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Intra-aortic balloon pump use and in-hospital mortality in acute myocardial infarction with Killip class III or IV: a nationwide cohort study

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Abstract

Background The intra-aortic balloon pump (IABP) remains widely used in acute myocardial infarction (AMI) complicated by severe heart failure or shock, particularly where access to advanced mechanical circulatory support is limited. Contemporary nationwide evidence in AMI presenting with Killip class III or IV is scarce. We therefore evaluated IABP use during hospitalization and in-hospital outcomes in this setting.

Methods We did a nationwide cohort study using the China Chest Pain Center Database (4089 hospitals; 2019 to 2023). Adults aged ≥ 18 years with AMI and Killip class III or IV who underwent percutaneous coronary intervention (PCI) were included. The exposure was IABP use during hospitalization versus no recorded mechanical circulatory support; the primary outcome was in-hospital all-cause mortality. Associations were estimated by stabilized inverse probability of treatment weighting based on Bayesian additive regression trees (sIPTW-BART) and weighted Cox models, supported by prespecified sensitivity analyses.

Results Among 37 477 patients, 6051 received IABP. In the sIPTW-BART-weighted cohort, IABP use was associated with higher in-hospital all-cause mortality (28.1% vs. 19.1%; hazard ratio [HR] 1.48, 95% CI 1.37–1.61) and cardiovascular mortality (27.5% vs. 18.8%; HR 1.48, 1.36–1.61), and recorded in-hospital complications differed between groups. Findings were consistent across prespecified sensitivity analyses. The E-value for the lower confidence limit was 2.08, indicating the minimum strength of unmeasured confounding required to explain away the primary association.

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Conclusions Among patients undergoing PCI for AMI with Killip class III or IV presentation, IABP use during hospitalization was associated with higher in-hospital all-cause and cardiovascular mortality. These findings suggest potential risk associated with routine IABP use in this population and support further prospective studies to identify patients most likely to benefit or be harmed. Residual confounding by indication cannot be excluded; these findings should therefore be interpreted as associations rather than as causal effects of IABP.

Keywords Intra-aortic balloon pump, Acute myocardial infarction, Cardiogenic shock, Mechanical circulatory support, Percutaneous coronary intervention, Registry

Background

Acute myocardial infarction complicated by cardiogenic shock (AMI-CS) remains a highly lethal condition [1–5]. For decades, the intra-aortic balloon pump (IABP) was the cornerstone of mechanical circulatory support (MCS) for these patients [6]. However, the landmark IABP-SHOCK II trial and subsequent meta-analyses failed to demonstrate a survival benefit with routine IABP use [7–10]. Accordingly, contemporary international guidelines recommend against routine IABP use in patients with AMI complicated by cardiogenic shock in the absence of mechanical complications [11–14]. The 2025 ACC/AHA/ACEP/NAEMSP/SCAI acute coronary syndromes guideline gives routine IABP use in AMI complicated by cardiogenic shock a Class III (No Benefit) recommendation [15].

Despite these guideline updates, IABP use remains heterogeneous across practice settings. In health systems where access to more advanced mechanical circulatory support is limited, the device continues to be used because it is available, familiar, and less resource-intensive than microaxial pumps or extracorporeal support [16–18]. Contemporary nationwide data from China may therefore inform routine clinical care. However, prior observational studies have been limited by confounding by indication and time-related bias [19–21]. Using the China Chest Pain Center Database, we evaluated the association between IABP use during hospitalization and in-hospital outcomes among adults undergoing percutaneous coronary intervention (PCI) for AMI with Killip class III or IV presentation and explored whether the association differed across prespecified clinically relevant subgroups.

Methods

Study design and data source

We conducted a retrospective nationwide registry-based cohort study using the China Chest Pain Center Database [22]. The registry is a national quality-improvement initiative for acute chest pain and acute coronary syndromes and includes 4089 tertiary and secondary hospitals across China. It captures demographics, presentation features, treatments, and in-hospital outcomes. The Ethics Committee of Zhongshan Hospital, Fudan University, approved the study (approval number B2024-045) and waived the requirement for informed consent for the use of anonymized registry data; the study was done in accordance with the Declaration of Helsinki. The study is reported in accordance with the STROBE reporting guideline for observational studies. The analysis was framed as an emulation of a hypothetical target trial contrasting IABP use during hospitalization with no mechanical circulatory support among eligible patients [23], as summarized in Table S1 (Additional file 1).

Study population

Patients admitted to participating hospitals between January 1, 2019, and December 31, 2023, were eligible for inclusion if they (1) were aged 18 years or older, (2) had a confirmed diagnosis of AMI, (3) presented with Killip class III or IV, and (4) underwent PCI during the index hospitalization. Killip class III was defined as acute pulmonary edema, and Killip class IV was defined as cardiogenic shock with hypotension and signs of peripheral hypoperfusion. Exclusion criteria were: (1) patients treated at hospitals with no recorded IABP use during the study period, because these hospitals were excluded from the study cohort rather than contributing patients to the control group; (2) patients who received other forms of mechanical circulatory support, including percutaneous extracorporeal ventricular assist systems, extracorporeal membrane oxygenation (ECMO), or left ventricular assist devices (LVAD); (3) patients with incomplete data on primary outcome measures; and (4) patients with prior coronary revascularization.

Exposure

Patients were classified according to whether IABP use was recorded during the index hospitalization. The exposure group included patients who underwent PCI and had recorded IABP use during hospitalization. The comparison group included patients who underwent PCI without any recorded mechanical circulatory support during hospitalization, including IABP, ECMO, or LVAD use.

Outcomes

The primary outcome was in-hospital all-cause mortality, defined as death from any cause during the index hospitalization. Follow-up was limited to the index

hospitalization and ended at in-hospital death or discharge. Secondary outcomes included in-hospital cardiovascular death and registry-recorded intraprocedural and postprocedural in-hospital complications. Outcome ascertainment was based on standardized records in the registry. In-hospital cardiovascular death was defined as death attributed to cardiovascular causes according to the standardized registry outcome record.

Covariates

Covariates for baseline characterization and adjustment were prespecified based on clinical relevance and availability in the registry and were assessed at presentation or using the earliest available information during the index hospitalization. These covariates included: demographics (age, sex); cardiovascular risk factors (history of hypertension, dyslipidemia, diabetes mellitus, smoking history, obesity, and family history of premature cardiovascular disease); comorbidities (coronary heart disease, atrial fibrillation, chronic heart failure, valvular heart disease, cerebrovascular disease, peripheral artery disease, aortic aneurysm, chronic obstructive pulmonary disease, chronic kidney disease, anemia, peptic ulcer disease, thyroid disorder, and malignancy); clinical presentation (Killip class, systolic blood pressure, diastolic blood pressure, alert on admission, heart rate, and chest pain on admission); diagnosis/angiography characteristics (type of myocardial infarction, left main coronary artery disease, and multivessel coronary disease); laboratory indicators (positive troponin, creatinine, and elevated BNP or NT-proBNP); hospital level (tertiary vs. secondary); and medications (antiplatelet therapy, pre-admission anticoagulation, statin therapy, and beta-blocker therapy). To approximate exchangeability, we constructed a directed acyclic graph (DAG) to identify a prespecified adjustment set based on clinical knowledge and data availability (Fig. S1, Additional file 1).

Statistical analysis

Preparation and handling of missing data

Baseline covariates with missing data were handled using random forest–based multiple imputation by chained equations (RF-MICE) [24], generating 40 completed datasets with 10 iterations per imputation chain. Only incomplete baseline covariates were imputed. IABP use, in-hospital all-cause death, in-hospital cardiovascular death, survival time, and admission year were included as predictors in the imputation models but were not themselves imputed. Analyses were performed separately within each completed dataset, and estimates were pooled using Rubin's rules. The extent of missingness and imputation status for baseline covariates are summarized in Table S2, and the detailed imputation specification is provided in Supplementary Methods 1 (Additional file 1).

Baseline characteristics and descriptive analysis

Baseline covariates were categorical and are presented as counts (percentages). Covariate balance before and after weighting/matching was assessed using standardized mean differences (SMDs), with an absolute SMD < 0.10 indicating adequate balance.

Analyses of primary and secondary outcomes

The primary analysis used stabilized inverse probability of treatment weighting based on a propensity score estimated using Bayesian additive regression trees [25–27]. Stabilized weights were constructed from the predicted treatment probabilities to create a weighted pseudo-population with balanced baseline covariates; balance was assessed using standardized mean differences and visualized with Love plots. Weighted cumulative incidence curves were used to depict the cumulative risk of in-hospital all-cause mortality and cardiovascular mortality by treatment group. Hazard ratios and 95% confidence intervals were estimated using sIPTW-BART–weighted Cox proportional hazards models with the control group as the reference. Registry-recorded binary secondary outcomes, including intraprocedural and in-hospital complications, were analyzed exploratorily using sIPTW-BART–weighted logistic regression models and reported as odds ratios with 95% confidence intervals. All model-based analyses were fitted separately within each of the 40 RF-MICE completed datasets, with robust sandwich standard errors clustered at the hospital level to account for within-hospital correlation, and estimates were pooled using Rubin's rules. The proportional hazards assumption was assessed using scaled Schoenfeld residuals for the treatment variable, with treatment-specific and global tests reported; when evidence of non-proportional hazards was detected, weighted Cox models including a treatment-by-log(time + 1) interaction were fitted as sensitivity analyses.

Sensitivity analyses

Prespecified sensitivity analyses included (1) the unadjusted association in the unmatched cohort; (2) 1:1 nearest-neighbor propensity score matching using generalized linear model (GLM)-, gradient boosting machine (GBM)-, and BART-estimated scores; (3) covariate balancing propensity score (CBPS) and sIPTW derived from GLM- and GBM-estimated scores; (4) multivariable Cox regression; and (5) complete-case analysis. We additionally adjusted for admission year and performed year-specific analyses (2019–2023); and (6) E-values were calculated using the method of VanderWeele and Ding to assess the robustness of the primary association to unmeasured confounding [28]. Propensity score overlap and stabilized-weight distribution were assessed (Supplementary Methods 2, Additional file 1), and positivity was

evaluated by truncating weights at the 1st and 99th percentiles and restricting to the common-support region.

Subgroup analyses

Prespecified subgroup analyses by baseline covariates (demographics, comorbidities, clinical presentation, hospital level) were performed using the same sIPTW-BART framework and weighted Cox models. Effect modification was evaluated using treatment-by-subgroup interaction terms with corresponding P values. Given multiple comparisons, subgroup results were considered exploratory. To further address heterogeneity between Killip class III and Killip class IV, additional Killip class-specific analyses re-estimated BART propensity scores separately within each Killip stratum, with untruncated and 99th-percentile weight-truncated estimates reported to assess the influence of extreme weights. All statistical tests were 2-sided, and a P value < 0.05 was considered statistically significant. All analyses were conducted in R (version 4.5.2; R Foundation for Statistical Computing).

Use of large language models

During the preparation of this manuscript, the authors used AI-based language tools to improve the language and readability of the text. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication. AI-based tools were not used for study design, data analysis, or interpretation of the results.

Results

Study population and baseline characteristics

Among 37 477 eligible patients, 6051 received IABP support and 31 426 served as controls (Fig. 1). Patients in the IABP group presented with more severe shock (Killip class IV: 80.2% vs. 60.1%; Killip class III: 19.8% vs. 39.9%). STEMI predominated in both groups (85.6% vs. 88.7%), with NSTEMI more common among IABP-treated patients (14.4% vs. 11.3%). After sIPTW using BART-estimated propensity scores, balance was achieved across all prespecified covariates (all SMDs < 0.1; Table 1; Table S3 and Fig. S2, Additional file 1). Because the primary analyses were weighted, patient counts reported for the weighted cohort are stabilized IPTW (pseudo-population) counts and therefore differ slightly from the corresponding unweighted counts (IABP group, 5928 vs. 6051; control group, 31 402 vs. 31 426).

Primary outcome: in-hospital all-cause mortality

In the sIPTW-BART-weighted cohort, the cumulative risk of in-hospital all-cause mortality was higher in the IABP group than in the control group (1663/5928 [28.1%] vs. 6013/31 402 [19.1%]). In weighted Cox models with hospital-clustered robust standard errors and Rubin's rules pooling across 40 RF-MICE completed datasets, IABP use was associated with a higher hazard of in-hospital all-cause mortality (HR, 1.48; 95% CI, 1.37–1.61; reference: control). Weighted cumulative risk curves with numbers at risk are shown in Fig. 2.

Secondary outcomes

Results were consistent for in-hospital cardiovascular mortality. The cumulative risk was higher among patients receiving IABP than among controls (1628/5928 [27.5%] vs. 5904/31 402 [18.8%]). In weighted Cox models with hospital-clustered robust standard errors and Rubin's rules pooling across 40 RF-MICE completed datasets, IABP use was associated with a higher risk of in-hospital cardiovascular death (HR, 1.48; 95% CI, 1.36–1.61; Fig. S3, Additional file 1).

In the weighted cohort, IABP use was associated with differences in intraprocedural and in-hospital events (Table 2). During PCI, intraprocedural hypotension was less frequently recorded in the IABP group (OR, 0.64; 95% CI, 0.58–0.71), whereas severe bradyarrhythmia (OR, 1.29; 95% CI, 1.06–1.57), slow-flow or no-reflow (OR, 1.70; 95% CI, 1.44–2.01), and coronary perforation (OR, 3.14; 95% CI, 1.25–7.90) were more frequently recorded.

For postprocedural in-hospital complications, IABP use was associated with higher odds of mechanical complications (OR, 1.45; 95% CI, 1.29–1.61), bleeding events (OR, 1.62; 95% CI, 1.33–1.97), and malignant arrhythmia (OR, 1.59; 95% CI, 1.40–1.81). Infection was less frequently recorded in the IABP group (OR, 0.71; 95% CI, 0.64–0.79), while other complications showed no statistically significant differences (Table 2).

Subgroup analyses

Across prespecified subgroups, association estimates were directionally consistent with the primary analysis, with hazard ratios above 1.0 (Fig. 3). Additional exploratory subgroup analyses for risk factors, comorbidities, angiographic characteristics, and medications are provided in Table S6 (Additional file 1). Tests for interaction were nominally significant for several subgroups in both the primary (Fig. 3) and supplementary (Table S6) analyses. Because of multiple comparisons, these subgroup analyses should be interpreted as exploratory and hypothesis generating. Given their clinical importance, Killip classes III and IV were further analyzed separately using stratum-specific BART propensity-score estimation and weighting. IABP use was associated with higher in-hospital mortality in both strata, although the Killip class III estimate should be interpreted cautiously because of limited overlap and residual imbalance (Table 3).

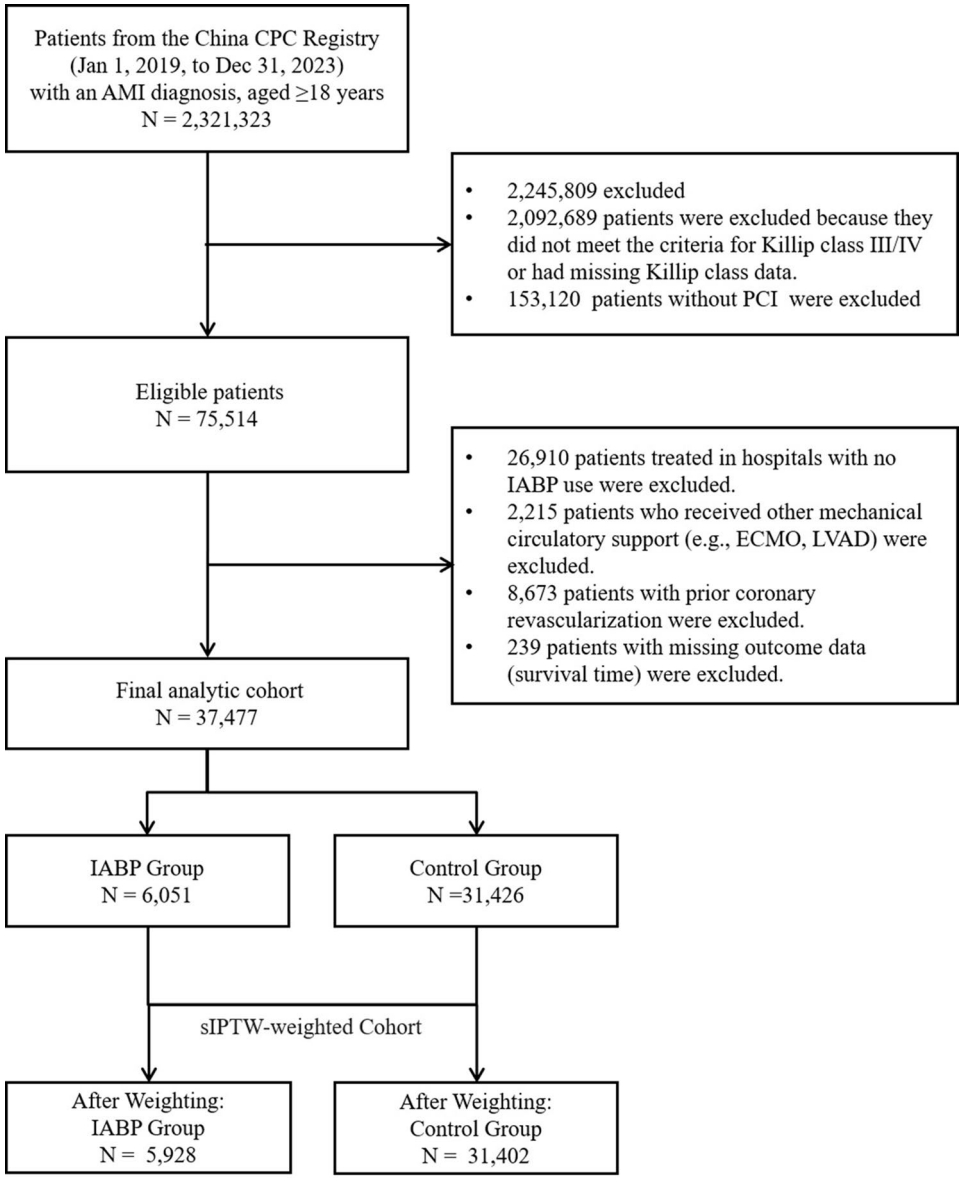


Fig. 1 Study cohort. This flow diagram illustrates the derivation of the analytic cohort from adult patients with acute myocardial infarction recorded in the China Chest Pain Center Registry from 2019 through 2023. Patients treated in hospitals with no recorded IABP use were excluded to restrict the analysis to hospitals in which the IABP strategy was observed in routine practice. Numbers above the weighting step represent unweighted patient counts; numbers below the weighting step represent weighted counts after sIPTW-BART. AMI indicates acute myocardial infarction; CPC, Chest Pain Center; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; PCI, percutaneous coronary intervention; sIPTW-BART, stabilized inverse probability of treatment weighting based on Bayesian additive regression trees–estimated propensity scores

Sensitivity analyses

Prespecified sensitivity analyses were consistent with the primary analysis (Table S4, Additional file 1). In the unmatched cohort, IABP use was associated with higher in-hospital all-cause mortality (HR, 2.18; 95% CI, 2.03–2.35). The direction of association remained unchanged across alternative confounding-control approaches, including 1:1 propensity score matching using propensity scores estimated by a generalized linear model, gradient boosting machine, or Bayesian additive regression trees; covariate balancing propensity score weighting; sIPTW using generalized linear model– or gradient boosting machine–estimated propensity scores; multivariable Cox regression; and complete-case analysis. Results were also consistent in analyses additionally adjusted for admission year and in year-specific analyses from 2019 to 2023. Positivity and weight-related sensitivity analyses, including truncation of stabilized weights at the overall 1st and 99th percentiles and restriction to the common-support region of the BART-estimated propensity score, yielded

Table 1 Baseline characteristics and in-hospital outcomes of the study cohort

Covariates	Unadjusted			sIPTW (BART-estimated PS)		
	Control group	IABP group	SMD	Control group	IABP group	SMD
No. of patients	31 426	6 051		31 402	5 928	
Demographics						
Age (years)			0.028			0.015
< 75 years	22 904 (72.9)	4 485 (74.1)		22 938 (73.0)	4 292 (72.4)	
≥ 75 years	8 522 (27.1)	1 566 (25.9)		8 464 (27.0)	1 636 (27.6)	
Sex			0.055			0.009
Male	22 738 (72.4)	4 524 (74.8)		22 829 (72.7)	4 286 (72.3)	
Female	8 688 (27.6)	1 527 (25.2)		8 573 (27.3)	1 643 (27.7)	
Clinical presentation						
Killip class			0.450			0.013
III	12 553 (39.9)	1 200 (19.8)		11 524 (36.7)	2 142 (36.1)	
IV	18 873 (60.1)	4 851 (80.2)		19 878 (63.3)	3 787 (63.9)	
Systolic blood pressure			0.252			0.001
< 90 mmHg	6 306 (20.1)	1 874 (31.0)		6 840 (21.8)	1 290 (21.8)	
≥ 90 mmHg	25 120 (79.9)	4 177 (69.0)		24 562 (78.2)	4 638 (78.2)	
Diastolic blood pressure			0.197			0.003
< 60 mmHg	7 681 (24.4)	2 018 (33.3)		8 113 (25.8)	1 538 (25.9)	
≥ 60 mmHg	23 745 (75.6)	4 033 (66.7)		23 289 (74.2)	4 390 (74.1)	
Consciousness on admission			0.192			0.007
Not awake	1 919 (6.1)	698 (11.5)		2 204 (7.0)	427 (7.2)	
Awake	29 507 (93.9)	5 353 (88.5)		29 198 (93.0)	5 501 (92.8)	
Chest pain on admission			0.071			0.008
Typical chest pain	25 702 (81.8)	5 060 (83.6)		25 759 (82.0)	4 879 (82.3)	
Atypical chest pain	5 079 (16.2)	921 (15.2)		5 037 (16.0)	936 (15.8)	
No chest pain	645 (2.1)	70 (1.2)		606 (1.9)	113 (1.9)	
Diagnosis / angiography						
AMI type			0.093			0.006
STEMI	27 866 (88.7)	5 177 (85.6)		27 689 (88.2)	5 238 (88.4)	
NSTEMI	3 560 (11.3)	874 (14.4)		3 713 (11.8)	690 (11.6)	
Laboratory indicators						
Troponin			0.101			0.004
Negative	4 869 (15.5)	726 (12.0)		4 692 (14.9)	893 (15.1)	
Positive	26 557 (84.5)	5 325 (88.0)		26 710 (85.1)	5 035 (84.9)	
Serum creatinine			0.215			0.013
44–115 μmol/L	23 703 (75.4)	3 975 (65.7)		23 187 (73.8)	4 370 (73.7)	
< 44 μmol/L	662 (2.1)	83 (1.4)		626 (2.0)	109 (1.8)	
116–176 μmol/L	4 901 (15.6)	1 404 (23.2)		5 284 (16.8)	1 008 (17.0)	
≥ 177 μmol/L	2 160 (6.9)	590 (9.7)		2 305 (7.3)	442 (7.5)	
Elevated BNP or NT-proBNP			0.205			0.014
Not elevated	16 416 (52.2)	2 544 (42.0)		15 875 (50.6)	2 955 (49.8)	
Elevated	15 010 (47.8)	3 507 (58.0)		15 527 (49.4)	2 974 (50.2)	
Hospital level						
Tertiary hospital	27 717 (88.2)	5 400 (89.2)	0.033	27 737 (88.3)	5 219 (88.0)	0.009
In-Hospital outcomes						
All-cause mortality	5 518 (17.6)	2 168 (35.8)		6 013 (19.1)	1 663 (28.1)	
Cardiovascular mortality	5 419 (17.2)	2 131 (35.2)		5 904 (18.8)	1 628 (27.5)	

Data are presented as n (%). Descriptive summaries were calculated separately within each of the 40 RF-MICE completed datasets and averaged across imputations. Weighted counts and percentages were calculated using sIPTW-BART weights within each imputed dataset and then averaged across the 40 datasets. BNP elevation was defined as BNP ≥ 300 pg/mL. NT-proBNP elevation was defined using age-specific thresholds: ≥450 pg/mL for patients aged < 50 years, ≥ 900 pg/mL for those aged 50–75 years, and ≥ 1800 pg/mL for those aged > 75 years. Troponin positivity was defined based on the final qualitative assessment; when unavailable, quantitative troponin levels > 0.03 ng/mL were used to derive the qualitative result. Standardized mean differences (SMDs) were calculated within each imputed dataset and averaged across imputations to assess covariate balance, with values < 0.10 indicating adequate balance. For model-based analyses reported in the manuscript, robust sandwich standard errors were clustered at the hospital level. BART, Bayesian additive regression trees; IABP, intra-aortic balloon pump; PS, propensity score; sIPTW, stabilized inverse probability of treatment weighting; SMD, standardized mean difference

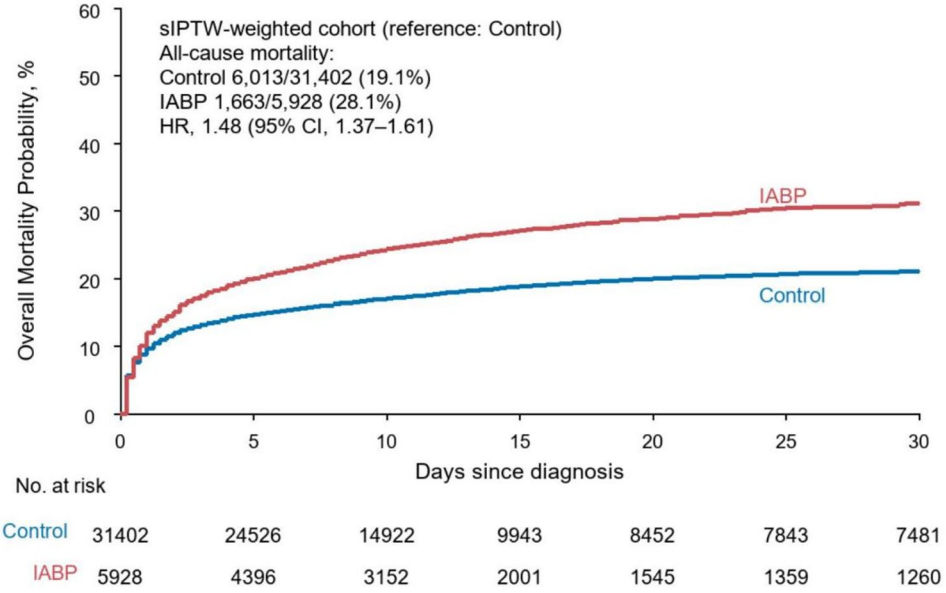


Fig. 2 Weighted cumulative risk of in-hospital all-cause mortality by treatment group. The curve shows the cumulative incidence of in-hospital all-cause mortality among patients with acute myocardial infarction and Killip class III or IV presentation. Weighted cumulative incidence curves were generated within each of the 40 RF-MICE completed datasets using sIPTW-BART weights and then averaged across imputations for display. Hazard ratios and 95% confidence intervals were estimated using weighted Cox proportional hazards models with hospital-clustered robust sandwich standard errors, fitted separately within each imputed dataset and pooled using Rubin's rules, with the control group as the reference. Numbers at risk are shown below the panel. Proportional hazards diagnostics and treatment-by-time interaction sensitivity analyses are reported in Table S5 (Additional file 1)

Table 2 In-hospital complications by treatment group in the sIPTW-BART–weighted cohort

Outcome	Control (*N* = 31 402)	IABP (*N* = 5928)	OR (95% CI) ref: Control	*P* value
Intraprocedural complications				
Hypotension	27 485 (87.5)	4 850 (81.8)	0.64 (0.58–0.71)	< 0.001
Severe bradyarrhythmia	1 020 (3.2)	246 (4.1)	1.29 (1.06–1.57)	0.011
Thromboembolism	123 (0.4)	20 (0.3)	0.85 (0.42–1.73)	0.663
Slow-flow / no-reflow	1 487 (4.7)	462 (7.8)	1.70 (1.44–2.01)	< 0.001
Coronary artery dissection	100 (0.3)	31 (0.5)	1.66 (0.87–3.19)	0.127
Non-target vessel occlusion	23 (0.1)	10 (0.2)	2.32 (0.95–5.66)	0.065
Coronary perforation	11 (0.0)	7 (0.1)	3.14 (1.25–7.90)	0.015
In-hospital complications				
Mechanical complications	2 778 (8.8)	729 (12.3)	1.45 (1.29–1.61)	< 0.001
Infection	22 488 (71.6)	3 804 (64.2)	0.71 (0.64–0.79)	< 0.001
Recurrent myocardial infarction	114 (0.4)	27 (0.4)	1.23 (0.77–1.97)	0.382
Thrombosis	260 (0.8)	48 (0.8)	0.98 (0.65–1.49)	0.928
Ischemic stroke	217 (0.7)	50 (0.8)	1.22 (0.83–1.79)	0.312
Transient ischemic attack	18 (0.1)	1 (0.0)	0.38 (0.09–1.64)	0.197
Bleeding	645 (2.1)	195 (3.3)	1.62 (1.33–1.97)	< 0.001
Malignant arrhythmia	2 457 (7.8)	705 (11.9)	1.59 (1.40–1.81)	< 0.001

Data are presented as weighted n (%). Weighted counts and percentages were calculated using sIPTW-BART weights within each of the 40 RF-MICE completed datasets and averaged across imputations. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using weighted logistic regression models with hospital-clustered robust sandwich standard errors, fitted separately within each imputed dataset and pooled using Rubin's rules, with the control group as the reference. Intraprocedural complications refer to events recorded during the PCI procedure, whereas in-hospital complications refer to events recorded after the procedure during the index hospitalization. Outcomes were based on validated registry-derived complication definitions. CI, confidence interval; IABP, intra-aortic balloon pump; OR, odds ratio; PCI, percutaneous coronary intervention; sIPTW-BART, stabilized inverse probability of treatment weighting based on Bayesian additive regression trees

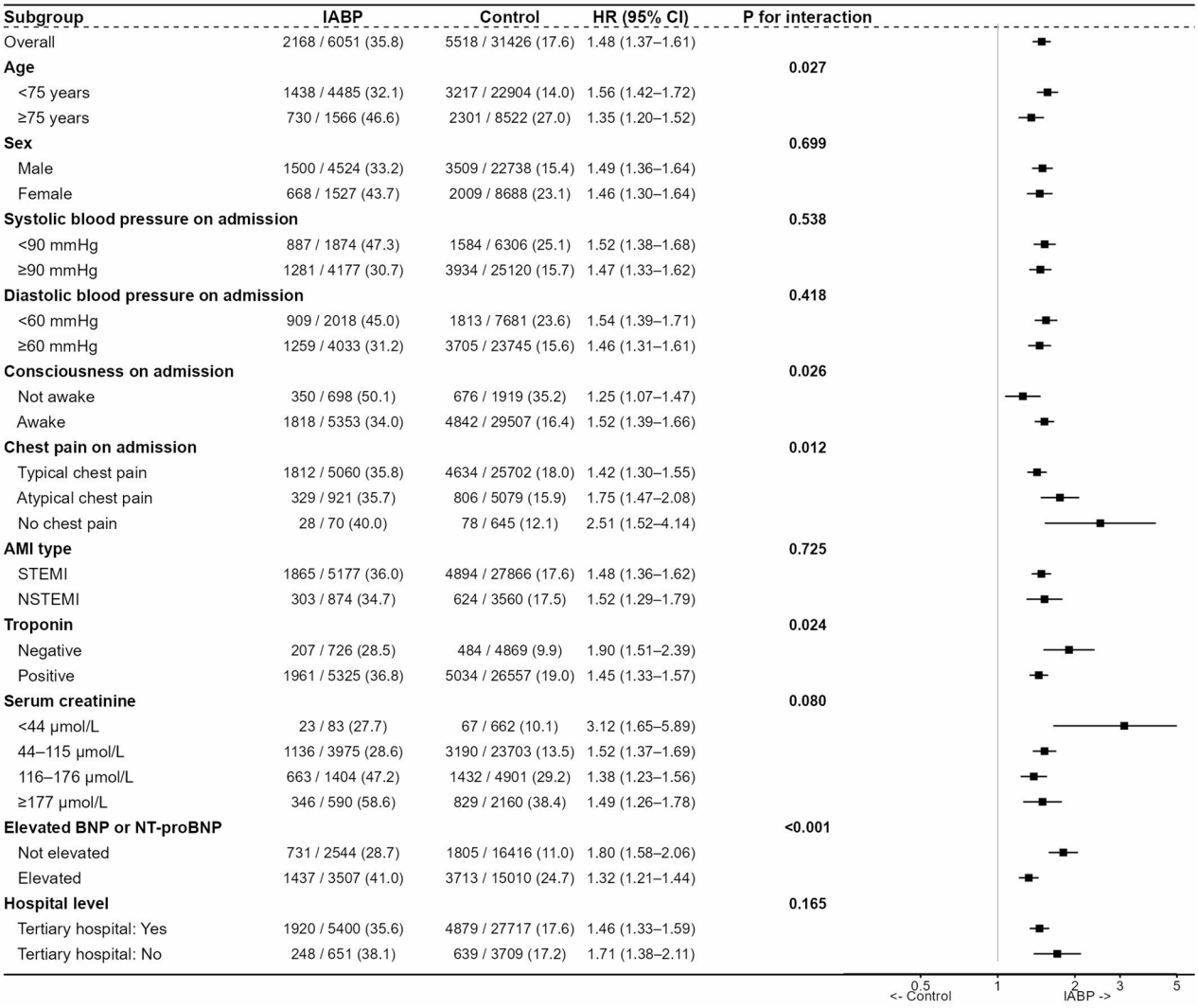


Fig. 3 Subgroup analyses of in-hospital all-cause mortality by treatment group. Hazard ratios and 95% confidence intervals for in-hospital all-cause mortality associated with intra-aortic balloon pump use versus control were estimated using sIPTW-BART–weighted Cox proportional hazards models fitted separately within each of the 40 RF-MICE completed datasets and pooled using Rubin's rules. Robust sandwich standard errors were clustered at the hospital level. Subgroup analyses were performed according to age, sex, systolic and diastolic blood pressure on admission, consciousness status, chest pain presentation, type of myocardial infarction, troponin status, creatinine level, B-type natriuretic peptide or N-terminal pro–B-type natriuretic peptide elevation, and hospital level. P values for interaction were calculated to assess association modification across subgroups. Subgroup analyses were exploratory

similar findings. Scaled Schoenfeld residual tests suggested evidence of non-proportional hazards for IABP use; in treatment-by-log(time + 1) interaction models, the direction of association remained consistent with the primary analysis (Table S5, Additional file 1). The E-value was 2.32 for the point estimate and 2.08 for the lower confidence limit, indicating the minimum strength of unmeasured confounding required to explain away the primary association.

Discussion

Principal findings

In this nationwide registry-based cohort study of adults undergoing PCI for AMI with Killip class III or IV presentation, IABP use during hospitalization was associated with higher in-hospital all-cause mortality and cardiovascular death compared with no recorded mechanical circulatory support. The direction and magnitude of this association were generally consistent across prespecified alternative confounding-control methods, admission-year adjusted and year-specific analyses, positivity and weight-related sensitivity analyses, and proportional hazards sensitivity analyses. Patients receiving IABP during hospitalization also had higher recorded rates of bleeding, malignant arrhythmia, and mechanical complications. These findings provide contemporary real-world evidence from a large national registry

Table 3 Killip class-stratified BART propensity-score analysis

Killip class	Analysis	Outcome	*N*	HR (95% CI)	*P* value
Killip III	Before truncation	All-cause mortality	13,753	1.68 (1.34–2.11)	< 0.001
	Before truncation	Cardiovascular death	13,753	1.65 (1.31–2.07)	< 0.001
	After 99th-percentile truncation	All-cause mortality	13,753	1.81 (1.48–2.20)	< 0.001
	After 99th-percentile truncation	Cardiovascular death	13,753	1.77 (1.46–2.16)	< 0.001
Killip IV	Before truncation	All-cause mortality	23,724	1.29 (1.18–1.40)	< 0.001
	Before truncation	Cardiovascular death	23,724	1.29 (1.18–1.40)	< 0.001
	After 99th-percentile truncation	All-cause mortality	23,724	1.31 (1.21–1.42)	< 0.001
	After 99th-percentile truncation	Cardiovascular death	23,724	1.31 (1.21–1.43)	< 0.001

Note: Values are hazard ratios (HRs) with 95% confidence intervals (CIs), with the control group as the reference. BART propensity scores were re-estimated separately within Killip class III and Killip class IV in each of the 40 RF-MICE completed datasets. Stratum-specific stabilized inverse probability of treatment weights were used in the analyses before truncation. In the weight-truncation analyses, weights were truncated at the corresponding 99th percentile within each Killip stratum and completed dataset. Weighted Cox proportional hazards models used hospital-clustered robust sandwich standard errors, and log-HRs and standard errors were pooled using Rubin's rules. The maximum absolute standardized mean differences before and after weight truncation were 0.204 and 0.114, respectively, in Killip class III, and 0.077 and 0.064, respectively, in Killip class IV. Because limited propensity-score overlap and modest residual imbalance remained in Killip class III, the Killip class III estimates should be interpreted cautiously

regarding outcomes associated with IABP use during hospitalization in this high-risk population.

Relation to prior studies and guidelines

Prior evidence on IABP use in infarct-related cardiogenic shock has been mixed. IABP-SHOCK II, the pivotal randomized trial informing contemporary guideline recommendations, was powered to detect a 12-percentage-point absolute difference in 30-day survival and did not show superiority of IABP over standard care; longer-term follow-up similarly showed no reduction in all-cause mortality [7–9]. Although these data provide strong evidence against a large mortality benefit from routine IABP use, the trial had limited statistical power to detect smaller treatment effects or heterogeneous effects across broader clinical phenotypes. In contrast, some observational studies reported lower mortality among selected patients receiving IABP, particularly in earlier reperfusion eras or selected cardiogenic shock cohorts [29–32].

Despite publication of IABP-SHOCK II in 2012 and subsequent guideline downgrading of routine IABP use, IABP continued to be used in routine practice. Current guidelines have moved away from routine IABP use in AMI complicated by cardiogenic shock, including the 2023 ESC acute coronary syndromes guideline and the 2025 ACC/AHA/ACEP/NAEMSP/SCAI acute coronary syndromes guideline, the latter giving routine IABP use in this setting a Class III (No Benefit) recommendation [14, 15]. In the present registry, IABP use during hospitalization was still recorded in 6051 of 37 477 eligible patients (16.1%) during 2019–2023, supporting the relevance of contemporary real-world evaluation.

Clinical interpretation of the observed association

Several clinical considerations may help explain the observed association between IABP use and higher in-hospital mortality. IABP provides hemodynamic support primarily through diastolic augmentation and afterload reduction, but the magnitude of this support is modest compared with contemporary advanced mechanical circulatory support strategies [4, 6]. In patients with severe shock, evolving multiorgan dysfunction, or profound metabolic compromise, this degree of support may be insufficient to restore systemic perfusion or alter the course of critical illness. In this cohort, lower recorded intraprocedural hypotension among patients receiving IABP was not accompanied by lower in-hospital mortality, suggesting that transient hemodynamic stabilization may not translate into survival benefit during the index hospitalization.

Killip class heterogeneity and subgroup analyses

Killip classes III and IV represent clinically distinct presentations. Killip class III reflects acute pulmonary edema, whereas Killip class IV reflects cardiogenic shock with hypotension and peripheral hypoperfusion. In the present cohort, IABP use was recorded in 1200 of 13,753 patients with Killip class III (8.7%) and 4851 of 23,724 patients with Killip class IV (20.4%), consistent with preferential use among patients with more severe hemodynamic compromise. In Killip class-specific analyses with BART propensity scores re-estimated within each stratum, the direction of association was consistent in both strata. Although the association was numerically stronger in Killip class III, this should not be interpreted as evidence that IABP is more harmful in the less severe stratum. The lower frequency of IABP use and less satisfactory propensity-score overlap and covariate balance in Killip class III suggest that the observed difference may reflect selective IABP use among patients with greater unmeasured clinical instability and residual confounding, rather than true effect modification.

Robustness of findings and potential bias

The association between IABP use and higher in-hospital mortality was generally consistent across multiple analytic approaches, including alternative propensity-score methods, multivariable Cox regression, complete-case analysis, models adjusted for admission year, year-specific analyses, weight truncation, and common-support restriction. The E-value was 2.32 for the observed HR and 2.08 for the lower confidence limit, indicating that an unmeasured confounder would need to be associated with both IABP use and in-hospital mortality by risk ratios of at least 2.08, conditional on the measured covariates, to explain away the lower confidence limit of the primary association. In addition, because IABP-treated patients had to survive until device insertion, any immortal-time bias introduced by this exposure definition may have attenuated, rather than exaggerated, the observed association. However, the exact timing of IABP insertion was unavailable, precluding formal landmark or time-dependent exposure analyses. Collectively, these findings support the robustness of the observed association, although residual confounding cannot be fully excluded in this observational registry.

Limitations

This study has several limitations. First, residual confounding by indication cannot be excluded because the registry did not uniformly capture important markers of shock severity, including lactate, acid-base status, vasoactive support, detailed cardiac arrest characteristics, and invasive hemodynamics. We used prespecified covariates, multiple imputation, propensity-score weighting, hospital-clustered robust standard errors, and multiple sensitivity analyses to mitigate measured confounding; however, unmeasured severity may still have influenced treatment selection and outcomes. Second, the registry did not reliably capture the exact timing of IABP insertion, including whether the device was inserted before PCI, during PCI, or after PCI. Therefore, the exposure should be interpreted as IABP use during hospitalization rather than a timed early-initiation strategy. Because patients classified as receiving IABP had to survive until device insertion, any immortal time introduced by this exposure definition would be expected to attenuate, rather than exaggerate, the observed association with higher in-hospital mortality. The registry also did not reliably capture the timing of registry-recorded complications, including mechanical complications, relative to IABP insertion. Because post-MI mechanical complications may themselves prompt IABP use as bridge therapy, the observed association may reflect reverse causation and confounding by indication and should not be interpreted as device-attributable harm. These registry-reported events may also have been subject to misclassification. In addition, in-hospital complications were analyzed as binary outcomes without accounting for the competing risk of death. Because in-hospital mortality was substantially higher in the IABP group, non-fatal events arising later during admission may have been systematically less likely to be observed in that group, and the corresponding odds ratios should be interpreted with this in mind.

Third, the cohort was defined by Killip class III or IV presentation, which may not fully capture contemporary shock phenotypes. We addressed this heterogeneity by performing Killip class-stratified subgroup analyses with stratum-specific propensity-score re-estimation; the direction of association was consistent across strata, although balance was less complete in Killip class III. Finally, hospitals with no recorded IABP use during the study period were excluded entirely and did not contribute patients to the control group. This restriction improved treatment comparability within hospitals where IABP was used, but may limit generalizability to centers without IABP use. The study also did not compare IABP with microaxial flow pumps, venoarterial extracorporeal membrane oxygenation, or other advanced mechanical circulatory support strategies; therefore, findings should not be extrapolated to those devices [16–18].

Conclusions

Among adults undergoing PCI for AMI with Killip class III or IV presentation, IABP use during hospitalization was associated with higher in-hospital all-cause mortality and cardiovascular death. These findings support caution regarding routine IABP use and highlight the need for prospective studies with detailed treatment timing and shock phenotyping.

Abbreviations

AMI	Acute myocardial infarction
AMI-CS	Acute myocardial infarction complicated by cardiogenic shock
BART	Bayesian additive regression trees
BNP	B-type natriuretic peptide
CBPS	Covariate balancing propensity score
CI	Confidence interval
DAG	Directed acyclic graph
ECMO	Extracorporeal membrane oxygenation
GBM	Gradient boosting machine
GLM	Generalized linear model
HR	Hazard ratio
IABP	Intra-aortic balloon pump
LVAD	Left ventricular assist device
MCS	Mechanical circulatory support
NSTEMI	Non-ST-segment elevation myocardial infarction
NT-proBNP	N-terminal pro–B-type natriuretic peptide
OR	Odds ratio
PCI	Percutaneous coronary intervention
PS	Propensity score
RF-MICE	Random forest–based multiple imputation by chained equations
sIPTW	Stabilized inverse probability of treatment weighting
sIPTW-BART	Stabilized inverse probability of treatment weighting based on Bayesian additive regression trees

SMD	Standardized mean difference
STEMI	ST-segment elevation myocardial infarction
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions
LY, LS and JG conceived and designed the study. HL, ZL, YW and SH curated the data and performed the formal analysis, with HL responsible for the statistical software and validation. LY, HL, ZL, YW and SH drafted the manuscript. MW and TZ contributed to the methodology, resources and validation. LHH and LS provided methodological guidance and supervision. JG acquired funding and provided overall supervision, project administration and resources. HL and LY directly accessed and verified the underlying data. LY, HL, ZL, YW and SH contributed equally to this work. All authors critically revised the manuscript for important intellectual content, had full access to all the data in the study, and read and approved the final manuscript.

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Data availability
The datasets generated and/or analysed during the current study are not publicly available owing to data governance restrictions of the China Chest Pain Center registry but are available from the corresponding author on reasonable request and with permission of the registry data custodian.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Zhongshan Hospital, Fudan University (approval number B2024-045) and was conducted in accordance with the Declaration of Helsinki. Because the analysis used anonymized data from the China Chest Pain Center registry, the Ethics Committee waived the requirement for individual informed consent.

Consent for publication
Not applicable. This study does not contain data from any individual person in a form that allows identification.

Authors' information
Not applicable.

Competing interests
The authors declare no competing interests.

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