



Changes in comorbidities, diagnoses, therapies and outcomes in a contemporary cardiac intensive care unit population

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Background Prior studies have demonstrated that the cardiac intensive care unit (CICU) patient population has evolved over time. We sought to describe the temporal changes in comorbidities, illness severity, diagnoses, procedures and adjusted mortality within our CICU practice in recent years.

Methods We retrospectively reviewed unique CICU admissions at the Mayo Clinic from January 2007 to April 2018. Comorbidities, severity of illness scores, discharge diagnosis codes and CICU procedures and therapies were recorded, and temporal trends were assessed using linear regression and Cochran-Armitage trend tests. Trends in adjusted hospital mortality over time were assessed using multivariable logistic regression.

Results We included 12,418 patients with a mean age of 67.6 years (including 37.7% females). Temporal trends in the prevalence of several comorbidities and discharge diagnoses were observed, reflecting an increase in the prevalence of non-coronary cardiovascular diseases, critical care diagnoses, and organ failure (all $P < .05$). The use of several CICU therapies and procedures increased over time, including mechanical ventilation, invasive lines and vasoactive drugs (all $P < .05$). A temporal decrease in adjusted hospital mortality was observed among the subgroup of patients with (adjusted OR per year 0.97, 95% CI 0.94–0.99, $P = .023$) and without (adjusted OR per year 0.91, 95% CI 0.85–0.96, $P = .002$) a critical care discharge diagnosis.

Conclusions We observed an increasing prevalence of critical care and organ failure diagnoses as well as increased utilization of critical care therapies in this CICU cohort, associated with a decrease in risk-adjusted hospital mortality over time. (Am Heart J 2019;215:12-9.)

The modern cardiac intensive care unit (CICU) has evolved from a unit primarily designed to monitor and treat acute myocardial infarction (MI) patients to a unit

that cares for an increasingly heterogeneous mix of patients with diverse acute cardiovascular diagnoses.¹⁻³ These temporal changes have led to a lower prevalence of ischemic heart disease and an increasing proportion of patients with heart failure (HF), complex non-cardiovascular comorbidities and multi-organ failure in the CICU.³⁻⁸ Accordingly, there has been a growing utilization of critical care restricted therapies such as mechanical ventilation and renal replacement therapy over time in CICU populations.³⁻¹⁰ This changing clinical profile and rise in CICU patient acuity and complexity has significant implications for resource utilization and optimal education and staffing models including specialized nurse and physician training pathways.^{1,2,11,12}

A seminal study of the Duke University CICU population examined temporal trends from 1989–2006, showing a rising prevalence of multi-organ comorbid non-cardiac critical illness and greater utilization of critical care restricted therapies and procedures over time.³

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The authors have no relevant financial disclosures or conflicts of interest related to this work. Submitted April 4, 2019; accepted May 26, 2019.

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<https://doi.org/10.1016/j.ahj.2019.05.012>

There have been no recent published studies with sufficient data granularity to determine whether similar changes have occurred in other large unselected CICU populations during subsequent years. A recent study administrative Medicare database study described broad national trends in CICU admission characteristics, demonstrating increases in non-cardiac diagnoses and a shift from acute coronary syndromes (ACS) to HF; however, inclusion of only Medicare beneficiaries limits its applicability to the broader CICU population.⁴

Understanding the changing landscape of contemporary CICU care is essential to address care deficiencies, define best practices and resource utilization, and to train the next generation of CICU physicians. The purpose of this study was to describe recent temporal trends in comorbidities, discharge diagnoses, illness severity, critical care restricted therapies and procedures, and risk-adjusted mortality in a large, unselected contemporary CICU cohort at a tertiary academic center.

Methods

Study population

This study was approved by the Institutional Review Board of Mayo Clinic as minimal risk, and was conducted under a waiver of informed consent. We analyzed a previously-constructed database of consecutive unique adult (aged ≥ 18 years) patients admitted to the CICU at Mayo Clinic Hospital St. Mary's Campus whose entire CICU admission occurred between January 1, 2007 and April 30, 2018.⁵⁻⁷ The Mayo Clinic CICU is a closed 16-bed unit serving critically-ill cardiac medical patients that excludes postoperative cardiac surgery patients and patients receiving extracorporeal membrane oxygenator support; critically-ill patients with pulmonary embolism are typically cared for in the medical intensive care unit. Initiation and titration of inotrope and vasopressor medication; initiation of antiarrhythmic therapy for ventricular arrhythmias; use of pulmonary artery catheter (PAC), arterial line and mechanical circulatory support; high-flow oxygen therapy, invasive and noninvasive ventilation; continuous renal-replacement therapy (CRRT); and targeted temperature management all require intensive care unit admission at the Mayo Clinic. A co-management model with consultation by a Critical Care Medicine physician has traditionally been available for assistance in management of patients with respiratory failure. The analyzed data are limited to the first CICU admission during the study period. We excluded patients in whom discharge diagnoses were not available; in addition, as per Minnesota state law, we excluded patients not providing Minnesota Research Authorization.

Data sources

Demographic, vital sign, laboratory, clinical, and outcome data were extracted electronically from the

medical record, as previously described.⁵⁻⁷ The dataset includes critical care restricted therapies and procedures, including placement of PAC, central venous catheter (CVC), arterial line, intra-aortic balloon pump (IABP) as well as dialysis (including CRRT), red blood cell transfusion, invasive and noninvasive ventilation, and administration of intravenous vasopressors and inotropes. Performance of coronary angiography and percutaneous coronary intervention (PCI) during hospitalization were also extracted. The following risk scores were automatically calculated using electronic health record data from the first 24 hours of CICU admission, with missing variables imputed as normal as the default: automated APACHE-III score, automated APACHE-IV predicted hospital mortality, automated Sequential Organ Failure Assessment (SOFA) score and Oxford Acute Severity of Illness Score (OASIS).^{5-7,13-16} According to prior studies in this population, all of these scores have very good discrimination in this CICU population, although calibration is generally suboptimal.⁵⁻⁷ The mean and maximum daily SOFA scores during CICU admission (up to the first 7 days) were recorded. The Charlson Comorbidity Index (CCI) and individual comorbidities were determined from the medical record based on a previously-validated electronic algorithm; we arbitrarily defined chronic cardiorenal syndrome (CRS) as the presence of chronic HF and chronic kidney disease (CKD).¹⁷

Discharge diagnoses were identified using *International Classification of Diseases (ICD)-9* and *ICD-10* diagnosis codes (Supplemental Table 1). Cardiovascular diagnoses of interest included ACS (including all forms of acute MI and unstable angina), ST-elevation MI (STEMI), non-ST-elevation ACS (NSTEMI), HF, atrial fibrillation (AF), ventricular fibrillation [VF], ventricular tachycardia [VT], complete heart block (CHB), pulmonary hypertension (PH), infective endocarditis, cardiomyopathy and stable coronary artery disease (CAD). High acuity CICU diagnoses of interest included shock, cardiac arrest, respiratory failure, and sepsis; collectively these diagnoses were considered as critical care diagnoses. We arbitrarily defined acute CRS as the presence of concomitant *ICD-9/10* discharge diagnosis codes for AKI and HF. Complicated ACS was defined as ACS with concomitant cardiac arrest, shock, respiratory failure, HF or VT/VF; ACS without these additional diagnoses was considered uncomplicated. Organ failure was defined using diagnosis codes for shock, respiratory failure, AKI, disseminated intravascular coagulation (DIC), encephalopathy/altered mental status and liver failure.

Statistical methods

All-cause CICU and hospital mortality were obtained from the electronic medical record. Data are reported as mean \pm standard deviation (SD) for continuous variables and number (%) for categorical variables. The cohort was

Table 1. Baseline characteristics, comorbidities and illness severity for each of the 4 study periods. Data are reported as mean \pm SD for continuous variables and number (%) for categorical variables. *P* value is for the temporal trends across groups.

	2007-2009 (n = 3687)	2010-2012 (n = 3280)	2013-2015 (n = 3027)	2016-2018 (n = 2424)	<i>P</i> (trend)
Demographics					
Age (years)	67.5 \pm 15.2	67.3 \pm 15.2	67.5 \pm 15.3	68.3 \pm 15.2	.0654
Female gender	1420 (38.5%)	1206 (36.8%)	1114 (36.8%)	940 (38.8%)	.9417
White race	3361 (91.2%)	3035 (92.5%)	2831 (93.5%)	2230 (92.0%)	.0434
Pre-admission comorbidities*					
Charlson Comorbidity Index	2.3 \pm 2.6	2.4 \pm 2.6	2.5 \pm 2.7	2.4 \pm 2.6	.0331
Myocardial infarction	795 (21.6%)	646 (19.7%)	538 (17.9%)	320 (13.2%)	\ll .0001
Heart failure	662 (18.0%)	633 (19.3%)	657 (21.9%)	568 (23.4%)	\ll .0001
Stroke	467 (12.7%)	386 (11.8%)	376 (12.5%)	254 (10.5%)	.0413
Chronic kidney disease	677 (18.4%)	682 (20.8%)	670 (22.3%)	530 (21.9%)	\ll .0001
Diabetes mellitus	1003 (27.2%)	951 (29.0%)	880 (29.3%)	707 (29.2%)	.0659
Liver disease	61 (1.6%)	60 (1.8%)	73 (2.4%)	65 (2.7%)	.0017
Cancer	782 (21.2%)	689 (21.0%)	660 (22.0%)	488 (20.1%)	.6082
Lung disease	714 (19.4%)	645 (19.7%)	585 (19.5%)	466 (19.2%)	.8945
Peripheral vascular disease	289 (7.8%)	232 (7.1%)	219 (7.3%)	132 (5.4%)	.0016
Prior dialysis	261 (7.1%)	168 (5.1%)	142 (4.7%)	49 (2.0%)	\ll .0001
Chronic cardiorespiratory syndrome	308 (8.4%)	294 (9.0%)	299 (10.0%)	247 (10.2%)	.0051
Severity of illness					
APACHE-III score	61.4 \pm 25.2	61.1 \pm 25.5	60.5 \pm 25.2	59.6 \pm 24.1	.0036
APACHE-IV predicted mortality	0.173 \pm 0.205	0.169 \pm 0.201	0.165 \pm 0.194	0.166 \pm 0.186	.1060
OASIS	25.4 \pm 10.5	25.0 \pm 10.3	25.6 \pm 10.2	26.6 \pm 10.1	\ll .0001
Day 1 SOFA score	3.4 \pm 3.1	3.5 \pm 3.2	3.4 \pm 3.2	3.7 \pm 3.3	.0017
Max week 1 SOFA score	3.8 \pm 3.3	3.9 \pm 3.3	3.9 \pm 3.4	4.2 \pm 3.5	.0016
Mean week 1 SOFA score	2.9 \pm 2.6	3.0 \pm 2.6	3.0 \pm 2.7	3.1 \pm 2.6	.0956

*Comorbidities and Charlson Comorbidity Index were determined using an electronic algorithm.¹⁷

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; OASIS, Oxford Acute Severity of Illness Score; SOFA, Sequential Organ Failure Assessment.

divided into 4 groups based on year of admission, ie, 2007–2009, 2010–2012, 2013–2015, and 2016–2018. Temporal trends across these time periods were analyzed using Cochran-Armitage trend tests for categorical variables and linear regression for continuous variables, with odds ratio (OR) values calculated for categorical variables as a function of time period using linear regression. In addition, linear regression as a function of year as a continuous variable was performed to determine OR values per year for categorical variables. Multivariable logistic regression was performed including year of CICU admission, age, gender, race, CCI, maximum week 1 SOFA score and CICU therapies and procedures; this multivariable analysis was repeated in patients with and without one or more critical care diagnoses. Statistical analyses were performed using JMP version 13.0 Pro (SAS Institute, Cary, NC). Two-tailed $P \ll .05$ were considered statistically significant.

Results

Baseline characteristics, comorbidities and illness severity

Among the 15,947 adult patients admitted to the CICU over the study period, 3529 were excluded (2472 readmissions, 1047 without Minnesota Research Authorization, 10 without available *ICD-9/10* diagnosis codes), leaving

12,418 unique CICU patients in the final study population (Supplemental Figure 1). Baseline characteristics, comorbidities and CCI for the 4 time periods are shown in Table 1. There were no significant temporal trends in age or gender. The CCI increased over time, reflecting increases in several comorbidities including HF and CKD, while prior MI became less prevalent; see also Supplemental Table 2. Illness severity based on Day 1 and maximum SOFA scores increased over time, whereas APACHE-III/IV scores and OASIS did not change significantly.

Discharge *ICD-9* diagnoses

Over the study period, temporal changes in several cardiovascular and non-cardiovascular discharge diagnoses were observed (Table 2 and Supplemental Table 2). The prevalence of ACS diagnoses decreased over time, reflecting a decrease in NSTEMI while the prevalence of STEMI did not change. During 2007–2009, most ACS cases (64.2%) were uncomplicated, but during 2016–2018 most ACS cases (70.9%) were complicated by a concomitant diagnosis of cardiac arrest, shock, HF, respiratory failure or VT/VF. All of the other examined cardiovascular diagnoses increased in prevalence over time, including HF, acute CRS, arrhythmias and valvular heart disease. The overall prevalence of pre-defined

Table 2. Discharge diagnoses based on *ICD-9* and *ICD-10* codes for each of the 4 study periods. Data are reported as mean ± SD for continuous variables and number (%) for categorical variables. *P* value is for temporal trends across groups using Cochran-Armitage trend tests for categorical variables across the 4 study periods.

Variable	2007-2009 (n = 3687)	2010-2012 (n = 3280)	2013-2015 (n = 3027)	2016-2018 (n = 2424)	<i>P</i> (trend)
Cardiovascular diagnoses					
ACS	1627 (44.1%)	1443 (44.0%)	1276 (42.2%)	977 (40.3%)	.0015
STEMI	890 (24.1%)	873 (26.6%)	801 (26.5%)	573 (23.6%)	.9856
NSTEMACS	737 (20.0%)	570 (17.4%)	475 (15.7%)	404 (16.7%)	<.0001
Uncomplicated ACS*	1045 (28.3%)	769 (23.4%)	543 (17.9%)	284 (11.7%)	<.0001
Complicated ACS*	582 (15.8%)	674 (20.6%)	733 (24.2%)	693 (28.6%)	<.0001
Chronic CAD	2323 (63.0%)	2009 (61.2%)	1841 (60.8%)	1675 (69.1%)	.0002
Cardiomyopathy	416 (11.3%)	467 (14.2%)	506 (16.7%)	538 (22.2%)	<.0001
Heart failure	1135 (30.8%)	1298 (39.6%)	1510 (49.9%)	1483 (61.2%)	<.0001
Acute CRS	362 (9.8%)	464 (14.2%)	572 (18.9%)	789 (32.6%)	<.0001
Pulmonary hypertension	405 (11.0%)	553 (16.9%)	519 (17.2%)	601 (24.8%)	<.0001
Valvular heart disease	976 (26.5%)	848 (25.8%)	966 (31.9%)	1140 (47.0%)	<.0001
Endocarditis	82 (2.2%)	94 (2.9%)	107 (3.5%)	87 (2.6%)	.0004
Ventricular arrhythmias	525 (14.2%)	570 (17.4%)	568 (18.8%)	773 (31.9%)	<.0001
Atrial fibrillation	1048 (28.4%)	1089 (33.2%)	1088 (35.9%)	1106 (45.6%)	<.0001
Complete heart block	190 (5.2%)	198 (6.0%)	238 (7.9%)	277 (11.4%)	<.0001
Critical-care diagnoses					
Any critical care diagnosis	853 (23.1%)	921 (28.1%)	1073 (35.4%)	1239 (51.1%)	<.0001
Shock	274 (7.4%)	359 (11.0%)	463 (15.3%)	576 (23.8%)	<.0001
Cardiogenic shock	211 (5.7%)	288 (8.8%)	362 (12.0%)	471 (19.4%)	<.0001
Cardiac arrest	249 (6.8%)	290 (8.8%)	289 (9.6%)	305 (12.6%)	<.0001
Respiratory failure	591 (16.0%)	625 (19.0%)	708 (23.4%)	880 (36.3%)	<.0001
Sepsis	197 (5.3%)	201 (6.1%)	278 (9.2%)	367 (15.1%)	<.0001
Organ dysfunction					
Any organ failure	1097 (29.8%)	1209 (36.9%)	1333 (44.0%)	1441 (59.4%)	<.0001
Multi-organ failure	443 (12.0%)	529 (16.1%)	641 (21.2%)	840 (34.6%)	<.0001
Non-cardiac organ failure	1033 (28.0%)	1144 (34.9%)	1244 (41.1%)	1360 (56.1%)	<.0001
Acute kidney injury	610 (16.5%)	702 (21.4%)	780 (25.8%)	971 (40.1%)	<.0001
Chronic kidney disease	532 (14.4%)	550 (16.8%)	585 (19.3%)	898 (37.0%)	<.0001
Liver failure	40 (1.1%)	47 (1.4%)	56 (1.8%)	139 (5.7%)	<.0001
DIC	21 (0.6%)	22 (0.7%)	24 (0.8%)	53 (2.2%)	<.0001
Anemia	457 (12.4%)	525 (16.0%)	566 (18.7%)	1117 (46.1%)	<.0001
Acute blood loss anemia	64 (1.7%)	149 (4.5%)	261 (8.6%)	386 (15.9%)	<.0001
Encephalopathy	202 (5.5%)	271 (8.3%)	308 (10.2%)	290 (12.0%)	<.0001

Abbreviations: ACS, acute coronary syndrome; CAD, coronary artery disease; CRS, cardiorenal syndrome; DIC, disseminated intravascular coagulation; NSTEMACS, non-ST-elevation ACS; STEMI, ST-elevation myocardial infarction.

* Complicated ACS is defined as ACS with concomitant diagnosis of HF, VT, VF, shock or cardiac arrest; uncomplicated ACS includes ACS without these diagnoses.

critical care diagnoses (ie, cardiac arrest, shock, respiratory failure, sepsis) increased more than 2-fold over the study period (from 23.1% in 2007–2009 to 51.1% in 2016–2018, $P \ll .001$ for trend). The prevalence of organ failure doubled and the prevalence of multi-organ failure nearly tripled over the study period, with increases in each individual organ failure diagnosis. The mean number of organ failure diagnoses per patient increased from 0.5 in 2007–2009 to 1.2 in 2016–2018, with a parallel increase in non-cardiac organ failure diagnoses (from 0.4 in 2007–2009 to 1.0 in 2018–2018).

CICU therapies and procedures

As shown in [Figure 1A](#) and [Figure 1B](#), temporal increases in the use of invasive and noninvasive ventilation, vasopressor and inotrope drugs, invasive lines and CRRT

were observed over the study period. Conversely, use of coronary angiography, PCI and RBC transfusion declined, with no change in the overall use of IABP or dialysis. Among patients with ACS, the use of coronary angiography and PCI decreased over time ($P \ll .001$ for trends). Use of any critical care therapy (ie, mechanical ventilation, invasive lines, vasoactive drugs or CRRT) increased over the study period ([Table 3](#) and [Supplemental Table 2](#)), from 51.9% in 2007–2009 to 66.4% in 2016–2018 (unadjusted OR 1.07 per year, 95% CI 1.06–1.08, $P \ll .001$). Overall CICU LOS did not change over the study period, although overall hospital LOS increased.

Hospital mortality trends

Overall crude in-hospital mortality was 9.2%, including a CICU mortality of 5.8%. Unadjusted hospital mortality

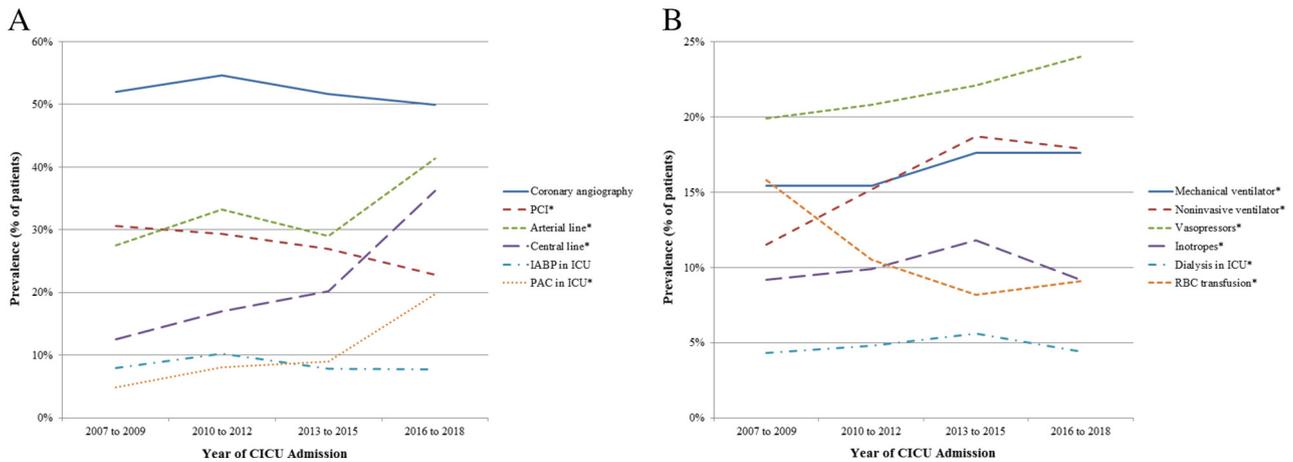


Figure 1

A and B, Use of selected procedures and therapies during each of 4 time periods. Panel A demonstrates use of invasive vascular procedures, and Panel B demonstrates other critical care therapies. * denotes $P < .05$ for trend.

Table 3. Procedures, therapies, complications and outcomes for each of the 4 study periods. Data are reported as mean \pm SD for continuous variables and number (%) for categorical variables. *P* value is for temporal trends across groups using Cochran-Armitage trend tests for categorical variables and linear regression for continuous variables.

Variable	2007-2009 (n = 3687)	2010-2012 (n = 3280)	2013-2015 (n = 3027)	2016-2018 (n = 2424)	<i>P</i> (trend)
Any ventilator	870 (23.6%)	883 (26.9%)	973 (32.1%)	757 (31.2%)	<<.0001
Invasive ventilator	569 (15.4%)	506 (15.4%)	532 (17.6%)	427 (17.6%)	.0038
Noninvasive ventilator	423 (11.5%)	499 (15.2%)	567 (18.7%)	434 (17.9%)	<<.0001
Vasopressors/inotropes	869 (23.6%)	818 (24.9%)	839 (27.7%)	663 (27.4%)	<<.0001
Vasopressors	735 (19.9%)	684 (20.8%)	668 (22.1%)	582 (24.0%)	<<.0001
Inotropes	341 (9.2%)	326 (9.9%)	357 (11.8%)	222 (9.2%)	.0882
IABP in ICU	296 (8.0%)	333 (10.2%)	236 (7.8%)	186 (7.7%)	.2198
PAC in ICU	182 (4.9%)	266 (8.1%)	273 (9.0%)	477 (19.7%)	<<.0001
CRRT	66 (1.8%)	43 (1.3%)	58 (1.9%)	77 (3.2%)	.0002
Dialysis in ICU	159 (4.3%)	159 (4.8%)	169 (5.6%)	107 (4.4%)	.3651
Coronary angiography	2193 (59.4%)	2004 (61.1%)	1786 (59.0%)	1271 (52.4%)	<<.0001
PCI	1460 (39.5%)	1203 (36.6%)	1061 (35.0%)	613 (25.3%)	<<.0001
RBC transfusion	581 (15.8%)	343 (10.5%)	247 (8.2%)	220 (9.1%)	<<.0001
Central line	462 (12.5%)	557 (17.0%)	610 (20.2%)	878 (36.2%)	<<.0001
Arterial line	1015 (27.5%)	1088 (33.2%)	879 (29.0%)	1003 (41.4%)	<<.0001
Any invasive line	1333 (36.1%)	1486 (45.3%)	1303 (43.0%)	1381 (57.0%)	<<.0001
Any critical care therapy*	1915 (51.9%)	1935 (59.0%)	1829 (60.4%)	1610 (66.4%)	<<.0001
CABG	260 (7.0%)	209 (6.4%)	198 (6.5%)	127 (5.2%)	.0114
Valve surgery	192 (5.2%)	188 (5.7%)	175 (5.8%)	195 (8.0%)	<<.0001
LVAD/transplant	53 (1.4%)	105 (3.2%)	90 (3.0%)	42 (1.7%)	.2098
CICU LOS	2.5 \pm 3.6	2.5 \pm 4.7	2.5 \pm 5.4	2.4 \pm 2.8	.7256
Hospital LOS	7.4 \pm 10.2	7.8 \pm 11.5	8.7 \pm 17.3	8.3 \pm 14.2	.0005
Unadjusted CICU mortality	226 (6.1%)	171 (5.2%)	172 (5.7%)	146 (6.0%)	.9125
Unadjusted hospital mortality	340 (9.2%)	272 (8.3%)	295 (9.8%)	241 (9.9%)	.1601

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CRRT, continuous renal replacement therapy; DIC, disseminated intravascular coagulation; IABP, intra-aortic balloon pump; LOS, length of stay; LVAD, left ventricular assist device; NSTEACS, non-ST-elevation ACS; PAC, pulmonary artery catheter; PCI, percutaneous coronary intervention; RBC, red blood cell; STEMI, ST-elevation myocardial infarction.

*Includes invasive/noninvasive ventilator, vasopressors/inotropes, invasive lines, CVVH.

during each of the 4 time periods is shown in **Figure 2A** ($P = .160$ for trend). There was no significant overall change in unadjusted CICU mortality or hospital mortality (unadjusted OR per year 1.01, 95% CI 0.99–1.03) over the

study period ($P \gg .1$). Unadjusted hospital mortality did not change significantly over the study period for patients with most cardiovascular discharge diagnoses (**Figure 2A**). By contrast, unadjusted hospital mortality decreased over

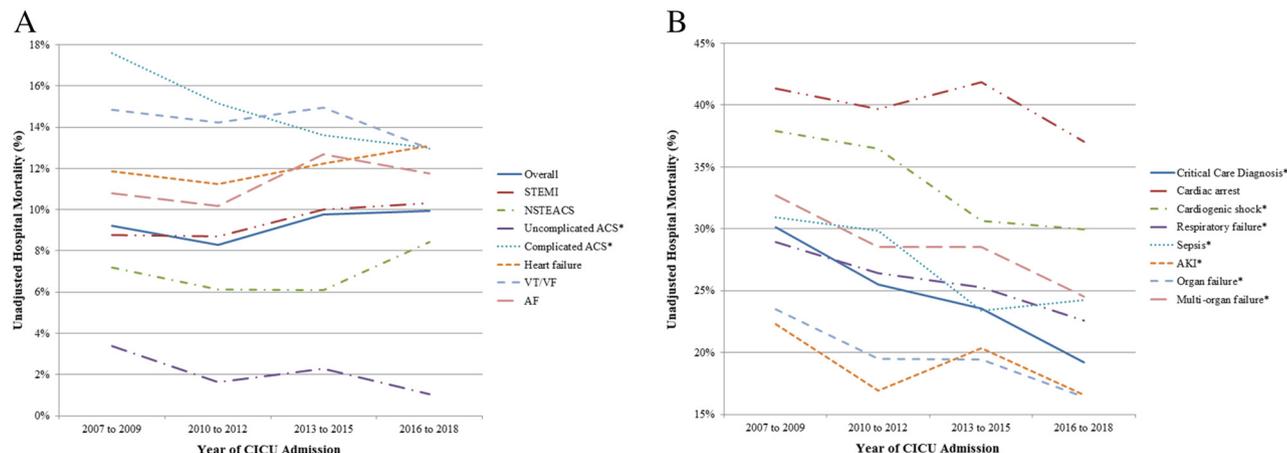


Figure 2

A and B, Unadjusted hospital mortality during each of the 4 time periods, overall and in patients with selected discharge diagnoses. Panel A demonstrates cardiovascular discharge diagnoses, and Panel B demonstrates critical care discharge diagnoses. * denotes $P < .05$ for trend.

time among patients with most critical care diagnoses, including organ failure (Figure 2B).

There was no significant change in adjusted hospital mortality over time after multivariable adjustment (adjusted OR per year 1.01, 95% CI 0.98-1.03, $P = .568$) across the entire population. However, a temporal decrease in adjusted hospital mortality was observed among the subgroup of patients with (adjusted OR per year 0.97, 95% CI 0.94-0.99, $P = .023$) and without (adjusted OR per year 0.91, 95% CI 0.85-0.96, $P = .002$) any critical care discharge diagnosis.

Discussion

We observed important clinical practice changes in this contemporary cohort of more than 12,000 unselected unique CICU patients over a 12-year period. An increasing number of patients presented with complicated ACS, HF, non-ACS cardiovascular diagnoses, critical care diagnoses and end-organ failure. At the end of the study period, more than 70% of ACS cases had concurrent complicating diagnoses, more than 50% of CICU patients carried a critical care diagnosis and nearly 60% of patients had organ failure. The use of critical care therapies such as invasive and noninvasive ventilation, vasopressors, inotropes and invasive lines increased over the study period; with two-thirds of contemporary patients receiving at least one critical care therapy. Despite the increasing patient complexity, overall mortality remained unchanged and we observed a decrease in adjusted hospital mortality over the study period among patients both with and without critical care diagnoses, even when accounting for the increasing utilization of CICU therapies and procedures.

The findings of our investigation corroborate and expand upon the findings of prior single-center and

multi-center studies.³⁻⁸ The prior Duke University study also demonstrated an increasing prevalence of sepsis, AKI and respiratory failure over 18 years, coupled with increased use of critical care procedures and therapies including mechanical ventilation and CVC placement; adjusted hospital mortality decreased over time in this study.³ Together, these studies at large, academic medical centers during sequential study periods spanning 3 decades demonstrate continued trends toward more non-cardiovascular and critical care diagnoses in CICU populations, which appear to have progressively influenced the use of critical care therapies over time leading to improved risk-adjusted mortality.

Although we adjusted our mortality analysis for measures of illness severity, we did not observe a trend toward decreasing mortality in the overall population, possibly due to an increased prevalence of critical care diagnoses over time. However, adjusted mortality decreased over time both in patients with and without critical care diagnoses. Therefore, the absence of an observed mortality trend in the overall population may have been due to the increased prevalence of critical illness over time, reflecting temporal changes in case-mix. We speculate that our observation of stable crude mortality despite an increasing prevalence of critical care diagnoses and organ failure could be due to improvements in the care of critically-ill CICU patients over time, as proposed by Katz, et al.³ However, this could simply be due to greater recognition and coding of these critical care diagnoses over time.

A broader view of national trends in CICU principal discharge diagnoses was provided by an analysis of a large Medicare cohort including 3.4 million CICU admissions from 2003-2013.⁴ This study demonstrated reductions in primary cardiovascular diagnoses (especially CAD) and

increases in primary non-cardiovascular diagnoses (especially infection) over time.⁴ As in our study, the rate of multi-morbidity rose over time, along with rates of invasive and noninvasive ventilator use and hemodialysis.⁴ The rates of PCI declined, consistent with the observed decrease in the prevalence of ischemic heart disease.⁴ The trends we observed in our mixed-age cohort corroborate those observed in the Medicare population, demonstrating an ongoing temporal shift from ischemic heart disease to HF among CICU patients. Our study provides greater data granularity, allowing evaluation of specific discharge diagnoses. A recent study from the Brigham and Women's Hospital including CICU patients from 2015–2017 demonstrated that the majority of CICU admissions were for shock/hypotension, cardiac arrest or arrhythmias, with many patients having respiratory failure and fewer patients having ACS.⁸ This study mirrors the high prevalence of critical care diagnoses during the later years of our study period.

These studies in patients from the United States contrast with a multicenter CICU study from France including 277,845 patients from 270 hospitals, demonstrating that ischemic heart disease remained by far the most common CICU admission diagnosis, followed by arrhythmias and then HF.¹⁸ Likewise, the multicenter Italian BLITZ-3 CICU registry has demonstrated a similar preponderance of ACS patients, with overall lower utilization of critical care restricted therapies than were observed in our study.¹⁹ In addition to distinct practice patterns and CICU case-mix across continents, the differences reported between CICU populations in the United States and other countries may in part relate to patient volume and the infrastructure of intermediate care units, as most published CICU studies have been performed in high-volume academic centers.^{3,5-10} A multicenter study from Canada demonstrated increased utilization of critical care therapies by CICU patients in high-volume centers.²⁰

The evolving patient population within the contemporary CICU emphasizes the need for more research to better understand the implications of these changes. Future studies should confirm and explore the factors driving the apparent improvements in risk-adjusted mortality, such as changes in care processes, early recognition of illness, improved treatment protocols or improved utilization of medical technology. We encourage collaborative development of standardized multidisciplinary treatment protocols for selected CICU patients that can be subjected to quality improvement strategies to determine the optimal care processes. The growing similarities between CICU and traditional medical ICU populations raise important questions about which patients with cardiovascular disease are best served in the CICU and how best to triage potential CICU admissions in terms of potential benefit of CICU care. As highlighted by recent professional society statements, the optimal CICU physician training and staffing models remains to be defined; the high prevalence of organ failure and utilization of critical care therapies such as mechanical

ventilation provides evidence supporting the need for dedicated training in critical care medicine for the next generation of CICU physicians.

Limitations

Despite similarities to other recently-reported CICU populations, the referral population reflected in this CICU cohort likely differs significantly from many CICU populations in terms of demographics and other important factors.⁸⁻¹⁰ Hospital mortality rates vary considerably in recent CICU studies based on geography, patient demographics, case-mix and hospital-based factors. The observed hospital mortality rate in this study is comparable to that reported by Goldfarb, et al., being lower than that reported in some recent single-center studies from the United States and higher than that reported in recent multicenter studies from Europe.^{8-10,18,19} Starting in 2015, our CICU staffing model changed to include 24/7 in-house attending physician coverage and hiring of new staff with board certification in both cardiovascular diseases and critical care medicine, in addition to an institutional protocol designed to facilitate admission of uncomplicated STEMI patients with low-risk clinical features directly to the cardiology ward rather than the CICU. Due to trends developing prior to institution of these changes, we cannot attribute the decreasing adjusted mortality seen in patients with critical care diagnoses to these staffing changes alone. The use of *ICD-9/10* diagnostic codes to define discharge diagnoses carries a number of potential limitations when compared to individual review of health records, and changes in diagnostic criteria and the utilization of specific *ICD-9/10* diagnostic codes over the study period could have created apparent temporal trends in some diagnoses independent of true disease prevalence. In particular, if a systematic increasing in coding acuity occurred over time, this could have potentially shifted a greater number of patients into higher-risk diagnostic categories. However, we expect that the impact on our main findings would be small because the recognition and coding of major critical care diagnoses such as shock and cardiac arrest is unlikely to have changed over time; likewise, this would not have influenced the observed trends in illness severity, procedure utilization and outcomes. The inability to capture the primary admission or discharge diagnosis remains an important limitation of this study. Data on resuscitation status were not available, although patients with a Do-Not-Resuscitate order are routinely admitted to our CICU if this is consistent with their goals of care.

Conclusions

This large, contemporary CICU cohort study demonstrated substantial temporal changes in the prevalence of cardiovascular, critical care and non-cardiac organ failure diagnoses, coupled with increased utilization of several critical care therapies and procedures. Despite this

increasing patient acuity and complexity, overall mortality rates remained stable and adjusted mortality rates decreased over the study period for patients with and without critical care diagnoses. Future research is needed to determine whether improvements in disease recognition, care coordination and/or quality of care have occurred among critically-ill CICU patients.

Sources of funding

No extramural funding was used to support this research. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

Acknowledgements

We would like to thank the dedicated physicians, nurses and allied health staff who provide tireless and exemplary care for our CICU patients every day. In addition, we would like to specifically thank Erica Portner RRT, whose hard work helped to bring this study to fruition.

Appendix. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ahj.2019.05.012>.

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