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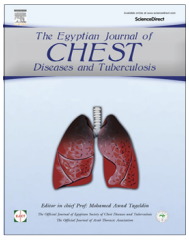

ORIGINAL ARTICLE

Outcome of community-acquired pneumonia with cardiac complications

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KEYWORDS

Pneumonia;
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Abstract *Background:* Although pneumonia is a leading cause of death, little consideration has been given to understanding the contributors to this mortality. Previous studies have suggested an increased mortality in pneumonia patients who develop cardiac complications. The aim of this study was to examine the risk factors and outcome of cardiac complications in admitted patients with community-acquired pneumonia.

Patients and methods: This study included 130 patients hospitalized with a primary diagnosis of community-acquired pneumonia. All patients were subjected to complete medical history, general and local chest examination, Laboratory investigations (complete blood count, renal and hepatic function tests, serum electrolytes, blood sugar, arterial blood gas analysis, CRP, procalcitonin, BNP, cardiac enzymes, blood and sputum Gram stain and culture, sputum PCR for *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Coxiella burnetii*, and *Chlamydophila* species, urine antigen testing for *S. pneumoniae* and *L. pneumophila*, pharyngeal swabs for viral PCR.), radiological investigations, electrocardiographic studies (ECG) and echocardiography.

Results: Among the studied 130 patients, 32 patients (24.6%) had cardiac complications [new or worsening heart failure in16 patients (12.3%), arrhythmias in 12 patients (9.2%), and acute myocardial infarction in 4 patients (3.1%)]. In comparing patients who developed cardiac complications with those who did not they had a significantly higher age (mean ± SD 69 ± 17.3 versus 49 ± 19.1, $p < 0.05$), included a significantly higher percentage of patients with preexisting cardiovascular diseases (40.6% versus 5.1%, $p < 0.05$), had a significantly higher pneumonia severity index (PSI) (mean ± SD 130 ± 27 versus 73 ± 29, $p < 0.05$), a significantly longer hospital stay (mean ± SD 22 ± 7.1 versus 9 ± 4.3, $P < 0.05$) and a significantly higher mortality (21.8% versus 6.1%, $P < 0.05$).

Conclusions: Cardiac complications are common in the admitted patients with pneumonia and they are associated with increased pneumonia severity and increased cardiovascular risk, these

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complications adds to the risk of mortality, so optimal management of these events may reduce the burden of death associated with this infection.

Introduction

Pneumonia is widely recognized as a major cause of morbidity and mortality. Clinically, pneumonia exhibits an extreme variety in the severity of presentation, from almost asymptomatic disease on one side to a fulminant event on the other [1].

Clinical risk scores have been developed for adult patients with pneumonia and are widely used to identify high risk patients in need of intensive treatment and careful monitoring, and low risk patients who may be suitable for out-patient treatment. These scores use clinical indicators from multiple organ systems, acknowledging the importance of systemic illness severity, advanced age, and reduced physiological reserve in determining mortality from pneumonia. For example, only four of the 20 measures in the pneumonia severity index (PSI) and one of five components of the widely used CURB 65 score (Confusion, Urea, and Respiratory rate, Blood pressure, and age $\geqslant$65 years) are direct measures of respiratory function [2]. Mortensen et al. [3] reported that about half of deaths in patients with CAP was attributable to worsening of a pre-existing condition.

Recent studies indicate that cardiac complications are common in patients with community-acquired pneumonia [4–7]. However, the frequency of these complications in unselected CAP patients, the contribution of specific cardiac events to this burden, the timing of these complications in the course of CAP, the factors associated with their development, and their association with the short-term mortality of this infection remain unclear.

Acute bacterial pneumonia stresses the heart by increasing myocardial oxygen demand at a time when oxygenation is compromised by a ventilation–perfusion mismatch. Pneumonia also raises circulating levels of inflammatory cytokines, which promote thrombogenesis and suppress ventricular function. Taken together, these pathophysiologic events might be expected to lead to major, acute cardiac events, such as myocardial infarction (MI), arrhythmia, and/or congestive heart failure (CHF) [8–10].

The aim of this study was to examine the risk factors and outcome of cardiac complications in admitted patients with community-acquired pneumonia as this might help to assess the risk of death and institute the appropriate level of care.

Patients and methods

This clinical study was carried out on 130 patients (68 males and 62 females with a mean age of 59 ± 19.3) hospitalized with a primary diagnosis of community-acquired Pneumonia (CAP) in the period between July 2012 and September 2014 after taking informed consent. Patients with presence of an alternative diagnosis that likely explained the pulmonary symptoms and X-ray infiltrate (e.g., lung carcinoma, pulmonary edema, or pulmonary embolus) were excluded.

All patients were subjected to:

- Complete medical history.
- General and local chest examination.
- Laboratory investigations: complete blood count, renal and hepatic function tests, serum electrolytes, blood sugar, arterial blood gas analysis, CRP, procalcitonin (Kryptor PCT, Brahms, Hennigsdorf, Germany), brain natriuretic peptide (NT-BNP) (Roche Diagnostics Corp., Indianapolis, IN, USA) and serum troponin I (cTnI) concentration using a Siemens Advia Centaur TnI-Ultra Assay (serum cTnI concentration was considered raised if it was $\geqslant$0.04 μg L).
- Microbial etiology: At least two sets of separate blood and sputum samples of each patient were Gram stained and cultured. Moreover, sputum samples were analyzed with TaqMan real-time polymerase chain reactions (PCRs) in order to detect DNA of *Mycoplasma pneumoniae*, *Legionella pneumophila*, *Coxiella burnetii*, and *Chlamydophila* species. Antigen testing of *S. pneumoniae* and *L. pneumophila* was performed in urine samples. Furthermore, pharyngeal swabs were taken for viral culture and viral PCR [11].
- Radiological investigations (plain x ray and computed tomography on the chest).
- Electrocardiographic studies (ECG).
- Echocardiography.

Definitions

Pneumonia was defined as the presence of a new pulmonary infiltrate on a chest radiograph at the time of hospitalization associated with one or more of the following: (1) new or increased cough with/without sputum production; (2) fever ($\geqslant$ 37.8 °C) or hypothermia ($\leqslant$ 35.6 °C); or (3) abnormal white blood cell count (either leukocytosis or leukopenia), or C-reactive protein values above the local upper limit [12].

Severity of pneumonia: on admission to the hospital, patients were assessed using the Pneumonia Severity Index (PSI), a validated prediction rule for 30-day mortality in patients with CAP [2].

Acute myocardial infarction (AMI) The diagnosis of AMI According to the WHO criteria as revised in 2000 [13], a cardiac troponin rise accompanied by either typical symptoms or ischemic ECG changes (ST-segment elevation 0.1 mV or greater in 2 or more contiguous leads, ST-segment depression, T-wave abnormality, and development of pathological Q waves).

New or worsening heart failure, i.e., the presence of clinical signs of new or worsening pulmonary edema or acute congestive heart failure detected by the managing physician.

New arrhythmias ECG monitor, or Holter monitor of newly recognized atrial fibrillation, atrial flutter,

supraventricular tachycardia, multifocal atrial tachycardia, ventricular tachycardia or ventricular fibrillation.

Statistical analysis

Results are given as numbers, percentage or mean ± SD. Demographic and physiologic characteristics of the two groups were compared with use of Student's *t*-test for continuous data and chi-square test for categorical data. The SPSS version 19 software package (SPSS, Chicago) was used for all analyses. $P < 0.05$ was considered as statistically significant.

Results

Demographic characteristics and comorbidities in the studied patients who developed and who did not develop cardiac complications are presented in Table 1. Patients who developed cardiac complications had a significantly higher age (mean ± SD 69 ± 17.3 vs. 49 ± 19.1, $P < 0.05$) and included a significantly higher percentage of patients with preexisting cardiovascular diseases (history of heart failure, prior cardiac arrhythmias, previously diagnosed coronary artery disease, hyperlipidemia or arterial hypertension) (40.6% vs. 5.1%, $P < 0.05$).

Table 2 shows distribution of cardiac complications among the studied 130 patients in which 32 patients (24.6%) had cardiac complications. New or worsening heart failure happened in 16 patients (12.3%). Arrhythmias happened in 12 patients (9.2%). Finally, MI was documented in 4 patients (3.1%).

In this study patients who developed cardiac complications compared with those who did not develop cardiac complications had a significantly higher PSI (130 ± 27 vs. 73 ± 29, $P < 0.05$), higher percentage of patients with altered mental status, Systolic blood pressure <90 mmHg, pulse ⩾125 bpm, Respiratory rate ⩾30 breaths/min (Table 3).

As regard to laboratory characteristics of the studied patients, the percentage of patients who had blood pH <7.35, blood urea nitrogen ⩾30 mg/dL, sodium <130 mmol/L, hematocrit <30%, and Po_2 <60 mmHg or O_2 sat <90 mmHg was significantly higher in patients who developed cardiac complications than those without cardiac complications (Table 4).

Table 5 shows that patients with cardiac complications had significantly higher procalcitonin levels than patients without cardiac complications (mean ± SD 20 ± 3.2 vs. 5.2 ± 1.3)

Table 1 Demographic characteristics and comorbidities in the studied patients.

Patient characteristics	With cardiac complications $n = 32$ (24.6%)	Without cardiac complications $n = 98$ (75.4%)	*P*
Age (mean ± SD, y)	69 ± 17.3	49 ± 19.1	<0.05
Sex (male/female)	17/15	51/47	>0.05
Smoking *n* (%)	7 (21.9)	19 (19.4)	>0.05
Comorbidities *n* (%)			
Cardiovascular diseases	13 (40.6)	5 (5.1)	<0.05
Diabetes	7 (21.9)	19 (19.4)	>0.05
COPD	6 (18.6)	17 (17.3)	>0.05
Cerebrovascular disease	3 (9.3)	10 (8.4)	>0.05
Chronic renal disease	3 (9.4)	8 (8.1)	>0.05

Table 2 Cardiac Complications of the studied patients.

Cardiac complications	No. of patients (%)
No cardiac complications	98 (75.4)
Cardiac complications	32 (24.6)
New or worsening heart failure	16 (12.3)
New arrhythmias	12 (9.2)
Acute myocardial infarction	4 (3.1)

Table 3 Initial clinical characteristics of the studied patients.

Clinical characteristics	With cardiac complications $N = 32$ (24.6%)	Without cardiac complications $N = 98$ (75.4%)	*P*
Altered mental status	12 (37.5)	7 (7.1)	<0.05
Pulse ⩾125 bpm	10 (31.1)	13 (13.3)	<0.05
Systolic blood pressure <90 mmHg	13 (40.6)	15 (15.3)	<0.05
Respiratory rate ⩾30 breaths/min	18 (56.3)	16 (16.3)	<0.05
Temperature <35 °C or ⩾40 °C	0	0	>0.05
PSI	130 ± 27	73 ± 29	<0.05

PSI: pneumonia severity index.

Table 4 Initial laboratory characteristics of the studied patients.

Laboratory characteristics	With cardiac complications $N = 32$ (24.6%)	Without cardiac complications $N = 98$ (75.4%)	*P*
Hematocrit <30%	12 (37.5)	4 (4.1)	<0.05
Blood urea nitrogen ⩾30 mg/dL	20 (62.5)	22 (22.4)	<0.05
Sodium <130 mmol/L	12 (37.5)	7 (7.1)	<0.05
pH <7.35	24 (75)	7 (7.1)	<0.05
Pao_2 <60 mmHg or O_2 sat <90 mmHg	25 (78.1)	31 (31.6)	<0.05
Glucose ⩾250 mg/dl	10 (31.2)	6 (6.1)	<0.05

Table 5 Initial inflammatory and myocardial injury markers in the studied patients.

Inflammatory and myocardial injury markers	With cardiac complications $N = 32$ (24.6%)	Without cardiac complications $N = 98$ (75.4%)	P
CRP (mg/mL) mean ± SD	15 ± 6.1	14 ± 7.2	> 0.05
Procalcitonin (ng/mL) mean ± SD	20 ± 3.2	5.2 ± 1.3	< 0.05
Patients with increased NT-BNP (n%)	19 (59.3)	12 (12.2)	< 0.05
Patients with increased troponin I (n%)	15 (46.7)	11 (11.2)	< 0.05

BNP: brain natriuretic peptide.

Table 6 Initial radiological characteristics of the studied patients.

Laboratory characteristics	With cardiac complications $N = 32$ (24.6%)	Without cardiac complications $N = 98$ (75.4%)	P
Lobar pattern	6 (18.8)	53 (54.1)	< 0.05
Interstitial pattern	18 (56.3)	24 (24.5)	< 0.05
Segmental pattern	4 (12.5)	11 (11.2)	> 0.05
Bronchopneumonia	4 (12.5)	10 (10.2)	> 0.05
Presence of pleural effusion	12 (37.5)	12 (12.2)	< 0.05

Table 7 Outcome of the studied patients with and without cardiac complications.

Outcome	With cardiac complications $N = 32$ (24.6%)	Without cardiac complications $N = 98$ (75.4%)	P
Need for MV	15 (46.9)	6 (6.1)	< 0.05
Need for inotropes and vasopressors	17 (53.1)	7 (7.1)	< 0.05
Acute renal failure	13 (40.6)	4 (4.1)	< 0.05
Hospital stay in days	22 ± 7.1	9 ± 4.3	< 0.05
Mortality	7 (21.8%)	6 (6.1)	< 0.05

MV: mechanical ventilation.

and that they had a higher percentage of patients with increased NT-BNP and increased troponin I (59.3% vs. 12.2% and 46.7% vs. 11.2%, respectively).

In the present study, as regard to radiology (Table 6) interstitial pattern of pneumonia and the presence of pleural effusion were significantly common in patients who developed cardiac complications compared to patients without cardiac complications (56.3% vs. 24.5% and 37.5% vs. 12.2%, $P < 0.05$).

Table 7 shows the outcome of the studied patients during the admission period in which patients who developed cardiac complications compared with those who did not, the percentage of patients who received mechanical ventilation was 46.9% vs. 6.1%, $P < 0.05$, those who received inotropes and vasopressors 53.1 vs. 7.1%, $P < 0.05$, occurrence of acute renal failure in 40.6% vs. 4.1%, hospital stay 22 ± 7.1 vs. 9 ± 4.3, $P < 0.05$ and mortality 21.8% vs. 6.1%, $P < 0.05$.

Discussion

Although CAP is a leading cause of death, little consideration has been given to understanding the contributors to this mortality. Recent studies indicate that cardiac complications are common in patients with community-acquired pneumonia [4–7]. However, the frequency of these complications in CAP patients, the contribution of specific cardiac events to this burden, the timing of these complications in the course of CAP, the factors associated with their development, and their association with the short-term mortality of this infection remains unclear. This study was carried out to examine the risk factors and outcome of cardiac complications in admitted patients with community-acquired pneumonia as this might help to assess risk of death and institute the appropriate level of care.

In this study 32 patients of 130 (24.6%) admitted patients with primary diagnosis of pneumonia, had cardiac complications: new or worsening heart failure in 16 patients (12.3%), new arrhythmias in 12 patients (9.2%) and AMI in 4 patients (3.1%). This finding agrees with Carlos et al. [5] who reported that major cardiac complications occurred in a substantial proportion (17.7%) of patients with community-acquired pneumonia, including incident heart failure, acute coronary syndromes, and arrhythmias.

Epidemiological studies have demonstrated that respiratory tract infections are associated with an increased risk for the development of acute myocardial infarction [14,9]. One recent study [15] that specifically sought non cardiac conditions in patients who had acute MI found that 7.2% of these patients had pneumonia; the authors emphasized, the tendency of admitting physicians to confine their assessment to a single diagnosis.

Musher et al. [16] reported that an associated AMI was found in 12 (7%) of 170 patients with pneumococcal pneumonia at time of hospital admission. Ramirez et al. [17] reported an incidence of myocardial infarction at the time of hospital admission of 5.8% in 500 patients hospitalized with community-acquired pneumonia. Corrales et al. [5] reported an incidence of myocardial infarction of 10.7% in 206 patients hospitalized with pneumonia. This incidence was measured during the first 15 days after hospital admission. The incidence of myocardial infarction occurring during hospitalization due to pneumonia in the study of Perry et al. [18] was 1.4%. Differences in these incidences may be explained by differences in the studied patient populations.

Several mechanisms, can account for the development of MI in patients with CAP. Hypoxemia decreases myocardial oxygen delivery and raises pulmonary arterial pressure and right ventricular afterload. Tachycardia increases myocardial

oxygen needs and shortens the diastole (when coronary perfusion occurs). Acute infections can promote inflammatory activity within coronary athero-sclerotic plaques and induce prothrombotic changes in the blood and endothelium, resulting in plaque instability and facilitating coronary thrombosis. Preexisting coronary artery disease that is insufficient to produce myocardial ischemia under baseline conditions can also result in significant ischemia in the face of increased myocardial oxygen demand [16].

In the study of Perry et al. [18] the incidence was 19.2% for new or repeat congestive heart failure and 6.4% for cardiac arrhythmias in the studied patients with pneumonia. Musher et al. [16] reported that the incidence of new-onset or worsening congestive heart failure for 14% of their sample and an incidence of new-onset arrhythmia (including atrial flutter, atrial fibrillation, and ventricular tachycardia of 5.8%. These incidences were measured at the time of admission for pneumonia. These findings agree with the present study which showed that new-onset or worsening congestive heart failure occurred in 12.3% and new-onset arrhythmia in 9.2% of the studied patients with community acquired pneumonia.

The ability of pneumonia to cause acute abnormalities in the cardiac conduction system has been recognized since the early 20th century and consistently confirmed thereafter [19].

The occurrence of CHF in pneumonia may be explained by many factors including increased myocardial demand for oxygen, lowered blood oxygen levels, and suppression of ventricular function by elevated levels of cytokines [20]. Biventricular impairment of intrinsic myocardial contractility, which may be present in 50% of patients with severe sepsis or septic shock [13].

This study identifies specific factors associated with the occurrence of cardiac complications in the admitted patients with pneumonia, these factors include higher age, presence of underlying cardiovascular diseases (previously diagnosed coronary artery disease, Congestive heart failure, arrhythmias and hypertension), and more severe pneumonia at presentation (respiratory rate $\geqslant 30$ breaths per minute, blood pH < 7.35, blood urea nitrogen $\geqslant 30$ mg/dL, sodium < 130 mmol/L, hematocrit $< 30\%$, which agrees with previous studies [5,7]. Elevated levels of B-type natriuretic peptides (markers of cardiac failure due to pressure or volume overload) are reported to be common in community-acquired lower respiratory tract infections and are associated with a higher risk of adverse outcome [8,9]. In this study elevated brain natriuretic peptide was present in 59.3% of patients with cardiac complications and 12.2% of patients without cardiac complications.

Elevated levels of cardiac troponins (indicating myocardial injury) have also been linked to increased disease severity in community-acquired pneumonia [10,21]. The present study showed that increased troponin I was present in 46.7% of patients with cardiac complications and 11.2% of patients without cardiac complications.

In this study there was a significant increase in hospital stay and mortality in the studied pneumonia patients with cardiac complications. As 7 of 32 (21.8%) patients who had cardiac events died, compared with 6 of 98 (6.1%) patients who did not experience cardiac events. This finding agrees with the study of Corrales et al. [5], in which the development of cardiac complications was associated with a substantial increase (60%) in the risk of death at 30 days, even after adjustment for patients' PSI score which is considered the most comprehensive and sensitive tool for predicting short-term mortality on presentation with CAP [2,22].

Conclusion: cardiac complications are common in the admitted patients with primary diagnosis of pneumonia and they are associated with increased pneumonia severity and increased cardiovascular risk, these complications add to the risk of mortality, so the prevention and optimal management of these events may significantly reduce the burden of death associated with this infection.

Conflict of interest

None.

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