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Outcomes of patients with systolic heart failure presenting with sepsis to the emergency department of a tertiary hospital: a retrospective chart review study from Lebanon

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ABSTRACT

Objectives Patients with congestive heart failure (CHF) may be at a higher risk of mortality from sepsis than patients without CHF due to insufficient cardiovascular reserves during systemic infections. The aim of this study is to compare sepsis-related mortality between CHF and no CHF in patients presenting to a tertiary medical centre.

Design A single-centre, retrospective, cohort study.

Setting Conducted in an academic emergency department (ED) between January 2010 and January 2015. Patients' charts were queried via the hospital's electronic system. Patients with a diagnosis of sepsis were included. Descriptive analysis was performed on the demographics, characteristics and outcomes of patients with sepsis of the study population.

Participants A total of 174 patients, of which 87 (50%) were patients with CHF.

Primary and secondary outcomes The primary outcome of the study was in-hospital mortality. Secondary outcomes included intensive care unit (ICU) and hospital lengths of stay, and differences in interventions between the two groups.

Results Patients with CHF had a higher in-hospital mortality (57.5% vs 34.5%). Patients with sepsis and CHF had higher odds of death compared with the control population (OR 2.45; 95% CI 1.22 to 4.88). Secondary analyses showed that patients with CHF had lower instances of bacteraemia on presentation to the ED (31.8% vs 46.4%). They had less intravenous fluid requirements in first 24 hours (2.75±2.28 L vs 3.67±2.82 L, p =0.038), had a higher rate of intubation in the ED (24.2% vs 10.6%, p=0.025) and required more dobutamine in the first 24 hours (16.1% vs 1.1%, p<0.001). ED length of stay was found to be lower in patients with CHF (15.12±24.45 hours vs 18.17±26.13 hours, p=0.418) and they were more likely to be admitted to the ICU (59.8% vs 48.8%, p=0.149).

Conclusion Patients with sepsis and CHF experienced an increased hospital mortality compared with patients without CHF.

BACKGROUND

Heart failure (HF) and sepsis are major public health concerns, with more than 5.7 million people in the USA affected by HF and more

Strengths and limitations of this study

► First study looking at the toll of sepsis in the high-risk congestive heart failure population.
► Eighty-seven patients with sepsis and heart failure were compared with 87 non-heart failure and septic patients. A descriptive analysis of the patient's demographics was done. The primary outcome was in-hospital mortality.
► Multivariable analysis conducted to minimise confounding bias by using statistically and clinically significant variables.
► A retrospective chart review cohort study. The study was not randomised and is subjected to information and selection bias.
► Single-centre study with a referral tertiary emergency department that deals with regional complicated cases, therefore, the applicability of the results would be affected.

than 1.5 million people diagnosed with sepsis each year.[1 2] Nearly half of the patients with HF die within 5 years of diagnosis, and about 250 000 Americans die from sepsis yearly.[1 3]

One study looked at severe sepsis and septic shock survivors after hospital discharge; they examined a subgroup of patients with HF and showed that they had increased 3-month and 1-year mortalities as compared with the general population.[4] Another study looked at pneumonia patients and studied the prognostic role of HF on mortality. The authors were able to show that the 30-day mortality was 24.4% among patients with heart failure and 14.4% among those without HF.[5] However, to the best of our knowledge, no study has examined the impact of HF on mortality in patients presenting to an emergency department (ED) with sepsis. The aim of this study is therefore to report on the mortality of

Table 1 Demographics

	CHF			
	Total n=174	**Negative n=87**	**Positive n=87**	**P values**
Age, mean±SD	72.80±14.26	72.61±13.91	73.00±14.68	0.663
Gender, male	105 (60.3)	50 (57.5)	55 (63.2)	0.438
Diagnosis				0.760
Sepsis	98 (56.3)	50 (57.5)	48 (55.2)	
Severe/shock	76 (43.7)	37 (42.5)	39 (44.8)	
Hypertension, yes	126 (72.4)	56 (64.4)	70 (80.5)	0.018
Diabetes mellitus, yes	78 (44.8)	34 (39.1)	44 (50.6)	0.127
Dyslipidaemia, yes	49 (28.2)	17 (19.5)	32 (36.8)	0.011
CAD, yes	95 (54.6)	29 (33.3)	66 (75.9)	<0.001
COPD/emphysema, yes	24 (13.8)	11 (12.6)	13 (14.9)	0.660
CKD no HD, yes	40 (23.0)	10 (11.5)	30 (34.5)	<0.001
CKD on HD, yes	16 (9.2)	9 (10.3)	7 (8.0)	0.600
Smoker, yes	50 (28.7)	23 (26.4)	27 (31.0)	0.503
Atrial fibrillation, yes	44 (25.3)	15 (17.2)	29 (33.3)	0.015
Bacteraemic, yes	66 (39.1%)	39 (46.4)	27 (31.8)	0.051
Site of infection				
Lung	71 (40.8)	33 (37.9)	38 (43.7)	0.441
Gastrointestinal	16 (9.2)	12 (13.8)	4 (4.6)	0.036
Urine	61 (35.1)	32 (36.8)	29 (33.3)	0.634
Skin	14 (8.0)	4 (4.6)	10 (11.5)	0.094
Blood	4 (2.3)	2 (2.3)	2 (2.3)	1.000
Gall bladder	8 (4.6)	4 (4.6)	4 (4.6)	1.000
Intravascular catheter	2 (1.1)	2 (2.3)	0 (0.0)	0.497
Others*	12 (6.9)	9 (10.3)	3 (3.4)	0.073

*Includes bone (one patient), heart (one patients), liver (two patients), kidneys (five patients), brain (one patient), colon (one patient), pacemaker (one patient).
CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; HD, haemodialysis.

patients—with and without HF—presenting with sepsis to the ED of a tertiary medical centre, and to examine the associations between HF and mortality in the septic population.

METHODS
Study design and setting
This was a single-centre, retrospective, cohort study conducted in an academic ED of a large tertiary care centre. All patients presenting from January 2010 to January 2015 had their medical records queried via the hospital's electronic health record (EHR) system. All clinical information, including comorbidities, vital signs, laboratory results and resuscitation parameters, were extracted from scanned charts by dedicated research fellows (MK, NEH, CK). Before the initiation of data collection, multiple meetings with the principal investigators were conducted to standardise the data extraction process.

Patient selection
Patients' ED encounters were filtered by an experienced data user using the hospital's EHR via an extensive structured keyword search and ICD-9 coding (International Statistical Classification of Diseases, Ninth Revision and Related Health Problems). The ICD-9 diagnoses retrieved were: sepsis (995.91), severe sepsis (995.92), septicaemia (038), septic shock (785.52) and bacteraemia (790.7). The medical records department at our institution assigns an ICD-9 code after compiling all diagnoses made throughout the patient's hospital stay and that includes the diagnosis made by the ED physician as well as by the intensivist and hospitalist. At the time of the study, sepsis was defined as having a documented or a presumed infection with two or more of the following: temperature >38°C or <36°C, heart rate of >90 bpm, respiratory rate of >20 breaths/min or arterial carbon dioxide tension <32 mm Hg, white cell count (WCC) >12×10^9/L or >10% bands. Septic shock

Table 2 Vital signs and laboratory parameters on presentation to the ED

	Total n=174	CHF Negative n=87	Positive n=87	P values
SIRS criteria				0.266
<2	61 (35.1)	34 (39.1)	27 (31.0)	
≥2	113 (64.9)	53 (60.9)	60 (69.0)	
SBP (mm Hg), mean (±SD)	112.16±27.23	114.12±29.92	110.22±24.29	0.348
DBP (mm Hg), mean (±SD)	62.01±17.42	60.70±17.31	63.30±17.53	0.316
MAP (mm Hg), mean (±SD)	78.34±18.69	78.54±19.69	78.15±17.76	0.774
HR (beats/min), mean (±SD)	97.84±25.70	100.71±27.31	95.01±23.83	0.145
O_2 saturation (%), mean (±SD)	94.74±6.02	94.42±6.28	95.02±5.81	0.181
Temperature (°C), mean (±SD)	37.53±1.15	37.61±1.11	37.45±1.18	0.363
RR (breaths/min), mean (±SD)	22.50±6.24	22.85±6.60	22.14±5.87	0.785
Glucose (mg/dL), mean (±SD)	167.21±105.35	153.69±79.16	175.46±118.42	0.662
Lactate (mmol/L), mean (±SD)	4.29±3.98	4.13±3.31	4.40±4.41	0.856
WCC (x10^9/L), mean (±SD)	14930.64±9671.00	16627.91±11 493.65	13252.87±7124.63	0.049
Absolute neutrophil count, mean (±SD)	12287.41±7739.01	13637.54±9054.72	10968.68±5954.86	0.072
Haemoglobin (g/dL), mean (±SD)	11.30±1.89	11.12±2.04	11.48±1.71	0.207
Haematocrit (%), mean (±SD)	33.76±5.74	32.95±6.09	34.56±5.28	0.065
Bicarbonate (mmol/L), mean (±SD)	20.86±6.07	20.72±5.57	21.00±6.55	0.761
BUN (mg/dL), mean (±SD)	47.11±32.45	39.70±29.63	54.53±33.60	<0.001
Creatinine (mg/dL), mean (±SD)	2.21±1.97	2.11±2.23	2.32±1.67	0.004
Arterial pH, mean (±SD)	7.35±0.13	7.35±0.13	7.35±0.14	0.867
$PaCO_2$ (mm Hg), mean (±SD)	34.86±12.82	32.97±9.72	36.28±14.65	0.387
PaO_2/FiO_2 (mm Hg), mean (±SD)	264.02±133.52	211.50±136.46	303.41±117.88	<0.001
Total bilirubin (mg/dL), mean (±SD)	1.58±2.32	1.82±2.79	1.41±1.94	0.862
Troponin (ng/mL), mean (±SD)	0.19±0.40	0.11±0.14	0.26±0.51	0.026
CKMB (µg/L), mean (±SD)	11.35±19.63	11.25±17.25	11.41±21.36	0.869
Pro-BNP (pg/mL), mean (±SD)	20619.57±26 500.81	9779.73±13 343.62	25587.83±29 644.64	0.012

Treatments received, lengths of stay and disposition.
BUN, blood urea nitrogen; CHF, congestive heart failure; CKMB, Creatine Kinase Muscle Brain; DBP, diastolic blood pressure; ED, emergency department; FiO_2, fractional inspired oxygen; HR, heart rate; MAP, mean arterial pressure; O2, oxygen saturation; $PaCO_2$, arterial carbon dioxide tension; PaO_2, arterial oxygen tension; Pro-BNp, Pro Brain Natriuretic Peptide; RR, respiratory rate; SBP, systolic blood pressure; SIRS, systemic inflammatory response syndrome; WBC, white cell count.

was defined as having sepsis with any of the following: systolic blood pressure <90 mm Hg or mean arterial pressure <65 mm Hg or lactate >2 mmol/L after an initial fluid challenge. Severe sepsis was considered positive if patients had evidence of organ dysfunction. Bacteraemia was coded if skin flora pathogens were grown from two blood cultures or non-skin flora pathogens were grown from a single blood culture.

Patients younger than 18 years of age, pregnant or presenting secondary to trauma were excluded.

Exposure: systolic heart failure

Patients who met the inclusion criteria were stratified according to the presence of underlying systolic HF (SHF). SHF was identified via the revision of echocardiography reports performed by American board-certified cardiologists at our institution. The echocardiography report was considered valid if the procedure was performed at most 1 year before the admission date. Patients with a left ventricular ejection fraction (EF) of ≤40% were included in the heart failure cohort. Patients exhibiting echocardiographic evidence of diastolic dysfunction or preserved EF HF were excluded. All other patients were included in the non-heart failure cohort.

Sample size calculation

After an extensive literature search for patients with congestive HF (CHF) and sepsis-related mortalities, we hypothesised that the sepsis-related mortality in patients with CHF would be around 38.7% and 18.4% for the non-CHF population.[6 7] Assuming a study power of 80% and a confidence level of 95%, the sample size needed was 174 patients.

Table 3 Sepsis treatment variables and patient's length of stay

		CHF		
	Total n=174	**Negative n=87**	**Positive n=87**	**P values**
Intravenous fluid requirement in first 6 hours (L), mean (±SD)	1.65±1.69	1.96±2.04	1.34±1.19	0.236
Intravenous fluid requirement in first 24 hours (L), mean (±SD)	3.20±2.59	3.67±2.82	2.75±2.28	0.038
Furosemide use within the first 24 hours, yes	33 (21.3)	9 (10.8)	24 (33.3)	0.001
Furosemide use in the ED, yes	24 (13.9)	7 (8.1)	17 (19.5)	0.030
Intubation in the ED, yes	25 (16.6)	9 (10.6)	16 (24.2)	0.025
Intubation within the first 48 hours, yes	51 (29.3)	18 (20.7)	33 (37.9)	0.012
Use of vasopressor in the first 24 hours, yes	59 (33.9)	24 (27.6)	35 (40.2)	0.078
Vasopressor use: norepinephrine, yes	54 (31.0)	23 (26.4)	31 (35.6)	0.190
Vasopressor use: dopamine, yes	17 (9.8)	4 (4.6)	13 (14.9)	0.022
Time to vasopressor use within first 24 hours (hours), mean (±SD)	7.47±7.23	7.92±7.73	7.16±6.97	0.911
Vasopressors treatment duration within first 24 hours (hours), mean (±SD)	108.12±158.29	117.21±111.96	101.89±184.84	0.046
Inotrope use in first 24 hours: dobutamine, yes within first 24 hours	15 (8.6)	1 (1.1)	14 (16.1)	<0.001
Time to dobutamine use within first 24 hours (hours), mean (±SD)	11.71±8.56	23	10.90±8.27	0.181
Dobutamine treatment duration within first 24 hours (hours), mean (±SD)	110.80±79.67	312	96.43±59.15	0.133
Steroid use, yes	49 (28.2)	25 (28.7)	24 (27.6)	0.866
Steroid treatment duration (hours), mean (±SD)	167.14±322.53	169.44±382.75	164.10±230.56	0.537

ED, emergency department; CHF, congestive heart failure.

Outcome measures

The primary outcome of the study was in-hospital mortality. Secondary outcomes included 72-hour mortality ED, intensive care unit (ICU) and hospital lengths of stay, and differences in interventions between the two groups. Lengths of stay were calculated for the patients who survived to discharge.

The infection site was determined from documentation in the medical record, culture results (blood, sputum, urine, other fluids) and/or radiology reports (such as chest X-rays). The infection source was deemed to be blood if the patients were bacteraemic and no other source of infection was identified. Vital signs were obtained from the scanned ED triage sheets. Laboratory results from blood drawn on the day of ED admission were obtained from the hospital's EHR system. Information about medications used, time to their initiation and duration of their use was obtained by reviewing the scanned ED order sheet.

Disposition status was also recorded by reviewing admission and discharge documents scanned to the hospital's EHR.

Patient and public involvement

This was a retrospective chart review study. Patients and the public were not involved in the design or the recruitment of the study.

Statistical analysis

Statistical analyses were performed using SPSS V.24.0 (IBM). The distributions of the continuous and categorical variables were presented as mean±SD and frequency/percentages,

respectively. The different parameters were then stratified by whether or not patients had CHF (CHF or non-CHF). Pearson's χ^2 test was used to assess for statistical significance for the categorical variables, while the Student's t-test and the Mann-Whitney U test were used for the continuous ones. All continuous variables were checked for normality of distribution using the Shapiro-Wilk test, Kurtosis and Skewness Z-score, and visualisation of histograms. Tests were interpreted at a significance level alpha=0.05. A multivariable analysis was performed to ascertain the association between HF status and mortality in the septic population via a logistic regression. A backward selection procedure, with the significance level for variable removal from the model set at 0.05, was conducted. The independent variables chosen for modelling were those found to be significant at the bivariate analysis level in addition to those considered clinically meaningful. The variables included in the model were: CHF status, age, gender, diagnosis of severe sepsis or septic shock (with sepsis as the reference), hypertension (HTN), diabetes mellitus (DM), dyslipidemia (DL), coronary artery disease (CAD), chronic obstructive pulmonary disease, smoking status, chronic kidney disease (CKD) on haemodialysis (HD), atrial fibrillation, bacteraemia, bicarbonate, blood urea nitrogen (BUN) and creatinine. The results were described as ORs and their corresponding 95% CI.

RESULTS
Population characteristics

A total of 174 patients were included in the study, of which 87 (50%) had CHF (table 1). The mean age was

Table 4	Lengths of stay (LOS) and in-hospital mortalities			
			CHF	
	Total n=174	Negative n=87	Positive n=87	P values
Admission disposition				0.149
ICU	94 (54.3)	42 (48.8)	52 (59.8)	
GPU	79 (45.7)	44 (51.2)	35 (40.2)	
Disposition from the hospital				0.003
Dead	80 (46.0)	30 (34.5)	50 (57.5)	
Discharge home	90 (51.7)	56 (64.4)	34 (39.1)	
Transfer to long-term facility	4 (2.3)	1 (1.1)	3 (3.4)	
Hospital mortality	80 (46.0)	30 (34.5)	50 (57.5)	0.002
72 hours mortality	13 (7.5)	4 (4.6)	9 (10.3)	0.149
Antibiotics initiated in the				0.346
ED	150 (86.2)	73 (83.9)	77 (88.5)	
GPU	13 (7.5)	9 (10.3)	4 (4.6)	
ICU	11 (6.3)	5 (5.7)	6 (6.9)	
Time to initiation of antibiotics (hours), mean (±SD)	2.83±1.75	2.99±1.84	2.66±1.65	0.234
ED LOS (hours), mean (±SD)	16.64±25.27	18.17±26.13	15.12±24.45	0.418
ED LOS (days), mean (±SD)	0.69±1.05	0.76±1.09	0.63±1.02	0.418
ICU LOS (hours), mean (±SD)	270.15±395.26	260.83±380.45	277.50±410.10	0.789
ICU LOS (days), mean (±SD)	11.26±16.47	10.87±15.85	11.56±17.09	0.789
GPU LOS (hours), mean (±SD)	200.56±193.89	190.15±164.66	213.65±227.24	0.935
GPU LOS (days), mean (±SD)	8.36±8.08	7.92±6.86	8.90±9.47	0.935
Hospital LOS (hours), mean (±SD)	276.14±265.90	289.13±298.35	256.11±208.57	0.482
Hospital LOS (days), mean (±SD)	11.51±11.08	12.05±12.43	10.67±8.69	0.482
Hospital LOS among discharge home (hours), mean (±SD)	277.20±268.28	284.22±298.71	265.65±212.55	0.699
Hospital LOS among discharge home (days), mean (±SD)	11.55±11.18	11.84±12.45	11.07±8.86	0.699

ED, emergency department; CHF, congestive heart failure; ICU, intensive care unit; GPU, general practice unit.

73.00 (±14.68) and 72.61 (±13.91) years for patients with and without CHF, respectively. There were more male patients among patients with CHF as compared with patients without CHF (63.2% vs 57.5%). The CHF cohort had a higher percentage of hypertensive (80.5% vs 64.4%), diabetic (50.6% vs 39.1%), CAD (75.9% vs 33.3%, p<0.001), as well as CKD (34.5% vs 11.5%, p<0.001) patients. Table 1 summarises the patients' comorbidities.

Presentation to the ED
Patients with CHF had lower instances of bacteraemia on presentation to the ED compared with patients without CHF (31.8% vs 46.4%). The most common infection sites for patients with CHF were lung (43.7%), followed by urine (33.3%), skin (11.5%) and gastrointestinal tract (4.6%). As compared with the control group, patients with CHF had less gastrointestinal infections (4.6% vs 13.8%) but more skin infections (11.5% vs 4.6%). A complete list of infection sites can be found in table 1.

Vital signs and laboratory tests
The two cohorts had comparable vital signs at presentation. They also had similar lactate, haemoglobin,

bicarbonate, bilirubin and Creatine Kinase Muscle Brain (CKMB) levels. The CHF cohort, however, had lower WCC (x10^9/L) (12711±7065 vs 15570±10 854; p=0.02) but higher BUN (in mg/dL) (54.53±33.60 vs 39.70±29.63, p<0.001) and creatinine (2.32±1.67 vs 2.11±2.23, p=0.004) levels. Table 2 summarises the laboratory values all the patients.

Patients with known CHF had less intravenous fluid requirements in the first 6 hours (1.34±1.19 L vs 1.96±2.04 L, p=0.236) and in the first 24 hours (2.75±2.28 L vs 3.67±2.82 L, p=0.038), as well as more furosemide use in the ED (19.5% vs 8.1%, p=0.03) and within the first 24 hours (23.4% vs 10.8%, p=0.041). Patients with CHF had higher rates of intubation in the ED (24.2% vs 10.6%, p=0.025) and within the first 48 hours (37.9% vs 20.7%, p=0.012). Patients with CHF received more dopamine (14.9% vs 4.6%, p=0.022) and more dobutamine in the first 24 hours (16.1% vs 1.1%, p<0.001) (table 3). In the majority of patients (86.2%), antibiotics were initiated in the ED, with no statistically significant difference in how rapidly (in hours) antibiotics were initiated among the two cohorts (2.66±1.65 vs 2.99±1.84, p=0.234). ED

Table 5 Multivariable logistic regression of the association of heart failure and hospital mortality

Hospital mortality (reference: no)		
Variables	OR (95% CI)	P values
CHF		
Positive	2.45 (1.22 to 4.88)	0.01
Diagnosis		
Severe sepsis/septic shock	4.45 (2.21 to 8.98)	<0.0001
Bacteraemia		
Yes	0.29 (0.14 to 0.61)	0.001
Gender		
Male	2.01 (0.98 to 4.13)	0.06

Variables included in the model were:
Age; gender (reference: female); CHF; Diagnosis (reference: sepsis); HTN (reference: no); DM (reference: no); DL (reference: no); CAD (reference: no); COPD (reference: no); smoker (reference: no); CKD on HD (reference: no); atrial fibrillation (reference: no); bacteraemia (reference: no); lactate; bicarbonate; BUN; creatinine.
BUN, blood urea nitrogen; CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; DM, diabetes mellitus; HD, haemodialysis; HTN, hypertension.

length of stay was found to be lower in patients with CHF (15.12±24.45 hours vs 18.17±26.13 hours, p=0.418). Of all the patients, 54.3% were admitted to the ICU and 45.7% to the general practice unit. One patient passed away before in-hospital admission. Patients with CHF were more likely to be admitted to the ICU (59.8% vs 48.8%, p=0.149) as compared with the control group. Furthermore, patients with CHF had a higher in-hospital mortality (57.5% vs 34.5%), a higher 72-hour mortality (10.3% vs 4.6%, p=0.149) and a lower chance of being discharged home (39.1% vs 64.4%) (p=0.003). Details about patient mortalities and lengths of stay can be seen in table 4.

In-hospital mortality analysis

A multivariable analysis was performed to determine association between HF status and hospital mortality considering all clinically relevant and statistically significant variables in the bivariate analysis (table 4). Age, gender, diagnosis (sepsis, severe sepsis or septic shock), comorbidities (CHF, HTN, DM, dyslipidemia (DL), CAD, CKD on HD, atrial fibrillation), bacteraemia were chosen as factors to be controlled for, due to their clinical relevance and the statistical difference between the patients with CHF and no CHF. A history of CHF was found to have greater odds of in-hospital mortality (OR 2.45, 95% CI 1.22 to 4.88), as well as diagnosis of severe sepsis or septic shock (OR 4.45, 95% CI 2.21 to 8.98), while adjusting for other confounders. Meanwhile, it was shown that patients who were bacteraemic (OR 0.29, 95% CI 0.14 to 0.61) had lower odds of death. The results of the multivariable analysis can be seen in table 5.

DISCUSSION

In this cohort study of 174 patients with sepsis, our results showed that the patients with SHF had 2.716 greater odds of dying in the hospital than non-HF patients. Although there is limited research on this topic, a study by Lemay *et al* showed that patients with sepsis and CHF had a 1.28 HR for mortality between 90 and 365 days after their admission, and an HR of 1.63 for mortality after 365 days.[8] One possible explanation for the increased mortality is the myocardial dysfunction caused by sepsis, which places further strain on the weak heart. Cardiac dysfunction in patients with sepsis manifests as a reduced EF, which prevents the heart from increasing its cardiac output and meeting the metabolic demands needed to fight off the infection. This vicious cycle continues and may hasten the plunge into severe sepsis and septic shock.[9]

Although the most common site of infection was the pulmonary system, our patients with sepsis and CHF had an unusually higher number of skin infections as compared with non-CHF patients. This can be due to several factors. First and foremost, the chronic oedema arising from the chronic fluid overload state can lead to small breaks in the skin which can act as an entry point for bacteria. Furthermore, the low cardiac output and poor skin microcirculation can prevent the body from fighting off the infection.[10 11]

Several laboratory abnormalities were highlighted in our results and are worth exploring in more depth. Our CHF cohort had a lower absolute neutrophil count, highlighting a possible underlying bone marrow dysfunction in patients with CHF. A previous study by Westenbrik *et al* showed a link between chronic HF and bone marrow dysfunction. This association was thought to arise through the activation of the tumor necrosis factor Alpha/(TNF-α/Fas) pathway, which ultimately leads to decreased haematopoiesis.[12 13] This bone marrow dysfunction and resulting leucopoenia might have contributed to the increased mortality in our patients. Furthermore, in our study, patients with CHF had a higher creatinine level compared with non-CHF patients. This can be due to the fact that CKD is very prevalent in patients with HF, as it is present in about 30%–40% of that population.[14–16] Sepsis has been shown to cause myocardial suppression as well cytokine-mediated systemic vasodilation. Both factors might have contributed to the higher creatinine in the CHF cohort.[17]

In our study, although patients with CHF received less intravenous fluids and more furosemide than their non-CHF counterparts, they still had higher rates of intubation as compared with those without CHF. The higher cardiac filling pressure of patients with CHF, and the latter's predisposition to develop pulmonary oedema can explain this.

The length of stay in the ED was found to be lower in patients with HF. To our knowledge, no previous study compared ED length of stay between two such cohorts. A possible explanation to our findings is the greater availability of beds in the cardiac ICU (CICU) at our

institution as compared with the medical ICU, and this is further highlighted in our study by the higher admission rate of patients with CHF to CICU as compared with non-CHF patients.

At the time of this study, the surviving sepsis campaign defined sepsis as a suspected or a documented source of infection plus 2 systemic inflammatory response syndrome (SIRS) criteria. The majority of patients in both cohorts presented with two or more SIRS criteria, showing that in accordance with the literature, SIRS criteria have a high sensitivity.[18] However, it is important to note that 37 (34.9%) patients with sepsis and HF were found to have less than two SIRS criteria at presentation. SIRS-negative sepsis is common, as it has been shown that about 12% of patients with sepsis have less than two SIRS criteria at presentation.[19 20] The low specificity of the SIRS criteria pushed the international community to change the definition of sepsis and to rely on the quick sepsis related organ failure assessment (qSOFA) score instead. Nevertheless, emergency physicians should always have a low threshold to suspect sepsis in patients with HF, as their vital signs may be misleading.[21]

Finally, in our multivariable regression, a history of HF was found to have greater odds of in-hospital mortality as compared with the non-HF population. While we showed this in our study, we are not aware of any studies that established HF as an independent risk factor for mortality in patients with sepsis. We find it interesting that in our study, bacteraemia was associated with lower odds of hospital mortality, despite existing evidence that suggests otherwise.[22] Information about the specific bacterial isolates along with their antimicrobial resistance and sensitivity patterns can lead to more appropriate, targeted antibacterial therapy, which may contribute to lowering the hospital mortality of bacteraemic patients.

LIMITATIONS

This was a retrospective chart review cohort study and, as such, the authors are aware of the inherent limitations of such a type of study. To minimise biases, frequent meetings were held between the principal investigator and data collectors to standardise the way in which data were collected, entered and cleaned. The increased mortality seen in the HF cohort could be due to several reasons. First and foremost, the study is from a referral tertiary centre ED that deals with regional complicated cases, which could limit the generalisability of the results to the whole HF subpopulation. Second, the delay in antibiotic administration might have led to the increased morality, as it has been shown in the literature.[23] In the analysis stage, the equally numbered groups were found to be unmatched and possibly difficult to compare and conclude meaningful evidence from. In an effort to correct for this, a bivariate analysis was performed, and characteristics that were statistically different between the populations—along with clinically meaningful elements—were controlled for in the multivariable analysis in order to minimise confounding variables. It is important to note that our secondary outcomes are the result of univariate analysis and as such are subject to confounders. These secondary outcomes are exploratory outcomes, as our study was powered to detect mortality differences. As such our results should be interpreted with caution. Another limitation of the study is the exclusion of patients with HF with EF. We understand that this is a substantial subgroup of patients with HF, but we chose to exclude these patients because we believe that these patients have a poorer prognosis than patients with SHF and we are conducting a study looking at the mortality of these specific patients as compared with the SHF population.

CONCLUSION

In summary, patients with CHF with sepsis experienced higher in-hospital mortality than patients without CHF, which was more pronounced in patients with severe sepsis and those intubated within 48 hours of ED admission. These vulnerable patients may benefit from a multidisciplinary approach and an admission to an ICU to ensure continued monitored aggressive care, optimised postdischarge follow-up and possibly improved clinical outcomes.

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