ORIGINAL ARTICLE

Prognostic value of chest radiographs in patients with acute heart failure: the Radiology in Acute Heart Failure (RAD-ICA) study

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Objective. To determine whether chest radiographs can contribute to prognosis in patients with acute heart failure (AHF).

Methods. Consecutive patients with AHF were enrolled by the participating emergency departments. Radiographic variables assessed were the presence or absence of evidence of cardiomegaly and pleural effusion and the pulmonary parenchymal pattern observed (vascular redistribution, interstitial edema, and/or alveolar edema). We gathered variables for the AHF episode and the patient's baseline state. Outcomes were in-hospital and 1-year mortality; hospital stay longer than 7 days, and a composite of events within 30 days of discharge (revisit, rehospitalization, and/or death). Crude and adjusted hazard ratios were calculated for the 3 categories of radiographic variables. The variables were also studied in combination.

Results. A total of 2703 patients with a mean (SD) age of 81 (19) years were enrolled; 54.5% were women. Cardiomegaly was observed in 1711 cases (76.8%) and pleural effusion in 992 (36.7%). A pulmonary parenchymal pattern was observed in all cases, as follows: vascular redistribution in 1672 (61.9%), interstitial edema in 629 (23.3%) and alveolar edema in 402 (14.9%). The adjusted hazard ratios showed that cardiomegaly lacked prognostic value. However, the presence of pleural effusion was associated with a 23% (95% CI, 2%–49%) higher rate of the 30-day composite outcome; in-hospital mortality was 89% (30%–177%) higher in the presence of alveolar edema, and 1-year mortality was 38% (14%–67%) higher in association with vascular redistribution. The results for the variables in combination were consistent with the results for individual variables.

Conclusions. A diagnostic chest radiograph can also contribute to the prediction of adverse events. Pleural effusion is associated with a higher rate of events after discharge, and alveolar edema is associated with higher mortality.

Keywords: Acute heart failure. Emergency department. Chest radiograph. Prognosis.

Estudio RAD-ICA: valor pronóstico de la radiografía de tórax obtenida en urgencias en pacientes con insuficiencia cardiaca aguda

Objetivos. Investigar si la radiografía de tórax en pacientes con insuficiencia cardiaca aguda (ICA) puede contribuir a establecer el pronóstico.

Método. Se incluyeron pacientes consecutivos diagnosticados de ICA en urgencias. Se valoró: cardiomegalia radiológica (CR), derrame pleural (DP) y el patrón parenquimatoso pulmonar (PPP: redistribución vascular, edema intersticial, edema alveolar). Se recogieron variables del estado basal del paciente y del episodio. Las variables de resultado evaluadas fueron mortalidad intrahospitalaria y al año, ingreso prolongado (> 7 días) y evento combinado (reconsulta, rehospitalización o muerte) a 30 días postalta, para las cuales se calcularon las *hazard ratio* crudas y ajustadas para las tres variables radiológicas y su combinación entre ellas.

Resultados. Se incluyeron 2.703 pacientes con una edad media de 81 (DE 19) años; el 54,5% eran mujeres. Se observó CR en 1.711 casos (76,8%), DP en 992 (36,7%) y todos los pacientes mostraron PPP (redistribución vascular el 61,9%, edema intersticial el 23,3% y edema alveolar el 14,9%). El análisis ajustado mostró que la CR no tuvo valor pronóstico; el DP incrementó un 23% (IC 95% 2-49%) los eventos combinados a los 30 días postalta; y el PPP edema alveolar aumentó un 89% (30-177%) la mortalidad intrahospitalaria y un 38% (14-67%) la mortalidad al año respecto al PPP redistribución vascular (referencia). El estudio de la combinación de estos tres hallazgos radiológicos mostró resultados similares y congruentes con los hallazgos del estudio individualizado.

Conclusiones. La radiografía de tórax, además de ayudar a establecer el diagnóstico de ICA, puede contribuir a estimar el pronóstico de eventos adversos. Así, el DP se asocia a un incremento de eventos adversos postalta y el PPP edema alveolar a una mayor mortalidad.

Palabras clave: Insuficiencia cardiaca aguda. Urgencias. Radiografía de tórax. Pronóstico.

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Introduction

Acute heart failure (AHF) is one of the main causes of hospitalization in Spain[1] and represents one of the greatest economic and health burdens within the public health system[2,3]. It is associated with high in-hospital and post-discharge mortality and high readmission rates[4]. In Spain, as in many countries with a public health system, the vast majority of patients with AHF are initially attended in hospital emergency departments (EDs). Among the complementary tests to determine the diagnosis of AHF, chest radiography is one of the most classic and frequently performed in EDs. Its diagnostic role is beyond doubt and, in fact, is part of the Framingham clinical diagnostic criteria established 40 years ago[4]. However, its role in helping to establish the prognosis of patients with AHF has not been studied widely. Perhaps this is why it is not part of any of the risk stratification scales of patients with AHF treated in the ED[5-9]. In order to study whether any of the main findings in chest radiography that can be found in the ICA relates to the prognosis of patients, the study RADiology in the ICA (RAD-ICA) was proposed.

Method

Characteristics of the EAHFE Register

The Registry "Epidemiology of Acute Heart Failure in Emergency departments" (EAHFE) is a multipurpose cohort of a non-interventional, multicentric, analytical nature, with a prospective follow-up, which to date has had five inclusive phases of patients in which 41 Spanish EDs have participated, representing 12% of the 339 public hospitals, including university hospitals, reference hospitals and county hospitals, with 13,791 patients included. The EAHFE Register includes consecutive patients diagnosed with AHF in the ED according to Framingham clinical criteria[4]. In addition, when possible, this diagnosis is confirmed by means of a study of natriuretic peptides or echocardiographic evaluation during the patient's stay in the emergency department or hospital (which was performed in approximately 92% of cases), following the criteria of the European Society of Cardiology[10]. However, patients with exclusively clinical diagnosis are included in the EAHFE Register in order to maintain a cohort as close as possible to the clinical reality of care. The head researcher of each centre is in charge of awarding the final diagnosis of each case. The only exclusion criterion in the EAHFE Register is that the patient presents an acute coronary syndrome with ST segment elevation and concomitant AHF, since these patients are often sent directly to the cardiac haemodynamics laboratory and do not receive direct assistance in the ED. Specific details of the EAHFE Registry have been published in previous studies[8,11-13].

Study design

This is an exploratory study conducted during Phase 5 of the EAHFE Register patient recruitment, which took place between January 1 and February 29, 2016 in 32 EDs, 22 of which participated in the present study. These centers collected specific data from chest radiography when available and the healthcare physician considered that it was of sufficient quality to be interpreted. Three fundamental radiological findings were assessed: 1) presence of radiological cardiomegaly (yes/no), which was defined as the presence of a cardiothoracic index greater than 0.5; 2) presence of pleural effusion (yes/no), regardless of the amount and uni or bilateral location; and 3) the pulmonary parenchymal pattern (PPP), which was grouped into three fundamental categories: vascular redistribution, interstitial edema and alveolar edema, following the classification proposed by Battler et al.[14] and Tattersfield et al.[15]. The classification was made by the physician in charge of the patient's care, and was reviewed by the head researcher of each center, who was in charge of the final allocation to a specific radiological category; in case of discrepancy, the evaluation was made by a radiologist.

Nineteen variables were collected from the patient's baseline, concerning demographic aspects, comorbidity, chronic treatment and the patient's baseline situation, and 14 referring to the current episode of decompensation (vital signs upon arrival at the emergency department, laboratory data, treatment and destination). The patients were followed for one year, by telephone contact and consultation of the electronic history of the hospital and primary care. Mortality from any cause after one year (from the date of the index episode in the emergency department) was defined as the main outcome variable, and the following three as secondary outcome variables: 1) in-hospital mortality from any cause; 2) prolonged hospital stay, which was considered when the duration of such stay, from arrival at the emergency department until discharge, was more than 7 days; and 3) combined event of reconsultation or re-hospitalization due to exacerbation or new episode of AHF or death from any cause in the 30 days following discharge (which were counted from the time the patient was discharged, either from the hospital or from the emergency department). All the researchers had a list of definitions for these variables and the outcome variables. A list with the definitions of the radiological groups was also provided (Table 1).

Statistical analysis

Qualitative variables are expressed as frequencies and percentages, with their 95% confidence interval (95% CI), and quantitative variables as mean and standard deviation (SD) or as median and interquartile range (IQR). Comparison between groups was done using the chi-square test for qualitative variables and the one-way ANOVA test for independent samples (Kruskal-Wallis test if the variable did not have a normal distri-

Table 1. Definitions of radiological groups

Radiological patterns	
Cardiomegaly	Cardiothoracic index equal to or greater than 0,5
Pleural effusion	Any radiological sign of pleural effusion (subdiaphragmatic or subpulmonary, free, localized, atypical or massive), of any occupation and in any location
Vascular Redistribution	Larger diameter of the pulmonary vessels in the upper quadrants of the chest opposite the lower lobes
Interstitial edema	Prominent pulmonary vasculature, blurred hilar margins, peribronchial and perivascular cuffs, and Kerley's B lines
Alveolar edema	Confluent alveolar infiltrates in both pulmonary fields or diffuse confluent densities with poorly defined borders and perihiliary distribution
Pulmonary edema or pulmonary parenchymal pattern	Presence of interstitial edema and alveolar edema

bution) for quantitative variables. The relationship between the different categories of radiological findings studied was calculated by means of the calculation of the hazard ratio (HR) using the Cox regression method for one year mortality, and by means of the calculation of the odds ratio (OR) using logistic regression for in-hospital mortality, prolonged admission and the combined 30-day postal event. These calculations were performed crudely and adjusted for those variables that in the univariate study had shown statistically significant differences. For this purpose, 10 sets of data were created by means of multiple imputation of the values requested in the variables that formed part of the multivariate models, after checking the random pattern of losses. In addition, the adjusted analysis of the results was repeated by combining the different radiological findings. It was accepted that statistical significance existed when the p value was lower than 0.05 or when the 95% CI of the OR or HR excluded the value 1. The analyses were performed with the SPSS 24 program (IBM, New Castle, NY, USA).

Ethical principles

The EAHFE Register is conducted in accordance with the Helsinki Declaration of Ethical Principles for Medical Research Involving Human Subjects, and patients give their consent to participate in it. The full protocol of the registry used in this study has been approved by the Ethics and Clinical Research Committee of the Hospital Central de Asturias in Oviedo, which acts as the main committee (protocol 160/15), as well as by the committees of the other participating hospitals.

Results

Of the 4,713 patients included in the EAHFE Register, the RAD-ICA study eventually studied 2,703 patients (Figure 1). The mean age was 81 (SD 19) years, and 54.5% were women. The rest of the characteristics of the sample are presented in Table 2. High comorbidity with 85% arterial hypertension, 50% atrial fibrillation, 43% diabetes mellitus, 30% chronic renal disease, 29% ischemic heart disease, 25% valvular heart disease and 22% associated chronic obstructive pulmonary disease. De novo heart failure accounted for 43% and 78% of patients were admitted to hospital. In terms of radiological findings, cardiomegaly was found in 2,076 cases (76.8%), pleural effusion in 992 (36.7%) and pulmonary parenchymal pattern was defined as vascular redistribution in 1,672 patients (61.9%), interstitial edema in 629 (23.3%) and alveolar edema in 402 (14.9%). The characteristics of the patients classified in each of these subgroups showed some significant differences and, thus, patients with and without cardiomegaly differed in 14 of the 33 characteristics evaluated, those with pleural effusion and those that did not differ in 10, and the groups of the different pulmonary parenchymal patterns differed in 15 (Table 3).

Considering the total population studied, 859 patients (31.8%) died after a year (primary event). Regarding secondary events, 233 in-hospital deaths (8.6%), 978 patients with prolonged stays (36.5%, 25 cases lost due to lack of discharge date) and 978 patients (among the 2,470 patients discharged alive from the index episode) who had a combined adverse event during the 30 days following discharge (26.0%, 28 patients without reconsultation or readmission data) were recorded.

The univariate study showed that radiological cardiomegaly was not associated with any significant increase in the adverse events studied, pleural effusion was associated with an increase in mortality after one year and combined events at 30 days, and pulmonary parenchymal pattern alveolar edema was associated with an increase in mortality at one year, in-hospital mortality and prolonged stays (Table 4).

The annual mortality curves for each radiological

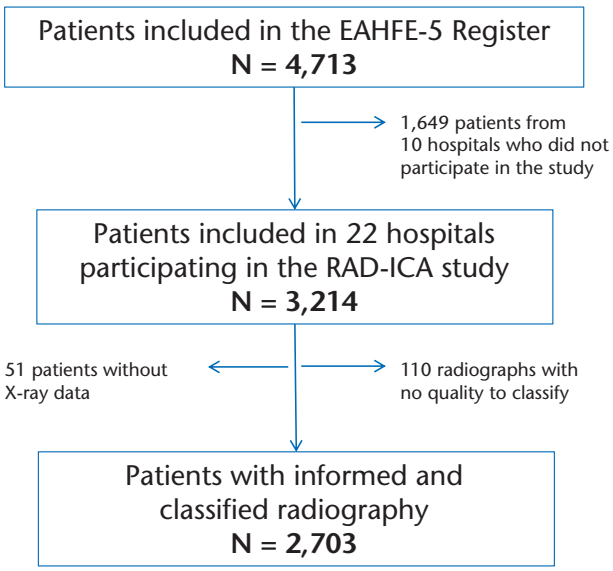

Figure 1. Patient inclusion diagram.

Table 2. Characteristics of the patients included in the study

	N = 2,703 n (%)	Lost values n (%)
Epidemiological data		
Age (years) [mean (SD)]	81 (10)	0 (0)
Women	1,468 (54,5)	11 (0.4)
Comorbidities		
High blood pressure	2,290 (84.7)	6 (0.2)
Diabetes mellitus	1,155 (42.8)	5 (0.2)
Ischemic heart disease	776 (28.8)	6 (0.2)
Chronic kidney disease	812 (30.1)	5 (0.2)
Cerebrovascular disease	362 (13.4)	5 (0.2)
Atrial fibrillation	1,354 (50.2)	5 (0.2)
Valvular heart disease	683 (25.3)	6 (0.2)
Peripheral arterial disease	289 (10.7)	6 (0.2)
Chronic obstructive pulmonary disease	591 (21.9)	6 (0.2)
Previous episodes of heart failure sharp	1,354 (57.0)	10 (0.2)
Previous chronic treatment		
Beta-blocker	1,257 (46.8)	15 (0.6)
System Inhibitors renin-angiotensin	1,488 (55.3)	12 (0.4)
Recipient antagonists mineralocorticoids	426 (15.8)	12 (0.4)
Digoxin	342 (12.7)	13 (0.5)
Baseline situation		
NYHA Class III/IV	641 (24.5)	83 (3.1)
Barthel Index (points) [mean (SD)]	79 (25)	148 (5.5)
LVEF (%) [mean (SD)]	51 (15)	986 (36.5)
Vital signs in the emergency department		
Systolic blood pressure (mmHg) [mean (SD)]	141 (27)	17 (0.6)
Heart rate (bpm) [mean (SD)]	88 (23)	28 (1.0)
Basal pulse oximetry (%) [mean (SD)]	92 (7)	56 (2.1)
Laboratory data in the ED		
Hemoglobin (g/l) [mean (SD)]	119 (21)	15 (0.6)
Creatinine (mg/dl) [mean (SD)]	1.37 (0.91)	13 (0.5)
Sodium (mmol/l) [mean (SD)]	139 (5)	53 (2.0)
Potassium (mmol/l) [mean (SD)]	4.42 (0.69)	182 (6.7)
NT-proBNP (pg/ml) [mean (IQR)]	4,101 (6422)	1,559 (57.7)
Elevated troponin	861 (61.3)	1,299 (48.1)
Treatment and ED destination		
Morphine (SC/IV)	194 (7.2)	6 (0.2)
Nitroglycerin (IV)	359 (13.3)	6 (0.2)
Inotropes or vasopressors (IV)	46 (1.7)	6 (0.2)
Non-invasive ventilation	199 (7.4)	6 (0.2)
Hospital admission	2,110 (78.1)	0 (0)

SD: standard deviation; LVEF: left ventricular ejection fraction; IV: intravenous; NT-proBNP: cerebral N-terminal natriuretic propeptide; NYHA: New York Heart Association; IQR: interquartile range; SC: subcutaneous.

subgroup are shown in Figure 2. After adjusting for potential confounding variables, there was a significant increase in combined postal events related to the presence of radiological pleural effusion (+23%; 95% CI +2% to +49%; p = 0.03), and a significant increase in mortality per year (+38%); 95% CI +14% to +67%; p = 0.001) and in-hospital mortality (+89%; CI 95 +30% to +177%; p = 0.001) in relation to the pattern of pulmonary edema (compared to vascular redistribution, which was the category taken as a reference) (Table 4).

When adverse events were analyzed by combining the different radiological categories (Figure 3), the results were similar and congruent with what was found in the individual analysis of each radiological sign. Thus, for patients with chest radiography in which there was no alveolar edema, no pleural effusion and no cardiomegaly (control category) in the PPP, those with pulmonary edema and pleural effusion without cardiomegaly had a higher mortality rate after a year (adjusted HR 2.697, 95% CI 1.622-4.483; p < 0.001) and in-hospital during the index episode (adjusted OR 6.993, 95% CI 2.672-18.302) (adjusted OR 6.993, 95% CI 2.672-18.302). Those with pulmonary edema and pleural effusion without cardiomegaly had increased mortality at one year (adjusted HR 2.697, 95% CI 1.622-4.483; p < 0.001) and in-hospital during the index episode (adjusted OR 6.993, 95% CI 2.672-18.302); p < 0.001); those with pulmonary edema, pleural effusion and cardiomegaly also had higher mortality at one year (adjusted HR 1.421, 95% CI 1.040-1.940; p = 0.027) and more combined postal events at 30 days (OR 1.627, 95% CI 1.027-2.579); P = 0.027) and those with pleural effusion without pulmonary edema or cardiomegaly had a higher frequency of combined postal events at 30 days (OR 1.662, 95% CI 1.058-2.610; P = 0.038).

Discussion

The first relevant finding of the RAD-ICA study is that radiological cardiomegaly was not associated with any significant increase in the adverse events studied. Its presence generally indicates an increase in ventricular volumes which, in turn, is a powerful predictor of adverse events, especially in patients with myocardial infarction[16,17]. However, the relationship between cardiomegaly and left ventricular ejection fraction (LVEF), although intimate, is not always concordant[18]. Furthermore, although sensitive, it is not specific for identifying dilation of the left ventricle[19]. Thus, some authors have published that half of patients with left ventricular systolic dysfunction present cardiomegaly on chest radiography. In different studies, cardiomegaly in heart failure behaves as a prognostic factor when associated with other variables, such as the existence of a reduced LVEF (which is related to an increased risk of progression of the functional class and hospitalization) or if associated with ventricular arrhythmias (related to increased mortality)[18].

Second, the presence of radiological pleural effusion produces a significant 23% increase in combined post-high events. In a previous study of 1,658 patients with AHF over 80 years of age, pleural effusion was associated with a 69% increase in short-term adverse events[20]. DeBiasi and Puchalski[21] showed that patients with heart failure with pleural effusion undergoing thoracentesis had higher mortality at 30 days and one year (22 and 53%, respectively). In a recent study, conducted in outpatients with heart failure, it was shown that the presence of pleural effusion was directly related to quality of life. And the study found that a reduction in pleural effusion was associated with an improvement in

Table 3. Comparison of patient characteristics according to the different radiological patterns studied

Factors	Radiological cardiomegaly		p	Pleural effusion		p	Pulmonary parenchymal pattern			p
	No N = 627 n (%)	Yes N = 2.076 n (%)		No N = 1.711 n (%)	Yes N = 992 n (%)		Vascular redistribution N = 1.672 n (%)	Interstitial edema N = 629 n (%)	Alveolar N = 402 n (%)	
Epidemiological data										
Age > 80 years	80 (10)	81 (10)	0.30	80 (10)	82 (10)	**0.002**	81 (10)	82 (9)	80 (11)	**0.04**
Women	309 (49.7)	1,159 (56.0)	**0.006**	939 (55.0)	529 (53.8)	0.54	896 (53.8)	359 (57.2)	213 (53.3)	0.31
Comorbidities										
High blood pressure	513 (81.9)	1,777 (85.8)	**0.02**	1,451 (85.1)	839 (84.7)	0.78	1,427 (85.6)	528 (83.9)	335 (83.5)	0.43
Diabetes mellitus	264 (42.2)	891 (43.0)	0.71	735 (43.1)	420 (42.4)	0.73	691 (41.4)	273 (43.4)	191 (47.6)	0.07
Ischemic heart disease	181 (28.9)	595 (28.7)	0.93	498 (29.2)	278 (28.1)	0.53	468 (28.1)	177 (28.2)	131 (32.7)	0.17
Chronic kidney disease (creatinine > 2 mg/dl)	170 (27.2)	642 (31.0)	0.07	481 (28.2)	331 (33.4)	**0.004**	486 (29.1)	184 (29.3)	142 (35.4)	**0.04**
Cerebrovascular disease	74 (11.8)	288 (13.9)	0.18	222 (13.0)	140 (14.1)	0.41	232 (13.9)	73 (11.6)	57 (14.2)	0.31
Atrial fibrillation	289 (46.2)	1,065 (51.4)	**0.02**	823 (48.2)	531 (53.6)	**0.007**	859 (51.5)	309 (49.1)	186 (46.4)	0.15
Valvular heart disease	133 (21.2)	550 (26.6)	**0.007**	421 (24.7)	262 (26.4)	0.31	434 (26.0)	148 (23.5)	101 (25.2)	0.47
Peripheral arterial disease	67 (10.7)	222 (10.7)	0.99	161 (9.4)	128 (12.9)	**0.005**	166 (10.0)	69 (11.0)	54 (13.5)	0.12
Chronic obstructive pulmonary disease	155 (24.8)	436 (21.1)	**0.04**	370 (21.7)	221 (22.3)	0.71	390 (23.4)	130 (20.7)	71 (17.7)	**0.03**
Previous episodes of acute heart failure	305 (48.7)	1,229 (59.5)	< **0.001**	955 (56.0)	579 (58.6)	0.19	953 (57.2)	343 (54.7)	238 (59.4)	0.32
Previous chronic treatment										
Beta-blockers	268 (43.2)	989 (47.8)	**0.04**	795 (46.7)	462 (46.9)	0.94	775 (46.5)	279 (44.6)	203 (51.1)	0.12
Renin-angiotensin system inhibitors	316 (50.9)	1,172 (56.6)	**0.01**	968 (56.8)	520 (52.6)	**0.03**	921 (55.3)	340 (54.2)	227 (57.0)	0.68
Mineralocorticoid receptor antagonists	75 (12.1)	351 (17.0)	**0.003**	282 (16.6)	144 (14.6)	0.17	270 (16.2)	93 (14.8)	63 (15.8)	0.72
Digoxin	57 (9.2)	285 (13.8)	**0.003**	210 (12.3)	32 (13.4)	0.44	222 (13.3)	71 (11.3)	49 (12.3)	0.42
Baseline situation										
NYHA Class III/IV	124 (20.4)	517 (25.7)	**0.008**	414 (24.9)	227 (23.7)	0.50	386 (23.8)	150 (24.5)	105 (27.1)	0.39
Barthel Index (points) [mean (SD)]	80 (26)	79 (25)	0.40	79 (26)	78 (25)	0.27	79 (25)	79 (25)	77 (26)	0.18
LVEF (%). mean (SD)	53 (13)	51 (16)	0.11	52 (15)	51 (15)	0.35	52 (15)	51 (15)	49 (16)	**0.03**
Vital signs in the emergency department										
Systolic blood pressure (mmHg) [mean (SD)]	140 (27)	142 (27)	0.13	141 (27)	142 (27)	0.52	142 (28)	145 (30)	141 (27)	**0.005**
Heart rate (bpm) [mean (SD)]	89 (23)	87 (23)	0.13	87 (23)	88 (23)	0.44	90 (25)	89 (23)	88 (23)	**0.003**
Basal pulse oximetry (%) [mean (SD)]	92 (6)	92 (7)	0.58	93 (6)	97 (7)	0.11	93 (6)	92 (8)	91 (7)	< **0.001**
Laboratory data										
Hemoglobin (g/l) [mean (SD)]	120 (22)	119 (21)	0.36	120 (20)	117 (22)	< **0.001**	120 (21)	119 (20)	116 (21)	**0.022**
Creatinine (mg/dl) [mean (SD)]	1.42 (0.96)	1.36 (0.90)	0.12	1.35 (0.90)	1.40 (0.93)	0.20	1.41 (1.06)	1.47 (0.96)	1.37 (0.91)	**0.01**
Sodium (mmol/l) [medium (SD)]	139 (5)	139 (5)	0.53	139 (5)	139 (6)	0.44	139 (5)	139 (5)	138 (6)	0.70
Potassium (mmol/l) [medium (SD)]	4.39 (0.65)	4.43 (0.71)	0.27	4.40 (0.70)	4.46 (0.69)	**0.03**	4.39 (0.69)	4.45 (0.67)	4.48 (0.75)	**0.02**
NT-proBNP (pg/ml) [median (IQR)]	3,594 (6.148)	4,380 (6.833)	0.12	3,597 (5.819)	4,903 (8.251)	< **0.001**	4,143 (6.440)	3,938 (6.233)	4,184 (6.215)	0.86
Elevated troponin	228 (67.9)	1,068 (59.3)	**0.005**	557 (63.2)	304 (58.1)	0.06	527 (63.8)	202 (56.9)	132 (59.2)	0.06
Treatment and ED destination										
Morphine (SC/IV)	56 (8.9)	138 (6.7)	0.06	130 (7.6)	64 (6.5)	0.26	75 (4.5)	50 (8.0)	69 (17.2)	< **0.001**
Nitroglycerin (IV)	63 (10.0)	296 (14.3)	**0.006**	196 (11.5)	163 (16.5)	< **0.001**	159 (9.5)	80 (12.7)	120 (29.9)	< **0.001**
Inotropes or vasopressors (IV)	8 (1.3)	38 (1.8)	0.34	30 (1.8)	16 (1.6)	0.78	22 81.3)	10 (1.6)	14 (3.5)	**0.01**
Non-invasive ventilation	56 (8.9)	143 (6.9)	0.09	120 (7.0)	79 (8.0)	0.36	68 (4.1)	60 (9.6)	71 (17.7)	< **0.001**
Hospital admission	458 (73.0)	1,652 (79.6)	**0.001**	1,261 (73.7)	849 (85.6)	< **0.001**	1,233 (73.3)	514 (81.7)	363 (90.3)	< **0.001**

SD: standard deviation; LVEF: left ventricular ejection fraction; IV: intravenous; NT-proBNP: cerebral N-terminal natriuretic propeptide; NYHA: New York Heart Association; IQR: interquartile range; SC: subcutaneous.

Statistically significant p values ($p < 0.05$) are highlighted in bold.

Table 4. Magnitude of the crude and adjusted effects of the different radiological characteristics

	Events	Univariable study		Multivariable study	
	n (%)	Ratio (95% CI)	p	Ratio (95% CI)	p
One-year mortality (HR)					
Radiological cardiomegaly					
No	197 (31.4)	1 (reference)	–	1 (reference)	–
Yes	662 (31.9)	1.01 (0.86-1.18)	0.95	1.05 (0.83-1.23)	0.56
Pleural effusion					
No	512 (29.9)	1 (reference)	–	1 (reference)	–
Yes	347 (35.0)	1.21 (1.06-1.39)	**0.006**	1.04 (0.90-1.19)	0.61
Pulmonary parenchymal pattern					
Vascular Redistribution	502 (30.0)	1 (reference)	–	1 (reference)	–
Interstitial edema	201 (32.0)	1.10 (0.93-1.29)	0.26	1.00 (0.84-1.18)	0.99
Pulmonary edema	156 (38.8)	1.44 (1.20-1.72)	< **0.001**	1.38 (1.14-1.67)	**0.001**
Intrahospital mortality (OR)					
Radiological cardiomegaly					
No	62 (9.9)	1 (reference)	–	1 (reference)	–
Yes	171 (8.2)	0.82 (0.60-1.11)	0.20	0.75 (0.53-1.01)	0.06
Pleural effusion					
No	137 (8.0)	1 (reference)	–	1 (reference)	–
Yes	96 (9.7)	1.23 (0.94-1.62)	0.14	0.98 (0.74-1.30)	0.89
Pulmonary parenchymal pattern					
Vascular Redistribution	115 (6.9)	1 (reference)	–	1 (reference)	–
Interstitial edema	58 (9.2)	1.37 (0.99-1.91)	0.06	1.09 (0.76-1.57)	0.63
Pulmonary edema	60 (14.9)	2.37 (1.70-3.31)	< **0.001**	1.89 (1.30-2.77)	**0.001**
Prolonged stay (> 7 days) (OR)					
Radiological cardiomegaly					
No	218 (35.7)	1 (reference)	–	1 (reference)	–
Yes	760 (36.8)	1.05 (0.87-1.26)	0.62	0.93 (0.75-1.15)	0.53
Pleural effusion					
No	600 (35.5)	1 (reference)	–	1 (reference)	–
Yes	378 (38.2)	1.12 (0.95 (1.32)	0.16	0.89 (0.74-1.06)	0.19
Pulmonary parenchymal pattern					
Vascular Redistribution	569 (34.3)	1 (reference)	–	1 (reference)	–
Interstitial edema	227 (36.5)	1.10 (0.91-1.33)	0.34	0.94 (0.76-1.16)	0.56
Pulmonary edema	182 (45.6)	1.60 (1.28-2.00)	< **0.001**	1.17 (0.91-1.50)	0.23
Combined event 30 days postal (OR)					
Radiological cardiomegaly					
No	142 (25.9)	1 (reference)	–	1 (reference)	–
Yes	494 (26.1)	1.01 (0.81-1.26)	0.91	1.01 (0.81-1.26)	0.95
Pleural effusion					
No	380 (24.5)	1 (reference)	–	1 (reference)	–
Yes	256 (28.7)	1.24 (1.03-1.49)	**0.023**	1.23 (1.02-1.49)	**0.03**
Pulmonary parenchymal pattern					
Vascular Redistribution	392 (25.4)	1 (reference)	–	1 (reference)	–
Interstitial edema	151 (26.8)	1.07 (0.86-1.34)	0.52	1.09 (0.87-1.37)	0.46
Pulmonary edema	93 (27.5)	1.11 (0.85-1.45)	0.43	1.09 (0.82-1.45)	0.57

HR: hazard ratio; 95% CI: 95% confidence interval; OR: odds ratio.
Statistically significant p values (p < 0.05) are highlighted in bold.

the quality of life tests - MLHFQ score - and in the functional class -NYHA-; thus, for each 1 cm reduction in pleural effusion, 3.2 points were reduced in the MLHFQ and 1.06 in the NYHA functional class[22].

Third, a pattern of pulmonary edema causes a significant increase of 89% in in-hospital mortality and 38% in annual mortality. Pulmonary congestion in AHF is a complex pathophysiological process that goes beyond fluid overload and hemodynamics. Inflammatory and oxidative lung injury causing blood-gas barrier dysfunction appears to be key to the pathogenesis of pulmonary edema[23]. Pulmonary edema is associated with pulmonary vascular disease and overload and dysfunction of both ventricles, and has been associated with increased mortality in different studies[24]. Hence the importance of intensive decongestion therapy in AHF to slow the progression of pulmonary vascular disease and biventricular heart failure and improve prognosis.

Finally, when adverse events were analysed combining the different radiological categories, the results were similar and consistent with what was found in the analysis of each radiological sign individually. Those showing PPP with pulmonary edema, pleural effusion and cardiomegaly had a greater frequency of combined postal events after 30 days (OR 1.627, 95% CI 1.027 - 2.579; P = 0.027) and mortality after one year (adjusted HR 1.421, 95% CI 1.040 - 1.940); P = 0.027); those who had PPP without pulmonary edema, with

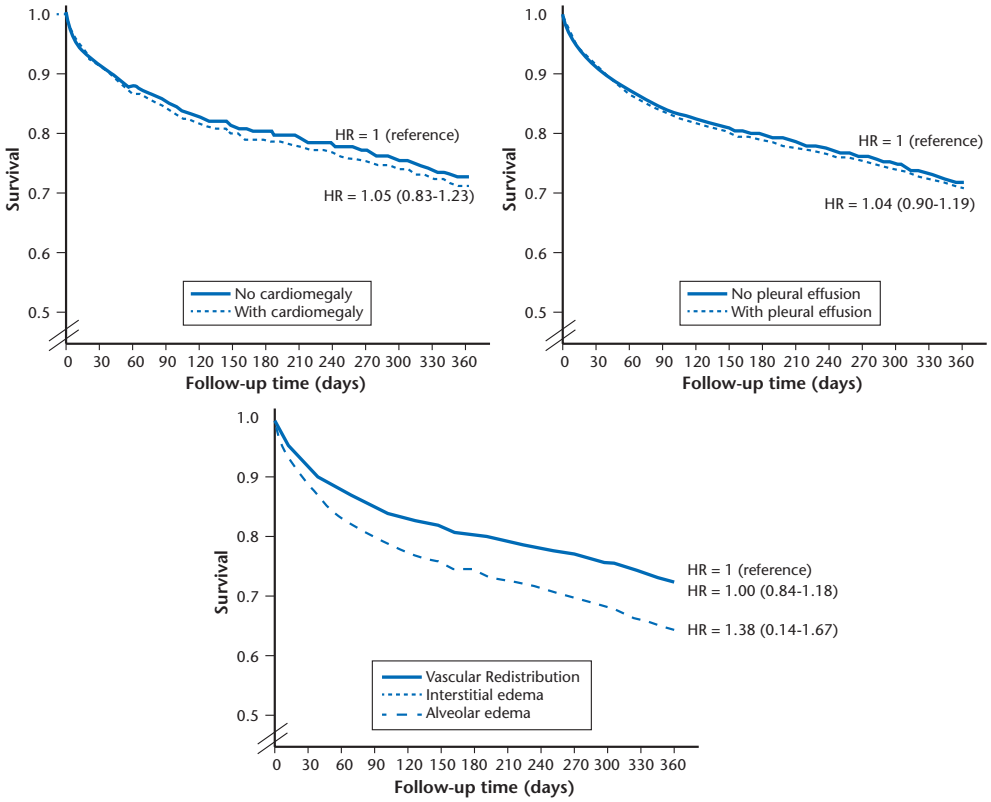

Figure 2. Adjusted survival curves of mortality at one year for the different radiological categories assessed in the present study.

pleural effusion and without cardiomegaly had a higher frequency of combined events after 30 days (OR 1.662, 95% CI 1.058-2.610); p = 0.038) and those with PPP pattern with pulmonary edema, pleural effusion and absence of cardiomegaly showed an increase in in-hospital mortality (adjusted OR 6.993, 95% CI 2.672-18.302; p < 0.001) and at one year (adjusted HR 2.697, 95% CI 1.622-4.483; p < 0.001). Congestion increases stress on the left ventricular wall and contributes to neurohormonal activation, promotes remodeling and contributes to progression. Radiological congestion (clinical congestion) is the reflection of elevated pulmonary capillary pressures (hemodynamic management), which are associated with volume overload and correlate with more severe symptoms and decreased survival[25]. Our study correlates with others where congestion has been defined as one of the main prognostic factors in patients with AHF and an important predictor of morbidity and mortality. However, hemodynamic congestion precedes clinical congestion over time and, therefore, the radiological presence of PPP is not always correlated with high pulmonary capillary pressures (PCP). In one study, altered PPP was absent in 53% of patients with a PCP of 16 to 29 mmHg and in 39% of patients with PCP ≥ 30 mmHg, so that the absence of congestion in chest radiography should not exclude the presence of elevated PCP26. In the study by Mahdyoon et al. only 7 of 22 patients (32%) with elevated PCP (≥ 25 mmHg) had moderate-severe pulmonary congestion detected by chest x-ray; and in 6 patients (27%) there was no evidence of radiological pulmonary congestion[27].

This study has certain limitations. First of all, it has been carried out in EDs that were chosen for convenience, because they were part of the EAHFE Registry. Secondly, the assignment to each radiological group was made by members of the ED itself, and not by a single awarding co-committee. Thirdly, there was no calculation of sample size as it was an exploratory study, so we cannot rule out the possibility of a beta error in some estimates. Fourthly, the size of the pleural effusion was not quantified and thoracentesis was required, since in previous studies larger size or the need for drainage were associated with greater adverse events[21].

In conclusion, the RAD-ICA study, conducted at a time of great development in advanced imaging techniques, shows that simple chest radiography can still provide information to the physician attending the patient. Beyond its unquestionable diagnostic value[28], which the present study does not evaluate, the interpretation of its findings in patients with AHF in the emergency department can help to detect those with a higher risk of adverse events and contribute to a better selection of patients who are subject to admission and those who can be discharged directly from the emergency department[9,29,30]. This, together with its universal availability in the emergency department and its low cost and risk,

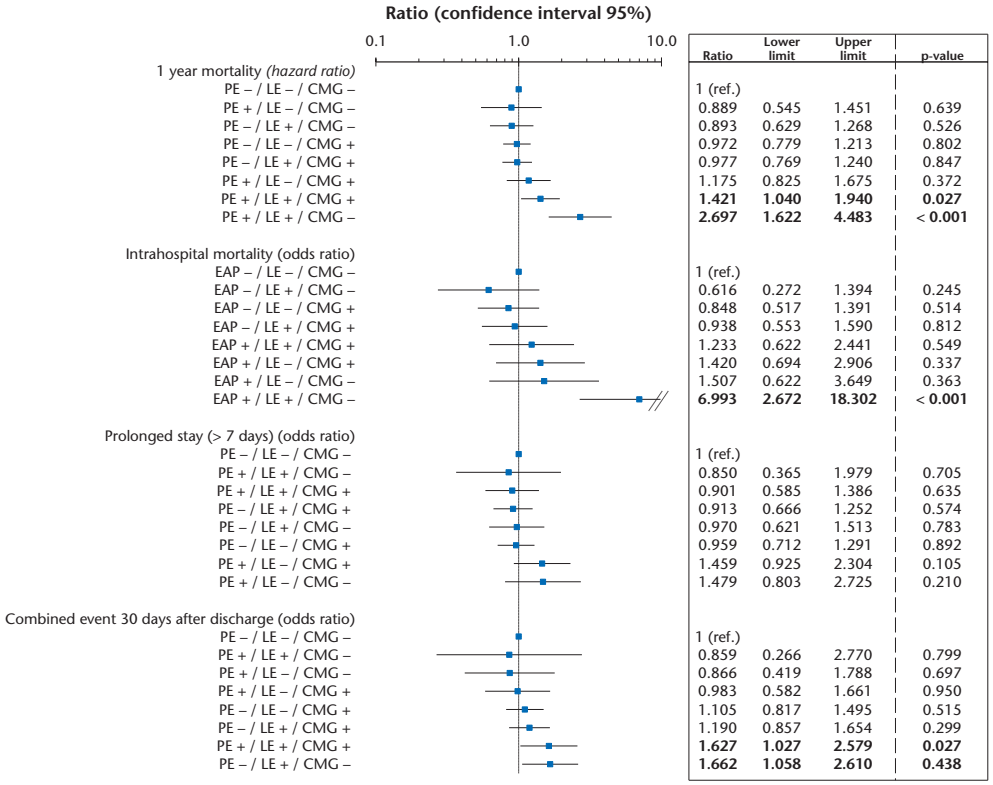

Figure 3. Adjusted analysis of the relationship between the combination of radiological findings and the adverse events evaluated in the present study.
CMG: cardiomegaly; PE: pleural effusion; LE: lung edema

means that it continues to be a fundamental test in the evaluation of these patients.

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