



## The Influence of Pre-Existing Heart Failure on Community-Acquired Pneumonia Outcomes

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### Abstract

**Background:** Community-acquired pneumonia is a common infectious disease, that is being associated with high mortality, especially in patients with comorbidities, such as heart failure. Also, preexisting heart failure increases pneumonia mortality by 30 - 50%, therefore it is important to identify patients who are in the risk group.

**Methods:** This is a retrospective study, where we examined causes of death in 62 patients with community-acquired pneumonia and heart failure, with emphasis on clinical, laboratory and microbiological characteristics.

**Results:** Our results show that cardiovascular disease, especially heart failure, represents a heavy load on the outcomes of community-acquired pneumonia patients and that progression of heart failure, it's complications and other co-morbidities increase the risk of death associated with pneumonia.

**Conclusion:** The obtained data suggests that community-acquired pneumonia is not only affecting the respiratory system, but it is also a systematic inflammation process that affects the cardiovascular system.

**Keywords:** Community-Acquired Pneumonia; Heart Failure; Outcomes; Risk Factors; Comorbidities

### Abbreviations

ACC/AHA: American College of Cardiology/American Heart Association; BNP: Brain Natriuretic Peptide; CAP: Community-Acquired Pneumonia; HF: Heart Failure; NYHA: New York Heart Association

### Introduction

Community-acquired pneumonia (CAP) is a common condition associated with substantial morbidity and mortality, irrespective of age [11]. The mortality of CAP has continued to increase over the years and short-term (30-day) mortality rates are consistently ranging from 10 to 12%. The most common risk factors include older age, severity of illness and pre-existing comorbidities [12].

The diagnosis of CAP in patients with heart failure (HF) highlights certain difficulties due to the common clinical picture. Signs and symptoms can appear in both pathologies, such as: dyspnea, tachycardia, tachypnea, cough, wet rales in the lower areas of the lungs, bilateral infiltrates on chest radiography. Radiological picture in patients with CAP and HF may also be inconclusive, which is due to bilateral infiltrative changes that may occur in patients with HF and which may lead to hyperdiagnosis of CAP [1].

Considering the fact that pre-existing HF increases pneumonia mortality by 30 - 50%, it is important to clarify which categories of patients are prone to a higher risk. HF is a cardiovascular complication that seems to be highly prevalent in patients with CAP [7]. Studies show a frequent association between CAP and the occur-

rence of acute cardiac complications such as HF, atrial fibrillation, and myocardial infarction [2]. Other factors, which are common to both pneumonia and HF, are also likely at play, including advanced age, reduced renal function, and the presence of other major comorbidities (e.g. atherosclerosis, diabetes, hypertension) are likely to contribute to an increased risk of heart failure in patients with CAP [2,4].

Retrospective clinical observations suggest that cardiac complications (new or worsening) occur in a significant proportion of high-risk CAP patients (e.g., elderly veterans and diabetics) [6]. However, there is still uncertainty regarding the actual incidence of these complications as it has varied widely in studies that have used different designs (retrospective versus prospective) and criteria to define these complications [3,5]. Corrales-Medina reported a persistent increased risk for cardiovascular events, including new onset HF, following pneumonia which declines with time, but remains elevated for at least 5 years [1]. Eurich also identified an increased risk of new onset HF over a 10 year follow up of adults with CAP [8-10].

**Materials and Methods**

We retrospectively analyzed 62 medical records of adults aged >18 years, who died between 01.2016-06.2019, with the final clinical diagnosis of community-acquired pneumonia and congestive heart failure.

The inclusion criteria were: bacteriological examination (blood culture, sputoculture), acute onset, muco-purulent/purulent sputum, fever, exacerbation of dyspnea, presence of criteria for congestive heart failure (dyspnea, cough, wet rales in the lower lungs, decreased exercise tolerance, acrocyanosis, orthopnoea), echocardiography (EF < 50%), elevation of BNP values ≥ 35 pg/mL, NT-pro-BNP ≥ 125 pg/mL, radiological confirmation of the infiltrate, morphopathological examination.

CAP severity was assessed accordingly PSI [23], CURB-65, CRB-65 [24], DS-CRB-65 [25] scores. NYHA (1994) and ACC/AHA (2005) classifications were used to describe HF in our patients.

The obtained data was processed using variational and correlational analysis. We showed n (%) for categorical variables and mean ± SD for continuous variables. Statistical analysis of the results was performed using the non-parametric test Spearman’s Rho.

The level of statistical significance was set at p < 0.05. The analyses were performed using IBM SPSS Statistics 23.

**Results**

The average age of the patients was 68.8 ± 12.6 years old, of which: men - 33 (53.2%), women - 29 (46.8%), and the average duration of hospitalization - 7.7 ± 8.07 days. The most common clinical manifestations: impaired consciousness - 27 cases (43.5%), dyspnea - 54 cases (87.1%), dry cough - 29 cases (46.8%), productive cough - 14 cases (22.6%), the presence of localized subcrepitant/crackling rales - 23 cases (37.1%), diffuse bullous rales - 17 cases (27.4%) (Table 1).

	The coincidence of CAP diagnosis, N (%)	CAP hyperdiagnosis, N (%)	p
Mean age, years	68.3 ± 13.2	71.2 ± 9.1	0.54
Men	29(58%)	4 (36.3%)	0.22
Days of hospitalization	7.8 ± 8.5	6.7 ± 5.3	0.98
Comorbidities ≥ 2	51 (100%)	11 (100%)	0.38
Impaired consciousness	23 (46%)	4 (36.3%)	0.6
Dyspnea	44 (88%)	10 (90%)	0.68
Muco-purulent expectorations	33 (66%)	10 (90%)	0.02
Body temperature ≥ 38°C	14 (28%)	2 (18.1%)	0.53
Unilateral rales	16 (32%)	7 (63.3%)	0.08
Bilateral rales	15 (30%)	2 (18.1%)	0.49

**Table 1:** Characteristics of the compared groups: group I - the coincidence of the clinical and morphopathological diagnosis of CAP, group II - CAP hyperdiagnosis.

Based on the results of the morphopathological analysis, patients were divided into 3 groups: group I - 50 patients (80.6%), in which the coincidence of the clinical and morphopathological diagnosis took place, group II - 11 patients (17.7%), in which pneumonia was not morphopathologically confirmed (hyperdiagnosis), group III - 1 patient (1.6%), in whom the clinical undiagnosis of pneumonia was confirmed at necropsy. The medical records of the patients included in group I and group II were statistically analyzed.

In most patients, CAP had a severe course, with a high risk of mortality. The CURB-65 and SIRS scores had a better predictability in the group with the coincidence of the diagnosis: the CURB-65  $\geq 2$  score was present in 46 cases (92%) vs. 7 cases (63.6%), ( $p = 0.01$ ), and the SIRS  $\geq 2$  score was present in 41 cases (82%) vs. 5 cases (45.4%), ( $p = 0.01$ ), in group I and group II, respectively.

According to the NYHA classification of heart failure, most patients had class II, III or IV of HF, with no significant differences between the two groups: class III (NYHA) was present in 28 cases (56%) vs. 5 cases (45.4%), and class IV (NYHA) - in 14 cases (28%) vs. 4 cases (36.3%), ( $p > 0.05$ ), in group I and group II, respectively.

In the researched groups, pulmonary edema occurred in 86% and 81% of cases, respectively ( $p > 0.05$ ). Comorbidities were present in all patients included in the study. Chronic renal disease (34% vs. 18%,  $p > 0.05$ ) and cerebrovascular disease (40% vs. 18%,  $p > 0.05$ ), predominated in the group of patients with the coincidence of CAP diagnosis, and diabetes was more common in patients with hyperdiagnosis (28% vs. 45%,  $p > 0.05$ ).

No statistically significant differences were observed in CAP etiology. It should be noted that *Staphylococcus aureus* and *Klebsiella pneumoniae* predominated in patients with the coincidence of CAP diagnosis. In 1/3 of the patients of both groups we found multilobar/bilateral infiltrates (36.6% vs 28%,  $p > 0.05$ ). Cases of hyperdiagnosis of community-acquired pneumonia had a significant weak positive correlation with the presence of mucopurulent sputum ( $r_s = 0.28$ ,  $p < 0.05$ ), and a negative correlation with positive blood cultures ( $r_s = -0.25$ ,  $p < 0.05$ ), and at the ultrasound - with dilation of the heart cavities ( $r_s = -0.27$ ,  $p > 0.05$ ).

## Discussion

All the patients included in our study presented some common characteristics: associated pathologies, high value of severity scores, identical clinical manifestation and multilobar/bilateral infiltrates. In our study the most affected were older patients (the mean age 68,9 years), this data was confirmed by Remar W, *et al.* who described age being one of the most important independent predictor for pneumonia and HF. The highest lethality (15-30%) is reached by patients  $> 60$  years old, being due to severe comorbidities and the presence of other risk factors [15].

Sirvent., *et al.* described the predictive factors of mortality in severe CAP as congestive heart failure with ventricular dysfunction,

documented by clinical symptoms, radiology and echocardiography; central nervous system disorders: acute or chronic vascular or nonvascular encephalopathy; diabetes mellitus: diagnosis of intolerance to glucose and treatment with oral antidiabetics or insulin; renal: pre-existing renal disease with documented abnormal serum creatinine levels outside the period of the pneumonia episode [15].

This comorbidities were present like predictive factors in all patients included in the both groups of our study: chronic renal disease (34% vs 18%,  $p > 0.05$ ) and cerebrovascular disease (40% vs 18%,  $p > 0.05$ ), predominated in the group of patients with the coincidence of CAP diagnosis, and diabetes was more common in patients with CAP hyperdiagnosis (28% vs 45%,  $p > 0.05$ ) [16]. Another study which included 1203 patients hospitalized with CAP for a period of 3 years (2012 - 2014) has evaluated the impact of co-morbidities on the CAP mortality. The most common comorbidities also were: diabetes mellitus (23,6%), cerebrovascular disease (17,2%) and chronic renal failure. The results of our study also show that common pathologies increase the risk of mortality in patients with CAP and HF [17].

In the present study, we investigated the accuracy in mortality prediction of CURB-65 and SIRS score systems. CURB-65 and SIRS scores had a better predictability in the group with the coincidence of CAP diagnosis: CURB-65  $\geq 2$  was present in 92% cases vs 63.6% cases, ( $p = 0.01$ ) and SIRS $\geq 2$  was present in 82% cases vs 45.4% cases, ( $p = 0.01$ ), in both groups. A strong relationship between mortality and CURB-65  $\geq 2$ /SIRS  $\geq 2$  scores was demonstrated in other studies [18-21]. Another study demonstrated that an altered mental state is a very important clinical sign to assess the severity of CAP, in our study altered mental state was present in 27 cases (43,5%) [22].

According to the data population-based cohort study in Western Denmark between 1994 and 2003, which included 33,736 patients, with HF NYHA class III-IV, seemed to be a particular high-risk group for death associated with pneumonia [12]. Compared with our results, most of the patients had class II, III or IV NYHA, with no significant differences between the two groups: class III (NYHA) was present in 28 cases (56%) vs 5 cases (45.4%), and class IV (NYHA) in 14 cases (28%) vs 4 cases (36.3%), ( $p > 0.05$ ), in group I and group II, respectively.

The hypothesis of another study was that radiological bilateral infiltrate is an independent risk factor for mortality. The prognosis

for bilateral involvement is worse comparatively with unilateral involvement. Chest radiography revealed bilateral lung involvement in 89 cases (47%) from 189 patients [13]. In our study, in 1/3 of the patients of both groups we found multilobar/bilateral infiltrates (36.6% vs 28%,  $p > 0.05$ ).

Our data shows that cases of hyperdiagnosis of CAP had a significant weak positive correlation with the presence of mucopurulent sputum ( $r_s = 0.28, p < 0.05$ ), a negative correlation with positive blood cultures ( $r_s = -0.25, p < 0.05$ ) and at the ultrasound - with dilation of the heart cavities ( $r_s = -0.27, p > 0.05$ ) (Table 2). In our study, the coincidence of the clinical and morphopathological diagnosis of CAP was present in 80.6% of cases with HF, in a similar clinical study, Tomashefski., *et al.* demonstrated at the autopsy a coincidence of the clinical diagnosis of CAP in 93 (78.1%) of 119 cases [14].

	rs, Spearman	p
Impaired consciousness	-0,06	p > 0.05
The presence of the rales	0,05	p > 0.05
Dyspnea	0,05	p > 0.05
Muco-purulent expectorations	0,28	p < 0.05
Body temperature $\geq 38^\circ\text{C}$	-0,04	p > 0.05
Multilobar/bilateral extension of the infiltrate	0,06	p > 0.05
Pleural effusion	-0,09	p > 0.05
Positive hemocultures	-0,25	p < 0.05
The dilation of the heart cavities (echocardiography)	-0,27	p > 0.05

**Table 2:** Clinical correlation in group with CAP hyperdiagnosis.

### Conclusion

The coincidence of the clinical and morphopathological diagnosis of CAP and HF was present in 80.6%. The most affected patients were elderly with multiple comorbidities. Chronic heart failure patients with NYHA class III-IV seem to be a particular high-risk group for death associated with pneumonia. No statistically significant differences were observed in CAP etiology. In 1/3 of the patients of both groups multilobar/bilateral infiltrates were present.

### Conflict of Interest

There is no conflict of interest.

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