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ORIGINAL RESEARCH

Association Between Systolic Blood Pressure and in-Hospital Mortality Among Congestive Heart Failure Patients with Chronic Obstructive Pulmonary Disease in the Intensive Care Unit: A Retrospective Cohort Study

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Background: There has been a growing body of research focusing on patients with Congestive Heart Failure (CHF) and chronic obstructive pulmonary disease (COPD) admitted to the intensive care unit (ICU). However, the optimal blood pressure (BP) level for such patients remains insufficiently explored. This study aimed to investigate the associations between systolic blood pressure (SBP) and in-hospital mortality among ICU patients with both CHF and COPD.

Methods: This retrospective cohort study enrolled 6309 patients from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database. SBP was examined as both a continuous and categorical variable, with the primary outcome being in-hospital mortality. The investigation involved multivariable logistic regression, restricted cubic spline regression, and subgroup analysis to determine the relationship between SBP and mortality.

Results: The cohort consisted of 6309 patients with concurrent CHF and COPD (3246 females and 3063 males), with an average age of 73.0 ± 12.5 years. The multivariate analysis revealed an inverse association between SBP and in-hospital mortality, both as a continuous variable (odds ratio = 0.99 [95% CI, 0.99~1]) and as a categorical variable (divided into quintiles). Restricted cubic spline analysis demonstrated an L-shaped relationship between SBP and mortality risk (P nonlinearity < 0.001), with an inflection point at 99.479 mmHg. Stratified analyses further supported the robustness of this correlation.

Conclusion: The relationship between SBP and in-hospital mortality in patients with both CHF and COPD follows an L-shaped pattern, with an inflection point at approximately 99.479 mmHg.

Keywords: systolic blood pressure, in-hospital mortality, congestive heart failure, chronic obstructive pulmonary disease, generalized additive model

Introduction

Congestive heart failure (CHF) impacts more than five million individuals in the United States, and its prevalence is predicted to increase by a quarter within the upcoming fifteen years.[1] It's important to note that CHF is not an isolated ailment; rather, it's a complex condition stemming from the progression of different cardiac issues into an advanced stage, resulting in heightened morbidity and mortality rates.[2] Chronic obstructive pulmonary disease (COPD) is a prevalent condition characterized by persistent limitation of airflow.[3] CHF and COPD frequently coexist due to shared

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risk factors such as smoking and advanced age, alongside common pathophysiological mechanisms like the "cardiopulmonary continuum" and low-grade systemic inflammation.[4–6] Prior research has established a strong link between heart failure and COPD, leading to an increasing number of combined patient cases.[7,8] Despite the growing recognition of COPD as a common and potentially deadly complication of CHF, the precise factors connecting these two conditions are not yet fully comprehended.

Systolic blood pressure (SBP) is a vital clinical parameter regularly evaluated to assess patient outcomes in various situations, encompassing sepsis[9], cardiovascular disease[10], and Acute Aortic Dissection.[11] Many studies have identified blood pressure as a significant determinant of adverse events in cardiovascular patients.[12,13] The J-curve phenomenon, examining the relationship between blood pressure levels and adverse cardiovascular events, has been observed in numerous studies, including instances of in-hospital mortality.[14,15] Consistent observational studies have linked admission systolic blood pressure (SBP) to the risk of mortality in acute cardiovascular conditions such as acute heart failure[16] and cardiogenic shock.[17] Additionally, prior research has associated SBP with stage 3 or 4 COPD.[18,19] Nevertheless, despite the established correlation between COPD and CHF, there exists limited research investigating the connection between SBP levels in COPD patients hospitalized for CHF and their subsequent outcomes.

Patients in the intensive care unit (ICU), as a special department, have high mortality risk, of which patients with COPD and CHF account for a certain proportion. Reducing the mortality of ICU patients with COPD and CHF has always been a major clinical objective. However, no study has focused on the association between BP and mortality risk and the optimal BP target in ICU patients with COPD and CHF. Considering the loss of cardiopulmonary function, the optimal value of BP in patients with COPD and CHF may differ from that in the general population, which would be of great clinical significance for defining thresholds of BP below which adverse events may increase or decline in frequency. As such, this study aims to explore the relationship between SBP and in-hospital mortality within a sizable cohort of American adults diagnosed with both congestive heart failure and COPD, all of whom are admitted to the intensive care unit.

Method

Data Source

This study is a population based, retrospective open cohort study using the Medical Information Mart for Intensive Care IV (MIMIC-IV) database. The Medical Information Mart for Intensive Care (MIMIC) database is a collaboration between the Beth Israel Deaconess Medical Center and the Laboratory for Computational Physiology at the Massachusetts Institute of Technology.[20,21] Detailed medical information is contained within the database, encompassing demographics, vital signs, diagnoses, laboratory test outcomes, caregiver annotations, and mortality statistics.[22] To obtain access to the MIMIC-IV version 2.0 database, a training course on the National Institutes of Health (NIH) website was completed, along with successful completion of the "Protecting Human Research Participants" exam (author certification number: 11639604). Approval for utilizing the MIMIC-IV database in this study was granted by the Institutional Review Boards of Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center.[23,24] Given the retrospective and de-identified nature of the data, the Beth Israel Deaconess Medical Center Institutional Review Board granted approval for the study and waived the necessity for patient consent.[21,25]

Study Population

In this nationwide cohort study, we retrospectively analyzed systolic blood pressure effects on mortality in patients with COPD-heart failure overlap. Patients included in the study were COPD-heart failure overlap cohorts during their stay in the intensive care unit (ICU). COPD and HF were identified using diagnostic codes from the International Classification of Diseases, 9th Revision, Clinical Modification (HF: 425.4, 425.9, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, and 428.xx; COPD: 491.xx, 492.xx, and 496.xx).

For patients with multiple ICU admissions, data from their initial ICU stay were considered. Exclusion criteria comprised individuals below 18 years of age, those with missing outcome data, and those without COPD. The study comprised both derivation and validation cohorts, each consisting of 6309 patients with both CHF and COPD. The selection process is visually illustrated in Figure 1.

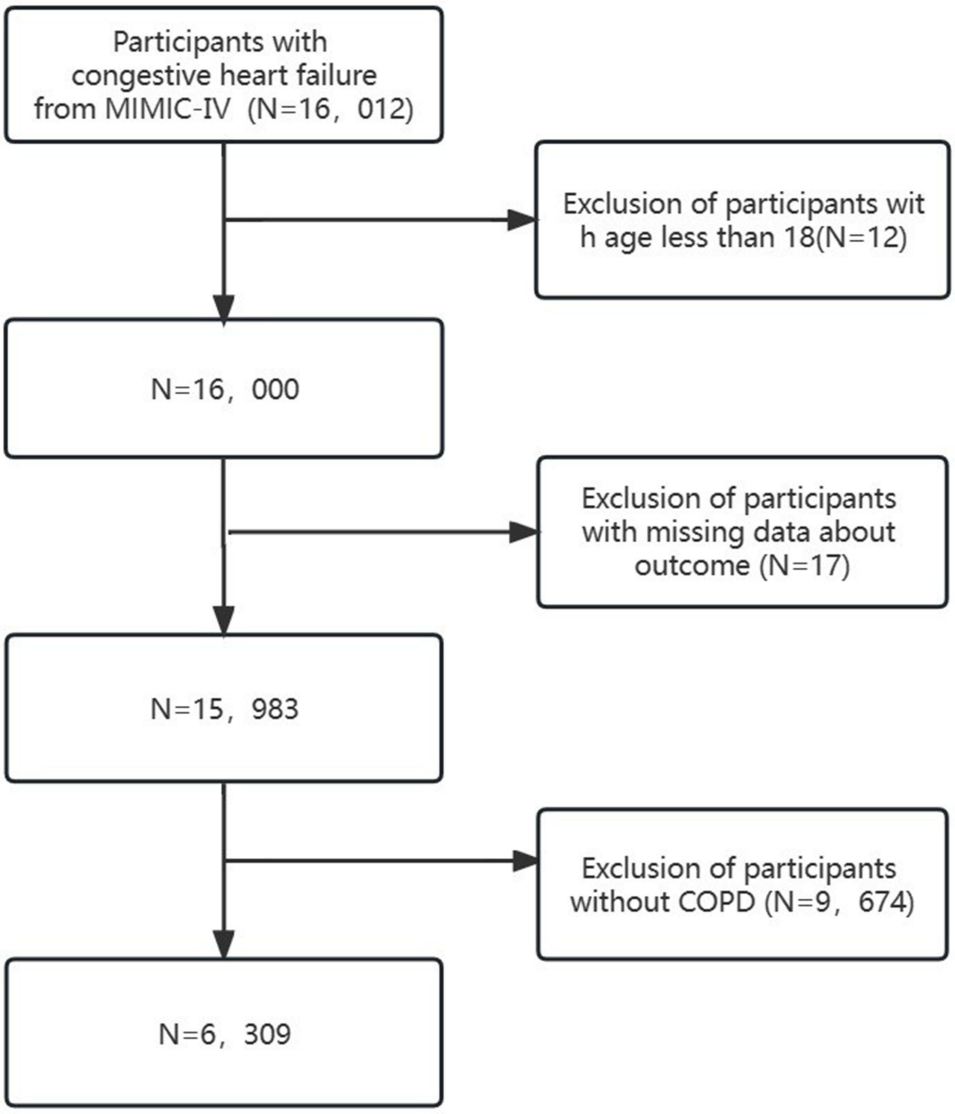

Figure 1 Flowchart of patient selection.

Exposure and Outcome

The primary exposure of interest in this study was systolic blood pressure. We performed all analyses using the main exposure variable as either a continuous or a categorical variable. Referring to previous articles, blood pressure was processed according to the five distinct categories when used as a categorical variable.[26–28] All-cause mortality assessed at hospital discharge (ie, in-hospital mortality) was the primary outcome of the study.

Data Retrieval and Outcomes

The investigation utilized Structured Query Language (SQL) for data retrieval within 24 hours following admission to the Intensive Care Unit (ICU). The scope of data encompassed crucial indicators such as vital signs (temperature, respiratory rate, heart rate), the Sequential Organ Failure Assessment (SOFA) score, and the Simplified Acute Physiology Score III (APS III). Additionally, demographic particulars, including age, race, gender, and illness severity evaluated via SOFA score and APS III during ICU admission, were also collected. Details regarding treatments, including ventilation and the application of vasoactive medications (yes or no) (norepinephrine, dopamine, epinephrine, phenylephrine, and vasopressin), as well as medical procedures like intubation and ventilation, were duly recorded. Furthermore, the

presence of comorbidities such as diabetes, acute myocardial infarction (AMI), malignant cancer (MC), and hepatic failure (HepF) was documented. The admission laboratory test values included arterial blood gases (AG), blood urea nitrogen (BUN), chloride, creatinine, hemoglobin (Hb), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), platelet count, potassium, sodium, red blood cell count (RBC), red cell distribution width (RDW), and white blood cell count (WBC).

Statistical Analyses

The dataset was categorized into two distinct types: continuous and categorical variables. Continuous variables underwent classification based on their distribution's normality. Normally distributed continuous variables were displayed as mean ± standard deviation and evaluated using Student's *t*-test, while non-normally distributed variables were depicted as median ± interquartile range (IQR) and assessed through the Wilcoxon rank-sum test. Categorical variables were presented as percentages and compared using the chi-square test. To ascertain differences among groups stratified by SBP, the Kruskal–Wallis test or one-way analysis of variance was employed.

For the examination of the relationship between SBP and in-hospital mortality, multivariate logistic regression was executed. The evaluation of this connection involved the calculation of odds ratios (ORs) and their corresponding 95% confidence intervals (CIs). A sequence of models was employed for adjustment, progressively introducing covariates: Model 1 (Unadjusted model without any covariate), Model 2 (Incorporating demographic variables: sex, age, race), Model 3 (Supplementing demographic variables and concurrent conditions: diabetes, AMI, MC, HepF), Model 4 (Further including demographic variables, comorbidities, Medical Procedures such as Vent and Intubation, Medication situation including Norepinephrine, Dopamine, Epinephrine, Phenylephrine, Vasopressin, essential vital signs such as Temperature, Respiratory Rate, Heart Rate, Blood biochemical indicators such as AG, BUN, Chloride, Creatinine, Hb, MCH, MCHC, MCV, Platelet, Potassium, Sodium, RBC, RDW, WBC), and Model 5 (Adjusted for demographic variables, comorbidities, Medical Procedures, Medication situation, basic vital signs, Blood biochemical indicators, APSIII, SOFA). Logistic regression, with SBP grouped into five categories, was utilized to detect trends.

To explore potential non-linear associations between SBP and in-hospital mortality, a Generalized Additive Model and a smooth curve fitting technique (penalized spline method) were employed. Adjustments and interactions within subgroups based on diverse factors were identified via stratified linear regression models and likelihood ratio tests.

All analyses were carried out using statistical software packages, specifically R version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria), and Free Statistics software version 1.7. A significance level of $P < 0.05$ (two-sided) was deemed as statistically significant. The present cross-sectional study's reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

Results

Baseline Characteristics of Selected Participants

Table 1 presents the baseline characteristics of 6309 patients diagnosed with both COPD and congestive heart failure (CHF). The patients were divided into five groups based on their SBP quintiles: Q1 (≤102 mmHg), Q2 (102–109 mmHg), Q3 (109–117 mmHg), Q4 (117–129 mmHg), and Q5 (>129 mmHg). The mean age of the entire patient cohort was 73.0 ± 12.5 years.

Compared to participants with lower SBP at baseline, those with higher SBP exhibited the following characteristics: a higher proportion of women, higher levels of Hb, platelets, blood sodium, RBC, and blood calcium; a lower proportion of white individuals; and a reduced use of Norepinephrine, Dopamine, Epinephrine, phenylalanine, and Vasopressin. Additionally, the higher SBP group showed lower HepF ratio, Heart rate, BUN, MCV, RDW, WBC, SOFA score, APS III score, and mortality rate (Table 1).

Table 1 Characteristics of the Study Population (N = 6309)

Variables	Total (n = 6309)	Q1 (n = 1248)	Q2 (n = 1122)	Q3 (n = 1288)	Q4 (n = 1383)	Q5 (n = 1268)	P value [a]
Age, Mean ± SD	73.0 ± 12.5	72.5 ± 12.7	72.8 ± 12.2	73.0 ± 12.0	73.3 ± 12.2	73.1 ± 13.2	0.481
Gender, n (%)							< 0.001
Male	3063 (48.5)	642 (51.4)	571 (50.9)	649 (50.4)	670 (48.4)	531 (41.9)	
Female	3246 (51.5)	606 (48.6)	551 (49.1)	639 (49.6)	713 (51.6)	737 (58.1)	
Race, n (%)							< 0.001
White	4339 (68.8)	919 (73.6)	807 (71.9)	913 (70.9)	956 (69.1)	744 (58.7)	
Black	901 (14.3)	155 (12.4)	107 (9.5)	142 (11)	202 (14.6)	295 (23.3)	
Other	1069 (16.9)	174 (13.9)	208 (18.5)	233 (18.1)	225 (16.3)	229 (18.1)	
Medication situation							
Norepinephrine, n (%)							< 0.001
No	4883 (77.4)	759 (60.8)	749 (66.8)	984 (76.4)	1193 (86.3)	1198 (94.5)	
Yes	1426 (22.6)	489 (39.2)	373 (33.2)	304 (23.6)	190 (13.7)	70 (5.5)	
Dopamine, n (%)							< 0.001
No	6126 (97.1)	1167 (93.5)	1083 (96.5)	1260 (97.8)	1356 (98)	1260 (99.4)	
Yes	183 (2.9)	81 (6.5)	39 (3.5)	28 (2.2)	27 (2)	8 (0.6)	
Epinephrine, n (%)							< 0.001
No	6086 (96.5)	1166 (93.4)	1066 (95)	1234 (95.8)	1362 (98.5)	1258 (99.2)	
Yes	223 (3.5)	82 (6.6)	56 (5)	54 (4.2)	21 (1.5)	10 (0.8)	
Phenylephrine, n (%)							< 0.001
No	5859 (92.9)	1075 (86.1)	1003 (89.4)	1193 (92.6)	1335 (96.5)	1253 (98.8)	
Yes	450 (7.1)	173 (13.9)	119 (10.6)	95 (7.4)	48 (3.5)	15 (1.2)	
Vasopressin, n (%)							< 0.001
No	5901 (93.5)	1078 (86.4)	1009 (89.9)	1203 (93.4)	1351 (97.7)	1260 (99.4)	
Yes	408 (6.5)	170 (13.6)	113 (10.1)	85 (6.6)	32 (2.3)	8 (0.6)	
Medical Procedures							
Vent, n (%)							0.004
No	678 (10.7)	142 (11.4)	103 (9.2)	113 (8.8)	156 (11.3)	164 (12.9)	
Yes	5631 (89.3)	1106 (88.6)	1019 (90.8)	1175 (91.2)	1227 (88.7)	1104 (87.1)	
Intubated, n (%)							< 0.001
No	4412 (69.9)	910 (72.9)	682 (60.8)	814 (63.2)	986 (71.3)	1020 (80.4)	
Yes	1897 (30.1)	338 (27.1)	440 (39.2)	474 (36.8)	397 (28.7)	248 (19.6)	
Complicating disease							
Diabetes, n (%)							< 0.001
No	3567 (56.5)	812 (65.1)	689 (61.4)	747 (58)	721 (52.1)	598 (47.2)	
Yes	2742 (43.5)	436 (34.9)	433 (38.6)	541 (42)	662 (47.9)	670 (52.8)	
AMI, n (%)							< 0.001
No	4509 (71.5)	873 (70)	799 (71.2)	897 (69.6)	970 (70.1)	970 (76.5)	
Yes	1800 (28.5)	375 (30)	323 (28.8)	391 (30.4)	413 (29.9)	298 (23.5)	
MC, n (%)							0.769
No	5661 (89.7)	1112 (89.1)	1014 (90.4)	1148 (89.1)	1245 (90)	1142 (90.1)	
Yes	648 (10.3)	136 (10.9)	108 (9.6)	140 (10.9)	138 (10)	126 (9.9)	
HepF, n (%)							< 0.001
No	6152 (97.5)	1203 (96.4)	1089 (97.1)	1256 (97.5)	1349 (97.5)	1255 (99)	
Yes	157 (2.5)	45 (3.6)	33 (2.9)	32 (2.5)	34 (2.5)	13 (1)	
Vital signs							
Temperature, Mean ± SD	36.7 ± 0.5	36.7 ± 0.5	36.8 ± 0.5	36.7 ± 0.5	36.7 ± 0.5	36.8 ± 0.4	< 0.001
RespiratoryRate, Mean ± SD	20.1 ± 3.7	20.2 ± 3.8	19.9 ± 3.7	20.0 ± 3.7	20.1 ± 3.7	20.3 ± 3.7	0.04
HeartRate, Mean ± SD	84.7 ± 15.6	88.5 ± 16.8	85.4 ± 14.9	84.7 ± 14.9	82.9 ± 15.6	82.1 ± 14.8	< 0.001
Blood biochemical indicators							
AG, Mean ± SD	14.9 ± 4.1	15.3 ± 4.4	14.9 ± 4.4	14.6 ± 4.0	14.8 ± 3.8	14.9 ± 3.8	< 0.001
BUN, Mean ± SD	35.4 ± 24.4	39.2 ± 27.0	35.7 ± 24.6	34.2 ± 23.8	34.2 ± 23.1	33.9 ± 23.3	< 0.001
Creatinine, Mean ± SD	1.8 ± 1.6	1.9 ± 1.6	1.8 ± 1.5	1.6 ± 1.3	1.7 ± 1.4	1.9 ± 1.9	< 0.001
Hb, Mean ± SD	10.2 ± 2.1	10.2 ± 2.1	10.2 ± 2.1	10.2 ± 2.1	10.2 ± 2.1	10.4 ± 2.1	0.021
MCH, Mean ± SD	29.3 ± 2.9	29.4 ± 3.1	29.4 ± 3.0	29.3 ± 2.8	29.2 ± 2.8	29.1 ± 2.9	0.084
MCHC, Mean ± SD	32.1 ± 1.8	32.0 ± 1.7	32.0 ± 1.8	32.2 ± 1.8	32.1 ± 1.7	32.0 ± 1.8	0.058
MCV, Mean ± SD	91.4 ± 7.6	92.0 ± 8.2	91.8 ± 7.8	91.2 ± 7.3	91.2 ± 7.4	91.0 ± 7.4	0.003

(*Continued*)

Table 1 (Continued).

Variables	Total (n = 6309)	Q1 (n = 1248)	Q2 (n = 1122)	Q3 (n = 1288)	Q4 (n = 1383)	Q5 (n = 1268)	P value [a]
Platelet, Mean ± SD	215.9 ± 100.1	212.3 ± 105.8	213.2 ± 101.4	214.2 ± 96.7	215.0 ± 99.4	224.8 ± 96.9	0.012
Potassium, Mean ± SD	4.3 ± 0.8	4.3 ± 0.8	4.3 ± 0.8	4.4 ± 0.8	4.3 ± 0.7	4.3 ± 0.8	0.735
Sodium, Mean ± SD	138.2 ± 5.1	137.3 ± 5.0	137.9 ± 5.3	138.1 ± 4.9	138.5 ± 5.0	138.9 ± 5.2	< 0.001
RBC, Mean ± SD	3.5 ± 0.7	3.5 ± 0.8	3.5 ± 0.8	3.5 ± 0.7	3.5 ± 0.8	3.6 ± 0.7	0.001
Calcium, Mean ± SD	8.5 ± 0.8	8.3 ± 0.8	8.4 ± 0.8	8.5 ± 0.8	8.6 ± 0.7	8.7 ± 0.7	< 0.001
Chloride, Mean ± SD	101.4 ± 6.9	101.0 ± 6.9	101.7 ± 7.3	101.9 ± 7.0	101.3 ± 6.5	101.1 ± 6.7	0.005
RDW, Mean ± SD	16.0 ± 2.4	16.4 ± 2.5	16.2 ± 2.5	15.9 ± 2.3	15.8 ± 2.2	15.7 ± 2.2	< 0.001
WBC, Mean ± SD	11.8 ± 8.6	12.1 ± 7.1	12.4 ± 7.3	12.8 ± 11.9	11.5 ± 9.6	10.2 ± 4.9	< 0.001
SOFA, Mean ± SD	3.3 ± 2.8	4.0 ± 3.1	3.7 ± 3.0	3.4 ± 2.9	3.0 ± 2.6	2.4 ± 2.2	< 0.001
APSIII, Mean ± SD	51.9 ± 21.3	58.6 ± 22.8	55.2 ± 22.0	51.8 ± 21.6	49.3 ± 19.8	45.2 ± 17.5	< 0.001
Hstatus, n (%)							< 0.001
Survival	5526 (87.6)	980 (78.5)	960 (85.6)	1137 (88.3)	1257 (90.9)	1192 (94)	
Death	783 (12.4)	268 (21.5)	162 (14.4)	151 (11.7)	126 (9.1)	76 (6)	

Notes: Q1(≤102Hg) Q2(102–109mmHg) Q3(109–117mmHg) Q4(117–129mmHg) Q5(>129mmHg). [a] P values of multiple comparisons were corrected by the False Discovery Rate method. Q1-Q5: according to SBP.

Abbreviations: %, weighted proportion.; Hstatus: hospital status; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; HepF, hepatic failure; AMI, acute myocardial infarction; APSIII, Acute Physiology III; SOFA, Sequential Organ Failure Assessment; SBP, systolic blood pressure; AG, anion gap; BUN, blood urea nitrogen; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular; hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; RDW, red blood cell distribution width; WBC, white blood cell count.

Association Between SBP and in-Hospital Mortality

Table 2 presents the relationship between systolic blood pressure (SBP) and in-hospital mortality among patients with congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD). The study assessed odds ratios (ORs) with corresponding 95% confidence intervals (CIs) across various body temperature ranges, while accounting for relevant demographic variables (sex, age, race), comorbidities (diabetes, acute myocardial infarction [AMI], malignant cancer [MC], hepatic failure [HepF]), medical procedures (ventilation, intubation), medication usage (norepinephrine, dopamine, epinephrine, phenylephrine, vasopressin), basic vital signs (temperature, respiratory rate, heart rate), blood biochemical indicators (arterial blood gases [AG], blood urea nitrogen [BUN], chloride, creatinine, hemoglobin [Hb], mean corpuscular hemoglobin [MCH], mean corpuscular hemoglobin concentration [MCHC], mean corpuscular volume [MCV], platelet count, potassium, sodium, red blood cell count [RBC], red cell distribution width [RDW], white blood cell count [WBC]), Acute Physiology and Chronic Health Evaluation III (APSIII) score, and Sequential Organ Failure Assessment (SOFA) score.

When SBP was analyzed as a continuous variable and confounding factors were controlled for, a significant negative association between SBP and in-hospital mortality was observed. Moreover, when SBP was analyzed using quintiles and potential confounders were adjusted for, individuals with higher SBP in Q2 (102mmHg-109mmHg), Q3 (109mmHg-117mmHg), Q4 (117mmHg-129mmHg), and Q5 (>129mmHg) showed lower adjusted OR values for in-hospital mortality compared to those in Q1 (≤102 mmHg). The adjusted OR values and corresponding 95% CIs for Q2, Q3, Q4, and Q5 were 0.7 (95% CI: 0.53~0.92, p = 0.01), 0.74 (95% CI: 0.56~0.98, p = 0.037), 0.72 (95% CI: 0.54~0.97, p = 0.028), and 0.75 (95% CI: 0.53~1.04, p = 0.084), respectively (Table 2). Notably, the trend test revealed a statistically significant trend for these changes ($p < 0.05$).

Dose–Response Relationships

We employed a restricted cubic spline model (Figure 2) to assess the relationship between systolic blood pressure (SBP) and in-hospital mortality among patients diagnosed with congestive heart failure and chronic obstructive pulmonary disease (COPD). The restricted cubic spline analysis revealed an L-shaped association between SBP and in-hospital mortality, accounting for relevant confounding factors. In the threshold analysis (Table 3), participants with an SBP of <99.479 mmHg exhibited an odds ratio (OR) of 0.939 (95% CI: 0.902~0.976, p = 0.0017) for the risk of in-hospital mortality. This finding indicates a reduction of 6.1% in the risk of in-hospital mortality with each 1 mg increase in SBP.

Table 2 Multivariable Logistic Regression to Assess the Association of SBP with in-Hospital Mortality Rate

	Model 1		Model 2		Model 3		Model 4		Model 5	
SBP	**OR_95CI**	**P value**	**OR_95CI**	**P value**	**OR_95CI**	**P value**	**OR_95CI**	**P value**	**OR_95CI**	**P value**
Continuous variable	**0.96 (0.96~0.97)**	**<0.001**	**0.96 (0.96~0.97)**	**<0.001**	**0.96 (0.96~0.97)**	**<0.001**	**0.99 (0.98~0.99)**	**<0.001**	**0.99 (0.99~1)**	**0.019**
Categorical variable										
Q1(≤102)	1(Ref)		1(Ref)		1(Ref)		1(Ref)		1(Ref)	
Q2(102–109)	0.62 (0.5~0.76)	<0.001	0.6 (0.48~0.74)	<0.001	0.6 (0.48~0.74)	<0.001	0.69 (0.53~0.89)	0.005	0.7 (0.53~0.92)	0.01
Q3(109–117)	0.49 (0.39~0.6)	<0.001	0.46 (0.37~0.58)	<0.001	0.46 (0.37~0.57)	<0.001	0.69 (0.53~0.9)	0.006	0.74 (0.56~0.98)	0.037
Q3(117–129)	0.37 (0.29~0.46)	<0.001	0.35 (0.28~0.44)	<0.001	0.35 (0.27~0.44)	<0.001	0.7 (0.53~0.92)	0.011	0.72 (0.54~0.97)	0.028
Q5(>129)	0.23 (0.18~0.3)	<0.001	0.22 (0.16~0.28)	<0.001	0.22 (0.17~0.29)	<0.001	0.62 (0.45~0.86)	0.004	0.75 (0.53~1.04)	0.084
P for tread		<0.001		<0.001		<0.001		0.003		0.05

Notes: Model 1: No adjustment. Model 2: Adjusted for demographic variables (sex, age, race). Model 3: Adjusted for demographic variables, comorbidities (diabetes, AMI, MC, Hep F). Model 4: Adjusted for demographic variables, comorbidities, Medical Procedures (Vent, Intubated), Medication situation (Norepinephrine Dopamine Epinephrine Phenylephrine Vasopressin), Basic vital signs (Temperature Respiratory Rate Heart Rate), Blood biochemical indicators (AG BUN Chloride Creatinine, Hb MCH MCHC MCV Platelet Potassium Sodium RBC RDW WBC). Model 5: Adjusted for demographic variables, comorbidities, Medical Procedures, Medication situation, Basic vital signs, Blood biochemical indicators, APSIII, SOFA.

Abbreviations: the unit of SBP is mmHg. CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; Hep F, hepatic failure; AMI, acute myocardial infarction; APSIII, Acute Physiology III; SOFA, Sequential Organ Failure Assessment; SBP, systolic blood pressure; AG, anion gap; BUN, blood urea nitrogen; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular; hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; RDW, red blood cell distribution width; WBC, white blood cell count; CI, confidence interval; OR, odds ratios; Ref, reference.

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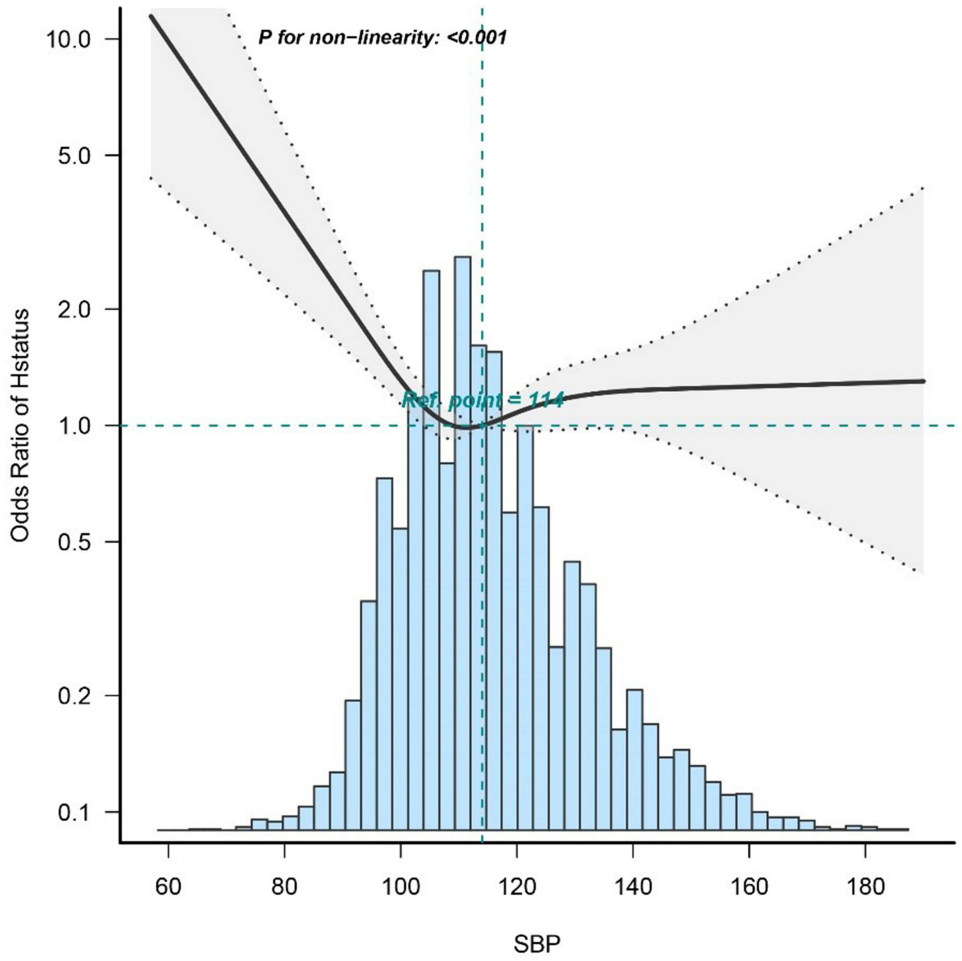

Figure 2 Dose–Response Relationships between SBP with In-hospital mortality rate odds ratio. Solid and dashed lines represent the predicted value and 95% confidence intervals. Adjusted for demographic variables (sex, age, race), Concomitant disease (diabetes, AMI, MC, Hep F, Medical Procedures (Vent, Intubated), Medication situation (Norepinephrine Dopamine Epinephrine Phenylephrine Vasopressin), Basic vital signs (Temperature Respiratory Rate Heart Rate), Blood biochemical indicators (AG BUN Chloride Creatinine calcium Hb MCH MCHC MCV Platelet Potassium Sodium RBC RDW WBC), APSIII, SOFA. Only 99% of the data is shown.
Abbreviations: %, weighted proportion. CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; Hep F, hepatic failure; AMI, acute myocardial infarction; APSIII, Acute Physiology III; SOFA, Sequential Organ Failure Assessment; SBP, systolic blood pressure; AG, anion gap; BUN, blood urea nitrogen; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular; hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; RDW, red blood cell distribution width; WBC, white blood cell count; CI, confidence interval; OR, odds ratios; Ref, reference.

However, when SBP was ≥99.479 mmHg, there was no significant association with the risk of in-hospital mortality (OR = 1.002 [95% CI 0.994~1.011], p = 0.599). Thus, the risk of in-hospital mortality ceased to decrease with increasing SBP beyond this threshold.

Subgroup Analysis

To investigate the potential impact of confounding factors on this association, we performed subgroup analyses, stratified by variables such as Age, Sex, Race, Nor epinephrine, Dopamine, Epinephrine, Phenylalanine, Vasopressin, acute myocardial infarction, Diabetes, and hepatic failure. The findings, including their interactions, are presented in the Supplement Figure 1. Remarkably, none of the subgroups demonstrated statistically significant associations (P > 0.05).

Discussion

This retrospective cohort study involving American ICU patients with COPD and CHF revealed an L-shaped relationship between systolic blood pressure (SBP) and in-hospital mortality. The critical inflection point was approximately 99.479 mmHg. The robustness of this relationship was affirmed by both stratified and sensitivity analyses.

Table 3 Threshold Effect Analysis of Relationship of SBP with in-Hospital Mortality Rate

	Adjusted OR_95CI	P value
Two model		
SBP≤99.479 mmHg	0.939 (0.902~0.976)	0.0017
SBP≥99.479 mmHg	1.002 (0.994~1.011)	0.599
Likelihood Ratio test	–	<0.001

Notes: Adjusted for demographic variables (sex, age, race), Concomitant disease (diabetes, AMI, MC, HepF), Medical Procedures (Vent, Intubated), Medication situation (Norepinephrine Dopamine Epinephrine Phenylephrine Vasopressin), Basic vital signs (Temperature Respiratory Rate Heart Rate), Blood biochemical indicators (AG BUN Chloride Creatinine Hb MCH MCHC MCV Platelet Potassium Sodium calcium RBC RDW WBC), APSIII, SOFA.

Abbreviations: %, weighted proportion. CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; HepF, hepatic failure; AMI, acute myocardial infarction; APSIII, Acute Physiology III; SOFA, Sequential Organ Failure Assessment; SBP, systolic blood pressure; AG, anion gap; BUN, blood urea nitrogen; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular; hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; RDW, red blood cell distribution width; WBC, white blood cell count; CI, confidence interval; OR, odds ratios; Ref, reference.

While multiple investigations have delved into SBP's impact on in-hospital mortality, certain specific patient populations have been studied. For instance, Bossone et al exclusively explored acute aortic dissection (AAD) patients and identified a nonlinear link between in-hospital mortality and SBP.[11] Conversely, a study of individuals with type 2 diabetes from LSU Health Care Services Division (LSUHCSD) indicated a U-shaped association between SBP and all-cause mortality.[29] This study recommended maintaining SBP within 130–150 mmHg, as levels below 120 mmHg or above 160 mmHg elevated all-cause mortality risk.

The Swedish National Diabetes Register studies[30,31] similarly reported U-shaped associations between SBP and all-cause mortality in diabetic patients, which contrasts with previous findings showing J-shaped associations between blood pressure (BP) and cardiovascular disease outcomes.[32] Notably, patients with pulmonary embolism (PE) displayed heightened risks of all-cause and PE-related mortality with low SBP, particularly below 70 mmHg.[33] In the case of frail older adults, SBP and mortality exhibited a U-shaped relationship, even when adjusted for diastolic blood pressure.[34] It's crucial to acknowledge that prior investigations mainly concentrated on patients with distinct medical conditions, with limited exploration of coexisting congestive heart failure (CHF) and diabetes mellitus (DM). CHF and COPD are significant global causes of morbidity and mortality[35,36], frequently co-occurring due to shared risk factors like tobacco smoking and advanced age. COPD affects around 20% to 30% of HF patients[37–43], contributing to poorer clinical outcomes[40,44], thereby complicating HF management. Our study discerned a notable negative correlation between SBP and mortality, even after accounting for these factors. Compared to patients admitted to general wards, those in the intensive care unit (ICU) experience higher mortality rates and longer hospital stays. Previous research has demonstrated a strong correlation between heart failure and COPD, indicating a rise in combined patient cases.[7,8] Given the elevated mortality rate among ICU patients, it is important to investigate the relationship between systolic blood pressure (SBP) and adverse clinical outcomes in these inpatients. Despite the lack of studies focusing on the association between blood pressure (BP) and mortality risk, as well as the optimal BP target in ICU patients with COPD and CHF, it is crucial to consider the impact of cardiopulmonary function on BP values. The optimal BP range for patients with COPD and CHF may differ from that of the general population, making it clinically significant to establish thresholds for BP levels that could either increase or decrease the frequency of adverse events. Our study addresses this gap in the literature by revealing a significant negative correlation between SBP and in-hospital mortality in patients with COPD and CHF.

Another vital discovery presented here is the compelling evidence for employing smooth curve fitting and generalized additive models to investigate the L-shaped linear relationship between SBP and in-hospital mortality among patients with congestive heart failure and COPD. On the lower side of the inflection point (SBP ≤ 99.479 mmHg), the risk of in-hospital deaths in COPD and CHF patients lessened by 6.1% for each additional 1 mmHg of admission SBP. Conversely, this relationship was not observable on the higher side of the inflection point (SBP > 99.479 mmHg) [1.002 (95% CI 0.994~1.011), p = 0.599]. These findings underscore the significance of controlling appropriate SBP in clinical practice. SBP, readily measurable in ICU settings, can promptly indicate changes in a patient's vital signs. Blood pressure reflects myocardial contractility, blood volume, and vascular tension changes, making dynamic monitoring vital. Moreover, subgroup analysis bolstered the robustness and consistency of these outcomes.

Our study boasts several notable strengths. It marks the first-ever exploration of the connection between systolic blood pressure (SBP) and in-hospital mortality among ICU-admitted patients with congestive heart failure (CHF) and COPD. By employing restricted cubic splines to model continuous variables, we could investigate nonlinear associations. To ensure the robustness of our findings, we employed logistic regression analysis with multiple models to account for confounding factors, complemented by pertinent subgroup analyses.

Nonetheless, we must acknowledge specific limitations inherent in our study. Initially, SBP values could have been influenced by diverse factors like pre-ICU vasopressor usage and pre-existing hypertension. Moreover, lung function indicators may prompt more information when subgrouping, and admission to the ICU is also important. Unfortunately, the MIMIC-IV database lacked these details, necessitating further investigations in subsequent studies to comprehend their impact on patients' prognosis. Furthermore, our study solely considered the initial SBP reading post-ICU admission, neglecting SBP's temporal dynamics. Nevertheless, this initial measurement likely offers valuable insights into SBP at the hospitalization's outset. Lastly, extending our study's outcomes to other countries or ICU settings demands caution, as the research was confined to a single US-based ICU facility. Nevertheless, the substantial and representative sample size bolsters our findings' reliability. To enhance future validation and applicability, we suggest conducting multicenter prospective studies.

Conclusions

The study reveals an L-shaped association between systolic blood pressure (SBP) and in-hospital mortality in patients with COPD and congestive heart failure (CHF). The association exhibits an inflection point at approximately 99.479 mmHg. These findings not only contribute to the existing literature but also offer valuable insights into the underlying pathogenesis of this relationship. To bolster the validity and coherence of these results, future research should consider adopting prospective, randomized, controlled study designs.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request. To obtain the application executable files, please contact the author Kai Zhang by Email zhangkai7018@jlu.edu.cn.

Ethics Approval and Consent to Participate

The studies involving human participants were reviewed and approved by the Beth Israel Women's Deaconess Medical Center and the MIT Institutional Review Board. This research scheme has been exempted from the requirement of informed consent and approved by the Ethics Committee of Jilin University Second Hospital. The ethics committee waived the requirement of written informed consent for participation.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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