

**ORIGINAL RESEARCH**

# Procedural Volume and Outcomes After Primary Percutaneous Coronary Intervention for ST-Segment–Elevation Myocardial Infarction in Kerala, India: Report of the Cardiological Society of India–Kerala Primary Percutaneous Coronary Intervention Registry

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**BACKGROUND:** There are limited data to inform policy mandating primary percutaneous coronary intervention (PPCI) volume benchmarks for catheterization laboratories in low- and middle-income countries.

**METHODS AND RESULTS:** This prospective state-wide registry included ST-segment–elevation myocardial infarction patients with symptoms of <12 hours, or with ongoing ischemia at 12 to 24 hours, reperfused with PPCI. From June 2013 to March 2016, we recruited 5560 consecutive patients. We categorized hospitals on the basis of annual PPCI volumes into low, medium, and high volume (<100, 100–199, and  $\geq$ 200 PPCIs per year, respectively). Kaplan-Meier curves and Cox regression models were used to examine the association between PPCI volume and 1-year mortality. Among 42 recruiting hospitals, there were 24 (57.2%) low-volume, 8 (19%) medium-volume, and 10 (23.8%) high-volume hospitals. The median (25th–75th percentile) TIMI (Thrombolysis in Myocardial Infarction) ST-segment–elevation myocardial infarction risk score was 3 (2–5). Cardiac arrest before admission occurred in 4.2%, 2.1%, and 2.9% of cases at low-, medium-, and high-volume hospitals, respectively ( $P=0.02$ ). Total ischemic time differed significantly among low-volume (median [25th–75th percentile], 3.5 [2.4–5.5] hours), medium-volume (median, 3.8 [25th–75th percentile, 2.58–6.05] hours), and high-volume hospitals (median, 4.16 [25th–75th percentile 2.8–6.3] hours) ( $P=0.01$ ). Vascular access was radial in 61.5%, 71.3%, and 63.2% of cases at low-, medium-, and high-volume hospitals, respectively ( $P=0.01$ ). The observed 1-year mortality rate was 6.5%, 3.4%, and 8.6% at low-, medium- and high-volume hospitals, respectively ( $P<0.01$ ), and the difference did not attenuate after multivariate adjustment (low versus medium: hazard ratio [95% CI], 1.80 [1.12–2.90]; high versus medium: hazard ratio [95% CI], 2.53 [1.78–3.58]) ( $P<0.01$ ).

**CONCLUSIONS:** Low- and middle-income countries, like India, may have a nonlinear relationship between institutional PPCI volume and outcomes, partly driven by procedural variations and inequalities in access to care.

**Key Words:** percutaneous coronary intervention ■ ST-segment–elevation myocardial infarction ■ stents

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## CLINICAL PERSPECTIVE

### What Is New?

- This large multicenter primary percutaneous coronary intervention (PPCI) registry from Kerala, India, reports long-term outcomes of patients presenting with ST-segment–elevation myocardial infarction to percutaneous coronary intervention–capable hospitals categorized according to institutional PPCI volume.
- There were significant variations in equity of access to ST-segment–elevation myocardial infarction care across low-, moderate-, and high-volume hospitals. Also, there were significant PPCI procedural variations as well as differences in the rates of guideline-directed medical therapy between low-, moderate-, and large-volume hospitals.
- Low- and middle-income countries, like India, may have a unique nonlinear relationship between institutional-level PPCI volumes and outcomes, with high-volume hospitals having the highest 1-year mortality rates.

### What Are the Clinical Implications?

- ST-segment–elevation myocardial infarction PPCI quality improvement initiatives in Kerala should at first focus on the relatively few high-volume hospitals.
- Process-of-care metrics, like timeliness of reperfusion and PPCI procedural characteristics, may be the key to improving ST-segment–elevation myocardial infarction outcomes in India rather than institutional-level PPCI volumes.
- Current global institutional-level PPCI volume benchmarks may not be appropriate for low- and middle-income countries, like India.

## Nonstandard Abbreviations and Acronyms

<b>ACS</b>	acute coronary syndrome
<b>LMIC</b>	low- and middle-income country
<b>PCI</b>	percutaneous coronary intervention
<b>PPCI</b>	primary percutaneous coronary intervention
<b>STEMI</b>	ST-segment–elevation myocardial infarction
<b>TIMI</b>	Thrombolysis in Myocardial Infarction

**G**lobal cardiovascular disease burden has been steadily increasing, with the disparate contribution of low- and middle-income countries (LMICs), like India, coming into focus.<sup>1–3</sup> Disease epidemiology in India, a country with 1.34 billion population, has made

a dramatic shift, with noncommunicable diseases accounting for a sizeable burden of disability-adjusted life years.<sup>1,2</sup> The southern Indian state of Kerala has been spearheading this national epidemiological transition to noncommunicable diseases.<sup>1</sup> Consequently, Kerala has had to pivot its healthcare delivery system traditionally designed to care for infectious diseases to increasingly face a significant burden of noncommunicable diseases, especially acute coronary syndromes (ACSs).<sup>4,5</sup> This shift is also apparent in the expansion of primary percutaneous coronary intervention (PPCI)–capable facilities in Kerala.<sup>4</sup> The rapid increase in the number of PPCI-capable hospitals in Kerala, with the attendant burgeoning of hospitals with low PPCI volumes, calls into question the safety and outcomes of PPCI at such hospitals.

An inverse relationship between both institutional- and operator-level percutaneous coronary intervention (PCI) volume and mortality has been observed.<sup>6,7</sup> Several international societies and regulatory bodies have issued institutional- and operator-level PPCI volume benchmarks, with wide variance in the recommended volume cutoffs.<sup>8–10</sup> However, there are limited data to inform policy mandating volume benchmarks for cardiac catheterization laboratories in LMICs that lack an organized prehospital system of ST-segment–elevation myocardial infarction (STEMI) care.<sup>11,12</sup> Prior ACS studies from Kerala showed the presence of extensive heterogeneity across hospitals in process and outcome measures.<sup>5,13</sup> Lower PPCI procedural volume may be driving some of this variability across hospitals. Analyzing the relationship between PPCI volumes and outcomes may enable LMICs to regionally adapt global PPCI institutional volume benchmarks and focus the limited healthcare resources on quality improvement initiatives across specific hospital groups.

The Cardiology Society of India–Kerala chapter developed and implemented a prospective state-wide PPCI registry to analyze the regional quality, procedural variations, and outcomes of PPCI services for STEMI. We report these results with a specific focus on the institutional PPCI volume–patient outcome relationship.

## METHODS

### Data Source and Study Population

The data that support the findings of this study are available from the corresponding author on reasonable request. The PPCI registry of Kerala is an investigator-initiated prospective state-wide multicenter registry of consecutive undergoing PPCIs at hospitals across Kerala, a state with a population of 33.4 million as per the 2011 Census. We performed a

baseline survey to identify PPCI-capable healthcare facilities in the state and updated it annually during the study period. During the study period, Kerala had a total of 255 hospitals providing emergency reperfusion services for STEMI. Of these hospitals, 92 had cardiac catheterization laboratories. Nine of the catheterization laboratory-equipped hospitals were public. After excluding 5 hospitals that were not offering PPCI services, we invited the remaining 87 hospitals to take part in the registry. Eighty-one percutaneous coronary intervention (PCI)-capable centers responded, of which 48 hospitals finally participated in the registry.

All adult patients presenting with acute STEMI, with ischemic symptoms of <12-hours' duration, designated to reperfusion therapy with PPCI were included. We also included patients with acute STEMI presenting to PCI-capable centers 12 to 24 hours after the onset of symptoms if the patient had clinical and electrocardiographic evidence of ongoing ischemia. At least one measurement of troponin I, troponin T, or creatinine kinase-MB above the upper reference limit was required for confirmation of diagnosis. New-onset left bundle branch block was also considered as a STEMI equivalent. We excluded patients presenting with STEMI >24 hours after symptom onset and those presenting between 12 and 24 hours with no clinical and electrocardiographic evidence of ongoing ischemia.

We enrolled patients in 2 phases. The first phase, extending from June 2013 to March 2015, enrolled 783 STEMI patients undergoing PPCI at hospitals in central Kerala. The second phase extended across the entire state and enrolled 5274 patients from April 2015 to March 2016. Follow-up was completed by March 2017. We obtained ethics committee clearance from participating hospitals and the central Cardiology Society of India-Kerala chapter ethics committee. Consent was obtained from all participating patients, except for very sick patients. An ethics committee waiver was obtained for patients who were deemed too ill to administer informed consent.

### Assessment of Hospital Volume and Outcomes

We stratified hospitals according to the annual PPCI volumes into low-, medium-, and high-volume centers (<100, 100–199, and >200 PPCIs per year, respectively) as well as based on whether they belonged to the public or private sector. The annual individual hospital PPCI volumes were corroborated with the numbers separately reported to the Interventional Cardiology Council of Kerala, an autonomous organization dedicated to the advancement of interventional cardiology regionally. We excluded hospitals

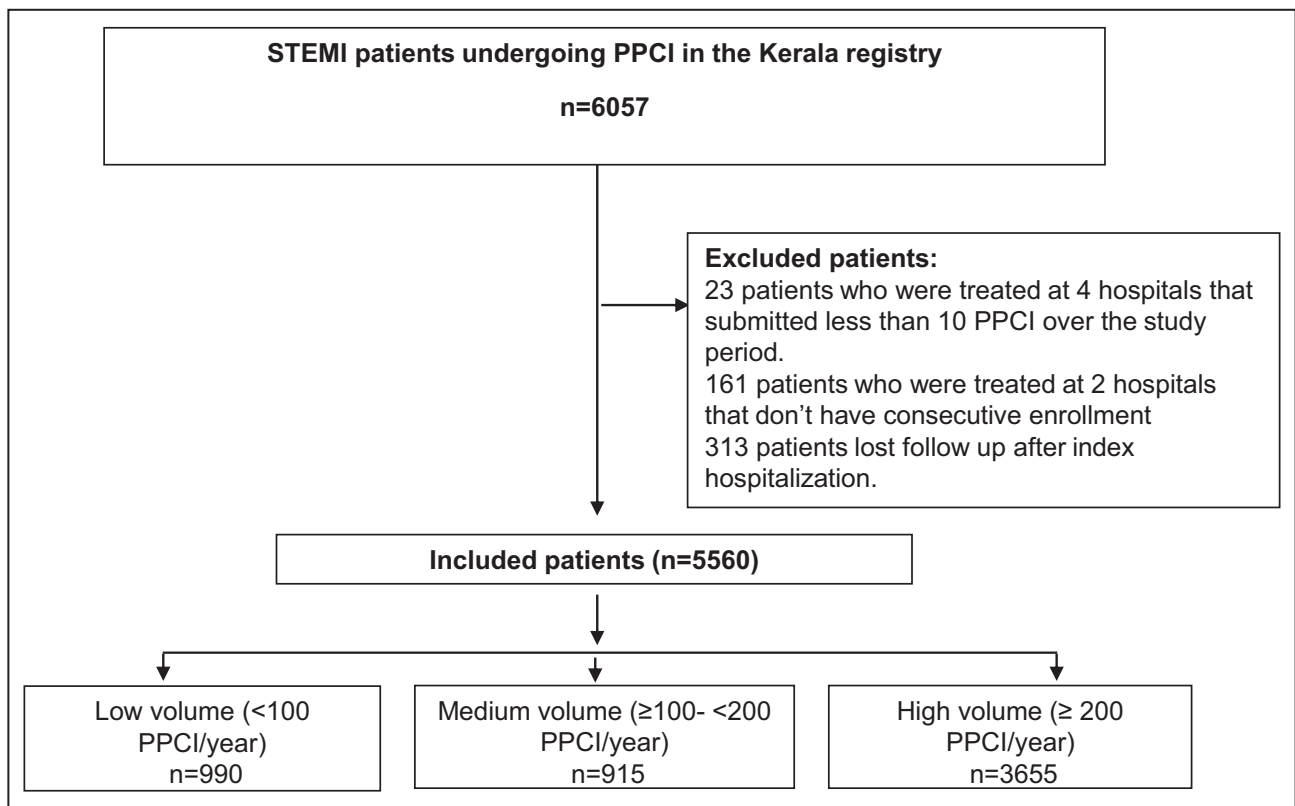
performing <10 PPCIs per year, as well as hospitals deemed to have recruited nonconsecutive patients, from the final analysis.

We recruited 6057 patients presenting with STEMI and undergoing PPCI across 48 hospitals in Kerala. We exclude the following groups of patients: 23 patients treated at 4 hospitals that submitted <10 PPCIs during the study period, 161 patients treated at 2 hospitals deemed to have recruited nonconsecutive patients, and 313 patients lost to follow-up after the index hospitalization. We also excluded 64 patients who did not consent to take part in the study. There was no difference between hospital groups in the proportion of nonconsenting patients. Thus, the overall study cohort included 5560 patients (Figure 1). The primary outcome was all-cause mortality within 1 year. Secondary outcomes included in-hospital mortality rates and stent thrombosis rates. We have provided additional details on methods in Data S1.

### Statistical Analysis

We summarized categorical variables as numbers and percentages, whereas continuous variables were presented as mean with SD. Continuous variables with skewed distribution were expressed as medians with 25th and 75th percentiles. Differences among groups (low-, medium-, and high-volume hospitals) were tested using Cochran-Mantel-Haenszel row mean scores for categorical variables and Cochran-Mantel-Haenszel correlation tests for continuous variables, thereby identifying trends. A descriptive analysis between public and private institutions in the high-volume group was performed to examine the difference in the quality of care and mortality within 1 year.

We plotted Kaplan-Meier curves to display the unadjusted relationship between hospital type and clinical outcomes (ie, the time to death within 30 days or 1 year). The groups were compared using the log-rank test. Follow-up time was censored at 365 days after symptom onset or discontinuation, whichever occurs first. The relative associations were estimated using Cox proportional hazard regression. We applied robust sandwich covariance estimates, by using maximum partial likelihood estimates in the model, to account for within-hospital clustering. We reported unadjusted and adjusted hazard ratios (HRs) and 95% CIs, with medium-volume hospitals as the reference group. To account for selection bias and confounders, we adjusted the PPCI volume-outcome association for sex, Thrombolysis in Myocardial Infarction (TIMI) risk score, insurance coverage, living below the poverty threshold, family history of coronary artery disease, smoking status, culprit lesion involving the proximal left anterior descending artery, number of years catheterization laboratory was performing PCI,



**Figure 1. CONSORT diagram of exclusions from the primary angioplasty registry of Kerala.** PPCI indicates primary percutaneous coronary intervention; and STEMI, ST-segment–elevation myocardial infarction.

and year of enrollment. We used a restricted cubic spline function to test the linearity assumption for continuous variables in the model. Spline transformations were applied when the linearity assumption was violated. As an exploratory analysis, we also examined the annual hospital volume as a continuous variable for mortality within 1 year using Cox proportional hazard regression model; hospital annual PPCI volume >300 was truncated to 300 because no hospital had yearly PPCI volumes between 300 and 500.

We performed a sensitivity analysis using individual components of the TIMI risk score for adjustment in the model instead of the score itself. We also repeated the analysis after excluding patients without insurance coverage treated at high-volume hospitals to see if this modified the mortality differential observed at high-volume centers.

All statistical tests were 2 sided, with  $P < 0.05$  considered nominally significant. We performed statistical analyses using SAS (version 9.4; SAS Institute, Cary, NC).

## RESULTS

### Hospital Characteristics

Forty-eight hospitals across the state of Kerala participated in the registry. We compared the institutional

characteristics of participating and nonparticipating hospitals. Hospital-level characteristics, including the proportion of urban hospitals (participating, 87.5%, versus nonparticipating, 92.7%;  $P = 0.49$ ), the number of hospital beds (participating,  $600 \pm 513$  beds, versus nonparticipating,  $469 \pm 253$  beds;  $P = 0.07$ ), and the number of years the catheterization laboratory has been performing PCI (participating,  $7.4 \pm 5.4$  years, versus nonparticipating,  $6.5 \pm 5.9$  years;  $P = 0.24$ ), were similar between participating and nonparticipating hospitals. However, participating hospitals had more interventionists performing PCI (median [25th–75th percentile], participating, 3 [2–4] interventionists, versus nonparticipating, 2 [1–2] interventionists;  $P = 0.01$ ). After excluding 6 ineligible hospitals, we categorized the remaining 42 enrolling hospitals into 24 (57.2%) low-volume, 8 (19.0%) medium-volume, and 10 (23.8%) high-volume hospitals. Of the 42 enrolling hospitals, 4 were public, with the remaining 38 being private. Public hospitals had high annual PPCI volumes and accounted for 29.3% of STEMI patients undergoing PPCI. Overall, the median (25th–75th percentile) annual hospital-level PPCI volume was 237 (115–520). The median (25th–75th percentile) annual PPCI volume was 563 (283–640) and 200 (99–237) for public and private

**Table 1. Baseline Characteristics Stratified Across Hospital Groups, Categorized According to Institutional-Level Annual PPCI Volume**

Baseline Characteristics	Missing Data	Total Cohort	Hospitals Categorized According to Hospital-Level Annual PPCI Volume			P Value
			Low Volume	Medium Volume	High Volume	
No. of patients	...	5560	990	915	3655	
Age, mean (SD) y	0	58.5 (11.4)	58.7 (11.4)	58.4 (11.6)	58.4 (11.4)	0.49
<40 y, n (%)	0	245 (4.4)	43 (4.3)	44 (4.8)	158 (4.3)	0.83
≥75 y, n (%)	0	521 (9.4)	96 (9.7)	80 (8.7)	345 (9.4)	0.96
Women, n (%)	0	1026 (18.5)	178 (18)	145 (15.8)	703 (19.2)	0.14
Below poverty level, n (%)	0	2009 (36.1)	248 (25)	273 (29.8)	1488 (40.7)	0.01
Self-paid, n (%)	1	3625 (65.2)	778 (78.6)	732 (80)	2115 (57.9)	0.01
Anterior STEMI, n (%)	0	2752 (49.5)	502 (50.7)	421 (46.0)	1829 (50)	0.05
LBBB, n (%)	10	118 (2.1)	44 (4.4)	20 (2.2)	54 (1.5)	0.01
Cardiac biomarker positive, n (%)	23	5537 (99.6)	984 (99.4)	913 (99.8)	3640 (99.6)	0.42
Hypertension, n (%)	0	2294 (41.3)	445 (44.9)	345 (37.7)	1504 (41.2)	0.15
Diabetes mellitus, n (%)	0	2383 (42.9)	506 (51.1)	377 (41.2)	1500 (41)	0.01
Total cholesterol, mean (SD), mg/dL	882	194 (59.6)	193.2 (62.2)	194.1 (50.9)	194.3 (61.0)	0.89
LDL cholesterol, mean (SD), mg/dL	1224	125.8 (47.8)	128.3 (51.4)	126 (43.6)	124.9 (47.8)	0.20
HDL cholesterol, mean (SD), mg/dL	1200	41.8 (11.7)	41.4 (12.6)	42.4 (12.5)	41.7 (11.2)	0.24
Chronic kidney disease, n (%)	0	160 (2.9)	36 (3.6)	34 (3.7)	90 (2.5)	0.02
Body mass index, mean (SD), kg/m <sup>2</sup>	262	23.9 (3.1)	24.1 (3.2)	23.9 (3.3)	23.9 (3.0)	0.18
Overweight, n (%)	262	1674 (30.1)	330 (26.3)	241 (26.3)	1103 (30.2)	0.01
Obesity, n (%)	262	179 (3.2)	39 (4.0)	38 (4.2)	102 (2.8)	0.01
Current smoker, n (%)	0	1972 (35.5)	285 (28.8)	255 (27.9)	1432 (39.2)	0.01
Family history of premature CAD, n (%)	0	1100 (19.9)	182 (18.4)	188 (20.5)	730 (20)	0.37
Cerebrovascular accident, n (%)	0	116 (2.1)	25 (2.5)	10 (1.1)	81 (2.2)	0.96
History of effort angina, n (%)	0	863 (15.5)	145 (14.6)	76 (8.3)	642 (17.6)	0.01
Prior MI, n (%)	0	277 (5.0)	56 (5.7)	52 (5.7)	169 (4.6)	0.11
Prior heart failure, n (%)	0	44 (0.8)	18 (1.8)	4 (0.4)	22 (0.6)	0.01
Aspirin use before MI, n (%)	0	274 (4.9)	75 (7.6)	53 (5.8)	146 (4.0)	0.01
Prior coronary revascularization, n (%)	0	126 (2.3)	24 (2.4)	30 (3.3)	72 (2)	0.15
TIMI risk score, median (25th–75th percentile)	0	3 (2–5)	3 (2–5)	3 (2–5)	3 (2–5)	0.01
Direct presentation to PCI-capable hospital, n (%)	0	2623 (47.2)	629 (63.5)	554 (60.5)	1440 (39.4)	0.01
Arrival at PCI-capable hospital by ambulance, n (%)	0	2470 (44.4)	291 (29.4)	290 (31.7)	1889 (51.7)	0.01
Ambulance use in direct presenting patients, n (%)	0	2623	66 (10.5)	57 (10.3)	187 (13)	0.02
Cardiac arrest before admission, n (%)	0	166 (3)	42 (4.2)	19 (2.1)	105 (2.9)	0.09
Systolic blood pressure at presentation, mean (SD), mm Hg	0	135 (30)	137 (30)	137 (28)	134 (30)	0.01
Shock at admission, n (%)	0	218 (3.9)	37 (3.7)	23 (2.5)	158 (4.3)	0.14
Angiographic characteristics, n (%)						
Single-vessel coronary artery disease	31	2861 (51.5)	454 (45.9)	446 (48.7)	1961 (53.6)	0.01

(Continued)

**Table 1. Continued**

Baseline Characteristics	Missing Data	Total Cohort	Hospitals Categorized According to Hospital-Level Annual PPCI Volume			P Value
			Low Volume	Medium Volume	High Volume	
Double-vessel coronary artery disease	31	1727 (31.1)	335 (33.8)	304 (33.2)	1088 (29.8)	0.01
Triple-vessel coronary artery disease	31	938 (16.9)	199 (20.1)	156 (17.1)	583 (16.0)	0.01
Left main disease	0	136 (2.5)	21 (2.1)	17 (1.9)	98 (2.7)	0.27
Proximal LAD artery culprit lesion	117	2009 (36.1)	352 (35.5)	320 (35.0)	1337 (36.5)	0.01

CAD indicates coronary artery disease; HDL, high-density lipoprotein; LAD, left anterior descending; LBBB, left bundle branch block; LDL, low-density lipoprotein; MI, myocardial infarction; PCI, percutaneous coronary intervention; PPCI, primary PCI; STEMI, ST-segment–elevation MI; and TIMI, Thrombolysis in Myocardial Infarction.

hospitals, respectively. Figure S1 depicts the histogram of institutional-level annual PPCI volumes. Catheterization laboratories at low-volume hospitals were performing PCI for a fewer number of years compared with medium- and high-volume hospitals (low-volume hospitals, 6.6±6.9 years; medium-volume hospitals, 8.6±3.8 years; and high-volume hospitals, 8.7±3.9 years; *P*<0.01). We reported the hospital-level details in Table S1.

**Patient Characteristics**

Table 1 depicts the baseline patient characteristics. We included a total of 5560 patients in the final analysis, with 990 (17.8%), 915 (16.5%), and 3655 (65.7%) patients treated in low-, medium-, and high-volume hospitals, respectively. These hospital groups differed considerably with regard to the clinical profile of patients subjected to PPCI. Overall, the mean age was 58.5±11.4 years, with women constituting 18.5% of the population. Patients classified as living in poverty represented 25%, 29.8%, and 40.7% of PPCI patients at low-, medium-, and high-volume hospitals, respectively (*P* for trend <0.01). Public health insurance schemes funded a larger proportion of patients undergoing PPCI in high-volume hospitals compared with other hospital groups (low-volume hospitals, 5.9%; medium-volume hospitals, 3.7%; and high-volume hospitals, 36.3%; *P* for trend <0.01).

In terms of underlying patient risk, patients undergoing PPCI in low-volume hospitals were more likely to have diabetes mellitus (low-volume hospitals, 51.1%; medium-volume hospitals, 41.2%; and high-volume hospitals, 41%; *P* for trend <0.01) and history of heart failure (low-volume hospitals, 1.8%; medium-volume hospitals, 0.4%; and high-volume hospitals, 0.6%; *P* for trend <0.01). Patients undergoing PPCI in low-volume hospitals had a higher TIMI risk score (proportion of patients with TIMI risk score ≥4: low-volume hospitals, 49.2%; medium-volume hospitals, 43%; and high-volume hospitals, 39.8%; *P* for trend <0.01) compared with medium- and high-volume hospitals. However, the

proportion of patients in shock on arrival (low-volume hospitals, 3.7%; medium-volume hospitals, 2.5%; and high-volume hospitals, 4.3%; *P* for trend=0.14) and the proportion of patients with resuscitated cardiac arrest before admission were similar across the 3 groups (low-volume hospitals, 4.2%; medium-volume hospitals, 2.1%; and high-volume hospitals, 2.9%; *P* for trend=0.09).

**Quality Indicators**

Table 2 lists quality indicators and outcomes. Key timeliness metrics, including the total ischemic time (median [25th–75th percentile]: low-volume hospitals, 3.5 [2.4–5.5] hours; medium-volume hospitals, 3.8 [2.6–6.1] hours; and high-volume hospitals, 4.2 [2.8–6.3] hours; *P* for trend <0.01) and ECG-to-balloon time (median [25th–75th percentile]: low-volume hospitals, 1.5 [1.0–2.4] hours; medium-volume hospitals, 1.5 [0.8–2.8] hours; and high-volume hospitals, 2 [1.2–3.1] hours; *P* for trend <0.01), differed significantly among hospital groups, with high-volume hospitals experiencing the most delays. However, the door-to-balloon time (measured at the PCI center and not including transfer hospital) did not differ significantly between the hospitals. The symptom onset to first medical contact time also did not differ. Radial vascular access rates (low-volume hospitals, 61.5%; medium-volume hospitals, 71.3%; and high-volume hospitals, 63.2%; *P* for trend=0.01) were higher at medium-volume hospitals. The rates of nonculprit vessel PCI (low-volume hospitals, 7.8%; medium-volume hospitals, 10.8%; and high-volume hospitals, 7.2%; *P* for trend=0.01) were also higher at medium-volume hospitals. A total of 359 (6.5%) patients underwent nonculprit vessel PCI during the index hospitalization, and 81 patients underwent staged elective nonculprit vessel PCI after discharge. High-volume hospitals had a significantly lower proportion of PPCI patients undergoing aspiration thrombectomy compared with low- and medium-volume hospitals (low-volume hospitals, 45.3%; medium-volume hospitals, 37.5%; and high-volume

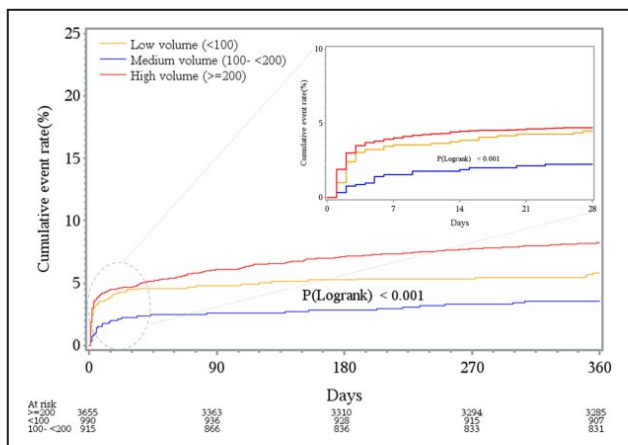
**Table 2. Quality Indicators and Outcomes**

Quality Indicators	Missing	Total, n (%)	Hospitals Categorized According to Hospital-Level Annual PPCI Volume			P Value
			Low Volume	Medium Volume	High Volume	
<b>Timeliness</b>						
Total ischemic time, median (25th–75th percentile), h	42	3.9 (2.7–6.1)	3.5 (2.4–5.5)	3.8 (2.6–6.1)	4.2 (2.8–6.3)	0.01
ECG-to-balloon time, median (25th–75th percentile), h	11	1.8 (1.1–3.0)	1.5 (1.0–2.4)	1.5 (0.8–2.8)	2 (1.2–3.1)	0.01
Door-to-balloon time, median (25th–75th percentile), h	7	1.2 (0.8–1.7)	1.2 (0.9–1.7)	1.16 (0.8–1.9)	1.13 (0.8–1.6)	0.60
Symptom onset to first medical contact, median (25th–75th percentile), h	0	1.5 (0.8–3.0)	1.33 (0.7–3.0)	1.5 (0.8–3.0)	1.5 (0.9–3.0)	0.96
<b>Procedural characteristics, n (%)</b>						
Radial access	0	3572 (64.2)	609 (61.5)	652 (71.3)	2311 (63.2)	0.01
Aspiration thrombectomy use	0	2062 (37.1)	448 (45.2)	343 (37.5)	1271 (34.8)	0.01
TIMI flow III final	0	5190 (93.3)	912 (92.1)	853 (93.2)	3425 (93.7)	0.08
Nonculprit vessel PCI during index admission	0	359 (6.5)	68 (6.9)	91 (9.9)	200 (5.5)	0.01
<b>Discharge medications, n (%)</b>						
Aspirin	8	5269 (98.5)	918 (96.5)	895 (99.4)	3456 (98.8)	0.01
Clopidogrel	7	3911 (73.1)	630 (66.3)	730 (81.1)	2551 (72.9)	0.01
Ticagrelor	8	847 (15.8)	246 (25.9)	109 (12.1)	492 (14.1)	0.01
Prasugrel	8	563 (10.5)	68 (7.1)	57 (6.3)	438 (12.5)	0.01
High-intensity statin	8	5120 (95.7)	875 (92.0)	826 (91.8)	3419 (97.7)	0.01
β Blocker	9	3497 (65.4)	649 (68.2)	570 (63.3)	2278 (65.1)	0.16
ACEI or ARB in patients with documented LV systolic dysfunction	7	1321 (50.6)	226 (37.7)	109 (25.8)	986 (62.1)	0.01
Aldactone	213	825 (14.8)	71 (7.2)	111 (12.1)	643 (17.6)	0.01
Eplerenone	213	109 (2.0)	11 (1.1)	3 (0.3)	95 (2.6)	0.01
<b>Outcomes</b>						
Stent thrombosis, n (%)	7	110 (2.0)	16 (1.6)	9 (1)	85 (2.3)	0.04
Definite stent thrombosis, n (%)	7	44 (0.8)	9 (0.9)	5 (0.5)	30 (0.8)	0.03
TIMI major bleed, n (%)	6	32 (0.6)	2 (0.2)	4 (0.4)	26 (0.7)	0.01
LVEF, mean (SD), %	270	39.2 (14.6)	32.8 (13.9)	39.6 (16.4)	40.8 (13.8)	0.01
Cardiogenic shock, in hospital, n (%)	7	363 (6.5)	50 (5.1)	30 (3.3)	283 (7.7)	0.01
30-d Mortality, n (%)	0	234 (4.2)	44 (4.4)	20 (2.2)	170 (4.6)	0.01
1-y Mortality, n (%)	0	410 (7.4)	64 (6.5)	31 (3.4)	315 (8.6)	0.01

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, aldosterone receptor blocker; LV, left ventricular; LVEF, LV ejection fraction; PCI, percutaneous coronary intervention; PPCI, primary PCI; and TIMI, Thrombolysis in Myocardial Infarction.

hospitals, 34.8%; *P* for trend <0.01). Discharge medication prescription patterns varied among hospital groups, with low-volume hospitals having the highest rate of newer P2Y12-inhibitor prescription (ticagrelor or prasugrel: low-volume hospitals, 33.1%; medium-volume hospitals, 18.4%; and high-volume hospitals, 26.6%; *P* for trend <0.01) and high-volume hospitals having more patients discharged on high-intensity statins (low-volume hospitals, 92.1%; medium-volume hospitals, 91.8%; and high-volume hospitals, 97.9%; *P*<0.01), angiotensin-converting enzyme inhibitors or

angiotensin receptor blockers in those with left ventricular ejection fraction <40% (low-volume hospitals, 37.7%; medium-volume hospitals, 25.8%; and high-volume hospitals, 62.1%; *P* for trend <0.01), and aldosterone blockers (low-volume hospitals, 8.3%; medium-volume hospitals, 12.4%; and high-volume hospitals, 20.2%; *P* for trend <0.01). There were significant differences in baseline characteristics and quality-of-care metrics between high-volume hospitals belonging to private and public sectors (Tables S2 and S3). Ninety (1.76%) patients underwent subsequent



**Figure 2.** Kaplan-Meier curves for the entire cohort (n=5560), displaying the unadjusted relationship between hospitals, categorized according to the hospital-level annual primary percutaneous coronary intervention volume, and all-cause mortality at 30 days (inset box) and 1 year with a comparison between groups using log-rank test.

coronary artery bypass grafting, of which 25 (0.45%) were in hospital and the rest after discharge.

### Association Between Hospital Type and Outcomes

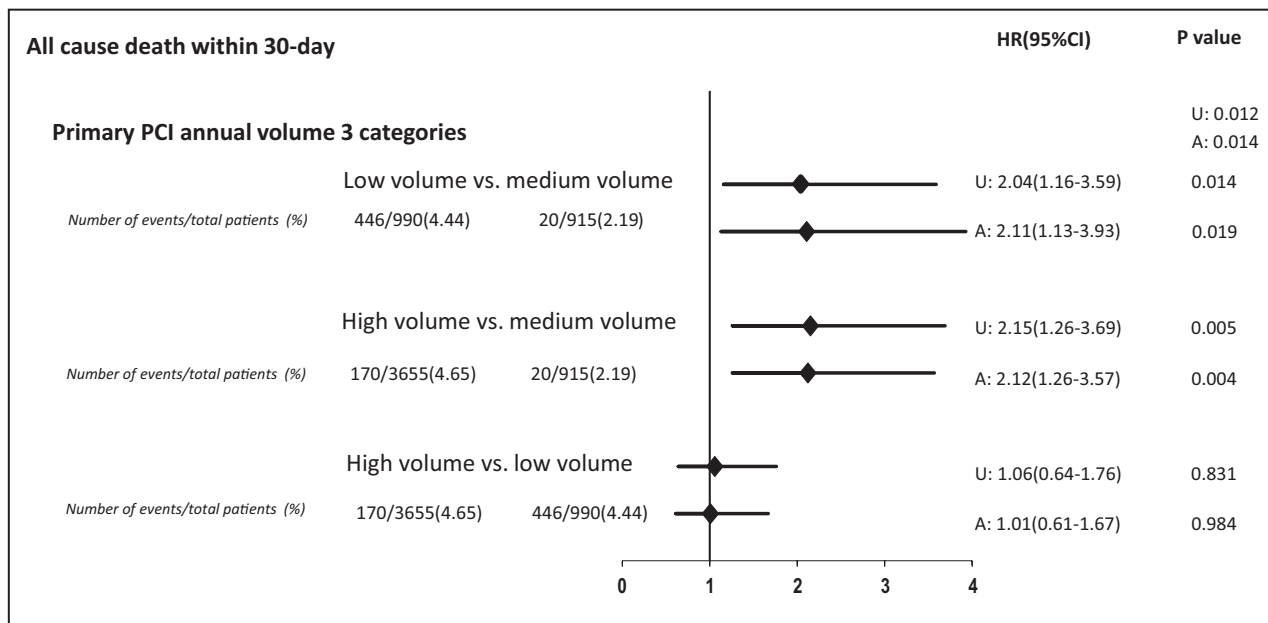
#### Short-Term Outcomes

The 30-day all-cause mortality for the entire cohort was 4.2%, with significant variation across low-, medium-, and high-volume hospitals (low-volume hospitals,

4.4%; medium-volume hospitals, 2.2%; and high-volume hospitals, 4.6%; *P* for trend <0.01). Figure 2 depicts Kaplan-Meier curves for the entire cohort, displaying the survival rates for low-, medium-, and high-volume hospitals. After multivariable adjustment, a higher HR for 30-day mortality was noted in both low-volume (HR, 2.11; 95% CI, 1.13–3.93; *P*=0.01) and high-volume hospitals (HR, 2.12; 95% CI, 1.26–3.57; *P*<0.01), compared with medium-volume hospitals. However, adjusted mortality at 30 days was not significantly different between high- and low-volume hospitals (HR, 1.01; 95% CI, 0.61–1.67; *P*=0.98). Figure 3 depicts the association between hospital-level annual PPCI volumes and 30-day mortality.

#### Long-Term Outcomes

The crude 1-year all-cause mortality for the entire cohort was 7.4%, with significant variation across low-, medium-, and high-volume hospitals (low-volume hospitals, 6.5%; medium-volume hospitals, 3.4%; and high-volume hospitals, 8.6%; *P* for trend <0.01). After multivariable adjustment, mortality within 1 year was higher among patients treated at high-volume PPCI centers (HR, 2.53; 95% CI, 1.78–3.58; *P*<0.01) and for those treated at low-volume centers (HR, 1.80; 95% CI, 1.12–2.90; *P*=0.01), compared with medium-volume hospitals. Mortality within 1 year was not significantly different between high- and low-volume hospitals (HR, 1.40; 95% CI, 0.91–2.17; *P*=0.13). We obtained consistent results in a sensitivity analysis performed after



**Figure 3.** Hazard ratios (HRs) of 30-day all-cause mortality between hospital groups, categorized into low-, medium-, and high-volume, according to the annual institutional primary percutaneous coronary intervention (PCI) volume.

A indicates adjusted for sex, CI, confidence interval, TIMI (Thrombolysis in Myocardial Infarction) risk score, insurance coverage, living in poverty, family history, smoking status, culprit lesion in proximal left anterior descending artery, number of years catheterization laboratory was performing percutaneous coronary interventions, and year of enrollment. U, unadjusted.



incorporating individual components of the TIMI STEMI risk score in the model as opposed to the risk score itself (Figure S2). We also performed this analysis with the exclusion of patients without insurance coverage treated at high-volume hospitals. In this analysis, we found that the volume-outcome relationship was maintained (high- versus medium-volume hospitals: HR, 2.42; 95% CI, 1.7–3.4;  $P < 0.01$ ). Figure 4 depicts the association between hospital-level annual PPCI volumes and the unadjusted and adjusted mortality within 1 year.

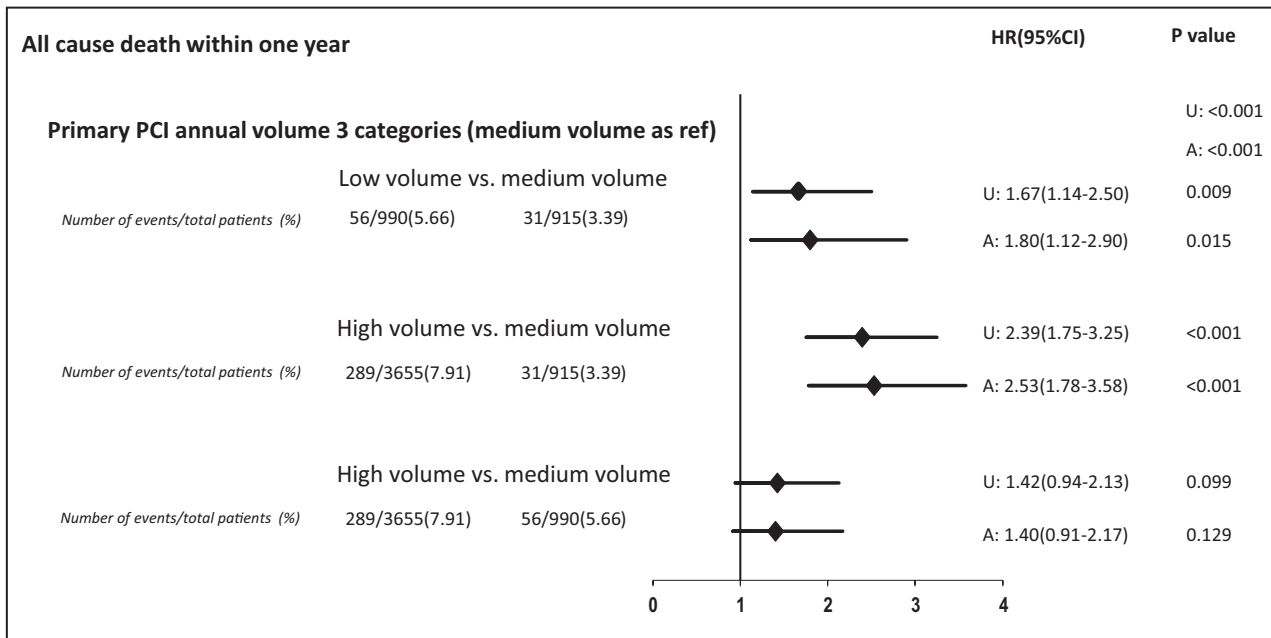
We then examined annual PPCI volume as a continuous variable. The relationship between the institutional annual PPCI volume and mortality within 1 year followed a nonlinear pattern, with low- and high-volume hospitals having increased mortality rates compared with medium-volume hospitals (Figure 5). Also, medium-volume hospitals had the lowest rates of cardiogenic shock in hospital (low-volume hospitals, 5.1%; medium-volume hospitals, 3.3%; and high-volume hospitals, 7.7%;  $P$  for trend=0.01) and stent thrombosis at 1 year (low-volume hospitals, 1.6%; medium-volume hospitals, 1.0%; and high-volume hospitals, 2.3%;  $P$  for trend=0.04).

## DISCUSSION

Improving care pathways for acute myocardial infarction management in LMICs constitutes one of the most crucial but arduous tasks on the path to reducing global cardiovascular disease burden.<sup>2,14</sup> In India, STEMI

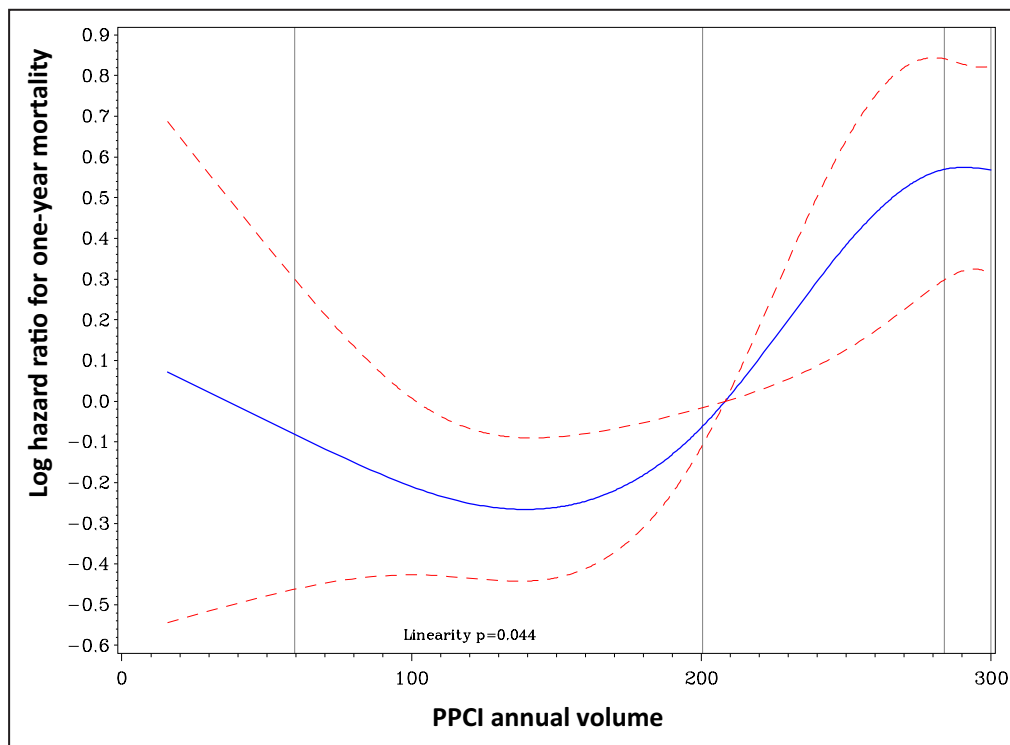
represents the most frequent ACS presentation.<sup>5,15</sup> The southern Indian state of Kerala adopted a pragmatic approach to improving STEMI care by locally adapting quality improvement tool kits for ACS management<sup>16</sup> and rapidly expanding the number of PPCI-capable hospitals.<sup>4</sup> However, several such hospitals have low PPCI volumes. Lower procedural volumes may be driving variability across hospitals in terms of quality of PPCI procedures, the use of guideline-directed medical therapy, and patient outcomes.

In this large PPCI STEMI registry, including 55.2% of all PPCI-capable hospitals in Kerala, several novel findings were observed. There were significant variations in the equity of access across hospital groups. Patients classified as living in poverty preferentially accessed high-volume hospitals, many of which were offering government-sponsored health insurance, possibly bypassing nearby low-volume hospitals. However, patients who could afford to pay for health care preferentially accessed the more prevalent low- and medium-volume hospitals. Such inequity in access resulted in the higher-volume hospitals having longer total ischemic time despite the similar door-to-balloon time. There were significant procedural variations across hospital groups. Medium-volume hospitals had higher rates of radial vascular access and nonculprit vessel PCI, compared with low- and high-volume hospitals. Contrastingly, high-volume hospitals had lower aspiration thrombectomy rates. Guideline-directed medical therapy rates were also not uniform across hospital



**Figure 4. Hazard ratios (HRs) of 1-year all-cause mortality between hospital groups, categorized into low-, medium-, and high-volume, according to the annual institutional primary percutaneous coronary intervention (PCI) volume.**

A indicates adjusted for sex, TIMI (Thrombolysis in Myocardial Infarction) risk score, insurance coverage, living in poverty, family history, smoking status, culprit lesion in proximal left anterior descending artery, number of years catheterization laboratory was performing percutaneous coronary interventions, and year of enrollment. U, unadjusted.



**Figure 5.** Relationship between institutional annual primary percutaneous coronary intervention (PPCI) volume as a continuous variable and risk of the primary outcome (1-year mortality).

groups. Low-volume hospitals discharged a higher proportion of patients on newer-generation P2Y12 inhibitors (ticagrelor or prasugrel). High-volume hospitals discharged a higher percentage of patients on high-intensity statins, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and aldosterone blockers. The level of affordability of the patient population, as well as the academic status of treating hospitals, likely impacted guideline-directed medical therapy rates.

We identified a nonlinear relationship between hospital-level annual PPCI volumes and 1-year mortality among patients who underwent PPCI for STEMI in Kerala. Medium-volume hospitals had lower rates of stent thrombosis, cardiogenic shock, and 30-day and 1-year mortality rates compared with low- and high-volume hospitals. Several factors can explain the paradoxical PPCI volume-outcome relationship in Kerala. First, the longer total ischemic time and ECG-to-balloon time documented at high-volume hospitals is one such factor potentially contributing to the differential in outcomes. Second, there were significant differences in the procedural quality indicators between hospital groups, which could be impacting outcomes. Medium-volume hospitals had significantly higher radial vascular access rates compared with low- and high-volume hospitals. Besides, medium-volume hospitals performed nonculprit vessel PCI in a higher proportion of patients compared with low- and

high-volume hospitals. The rates of nonculprit vessel PCI may be a surrogate marker of complete revascularization. In STEMI patients with multivessel coronary artery disease, complete revascularization reduces the risk of cardiovascular death and myocardial infarction.<sup>17</sup> Similarly, low-volume hospitals used aspiration thrombectomy in 45.2% of PPCIs, a rate much higher than in medium- and low-volume hospitals. Third, all public hospitals were high-volume hospitals. There were significant differences between private and public hospitals in terms of baseline patient characteristics, the clinical process-of-care metrics, and outcomes. Finally, there could be multiple unmeasured confounders influencing the PPCI volume-outcome relationship in LMICs. Lower drug compliance among patients living in poverty may potentially explain the divergence in survival curves between low- and high-volume hospitals after the first month. Although high-volume hospitals had significantly higher rates of guideline-directed medical therapy prescription at discharge compared with other hospital groups, compliance issues stemming from catastrophic healthcare expenditure could compromise this early advantage. Catastrophic healthcare expenditure and distress financing are typical after ACS in this geographic area.<sup>18</sup> In our cohort, 65.2% of patients undergoing PPCI paid for their treatment expenses out of pocket, comparable to the 75.9% of patients lacking health insurance coverage in the Kerala ACS QUIK (Acute Coronary Syndrome

Quality Improvement in Kerala) trial.<sup>16,18</sup> Furthermore, fellows or early-career interventionists typically train at high-volume hospitals. Lifetime operator-level PCI volume may thus be a potential confounder affecting the volume-outcome relationship.

The association between both hospital- and operator-level volume benchmarks and cardiac interventional procedural quality would appear logical. Also, volume benchmarks have remained the cornerstone of surgical quality assurance programs. National cardiac societies and governmental agencies in many LMICs, including India, grapple with the need to adopt globally recognized institutional volume benchmarks to regulate the growth of cardiac catheterization laboratories and to mandate which hospitals can perform PPCI. Several international societies and regulatory bodies have issued institutional- and operator-level volume benchmarks, with wide variance in the recommended volume cutoffs. The British Cardiovascular Intervention Society, for example, has endorsed that STEMI patients should undergo PPCI in hospitals performing a minimum of 100 PPCIs annually.<sup>8</sup> However, the American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Interventions guidelines recommended an annual institutional cutoff of at least 36 PPCIs and an operator-level cutoff of 11 PPCIs.<sup>9,10</sup> The volume benchmarks are more stringent for hospitals without on-site cardiac surgical support.<sup>9</sup> Low-volume hospitals, especially using low-volume operators, may have worse outcomes<sup>6</sup> and may require extra surveillance and operator backup.

Several concerns temper the enthusiasm to adapt globally recognized PCI volume benchmarks to STEMI care in LMICs. First, volume benchmarks may result in regionalization of care, creating further unintended hurdles to access to care. Impediments to the access of care may disproportionately impact lower socioeconomic strata patients residing in remote areas. Second, all structural and process metrics may not be equal. Quality improvement initiatives designed to improve total ischemic time may differently impact outcomes compared with efforts intended to strengthen structural parameters, like institutional PPCI volumes. LMICs may incur a high opportunity cost by basing quality improvement programs on benchmarks that are not methodically selected. Third, at least in some countries, PPCI as a procedure may be maturing, and the volume-outcome relationship may have weakened.<sup>7,19</sup> There are limited data to indicate where LMICs stand with regard to the maturity of PPCI procedures. Institutional-level variations in process metrics may explain many of the differences in outcomes,<sup>6,20</sup> especially in LMICs.<sup>13</sup>

Our study has certain limitations. Our study involved only 55.2% of the PCI-capable hospitals in this

region. However, we have demonstrated that there are no significant differences between the participating and nonparticipating hospitals but for the number of interventionalists employed at each center. Also, 5.2% of patients were lost to follow-up. Some of these patients could have died or switched healthcare providers. We did not measure the operator-level procedural volume. Both lifetime and annual operator-level procedure volumes may influence outcomes. Low-volume operators performing PPCI at low-volume hospitals may have worse results.<sup>6</sup> We have not documented cardiac rehabilitation participation because most participating hospitals were not offering formal cardiac rehabilitation to STEMI patients during the study period. Nonetheless, our registry is the first multicenter PPCI STEMI registry from India and represents one of the earliest studies looking at long-term outcomes following STEMI in India.

## CONCLUSIONS

In conclusion, LMICs, like India, may have a unique nonlinear relationship between institutional-level PPCI volumes and outcomes that appears to be partly driven by inequities in access to health care and institutional-level variance of procedural quality metrics. STEMI quality improvement initiatives in Kerala should mainly focus on the relatively few high-volume hospitals, especially those in the public sector. Process-of-care metrics, like timeliness of reperfusion and procedural characteristics, may be more vital than institutional-level PPCI volumes in the quest to improve STEMI outcomes in India. Our data call into question the need for LMICs, like India, to regionally adapt global institutional-level PPCI volume benchmarks.

## ARTICLE INFORMATION

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## Supplementary Materials

Data S1

Tables S1–S3

Figures S1–S2

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# **SUPPLEMENTAL MATERIAL**

## **Data S1**

### **Supplemental Methods**

We identified public PCI-capable hospitals through the Directorate of Health Services and private PCI-capable hospitals by collating information from local physician bodies in each district, private teaching hospitals, medical device manufacturing and distributing companies, and the from the updated CSI-K list of PCI-capable hospitals. Detailed demographic data, risk factors, procedural details, and post-procedure complications were entered prospectively by clinical staff members at each hospital.

Data elements were entered by pre-designated patient care team members at specific points along the chain of STEMI care using an internet-based standardized electronic case report form.

Data were recorded in real-time or as soon as the patient was transferred out of a hospital location. A supplementary paper-based case report form was utilized in select areas or wards, where internet access was not available. Research nurses/data abstracters visited the participating hospitals once a month and audited data accuracy against source documents.

Also, they reviewed patient medical records to determine if any in-hospital adverse outcomes were left undocumented or misclassified. Follow-up information was also prospectively obtained, during these monthly site visits, from the medical records, or by telephonic interviews with patients. Coronary angiography and PPCI images were reviewed. We followed-up patients at pre-defined time intervals of 30 days and one year.

Patients who were thrombolized, either at the referring hospital or at the STEMI receiving center, were excluded irrespective of the dose of the lytic therapy. Patients presenting initially with unstable angina

or non-ST elevation myocardial infarction and subsequently developing STEMI in-hospital were excluded. Diagnostic ST- elevation, in the absence of LV hypertrophy or left bundle branch block, was defined as new ST- elevation at the J-point in at least two contiguous leads measuring  $>2$  mm in men or  $>1.5$  mm in women involving leads V2-V3 and/or  $\geq 1$  mm in other contiguous chest leads or limb leads. We first established the upper reference limit for cardiac biomarkers at each hospital and then documented cardiac biomarker elevation as a categorical variable. All recruited patients had at least one biomarker elevation, but for 23 patients. In these 23 patients, the steering committee reviewed the ECG and coronary angiogram findings to confirm that the diagnosis is consistent with acute STEMI. We defined total ischemic time as the time interval between onset of chest pain and first balloon inflation during primary PCI. Door-to-balloon time was defined as the time interval between arrival at the PCI-capable hospital to first inflation of balloon during primary PCI. Annual PPCI volumes for each hospital was calculated as the total number of PPCI patients in a hospital after first enrollment times 4 divided by the total number of quarters the hospital has been reporting data after first enrollment.

**Table S1. Hospital characteristics.**

Hospital characteristics	Total cohort	Hospitals categorized according to hospital-level annual primary PCI volume			p-value
		Low-volume	Medium-volume	High volume	
Patients treated in academic hospitals, n (%)	2444/5560 (44)	115 (11.6)	135 (14.7)	2194 (60)	0.01
Patients treated in hospitals with surgical back-up, n (%)	4543/5560 (81.7)	628 (63.4)	471 (41.5)	3444 (94.2)	0.01
Patients treated in hospitals with 24x7 primary PCI, n (%)	5441/5560 (97.8)	871 (88)	915 (100)	3655 (100)	0.01
Patients treated in hospitals with trainees/fellows performing primary PCI, n (%)	1705/5560 (30.7)	89 (9)	0 (0)	1616 (44.2)	0.01
Number of hospitals	42	24	8	10	
Number of interventionists per hospital, median (IQR)	3 (2-4)	2 (2-4)	3 (2-5)	4 (3-4)	
Number of Academic/teaching hospitals, n (%)	8 (19)	2 (8.30)	1 (12.5)	5 (50)	
Number of hospitals with on-site surgical back up available, n (%)	26 (61.9)	12 (50)	5 (62.5)	9 (90)	
Number of hospitals with 24x7 primary PCI available, n (%)	36 (85.7)	18 (75)	8 (100)	10 (100)	
Number of hospitals with fellows/trainees performing primary PCI as first operators, n (%)	5 (11.9)	1 (4.2)	0 (0)	4 (50)	



**Table S2. Private- versus public- hospitals: baseline characteristics.**

	<b>Total</b>	<b>Private hospitals</b>	<b>Public hospitals</b>	<b>p-value</b>
Number of patients, n(%)	5560	3932 (70.7)	1628 (29.3)	
Age, mean (SD) years	58.5 (11.45)	58.4 (11.6)	58.7 (11.2)	0.89
<40 years, n (%)	245 (4.4)	182 (4.6)	63 (3.9)	0.21
≥75 years, n (%)	521 (9.4)	373 (9.5)	148 (9.1)	0.65
Women, n (%)	1026 (18.5)	689 (17.5)	337 (20.7)	0.01
Below poverty level, n (%)	2009 (36.1)	913 (23.2)	1096 (67.3)	0.01
Self-paid, n (%)	3625 (65.2)	3190 (81.1)	435 (26.7)	0.01
Anterior STEMI, n(%)	2752 (49.5)	1907 (48.5)	845 (51.9)	0.02
LBBB, n(%)	118 (2.1)	91 (2.3)	27 (1.7)	0.12
Hypertension, n (%)	2294 (41.3)	1734 (44.1)	560 (34.4)	0.01
Diabetes, n (%)	2383 (42.8)	1778 (45.2)	605 (37.2)	0.01
Total cholesterol, mean±SD (mg/dl)	194.1 ± 59.6	196.1 ± 63.4	188 ± 48.0	0.01
LDL, mean±SD (mg/dl)	125.8±47.8	126.2±46.2	124±53.4	0.31
HDL, mean±SD (mg/dl)	41.8±11.7	41.8±11.9	41.6±11.1	0.65

Chronic kidney disease, n (%)	160 (2.9)	116 (2.9)	44 (2.7)	0.61
COPD, n (%)	329 (5.9)	265 (6.7)	64 (3.9)	0.01
BMI, mean (SD) Kg/m <sup>2</sup>	24.0±3.1	23.9±3.3	24.1±2.5	0.18
Overweight, n (%)	1674 (31.6)	1160 (31.1)	514 (32.8)	0.22
Obesity, n (%)	179 (3.4)	158 (4.2)	21 (1.3)	0.01
Current smoker, n (%)	1972 (35.5)	1308 (33.3)	664 (40.8)	0.01
Family history of premature CAD, n (%)	1100 (19.8)	908 (23.1)	192 (11.8)	0.01
CVA, n (%)	116 (2.1)	98 (2.5)	18 (1.1)	0.01
History of effort angina, n(%)	863 (15.5)	701 (17.8)	162 (9.9)	0.01
Prior myocardial infarction, n (%)	277 (5.0)	213 (5.4)	64 (3.9)	0.02
Prior heart failure, n (%)	44 (0.8)	34 (0.8)	10 (0.6)	0.34
Aspirin use prior to MI, n (%)	274 (4.9)	192 (4.9)	82 (5.1)	0.80
Prior coronary revascularization	126 (2.3)	99 (2.5)	27 (1.7)	0.05
TIMI risk score, median (IQR)	3 (2-5)	3 (2-5)	3 (2-.4)	0.01

**Table S3. Private- versus public-high-volume hospitals: process metrics and outcomes.**

	<b>High-volume hospitals (&gt;200 PPCI per year)</b>	<b>Private high-volume</b>	<b>Public high-volume</b>	<b>p-value</b>
Total ischemic time, median (IQR) hours	4.2 (2.8-6.3)	3.9 (2.8-6.2)	4.3 (2.9-6.4)	0.03
ECG to balloon time, median (IQR) hours	2 (1.2-3.1)	1.8 (1.1-2.9)	2.2 (1.2-3.4)	0.01
Door to balloon time, median (IQR) hours	1.1 (0.8-1.6)	1.1 (0.8-1.5)	1.2 (0.8-1.75)	0.05
Symptom onset to first medical contact, median (IQR) hours	1.5 (0.8-3.0)	1.6 (0.8-3.1)	1.5 (1.0-3.0)	0.28
Radial access, n(%)	2311 (63.2)	1457 (71.9)	854 (52.5)	0.001
Aspiration thrombectomy use, n(%)	1271 (34.8)	792 (39.1)	479 (29.4)	0.001
Post-dilatation, n(%)	2187 (61.3)	1391 (69.3)	796 (51.1)	0.001
TIMI flow III final, n(%)	3425 (93.7)	1892 (93.3)	1533 (94.2)	0.31
Aspirin, n(%)	3472 (98.9)	1958 (99.1)	1514 (98.8)	0.42

Clopidogrel , n(%)	2567 (73.13)	1244 (62.9)	1323 (86.3)	0.001
Ticagrelor, n(%)	492 (14.1)	437 (22.2)	55 (3.6)	0.001
Prasugrel, n(%)	438 (12.5)	286 (14.5)	152 (10.0)	0.001
High intensity statin, n(%)	3433 (97.9)	1937 (98.1)	1496 (97.7)	0.384
Beta-blocker, n(%)	2283 (65.1)	1327 (67.2)	956 (62.4)	0.003
ACEI or ARB in patients with documented LV systolic dysfunction, n(%)	1058 (61.2)	634 (65.7)	424 (55.4)	0.001
Stent thrombosis, n(%)	85 (2.3)	53 (2.6)	32 (2.0)	0.20
Definite stent thrombosis, n(%)	30 (0.8)	22 (1.1)	8 (0.5)	0.015
Mortality at 1 year, n(%)	315 (8.6)	150 (7.4)	165 (10.1)	0.003

Figure S1. Hospital level annual primary percutaneous coronary intervention volumes.

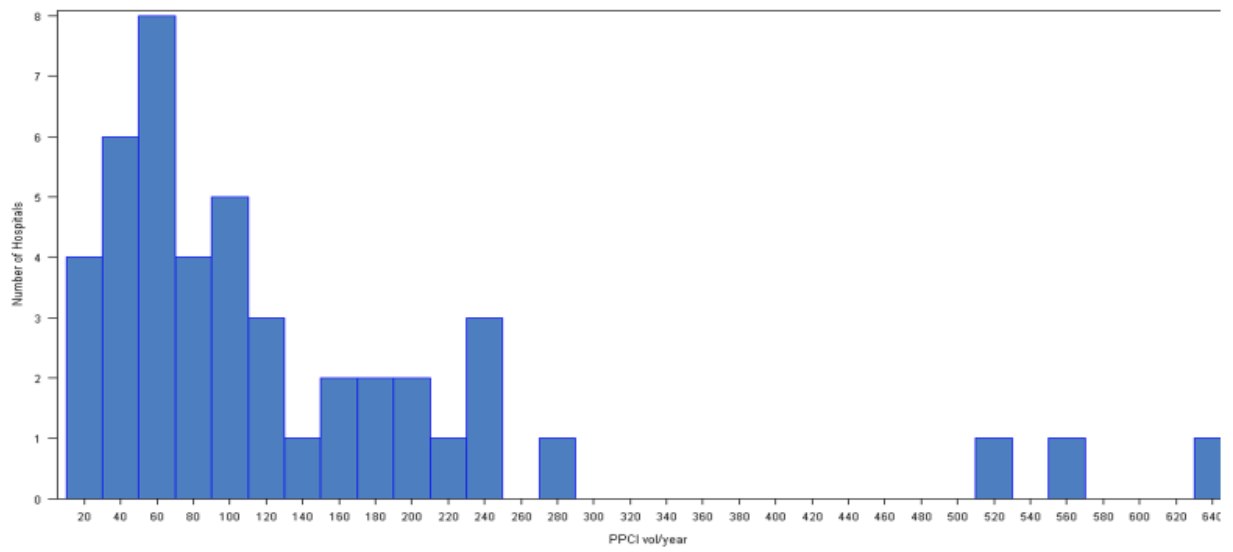


Figure S2. Sensitivity analysis adjusted for components of TIMI risk score.

