# Intraventricular conduction defects in patients with congestive heart failure: left but not right bundle branch block is an independent predictor of prognosis. A report from the Italian Network on Congestive Heart Failure (IN-CHF database)

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*Key words:*
**Bundle branch block; Congestive heart failure; Prognosis.**

*Background.* **In industrialized countries the prevalence of congestive heart failure (CHF) is increasing. Many clinical factors have been shown to influence the prognosis of CHF. The effect of a wide QRS on mortality is debated; while left bundle branch block (LBBB) has been already identified as a negative prognostic factor, the effect of right bundle branch block (RBBB) is still unknown. The aim of this study was to compare the association of these two intraventricular conduction defects on the prognosis of CHF.**

*Methods.* **Data were derived from the Italian Registry of CHF. Entry in the Registry required that patients had a diagnosis of CHF based on the European Society of Cardiology guidelines. We analyzed the 1-year follow-up data of 5517 outpatients with CHF of different etiologies. The presence of a wide QRS was defined if the duration was > 120 ms.**

*Results.* **A wide QRS was present in 2066 patients (37.5%), 25.2% with LBBB, 6.1% with RBBB, 6.2% with other intraventricular defects. At univariate analysis patients with complete LBBB had a significantly higher 1-year mortality than those without (16.1 vs 11.9%) but this was not true for complete RBBB (11.9 vs 11.9%). Even after multivariate adjustment, complete LBBB still remained an independent predictor of death (relative risk 1.36, 95% confidence interval 1.15-1.61).**

*Conclusions.* **LBBB but not RBBB is an independent predictor of death in CHF.**

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## Introduction

In spite of major reductions in the mortality due to cardiovascular diseases in industrialized countries[1,2], congestive heart failure (CHF) still continues to be a life-threatening condition[2] and one of the first-line problems to be managed by health care systems[3,4]. Many epidemiological, clinical and pathophysiological factors influence the prognosis of patients with CHF[5-9]. Among these, more attention has been recently focused on the role of intraventricular conduction defects, and a wide QRS in particular[10-13].

The presence of a wide QRS induces significant mechanical and electrical alterations during both the systolic and diastolic phases of the cardiac cycle[14,15]. This electrical alteration produces an additional impairment on the cardiac performance in patients with a depressed left ventricular function[16].

Although the effects of a wide QRS on left ventricular function have been elucidated[17,18], the prognostic power of this alteration has not yet been clearly established. This is particularly true in heart failure.

We have recently defined the prevalence and the role of complete left bundle branch block (LBBB) in ambulatory patients affected by CHF[19] and also their synergistic effects with other arrhythmias such as atrial fibrillation[20]. Nevertheless, the prevalence and the role of right bundle branch block (RBBB) in CHF are still unknown. Several studies have demonstrated that RBBB is associated with increased

mortality in patients with chronic ischemic heart disease and during acute myocardial infarction[21-23]. Recently, Hesse et al. reported that LBBB and RBBB had similar effects on mortality in a large cohort of patients with confirmed or suspected coronary artery disease[24,25]. In contrast, few data are available in the literature on the role of RBBB in patients affected by CHF.

The difference in the prognostic role of these two intraventricular conduction defects in patients with CHF is still debated. The aim of this study was to define their prevalence and independent prognostic value in a large unselected outpatient population affected by CHF.

## Methods

**Study design, collected data and definitions.** Data for the present analysis have been derived from the database of the Italian Network on Congestive Heart Failure (IN-CHF) Registry[26], a survey designed by an *ad hoc* Committee of the Italian Association of Hospital Cardiologists (ANMCO, Florence, Italy) in 1995. One hundred and fifty cardiology centers accepted to participate in the study. Centers were distributed across the national territory. Training sessions were organized to prepare clinicians to collect and enter data following standardized methods. Using an *ad hoc* designed software, the patients' data were recorded at each center by trained cardiologists and were then pooled into a single national database at the ANMCO Research Center. Entry into the database required that the patient had a diagnosis of CHF based on the European Society of Cardiology guidelines[27]. Demographic, clinical, instrumental and laboratory variables, and information on drug therapy were collected for each patient. At baseline, a 12-lead ECG was recorded and coded by a single cardiologist at each participating center, using a standardized format outlined in the database. In particular, the definition of a wide QRS was established when the QRS duration > 120 ms; the definition of complete LBBB or RBBB was coded when the QRS duration > 120 ms was associated with morphological criteria; otherwise, we defined it as other intraventricular conduction defects (OICD). Patients were followed according to the routine clinical practice of the participating centers. In this context, patients underwent standard chest X-ray, 24-hour Holter ECG monitoring, two-dimensional echocardiography, and blood sampling for the most common laboratory tests (e.g. creatinine, electrolytes, etc.), when the attending cardiologists deemed them necessary. Cardiologists at the participating centers were responsible for defining the etiology of CHF and the NYHA functional class, noting whether a third heart sound was audible, and computing the cardiothoracic ratio. When an echocardiogram was performed, the left ventricular ejection fraction was also calculated using a 4-chamber apical echocardiographic view. Ventricular tachycardia was defined as an episode of tachycardia with a widened QRS that lasted > 3 beats with a heart rate > 100 b/min, as revealed by 24-hour Holter ECG monitoring. Renal dysfunction was diagnosed for serum creatinine levels > 2.5 mg/dl. Hospitalizations for CHF during the last year were also recorded. After the baseline visit, patients were followed up according to the clinical practice of the participating centers. In case of an out-of-hospital death, the event was confirmed by telephone interview of the patient's relatives, using a standardized questionnaire.

**Study population.** The study population consisted of 6593 patients; the 1-year follow-up data were complete for all patients. One thousand and seventy six of these patients were excluded from the present analysis for any of the following reasons: CHF due to primary valvular heart disease (n = 745); inadequate quality of the ECG (n = 270); cardiac transplantation within the first year of follow-up (n = 61). Therefore, the study population for this analysis consisted of 5517 patients.

**Statistical analysis.** Data were analyzed using the SAS statistical package[28] and are presented as mean ± SD. The univariate associations of complete LBBB, complete RBBB, OICD and a wide QRS with several demographic and clinical characteristics and with the 1-year mortality were analyzed using the $\chi^2$ test. To compare the relative risk (RR) of death at 1 year among the groups with different intraventricular conduction alterations we used a logistic regression model attributing the reference risk to the group without a wide QRS. Cox proportional hazards multivariate models including the calculation of the adjusted hazard ratio and 95% confidence intervals (95% CI) were used to identify the independent determinants of all-cause mortality. The following variables, evaluated at the baseline visit, were included in the model: age, gender, NYHA classes III to IV vs I to II, ischemic vs non ischemic etiology, left ventricular ejection fraction ≤ 30 vs > 30%, atrial fibrillation, third heart sound, a cardiothoracic ratio ≥ 0.55 vs < 0.55, renal failure defined as a creatinine serum level ≥ 2.5 vs < 2.5 mg/dl, hospitalization for heart failure during the previous year, ventricular tachycardia, systolic blood pressure, and heart rate. In the model age, systolic blood pressure and heart rate were considered as continuous variables. A two-tailed $p < 0.05$ was considered statistically significant.

## Results

**Wide QRS.** *Prevalence and associated clinical characteristics.* In the total population of 5517 outpatients we found that the prevalence of a wide QRS was 37.5% (n = 2066); 25.2% (n = 1391) of the patients presented with complete LBBB, 6.1% (n = 336) of the study population had complete RBBB, and 6.2% (n = 339) showed the presence of OICD at the 12-lead ECG.

In table I the demographic and clinical characteristics of the study population considering patients with or without a wide QRS are reported. In table II we report the characteristics of the study population considering three groups of patients; patients with complete LBBB, those with complete RBBB, and those with OICD.

**Table I.** Demographic and clinical characteristics of the two groups of patients according to the presence or absence of a wide QRS.

| Variable | Wide QRS (%) | | p |
|---|---|---|---|
| | Present (n=2066) | Absent (n=3451) | |
| Age > 70 years | 31.3 | 31.1 | NS |
| Sex (female) | 25.0 | 22.6 | 0.04 |
| CHF etiology | | | 0.001 |
| Dilated cardiomyopathy | 42.7 | 32.1 | |
| Ischemic heart disease | 39.7 | 49.0 | |
| Other etiologies | 17.6 | 18.9 | |
| Previous hospitalization for CHF | 56.3 | 54.0 | NS |
| NYHA class III-IV | 31.2 | 26.1 | 0.001 |
| Heart rate > 100 b/min | 10.6 | 10.7 | NS |
| SBP < 100 mmHg | 3.9 | 2.5 | 0.001 |
| Third heart sound | 31.0 | 21.8 | 0.001 |
| Cardiothoracic ratio > 0.55 | 61.8 | 54.3 | 0.03 |
| LVEF < 30% | 43.6 | 30.0 | 0.001 |
| Chronic atrial fibrillation | 14.8 | 19.6 | 0.001 |
| Ventricular tachycardia | 28.4 | 28.8 | NS |
| Renal failure | 2.2 | 2.5 | NS |

CHF = congestive heart failure; LVEF = left ventricular ejection fraction; SBP = systolic blood pressure.

When we considered the population with a wide QRS vs those without conduction disturbances, no differences were detected in terms of age, previous hospitalization for CHF, sinus and ventricular tachycardia, and renal dysfunction. However, a wide QRS was associated more frequently with female gender, dilated cardiomyopathy, an advanced NYHA class, hypotension, other signs of advanced heart failure and chronic atrial fibrillation (Table I). A similar demographic and clinical profile was found considering the patients with complete LBBB, being this alteration associated with clinical and hemodynamic features of a greater impairment of cardiac function (Table II).

On the contrary, outpatients with complete RBBB were older, more frequently had CHF of ischemic etiology, cardiac enlargement and a reduced ejection fraction, but RBBB was not correlated with a more symptomatic CHF (Table II). Patients with OICD substantially showed similar clinical and hemodynamic profiles in respect of patients with no wide QRS (Table II).

*Prognosis.* The effects of intraventricular conduction defects on the 1-year total mortality were analyzed considering patients with a wide QRS, patients with complete LBBB and those with complete RBBB.

The total 1-year mortality in the overall population of the study was 11.9%; the patients with a wide QRS had a significantly higher mortality with respect to patients without (14.2 vs 10.6%, p = 0.001). A similar risk ratio was found when the population with complete LBBB was compared with that without LBBB (16.1 vs 10.5%, p = 0.001) (Fig. 1). In contrast, the mortality was similar in patients with or without complete RBBB (11.9 vs 11.9%, p = NS) (Fig. 1).

**Table II.** Demographic and clinical characteristics of the three groups of patients according to the different types of intraventricular conduction defects.

| Variable | LBBB | | | RBBB | | | OICD | | |
|---|---|---|---|---|---|---|---|---|---|
| | LBBB (%) | No wide QRS (%) | p | RBBB (%) | No wide QRS (%) | p | OICD (%) | No wide QRS (%) | p |
| Age > 70 years | 31.2 | 30.0 | | 38.7 | 31.2 | | 29.5 | 31.2 | |
| Sex (female) | 22.6 | 29.3 | | 11.9 | 22.6 | | 20.4 | 22.6 | |
| CHF etiology | | | | | | | | | |
| Dilated cardiomyopathy | 49.3 | 32.1 | NS | 20.5 | 32.0 | 0.004 | 32.1 | 37.5 | NS |
| Ischemic heart disease | 33.7 | 49.0 | 0.0001 | 61.6 | 49.1 | 0.0001 | 49.0 | 42.5 | NS |
| Other etiologies | 17.0 | 18.9 | 0.0001 | 17.9 | 18.9 | 0.0001 | 18.9 | 20.0 | NS |
| Previous hospitalization for CHF | 56.4 | 54.0 | NS | 54.5 | 54.0 | NS | 57.5 | 54.0 | NS |
| NYHA class III-IV | 32.8 | 26.1 | 0.0001 | 31.0 | 26.1 | NS | 24.8 | 26.1 | NS |
| Heart rate > 100 b/min | 10.9 | 10.7 | NS | 8.6 | 10.8 | NS | 11.7 | 10.7 | NS |
| SPB < 100 mmHg | 3.9 | 2.5 | 0.01 | 3.8 | 2.5 | NS | 3.8 | 2.5 | NS |
| Third heart sound | 34.1 | 21.8 | 0.0001 | 28.0 | 21.8 | 0.009 | 21.2 | 21.8 | NS |
| Cardiothoracic ratio > 0.55 | 63.2 | 54.4 | 0.03 | 61.9 | 54.4 | NS | 52.9 | 54.4 | NS |
| LVEF < 30% | 49.2 | 30.0 | 0.0001 | 31.1 | 30.0 | NS | 32.8 | 30.0 | NS |
| Chronic atrial fibrillation | 13.3 | 19.6 | 0.0001 | 20.2 | 19.6 | NS | 15.6 | 19.6 | NS |
| Ventricular tachycardia | 28.4 | 28.9 | NS | 24.7 | 28.9 | NS | 31.6 | 28.9 | NS |
| Renal failure | 2.1 | 2.5 | NS | 2.4 | 2.5 | NS | 2.9 | 2.5 | NS |

Renal failure defined as creatinine > 2.5 mg/dl. CHF = congestive heart failure; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; RBBB = right bundle branch block; SBP = systolic blood pressure.

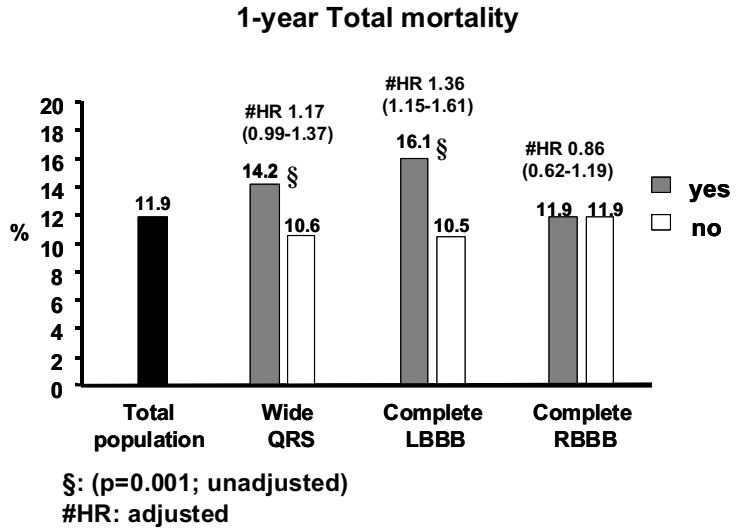


**Figure 1.** *One-year total mortality as related to the presence or absence of the three different intraventricular conduction defects. HR = hazard ratio; LBBB = left bundle branch block; RBBB = right bundle branch block.*

As reported in figure 2, RR analysis confirmed that complete RBBB did not have any significant effect on mortality in patients with CHF (RR 1.14, 95% CI 0.80-1.61); similarly, neither did OICD influence the prognosis (RR 0.82, 95% CI 0.56-1.21).

In contrast, complete LBBB characterized a subgroup of patients with CHF at high risk of death (RR 1.62, 95% CI 1.35-1.94).

Finally, we planned a Cox multivariate regression model in which we introduced all clinical and demographic variables. First, we introduced a wide QRS as a single variable and it lost its independent prognostic value for CHF (Table III). When we introduced complete LBBB and complete RBBB separately, only complete LBBB maintained a statistical power which significantly predicted death in patients affected by CHF. In fact, even after adjusting for all clinical variables, patients with complete LBBB still had a 36% increased 1-year total mortality risk in respect of the others (Table III).

## Discussion

In this study we analyzed the epidemiological profile and the clinical effects of different alterations of intraventricular conduction in a large group of unselected outpatients affected by CHF.

First, we found that the prevalence of a wide QRS is very high in outpatients with CHF; in fact, more than one third of the overall population presented this electrical disturbance and complete LBBB is the prevalent intraventricular conduction defect. In accordance with other studies[29,30], dilated cardiomyopathy was the most frequent etiology of CHF in patients presenting with complete LBBB. In contrast, patients with RBBB more frequently presented with CHF of ischemic etiology, confirming that this electrical defect is strictly related to coronary heart disease[31].

Complete LBBB was associated with more severe left ventricular dysfunction as demonstrated by the

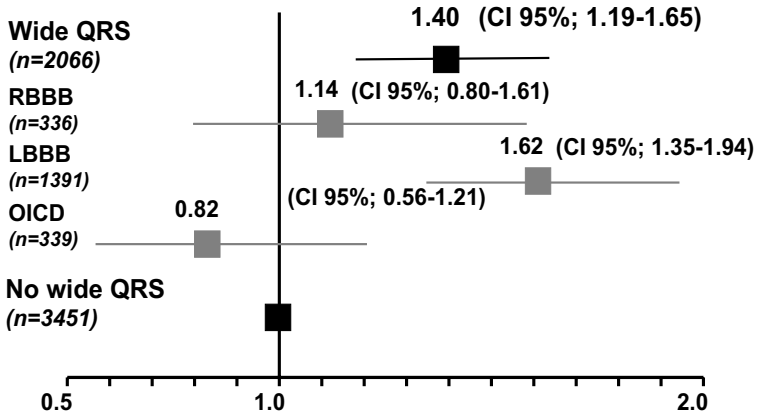


**Figure 2.** *Relative risk of death as a function of the presence of different intraventricular conduction defects. CI = confidence interval; LBBB = left bundle branch block; OICD = other intraventricular conduction defects; RBBB = right bundle branch block.*

**Table III.** Multivariate predictors of the 1-year all-cause mortality in patients with a wide QRS, right bundle branch block (RBBB) and left bundle branch block (LBBB).

| | Wide QRS | | | RBBB | | | LBBB | | |
|---|---|---|---|---|---|---|---|---|---|
| | HR | 95% CI | p | HR | 95% CI | p | HR | 95% CI | p |
| Yes vs no | 1.168 | 0.997-1.368 | NS | 0.862 | 0.624-1.190 | NS | 1.360 | 1.148-1.610 | 0.0004 |
| Age (years)* | 1.026 | 1.018-1034 | 0.0001 | 1.027 | 1.019-1035 | 0.0001 | 1.023 | 1.015-1031 | 0.0001 |
| Ischemic heart disease | 1.215 | 1.033-1.430 | 0.0188 | 1.202 | 1.022-1.441 | 0.0262 | 1.247 | 1.054-1.474 | 0.0100 |
| Previous hospitalization for CHF | 1.771 | 1.482-2.117 | 0.0001 | 1.769 | 1.480-2.114 | 0.0001 | 1.749 | 1.463-2.092 | 0.0001 |
| NYHA class III-IV | 1.975 | 1.677-2.326 | 0.0007 | 1.989 | 1.689-2.342 | 0.0001 | 1.931 | 1.639-2.276 | 0.0001 |
| Heart rate* | 1.008 | 1.003-1.013 | 0.0008 | 1.008 | 1.003-1.013 | 0.0008 | 1.008 | 1.003-1.013 | 0.0019 |
| SBP* | 0.985 | 0.981-0.989 | 0.0001 | 0.985 | 0.981-0.989 | 0.0001 | 0.986 | 0.982-0.990 | 0.0001 |
| Third heart sound | 1.456 | 1.233-1.718 | 0.0001 | 1.477 | 1.252-1.743 | 0.0001 | 1.421 | 1.203-1.678 | 0.0001 |
| Chronic atrial fibrillation | 1.318 | 1.092-1.591 | 0.0040 | 1.303 | 1.080-1.572 | 0.0058 | 1.316 | 1.088-1.590 | 0.0046 |
| Ventricular tachycardia | 1.791 | 1.302-2.464 | 0.0003 | 1.769 | 1.286-2.434 | 0.0005 | 1.758 | 1.278-2.419 | 0.0005 |
| Renal failure | 1.801 | 1.157-2.802 | 0.0091 | 1.770 | 1.138-2.775 | 0.0114 | 1.664 | 1.063-2.604 | 0.0260 |

CHF = congestive heart failure; CI = confidence interval; HR = hazard ratio; SBP = systolic blood pressure. * introduced as continuous variables; not significant variable ($p < 0.10$): gender; cardiothoracic ratio; left ventricular ejection fraction.

higher prevalence of a third heart sound, hypotension, and a reduced left ventricular ejection fraction. This disorder was also associated with more significant clinical impairment as confirmed by the higher number of patients in NYHA class III-IV. This association is probably also related to the functional effects of left intraventricular delay. In fact, this alteration causes several disorders such as: a) desynchronized atrioventricular activation with a mismatch between the end of atrial systole and the onset of ventricular systole, b) interventricular asynchrony with a severely impaired chamber relaxation and subsequent diastolic filling, and finally, c) a heterogeneous left intraventricular contraction, in particular of the septal segment, with the consequent effect that some ventricular segments contract while diastolic filling has already begun. All these events contribute to reduce the systolic ejection volume and to impair the ventricular diastolic phase[14,32]. The relevant effects of left intraventricular conduction defects on cardiac function have been confirmed by the beneficial results of biventricular pacing in terms of exercise tolerance, oxygen consumption and of the quality of life of patients with CHF[33,34].

On the contrary, complete RBBB does not seem to be associated with more advanced heart failure; the pathophysiological reasons why complete RBBB does not significantly impair left ventricular systolic function are not clear because few data regarding this issue are present in the literature[35]. This alteration may be correlated with the degree of impairment of the left ventricular ejection fraction probably because it is usually a marker of the extent of an acute myocardial infarction. This is especially true for anterior wall acute myocardial infarctions in which RBBB has been demonstrated to be an independent predictor of death[35]. Our data not only confirm the role of a wide QRS in patients with heart failure in accordance with other previous studies[13], but also contribute to accurately identify, in the myriad of these electrical alterations, which defect has an independent predictive role in CHF patients.

These findings should be considered applicable to the population of patients with CHF followed by cardiology clinics. Their applicability to all patients with CHF, particularly those followed by internists or general practitioners, is yet to be verified.

Other studies with similar cohorts of patients that compared the different effect of complete LBBB vs RBBB usually excluded subjects with heart failure, and usually considered only patients with ischemic heart disease[24].

Some limitations in our study must be acknowledged. Analysis of the ECG and measurement of the QRS duration were not carried out in a single, core laboratory using standardized, blinded methods and quality control techniques. Further, the duration of the QRS was expressed as a dichotomous variable (> 120 ms); thus, any correlation between the different durations of the QRS and prognosis is not possible. Finally, our registry of outpatients followed by cardiologists included a population with CHF younger than that generally observed in surveys conducted by internal medicine doctors, general practitioners or geriatricians.

In spite of these limitations, present data support the hypothesis that in the myriad of intraventricular conduction alterations defined as a wide QRS, only complete LBBB has a negative prognostic power which is maintained even after adjusting for clinical and demographic variables. The cause-effect relationship of this association, and whether correction of the left ventricular asynchrony secondary to the intraventricular conduction defect may improve survival, should be investigated by adequately powered and properly designed studies.

## Appendix

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