# Prevalence, Related Factors and Association of Left Bundle Branch Block With Prognosis in Patients With Acute Heart Failure: a Simultaneous Analysis in 3 Independent Cohorts

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**ABSTRACT**

**Objectives:** To determine the prevalence, characteristics and association with prognosis of left bundle branch block (LBBB) in 3 different cohorts of patients with acute heart failure (AHF).

**Methods and Results:** We retrospectively analyzed 12,950 patients with AHF who were included in the EAHFE (Epidemiology Acute Heart Failure Emergency), RICA (National Heart Failure Registry of the Spanish Internal Medicine Society), and BASEL-V (Basics in Acute Shortness of Breath Evaluation of Switzerland) registries. We independently analyzed the relationship between baseline and clinical characteristics and the presence of LBBB and the potential association of LBBB with 1-year all-cause mortality and a 90-day postdischarge combined endpoint (Emergency Department reconsultation, hospitalization or death). The prevalence of LBBB was 13.5% (95% confidence interval: 12.9%−14.0%). In all registries, patients with LBBB more commonly had coronary artery disease and previous episodes of AHF, were taking chronic spironolactone treatment, had lower left ventricular ejection fraction and systolic blood pressure values and higher NT-proBNP levels. There were no differences in risk for patients with LBBB in any cohort, with adjusted hazard ratios (95% confidence interval) for 1-year mortality in EAHFE/RICA/BASEL-V cohorts of 1.02 (0.89−1.17), 1.15 (0.95−1.38) and 1.32 (0.94−1.86), respectively, and for 90-day postdischarge combined endpoint of 1.00 (0.88−1.14), 1.14 (0.92−1.40) and 1.26 (0.84−1.89). These results were consistent in sensitivity analyses.

**Conclusions:** Less than 20% of patients with AHF present LBBB, which is consistently associated with cardiovascular comorbidities, reduced left ventricular ejection fraction and more severe decompensations. Nonetheless, after taking these factors into account, LBBB in patients with AHF is not associated with worse outcomes. (*J Cardiac Fail 2022;28:1104−1115*)

**Key Words:** Acute heart failure, left bundle branch block, prognosis, mortality.

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Manuscript received August 18, 2021; revised manuscript received November 13, 2021; revised manuscript accepted November 19, 2021.

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1071-9164/$ - see front matter



https://doi.org/10.1016/j.cardfail.2021.11.022

### Bullet points

- The prevalence of left bundle branch block in patients with acute heart failure ranges between 10% and 20%.
- The presence of left bundle branch block in acute heart failure is associated with cardiovascular comorbidities, reduced left ventricular ejection fraction and more severe decompensations.
- Left bundle branch block is associated with a non-significant increased risk of mortality in patients with acute heart failure.

### Brief lay Summary

The prognosis of left bundle branch block in acute heart failure remains controversial. While some studies have suggested that it is associated with higher mortality others have failed to demonstrate this relationship. To answer this question more studies including systematic reviews and meta-analysis are needed.

Tweet: "Prevalence and association with prognosis of left bundle branch block in acute heart failure: analysis in three independent cohorts" (RICA from @icyfasemi, EAHFE from @IcaSemes and BASEL-V)" by @jc_trullas @OmiroOscar et al.

Heart failure (HF) is highly prevalent in people over the age of 65 years and constitutes the first cause of hospitalization in this population. During recent decades, there has been an increase in the percentage of patients with HF who also have multiple comorbidities, due mainly to the increase in cardiovascular diseases (such as hypertension, obesity and diabetes) and the aging of the population (which is frequently associated with frailty and dependence).[1,2] In addition, mortality and the need for rehospitalization that is associated with decompensations (acute HF [AHF]) are high, and these adverse outcomes start from the first episode of decompensation, even in low-risk patients with HF.[3–5]

Accordingly, many variables related to patient baseline characteristics and to the acute episode of decompensation able to predict such adverse outcomes in patients with AHF have been investigated, and some risk factors have been defined unequivocally.[5–8] Conversely, the importance of electrocardiographic abnormalities has been poorly explored. In fact, observational studies have shown that left bundle branch block (LBBB) is present in the electrocardiograms (ECGs) of 15%–30% of patients with AHF, but the association of LBBB with prognosis still remains controversial; some studies have suggested it is associated with higher mortality rates,[9,10] whereas others have failed to demonstrate this relationship.[11–15] Many of these results, however, come from either highly selected patients in randomized controlled trials,[10] patients admitted to intensive care units,[13,14] studies including patients with right bundle branch block and LBBB together,[12] or patients included in developing countries.[11] All these factors impose a large selection bias. In addition, it is of note that around one-quarter of patients with AHF are managed entirely in the emergency department without hospitalization, and around one-quarter of patients requiring hospitalization are admitted to cardiology departments.[16] Accordingly, we designed the present study with the objectives of determining the prevalence of LBBB in patients with AHF, defining common risk factors associated with the presence of LBBB and analyzing the association between LBBB and the prognosis of patients with AHF in 3 different cohorts representing different clinical scenarios in an attempt to avoid the aforementioned recruitment partiality.

## Methods

### Study Population

The present study is a secondary analysis of patients included in 3 independent cohorts of people with AHF, the designs of which have been explained in greater detail elsewhere.[16–19] Briefly, the EAHFE (Epidemiology of AHF in Emergency departments) cohort is a prospective multicenter registry that includes patients with AHF attended to in 45 Spanish emergency departments (EDs) independent of their final disposition after the first medical presentation (admission to a general ward, admission to an intensive care unit or discharged home);[16,17] the RICA (from Registro de Insuficiencia Cardiaca Aguda, in Spanish, or AHF Registry, in English) cohort is a prospective multicenter registry that includes patients consecutively admitted to 34 Spanish internal medicine departments (IMDs) for AHF who were discharged alive after the index AHF episode that caused the hospitalization;[17,18] and the BASEL-V (Basics in Acute Shortness of Breath EvaLuation) cohort is a prospective multicenter diagnostic study that enrolled adult patients presenting with acute dyspnea to 2 Swiss EDs.[19] For the current study, only patients in the BASEL-V cohort with adjudicated final diagnoses of AHF were included. The 3 registries were approved by their respective ethics committees, and written informed consent was obtained from all participating patients.

### Patient Selection and Classification

For the present secondary analysis, we included patients from the 3 cohorts for whom information about the ECG at baseline and vital status after 1

year of follow-up were available. We excluded patients with pacemakers at admission and those who required pacemaker implantation during the index admission for 3 reasons: (1) a pacemaker rhythm on the baseline ECG does not allow an adequate assessment of the patient's baseline heart rhythm; (2) pacemaker implementation could influence the prognosis; and (3) all studies that have analyzed conduction abnormalities in AHF have systematically excluded patients with pacemakers. Patients were then divided into 2 groups, according to whether LBBB was or was not present in the first resting 12-lead ECG, recorded either at the time of ED presentation or during hospital admission. Adjudication of LBBB was made at a local level by the principal investigator of each center and was based on the presence in the ECG of a QRS duration $>$ 120 ms; delayed onset of the intrinsicoid deflection in leads I, V5 and V6 of $>$ 50 ms; the presence of a broad monophasic, often notched, R-wave in leads I, V5 and V6, with rS or QS complexes in leads V1 and V2; and ST-T-wave vectors opposite in direction from the major QRS vector.[20]

#### Independent Variables

We selected 2 different types of variables: 1 set corresponded to the baseline characteristics of the patients, and 1 set corresponded to the clinical characteristics of the acute episode of decompensation. Among all the variables reported in the registries, we prioritized those that were present and commonly defined in at least 2 of the 3 registries. The only exceptions were the Charlson and Pfeifer indexes (recorded only in the RICA cohort) and treatments provided in the ED (recorded only in the EAHFE cohort). Regarding baseline variables, we finally included 28 items: 3 demographic (age, sex, body mass index); 14 comorbidities (active smoker, hypertension, dyslipidemia, diabetes mellitus, coronary artery disease, heart valve disease, peripheral artery disease, cerebrovascular disease, atrial fibrillation, previous episodes of AHF, chronic kidney disease, chronic obstructive pulmonary disease, dementia, active cancer); 5 corresponding to baseline status (New York Heart Association class, left ventricular ejection fraction (LVEF), Barthel index, Charlson index, Pfeifer index); and 6 chronic treatments (diuretics, renin-angiotensin system inhibitors, beta-blockers, mineralcorticosteroid-receptor antagonists, digoxin, amiodarone). Regarding clinical variables, we included 21 items: 6 triggers of AHF episodes (infection, rapid atrial fibrillation, anemia, hypertensive crisis, dietetic/pharmacologic transgression, acute coronary syndrome); 3 vital signs at arrival (systolic blood pressure [SBP], heart rate, room air oximetry); 6 analytical parameters (hemoglobin, creatinine, potassium, sodium, NT-proBNP, troponin); 1 variable assessing severity (MEESSI risk stratification);[21] and 5 variables related to ED management (intravenous diuretics, vasodilators and inotropes/vasopressors, noninvasive ventilation, hospitalization).

#### Endpoints

We selected 2 coprimary endpoints. The first was 1-year all-cause mortality. Time was counted from the day of ED admission by the EAHFE and BASEL-V cohorts and from hospital discharge by the RICA cohort. The second endpoint corresponded to a 90-day postdischarge combined event, which was formed by all-cause mortality or need for hospitalization due to AHF. ED revisit due to AHF was also included in the combined endpoint for the EAHFE cohort. By definition, patients dying during the index AHF episode before discharge (in-hospital mortality) were not included in the analysis of the 90-day postdischarge combined event. In all 3 cohorts, the time to the combined endpoint was counted from the day of hospital discharge after the index AHF episode, either from the ED or after hospitalization. Outcome adjudication was carried out at a local level by the principal investigators of each center in the EAHFE and RICA cohorts, whereas central adjudication by 2 independent cardiologists was performed in the BASEL-V cohort.

#### Statistical Analysis

All statistical analyses were independently performed for each individual cohort. Quantitative variables are expressed as median and interquartile range. Qualitative variables are expressed as the number of patients and percentages. The $\chi^2$ or Fisher exact tests (as needed) were used to compare qualitative variables. The *t* test was used to compare normally distributed quantitative variables (assessed by the Kolmogorov-Smirnov test), and the nonparametric Mann-Whitney U test was used when distribution was not normal. Kaplan-Meier curve analysis was used to plot the survival of patients with and without LBBB and compared using the log-rank test. Differences in 1-year mortality and the 90-day postdischarge combined endpoint for patients with LBBB with respect to patients without LBBB were expressed as hazard ratios (HRs) with the 95% confidence interval (CI) using the Cox regression model, first unadjusted and then adjusted for variables with a $P < 0.05$ in the bivariate comparison in each particular cohort. Adjustments were made progressively, first for baseline variables ($P < 0.05$), then for clinical variables ($P < 0.05$) and, finally, for both (fully adjusted model). Results of unadjusted analyses and partial adjustments by baseline or acute-

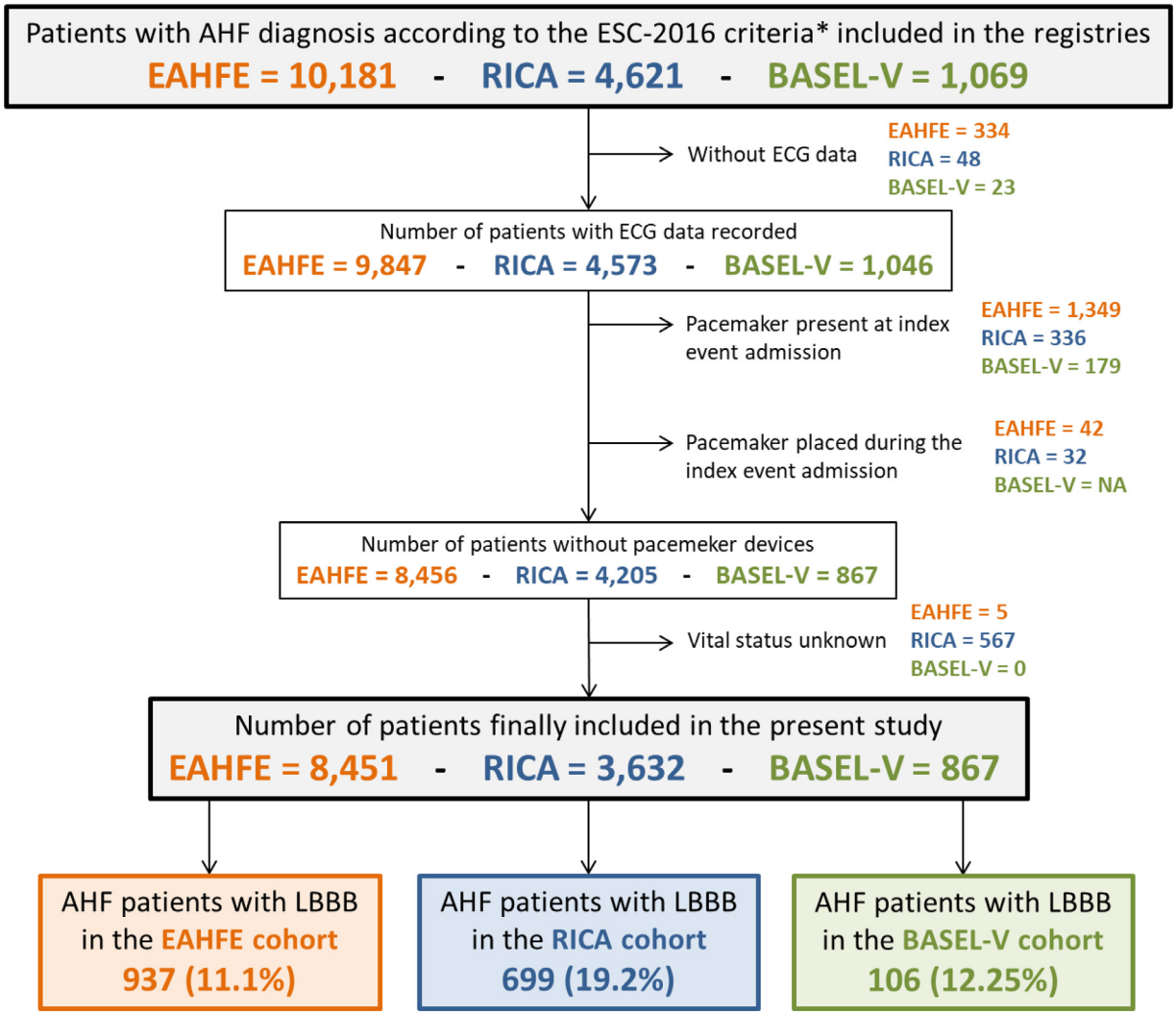



**Fig. 1.** Triage flow chart for patient inclusion.

episode characteristics were quite similar and, for this reason, were not included in Table 3. We created 5 sets of data with replacement of missing values by multiple imputation using chained equations before proceeding with adjustments. The Rubin rule was used to pool parameter estimates in the 5 datasets with multiple imputation. Finally, we ran 3 different sensitivity analyses of outcomes: by removing from the control group patients with other electric abnormalities in the ECG (including right bundle branch block and left ventricular hypertrophy; sensitivity analysis A); by including only cases and controls in sinus rhythm (sensitivity analysis B); and by including only cases and controls with valid values in all variables included in the fully-adjusted model (ie, without applying multiple imputation for missing values; sensitivity analysis C). Statistical significance was accepted if $P < 0.05$ or 95% CI excluded the value 1. The analyses were performed using the Statistical Package for Social Sciences, version 23.0 (IBM, Armonk, New York, USA).

## Results

### Relative Frequency of LBBB

Of the total of 15,871 patients with AHF included in the 3 cohorts, the present study finally selected 12,950 patients for analysis: 8451 from EAHFE, 3632 from RICA and 867 from BASEL-V cohorts (Fig. 1). The number of patients with LBBB (and the relative frequency of LBBB) was 937 (11.1%), 699 (19.2%) and 106 (12.2%) in the EAHFE, RICA and BASEL-V cohorts, respectively, and considering all the patients together, the relative frequency of LBBB was 13.5% (95% CI: 12.9%–14.0%)

### Baseline and Acute Episode Characteristics

Patients included in the 3 cohorts had a median age between 79 and 82 years, and there was a similar proportion of females and males (Table 1). Comorbidities were common in every cohort; hypertension, dyslipidemia, atrial fibrillation, and

**Table 1.** Baseline Characteristics

| | Epidemiology Acute Heart Failure Emergency (EAHFE) Cohort | | | | | National Heart Failure Registry of the Spanish Internal Medicine Society (RICA) Cohort | | | | | Basics in Acute Shortness of Breath Evaluation of Switzerland (BASEL-V) Cohort | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | All patients N = 8451 n (%) | Missing valuesn n(%) | Patients with LBBB n = 937 n (%) | Patients without LBBB n = 7514 n (%) | *P*** | All patients | Missing values | With LBBB | Without LBBB | *P*** | All patients n = 867 | Missing valuesn (%) | With LBBB n = 106 | Without LBBB n = 761 | *P*** |
| **Demographic data** | | | | | | | | | | | | | | | |
| Age (years) (median (IQR)) | 82 (76-88) | 7 (0.1) | 83 (75-88) | 82 (76-88) | 0.769 | 81 (75-86) | 0 (0.0) | 82 (76-86) | 81 (75-86) | **0.012** | 79.0 [71.0, 85.0] | 0 (0) | 81.0 [74.2, 86.0] | 79.0 [71.0, 84.0] | **0.024** |
| Sex female | 4684 (55.5) | 15 (0.2) | 492 (52.5) | 4192 (55.9) | **0.049** | 1,797 (49) | 0 (0.0) | 374 (54) | 1,423 (48) | **0.016** | 404 (46.6) | 0 (0) | 47 (44.3) | 357 (46.9) | 0.694 |
| BMI (kg/m$^2$) (median (IQR)) | 28.7 (22.4-31.2) | 3380 (40.0) | 27.3 (24.5-30.1) | 27.7 (24.8-31.2) | **0.014** | 28.1 (25.0-31.6) | 1 (0.0) | 27.6 (24.7-31.1) | 28.3 (25.1-32.0) | **0.002** | 26.1 [23.1, 30.2] | 10 (1.2) | 25.7 [23.1, 29.4] | 26.2 [23.0, 30.4] | 0.509 |
| Comorbidity | | | | | | | | | | | | | | | |
| Active smoker | 599 (9.8) | 2344 (27.7) | 57 (8.1) | 542 (10.0) | 0.097 | 1,387 (38) | 0 (0.0) | 286 (41) | 1,101 (37) | 0.091 | 161 (19.0) | 20 (2.3) | 20 (19.8) | 141 (18.9) | 0.935 |
| Hypertension | 7015 (83.1) | 14 (0.2) | 789 (84.3) | 6226 (83.0) | 0.319 | 3,098 (85) | 0 (0.0) | 604 (86) | 2,494 (85) | 0.315 | 692 (80.0) | 2 (0.2) | 87 (82.1) | 605 (79.7) | 0.659 |
| Dyslipidemia | 3715 (44.0) | 16 (0.2) | 437 (46.7) | 3278 (43.7) | 0.078 | 1,932 (53) | 0 (0.0) | 370 (53) | 1,562 (53) | 0.933 | 435 (50.3) | 3 (0.3) | 64 (60.4) | 371 (48.9) | **0.036** |
| Diabetes mellitus | 3546 (42.0) | 14 (0.2) | 421 (45.0) | 3125 (41.7) | 0.053 | 1,674 (46) | 0 (0.0) | 313 (45) | 1,361 (46) | 0.473 | 250 (28.8) | 0 (0) | 42 (39.6) | 208 (27.3) | **0.012** |
| Coronary artery disease | 2407 (28.5) | 14 (0.2) | 316 (33.8) | 2091 (27.9) | <**0.001** | 957 (26) | 0 (0.0) | 210 (30) | 747 (25) | **0.015** | 393 (45.4) | 2 (0.2) | 67 (63.2) | 326 (43.0) | <**0.001** |
| Heart valve disease | 2121 (25.1) | 13 (0.2) | 277 (29.6) | 1844 (24.6) | **0.001** | 1,207 (33) | 0 (0.0) | 253 (36) | 954 (32) | 0.061 | NA | - | NA | NA | NA |
| Peripheral arterial disease | 804 (9.5) | 17 (0.2) | 94 (10.0) | 710 (9.5) | 0.573 | 393 (11) | 0 (0.0) | 92 (13) | 301 (10) | **0.030** | 145 (16.7) | 0 (0) | 18 (17.0) | 127 (16.7) | 1.000 |
| Cerebrovascular disease | 1060 (12.6) | 14 (0.2) | 125 (13.4) | 935 (12.5) | 0.439 | 475 (13) | 0 (0.0) | 90 (13) | 385 (13) | 0.901 | 136 (15.7) | 0 (0) | 13 (12.3) | 123 (16.2) | 0.373 |
| Atrial fibrillation | 4363 (51.7) | 14 (0.2) | 409 (43.7) | 3954 (52.7) | <**0.001** | 2,301 (63) | 0 (0.0) | 399 (57) | 1,902 (65) | <**0.001** | 349 (40.3) | 0 (0) | 39 (36.8) | 310 (40.7) | 0.503 |
| Chronic heart failure | 5110 (63.1) | 349 (4.1) | 628 (69.8) | 4482 (62.2) | <**0.001** | 2,353 (65) | 0 (0.0) | 481 (69) | 1,872 (64) | **0.011** | 423 (49.0) | 3 (0.3) | 71 (67.0) | 352 (46.4) | <**0.001** |
| Chronic kidney disease* | 2238 (26.5) | 13 (0.2) | 255 (27.2) | 1983 (26.4) | 0.596 | 2,073 (57) | 0 (0.0) | 418 (60) | 1,655 (56) | 0.097 | 346 (40.0) | 2 (0.2) | 52 (49.1) | 294 (38.7) | 0.054 |
| COPD | 1989 (23.6) | 19 (0.2) | 196 (21.0) | 1793 (23.9) | **0.047** | 888 (24) | 0 (0.0) | 173 (25) | 715 (24) | 0.807 | 230 (26.5) | 0 (0) | 26 (24.5) | 204 (26.8) | 0.704 |
| Dementia | 906 (11.6) | 654 (7.7) | 87 (10.5) | 819 (11.7) | 0.302 | 199 (5.5) | 0 (0.0) | 53 (7.6) | 146 (5.0) | **0.009** | 86 (10.5) | 45 (5.2) | 10 (9.6) | 76 (10.6) | 0.896 |
| Active cancer | 1079 (13.8) | 656 (7.8) | 114 (13.8) | 965 (13.8) | 0.971 | 430 (12) | 0 (0.0) | 86 (12) | 344 (12) | 0.649 | 48 (6.0) | 73 (8.4) | 3 (3.2) | 45 (6.4) | 0.326 |
| **Baseline status** | | | | | | | | | | | | | | | |
| NYHA class | | 304 (3.6) | | | 0.716 | | | | | **0.049** | | 0 (0) | | | 0.949 |
| I | 2029 (24.9) | | 214 (24.0) | 1815 (25.0) | | 317 (8.8) | 49 (1.3) | 57 (8.2) | 260 (9.0) | | 0 (0) | | 0 (0) | 0 (0) | |
| II | 4225 (51.9) | | 464 (52.0) | 3761 (51.8) | | 1,929 (54) | 49 (1.3) | 350 (51) | 1,579 (54) | | 67 (7.7) | | 9 (8.5) | 58 (7.6) | |
| III | 1779 (21.8) | | 209 (23.4) | 1570 (21.6) | | 1,230 (34) | 49 (1.3) | 267 (39) | 963 (33) | | 393 (45.3) | | 48 (45.3) | 345 (45.3) | |
| IV | 114 (1.4) | | 5 (0.6) | 109 (1.5) | | 113 (3.1) | 49 (1.3) | 17 (2.5) | 96 (3.3) | | 407 (46.9) | | 49 (46.2) | 358 (47.0) | |
| LVEF (%) (median (IQR)) | 51 (37-60) | 3523 (41.7) | 39 (30-55) | 63 (40-61) | <**0.001** | 50 (35-60) | 0 (0.0) | 36 (29-52) | 54 (36-62) | <**0,001** | 50.0 [35.0, 60.0] | 319 (36.8) | 35.0 [21.6, 45.0] | 50.0 [35.0, 60.0] | <**0.001** |
| Charlson index (points) (median (IQR)) | NA | - | NA | NA | - | 3 (1-5) | 0 (0.0) | 3 (1-5) | 3 (1-5) | 0.307 | NA | - | NA | NA | NA |
| Barthel index (points) (median (IQR)) | 90 (70-100) | 610 (7.2) | 90 (70-100) | 90 (709-100) | 0.824 | 95 (75-100) | 2 (0.1) | 95 (75-100) | 95 (75-100) | 0.911 | NA | - | NA | NA | NA |
| Pfeiffer index (points) (median (IQR)) | NA | - | NA | NA | - | 1 (0-2) | 292 (8.0) | 1 (0-3) | 1 (0-2) | 0.318 | NA | - | NA | NA | NA |
| **Chronic treatments at home** | | | | | | | | | | | | | | | |
| Receiving diuretics (any) | 6163 (73.5) | 108 (1.3) | 717 (77.6) | 5419 (73.0) | **0.003** | 3284 (90) | 0 (0.0) | 643 (92) | 2,641 (90) | 0.089 | 574 (66.7) | 6 (0.7) | 84 (80.0) | 490 (64.8) | **0.003** |
| Receiving RASI | 4644 (55.7) | 109 (1.3) | 576 (62.4) | 4068 (54.8) | <**0.001** | 2507 (69) | 0 (0.0) | 522 (75) | 1,985 (68) | <**0.001** | 513 (59.6) | 6 (0.7) | 68 (64.8) | 445 (58.9) | 0.295 |
| Receiving beta-blockers | 3823 (45.8) | 112 (1.3) | 470 (50.9) | 3353 (45.2) | **0.001** | 2330 (64) | 0 (0.0) | 480 (69) | 1,850 (63) | **0.005** | 496 (57.6) | 6 (0.7) | 68 (64.8) | 428 (56.6) | 0.139 |
| Receiving MRA | 1343 (16.1) | 107 (1.3) | 184 (19.9) | 1159 (15.6) | **0.001** | 1135 (31) | 0 (0.0) | 271 (39) | 864 (29) | <**0.001** | 77 (9.0) | 16 (1.8) | 20 (19.0) | 57 (7.6) | <**0.001** |
| Receiving digoxin | 1217 (14.6) | 116 (1.4) | 112 (12.1) | 1105 (14.9) | **0.024** | 634 (17) | 0 (0.0) | 101 (14) | 533 (18) | **0.023** | 42 (4.9) | 16 (1.8) | 3 (2.9) | 39 (5.2) | 0.418 |
| Receiving amiodarone | 383 (4.6) | 112 (1.3) | 64 (6.9) | 319 (4.3) | <**0.001** | 114 (3.1) | 0 (0.0) | 28 (4.0) | 86 (2.9) | 0.147 | NA | - | NA | NA | NA |

*Chronic kidney disease was defined as previous creatinine $\geq$ 2 mg/dL for the EAHFE cohort, estimated glomerular filtration rate $<$ 60 mL/min/m$^2$ for the RICA cohort and the BASEL-V cohort.

**Bold *P* values in shadowed cells denote statistical significance ($P < 0.05$).BMI, body mass index; COPD, chronic pulmonary obstructive disease; IQR: interquartile range; LBBB: left bundle branch block; LVEF: left ventricular ejection fraction; MRA: mineralcorticosteroid-receptor blockers; NA, not available; NYHA, New York Heart Association; RASI, renin-angiotensin system inhibitors.

previous episodes of AHF were present in more than half of the patients. There were significant differences between patients with and without LBBB in every cohort in relation to the frequency of many baseline characteristics (in 14 of 26 in the EAHFE cohort, in 14 of 28 in the RICA cohort, in 8 of 24 in the BASEL-V cohort), but 4 differences were consistently found in the 3 cohorts: patients with LBBB more commonly had coronary artery disease (CAD) and previous episodes of AHF, were on chronic treatment with mineralcorticosteroid-receptor antagonists, and had lower LVEFs (Table 1).

With respect to the clinical characteristics of the AHF episodes, the most common triggers for decompensation were infections (in the EAHFE and RICA cohorts) and rapid atrial fibrillation (in the BASEL-V cohort) (Table 2). At admission, the median SBP was between 134 and 139 mmHg, and the median NT-proBNP level ranged from 3486 to 4465 pg/mL. There were significant differences between patients with and without LBBB in the frequency of some baseline characteristics in every cohort (in 9 of 21 in the EAHFE cohort, in 5 of 14 in the RICA cohort and in 5 of 16 in the BASEL-V cohort). Among the 13 common clinical variables assessed in the 3 cohorts, 2 were consistently different in patients with LBBB: SBP was lower, and NT-proBNP levels were higher (Table 2).

### Outcomes

The cumulative all-cause mortality rate at 1 year was 31.9% (95% CI 30.9−32.9) in the EAHFE cohort, 16.9% (95% CI 15.2-18.5) in the RICA cohort, and 31.0% (95% CI 27.9-34.1) in the BASEL-V cohort. There were no statistically significant differences in survival between patients with and without LBBB in the EAHFE cohort, whereas the mortality rate was higher in patients with LBBB in the RICA and BASEL-V cohorts (Fig. 2). On the other hand, the cumulative postdischarge combined event at 90 days was 49.0% (95% CI 47.2−50.8) in the EAHFE cohort, 15.8% (95% CI 14.6−17.0) in the RICA cohort, and 22.0% (95% CI 19.3−24.8) in the BASEL-V cohort. For this outcome, statistically significant differences between patients with and without LBBB were observed only in the BASEL-V cohort, where patients with LBBB had an increased risk (Fig. 2).

The risk of adverse outcomes after adjustments are presented in Table 3. LBBB was not associated with significant differences in either 1-year mortality or the 90-day postdischarge combined event in the EAHFE cohort in any of the adjusted models. In the other 2 cohorts, the increased risk of crude 1-year mortality in patients with LBBB was maintained in the models adjusted for baseline characteristics (BASEL-V cohort) or for characteristics of the acute episode (RICA cohort), but this significance was not maintained in the remaining models, including the fully adjusted model. On the other hand, the increased risk of the crude 90-day postdischarge combined event in patients with LBBB found in the BASEL-V cohort was not observed in any of the adjusted models. In summary, and remarkably, the fully adjusted models did not uncover statistically significant differences between patients with and without LBBB for any of the outcomes analyzed. Sensitivity analyses (which could not be run in the BASEL-V cohort due to the small group size and low number of events) confirmed this lack of association between LBBB and adverse outcomes in the EAHFE and RICA cohorts (Table 3).

## Discussion

The main strength of this study is the inclusion of a large number of real-world AHF patients from 3 independent cohorts, representing 3 different scenarios and covering a wide spectrum of this syndrome, with no limitations in age, comorbidities, HF etiology, or LVEF values. From this unique perspective, we herein report 3 main findings. First, the prevalence of LBBB in patients with AHF ranges between 10% and 20%. Second, the presence of LBBB is consistently associated with some baseline and acute episode clinical characteristics. And third, after adjusting for differences between patients with and without LBBB, the presence of LBBB in the ECG does not seem to be associated with adverse outcomes.

The prevalence of LBBB was higher in the RICA cohort (19%; hospitalized patients) than in the EAHFE and BASEL-V cohorts (11%−12%; patients recruited in the ED). LBBB probably constitutes a marker of a more evolved cardiac disease (regardless of the main cause leading to HF), so it is expected to be more prevalent in hospitalized patients because they probably have more severe cardiac diseases and/or decompensations. In fact, the prevalence found in the hospitalized patients of the RICA cohort (19%) was close to that reported in previous studies, ranging between 15% and 30%, and all of these studies exclusively referred to hospitalized patients.[9−15]

This result is likely to be linked to our second finding: LBBB was more common in patients with CAD, previous AHF episodes, reduced LVEF, and higher increments of NT-proBNP in the 3 cohorts analyzed in the present study. All these findings suggest a prominent role of ischemic cardiomyopathy in the development of LBBB and that LBBB could be related to more highly evolved cardiac diseases. In this regard, MEESSI risk stratification also agrees with this concept, as patients with LBBB presented

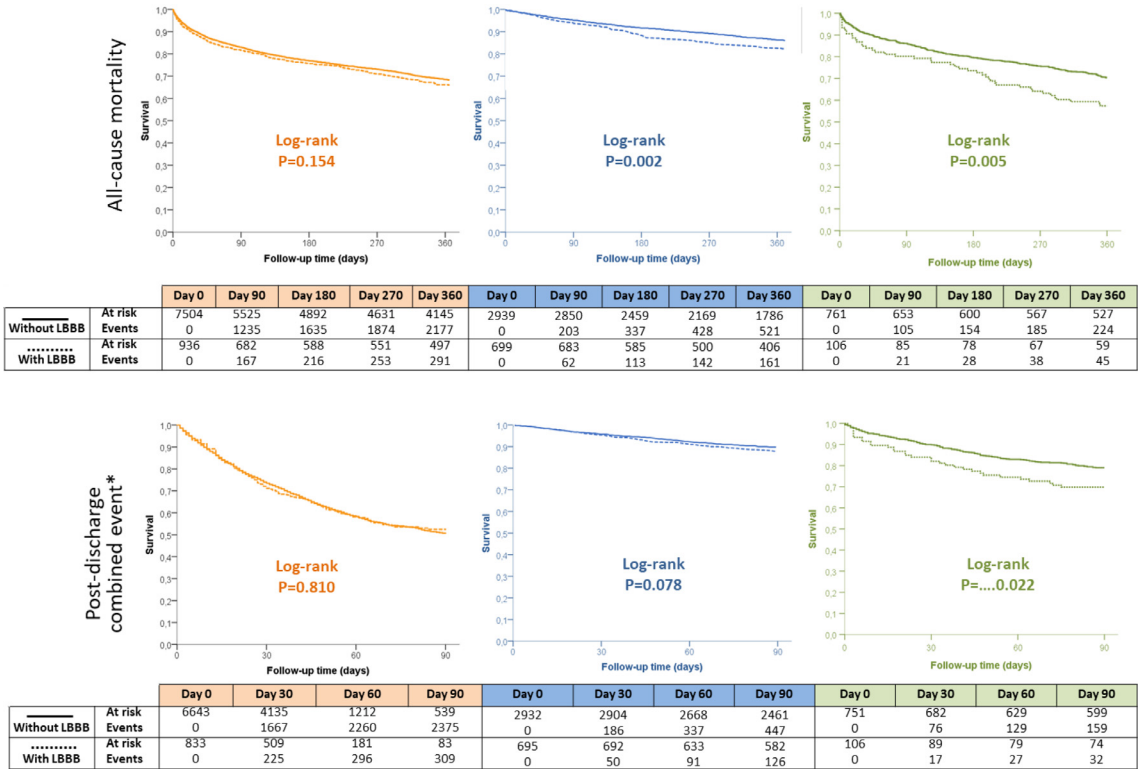
**Table 2.** Characteristics of Acute Episodes

| | EAHFE cohort | | | | | RICA cohort | | | | | BASEL-V cohort | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | All patients n = 9098 n (%) | Missing values n (%) | Patients with LBBB n = 1035 n (%) | Patients without LBBB n = 8063 n (%) | *P*** | All patients | Missing values | With LBBB | Without LBBB | *P*** | All patients n = 867 | Missing values | With LBBB n = 106 | Without LBBB n = 761 | *P*** |
| **Triggers of AHF episode** | | | | | | | | | | | | | | | |
| Infection | 3009 (39.4) | 810 (9.6) | 265 (33.0) | 2744 (40.1) | <**0.001** | 1,155 (32) | 0 (0.0) | 225 (32) | 930 (32) | 0.786 | 235 (27.1) | 0 (0) | 22 (20.8) | 213 (28.0) | 0.146 |
| Rapid atrial fibrillation[1] | 1275 (16.7) | 811 (9.6) | 91 (11.3) | 1184 (17.3) | <**0.001** | 933 (26) | 0 (0.0) | 155 (22) | 778 (26) | **0.021** | 271 (31.3) | 0 (0) | 24 (22.6) | 247 (32.5) | 0.054 |
| Anaemia | 533 (7.0) | 809 (9.6) | 50 (6.2) | 483 (7.1) | 0.377 | 286 (7.9) | 0 (0.0) | 45 (6.4) | 241 (8.2) | 0.137 | 69 (8.0) | 0 (0) | 11 (10.4) | 58 (7.6) | 0.429 |
| Hypertensive crisis[2] | 435 (5.7) | 808 (9.6) | 54 (6.7) | 381 (5.6) | 0.183 | 243 (6.7) | 0 (0.0) | 40 (5.7) | 203 (6.9) | 0.274 | 95 (11.0) | 0 (0) | 12 (11.3) | 83 (10.9) | 1.000 |
| Dietetic/pharmaco-logic transgression | 260 (3.4) | 810 (9.6) | 26 (3.2) | 234 (3.4) | 0.783 | 429 (12) | 0 (0.0) | 90 (13) | 339 (12) | 0.328 | 90 (10.4) | 0 (0) | 8 (7.5) | 82 (10.8) | 0.395 |
| Acute coronary syndrome[3] | 185 (2.2) | 40 (0.5) | 26 (2.8) | 159 (2.1) | 0.186 | 270 (7.4) | 0 (0.0) | 59 (8.4) | 211 (7.2) | 0.261 | 98 (11.3) | 0 (0) | 11 (10.4) | 87 (11.4) | 0.875 |
| **Severity of AHF episode** | | | | | | | | | | | | | | | |
| SBP (mmHg) (median (IQR)) | 139 (121-158) | 92 (1.1) | 136 (120-155) | 139 (121-158) | **0.012** | 134 (119-151) | 0 (0.0) | 131 (115-150) | 135 (120-152) | **0.002** | 138 [121-157] | 0 (0) | 130 [110-151] | 139 [122-157] | **0.012** |
| Heart rate (bpm) (median (IQR)) | 87 (73-104) | 150 (1.8) | 89 (75-103) | 87 (73-104) | 0.376 | 84 (72-100) | 0 (0.0) | 82 (71-100) | 85 (72-100) | 0.343 | 92 [74-111] | 2 (0.2) | 85 [72-102] | 92 [75-111] | 0.061 |
| Pulse oxymetry (%) (median (IQR)) | 94 (90-97) | 215 (2.5) | 94 (90-96) | 94 (90-97) | 0.237 | NA | - | NA | NA | - | 96 [93-98] | 1 (0.1) | 97 [95-99] | 96 [93-98] | **0.030** |
| Hemoglobin (g/L) (median (IQR)) | 120 (107-134) | 44 (0.5) | 121 (109-134) | 120 (106-134) | **0.036** | 12 (11−14) | 0 (0.0) | 12 (11−14) | 12 (11−14) | <**0,001** | 128 [113-141] | 16 (1.8) | 125 [110-139] | 128 [113-142] | 0.257 |
| Creatinine (mg/dL) (median (IQR)) | 1.16 (0.89-1.57) | 63 (0.7) | 1.19 (0.90-1.58) | 1.15 (0.88-1.57) | 0.079 | 1.16 (0.90-1.52) | 0 (0.0) | 1.20 (0.96-1.54) | 1.15 (0.90-1.51) | **0.009** | 1.13 [0.89-1.61] | 9 (1.0) | 1.27 [0.94-1.95] | 1.11 [0.88-1.56] | **0.009** |
| Potassium (mmol/L) (median (IQR)) | 4.4 (4.0-4.8) | 537 (6.4) | 4.3 (4.0-4.8) | 4.4 (4.0-4.8) | 0.518 | 4.3 (3.9-4.7) | 156 (4.3) | 4.3 (3.9-4.7) | 4.3 (3.9-4.7) | 0.211 | 4.1 [3.8-4.5] | 36 (4.2) | 4.2 [3.8-4.5] | 4.1 [3.8-4.5] | 0.516 |
| Sodium (mmol/L) (median (IQR)) | 139 (136-141) | 141 (1.7) | 139 (136-141) | 139 (136-141) | 0.307 | 140 (137-142) | 0 (0.0) | 139 (136-142) | 140 (137-142) | 0.855 | 139 [136-141] | 15 (1.7) | 139 [136-141] | 139 [136-141] | 0.706 |
| NT-proBNP (ng/mL) (median (IQR)) | 3764 (1936-8143) | 1394 (16.5) | 4828 (2416-11170) | 3685 (1900-7898) | <**0.001** | 3,486 (1,666-7,898) | 1165 (32.0) | 4,763 (2,130-9,247) | 3,329 (1,568-7,506) | <**0,001** | 4,465 [1,951-9,257] | 22 (2.5) | 6,032 [2,210-12,367] | 4,275 [1,923-9,054] | **0.013** |
| Raised troponin (above 99$^{th}$ percentile) | 2657 (51.6) | 3307 (39.1) | 338 (53.6) | 2319 (51.3) | 0.292 | 48 (4.7) | 2,607 (71.7) | 14 (6.3) | 34 (4.2) | 0.206 | 747 (86.8) | 6 (0.7) | 98 (92.5) | 649 (86.0) | 0.090 |
| MEESSI-AHF risk category* | | 3467 (41.0) | | | 0.054 | NA | - | NA | NA | - | | 130 (15.0) | | | **0.026** |
| Low risk | 1946 (39.0) | | 211 (36.3) | 1735 (39.4) | | | | | | | 309 (41.9) | | 26 (28.9) | 283 (43.7) | |
| Intermediate risk | 2015 (40.4) | | 240 (41.2) | 1775 (40.3) | | | | | | | 304 (41.2) | | 44 (48.9) | 260 (40.2) | |
| High risk | 554 (11.1) | | 62 (10.7) | 492 (11.2) | | | | | | | 65 (8.8) | | 8 (8.9) | 57 (8.8) | |
| Very high risk | 474 (9.5) | | 69 (11.9) | 405 (9.2) | | | | | | | 59 (8.0) | | 12 (13.3) | 47 (7.3) | |
| **Treatment at ED** | | | | | | | | | | | | | | | |
| IV diuretics | 7184 (85.8) | 81 (1.0) | 825 (88.3) | 6359 (85.5) | **0.018** | NA | - | NA | NA | - | NA | - | NA | NA | - |
| IV vasodilators | 1062 (12.7) | 82 (1.0) | 144 (15.4) | 918 (12.3) | **0.008** | NA | - | NA | NA | - | NA | - | NA | NA | - |
| Inotrope/vasoactive drugs | 126 (1.5) | 87 (1.0) | 25 (2.7) | 101 (1.4) | **0.002** | NA | - | NA | NA | - | NA | - | NA | NA | - |
| Non-invasive ventilation | 678 (8.1) | 82 (1.0) | 95 (10.2) | 583 (7.8) | **0.013** | NA | - | NA | NA | - | NA | - | NA | NA | - |
| Need of hospitalization | 6715 (79.4) | 4 (0.0) | 724 (77.2) | 5991 (79.7) | 0.069 | NA | - | NA | NA | - | NA | - | NA | NA | - |

[1]Defined as arrhythmia in BASEL V.
[2]Defined as hypertension in BASEL V.
[3]Defined as Ischemia in BASEL V.

*The MEESSI-AHF score is calculated based on 13 variables obtained at patient arrival at emergency department: age, acute coronary syndrome as trigger of decompensation, systolic blood pressure, oxygen saturation, low output signs and symptoms, creatinine, potassium, troponin, NTproBNP, hypertrophy in the ECG, and Barthel Index and NYHA class at the moment of patient presentation to the emergency department.MEESSI-AHF risk score in the BASEL V cohort is calculated using an established reduced (Model D: without Barthel Index Score) and recalibrated model as described elsewhere (Wussler et al., 2019).

**Boldface *P* values in shadowed cells denote statistical significance ($P < 0.05$)ED, emergency department; EMS, emergency medical services; NA, not available.




| | | Day 0 | Day 90 | Day 180 | Day 270 | Day 360 | Day 0 | Day 90 | Day 180 | Day 270 | Day 360 | Day 0 | Day 90 | Day 180 | Day 270 | Day 360 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Without LBBB | At risk | 7504 | 5525 | 4892 | 4631 | 4145 | 2939 | 2850 | 2459 | 2169 | 1786 | 761 | 653 | 600 | 567 | 527 |
| | Events | 0 | 1235 | 1635 | 1874 | 2177 | 0 | 203 | 337 | 428 | 521 | 0 | 105 | 154 | 185 | 224 |
| With LBBB | At risk | 936 | 682 | 588 | 551 | 497 | 699 | 683 | 585 | 500 | 406 | 106 | 85 | 78 | 67 | 59 |
| | Events | 0 | 167 | 216 | 253 | 291 | 0 | 62 | 113 | 142 | 161 | 0 | 21 | 28 | 38 | 45 |




| | | Day 0 | Day 30 | Day 60 | Day 90 | Day 0 | Day 30 | Day 60 | Day 90 | Day 0 | Day 30 | Day 60 | Day 90 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Without LBBB | At risk | 6643 | 4135 | 1212 | 539 | 2932 | 2904 | 2668 | 2461 | 751 | 682 | 629 | 599 |
| | Events | 0 | 1667 | 2260 | 2375 | 0 | 186 | 337 | 447 | 0 | 76 | 129 | 159 |
| With LBBB | At risk | 833 | 509 | 181 | 83 | 695 | 692 | 633 | 582 | 106 | 89 | 79 | 74 |
| | Events | 0 | 225 | 296 | 309 | 0 | 50 | 91 | 126 | 0 | 17 | 27 | 32 |

**Fig. 2.** Kaplan-Meier curves for 1-year survival (up) and 90-day combined event (down) for the EAHFE cohort (left), RICA cohort (middle) and BASEL-V cohort (right).

to the ED with more severe decompensations than patients without LBBB in the BASEL-V cohort ($P = 0.026$) and also with a marked trend in this direction in the EAHFE cohort ($P = 0.054$).

Although several studies have analyzed the relationship between LBBB and the prognosis of patients with HF,[9–15,22–24] only 2 have found worse outcomes in patients with AHF and LBBB. Abdel-Qadir et al.[9] analyzed 9487 patients and found an increase in mortality rate and the need for rehospitalization because of HF in patients with LBBB; however, their analysis was limited to patients hospitalized for AHF. On the other hand, Wang et al.[10] also found an increased risk of death associated with LBBB in a cohort of 2962 patients, although their analysis was limited to patients with reduced LVEF. No differences in mortality rates were reported in the remaining studies carried out to date in patients with AHF.[11–15] Again, patients included in these studies were highly selected and, therefore, they could have ascertained the problem only in a limited number of situations. Interestingly, Tabrizi et al.[14] suggested that an apparent increased mortality rate in patients with LBBB could be, in fact, due to the higher number of cardiac comorbidities and myocardial dysfunction than to LBBB per se. This hypothesis agrees with our findings; we found an apparent increase in mortality rates in the unadjusted analyses, which disappeared after adjustment using, among others, CAD and previous AHF episodes (higher in patients with LBBB) and LVEF (decreased in patients with LBBB). In summary, and in concordance with our results, most of the previous studies did not show a clearly significant increase in mortality rates in the group of patients with LBBB when adjusting for comorbidities, echocardiographic data and laboratory tests.

Patients with AHF and LBBB surviving the index episode did not exhibit a higher risk of a 90-day postdischarge combined adverse events than did patients with AHF but without LBBB. This early phase after discharge has been defined as the vulnerability period, in which the risk of complications is higher.[25–27] In fact, 20% of rehospitalizations for AHF are seen within the first 30 days following hospital discharge, and up to 50% occur within 6 months.[28] However, LBBB does not seem to play a role during this vulnerable period, even taking into account ED revisits (not needing hospitalization) due to mild episodes of AHF (as we described in the EAHFE cohort). It is important to note that when LBBB is associated with LVEF below 40% there is an opportunity for further treatment with a cardiac resynchronization therapy device (in most of these patients LBBB persists, but in others LVEF improves and cardiac resynchronization therapy is not necessary). On the other hand, in most cases LVEF stays below 40% if it was below 40% initially. For this

**Table 3.** Cox Regression Analyses for 1-Year All-Cause Mortality and 90-Day Postdischarge Combined Event for Patients With Left Bundle Branch Block in the 3 Cohorts, Including Sensitivity Analyses in the Fully Adjusted Model

| | EAHFE cohort HR (IC 95%) | P** | RICA cohort HR (IC 95%) | P** | BASEL-V cohort HR (IC 95%) | P** |
|---|---|---|---|---|---|---|
| **1-year all-cause mortality** | | | | | | |
| **Main analyses** | | | | | | |
| Unadjusted | 1.093 (0.967-1.235) | 0.155 | **1.320 (1.107-1.573)** | **0.002** | 1.572 (1.141-2.166) | **0.006** |
| Adjusted by baseline characteristics[2] | 1.055 (0.931-1.194) | 0.403 | 1.131 (0.940-1.360) | 0.192 | 1.433 (1.032-1.989 | **0.032** |
| Adjusted by acute episode characteristics[3] | 1.038 (0.911-1.183) | 0.574 | **1.303 (1.092-1.555)** | **0.003** | 1.333 (0.952-1.864) | 0.094 |
| Fully-adjusted model | 1.021 (0.894-1.166) | 0.756 | 1.148 (0.953-1.382) | 0.146 | 1.321 (0.937-1.860) | 0.112 |
| **Sensitivity analyses for the fully adjusted model** | | | | | | |
| Sensitivity analysis A* | 1.007 (0.882-1.151) | 0.916 | 1.138 (0.908-1.427) | 0.262 | NA[1] | |
| Sensitivity analysis B* | 1.174 (0.950-1.450) | 0.138 | 0.943 (0.688-1.294) | 0.718 | NA[1] | |
| Sensitivity analysis C* | 1.124 (0.886-1.425) | 0.337 | 1.037 (0.813-1.323) | 0.771 | NA[1] | |
| **90-day post-discharge combined event** | | | | | | |
| **Main analyses** | | | | | | |
| Unadjusted | 1.015 (0.901-1.142) | 0.810 | 1.193 (0.980-1.453) | 0.078 | 1.554 (1.063-2.272) | **0.023** |
| Adjusted by baseline characteristics[2] | 0.979 (0.868-1.105) | 0.736 | 1.106 (0.899-1.362) | 0.340 | 1.382 (0.938-2.037) | 0.102 |
| Adjusted by acute episode characteristics[3] | 1.033 (0.910-1.172) | 0.620 | 1.178 (0.965-1.437) | 0.107 | 1.289 (0.871-1.909) | 0.204 |
| Fully-adjusted model | 1.004 (0.883-1.142) | 0.950 | 1.138 (0.923-1.403) | 0.226 | NA[1] | |
| **Sensitivity analyses for the fully-adjusted model** | | | | | | |
| Sensitivity analysis A* | 1.007 (0.885-1.146) | 0.911 | 1.155 (0.903-1.476) | 0.252 | NA[1] | |
| Sensitivity analysis B* | 0.978 (0.797-1.199) | 0.831 | 1.223 (0.861-1.739) | 0.261 | NA[1] | |
| Sensitivity analysis C* | 0.907 (0.711-1.156) | 0.431 | 1.156 (0.877-1.523) | 0.303 | NA[1] | |

*Sensitivity Analysis A consisted of removing from the control group patients with other electric abnormalities in the ECG (including right bundle branch block, left ventricular hypertrophy); sensitivity analysis B included only cases and controls in sinus rhythm; and Sensitivity Analysis C included only cases and controls with valid values in all variables included in the fully adjusted model, without applying multiple imputation for missing values.

**Bold *P* values in shadowed cells denote statistical significance ($P < 0.05$)BASEL V: 90-day combined event: CHF-Rehosp, all-cause mortality.

[1]These analyses were not performed in the BASEL V study because there were fewer than 10 events per included variable.

[2]For every cohort, covariates included in the adjustment by baseline characteristics were those variables with a *P* value $< 0.05$ in the bivariate analysis for each particular cohort.

[3]For every cohort, covariates included in the adjustment by acute episode characteristics were those variables with a *P* value $< 0.05$ in the bivariate analysis for each particular cohort.

reason, the lack of independent effect on mortality could be explained also by the therapy applied in those with persistent LVEF below 40% and LBBB.

It is worthy of note that in our study, the results of the 3 cohorts show some differences in their main outcomes. These differences are easily explained by differences in cohort definition and composition. For example, the RICA cohort accounted only for hospitalized patients in IMD, and the AHF case mix in the IMD is more heterogeneous than the AHF case mix in cardiology departments. Moreover, the follow-up in the RICA cohort was initiated just after hospital discharge and, therefore, in-hospital mortality did not account for 1-year mortality. This resulted in a 1-year mortality of around half that 1 observed in the EAHFE and BASEL-V registries. On the other hand, in the BASEL-V cohort up to 67% of patients with CAD in the group had LBBB (around double that of the EAHFE and RICA cohorts) and the proportion of patients with advanced (III or IV) New York Heart Association functional class was higher than 90% (about triple that of the EAHFE and RICA cohorts). This probably explains why, in the unadjusted analysis, we found higher differences in 1-year mortality and 90-day postdischarge combined event in patients with LBBB compared to those without LBBB in the BASEL-V cohort in comparison with the narrower differences found in the other 2 cohorts, as well as why a large part of these differences between patients with and without LBBB disappears after adjustment for these confounders in the BASEL-V cohort.

### Limitations

There are some limitations that should be considered. First, the 3 cohorts included patients with AHF but with heterogeneity in their characteristics and with different perspectives at the time of inclusion (EDs and IMDs) that may contribute to the differences shown in the results. However, this was intentionally sought by the authors in order to provide 3 different perspectives on the same clinical problem and, in some aspects, this should be taken into account as a strength of our study. Second, as in every observational study, causal relationships cannot be inferred. Therefore, the results of the current analysis are limited by the retrospective design, and some important data could be lacking. For example,

the onset of LBBB and its potential disappearance during follow-up was unknown. Even more important, a large number of LVEF values were missing in the EAHFE and BASEL-V cohorts, and information regarding cardiac resynchronization therapy implementation (that could modify the prognosis of patients) is not available for any of the 3 cohorts. Although we tried to manage this limitation by using multiple imputation, we cannot exclude bias. Therefore, our results should be considered to be hypothesis generating. Third, there was no sample-size calculation, and this could have influenced the lack of statistical significance in some comparisons (beta error). Indeed, a sensitivity analysis cohort could not be performed in the BASEL-V cohort due to the limitation of sample size. Fourth, Spain and Switzerland have a nationwide universal public health care system, and external validation of our results might be needed to confirm their generalizability. For example, Spanish EDs are able to provide observation for up to 24 hours, which is not the rule in other countries, and this can influence the percentage of patients who are sent home directly from the ED, without hospitalization, and their prognoses.[29] Fifth, our study included a high percentage of elderly patients with AHF in whom frailty and dependence are common, and these 2 factors are strongly related to mortality.[1,30] And sixth, outcome adjudication was performed externally only in the BASEL-V cohort.

## Conclusions

The prevalence of LBBB in our 3 large cohorts of patients with AHF ranged between 11% and 19%, and it is associated with some cardiovascular comorbidities, a reduced LVEF and probably more severe decompensations. Nonetheless, after taking these factors into account, the presence of LBBB in patients with AHF does not seem to be associated with a statistically significant increased risk of adverse outcomes.

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## Conflicts of interest

None of the authors have conflicts of interest to declare.

**Funding:** No funding was received for the present study

**Acknowledgments:** We thank all the researchers who are part of the EAHFE, RICA and BASEL-V cohorts. We also thank Ms. Alicia Díaz and her strong professionalism as data manager of the EAHFE cohort; and the RICA's coordinating center, S&H Medical Science Service, for the data quality-control, logistical and administrative support, as well as to Professor Salvador Ortiz (Autonomous University of Madrid and Statistical Advisor of S&H Medical Science Service) for the statistical analysis of the RICA data presented in this document.

## Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2021.11.022.

## References

1. Martín-Sánchez FJ, Parra Esquivel P, Llopis García G, González Del Castillo J, Rodríguez Adrada E, Espinosa B, et al. Thirty-day outcomes in frail older patients discharged home from the emergency department with acute heart failure: effects of high-risk criteria identified by the DEED FRAIL-AHF trial. Emergencias 2021;33:165–73.
2. Aguilar Ginés S. Prognosis in heart failure: importance of physical frailty at the time of admission. Emergencias 2020;32:147–8.
3. Fonarow GC, Corday E. ADHERE Scientific Advisory Committee. Overview of acutely decompensated congestive heart failure (ADHF): a report from the ADHERE registry. Heart Fail Rev 2004;9:179–85.
4. Miró Ò, García Sarasola A, Fuenzalida C, Calderón S, Jacob J, Aguirre A, et al. Departments involved during the first episode of acute heart failure and subsequent emergency department revisits and rehospitalisations: an outlook through the NOVICA cohort. The NOVICA-3 study. Eur J Heart Fail 2019;21:1231–44.
5. Miró O, Rossello X, Platz E, Masip J, Gualandro DM, Peacock WF, Study Group on Acute Heart Failure of the Acute Cardiovascular Care Association of the European Society of Cardiology. Risk stratification scores for patients with acute heart failure in the emergency department: a systematic review. Eur Heart J Acute Cardiovasc Care 2020;9:375–98.
6. Farmakis D, Parissis J, Lekakis J, Filippatos G. Acute heart failure: epidemiology, risk factors, and prevention. Rev Esp Cardiol (Engl Ed) 2015;68:245–8.
7. Kimmoun A, Takagi K, Gall E, Ishihara S, Hammoum P, El Bèze N, METAHF Team. Temporal trends in mortality and readmission after acute heart failure: a systematic review and meta-regression in the past four decades. Eur J Heart Fail 2021;23:420–31.
8. Llauger L, Jacob J, Moreno LA, Aguirre A, Martín-Mojarro E, Romero-Carrete JC, et al. Worsening renal function during an episode of acute heart failure and its relation to short- and long-term mortality: associated factors in the Epidemiology of Acute heart failure in Emergency Departments–Worsening Renal Function study. Emergencias 2020;32:332–9.
9. Abdel-Qadir HM, Tu JV, Austin PC, Wang JT, Lee DS. Bundle branch block patterns and long-term outcomes in heart failure. Int J Cardiol 2011;146:213–8.
10. Wang NC, Maggioni AP, Konstam MA, Zannad F, Krasa HB, Burnett JC Jr, et al. Clinical implications of QRS duration in patients hospitalized with worsening heart failure and reduced left ventricular ejection fraction. JAMA 2008;299:2656–66.
11. Dzudie A, Milo O, Edwards C, Cotter G, Davison BA, Damasceno A, et al. Prognostic significance of ECG abnormalities for mortality risk in acute heart failure: insight from the Sub-Saharan Africa Survey of Heart Failure (THESUS-HF). J Card Fail 2014;20:45–52.
12. Hong SJ, Oh J, Kang SM, Chan Youn J, Han S, Jeon ES, et al. Clinical implication of right bundle branch block in hospitalized patients with acute heart failure: data from the Korean Heart Failure (KorHF) Registry. Int J Cardiol 2012;157:416–8.
13. Huvelle E, Fay R, Alla F, Cohen Solal A, Mebazaa A, Zannad F. Left bundle branch block and mortality in patients with acute heart failure syndrome: a substudy of the EFICA cohort. Eur J Heart Fail 2010;12:156–63.
14. Tabrizi F, Englund A, Rosenqvist M, Wallentin L, Stenestrand U. Influence of left bundle branch block on long-term mortality in a population with heart failure. Eur Heart J 2007;28:2449–55.
15. Tolppanen H, Siirila-Waris K, Harjola VP, Marono D, Parenica J, Kreutzinger P, et al. Ventricular conduction abnormalities as predictors of long-term survival in acute de novo and decompensated chronic heart failure. ESC Heart Fail 2016;3:35–43.
16. Llorens P, Javaloyes P, Martín-Sánchez FJ, Jacob J, Herrero-Puente P, Gil V, et al. Time trends in characteristics, clinical course, and outcomes of 13,791 patients with acute heart failure. Clin Res Cardiol 2018;107:897–913.
17. Trullàs JC, Miró Ò, Formiga F, Martín-Sánchez FJ, Montero-Pérez-Barquero M, Jacob J, et al. The utility of heart failure registries: a descriptive and comparative study of two heart failure registries. Postgrad Med J 2016;92:260–6.
18. Trullàs JC, Formiga F, Montero M, Conde A, Casado J, Carrasco FJ, et al. Paradox of obesity in heart failure:

results from the Spanish RICA Registry. Med Clin (Barc) 2011;137:671–7.
19. Wussler D, Kozhuharov N, Sabti Z, Walter J, Strebel I, Scholl L, et al. External validation of the MEESSI acute heart failure risk score: a cohort study. Ann Intern Med 2019;170:248–56.
20. Hecht HH, Kossmann CE, Childers RW, Langendorf R, Lev M, Rosen KM, et al. Atrioventricular and intraventricular conduction: revised nomenclature and concepts. Am J Cardiol 1973;31:232–44.
21. Miró Ò, Rossello X, Gil V, Martín-Sánchez FJ, Llorens P, Herrero-Puente P, ICA-SEMES Research Group. Predicting 30-day mortality for patients with acute heart failure in the emergency department: a cohort study. Ann Intern Med 2017;167:698–705.
22. Baldasseroni S, Opasich C, Gorini M, Lucci D, Marchionni N, Marini M, et al. Left bundle-branch block is associated with increased 1-year sudden and total mortality rate in 5517 outpatients with congestive heart failure: a report from the Italian network on congestive heart failure. Am Heart J 2002;143:398–405.
23. Barsheshet A, Leor J, Goldbourt U, Garty M, Schwartz R, Behar S, et al. Effect of bundle branch block patterns on mortality in hospitalized patients with heart failure. Am J Cardiol 2008;101:1303–8.
24. Lund LH, Jurga J, Edner M, Benson L, Dahlström U, Linde C, Alehagen U. Prevalence, correlates, and prognostic significance of QRS prolongation in heart failure with reduced and preserved ejection fraction. Eur Heart J 2013;347:529–39.
25. Latif A, Lateef N, Lundgren S, Kapoor V, Ahsan MJ, Aboeata A. Vulnerable phase of acute heart failure and its association with hospital readmissions reduction program. Curr Probl Cardiol 2021:100904. https://doi.org/10.1016/j.cpcardiol.2021.100904.
26. Kitakata H, Kohno T, Kohsaka S, Shiraishi Y, Parizo JT, Niimi N, et al. Prognostic implications of early and midrange readmissions after acute heart failure hospitalizations: a report from a Japanese multicenter registry. J Am Heart Assoc 2020;9:e014949.
27. Cheng RK, Cox M, Neely ML, Heidenreich PA, Bhatt DL, Eapen ZJ, et al. Outcomes in patients with heart failure with preserved, borderline, and reduced ejection fraction in the Medicare population. Am Heart J 2014;168:721–30.
28. Rizzi MA, Sarasola AG, Arbé AA, Mateo SH, Gil V, Llorens P, et al. Factors associated with in-hospital mortality and adverse outcomes during the vulnerable post-discharge phase after the first episode of acute heart failure: results of the NOVICA-2 study. Clin Res Cardiol 2021;110:993–1005.
29. Miró Ò, Rossello X, Gil V, Martín-Sánchez FJ, Llorens P, Herrero-Puente P, et al. Analysis of how emergency physicians' decisions to hospitalize or discharge patients with acute heart failure match the clinical risk categories of the MEESSI-AHF Scale. Ann Emerg Med 2019;74:204–15.
30. García-Álvarez A. Safety and the identification of modifiable factors in older patients discharged from the emergency department with acute heart failure. Emergencias 2021;33:161–2.