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In-hospital Outcomes of Aspiration Pneumonia Hospitalizations With Acute Heart Failure: A Nationwide Analysis

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ABSTRACT

Background and Objectives: There is a paucity of data regarding the impact of acute heart failure (AHF) on the outcomes of aspiration pneumonia (AP).
Methods: Using National Inpatient Sample datasets (2016 to 2019), we identified admissions for AP with AHF vs. without AHF using relevant International Classification of Diseases, Tenth Revision codes. We compared the demographics, comorbidities, and outcomes between the two groups.
Results: Out of the 121,097,410 weighted adult hospitalizations, 488,260 had AP, of which 13.25% (n=64,675) had AHF. The AHF cohort consisted predominantly of the elderly (mean age 80.4 vs. 71.1 years), females (47.8% vs. 42.2%), and whites (81.6% vs. 78.5%) than non-AHF cohort (all p<0.001). Complicated diabetes and hypertension, dyslipidemia, obesity, chronic pulmonary disease, and prior myocardial infarction were more frequent in AHF than in the non-AHF cohort. AP-AHF cohort had similar adjusted odds of all-cause mortality (adjusted odds ratio [AOR], 0.9; 95% confidence interval [CI], 0.78–1.03; p=0.122), acute respiratory failure (AOR, 1.0; 95% CI, 0.96–1.13; p=0.379), but higher adjusted odds of cardiogenic shock (AOR, 2.2; 95% CI, 1.30–3.64; p=0.003), and use of mechanical ventilation (MV) (AOR, 1.3; 95% CI, 1.17–1.56; p<0.001) compared to AP only cohort. AP-AHF cohort more frequently required longer durations of MV and hospital stays with a higher mean cost of the stay.
Conclusions: Our study from a nationally representative database demonstrates an increased morbidity burden, worsened complications, and higher hospital resource utilization, although a similar risk of all-cause mortality in AP patients with AHF vs. no AHF.

Keywords: Aspiration pneumonia; Heart failure; Outcome assessment; In hospital mortality; United States Agency for Health Care Policy and Research

INTRODUCTION

Aspiration pneumonia (AP) is a frequent condition encountered in a clinical setting and accounts for about 5–15% of patients with community-acquired pneumonia. However, there is a lack of conclusive data regarding its prevalence in hospital-acquired pneumonia.[1] Some of the significant risk factors for developing AP include oropharyngeal dysphagia, which could be a complication of neurological illness like an ischemic stroke or an intraparenchymal hemorrhage; head and neck cancers, motility disorders of the esophagus, alcohol/substance use disorder, and seizure disorder.[1]

Mortality in patients with AP is high. AP has a higher mortality than other forms of pneumonia acquired in the community.[2] A recent study by Gupte et al.[3] showed a mortality rate in patients with AP of 30.1% and a staggering 76% in patients 75 years or older. Elderly patients have a higher incidence of AP.[4] This population is also at risk of having significant heart failure, which can worsen respiratory symptoms and complicate the recovery process. A study revealed a 6.6–7.9% incidence of heart failure in octogenarians.[5] AP may cause sepsis, which worsens heart failure and increases the risk of both cardiogenic and septic shock. These patients may also receive up to 30 mL/kg crystalloid bolus, which can significantly contribute to fluid overload, especially in patients with pre-existing heart failure.[6] To our best knowledge, no studies have been performed that specifically look at the outcomes of AP in patients with or without acute heart failure (AHF). Thus, we aim to identify this unmet research need, study in-hospital mortality, and analyze the length of stay (LOS) and cost of hospitalization in patients of AP with AHF through a nationally representative sample.

METHODS

Data overview/source

We used the National Inpatient Sample (NIS) datasets from 2016 to 2019 to obtain our study cohort. The NIS is supported by the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Projects. The NIS contains about 35 million discharges (weighted) annually. The International Classification of Diseases is used in the NIS to record diagnoses and procedure codes. NIS datasets 2016-2019 utilize the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), and Procedure Coding System (ICD-10-PCS). Variable "KEY_NIS" is associated with an individual hospitalization and subsequent discharge. Since all datasets are de-identified and openly accessible, our study did not require Institutional Review Board permission.

Data selection and study population

AP hospitalizations were identified using appropriate ICD-10-CM codes (**Supplementary Table 1**) in the primary disease diagnosis field. Relevant ICD-10-CM codes were used in the secondary diagnosis fields to extract patients with AHF (**Supplementary Table 1**). The two cohorts comprised the study arms: the AHF cohort and the non-AHF cohort (**Figure 1**).

Baseline variables

Demographic characteristics including age, race, and sex; hospital characteristics including size, region, and teaching status; and patient-specific characteristics, such as the median household income, the primary payer source, and the type of admission, were

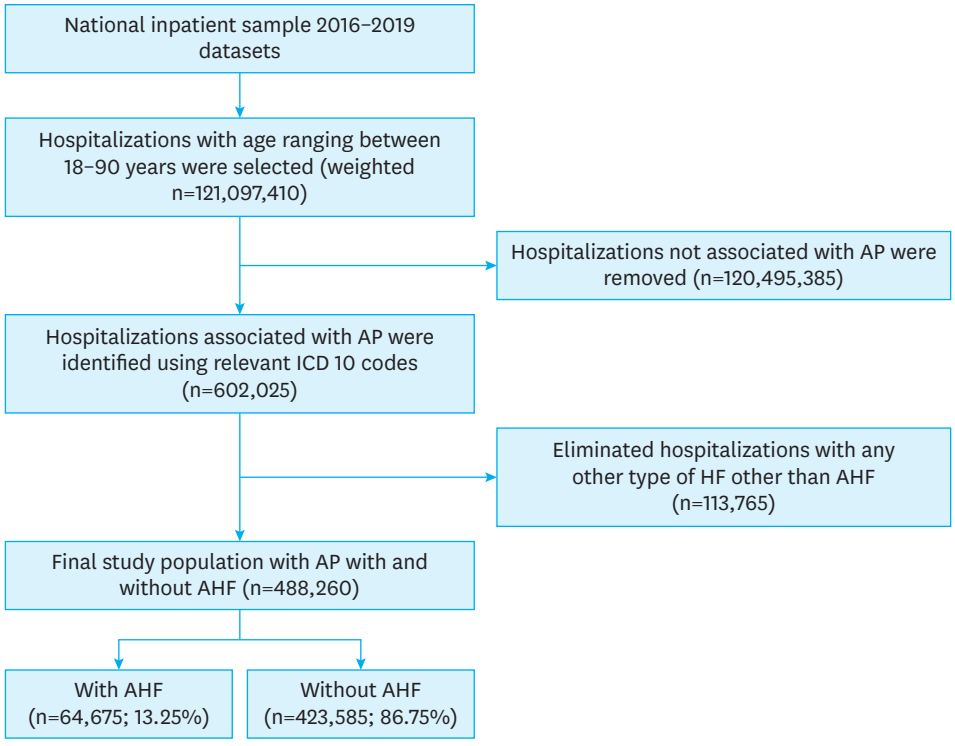

Figure 1. Patient selection and design.
AP = aspiration pneumonia; ICD-10 = International Classification of Diseases, Tenth Revision; AHF = acute heart failure.

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identified using the NIS variables. We used the Elixhauser comorbidity software[7] to compare the prevalence of comorbidities between the two cohorts. Elixhauser comorbidity software uses ICD-10-CM codes in the diagnosis fields and generates the comorbidities as binary variables (**Supplementary Tables 2** and **3**). The comorbidities included hypertension, diabetes mellitus, valvular disease, peripheral vascular disease, cerebrovascular disease, obesity, renal failure, chronic pulmonary disease, liver disease, hypothyroidism and other thyroid disorders, paralysis, dementia, depression, autoimmune disorders, HIV/AIDS, alcohol abuse, and drug abuse. Besides these software-generated comorbidities, we included dysphagia, atrial fibrillation/flutter (aff), dyslipidemia, prior myocardial infarction, prior percutaneous coronary intervention (PCI), prior coronary artery bypass graft, obstructive sleep apnea, tobacco use, cocaine, and cannabis use as the other comorbidity binary variables in our study by utilizing the corresponding ICD-10-CM codes in the secondary diagnosis fields (**Supplementary Tables 2** and **3**).

Outcomes

Our primary outcome was in-hospital all-cause mortality (NIS in-built variable). Secondary outcomes included sepsis, septic shock, cardiogenic shock, need for mechanical ventilation (MV), acute respiratory failure, duration of the requirement of MV, LOS, cost of hospitalization (generated using ICD-10-CM or ICD-10-PCS codes), and 30-day readmission risk (generated from Elixhauser comorbidity software) (**Supplementary Tables 2** and **3**). The cost of hospitalization was generated after matching the variable "TOTCHG," representing the edited total charges of hospitalization per the hospital services for March 2022 provided by the US Bureau of Labor Statistics as consumer price index (**Supplementary Table 4**).

Analysis

We used Stata (version 16) MP edition (Stata Statistical Software, Release 16.; StataCorp LLC, College Station, TX, USA) for statistical analysis. Pearson's chi-square test was used to analyze categorical variables, Student's t-test was used to analyze continuous variables, and the differences between the AHF and non-AHF cohorts were measured. Survey data analysis was further used for univariate and multivariate analysis for the odds ratio (OR) and adjusted odds ratio (AOR) with a 95% confidence interval (95% CI) of the primary and secondary outcomes. We used baseline demographics, patient- and hospital-specific admitting characteristics, and comorbidities in **Table 1** as adjusting variables for multivariate regression analysis. Elixhauser comorbidity index and risk of 30-day all-cause mortality, generated via Elixhauser comorbidity software, were also compared between the two cohorts as a baseline comorbidity.[7]

Table 1. Baseline characteristics of patients hospitalized with aspiration pneumonia from national inpatient sample (2016–2019) stratified by AHF

Characteristics of AP patients (n=488,260, weighted)	AHF absent (n=423,585, weighted 86.75%)	AHF present (n=64,675, weighted 13.25%)	p value
Demographics			
Age at admission (mean, years)	71.1	80.4	<0.001
Sex			<0.001
Males	57.8	52.2	
Females	42.2	47.8	
Race			<0.001
White	78.5	81.6	
African American	10.9	8.7	
Hispanics	7.2	6.3	
Asian/Pacific Islanders	2.9	3.0	
Native Americans	0.6	0.4	
Median household income*			<0.001
0–25th	26.8	24.4	
26–50th	25.9	25.7	
51–75th	24.5	25.1	
76–100th	22.7	24.9	
Primary expected payer			<0.001
Medicare	77.3	89.9	
Medicaid	9.5	3.5	
Private	11.4	6.0	
Self-pay	1.7	0.6	
Hospital-specific admitting characteristics			
Type of admission			<0.001
Non-elective	95.7	97.2	
Elective	4.3	2.8	
Day of admission			0.039
Weekday	73.8	73.0	
Weekend	26.2	27.0	
Bed size of hospital†			0.094
Small	24.7	24.0	
Medium	31.1	32.2	
Large	44.2	43.8	
Location and teaching status of hospital‡			<0.001
Rural	12.7	9.6	
Urban non-teaching	26.0	27.9	
Urban teaching	61.3	62.5	
Region of hospital			<0.001
Northeast	21.3	21.8	
Midwest	21.7	23.3	
South	38.4	35.6	
West	18.6	19.3	
Comorbidities			
Dysphagia§	34.7	33.3	0.003
HTN uncomplicated‖	46.1	9.7	<0.001
HTN complicated‖	15.4	75.6	<0.001
DM without chronic complications‖	12.0	11.1	0.003
DM with chronic complications‖	12.9	26.6	<0.001
Valvular disease‖	1.0	4.3	<0.001
Atrial fibrillation/flutter§	18.5	53.4	<0.001
Peripheral vascular disease‖	6.1	10.6	<0.001
Dyslipidemia§	35.4	48.9	<0.001
Cerebrovascular disease‖	9.3	9.7	<0.001
Paralysis‖	6.8	7.3	0.064
Prior MI§	4.5	11.1	<0.001

(continued to the next page)

Table 1. (Continued) Baseline characteristics of patients hospitalized with aspiration pneumonia from national inpatient sample (2016–2019) stratified by AHF

Characteristics of AP patients (n=488,260, weighted)	AHF absent (n=423,585, weighted 86.75%)	AHF present (n=64,675, weighted 13.25%)	p value
Prior PCI§	3.8	7.8	<0.001
Prior CABG§	4.0	11.3	<0.001
Obesity‖	7.2	13.2	<0.001
Renal failure‖	1.8	2.8	<0.001
Chronic pulmonary disease‖	32.1	43.4	<0.001
OSA§	6.1	10.9	<0.001
Liver disease‖	0.1	0.1	0.485
Hypothyroidism‖	19.7	23.4	<0.001
Other thyroid disorders‖	1.1	1.3	0.018
Dementia‖	29.9	31.3	0.001
Depression‖	16.4	14.5	<0.001
HIV/AIDS‖	0.4	0.1	<0.001
Autoimmune disorders‖	3.4	4.2	<0.001
Tobacco use§	26.5	26.6	0.946
Alcohol abuse‖	5.6	2.8	<0.001
Cocaine use§	0.8	0.3	<0.001
Cannabis use§	1.2	0.4	<0.001
Drug abuse‖	4.0	2.0	<0.001
Elixhauser comorbidity index[8]	3.8	6.3	<0.001

Values are presented as % unless otherwise indicated.
AHF = acute heart failure; AP = aspiration pneumonia; HTN = hypertension; DM = diabetes mellitus; MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; OSA = obstructive sleep apnea; HIV = human immunodeficiency virus; AIDS = acquired immunodeficiency syndrome.
*Represents a quartile classification of the estimated median household income of residents within the patient's zip code, https://www.hcup-us.ahrq.gov/db/vars/zipinc_qrtl/nrdnote.jsp.
†The bed size cutoff points divided into small, medium, and large have been done so that approximately one-third of the hospitals in a given region, location, and teaching status combination would fall within each bed size category. https://www.hcup-us.ahrq.gov/db/vars/hosp_bedsize/nrdnote.jsp.
‡A hospital is considered to be a teaching hospital if it has an American Medical Association-approved residency program. https://www.hcup-us.ahrq.gov/db/vars/hosp_ur_teach/nrdnote.jsp.
§Comorbidities generated separately using relevant International Classification of Diseases, Tenth Revision, Clinical Modification diagnosis codes (**Supplementary Tables 2** and **3**).
‖Comorbidities generated using Elixhauser comorbidity software (**Supplementary Tables 2** and **3**).

To eliminate the baseline differences between the AHF and non-AHF cohorts, we used entropy balancing (EB) as the reweighting method to adjust for covariate imbalances between the two cohorts. Originally, Hainmueller et al.[9] described EB as a generalization of the conventional propensity score method, directly estimating the unit weights from the balanced constraints and matching the two cohorts for mean, variance, and skewness. This allows the researcher to obtain a high degree of covariate balance by imposing a potentially large set of balance constraints as well as helps retain valuable information in the preprocessed data by allowing the unit weights to vary smoothly across units.[9] Next, in the post-EB population (n=6,406 in each cohort), multivariate logistic regression for AOR for categorical outcomes and Poisson regression for incidence rate ratio for continuous outcomes was performed. EB was successful for age, sex, hospital-specific admitting characteristics, median household income, and all the comorbidities, as mentioned in **Table 1**. After that, the multivariate model was used to obtain the predicted probability of all-cause in-hospital mortality (ACM) and adjusted risk ratio between the two cohorts. A p value of < 0.05 (95% CI) was chosen.

Ethics statements

We used the publicly available National Inpatient Sample (NIS) datasets from 2016 to 2019 without any way to trace the identity of the patients. Therefore, this study did not require Institutional Review Board approval and informed consent was not obtained.

RESULTS

Out of the 121,097,410 weighted discharges in the NIS datasets 2016–2019, 602025 AP-related hospitalizations were obtained between 2016 and 2019. Next, using the relevant ICD-10-CM codes, we included only patients with AHF and eliminated those individuals who had heart failure of any other type. Thus, there were 488260 hospitalizations for AP in our study population, of which 13.25% (n=64,675) had AHF and 86.75% (n=423,585) did not.

We compared the baseline demographics, patient-specific, hospital-specific characteristics and comorbidities between the two cohorts (**Table 1**). The AHF cohort consisted predominantly of elderly (mean age, 80.4 years vs. 71.1 years), females (47.8% vs. 42.2%), whites (81.6% vs. 78.5%), and Medicare enrollees (89.9% vs. 77.3%) as compared to the non-AHF cohort (p<0.001). Looking at hospital-specific admitting characters, the AHF cohort demonstrated a higher percentage of non-elective (97.2% vs. 95.7%, p<0.001), weekend (27% vs. 26.2%, p=0.039), urban teaching, and non-teaching (62.5% vs. 61.3% and 27.9% vs. 26.0%, p<0.001) hospitalizations than non-AHF. Significant regional differences were observed, with Southern centers having the highest number of AP hospitalizations in both population cohorts (p<0.001). AP hospital admissions in the West, Midwest, and Northeast were more likely to have AHF than non-AHF (19.3% vs. 18.6%, 23.3% vs. 21.7%, and 21.8% vs. 21.3%, respectively) whereas, in the South, non-AHF was more common (38.4% vs. 35.6%, p<0.001). There was no difference in the median household income between the cohorts.

Cardiovascular and non-cardiovascular risk factors were compared between the groups. Complicated hypertension (75.6% vs. 15.4%), atrial fibrillation/flutter (53.4% vs. 18.5%), diabetes with chronic complications (26.6% vs. 12.9%), dyslipidemia (48.9%

vs. 35.4%), obesity (13.2% vs. 7.2%), valvular heart disease (4.3% vs. 1.00%), peripheral vascular disease (10.6% vs. 6.1%), cerebrovascular disease (9.7% vs. 9.3%), obstructive sleep apnea (10.9% vs. 6.1%), chronic pulmonary disease (43.4% vs. 32.1%), renal failure (2.8% vs. 1.8%), hypothyroidism (23.4% vs. 19.7%), autoimmune conditions (4.2% vs. 3.4%), dementia (31.3% vs. 29.9%), prior MI (11.1% vs. 4.5%), prior PCI (7.8% vs. 3.8%), and prior CABG (11.3% vs. 4.0%) were significantly more frequent in AHF than the non-AHF cohort (p≤0.001).

We compared the outcomes of patients stratified by AHF with Pearson coefficient p values (**Table 2**) and performed regression analysis for the outcomes (**Table 3**). We then compared the primary and secondary outcomes between the two cohorts before and after EB (**Table 4**, **Figure 2**). For the entropy balanced cohorts, we performed post-regression estimation for predictive probabilities and adjusted risk ratios of outcomes (**Table 5**). All-cause in-hospital mortality, which was the primary outcome of the study, was noted to be 10.5% in the AHF cohort as compared to 6.3% in the non-AHF cohort with higher odds seen in both univariate (OR, 1.70; 95% CI, 1.63–1.85; p<0.001), and multivariate logistic regression before EB (AOR, 1.50; 95% CI, 1.36–1.71; p<0.001). However, after EB, the odds of mortality were similar between the two cohorts (AOR, 0.9; 95% CI, 0.78–1.03; p=0.122). For secondary outcomes, AHF hospitalizations were more likely to experience cardiogenic shock (1.1% vs. 0.2%, post-EB: AOR, 2.2; 95% CI, 1.30–3.64; p=0.003), and use of mechanical ventilation (9.5% vs. 7.5%, post-EB: AOR, 1.3; 95% CI, 1.17–1.56; p<0.001). Use of mechanical ventilation was further sub-grouped based on the duration of ventilation provided; patients with AHF more frequently required therapy for 24 hours to 96 hours (4.5% vs. 3.5%, post-EB: AOR, 1.4; 95% CI, 1.12–1.65; p=0.002) and more than 96 hours (3.8% vs. 2.3%, post-EB: AOR, 2.0; 95% CI, 1.53–2.51; p<0.001). However, after EB, acute respiratory failure, sepsis, septic shock, and the need for mechanical ventilation within 24 hours of admission showed no significant difference. The mean length of hospital stay was longer in the AHF cohort than in the non-AHF cohort (8.3 days vs. 6.0 days, post-EB: AOR, 1.3; 95% CI, 1.26–1.34; p<0.001) with a higher associated mean cost of stay (92,769.8 USD vs. 62,800.4 USD, post-EB: AOR, 1.4; 95% CI, 1.24–1.38; p<0.001). The comorbidity index for the risk of 30-day all-cause readmission was higher in the AHF cohort than in the non-AHF one (4.6 vs. 4.1, p<0.001). The predictive probabilities (**Figure 3**) were higher in AHF for all-cause in-hospital mortality (0.102 vs. 0.073), cardiogenic shock (0.013 vs. 0.006), use of mechanical ventilation (0.097 vs. 0.076), mechanically ventilated of 24–96 hours (0.050 vs. 0.037), mechanically ventilated for 96 hours (0.036 vs. 0.019), acute respiratory failure (0.412 vs. 0.313) than non-AHF (p<0.001).

DISCUSSION

Concomitant acute pulmonary and cardiac failures may portend a poor prognosis. Contemporary data for short-term in-hospital outcomes of AP in AHF patients is unavailable, and therefore we conducted this study from the NIS database. We provide current data with our analysis on the following major points: 1) AHF cohort had a similar ACM compared to non-AHF patients. 2) Higher overall utilization and longer duration of mechanical

Table 2. Outcomes of patients hospitalized with aspiration pneumonia from national inpatient sample (2016–2019) stratified by AHF: outcomes with Pearson coefficient p values

Outcomes	AHF absent (n=423,585, weighted 86.75%)	AHF present (n=64,675, weighted 13.25%)	p value
All-cause in-hospital mortality	6.3	10.5	<0.001
Cardiogenic shock	0.2	1.1	<0.001
Need for mechanical ventilation within 24 hours of admission	5.6	5.6	0.849
Use of mechanical ventilation	7.5	9.5	<0.001
Mechanically ventilated for 24 hours	2.0	1.6	0.013
Mechanically ventilated for 24–96 hours	3.5	4.5	<0.001
Mechanically ventilated for 96 hours	2.3	3.8	<0.001
Acute respiratory failure	27.1	39.8	<0.001
Sepsis	4.3	5.3	<0.001
Septic shock	1.3	2.2	<0.001
Length of hospital stay (mean, days)	6.0	8.3	<0.001
Total cost of hospitalization (mean, USD)*	62,800.4	92,769.8	<0.001
Comorbidity index for risk of 30-day all-cause mortality	1.6	1.7	0.207
Comorbidity index for risk of 30-day all-cause readmission	4.1	4.6	<0.001

AHF = acute heart failure.
*NIS variable "TOTCHG" depicting total charges of hospitalization converted to the total cost of hospitalization in accordance with Consumer Price Index Hospital Expenditure adjustments to March 2022 (**Supplementary Table 4**).

Table 3. Outcomes of patients hospitalized with aspiration pneumonia from national inpatient sample (2016–2019) stratified by acute heart failure: regression analysis for outcomes

Univariate regression analysis	Unadjusted OR	95% CI	p value
All-cause in-hospital mortality	1.7	1.63–1.85	<0.001
Cardiogenic shock	5.4	4.37–6.78	<0.001
Need for mechanical ventilation within 24 hours of admission	1.0	0.93–1.10	0.848
Use of Mechanical ventilation	1.3	1.20–1.37	<0.001
Mechanically ventilated for 24 hours	0.8	0.72–0.96	0.013
Mechanically ventilated for 24–96 hours	1.3	1.19–1.43	<0.001
Mechanically ventilated for 96 hours	1.7	1.50–1.83	<0.001
Acute respiratory failure	1.8	1.71–1.85	<0.001
Sepsis	1.3	1.15–1.36	0.000
Septic shock	1.7	1.46–1.91	<0.001
Length of hospital stay (mean, days)	1.4	1.38–1.43	<0.001
Total cost of hospitalization (mean, USD)*	1.5	1.44–1.51	<0.001

OR = odds ratio; CI = confidence interval.
*NIS variable "TOTCHG" depicting total charges of hospitalization converted to the total cost of hospitalization in accordance with Consumer Price Index Hospital Expenditure adjustments to March 2022 (**Supplementary Table 4**).

Table 4. Multivariate analysis of outcomes in aspiration pneumonia between entropy balanced acute heart failure cohorts from national inpatient sample: multivariate logistic regression analysis for AOR

Multivariate regression analysis	Before entropy balancing			After entropy balancing		
	AOR	95% CI	p value	AOR	95% CI	p value
All-cause in-hospital mortality	1.4	1.22–1.55	<0.001	0.9	0.78–1.03	0.122
Cardiogenic shock	3.8	2.20–6.68	<0.001	2.2	1.30–3.64	0.003
Need for mechanical ventilation within 24 hours of admission	1.1	0.95–1.27	0.221	1.1	0.93–1.31	0.252
Use of mechanical ventilation	1.4	1.22–1.55	<0.001	1.3	1.17–1.56	<0.001
Mechanically ventilated for 24 hours	0.9	0.73–1.22	0.657	0.8	0.61–1.10	0.186
Mechanically ventilated for 24–96 hours	1.3	1.11–1.57	0.001	1.4	1.12–1.65	0.002
Mechanically ventilated for 96 hours	1.9	1.56–2.34	<0.001	2.0	1.53–2.51	<0.001
Acute respiratory failure	1.1	1.04–1.15	<0.001	1.0	0.96–1.13	0.379
Sepsis	1.1	0.92–1.23	0.399	1.0	0.81–1.14	0.651
Septic shock	1.3	0.99–1.61	0.061	1.1	0.83–1.47	0.486
Length of hospital stay (mean, days)	1.3	1.29–1.38	<0.001	1.3	1.26–1.34	<0.001
Total cost of hospitalization (mean, USD)*	1.4	1.29–1.42	<0.001	1.3	1.24–1.38	<0.001

AOR = adjusted odds ratio; CI = confidence interval.

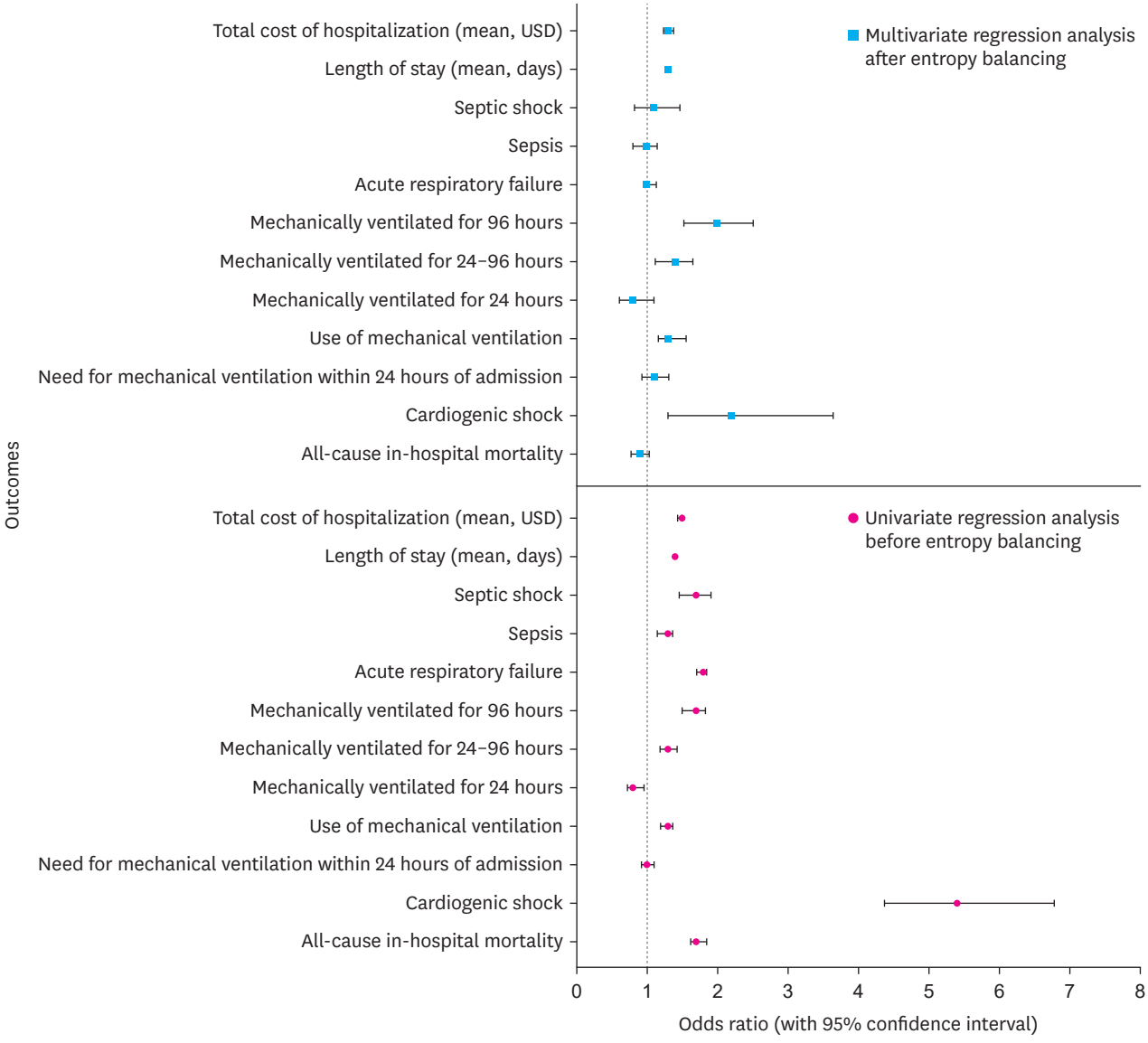

Figure 2. Odds ratio of outcomes before and after entropy balancing.

Table 5. Multivariate analysis of outcomes in aspiration pneumonia between entropy balanced acute heart failure cohorts from national inpatient sample: post-regression estimation for predictive probabilities and adjusted risk ratios of outcomes for entropy balanced AHF cohorts

Outcomes	Probability for non-AHF	Probability for AHF	ARD	ARR	95% CI		p value
All-cause in-hospital mortality	0.073	0.102	0.029	1.4	1.22	1.58	<0.001
Cardiogenic shock	0.006	0.013	0.007	2.1	1.25	3.49	<0.001
Need for mechanical ventilation within 24 hours of admission	0.054	0.059	0.005	1.1	0.94	1.27	0.248
Use of mechanical ventilation	0.076	0.097	0.022	1.3	1.14	1.46	<0.001
Mechanically ventilated for 24 hours	0.021	0.017	−0.004	0.8	0.62	1.10	0.197
Mechanically ventilated for 24–96 hours	0.037	0.050	0.012	1.3	1.11	1.58	0.001
Mechanically ventilated for 96 hours	0.019	0.036	0.017	1.9	1.48	2.36	<0.001
Acute respiratory failure	0.313	0.412	0.099	1.3	1.25	1.39	<0.001
Sepsis	0.062	0.060	−0.002	1.0	0.83	1.12	0.652
Septic shock	0.022	0.024	0.002	1.1	0.84	1.44	0.480

Multivariate regression analysis: adjusted for patient demographics, hospital-admitting characteristics, and comorbidities as in **Table 1**.
AHF = acute heart failure; ARD = adjusted risk difference; ARR = adjusted risk ratio; CI = confidence interval.
*NIS variable "TOTCHG" depicting total charges of hospitalization converted to total cost of hospitalization in accordance to Consumer Price Index Hospital Expenditure adjustments to March 2022 (**Supplementary Table 4**).

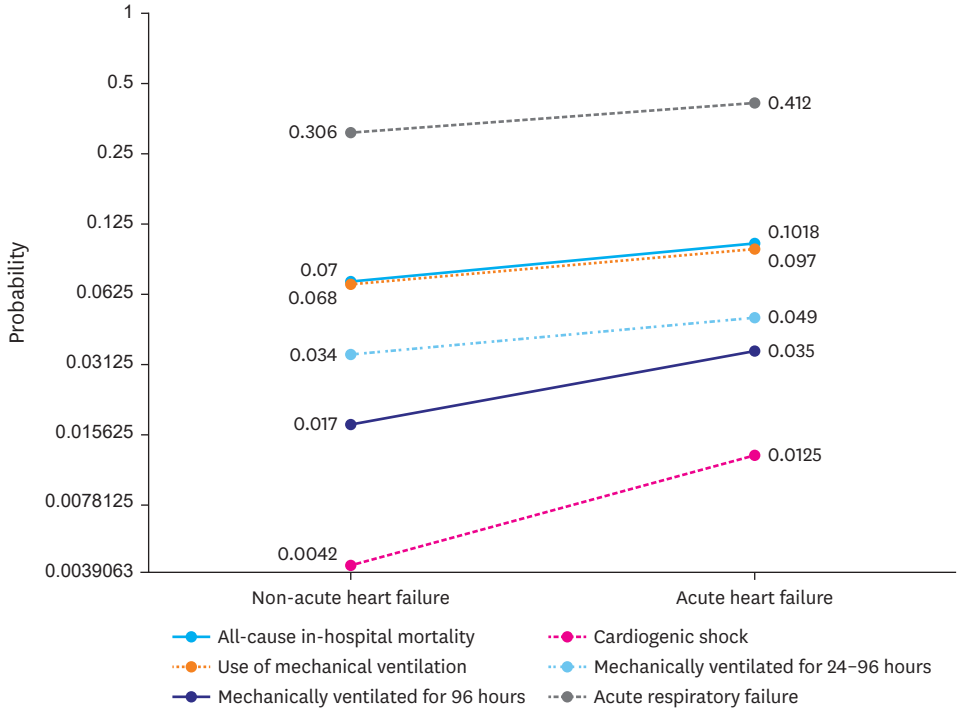

Figure 3. Post-regression estimation for predictive probabilities and adjusted risk ratios of outcomes for entropy-balanced cohorts.

ventilation in the AHF cohort. 3) Resource utilization, including LOS and cost of hospitalization, was significantly higher in the AHF cohort. 4) Serious complications, including cardiogenic shock, were higher in the AHF cohort.

The prevalence of heart failure in patients with AP has varied widely from 7.5% to 52.4% in various studies.[10,13] We believe such a high variation in heart failure prevalence in the study group is likely due to single-center studies, which are prone to variations due to population demographics. None of these studies, however, had a sample size as our study from the NIS database. We report a 13.25% prevalence of AHF in patients with AP. Advanced age significantly contributes to morbidity and mortality in patients with AP and AHF. Older patients are at an increased risk of frailty, oropharyngeal dysphagia, stroke, altered mental status, and dementia – all of which are risk factors for AP. Our study reports a higher mean age in the AHF cohort of 80.4 years compared to the non-AHF group. Heart failure primarily affects older patients, and with each decade after age 65, the incidence of HF doubles in men and triples in women.[14] More than half of patients hospitalized with heart failure are over 75 years old.[15] A retrospective study by Christiansen et al. from national registries of Denmark looking at age-specific trends observed the mean age to be 74 in patients with heart failure.[16] The proportion of females was higher in the AHF cohort in our study, and this is simi-

lar to a previous study by Tandon et al. observing gender disparities in heart failure patients.[17]

Studies have been conducted previously that look at heart failure as a risk factor for mortality in patients with AP; however, it was not the primary goal of these studies. Yoon et al.,[10] in their study on factors implicated in the mortality of patients with AP, did not find heart failure to be a significant factor. The limitation of this study was that it was a single-center retrospective study, and thus data cannot be generalized.[10] Won et al.[18] conducted a study based on data from a national database. They also did not find heart failure statistically significant in increasing the risk of mortality.[18] This study from the Korean national database specifically looked at patients with Parkinson's disease. These are high-risk patients who have Parkinson's disease and AP and are deemed to have higher mortality, irrespective of the comorbidities. Other comorbidities such as hypertension, diabetes, ischemic heart disease, cancer, atrial fibrillation, and chronic kidney disease were also not associated with higher mortality in the patient population in this study. Therefore, as this study looks at a subset of high-risk populations, the results cannot be considered conclusive. Our study from a nationally representative database demonstrates similar in-hospital all-cause mortality in the AHF cohort when compared to the non-AHF cohort despite worse outcomes in terms of increased cardiogenic shock, use of mechanical ventilation, LOS, and total cost of hospitalization. This suggests that the mortality in both groups is likely secondary to the disease of AP itself. We could not analyze the cardiovascular mortality in this study; however, it would be interesting to see whether AHF would lead to higher cardiovascular mortality in AP patients.

Various factors could be attributed to this result and may be considered a limitation of the current study. AP leads to stress in the body and the development of systemic inflammatory response syndrome and, thus, sepsis. Some of the major inflammatory cytokines involved in this process include tumor necrosis factor-alpha, interleukin 1 beta, and interleukin 6.[19] They play a significant role in myocardial depression. An increase in systemic catecholamine and multiorgan failure augments this inflammatory response.[20] These cytokines can also lead to the worsening of diastolic function and an increase in the permeability of the vascular bed. This leads to a clinical picture of hypovolemia which reflexively causes tachycardia, increases myocardial demand, and worsens diastolic function by reducing the diastolic filling time.[21] The results of our study, although specific to AP, are in conjunction with available literature for a broader etiology of sepsis.

Another mechanism by which AHF can lead to worse outcomes is the alteration in lipoprotein metabolism. Infective conditions such as AP predispose to increased plasma triglyceride and free fatty acid levels. This is also associated with decreased energy utilization in the myocardium and other organs. With the majority of the cardiac energy being derived from lipid oxidation, conditions like AP which cause reduced fatty acid oxidation, lead to significant demand-supply mismatch leading to myocardial depression.[22] Patients with baseline congestive heart failure are at increased risk of further such complications and thus contribute to worse outcomes like AHF, mortality, and morbidity. As noted above, patients with AP and AHF are typically elderly. This population is at significant risk of undiagnosed coronary artery disease (CAD) if not yet already diagnosed. AP can lead to significant variations in the hemodynamics of the patient. This, coupled with CAD, can trigger global or regional myocardial ischemia or infarction, leading to increased cardiogenic shock.[23]

Acute respiratory failure from AP further complicates AHF. Decreased oxygen saturation and oxygen supply to the myocardium due to inadequate ventilation by the affected lung segment offer an additional strain on the myocardium. Experiments in animal models have shown that hypoxia induces a reduction in the heart's mechanical function.[24] The results of our study in terms of time to onset and duration of invasive mechanical ventilation in AHF versus non-AHF cohorts of AP are very interesting. Our study shows that patients with AHF and AP have a longer time until mechanical ventilation initiation than the non-AHF group. Once mechanical ventilation is initiated, its duration is also longer in the AHF cohort. This may be due to the early use of non-invasive mechanical ventilation in patients with AHF, which has been shown to be beneficial in preventing/delaying the need for invasive mechanical ventilation.[25] The use of continuous or bilevel positive airway pressure ventilation helps in providing relief and avoiding intubation in patients in the early days. However, once invasive mechanical ventilation is initiated, AHF significantly contributes to respiratory failure from AP and increases the duration of invasive mechanical ventilation required for these patients.

Wu et al.,[26] in their study of the NIS database from 2002 to 2012, noted a median LOS of 6 days for patients admitted with AP. Our study also shows similar results for patients without AHF, but the presence of AHF increases the LOS to a mean of 8.3 days. As noted in the mechanisms above, the presence of AHF increases the risk of complications from AP. Thus, patients with a combination of both AHF and AP are likely to be sicker, requiring longer LOS. The cost of hospitalization is directly associated with LOS. Also, the concurrent management of multiple conditions increases resource utilization and, thus, the cost associated with the hospital stay. However, it is essential to note the increase in the cost of hospitalization in these years. Wu et al.[26] reported a

median cost of $30,280 in 2012 for the management of AP in patients with ages >65 years. Even the non-AHF cohort in our study had a mean cost of $62,800 for the hospitalization, with the AHF cohort having an even higher cost of $92,769. Judicial use of resources is of utmost importance in controlling the rise in hospital prices and expenditures.

The NIS database only allows retrospective analysis of datasets. Despite our careful use of validated ICD 10 diagnosis and procedure codes, there is still a possibility of error in the inclusion and exclusion of the sample population due to coding errors in administrative datasets like NIS. NIS does not provide data on the type, cause, and severity of AP, nor does it provide data on cardiovascular mortality, the hemodynamic parameters of AHF, ejection fraction, number of vasopressors, or pre-or post-procedural status for stratification, and therefore, sub-group analysis was not possible. Based on NIS data, it is not possible to study the procedure's outcomes by high or low-volume hospitalizations. Owing to the possibility of these unmeasured confounders, we preferred to choose EB for reweighting as it balances covariates with mean, variance, and skewness between the two cohorts. Despite these limitations, we provide the contemporary data on the in-hospital outcomes of AHF in AP patients from the large nationally representative database.

Our study from a nationally representative database demonstrates that AP patients with AHF have similar odds of mortality than that those without AHF. However, those with AHF are more prone to developing serious complications, including cardiogenic shock, and the need for mechanical ventilation. This translates to significantly higher hospital resource utilization in those with AHF.

SUPPLEMENTARY MATERIALS

Supplementary Table 1
ICD-10-CM/PCS Codes used in our study

Click here to view

Supplementary Table 2
Comorbidities

Click here to view

Supplementary Table 3
Comorbidities generated using Elixhauser

Click here to view

Supplementary Table 4
Adjusting total cost of hospitalization*

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Conflict of Interest
The authors have no financial conflicts of interest.

Data Availability Statement
We used a publically available anonymous national database, i.e., National Inpatient Sample (datasets from 2016 to 2019).

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REFERENCES

1. Mandell LA, Niederman MS. Aspiration pneumonia. N Engl J Med 2019;380:651-63.
PUBMED | CROSSREF
2. Lindenauer PK, Strait KM, Grady JN, et al. Variation in the diagnosis of aspiration pneumonia and association with hospital pneumonia outcomes. Ann Am Thorac Soc 2018;15:562-9.
PUBMED | CROSSREF
3. Gupte T, Knack A, Cramer JD. Mortality from aspiration pneumonia: incidence, trends, and risk factors. Dysphagia 2022;37:1493-500.
PUBMED | CROSSREF
4. Khadka S, Khan S, King A, Goldberg LR, Crocombe L, Bettiol S. Poor oral hygiene, oral microorganisms and aspiration pneumonia risk in

older people in residential aged care: a systematic review. Age Ageing 2021;50:81-7.
PUBMED | CROSSREF

5. Modi K, Pannu AK, Modi RJ, et al. Utilization of left ventricular assist device for congestive heart failure: inputs on demographic and hospital characterization from nationwide inpatient sample. Cureus 2021;13:e16094.
PUBMED | CROSSREF
6. Arfaras-Melainis A, Polyzogopoulou E, Triposkiadis F, et al. Heart failure and sepsis: practical recommendations for the optimal management. Heart Fail Rev 2020;25:183-94.
PUBMED | CROSSREF
7. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care 1998;36:8-27.
PUBMED | CROSSREF
8. Moore BJ, White S, Washington R, Coenen N, Elixhauser A. Identifying increased risk of readmission and in-hospital mortality using hospital administrative data: the AHRQ Elixhauser Comorbidity Index. Med Care 2017;55:698-705.
PUBMED | CROSSREF
9. Hainmueller J. Entropy balancing for causal effects: a multivariate reweighting method to produce balanced samples in observational studies. Polit Anal 2012;20:25-46.
CROSSREF
10. Yoon HY, Shim SS, Kim SJ, et al. Long-term mortality and prognostic factors in aspiration pneumonia. J Am Med Dir Assoc 2019;20:1098-104.e4.
PUBMED | CROSSREF
11. Hayashi M, Iwasaki T, Yamazaki Y, et al. Clinical features and outcomes of aspiration pneumonia compared with non-aspiration pneumonia: a retrospective cohort study. J Infect Chemother 2014;20:436-42.
PUBMED | CROSSREF
12. Lanspa MJ, Peyrani P, Wiemken T, Wilson EL, Ramirez JA, Dean NC. Characteristics associated with clinician diagnosis of aspiration pneumonia: a descriptive study of afflicted patients and their outcomes. J Hosp Med 2015;10:90-6.
PUBMED | CROSSREF
13. Lanspa MJ, Jones BE, Brown SM, Dean NC. Mortality, morbidity, and disease severity of patients with aspiration pneumonia. J Hosp Med 2013;8:83-90.
PUBMED | CROSSREF
14. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. Circulation 2017;135:e146-603.
PUBMED | CROSSREF
15. Chen J, Dharmarajan K, Wang Y, Krumholz HM. National trends in heart failure hospital stay rates, 2001 to 2009. J Am Coll Cardiol 2013;61:1078-88.
PUBMED | CROSSREF
16. Christiansen MN, Køber L, Weeke P, et al. Age-specific trends in incidence, mortality, and comorbidities of heart failure in Denmark, 1995 to 2012. Circulation 2017;135:1214-23.
PUBMED | CROSSREF
17. Tandon V, Stringer B, Conner C, et al. An observation of racial and gender disparities in congestive heart failure admissions using the national inpatient sample. Cureus 2020;12:e10914.
PUBMED | CROSSREF
18. Won JH, Byun SJ, Oh BM, Park SJ, Seo HG. Risk and mortality of aspiration pneumonia in Parkinson's disease: a nationwide database study. Sci Rep 2021;11:6597.
PUBMED | CROSSREF
19. Reina-Couto M, Pereira-Terra P, Quelhas-Santos J, Silva-Pereira C, Albino-Teixeira A, Sousa T. Inflammation in human heart failure: major mediators and therapeutic targets. Front Physiol 2021;12:746494.
PUBMED | CROSSREF
20. Mankowski RT, Yende S, Angus DC. Long-term impact of sepsis on cardiovascular health. Intensive Care Med 2019;45:78-81.
PUBMED | CROSSREF
21. Chebl RB, Berbari I, Safa R, et al. Clinical outcome of septic patients with heart failure with preserved ejection fraction presenting to the emergency department of a tertiary hospital: a retrospective cohort study. Front Med (Lausanne) 2020;7:517999.
PUBMED | CROSSREF
22. Drosatos K, Lymperopoulos A, Kennel PJ, Pollak N, Schulze PC, Goldberg IJ. Pathophysiology of sepsis-related cardiac dysfunction: driven by inflammation, energy mismanagement, or both? Curr Heart Fail Rep 2015;12:130-40.
PUBMED | CROSSREF
23. Merx MW, Weber C. Sepsis and the heart. Circulation 2007;116:793-802.
PUBMED | CROSSREF
24. Pine MB, Caulfield JB, Bing OH, Brooks WW, Abelmann WH. Resistance of contracting myocardium to swelling with hypoxia and glycolytic blockade. Cardiovasc Res 1979;13:215-24.
PUBMED | CROSSREF
25. Miller PE, van Diepen S, Ahmad T. Acute decompensated heart failure complicated by respiratory failure. Circ Heart Fail 2019;12:e006013.
PUBMED | CROSSREF
26. Wu CP, Chen YW, Wang MJ, Pinelis E. National trends in admission for aspiration pneumonia in the United States, 2002–2012. Ann Am Thorac Soc 2017;14:874-9.
PUBMED | CROSSREF