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Original Article

Pleural effusions in acute decompensated heart failure: Prevalence and prognostic implications

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ABSTRACT

Background: The incidence of pleural effusions (PEs) in acute decompensated heart failure (ADHF) is not well established. We aimed to determine their prevalence, clinical characteristics and prognostic implications.
Methods: Retrospective review of 3245 consecutive patients with ADHF from the Spanish RICA Registry. The clinical characteristics of those with or without PEs on chest radiographs were compared and a predictive PE model was generated.
Results: Patient's median age was 80 years and 60% had a left ventricular ejection fraction (LVEF) > 50%. PEs were seen in 46% of the cases, and their distribution was as follows: 58% bilateral, 27% right-sided and 14% left-sided. Male gender (OR 2.18; 95%CI 1.23–3.87), serum amino-terminal fraction of the pro-brain natriuretic peptide (NT-pro-BNP) levels > 3500 pg/ml (OR 2.2; 95%CI 1.25–3.77), estimated systolic pulmonary artery pressure (sPAP) > 55 mm Hg by echocardiography (OR 2.05; 95%CI 1.12–3.75), and serum prealbumin < 15 mg/l (OR 1.96; 95%CI 1.08–3.52) were associated with PE development in a multivariate analysis. Serum NT-proBNP > 8000 pg/ml, and systolic arterial pressure < 110 mm Hg, but not PEs, independently predicted overall 1-year mortality.
Conclusions: PEs are present on chest radiographs in nearly half of ADHF patients. They are mainly bilateral or right-sided and predominate in males with elevated sPAP on echocardiography and high serum levels of NT-proBNP. PEs do not independently predict 1-year mortality.

1. Introduction

Heart failure (HF) is a prevalent condition with high morbidity and mortality rates, particularly in the elderly population [1,2]. Body fluid retention accompanies worsening HF, and pleural effusion (PE) is included as one of the minor Framingham criteria for the diagnosis of HF [3]. Despite acute decompensated HF (ADHF) being the most probable common cause of PEs, the real incidence of PE in this population has not been well established and depends on the accuracy of the selected reference imaging [1–5]. Some issues about PEs secondary to HF remain controversial. For example, previous reports suggest that unilateral left-sided effusions in the context of HF may not be an atypical finding [1,4]. Similarly, it is thought that the probability of HF-related PE decreases in patients with a normal cardiac silhouette on chest radiographs; a concept, however, which is based on studies where the proportion of patients with a preserved left ventricular ejection fraction (LVEF) was small [6]. Finally, the prognostic implications of PEs in the setting of ADHF have not been previously addressed.

The aim of this study was to determine the prevalence, clinical characteristics and prognosis of PEs in patients with ADHF who were

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admitted to Internal Medicine wards.

2. Patients and methods

2.1. Data source

Patient data were extracted from the **R**egistro de **I**nsuficiencia **Ca**rdiaca (RICA) supported by the Heart Failure Working Group of the Spanish Society of Internal Medicine. RICA is an ongoing multicenter, prospective cohort registry of patients with HF, which has been described elsewhere [7,8]. For the current investigation, the study population was represented by all consecutive patients aged 50 years or more with ADHF (defined according to the criteria of the European Society of Cardiology) [9,10] as a primary diagnosis, who were admitted to the Internal Medicine wards of 52 public and private hospitals in Spain between February 2008 and March 2016. They were followed up for a minimum of 1 year, with outpatient visits at 3 and 12 months after their inclusion in the study. Unscheduled additional visits were performed at the discretion of the attending physician.

Patients were included only once in the registry and subsequent admissions were coded as readmissions. The Ethics Committee of the University Hospital "Reina Sofia" (Córdoba, Spain) approved the study protocol. All patients signed an informed consent before being included in the RICA registry. Patient data were introduced through a web site (https://www.registrorica.org), with the use of a personal password. Confidentiality was preserved since no personal information was collected, except for date of birth and name initials.

2.2. Variables

Complete data included in the registry have been previously reported [7]. For the current study, the following parameters were collected during hospitalization for an ADHF: past medical history, comorbidities, vital signs (blood pressure, heart rate), heart rhythm on electrocardiogram, body mass index (BMI), precipitants of HF decompensation, pre-admission baseline treatments for HF, blood chemistries (i.e., kidney function, glucose, prealbumin and, when available, the natriuretic peptides BNP and NT-pBNP), New York Heart Association (NYHA) scale for functional class before ADHF admission, 2-D echocardiography data during admission or the next 90 days (including LVEF calculated by the Teichholz formula or the Simpson method, the estimated systolic pulmonary artery pressure (sPAP) after applying the Bernoulli equation, and the presence of valvular heart disease), findings from a chest radiograph (PE and its laterality, cardiomegaly defined by a cardiothoracic ratio > 0.5, and vascular redistribution or cephalization), and mortality (either global or related to cardiovascular diseases) during follow-up and readmissions. Glomerular filtration rate (GFR) was estimated with the Modification of Diet in Renal Disease (MDRD) Study equation, and chronic kidney disease was defined by an estimated GFR (eGFR) < 60 ml/min/1.73 m^2. Patients excluded were those with HF triggered by a pulmonary embolism, those without echocardiographic examination or a 1-year follow-up, and those who died before hospital discharge.

2.3. Statistical analysis

Categorical variables are presented as percentages of non-missing values, and continuous variables as medians and 25th–75th quartiles. Between-group comparisons of epidemiological, clinical, biochemical, radiographic and echocardiographic variables in patients with or without PEs were analyzed with the Chi-squared or Mann-Whitney *U* tests, as appropriate. Receiver operating characteristic (ROC) curve analysis helped to decide the optimal cutoff points of continuous variables (e.g., sPAP, NT-proBNP and prealbumin) for predicting the presence of PEs or mortality. A logistic regression analysis with a backward conditional method served to select the best variables related to the development of PEs. To adjust for confounders (i.e., age, heart rate, blood pressure, hemoglobin, eGFR, sodium, NT-proBNP, sPAP, LVEF, NYHA functional class, baseline medical therapy, and the presence of moderate to severe mitral regurgitation or aortic stenosis), a Cox regression analysis estimated the prognostic impact of PEs and other variables. Analyses were performed with the statistical software SPSS version 18.0 (SPSS, Inc., Chicago, Illinois).

3. Results

Of 4648 patients included in the RICA registry during the study period, 3245 received a 1-year follow-up and represented the study population. Baseline characteristics of these patients are listed in Table 1. Median age was 80 (74–84) years, and 53% were women. LVEF was objectively calculated in 3048 patients, of whom 1211 (40%) showed values < 50%.

PEs were detected in 1504 (46%) patients, and their radiological distribution was: bilateral in 881 (58%), isolated right-sided in 414 (27%) and isolated left-sided in 209 (14%). Other radiological and echocardiographic characteristics of the study population are shown in Table 1. No differences in the baseline characteristics (listed in Table 1) were observed between patients with isolated left-sided PEs and those with either bilateral or right-sided PEs (data not shown).

Patients with PEs were significantly older, more often men, and had lower LVEF in comparison to those without PEs. The etiology of HF had no influence on the development of PEs, nor did the echocardiographic detection of moderate-severe mitral regurgitation (24.6% in patients with PE vs 23.6% in those without, p = 0.694) or aortic stenosis (10.5% vs 9.6%, p = 0.715). Patients who were obese or overweight exhibited PEs less frequently, while the opposite was noted in those receiving potassium-sparing diuretics. Although serum creatinine levels were slightly higher in patients with PEs, no significant differences in the eGFR between the groups were observed. Levels of prealbumin were significantly lower in patients with PEs (15.8 vs 18.9 mg/l, p < 0.01).

Natriuretic peptides were measured in the serum of 1886 (58%) patients: B-type natriuretic peptide (BNP) in 452 and the aminoterminal proBNP (NT-proBNP) in 1434. Patients with PEs had higher levels of both natriuretic peptides (779 pg/ml vs 644 pg/ml, and 4426 pg/ml vs 3000 pg/ml, respectively). NT-proBNP levels were found to be associated with the presence of PEs even after considering factors that could modify their concentrations, such as age, gender, BMI and serum creatinine (data not shown).

Patients with PEs more often showed cardiomegaly on chest radiographs. The presence of PEs was also associated with a more dilated left atrium and slightly higher estimated sPAP.

A predictive model was constructed with those variables that had shown a significant association with the presence of PEs. The model selected the following as independent predictors of PE development: male gender, estimated sPAP > 55 mm Hg, serum NT-proBNP > 3500 pg/ml, and serum prealbumin < 15 mg/l (Table 2).

The overall mortality rate at the 1-year follow-up from the ADHF episode was 29% (840 of 3245 patients). A higher mortality rate was observed in patients with PEs (32.4% vs 26.1%, p < 0.01). However, there were no differences in mortality attributable to HF in patients with PEs (15.8% vs 13.5%, p = 0.09). PE development had no influence on the readmission rate, which was 42% overall.

After accounting for confounders, the presence of PEs was not an independent predictor of either cardiovascular or overall mortality. In contrast, serum NT-proBNP levels > 8000 ng/ml (hazard ratio -HR- 2.14, 95%CI 1.75–2.62), and systolic arterial pressure < 110 mm Hg (HR 1.52, 95%CI 1.18–1.96) predicted a worse overall 1-year survival rate, whereas the use of beta blockers (HR 0.59, 95%CI 0.49–0.72) or angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (HR 0.63, 95%CI 0.51–0.77) were protective.