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Echocardiographic left ventricular filling pressure (E/e') and incident acute kidney injury in critically ill adults with preserved ejection fraction

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Abstract

Acute kidney injury (AKI) is common in critical illness, and elevated left ventricular filling pressure may contribute through venous congestion. We examined whether the echocardiographic ratio E/e', a non-invasive estimate of filling pressure, is independently associated with incident AKI in critically ill adults with preserved ejection fraction. Using the MIMIC-IV critical care database linked to the MIMIC-IV-ECHO module (single US centre, 2008–2022), we conducted a retrospective cohort study of 3,067 adults with a first ICU admission, preserved ejection fraction (≥ 50%) and an interpretable mean E/e' on peri-admission echocardiography, excluding those with end-stage renal disease, significant mitral disease or prevalent AKI. The outcome was incident AKI (KDIGO serum-creatinine criteria) within 7 days of the index echocardiogram, with early death as a competing event. AKI occurred in 588 patients (19.2%), and crude 7-day incidence rose across E/e' categories (16.1%, 18.7%, 26.7%). In a Fine–Gray model adjusted for acute-severity and comorbidity covariates, each 1-unit higher E/e' was associated with incident AKI (subdistribution hazard ratio 1.030, 95% CI 1.013–1.047), with concordant estimates across logistic, modified-Poisson and dichotomous (> 14 versus ≤ 14: odds ratio 1.47, 1.15–1.87) analyses. The association was independent of acute illness severity. Prospective, multicentre confirmation is warranted.

Introduction

Acute kidney injury (AKI) is among the most common and consequential complications of critical illness, affecting close to one in five hospitalized patients and more than half of those admitted to the intensive care unit (ICU) [1,2]. Even when transient or mild, AKI is independently associated with prolonged hospitalization, progression to chronic kidney disease, and increased short- and long-term mortality [1,2]. Because few targeted therapies exist once AKI is established, identifying those at elevated risk—ideally from information already at the bedside—remains a clinical priority.

Although AKI in critically ill patients has traditionally been attributed to arterial hypoperfusion and tubular injury, venous congestion and elevated cardiac filling pressures are increasingly recognized contributors to renal dysfunction [3]. Across acute decompensated heart failure and a broad spectrum of cardiovascular disease, elevated central venous pressure—rather than reduced cardiac output—correlates most strongly with worsening renal function and mortality, supporting a congestive mechanism of kidney injury [4,5]. Consistent with this paradigm, bedside indices of systemic venous congestion predict subsequent AKI, including after cardiac surgery [6].

Left ventricular (LV) diastolic dysfunction, the functional hallmark of elevated LV filling pressure, is a plausible upstream driver of such congestion. The ratio of early transmitral inflow velocity to early diastolic mitral annular velocity (E/e') is the recommended noninvasive echocardiographic estimate of LV filling pressure [7] and correlates with invasively measured pressures [8]. Diastolic dysfunction is highly prevalent among the critically ill, and in patients with sepsis it has been independently associated with mortality in both single-center cohorts and a meta-analysis [9,10]. Because E/e' is reported on most routine

transthoracic studies, it is available without the additional procedures required for invasive monitoring or dedicated congestion ultrasound.

Direct evidence linking E/e' to AKI, by contrast, remains limited and largely confined to specific settings [11,12]. The available studies have generally relied on baseline or remote echocardiography rather than a measurement made at the time of acute illness, have not required the filling-pressure estimate to precede incident AKI, and have not accounted for the competing risk of early death; nor have they focused on critically ill patients with preserved ejection fraction. It therefore remains unresolved whether a filling-pressure estimate obtained at the time of ICU admission predicts subsequent AKI, independently of acute illness severity, in this population.

The recent release of the MIMIC-IV-ECHO module, which links structured echocardiographic measurements to the MIMIC-IV critical care database [13,14], makes it possible to address this question at scale and with explicit attention to temporality. In a cohort of critically ill adults with preserved ejection fraction, we examined the association between peri-admission E/e' and incident AKI within 7 days using a competing-risk framework that accounts for early death, adjusting for a panel of acute-severity and chronic-comorbidity covariates to determine whether any association is independent of concurrent illness severity.

Methods

Study design and data source

We conducted a retrospective cohort study using the Medical Information Mart for Intensive Care IV (MIMIC-IV) clinical database (version 3.1) and the linked MIMIC-IV-ECHO module (Echocardiogram Matched Subset, version 1.0) [13,14]. MIMIC-IV comprises de-identified records of patients cared for at the Beth Israel Deaconess Medical Center (Boston, Massachusetts, USA). The echocardiography module, derived from MIMIC-IV version 2.2, provides structured measurements from 206,488 echocardiographic studies in 91,372 unique patients; these structured measurements derive from studies performed between 2008 and 2022. Because the de-identified patient identifiers and the per-patient temporal offsets are preserved across MIMIC-IV releases, echocardiographic records were linked to clinical data by these identifiers, with successful linkage for all echocardiography patients. Data were extracted using Google BigQuery (Google LLC, Mountain View, CA, USA). The databases are publicly available to credentialed users and contain only de-identified records; ethics approval and the consent waiver are detailed in the Ethics declaration below. The study is reported in accordance with the STROBE [15] and RECORD [16] statements.

Study population

We included adults (≥ 18 years) admitted to an intensive care unit (ICU) who underwent transthoracic echocardiography within a peri-admission window extending from 24 hours before to 48 hours after ICU admission. For patients with more than one qualifying study, the study closest to ICU admission was retained, and the time of that echocardiogram served as the index time (time zero) for all subsequent analyses. To isolate the contribution of diastolic filling, the cohort was restricted to patients with preserved left ventricular systolic function (left ventricular ejection fraction [LVEF] ≥ 50%) [17] and an interpretable mean E/e'. Only the first ICU admission per patient was analysed. We excluded patients with end-stage renal disease or chronic dialysis dependence; those with moderate or greater mitral regurgitation or mild or greater mitral stenosis, conditions that invalidate the estimation of left ventricular filling pressure from E/e'; patients who already met acute kidney injury (AKI) criteria at the index echocardiogram (prevalent AKI); and patients without a pre-index baseline serum creatinine value. Derivation of the analytic cohort is summarised in Fig. 1.

Exposure: echocardiographic estimate of left ventricular filling pressure

The exposure was the mean E/e' ratio—the ratio of early transmitral inflow velocity (E) to the average of the septal and lateral early diastolic mitral annular velocities (e')—a non-invasive index of left ventricular filling pressure, obtained from the structured echocardiographic measurements. E/e' was analysed both as a continuous variable and according to guideline-informed categories [7]: ≤ 8 (normal), > 8 to 14 (intermediate), and > 14 (elevated filling pressure).

Outcomes

The primary outcome was incident AKI within 7 days after the index echocardiogram, defined by the serum-creatinine criteria of the Kidney Disease: Improving Global Outcomes (KDIGO) guideline [18]—an increase in serum creatinine of ≥ 0.3 mg/dL (26.5 μmol/L) or to ≥ 1.5 times the baseline value. The baseline creatinine was the lowest value measured during the 7 days preceding the index echocardiogram. AKI was ascertained from serum creatinine alone; the urine-output criterion was not applied because hourly urine output is incompletely recorded in the database. The 0.3 mg/dL absolute-increase criterion, conventionally evaluated over 48 hours, was assessed across the 7-day post-index window—a deliberate, transparent deviation from the strict KDIGO timeframe—with a sensitivity analysis restricting AKI to events within 48 hours reported in the Results. To preserve temporality and minimise reverse causation, AKI was required to develop after the index echocardiogram; patients meeting AKI criteria at or before the index time were excluded as prevalent cases, and the time of AKI onset was taken as the time of the first qualifying creatinine value. In-hospital mortality was reported descriptively and was additionally related to E/e' in an exploratory logistic model; death within 7 days of the index echocardiogram served as the competing event in the primary analysis.

Covariates

Covariates were specified a priori and comprised age, sex, the Sequential Organ Failure Assessment (SOFA) score [19] during the first 24 hours of ICU admission, the Charlson comorbidity index, chronic kidney disease, diabetes mellitus, hypertension, baseline serum creatinine, vasopressor or inotrope administration during the first 24 hours, invasive mechanical ventilation during the first 24 hours, and sepsis defined by the Sepsis-3 criteria [20]. Detailed variable definitions, including the diagnostic codes and item identifiers used for extraction, are provided in the Supplementary Methods (Supplementary Table S4). The covariates summarising acute illness severity were defined over the first 24 hours after ICU admission, a window that for some patients preceded or only partially overlapped the index echocardiogram (performed a median of 16 hours after admission, range 24 hours before to 48 hours after); we retained these first-24-hour definitions because they capture early-stay severity, a constraint inherent to the data source.

Statistical analysis

Continuous variables are summarised as mean (standard deviation) or median (interquartile range) and categorical variables as counts (percentages). Baseline characteristics were compared across E/e' categories using one-way analysis of variance or the Kruskal–Wallis test for continuous variables and the chi-square test for categorical variables; between-group imbalance was additionally quantified using the standardized mean difference (SMD).

The primary analysis modelled the association between E/e' and incident AKI using a Fine–Gray subdistribution hazard model [21], with death within 7 days of the index echocardiogram treated as the competing event and patients without an event censored at day 7; the model was adjusted for all prespecified covariates, and the effect of E/e' was expressed per 1-unit increase. The cumulative incidence of AKI was estimated by E/e' category while accounting for the competing risk of death. Because the 7-day cumulative outcome was common, we performed sensitivity analyses using multivariable logistic regression (odds ratio) and a modified Poisson model with robust (sandwich) variance to estimate risk ratios [22], and we additionally modelled E/e' as a binary variable (> 14 versus ≤ 14). The shape of the dose–response relationship was examined with restricted cubic splines (four knots) [23], and departure from linearity was assessed by the Wald test. Effect modification by sepsis was evaluated using a multiplicative interaction term. The robustness of the primary association to unmeasured confounding was quantified using the E-value [24]. All tests were two-sided, with a significance threshold of 0.05. Analyses were performed in R (version 4.5.2; R Foundation for Statistical Computing, Vienna, Austria) using the cmprsk, rms, tableone, sandwich, lmtest, and EValue packages.

Ethics

This study was conducted in accordance with the principles of the Declaration of Helsinki. It is a secondary analysis of the MIMIC-IV (version 3.1) and MIMIC-IV-ECHO (version 1.0) databases, which are publicly available and contain only de-identified records. The establishment of these databases was approved by the Institutional Review Boards of the Massachusetts Institute of Technology (MIT; Cambridge, Massachusetts, USA) and the Beth Israel Deaconess Medical Center (BIDMC; Boston, Massachusetts, USA), with a waiver of informed consent because all records are de-identified. As a secondary analysis of a publicly available, fully de-identified database, this study did not require additional institutional review board approval, and the requirement for individual informed consent did not apply. The authors completed the required human-subjects research training (CITI "Data or Specimens Only Research") and accessed the data as credentialed users under a signed PhysioNet Credentialed Health Data Use Agreement.

Results

Cohort characteristics

A total of 3,067 critically ill adults with a first ICU admission, preserved left ventricular ejection fraction, and an interpretable mean E/e' were analysed. The index echocardiogram was performed a median of 16 hours after ICU admission (range, 24 hours before to 48 hours after). The mean E/e' was 10.5 (SD 4.6; median 9.4, interquartile range 7.4–12.3); 1,025 patients (33.4%) had a normal value (≤ 8), 1,522 (49.6%) an intermediate value (> 8–14), and 520 (17.0%) an elevated value (> 14). The mean LVEF was 60.1% (SD 6.8), and 1,359 patients (44.3%) met Sepsis-3 criteria. Across increasing E/e' categories, patients were progressively older and had a greater burden of cardiovascular and renal comorbidity, higher baseline serum creatinine, and a higher proportion of women (all $P < 0.001$), whereas indices of acute illness severity—the SOFA score, vasopressor or inotrope use, invasive mechanical ventilation, and sepsis—were similar across categories ($P \geq 0.12$; Table 1).

Table 1
Baseline characteristics of the study cohort, overall and by category of mean E/e'.

Characteristic	Overall (n = 3067)	Normal ≤ 8 (n = 1025)	Intermediate > 8–14 (n = 1522)	Elevated > 14 (n = 520)	P value	SMD
Demographics and illness severity						
Age, years	64.68 (16.83)	55.35 (16.31)	67.23 (15.04)	75.61 (13.26)	< 0.001	0.90
Female sex	1500 (48.9)	369 (36.0)	780 (51.2)	351 (67.5)	< 0.001	0.44
SOFA score, first 24 h	3.99 (3.18)	3.93 (3.29)	4.01 (3.16)	4.04 (2.99)	0.746	0.03
Sepsis (Sepsis-3)	1359 (44.3)	439 (42.8)	685 (45.0)	235 (45.2)	0.503	0.03
Vasopressor or inotrope use, first 24 h	779 (25.4)	257 (25.1)	390 (25.6)	132 (25.4)	0.952	0.01
Invasive mechanical ventilation, first 24 h	888 (29.0)	298 (29.1)	458 (30.1)	132 (25.4)	0.123	0.07
Comorbidities						
Charlson comorbidity index	4.74 (2.87)	3.56 (2.90)	5.04 (2.70)	6.18 (2.40)	< 0.001	0.65
Hypertension	1881 (61.3)	444 (43.3)	1006 (66.1)	431 (82.9)	< 0.001	0.59
Diabetes mellitus	860 (28.0)	172 (16.8)	474 (31.1)	214 (41.2)	< 0.001	0.37
Chronic kidney disease	494 (16.1)	76 (7.4)	260 (17.1)	158 (30.4)	< 0.001	0.41
Echocardiography and laboratory						

Data are presented as mean (standard deviation) for continuous variables and as number (percentage) for categorical variables. P values are derived from one-way analysis of variance or the Kruskal–Wallis test for continuous variables and from the chi-square test for categorical variables, comparing the three E/e' categories. SMD denotes the standardized mean difference across the three categories (mean of pairwise comparisons); values ≥ 0.10 indicate meaningful imbalance, and the SMD is not reported for mean E/e', the variable defining the strata. The first-24-hour window refers to the first 24 hours after ICU admission. Acute kidney injury and in-hospital mortality are shown by exposure category to display crude associations; adjusted analyses are reported in the main text. To convert serum creatinine from mg/dL to µmol/L, multiply by 88.4. Abbreviations: AKI, acute kidney injury; E/e', ratio of early transmitral inflow velocity to early diastolic mitral annular velocity; ICU, intensive care unit; SMD, standardized mean difference; SOFA, Sequential Organ Failure Assessment.

Characteristic	Overall (n = 3067)	Normal ≤ 8 (n = 1025)	Intermediate > 8–14 (n = 1522)	Elevated > 14 (n = 520)	P value	SMD
Demographics and illness severity						
Left ventricular ejection fraction, %	60.08 (6.77)	59.90 (6.68)	59.99 (6.71)	60.67 (7.12)	0.089	0.07
Mean E/e'	10.51 (4.55)	6.59 (1.04)	10.48 (1.59)	18.32 (4.64)	< 0.001	—
Baseline serum creatinine, mg/dL	1.13 (0.97)	1.04 (0.87)	1.12 (1.00)	1.33 (1.03)	< 0.001	0.19
Outcomes						
Incident AKI within 7 days	588 (19.2)	165 (16.1)	284 (18.7)	139 (26.7)	< 0.001	0.17
In-hospital mortality	286 (9.3)	81 (7.9)	147 (9.7)	58 (11.2)	0.095	0.07

Data are presented as mean (standard deviation) for continuous variables and as number (percentage) for categorical variables. P values are derived from one-way analysis of variance or the Kruskal–Wallis test for continuous variables and from the chi-square test for categorical variables, comparing the three E/e' categories. SMD denotes the standardized mean difference across the three categories (mean of pairwise comparisons); values ≥ 0.10 indicate meaningful imbalance, and the SMD is not reported for mean E/e', the variable defining the strata. The first-24-hour window refers to the first 24 hours after ICU admission. Acute kidney injury and in-hospital mortality are shown by exposure category to display crude associations; adjusted analyses are reported in the main text. To convert serum creatinine from mg/dL to μmol/L, multiply by 88.4. Abbreviations: AKI, acute kidney injury; E/e', ratio of early transmitral inflow velocity to early diastolic mitral annular velocity; ICU, intensive care unit; SMD, standardized mean difference; SOFA, Sequential Organ Failure Assessment.

Incidence of acute kidney injury

Incident AKI within 7 days of the index echocardiogram occurred in 588 patients (19.2%), and 286 (9.3%) died in hospital. Within 7 days of the index echocardiogram, 186 patients (6.1%) died, of whom 117 (3.8%) died without antecedent acute kidney injury and constituted the competing events in the primary analysis. The crude 7-day incidence of AKI increased monotonically across E/e' categories, from 16.1% (165/1,025) in the normal category to 18.7% (284/1,522) in the intermediate category and 26.7% (139/520) in the elevated category (P < 0.001; Table 1). The cumulative incidence of AKI accounting for the competing risk of death showed the same ordering (Fig. 2).

Association between E/e' and acute kidney injury

In the primary Fine–Gray model with death within 7 days as the competing event and adjustment for all prespecified covariates, each 1-unit increase in E/e' was associated with a higher subdistribution hazard of AKI (subdistribution hazard ratio [sHR] 1.030, 95% confidence interval [CI] 1.013–1.047; P < 0.001), corresponding to an sHR of 1.16 (95% CI 1.07–1.26) per 5-unit increase. The association was consistent

across alternative approaches to the 7-day cumulative outcome: the adjusted odds ratio was 1.038 (95% CI 1.015–1.060) per unit by logistic regression, and the adjusted risk ratio was 1.026 (95% CI 1.012–1.041) per unit by modified Poisson regression. Modelled dichotomously, an elevated E/e' (> 14) was associated with 47% higher adjusted odds of AKI relative to E/e' ≤ 14 (odds ratio 1.47, 95% CI 1.15–1.87; P = 0.002). All model estimates are summarised in Table 2. The close agreement between the competing-risk and non–competing-risk estimates indicates that the finding was not materially affected by the competing risk of death. In a quantitative bias analysis, an unmeasured confounder would need to be associated with both an elevated E/e' and AKI by a risk ratio of approximately 1.7, and by 1.35 for the lower confidence limit, over and above the measured covariates, to fully explain the observed association (E-value, computed for the dichotomous E/e' > 14 vs ≤ 14 contrast). Findings were unchanged when septal E/e' was substituted for mean E/e' (adjusted odds ratio 1.03 per unit, 95% CI 1.02–1.05; n = 3065, two patients lacking a septal e' measurement). Because E/e' is less reliable in atrial fibrillation, the association was reassessed with adjustment for atrial fibrillation and after restriction to the sinus-rhythm subgroup; it remained essentially unchanged in both analyses (Table S5). Restricting incident AKI to events occurring within 48 hours of the index echocardiogram (375 events, 12.2%) left the association with continuous E/e' essentially unchanged (adjusted odds ratio 1.03 per unit, 95% CI 1.00–1.06), although the dichotomized E/e' > 14 contrast was attenuated and no longer significant over this shorter window, consistent with the smaller number of events. In an exploratory analysis, E/e' was not associated with in-hospital mortality (adjusted odds ratio 1.01 per unit, 95% CI 0.98–1.04).

Table 2
Adjusted association between mean E/e' and incident 7-day acute kidney injury across analytic models.

Model and E/e' scaling	Effect measure	Adjusted estimate (95% CI)	P value
Fine–Gray model, per 1-unit (primary)	sHR	1.030 (1.013–1.047)	< 0.001
Fine–Gray model, per 5-unit	sHR	1.16 (1.07–1.26)	< 0.001
Logistic regression, per 1-unit	OR	1.038 (1.015–1.060)	< 0.001
Modified Poisson, per 1-unit	RR	1.026 (1.012–1.041)	< 0.001
Logistic regression, E/e' > 14 vs ≤ 14	OR	1.47 (1.15–1.87)	0.002

All models were adjusted for age, sex, SOFA score, Charlson comorbidity index, chronic kidney disease, diabetes mellitus, hypertension, baseline serum creatinine, first-24-hour vasopressor or inotrope use, first-24-hour invasive mechanical ventilation, and sepsis. The Fine–Gray model is the primary analysis and treats death within 7 days as a competing event; the per-5-unit estimate is derived from the per-1-unit subdistribution hazard. The logistic and modified Poisson models address the 7-day cumulative outcome. Full covariate-adjusted estimates are provided in Supplementary Tables S1 and S2. Abbreviations: CI, confidence interval; E/e', ratio of early transmitral inflow velocity to early diastolic mitral annular velocity; OR, odds ratio; RR, risk ratio; sHR, subdistribution hazard ratio; SOFA, Sequential Organ Failure Assessment.

Dose–response and effect modification

In restricted cubic spline analysis, the adjusted risk of AKI increased across the range of E/e', with no significant departure from linearity (P for nonlinearity = 0.31; Fig. 3 and Supplementary Table S3); estimates at the highest E/e' values were imprecise, reflecting the sparse data in that range. The association between E/e' and AKI did not differ significantly between patients with and without sepsis (P for interaction = 0.15). As expected, established determinants of AKI such as a higher SOFA score and chronic kidney disease were associated with the outcome in the same models; these secondary covariate estimates are susceptible to the table-2 fallacy and are not interpreted causally. After adjustment, the coefficient for age was inverse, consistent with its collinearity with the comorbidity measures and baseline renal function included in the same models. Full covariate-adjusted estimates are provided in Supplementary Tables S1 and S2.

Discussion

In a cohort of 3,067 critically ill adults with preserved left ventricular ejection fraction, a higher echocardiographic estimate of left ventricular filling pressure (E/e') was associated with a greater 7-day risk of incident AKI. The association was consistent in direction and magnitude across a competing-risk Fine–Gray model, logistic and modified Poisson regressions, and a dichotomous (> 14) specification, and the dose–response relationship showed no significant departure from linearity. Most telling is that E/e' rose in parallel with age, comorbidity, and baseline renal impairment yet was unrelated to concurrent indices of acute illness severity: the SOFA score, vasopressor or inotrope use, mechanical ventilation, and sepsis were balanced across E/e' categories. The E/e'–AKI association therefore captures a dimension of risk that is largely independent of the acute physiologic derangement usually emphasized in the ICU, and it persisted after adjustment for that derangement and for the competing risk of early death.

These findings are biologically coherent. E/e' is a validated noninvasive marker of elevated left ventricular filling pressure, which is transmitted backward to the pulmonary and systemic venous circulations; the resulting venous congestion raises renal venous and interstitial pressure, reduces the trans-renal perfusion gradient, and promotes a congestive form of kidney injury [3–5]. Consistent with this mechanism, elevated central venous pressure rather than reduced cardiac output is the hemodynamic variable most strongly associated with worsening renal function [4,5], and bedside measures of venous congestion predict AKI after cardiac surgery [6]. These mechanisms are echoed in the critical-care literature: an elevated central venous pressure or clinical venous congestion has been associated with subsequent AKI in critically ill patients [25,26], impaired intrarenal venous flow tracks the severity of cardiorenal dysfunction [27], and kidney function deteriorates in parallel with congestion across the heart-failure trajectory [28]. A chronically elevated filling pressure may additionally mark a diminished cardiorenal reserve that lowers the threshold for AKI when an acute insult is superimposed—an interpretation in keeping with the independence of the association from acute illness severity.

Our results extend a limited body of prior work linking diastolic function to adverse outcomes [9–12]. The present study advances that literature in three respects that bear directly on interpretation. First, it anchors the exposure to a peri-admission echocardiogram and enforces a strict temporal sequence—requiring AKI to arise after the index study and excluding prevalent cases—so that an acute, on-admission estimate of filling pressure precedes the outcome, whereas earlier studies relied on baseline or remote imaging. Second, it accounts for the competing risk of early death. Third, by restricting the cohort to preserved ejection fraction, it characterises the filling-pressure signal without the overlay of overt systolic dysfunction. The stability of the estimate across these design and modelling choices argues that the signal reflects a genuine association rather than reverse causation or an artifact of a particular analytic specification.

As an observational analysis, this study cannot establish causation, and residual or unmeasured confounding cannot be excluded. Volume status is the most important consideration: an elevated E/e' and systemic venous congestion are physiologically intertwined, so the association probably reflects, at least in part, the congestive pathway that links elevated filling pressure to kidney injury [3,29]. Because that pathway is the proposed mechanism rather than an extraneous confounder, this overlap supports rather than negates the value of E/e' as a risk marker, although it does mean E/e' should not be read as a purely intrinsic myocardial property. The E-value indicated that an unmeasured confounder would need to be associated with both E/e' and AKI by a risk ratio of about 1.7, beyond the measured covariates, to account fully for the association; while such confounding cannot be excluded, the finding is best interpreted as a robust and mechanistically plausible association rather than definitive proof of an independent causal effect. We deliberately did not adjust for fluid balance or diuretic exposure, which lie on the causal pathway [30], and several first-24-hour severity covariates may themselves be downstream of an elevated filling pressure; adjusting for these would, if anything, bias the association toward the null, so the reported estimates are likely conservative.

Measurement and cohort definition also warrant comment. E/e' estimates rather than directly measures filling pressure, and its reliability is reduced in atrial fibrillation, marked tachycardia and significant mitral disease [7,31]; accordingly, patients with at least moderate mitral regurgitation or any significant mitral stenosis were excluded, and the association was unchanged after accounting for atrial fibrillation and within the sinus-rhythm subgroup. AKI was ascertained from serum creatinine alone, which may under-ascertain or delay its detection [32], and the baseline creatinine was the lowest pre-index inpatient value, a surrogate for stable renal function [33]. Because ICU echocardiography is performed for clinical indications rather than at random, a cohort defined by an interpretable peri-admission study may not represent all critically ill patients; reassuringly, the association was independent of sepsis, the most common precipitant of AKI in this setting [34], a population that overlaps clinically with heart failure with preserved ejection fraction and its limited cardiorenal reserve [35]. Finally, the data derive from a single centre over 2008–2022, a period during which reporting and practice evolved, so external validation in independent, multicentre cohorts is needed.

These findings have potential clinical relevance. E/e' is already reported on most routine echocardiograms and is obtainable without any additional procedure, and it appears to carry information about short-term AKI risk that is largely independent of conventional severity scores. Because risk rose continuously with E/e', a higher value—operationally, one above the guideline threshold of 14—may help identify critically ill patients with preserved ejection fraction who merit closer monitoring of renal function and more deliberate fluid management, given the contribution of fluid accumulation to AKI [36,37]. Because AKI in this setting is associated with substantial short- and long-term morbidity, including progression to chronic kidney disease [38,39], even modest improvements in early risk identification could be clinically meaningful. These results are best regarded as hypothesis-generating: they support, but do not establish, a role for E/e' as a risk-stratification adjunct, ideally combined with emerging biomarkers of kidney stress [40], and they motivate prospective, multicenter studies that incorporate direct assessment of venous congestion [6] and urine-output–based AKI criteria.

In critically ill adults with preserved left ventricular ejection fraction, a higher echocardiographic estimate of left ventricular filling pressure was independently associated with incident acute kidney injury within 7 days, with adjusted risk increasing at higher values (no significant departure from linearity) and independently of acute illness severity. Because E/e' is routinely reported at the bedside, it may serve as a readily available marker of elevated AKI risk; whether it improves risk identification beyond established factors requires prospective evaluation. Prospective, multicenter studies that incorporate direct measures of congestion and urine-output criteria are warranted to confirm these findings and to define their clinical utility.

Declarations

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Author contributions

LW conceived and designed the study, supervised the project and the statistical analysis, contributed to the interpretation of the results, and critically revised the manuscript for important intellectual content. LS performed the data extraction, statistical analysis, and model development, and drafted the manuscript. YL contributed to the study design and methodology, interpreted the results, and critically revised the manuscript for important intellectual content. CX contributed to data curation, statistical analysis, and validation of the results. HT contributed to the interpretation of the results, to visualisation, and to critical revision of the manuscript. JS contributed to the interpretation of the findings and to project administration, and critically revised the manuscript for important intellectual content. As corresponding authors, LW and JS share responsibility for communication with the journal and for the

integrity of the work as a whole, with LW serving as the primary corresponding author and JS as the co-corresponding author. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

Data availability

The MIMIC-IV and MIMIC-IV-ECHO databases are available to credentialed users on PhysioNet (https://physionet.org). The SQL and R code used to derive the cohort and perform all analyses is openly available at Zenodo (https://doi.org/10.5281/zenodo.20576321).

Competing interests

The authors declare no competing interests.

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Figures

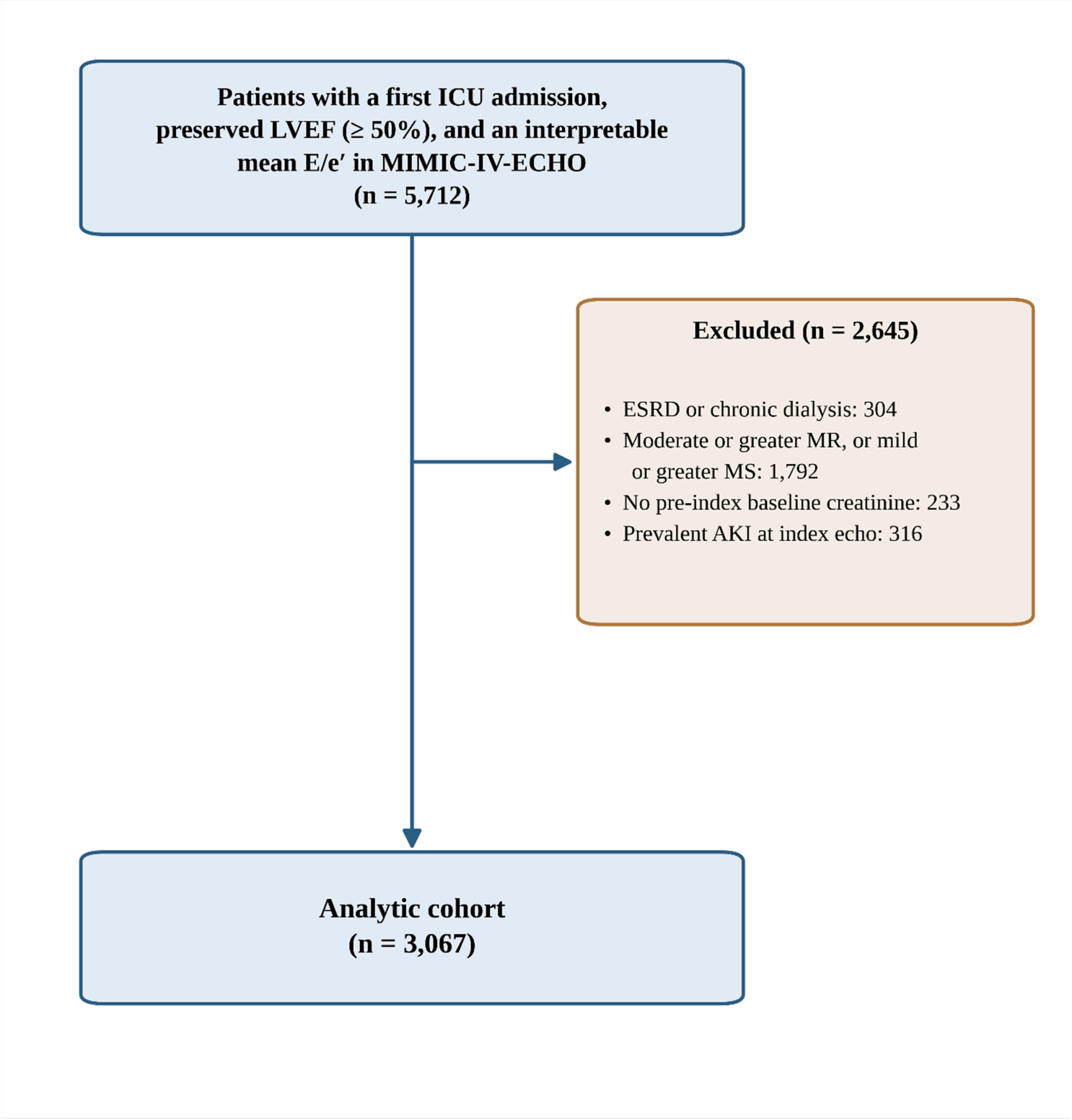


Figure 1

Derivation of the analytic cohort. Of 5,712 patients with a first ICU admission, preserved left ventricular ejection fraction (≥ 50%), and an interpretable mean E/e' in the MIMIC-IV-ECHO module, 304 were excluded for end-stage renal disease or chronic dialysis, 1,792 for moderate or greater mitral regurgitation or mild or greater mitral stenosis, 233 for absence of a pre-index baseline serum creatinine, and 316 for prevalent acute kidney injury at the index echocardiogram, leaving 3,067 patients in the analytic cohort. Abbreviations: AKI, acute kidney injury; E/e', ratio of early transmitral inflow velocity to early diastolic mitral annular velocity; ESRD, end-stage renal disease; ICU, intensive care unit; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MS, mitral stenosis.

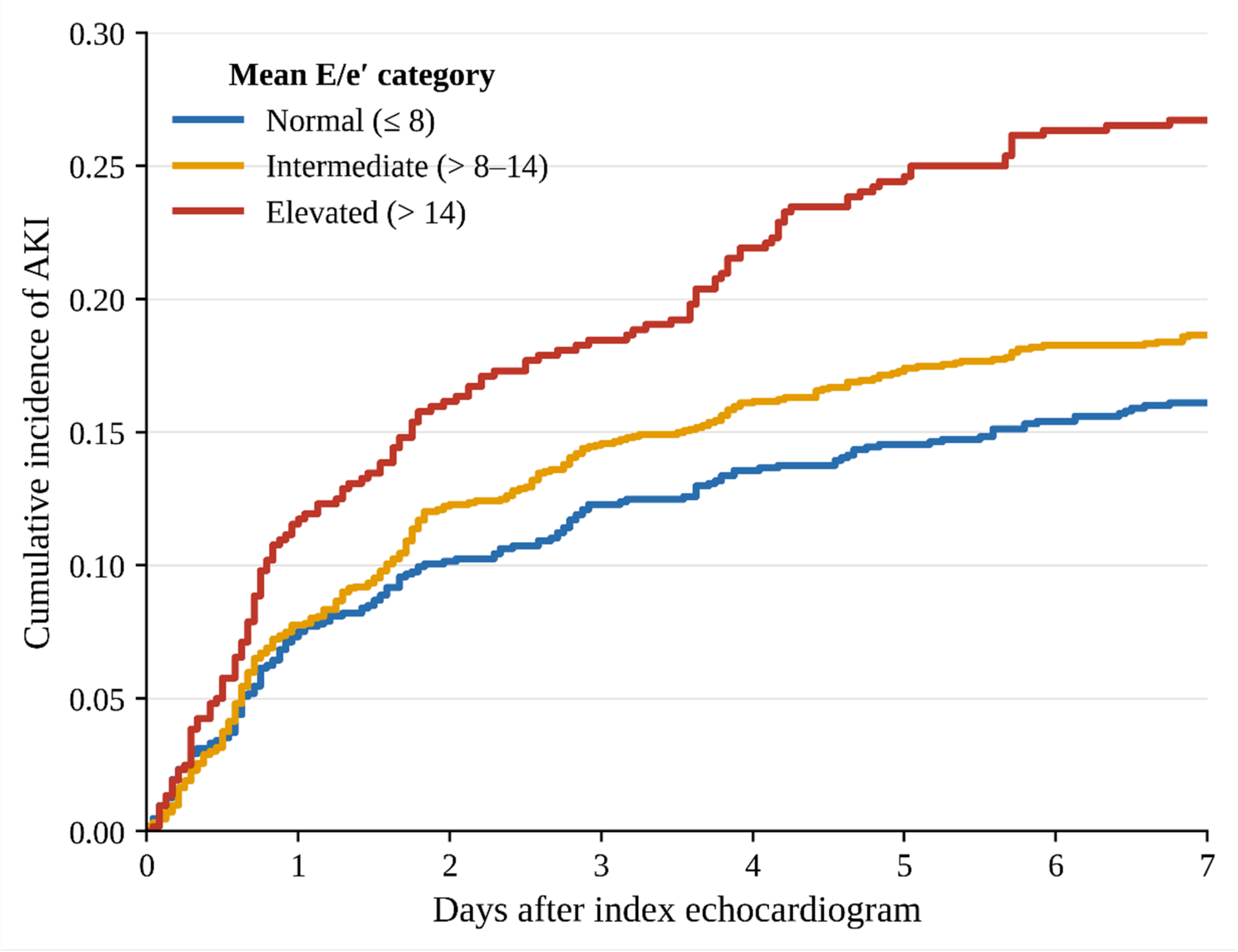


Figure 2

Cumulative incidence of acute kidney injury by category of mean E/e'. Cumulative incidence functions of incident acute kidney injury within 7 days after the index echocardiogram for the normal (≤ 8), intermediate (> 8–14), and elevated (> 14) categories of mean E/e', estimated under a competing-risk framework in which death within 7 days is the competing event. Abbreviations: AKI, acute kidney injury; E/e', ratio of early transmitral inflow velocity to early diastolic mitral annular velocity.

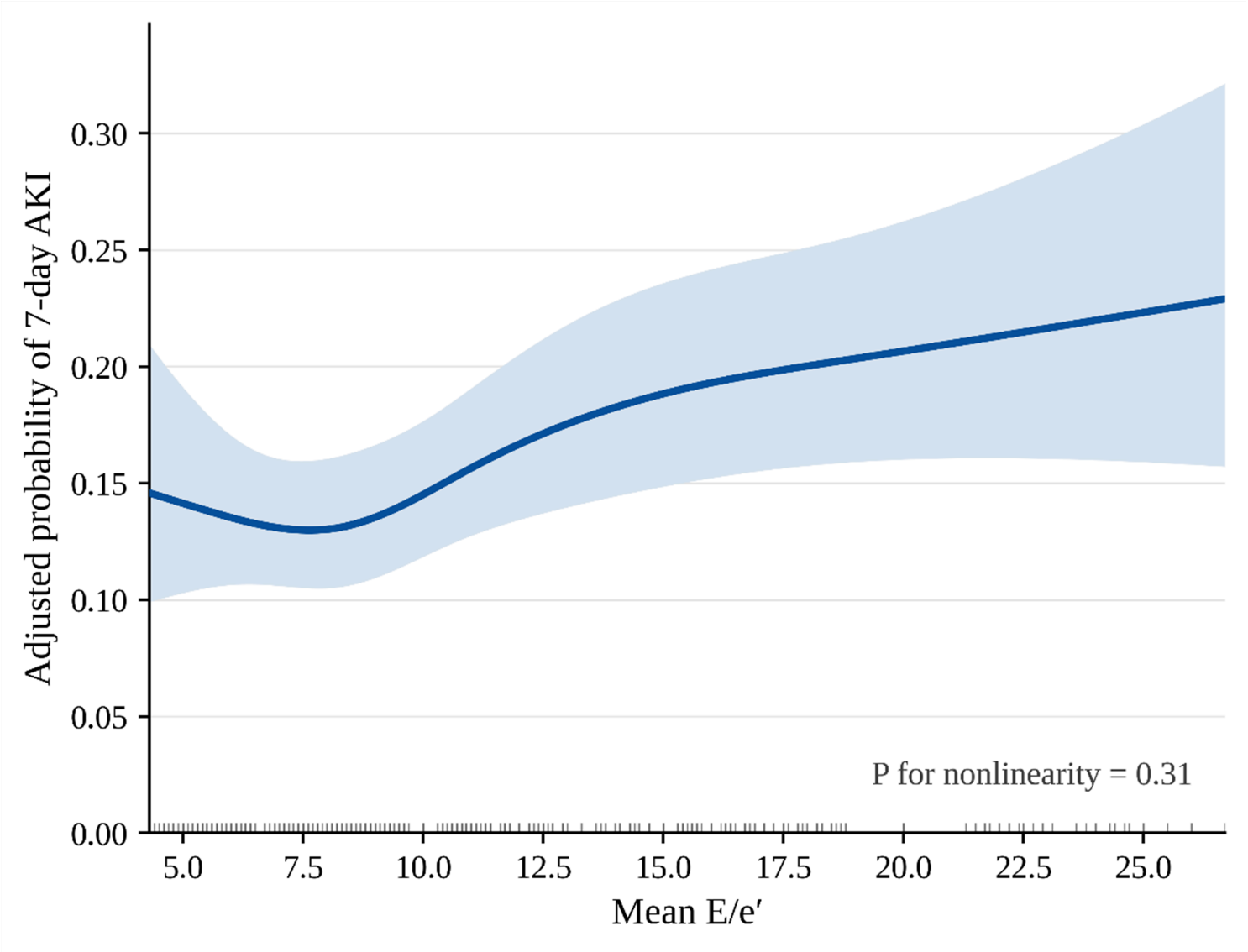


Figure 3

Adjusted dose–response relationship between mean E/e' and acute kidney injury. Adjusted probability of incident 7-day acute kidney injury as a function of mean E/e', modelled with restricted cubic splines (four knots) in a multivariable model adjusted for the prespecified covariates. The solid line denotes the point estimate and the shaded area the 95% confidence interval; the test for nonlinearity was not significant (P = 0.31). Abbreviations: AKI, acute kidney injury; CI, confidence interval; E/e', ratio of early transmitral inflow velocity to early diastolic mitral annular velocity.

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