



## A small pericardial effusion is a marker of complicated hospitalization in patients with community-acquired pneumonia<sup>☆</sup>

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### ARTICLE INFO

#### Keywords:

Community acquired pneumonia  
Echocardiography  
small pericardial effusion

### ABSTRACT

**Objective:** Although often asymptomatic, presence of small pericardial effusion (SPE) is shown to be associated with adverse events and increased mortality in various conditions. This study aimed to evaluate the frequency and prognostic importance of SPE in a cohort of patients hospitalized for community-acquired pneumonia (CAP). **Methods:** We prospectively followed 154 consecutive adult patients hospitalized with CAP. The severity of CAP was evaluated with the pneumonia severity index (PSI) and the CURB-65 (confusion, urea, respiratory rate, arterial blood pressure and age) score. All patients underwent transthoracic echocardiography within the first 48 h of admission. Patients were followed-up until hospital discharge or death. The outcomes of interest were length of stay in hospital and complicated hospitalization (CH) which is defined as intensive care unit admission, need for mechanical ventilation or in-hospital mortality. This study was registered with [ClinicalTrials.gov](http://ClinicalTrials.gov), number NCT02441855.

**Results:** A total 34 episodes of CHs occurred in 21 (13.6%) patients. Older patients and those with more co-morbid conditions such as diabetes, coronary artery diseases, cerebrovascular diseases, and chronic obstructive pulmonary diseases tended to have a higher rate of CH. Patients with CH had higher N-terminal pro-brain natriuretic peptide, troponin and creatinine levels on admission compared to patients without CH. Patients with CH had also higher CURB-65 and PSI scores and had longer durations of stay compared to patients with uncomplicated course. SPE was noted in 24 (15.6%) of the patients in our study cohort. Incidence of CH was greater for patients with a SPE (26 CHs occurred in 14 of the 24 patients) compared to those without an effusion (8 CHs occurred in 7 of the 130 patients,  $p < 0.001$ ). Logistic multivariate analysis revealed that the presence of SPE was an independent predictor of CH (OR: 3.26; 95% CI: 2.19–8.71;  $p = 0.008$ ).

**Conclusion:** This study is the first to demonstrate that the presence of SPE is associated with increased adverse events in patients with CAP.

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### 1. Introduction

Community acquired pneumonia (CAP) remains a major health concern worldwide and a cause of morbidity and mortality especially in underdeveloped and developing countries such as Turkey [1]. Several predictors of adverse events in patients with CAP have been developed to identify individuals at risk of complicated hospitalizations (CH). The pneumonia severity index (PSI) and CURB-65 (confusion, urea nitrogen, respiratory rate, blood pressure, age  $\geq 65$  years), are the most widely

known scores for the assessment the severity of CAP [2–4]. However, due to some limitations of these scores, increasing attention has been paid to research on new predictors in recent years [5,6]. Infections such as CAP increase myocardial oxygen demand due to fever and tachycardia and raises circulating levels of inflammatory cytokines, which promote arrhythmias, and heart failure [7]. High platelet activation may also provide a mechanistic explanation for increased myocardial infarction risk in CAP [8]. As a result, recent studies have demonstrated the prognostic value of biomarkers of cardiopulmonary or myocardial dysfunction in CAP [5–8]. Although incidence of CAP is greatest among middle-aged and elderly patients, who are also at the greatest risk for cardiovascular diseases, the association between cardiac events at the time of hospitalization for CAP has not been well-studied before. Transthoracic echocardiography is a first-line

<sup>☆</sup> All authors had access to the data and a role in writing the manuscript.

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non-invasive technique for evaluation of cardiac function and it can be easily performed at the bedside in patients with CAP. However, there are only 2 studies in the literature evaluating the value of echocardiography in these patients [9,10]. In the first study we compared 111 CAP patients with 100 sex- and age-matched control patients [9]. This preliminary study showed that the 2 groups did not differ in terms of left and right ventricle ejection fraction, left atrial diameter, pulmonary artery systolic pressure, and left ventricular end-diastolic and end-systolic diameter, but tricuspid annular plane systolic excursion (a measure of right ventricular systolic function), aortic distensibility, and aortic strain were significantly reduced in CAP group than in controls.

In the second study we showed that the decreased right ventricular systolic function was associated with increased rates of adverse events in patients with CAP [10].

Pericardial effusion is the abnormal accumulation of fluid in the pericardial space which may occur as a result of a variety of clinical conditions [11]. The mortality and morbidity of pericardial effusion depends on the underlying etiology and comorbid conditions [11]. Although often asymptomatic, presence of small pericardial effusion (SPE) is shown to be associated with increased mortality in patients with human immunodeficiency virus infection [12], in a cohort of patients undergoing transthoracic echocardiography [13], in patients with lung cancer [14] and acute ischemic stroke [15]. However, there is no data in the literature regarding the prevalence and importance of pericardial effusion in patients with CAP. Therefore, in this study we sought to examine the prevalence of SPE in CAP, and its association with CHs.

## 2. Methods

### 2.1. Study design

The study was a prospective, observational, and single-center study, conducted at the Muğla Sıtkı Koçman University Hospital, Muğla, Turkey, from March 2015 to March 2016. All patients included in this study were treated according to the Infectious Diseases Society of America/American Thoracic Society consensus guidelines for the management of CAP in adults [16]. All patients were followed up during hospitalization or until death. This project was approved by the regional ethics committee and registered with [ClinicalTrials.gov](http://ClinicalTrials.gov), number NCT02441855. All patients or their relatives gave informed written consent.

### 2.2. Selection of participants

All patients with  $\geq 18$  years of age and CAP diagnosis hospitalized through emergency department were prospectively recruited. We excluded patients who met any of the following criteria: younger than 18 years, active pulmonary tuberculosis, hospital-acquired pneumonia, pregnancy, severely immunocompromised patients, patients undergoing chronic dialysis and patients sent for ambulatory treatment. Patients were also excluded if they had cardiothoracic surgery or acute myocardial infarction within the previous 6 months, a moderate or greater pericardial effusion ( $>1$  cm if circumferential), and inadequate visualization of the pericardial space. Pneumonia was defined by the presence of two or more of the following recently acquired symptoms or signs: temperature  $>38$  °C, dyspnea, cough, sputum production, pleuritic chest pain, or bronchial sounds or crackles on chest auscultation, plus radiographical findings of pneumonia. Community-acquired pneumonia is defined as pneumonia acquired outside a hospital or long-term care facility that occurs within 48 h of hospital admission or in a patient presenting with pneumonia who does not have any of the characteristics of health care-associated pneumonia (i.e., hospitalized in an acute care hospital for 2 or more days within 90 days of infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past

30 days of the current infection; or attended a hospital or hemodialysis clinic).

### 2.3. Measurements

Demographic information, past medical history, vital signs, electrocardiographic, radiographic and laboratory data were collected. Complete blood count, routine biochemical analyses, N-terminal pro-brain natriuretic peptide (NT-proBNP) and troponin I concentrations were measured within the first 24 h of admission.

For all patients with CAP, severity of pneumonia was quantified by the PSI and CURB-65 (confusion, blood urea nitrogen  $>20$  mg/dL, respiratory rate  $>30$  breaths/min, blood pressure  $<90/60$  mm Hg, and age  $\geq 65$  years) scores which were calculated upon admission as previously described [17,18].

### 2.4. Transthoracic echocardiography

Standard M-mode and 2-dimensional color Doppler echocardiography was performed in all patients using Philips System (Philips Epiq 7G, Andover, MA, USA) within two days of hospital admission. Standard views, including the left lateral decubitus and supine positions, were obtained. A pericardial effusion was diagnosed if an echo-free space between the visceral and parietal pericardium persisted throughout the cardiac cycle. The size of the pericardial effusion was defined as follows: small when the maximum pericardial space at end-diastole was  $<10$  mm, moderate when the space was 10 mm–20 mm, and large when the pericardial space was  $>20$  mm (Fig. 1). Patients with a moderate or greater pericardial effusion were excluded from the study.

### 2.5. Study Endpoints

The primary study endpoint was CH defined as at least one of the following: in-hospital mortality, intensive care unit admission or need for mechanical ventilation. The secondary outcome of interest was length of stay in hospital. Univariate and multivariate Cox regression analyses were performed to assess the associations between initial prognostic indicators (PSI, CURB-65, biomarkers and SPE) and outcome.

### 2.6. Statistical analysis

Data were analyzed using SPSS for Windows (version 15; SPSS Inc, Chicago, IL). The continuous variables were expressed as mean  $\pm$  standard deviation and were compared between groups by 2-tailed Student *t*-test. Nonparametric tests were also used when necessary (Mann-Whitney *U* test). Fisher exact ( $\chi^2$ ) test was used in comparison of categorical variables. Comparing of patients characteristics from two groups (complicated and uncomplicated) was done by using chi-square test. Statistical differences among groups were tested by one-way analysis of variance and Kruskal-Wallis tests for parametric and nonparametric variables, respectively. Univariate and multivariate logistic regression analyses were applied to determine crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the relationship between SPE and CH. For all analyses,  $P < 0.05$  was considered statistically significant.

## 3. Results

A total of 154 patients with CAP (mean age  $66.8 \pm 13.7$  and 51% male) were enrolled. Hypertension was the most frequent comorbidity, followed by hyperlipidemia, coronary artery disease, diabetes mellitus, malignancy, chronic obstructive pulmonary disease, cerebrovascular disease and heart failure. The mean CURB-65 and PSI score values were  $1.8 \pm 1.3$  and  $3.1 \pm 1.2$  in our patient group, respectively. Respiratory rate was  $24.3 \pm 4.5$  breaths per minute, heart rate was  $79.21 \pm 13.2$  bpm and body temperature was  $37.6 \pm 0.7$  °C on admission. Median length of stay was 6 days.

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