

Reported mitral annular calcification grade and in-hospital mortality: a retrospective linked echocardiographic cohort study

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Abstract

Background

The short-term prognostic meaning of routinely reported mitral annular calcification (MAC) grade during hospitalization remains uncertain, especially when unreported MAC cannot be equated with imaging-confirmed absence.

Methods

This retrospective linked echocardiographic cohort study analyzed MIMIC-IV-ECHO linked to MIMIC-IV hospital and ICU data. Admissions with inpatient transthoracic echocardiography and structured MAC severity were included. The primary analysis compared moderate and severe reported MAC with mild MAC. Logistic regression used subject-level cluster-robust standard errors and adjusted for demographics, admission factors, prior comorbidities, index diagnoses, ICU stay, ventilation, vasopressor exposure, first-day SOFA, and procedure markers.

Results

The cohort included 83436 admissions from 59586 subjects, with 5669 in-hospital deaths. Among admissions with reported MAC, mortality was 7.0% with mild MAC, 8.7% with moderate MAC, and 10.7% with severe MAC. The reported-MAC-only analysis included 27964 admissions and 2115 deaths. In the clinical and acute-support adjusted model, moderate MAC (odds ratio [OR] 1.28, 95% confidence interval [CI] 1.13–1.45; $p < 0.001$) and severe MAC (OR 1.49, 95% CI 1.20–1.85; $p < 0.001$) were associated with higher mortality than mild MAC. In an echocardiographic complete-case sensitivity model, the moderate-MAC association persisted (OR 1.19, 95% CI 1.02–1.39), whereas the severe-MAC estimate was less precise (OR 1.29, 95% CI 0.97–1.71).

Conclusions

Routinely reported moderate and severe MAC grades were associated with higher in-hospital mortality than mild MAC. Reported MAC grade should be interpreted as a marker of short-term inpatient risk context rather than causal evidence or confirmed absence-versus-presence stratification.

Trial registration

Not applicable.

Background

Mitral annular calcification (MAC) is a chronic degenerative process of the mitral annulus that is frequently encountered in older and multimorbid cardiovascular populations [1]. Previous echocardiographic studies have linked MAC with endothelial dysfunction, carotid intima-media thickness, altered left atrial volume, and impaired left atrial mechanics [2, 3]. These observations support the view that MAC is more than an incidental imaging descriptor.

Contemporary echocardiographic cohorts have clarified the prevalence and natural history of MAC-related valve dysfunction, but the short-term prognostic meaning of routinely reported MAC grade during hospitalization remains less certain [4]. A central reporting problem is that an unreported MAC field cannot be assumed to represent imaging-confirmed absence of MAC.

The present study evaluated whether explicitly reported MAC grade on routine inpatient transthoracic echocardiography (TTE) was associated with in-hospital mortality among hospitalized adults. The primary analysis compared moderate and severe MAC with mild MAC among admissions with reported MAC. Full-cohort analyses that included no reported/unreported MAC were treated as sensitivity analyses.

Methods

Study design, reporting framework, data source, and cohort construction

This retrospective linked echocardiographic cohort study used MIMIC-IV hospital and ICU data linked to MIMIC-IV-ECHO [5, 6]. Reporting followed STROBE and RECORD guidance for observational studies using routinely collected health data [10, 11]. Structured echocardiographic metadata were processed in Google BigQuery and linked to deidentified hospital admissions through subject and admission identifiers.

Hospital admissions were eligible if a structured inpatient TTE record was available and a structured MAC severity entry was present. Time zero for the hospitalization-level analysis was hospital admission. MAC grade was ascertained from the earliest eligible inpatient TTE during that admission, and the outcome window was the same hospitalization through discharge. Because TTE necessarily occurred after admission in some patients, admission-to-TTE time was included in adjusted models and the results were interpreted as hospitalization-level associations rather than admission-time prediction.

If more than one eligible TTE was present during an admission, the earliest TTE was retained as the index study. The locked analytic cohort included 83436 admissions from 59586 subjects; all admissions matched to the acute-illness add-on extraction.

Exposure, outcome, and covariates

The exposure was structured TTE-reported MAC severity. Explicitly reported MAC was categorized as mild, moderate, or severe. The primary reported-MAC-only analysis used mild MAC as the reference category. The no reported/unreported category was retained for descriptive and sensitivity analyses but was not interpreted as imaging-confirmed absence of MAC.

The primary outcome was in-hospital mortality, defined by the MIMIC-IV hospital discharge mortality flag and attributed at the admission level. Demographic and admission-level covariates included age, sex, admission type, admission location, insurance, race, and time from hospital admission to TTE.

Prior comorbidities were derived from ICD diagnosis codes recorded before the index admission. Index-admission diagnosis indicators included heart failure, myocardial infarction, atrial fibrillation, sepsis or shock, acute kidney injury, acute respiratory failure, and cardiac arrest. Acute-illness and support markers included ICU admission, invasive ventilation, noninvasive ventilation, vasopressor exposure, first-day SOFA score, and ICD procedure-code count during the index hospitalization. These variables were included to account for measured hospitalization-level illness burden and life-support intensity, not to create a baseline prediction model. Because some may also lie on pathways linking structural cardiac disease, acute decompensation, and mortality, the adjusted estimates were interpreted as severity-adjusted associations rather than total causal effects. Raw first-day SOFA was available only for ICU stays; the model covariate used zero-fill for non-ICU admissions to avoid excluding all non-ICU admissions from acute-support models.

Echocardiographic covariates included moderate/severe aortic stenosis, moderate/severe mitral regurgitation, moderate/severe mitral stenosis, left ventricular ejection fraction, left atrial enlargement, right ventricular dysfunction, moderate/severe tricuspid regurgitation, and tricuspid regurgitation velocity when available. Valve and pulmonary-pressure terminology followed contemporary guideline frameworks [7–9].

Statistical analysis

Continuous variables are summarized as mean (standard deviation) or median [interquartile range], and categorical variables as number (percentage). Multivariable logistic regression estimated odds ratios (ORs) and 95% confidence intervals (CIs) for in-hospital mortality. Subject-level cluster-robust standard errors accounted for repeated admissions from the same subject.

The primary reported-MAC-only model compared moderate and severe MAC with mild MAC and adjusted for demographics, admission characteristics, prior comorbidities, index-admission diagnoses, and acute-support markers. An echocardiographic complete-case model added valve and cardiac remodeling covariates and was treated as a sensitivity analysis because echocardiographic covariate missingness reduced the analytic sample. Full-cohort models using no reported/unreported MAC as a category were considered descriptive or sensitivity analyses because the category did not represent confirmed MAC absence.

Data extraction was performed with Google BigQuery. Statistical analyses were performed with Python using pandas, NumPy, and statsmodels. Reproducibility records, source hashes, and package-generation notes are provided in Additional file 1. Outcome language was matched to the observational design, and causal claims were avoided [12].

Results

Cohort and reported MAC distribution

The cohort included 83436 admissions from 59586 unique subjects, with 5669 in-hospital deaths (6.8%). No duplicate hospital admissions were present in the merged analytic dataset.

The distribution by MAC reporting category was as follows: no reported/unreported MAC severity, 55351 admissions and 3533 deaths (6.4%); mild MAC, 19530 admissions and 1366 deaths (7.0%); moderate MAC, 7136 admissions and 618 deaths (8.7%); and severe MAC, 1419 admissions and 152 deaths (10.7%). Among admissions with reported MAC, crude mortality increased from mild to severe MAC (Fig. 1).

Acute-illness burden was broadly similar but slightly higher in the severe-MAC group for several support markers. ICU admission occurred in 41.6% of mild, 42.2% of moderate, and 44.7% of severe MAC admissions; vasopressor exposure occurred in 17.5%, 17.9%, and 19.9%, respectively (Table 1).

Table 1
Mortality and acute-illness markers by MAC reporting category

Characteristic	No reported/unreported MAC	Mild MAC	Moderate MAC	Severe MAC
Admissions, n	55351	19530	7136	1419
In-hospital deaths, n (%)	3533 (6.4)	1366 (7.0)	618 (8.7)	152 (10.7)
ICU admission, n (%)	23226 (42.0)	8114 (41.5)	3013 (42.2)	634 (44.7)
Invasive ventilation, n (%)	11344 (20.5)	3748 (19.2)	1316 (18.4)	274 (19.3)
Noninvasive ventilation, n (%)	1084 (2.0)	453 (2.3)	185 (2.6)	40 (2.8)
Vasopressor exposure, n (%)	9697 (17.5)	3411 (17.5)	1279 (17.9)	282 (19.9)
ICD-10 procedure marker, n (%)	20478 (37.0)	6955 (35.6)	2489 (34.9)	563 (39.7)
ICD-9 procedure marker, n (%)	16977 (30.7)	6054 (31.0)	2246 (31.5)	405 (28.5)
Values are n (%). ICU indicates intensive care unit; MAC, mitral annular calcification.				

Main reported-MAC-only models

In the primary reported-MAC-only model adjusted for demographics, admission characteristics, prior comorbidities, index-admission diagnoses, and acute-support markers, moderate MAC was associated with higher in-hospital mortality compared with mild MAC (OR 1.28, 95% CI 1.13–1.45; $p < 0.001$). Severe MAC was also associated with higher mortality compared with mild MAC (OR 1.49, 95% CI 1.20–1.85; $p < 0.001$) (Table 2 and Fig. 2).

Table 2
Reported-MAC-only logistic regression models for in-hospital mortality

Analysis	Comparison	N	Deaths	OR	95% CI	p value
Demographic and admission adjusted	Moderate vs mild MAC	27964	2115	1.23	1.11–1.36	p < 0.001
Demographic and admission adjusted	Severe vs mild MAC	27964	2115	1.58	1.32–1.90	p < 0.001
Clinical and acute-support adjusted	Moderate vs mild MAC	27964	2115	1.28	1.13–1.45	p < 0.001
Clinical and acute-support adjusted	Severe vs mild MAC	27964	2115	1.49	1.20–1.85	p < 0.001
Echocardiographic complete-case sensitivity	Moderate vs mild MAC	18084	1378	1.19	1.02–1.39	p = .029
Echocardiographic complete-case sensitivity	Severe vs mild MAC	18084	1378	1.29	0.97–1.71	p = .080
Reference category is mild MAC. Cluster-robust standard errors were used at subject level.						

After additional adjustment for echocardiographic valve and remodeling variables in the complete-case sensitivity model, the moderate-MAC association persisted (OR 1.19, 95% CI 1.02–1.39; p = 0.029). The severe-MAC estimate remained directionally similar but had wider precision and did not meet conventional statistical significance (OR 1.29, 95% CI 0.97–1.71; p = 0.080).

Full-cohort sensitivity analyses

Full-cohort analyses that included the no reported/unreported category were interpreted cautiously. Compared with mild MAC, moderate MAC (OR 1.32, 95% CI 1.17–1.49; p < 0.001) and severe MAC (OR 1.57, 95% CI 1.27–1.95; p < 0.001) were associated with higher mortality after adjustment for demographics, admission characteristics, prior comorbidities, index diagnoses, and acute-support markers. The no reported/unreported category was not independently associated after acute-support adjustment (OR 1.07, 95% CI 0.98–1.16; p = 0.127) (Table 3).

Table 3
Full-cohort sensitivity models including no reported/unreported MAC

Analysis	Comparison	N	Deaths	OR	95% CI	p value
Full cohort, clinical and acute-support adjusted	Moderate vs mild MAC	82662	5563	1.32	1.17–1.49	p < 0.001
Full cohort, clinical and acute-support adjusted	Severe vs mild MAC	82662	5563	1.57	1.27–1.95	p < 0.001
Full cohort, clinical and acute-support adjusted	No reported/unreported vs mild MAC	82662	5563	1.07	0.98–1.16	p = .127
Full cohort, echocardiographic complete-case sensitivity	Moderate vs mild MAC	47719	3228	1.21	1.04–1.41	p = .014
Full cohort, echocardiographic complete-case sensitivity	Severe vs mild MAC	47719	3228	1.33	1.01–1.75	p = .044
Full cohort, echocardiographic complete-case sensitivity	No reported/unreported vs mild MAC	47719	3228	1.03	0.92–1.15	p = .598
Reference category is mild MAC. The no reported/unreported category was not interpreted as confirmed absence of MAC.						

In the full-cohort echocardiographic complete-case sensitivity model, moderate MAC (OR 1.21, 95% CI 1.04–1.41; p = 0.014) and severe MAC (OR 1.33, 95% CI 1.01–1.75; p = 0.044) remained associated with mortality compared with mild MAC, whereas the no reported/unreported category did not (OR 1.03, 95% CI 0.92–1.15; p = 0.598).

Discussion

Among hospitalized adults undergoing routine inpatient TTE, explicitly reported moderate and severe MAC grades were associated with higher in-hospital mortality than mild MAC after adjustment for demographics, prior comorbidity burden, index-admission diagnoses, ICU-level care, ventilation, vasopressor exposure, first-day SOFA, and procedure markers. The severe-MAC estimate remained directionally similar after additional echocardiographic adjustment, but the wider confidence interval in the complete-case model indicates that the most defensible primary message is a reported-grade association rather than a fully adjudicated anatomical severity effect.

The association is biologically plausible because higher-grade MAC may mark a combined structural and systemic vulnerability phenotype. MAC can coexist with mitral valve dysfunction, left atrial remodeling, pulmonary pressure surrogates, right-sided dysfunction, renal disease, and multimorbidity. In this inpatient cohort, the association persisted after acute-support adjustment, suggesting that reported

MAC grade was not simply a marker of ICU admission, ventilation, vasopressor exposure, or first-day SOFA. The attenuation after echocardiographic complete-case adjustment is clinically informative because valve dysfunction and cardiac remodeling may be confounders, mediators, or both.

The findings are directionally consistent with the Framingham Heart Study, in which MAC identified higher long-term cardiovascular morbidity and mortality in a community cohort [13]. The present study differs in population and endpoint: it evaluated acutely hospitalized adults selected for clinically indicated inpatient TTE and assessed in-hospital mortality rather than long-term cardiovascular events.

Contemporary echocardiographic literature also supports a cautious structural-risk interpretation. Kato and colleagues reported that MAC was common among adults undergoing echocardiography and that mortality was higher when MAC and mitral valve dysfunction coexisted [4]. Mendez-Hirata and colleagues similarly described MAC-related mitral valve dysfunction as prognostically relevant in a large contemporary cohort [14]. The present analysis adds a narrower inpatient finding: routine report-grade MAC remained associated with short-term mortality even after explicit adjustment for acute illness and life-support markers.

Clinical outcome studies of MAC-related mitral valve disease have generally focused on significant mitral regurgitation or stenosis, intervention candidacy, or longer-term survival. Fukui and colleagues reported poor survival among patients with MAC-related mitral valve disease, with better survival among those who underwent mitral intervention [15]. The present study was not designed to evaluate procedural candidacy or treatment effect. Its clinical use is more limited: moderate or severe MAC in an inpatient TTE report should prompt deliberate review of coexisting valve disease, cardiopulmonary remodeling, renal disease, acute illness severity, and discharge-risk context.

Procedure-oriented MAC literature provides an important contrast. CT-based MAC scores were developed for anatomic risk stratification in transcatheter mitral procedures, whereas studies in aortic stenosis and TAVR populations show that isolated MAC may behave differently when mitral valve function is preserved [16–18]. The present findings should therefore not be generalized to CT-based procedural risk, intervention benefit, or isolated anatomical MAC. Reported MAC grade in this study functioned as a routine echocardiographic marker embedded in a broader inpatient illness context.

Several limitations should guide interpretation. This was an observational retrospective analysis; residual and unmeasured confounding cannot be excluded. MAC severity was based on structured TTE report fields and was not independently adjudicated from images or quantified by CT. The no reported/unreported MAC category did not represent imaging-confirmed absence of MAC, so full-cohort analyses including that category were sensitivity analyses rather than an absence-versus-presence comparison. The outcome was restricted to in-hospital mortality, and post-discharge outcomes were unavailable. The cohort reflects hospitalized patients who underwent TTE and may not generalize to patients without an echocardiographic indication. Echocardiographic covariate missingness reduced the complete-case sensitivity sample.

Conclusions

Among hospitalized adults undergoing routine inpatient TTE, reported moderate and severe MAC grades were associated with higher in-hospital mortality than mild MAC after adjustment for clinical characteristics, prior comorbidities, index-admission diagnoses, and acute-support markers. Reported MAC grade should be interpreted as a marker of short-term inpatient risk context. The absence of a confirmed no-MAC reference group and image adjudication limits causal, anatomical, and absence-versus-presence interpretations.

Abbreviations

AS
aortic stenosis
CI
confidence interval
CT
computed tomography
ICD
International Classification of Diseases
ICU
intensive care unit
LA
left atrial
LVEF
left ventricular ejection fraction
MAC
mitral annular calcification
MR
mitral regurgitation
MS
mitral stenosis
OR
odds ratio
RV
right ventricular
SOFA
Sequential Organ Failure Assessment
TAVR
transcatheter aortic valve replacement
TR
tricuspid regurgitation

TTE
transthoracic echocardiography.

Declarations

Ethics approval and consent to participate

This non-interventional retrospective study used deidentified data from MIMIC-IV and MIMIC-IV-ECHO. Original data collection was approved by the institutional review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center, and informed consent was waived because protected health information had been removed. The study was approved as non-interventional research by the Bezmialem Foundation University Department of Cardiology Academic Board (meeting no. 5, decision no. 1, dated 31 March 2026).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Use of AI-assisted technology

AI-assisted technology was used only to improve readability and language consistency. It was not used to generate data, perform statistical analyses, or make scientific decisions. The authors reviewed and take full responsibility for all submitted content.

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Author Contribution

CA conceptualized the study, contributed to clinical interpretation, and drafted the manuscript. NKA contributed to data curation, literature review, and manuscript revision. BI designed the study, performed data extraction and statistical analysis, prepared the figures and tables, supervised the work, and finalized the manuscript. All authors reviewed and approved the final manuscript.

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Not applicable.

Data Availability

The data used in this study were derived from MIMIC-IV and MIMIC-IV-ECHO, which are available through PhysioNet to credentialed users under the applicable data use agreement. The analytic derivatives generated for this study are available from the corresponding author upon reasonable request, subject to PhysioNet data-use requirements.

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Figures

Crude mortality among admissions with reported MAC

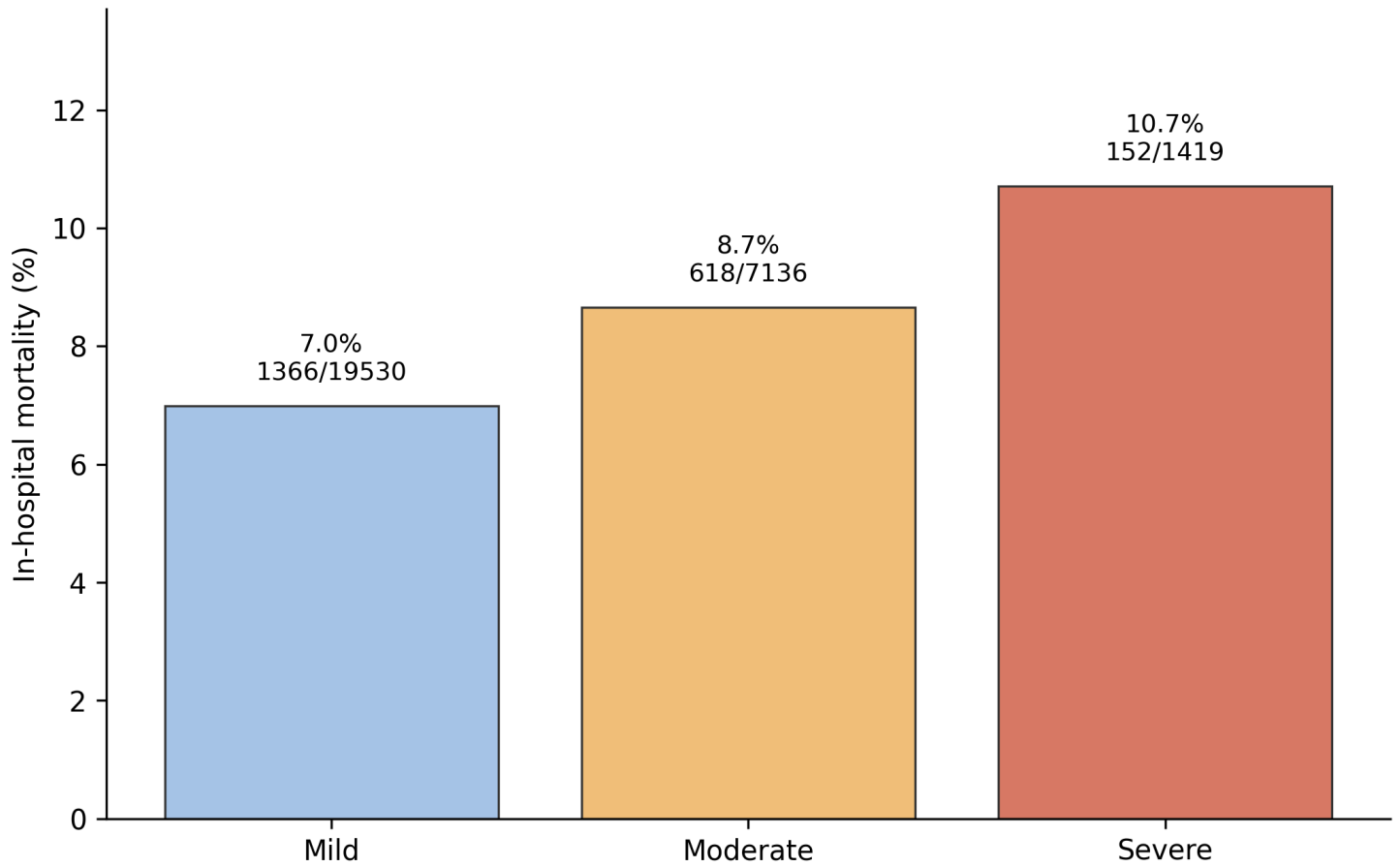


Figure 1

Crude in-hospital mortality among admissions with reported MAC. Bars show mortality percentages with deaths/admissions annotated above each bar.

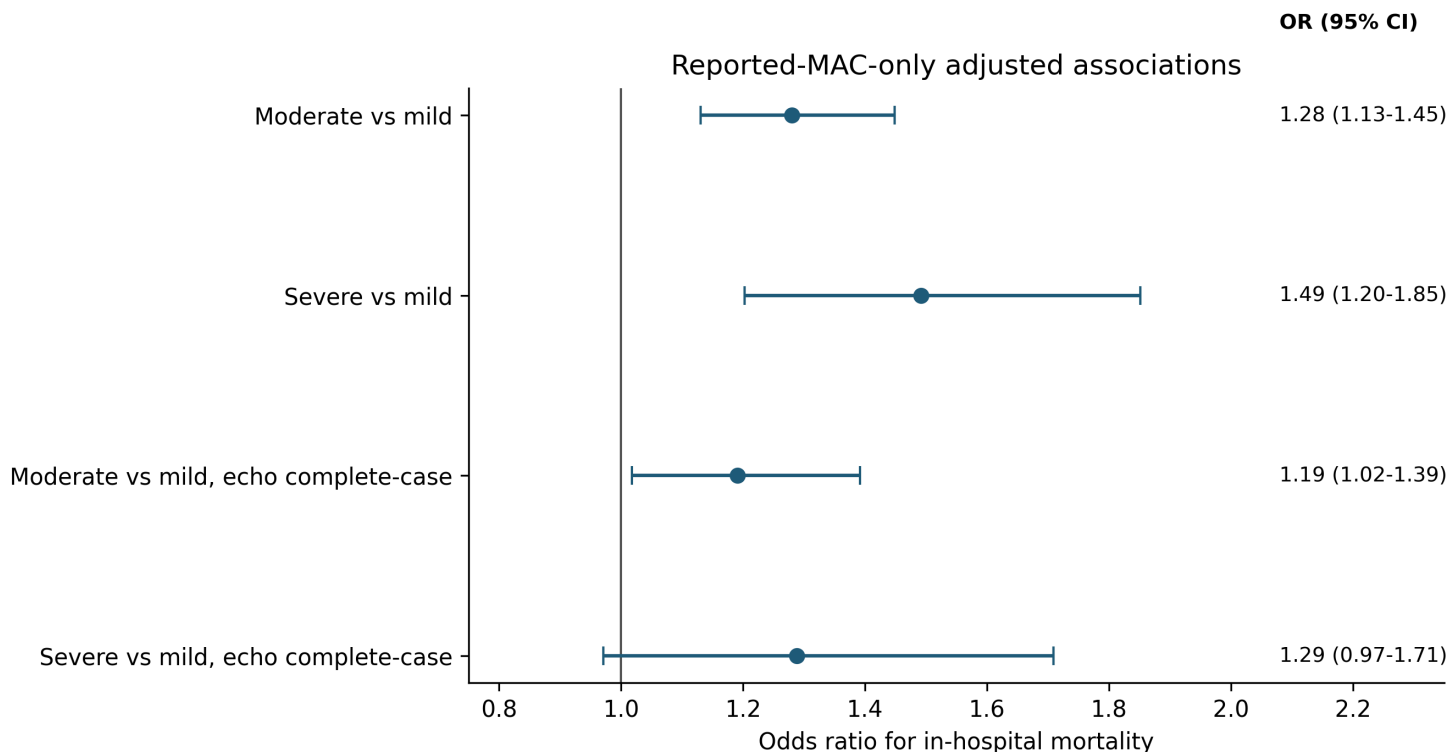


Figure 2

Reported-MAC-only adjusted associations with in-hospital mortality. Odds ratios and 95% confidence intervals are shown for the clinical and acute-support adjusted model and the echocardiographic complete-case sensitivity model.

Supplementary Files

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- [Supplementarytables.docx](#)