</td>
<td></td>
</tr>
<tr>
<td><strong>Demographics, medical history</strong></td>
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<tr>
<td>Sex (men), n (%)</td>
<td>8009 (77.7)</td>
<td>11,914 (77.2)</td>
<td>0.31</td>
<td>8790 (77.1)</td>
<td>10,374 (77.7)</td>
<td>0.29</td>
</tr>
<tr>
<td>Age, y (SD)</td>
<td>60.3 (12)</td>
<td>60.6 (12)</td>
<td>0.12</td>
<td>60.4 (12)</td>
<td>60.5 (12)</td>
<td>0.24</td>
</tr>
<tr>
<td>Unemployed, n (%)</td>
<td>3788 (37.1)</td>
<td>5974 (39.0)</td>
<td>&lt;0.001</td>
<td>4271 (37.8)</td>
<td>5107 (38.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior MI, n (%)</td>
<td>1227 (11.9)</td>
<td>2428 (15.7)</td>
<td>&lt;0.001</td>
<td>1471 (12.9)</td>
<td>2005 (15.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of HTN, n (%)</td>
<td>5837 (56.6)</td>
<td>7443 (48.2)</td>
<td>&lt;0.001</td>
<td>6097 (53.5)</td>
<td>6683 (50.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of diabetes mellitus, n (%)</td>
<td>4104 (39.8)</td>
<td>5579 (36.1)</td>
<td>&lt;0.001</td>
<td>4495 (39.4)</td>
<td>4769 (35.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of smoking, n (%)</td>
<td>4451 (43.8)</td>
<td>4416 (28.6)</td>
<td>&lt;0.001</td>
<td>4741 (41.6)</td>
<td>3788 (28.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Presentation, clinical data</strong></td>
<td></td>
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<tr>
<td>STEMI, n (%)</td>
<td>3407 (36.0)</td>
<td>6162 (42.0)</td>
<td>&lt;0.01</td>
<td>3850 (36.8)</td>
<td>4935 (38.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI, kg/m² (SD)</td>
<td>23.1 (3.6)</td>
<td>23.1 (3.6)</td>
<td>0.44</td>
<td>23.0 (3.6)</td>
<td>23.1 (3.6)</td>
<td>0.05</td>
</tr>
<tr>
<td>Heart rate, bpm (SD)</td>
<td>80.2 (20)</td>
<td>80.2 (19)</td>
<td>0.29</td>
<td>79.7 (19)</td>
<td>80.1 (20)</td>
<td>0.09</td>
</tr>
<tr>
<td>SBP, mmHg (SD)</td>
<td>140.6 (30)</td>
<td>141.3 (29)</td>
<td>0.06</td>
<td>141.1 (29)</td>
<td>140.9 (31)</td>
<td>0.53</td>
</tr>
<tr>
<td>Creatinine, mg/dL (SD)</td>
<td>1.2 (0.8)</td>
<td>1.2 (0.6)</td>
<td>0.003</td>
<td>1.2 (0.7)</td>
<td>1.2 (0.6)</td>
<td>0.51</td>
</tr>
<tr>
<td>Killip class &gt;1</td>
<td>1045 (18.6)</td>
<td>1951 (23.8)</td>
<td>&lt;0.001</td>
<td>1062 (17.1)</td>
<td>1763 (24.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior/in-hospital ASA, n (%)</td>
<td>1650 (16.0)</td>
<td>2456 (15.9)</td>
<td>0.83</td>
<td>11,300 (99.2)</td>
<td>11,735 (87.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior/in-hospital clopidogrel, n (%)</td>
<td>1550 (15.0)</td>
<td>2384 (15.4)</td>
<td>0.38</td>
<td>11,263 (98.8)</td>
<td>12,294 (92.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior/in-hospital β-blocker, n (%)</td>
<td>1298 (12.6)</td>
<td>1792 (11.6)</td>
<td>0.02</td>
<td>10,333 (91.1)</td>
<td>5994 (44.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior/in-hospital statin, n (%)</td>
<td>1109 (10.8)</td>
<td>1832 (11.9)</td>
<td>&lt;0.001</td>
<td>10,550 (92.6)</td>
<td>8992 (66.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Procedures, other treatment</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital coronary angiography, n (%)</td>
<td>2115 (20.5)</td>
<td>2896 (18.8)</td>
<td>&lt;0.001</td>
<td>2391 (21.0)</td>
<td>2359 (17.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>In-hospital PCI, n (%)</td>
<td>1284 (12.5)</td>
<td>1776 (11.5)</td>
<td>0.02</td>
<td>1427 (12.5)</td>
<td>1448 (10.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>In-hospital CABG, n (%)</td>
<td>174 (1.7)</td>
<td>173 (1.1)</td>
<td>&lt;0.001</td>
<td>167 (1.5)</td>
<td>164 (1.2)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

ASA indicates aspirin; BMI, body mass index; CABG, coronary artery bypass graft; HTN, hypertension; MI, myocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; and STEMI, ST-segment–elevation MI.
to receive optimal discharge care (adjusted OR [95% CI], 3.93 [1.15, 1.68]). The unadjusted OR (95% CI) of optimal in-hospital care on the outcome of optimal discharge care is 9.33 (8.80, 9.90), which increases to OR=10.48 (9.37, 11.72; Table 5) after adjustment for within-hospital clustering and patient characteristics, although we note overlap of the 95% CI. We have also explored the correlation coefficient between optimal in-hospital and discharge care across all hospitals, which ranges widely from −0.24 to 1.00 (data not shown).

**Discussion**

**Summary of Results**

In a secondary analysis of the Kerala ACS Registry, we demonstrate that optimal in-hospital and discharge medical care, defined as receiving aspirin, clopidogrel, β-blockade, statin, and heparin (in-hospital only), were delivered in 40% and 46% of admissions, respectively. Wide variability in both in-hospital and discharge medical care was present across the range of participating hospitals, with few hospitals participating at consistently high (>90%) levels. When we excluded heparin in our definition of optimal in-hospital medical care, n of every 2 patients received the combination of aspirin, clopidogrel, β-blocker, and statin during ACS hospitalization. The lower rate of inappropriate thrombolysis in patients receiving optimal medical care also suggests that hospital- and provider-level processes of care extend beyond the optimal care package. In fact, patients who received optimal in-hospital medical care had a 21% lower rate of in-hospital MACE after adjustment and a trend toward lower in-hospital death rates.

In our evaluation of associations with receiving optimal medical care, we found that optimal in-hospital medical care had the strongest association with receiving optimal discharge care (OR [95% CI], 10.48 [9.37, 11.72]). We interpret these results to suggest that patient- and hospital-level factors that are associated with in-hospital optimal care are likely associated with optimal discharge care, which highlights the importance of optimal in-hospital care as a key step for improving ACS quality of care. β-Blocker use had the highest correlation with clopidogrel and statin use, suggesting that targeted efforts to increase the uptake of β-blockers may lead to greater increases in other medications particularly because β-blockers were the least commonly prescribed medication among both in-hospital and discharge groups. However, β-blocker prescription may be confounded by the presence of other, unmeasured variables of high-quality care.

Rural, nonacademic hospitals were less likely to provide both in-hospital and discharge optimal medical care. In subsequent interviews and focus group discussions with participating cardiologists after these data were collected, we have learned of the near impossibility of administering unfractionated heparin in the crowded wards of public hospitals, where measuring partial thromboplastin times is infeasible, and the cost of low molecular weight heparin is unaffordable. Such local factors likely play crucial roles in determining the definition of optimal care. We also note similarities in receiving optimal in-hospital and discharge medical care from hospitals with and without cardiologists, which suggests that task shifting in the care of patients with low-risk ACS to noncardiologists may be 1 strategy to provide high-quality, high-throughout care in regions with limited resources. However, we remain cautious in our interpretation of the association between hospital-level characteristics and optimal care given for the potential for reverse causality, such that sicker patients may be more likely to seek care at facilities with cardiac catheterizations laboratories, may be more likely to undergo invasive procedures, and may have more contraindications to components of optimal medical care.

**Comparison With Prior Studies**

One small study of 137 patients at a single center in Mangalore, India, reported similar rates of discharge optimal medical care.
care (41%) for patients with ACS, although the definition included a single antiplatelet agent, β-blocker, statin, and ACE-I inhibitor/angiotensin receptor blocker (ACE-I/ARB) use. The CREATE investigators have not reported analyses evaluating combination therapy for patients with ACS, but β-blocker and statins rates were lower than in our analyses; however, anticoagulant (and ACE-I/ARB) rates were higher in CREATE compared with the Kerala ACS Registry. Optimal combination secondary prevention of cardiovascular disease (CVD; aspirin, β-blocker, statin, and ACE-I/ARB) in the outpatient setting seems low as well, ranging from 7% to 44% in a recent report of 2993 prescriptions from the Indian state of Rajasthan, compared with rates of 54% at the time of CVD discharge from tertiary medical centers.

Investigators from other low- and middle-income countries have also evaluated the prevalence of optimal medical care in their registries. For example, the prevalence of optimal medical care at discharge, defined by the concurrent use of aspirin, β-blockers, statin, and ACE-I/ARB, was evaluated in the Clinical Pathways for ACSs (CPACS) in China registry of 2901 ACS admissions from 49 hospitals. In this registry, optimal discharge medical care was present in ≈1 of every 2 patients (48%). Similar to our data, patients with higher GRACE scores had lower rates of optimal care at discharge (OR per 1-point increase in GRACE score [95% CI], 0.99 [0.99, 0.99]), patients with cardiogenic shock in the Gulf RACE were far less likely to receive optimal discharge medications (OR [95% CI], 0.27 [0.21, 0.36]).

Building on these previous publications, investigators from the Brazilian Intervention to Increase Evidence Usage

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**Figure.** Proportion of each drug and drug combination for in-hospital and discharge care in Kerala Acute Coronary Syndrome Registry patients. A indicates aspirin; B, β-blocker; C, clopidogrel; H, heparin; and S, statin.

**Table 4.** Unadjusted and Multivariable Adjusted Random Effects Logistic Regression Model to Evaluate the Association (OR [95% CI]) Between Optimal vs Nonoptimal In-Hospital Medical Therapy and In-Hospital Events

<table>
<thead>
<tr>
<th></th>
<th>Optimal In-Hospital Medical Therapy</th>
<th>Nonoptimal In-Hospital Medical Therapy (ref)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>10 307 (40)</td>
<td>15 411 (60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital death</td>
<td>366 (3.6)</td>
<td>632 (4.1)</td>
<td>0.86 (0.76, 0.98)</td>
<td>0.93 (0.71, 1.22)</td>
</tr>
<tr>
<td>In-hospital death,</td>
<td>532 (5.2)</td>
<td>938 (6.1)</td>
<td>0.84 (0.75, 0.94)</td>
<td>0.79 (0.63, 0.99)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; GRACE, Global Registry of Acute Coronary Events; and OR, odds ratio.

*Adjusted for within-hospital clustering and modified GRACE risk score variables: age, heart rate, systolic blood pressure, serum creatinine, Killip class, cardiac enzyme (positive versus negative), and ST-segment deviation. Cardiac arrest at presentation excluded (N/A).
in ACS (BRIDGE ACS) cluster-randomized clinical trial of 1150 patients with ACS in 34 clusters demonstrated increased rates of optimal acute (first 24 hours) and discharge medical therapy through a multifaceted quality improvement intervention.\(^\text{11}\) The intervention led to an increase in acute medical care, defined by the concurrent use of aspirin, clopidogrel, anticoagulant, and statin from 50% to 68% (OR [95% CI], 2.64 [1.28, 5.45]). Optimal discharge medical therapy, defined as the use of aspirin, β-blocker, statin, and ACE-I/ARB, also increased from 57% in the control arm to 66% in the intervention arm (OR [95% CI], 1.55 [0.75, 3.18]).

Reasons for the differences between our data and other investigators are likely multifactorial and include: (1) differences in definitions of optimal care. We included clopidogrel given its class I recommendation for all patients in 2007, which is not the case with ACE-I/ARB, which requires concomitant heart failure, left ventricular systolic dysfunction, diabetes mellitus, or hypertension for a class I indication;\(^\text{12}\) (2) wider range of hospitals. We included 125 hospitals compared with 49, 65, and 34 hospitals from CPACS, Gulf RACE, and BRIDGE ACS, respectively. These registries included a higher proportion of academically affiliated hospitals (all >70%, compared with 8% of hospitals in the Kerala ACS Registry), which may bias their results to centers more likely to provide optimal care,14 low rates of optimal medical care in our data, in other observational studies from other low- and middle-income countries, and in carefully monitored clinical trials in high-income countries argue for comprehensive, continuous quality improvement and different paradigms (eg, inpatient and postdischarge use of 3-drug [aspirin, clopidogrel, and statin] fixed-dose combination, or polypill, therapy, which is already available in India, or alternative [nonoral] drug delivery systems) for secondary prevention of CVD. These data may also have implications for the ongoing debate on universal health insurance in India and other low- and middle-income countries because patients frequently bear high out-of-pocket expenses for treatment, including for in-hospital medications. More than 1 of every 2 patients hospitalized for ACS or stroke in Kerala experience financial catastrophe as a result of their medical expenditures (or catastrophic health spending, defined as spending >40% of total, nonfood expenditures on health),\(^\text{13}\) which likely affects not only in-hospital medical treatment but also discharge medical treatment. Lack of private or social health insurance has been associated with a 4-fold higher risk of catastrophic health spending (OR [95% CI], 3.93 [2.23, 6.90]) within 15 months of CVD hospitalization in India, as well as Argentina, China, and Tanzania.\(^\text{15}\) Scalable strategies to increase the proportion of patients with ACS who receive the optimal combination of in-hospital and discharge medications in low- and middle-income country settings seem to have substantial potential impact particularly because ischemic heart disease is the leading cause of death worldwide, and the majority (80%) of global CVD deaths occur in low- and middle-income countries.

### Strengths/Limitations

These data represent the largest ACS registry in India to date and provide the first large-scale evaluation of optimal in-hospital and discharge medical care in India. We will leverage these data in the development of our regional ACS QUIK for improved process-of-care measures. We also aim to explore quality-of-care data may lead to changes in process-of-care measures through a Hawthorne effect, which may wane over time and lead to lower rates of optimal process-of-care measures through regression to the mean, particularly in lower performing hospitals.

Postdischarge rates of optimal medical care in the outpatient setting are unfortunately even lower. Data from the Prospective Urban Rural Epidemiology registry suggest that less than half of patients with prevalent CVD take ≥1 medication for secondary prevention.\(^\text{9}\) Even large contemporary, US-based clinical trials (Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals With Diabetes [FREEDOM], Bypass Angioplasty Revascularization Investigation 2 Diabetes [BARI 2D], and Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation [COURAGE]) suggest that research participants simultaneously reach clinical cholesterol, blood pressure, smoking, and hemoglobin A1c targets only ≈20% of the time, due at least in part to low adherence.\(^\text{13}\) Although others have demonstrated ≈40% lower mortality rates (hazard ratio [95% CI], 0.61 [0.43, 0.88]) at 12 months at a single US center in patients with ≥80% adherence, or concordance, to guideline-based care,\(^\text{14}\) low rates of optimal medical care in our data, in other observational studies from other low- and middle-income countries, and in carefully monitored clinical trials in high-income countries argue for comprehensive, continuous quality improvement and different paradigms (eg, inpatient and postdischarge use of 3-drug [aspirin, clopidogrel, and statin] fixed-dose combination, or polypill, therapy, which is already available in India, or alternative [nonoral] drug delivery systems) for secondary prevention of CVD. These data may also have implications for the ongoing debate on universal health insurance in India and other low- and middle-income countries because patients frequently bear high out-of-pocket expenses for treatment, including for in-hospital medications. More than 1 of every 2 patients hospitalized for ACS or stroke in Kerala experience financial catastrophe as a result of their medical expenditures (or catastrophic health spending, defined as spending >40% of total, nonfood expenditures on health),\(^\text{13}\) which likely affects not only in-hospital medical treatment but also discharge medical treatment. Lack of private or social health insurance has been associated with a 4-fold higher risk of catastrophic health spending (OR [95% CI], 3.93 [2.23, 6.90]) within 15 months of CVD hospitalization in India, as well as Argentina, China, and Tanzania.\(^\text{15}\) Scalable strategies to increase the proportion of patients with ACS who receive the optimal combination of in-hospital and discharge medications in low- and middle-income country settings seem to have substantial potential impact particularly because ischemic heart disease is the leading cause of death worldwide, and the majority (80%) of global CVD deaths occur in low- and middle-income countries.

### Table 5. Multivariable Random Effects Logistic Regression Model to Evaluate the Association (OR [95% CI]) Between Patient and Process Characteristics With Optimal In-Hospital and Discharge Medical Care

<table>
<thead>
<tr>
<th>Variable</th>
<th>Optimal In-Hospital Medical Therapy</th>
<th>Optimal Discharge Medical Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.00 (1.00, 1.01)</td>
<td>1.00 (0.99, 1.00)</td>
</tr>
<tr>
<td>Women vs men (ref)</td>
<td>1.00 (0.90, 1.12)</td>
<td>1.00 (0.89, 1.13)</td>
</tr>
<tr>
<td>Heart rate, per bpm</td>
<td>1.01 (1.00, 1.01)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Systolic blood pressure (per mm Hg)</td>
<td>1.00 (1.00, 1.00)</td>
<td>1.00 (1.00, 1.00)</td>
</tr>
<tr>
<td>Killip &gt;1 vs =1 (ref)</td>
<td>0.56 (0.50, 0.63)</td>
<td>0.67 (0.59, 0.75)</td>
</tr>
<tr>
<td>NSTEMI vs unstable angina (ref)</td>
<td>1.17 (0.95, 1.45)</td>
<td>1.71 (1.35, 2.16)</td>
</tr>
<tr>
<td>STEMI vs unstable angina (ref)</td>
<td>0.51 (0.42, 0.62)</td>
<td>1.39 (1.15, 1.68)</td>
</tr>
<tr>
<td>Enzyme positive vs negative (ref)</td>
<td>2.14 (1.75, 2.62)</td>
<td>0.74 (0.60, 0.90)</td>
</tr>
<tr>
<td>Creatinine, per mg/dL</td>
<td>1.03 (0.97, 1.10)</td>
<td>0.97 (0.90, 1.04)</td>
</tr>
<tr>
<td>Optimal in-hospital medical therapy vs nonoptimal in-hospital medical therapy (ref)</td>
<td>...</td>
<td>10.48 (9.37, 11.72)</td>
</tr>
</tbody>
</table>

\(\text{CI}\) indicates confidence interval; GRACE, Global Registry of Acute Coronary Events; NSTEMI, non-ST-segment-elevation myocardial infarction; OR, odds ratio; and STEMI, ST-segment–elevation myocardial infarction.

\(\text{Adjusted for within-hospital clustering and modified GRACE risk score variables: age, heart rate, systolic blood pressure, serum creatinine, Killip class, enzyme positive versus negative, and ST-segment elevation and within-hospital clustering. Cardiac arrest at presentation excluded (N/A).} \)
reasons for successes, including high rates of dual antiplatelet use, which are comparable with contemporary registries from high-income countries. However, our data also have several limitations. First, patients receiving optimal medical care may have had fewer contraindications or been less ill than patients who did not receive optimal care, as demonstrated by patients with Killip class >1 being 44% and 33% less likely to receive optimal in-hospital and discharge care, respectively, compared with patients who were Killip class=1. This example of reverse causality may also partially explain the lower mortality and MACE rates in patients receiving optimal medical care. Second, these data are susceptible to residual confounding, which might change the strength or direction of the associations between process-of-care measures and outcomes, which may be reflected by the imprecision of our results. However, we restricted our evaluation to contemporary medications that have been shown to improve in-hospital and postdischarge outcomes and are class I recommendations in major cardiovascular society guidelines for all patients with ACS. Although we appreciate the potential for residual confounding, even after controlling for GRACE risk score variables, we argue that these process-of-care measures are generally considered the standard of care. Third, we did not include ACE-I/ARBs in our definition of optimal medical care, which some may argue for inclusion. Rates of left ventricular systolic dysfunction (ejection fraction, <30%) were very low (<2%), and we were missing data on ejection fraction on one-third of participants. Given these low rates of severe left ventricular systolic dysfunction and the lack of a class I recommendation of administering ACE-I/ARB in patients with preserved ejection fraction, we excluded ACE-I/ARB in our definition. Fourth, our outcome data are limited to in-hospital events, and so potential outcome benefits from optimal discharge medical care could not be explored. Fifth, our data are geographically limited to the state of Kerala and thus cannot represent the whole of India. However, the Kerala ACS Registry has broad coverage throughout the state.

Implications/Conclusions
Rates of optimal in-hospital (40%) and discharge (46%) medical care for ACS are suboptimal in Kerala, and these process-of-care gaps represent opportunities for improvement. Even after adjustment, patients at higher risk (Killip >1, STEMI) were less likely to receive optimal in-hospital medical therapy, which was associated with increased MACE rates. In-hospital ACS medical therapy is a powerful predictor of discharge medical therapy and provides an important target for quality improvement of discharge medical therapy. Strategies to improve in-hospital medical therapy (checklists, audit/feedback systems for continuous quality improvement) and discharge/postdischarge adherence are needed to improve local process-of-care measures and ACS outcomes. Novel paradigms might also be useful to increase optimal medical care for patients with ACS, including inpatient and postdischarge use of fixed-dose combination or polypill therapies, alternative drug delivery mechanisms, and universal health insurance to improve access to essential medicines.

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References


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SUPPLEMENTAL MATERIAL.

Supplemental Figure 1. Flowchart of hospitals participating in the Kerala ACS Registry and ACS admissions included in this analysis (2007-2009).

300 acute care hospitals in Kerala (2007 estimate)

185 hospitals admit patients with ACS and all were invited to participate

140 hospitals responded to invitation

125 hospitals participated in Kerala ACS Registry
n=25,748 ACS admissions

30 admissions excluded due to incomplete data

n=25,418 ACS admissions for analysis
Supplemental Figure 2. Distribution of optimal in-hospital medical care, by hospital.
Supplemental Figure 3. Distribution of optimal discharge medical care, by hospital.