Original article

Clinical significance and prognostic value of right bundle branch block in permanent pacemaker patients

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Aims In patients undergoing pacemaker implantation with no prior history of heart failure (HF), the presence of left bundle branch block (LBBB) has been identified as an independent predictor of HF-related death or hospitalization, while the prognostic significance of right bundle branch block (RBBB) remains uncertain. We aimed to assess the long-term risk of all-cause mortality in patients with a standard indication for permanent pacing and normal or moderately depressed left ventricular function when RBBB is detected at the time of implantation.

Methods We retrospectively enrolled 1348 consecutive patients who had undergone single- or dual-chamber pacemaker implantation at the study center, from January 1990 to December 2022. Patients with a left ventricular ejection fraction ≤ 35% or a prior diagnosis of HF were excluded.

Results The baseline 12-lead electrocardiogram revealed an RBBB in 241 (18%) and an LBBB in 98 (7%) patients. During a median follow-up of 65 [25th–75th percentile: 32–117] months, 704 (52%) patients died. The combined endpoint of cardiovascular death or HF hospitalization was reached by 173 (13%) patients. On multivariate analysis, RBBB was confirmed as an independent predictor of death [hazard ratio, 1.33; 95% confidence interval (CI), 1.09–1.63; $P = 0.005$]. However, when considering the combined endpoint of cardiovascular death and HF hospitalization, this endpoint was independently associated with LBBB (hazard ratio, 2.13; 95% CI, 1.38–3.29; $P < 0.001$), but not with RBBB.

Conclusion In patients with standard pacemaker indications and normal or moderately depressed left ventricular function, the presence of basal RBBB was an independent predictor of mortality. However, it was not associated with the combined endpoint of cardiovascular death and HF hospitalization.

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Keywords: bradycardia, left bundle branch block, pacemaker, pacing, right bundle branch block

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Introduction

Previous studies have established a significant association between the presence of left bundle branch block (LBBB) and the development of new-onset heart failure (HF) during long-term follow-up.[1] Over extended periods, isolated LBBB has been linked to an elevated risk of cardiac mortality and HF progression.[2,3] Similarly, multiple investigations have revealed that right bundle branch block (RBBB) serves as an independent predictor of mortality in patients with cardiovascular diseases,[4–6] while the relationship between RBBB and mortality is less firmly established in patients without cardiovascular disease. Notably, in patients undergoing pacemaker implantation with no prior history of HF and no indication for cardiac resynchronization therapy (CRT), the presence of LBBB has been identified as an independent predictor of HF-related death or hospitalization,[7] while the prognostic significance of RBBB remains uncertain.

In the present study, we aimed to assess the long-term risk of all-cause mortality in patients with a standard indication for permanent single- or dual-chamber pacing and normal or moderately depressed left ventricular (LV) function when RBBB is detected at the time of implantation.

Methods

Patient selection, pacemaker implantation and follow-up

We retrospectively enrolled all consecutive adult patients in whom pacemaker implantation had been performed from January 1990 to December 2022 at the Santa Maria della Stella Hospital in Orvieto, Italy. Patients were

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required to have standard indications for permanent single- or dual-chamber pacing. Patients with evidence of systolic dysfunction [LV ejection fraction (LVEF) $\leq$ 35%] or a prior diagnosis of HF were excluded from the analysis. The study was approved by the Local Ethics Committee and informed consent was obtained from all patients. Devices and pacing leads were implanted by means of standard techniques. Atrial leads were routinely implanted in the right atrial appendage and ventricular leads in the right apex. Baseline evaluation included demographics and medical history, clinical examination, 12-lead electrocardiogram, and echocardiographic evaluation of LVEF. Optimization of pacing parameters and pharmacological treatments were based on clinical evaluation by the attending physicians. During follow-up, patients returned for regular clinic visits every 6 months. At each scheduled or unscheduled visit, the pacemaker was interrogated and stored data were retrieved.

Twelve-lead ECG

A standard ECG was recorded at the time of pacemaker implantation in the supine position during quiet respiration, at a paper speed of 25 and 50 mm/s and at a standard gain of 1 mV/cm. For the purpose of the study, RBBB was defined using the American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Rhythm Society criteria.[8] These criteria consist of three parameters: a QRS duration of >120 ms; a secondary R wave in V1 or V2; a wide, slurred S wave in leads I, V5, and V6. LBBB was defined as: a QRS duration of $\geq$120 ms; broad (frequently notched or slurred) R waves in leads I, aVL, V5, or V6; absent q waves in leads I, V5, and V6; R peak time of >60 ms in leads V5 and V6 but normal in leads V1, V2, and V3, when small initial r waves can be discerned in the above leads. In patients requiring continuous ventricular pacing, intrinsic conduction was sought by slowing down the pacing rate. In the case of pacemaker dependency, patients were excluded from the QRS analysis. Pacemaker dependency was defined as the absence of intrinsic conduction for at least 30 s after gradual slowing-down of the pacing rate to 30 beats/min.[9] Substantial right ventricular pacing was defined as a percentage of ventricular pacing of >40% at the first follow-up.[10]

Clinical events

The study endpoints consisted of all-cause death and the combined endpoint of cardiovascular death and HF hospitalization. The diagnosis of HF was based on the presenting symptoms, clinical findings, and appropriate investigations, in accordance with the guidelines for the diagnosis and treatment of acute and chronic HF.[11] Mortality data were obtained by means of hospital file review or direct telephone contact, and hospitalizations were collected from medical records.

Statistical analysis

Quantitative variables are reported as means $\pm$ SD if normally distributed, or medians with 25th to 75th percentiles in the case of skewed distribution. Normality of distribution was tested by means of the nonparametric Kolmogorov–Smirnov test. Categorical data were expressed as percentages. Event rates were summarized by constructing Kaplan–Meier curves. The log-rank test was applied to evaluate differences between trends (level of significance adjusted for multiple testing by Bonferroni correction). Cox regression was used to analyze possible predictors of the endpoints. All variables associated with a *P*- value of <0.05 on univariate analysis were entered into the multivariate regression analysis. A *P*- value of <0.05 was considered significant for all tests. All statistical analyses were performed by means of R: a language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population and baseline evaluation

From January 1990 to December 2022, a total of 1348 consecutive patients with a standard indication for permanent single- or dual-chamber pacing underwent pacemaker implantation in our center. All procedures were performed by three expert operators. Patients included in the present analysis had no history of HF and had an LVEF of >35%. Table 1 shows baseline clinical variables and the indications for pacemaker implantation. The baseline 12-lead electrocardiogram revealed an RBBB in 241 (18%) and an LBBB in 98 (7%) patients, and other conduction defects were diagnosed in 10 (0.7%) patients; the absence of intrinsic rhythm was recorded in 174 patients. The following peri-implantation complications occurred during the study period: 24 (1.8%) lead-related reinterventions, 11 (0.8%) pneumothorax, 10 (0.7%) pocket revisions, 8 (0.6%) device-related infections. All events were effectively managed, resulting in a positive outcome.

Follow-up

During a median follow-up of 65 [25th–75th percentile: 32–117] months, 704 (52%) patients died. Death for cardiovascular reasons was reported in 94 (7%) patients and 140 (10%) were hospitalized for HF. The combined endpoint of cardiovascular death or HF hospitalization was reached by 173 (13%) patients. Fig. 1 shows the Kaplan–Meier survival curves regarding all-cause death, stratified by the presence or absence of conduction defects. Patients with RBBB or LBBB displayed significantly higher rates of death than those without blocks (log-rank test, all

Table 1 Demographics, baseline clinical parameters and indications for pacing of the study population and of the groups

Parameter	Total (1348)	RBBB (241)	LBBB (98)	No conduction defects (825)
Male gender, *n* (%)	763 (57)	167 (69)[a]	47 (48)	445 (54)
Age, years	78 ± 9	81 ± 8[a]	79 ± 8	77 ± 9
Body mass index, kg/m^2	27 ± 4	27 ± 4	26 ± 3[a]	27 ± 4
Right bundle branch block	241 (18)	–	–	–
Left bundle branch block	98 (7)	–	–	–
QRS duration [b], ms	96 ± 23	126 ± 12[a]	135 ± 14[a]	83 ± 7
History of AF, *n* (%)	595 (44)	86 (36)[a]	39 (40)	449 (54)
Coronary artery disease, *n* (%)	208 (15)	35 (15)	12 (12)	135 (16)
Hypertension, *n* (%)	1029 (76)	196 (81)	74 (76)	626 (76)
Diabetes mellitus, *n* (%)	307 (23)	58 (24)	27 (28)	167 (20)
COPD, *n* (%)	192 (14)	42 (17)	12 (12)	107 (13)
Chronic kidney disease, *n* (%)	222 (16)	49 (20)[a]	23 (23)[a]	1116 (14)
Peripheral arterial disease, *n* (%)	141 (10)	29 (12)	13 (13)	78 (9)
LV ejection fraction 36–50%, *n* (%)	154 (11)	32 (13)[a]	24 (24)[a]	74 (9)
NYHA class				
NYHA I, *n* (%)	821 (61)	135 (56)	55 (56)	528 (64)
NYHA II, *n* (%)	476 (35)	92 (38)	31 (32)	281 (34)
NYHA III, *n* (%)	51 (4)	14 (6)	12 (12)	16 (2)
CHA2DS2-VASc score	3.4 ± 1.2	3.5 ± 1.1	3.7 ± 1.2[a]	3.4 ± 1.2
Clinical indication for pacing				
Sick sinus syndrome	567 (42)	75 (31)[a]	27 (28)[a]	456 (55)
Atrioventricular block	449 (33)	115 (48)[a]	43 (44)[a]	134 (16)
AF with slow ventricular response	229 (17)	39 (16)	21 (21)	154 (19)
Carotid sinus syndrome	97 (7)	12 (5)	7 (7)	75 (9)
Vasovagal syncope	6 (0.4)	0 (0)	0 (0)	6 (1)
Dual-chamber pacemaker, *n* (%)	1083 (80%)	195 (81)	71 (72)	652 (81)

AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; LV, left ventricular; NYHA, New York Heart Association. [a] $P < 0.005$ versus no conduction defects. [b] Missing values in 172 patients.

$P < 0.001$). Figure. 2 shows the Kaplan–Meier survival curves regarding the combined endpoint of cardiovascular death and HF hospitalization. Patients with LBBB displayed significantly higher rates of events (log-rank test, $P < 0.001$).

At the time of the first follow-up visit, the median cumulative ventricular pacing percentage was 61% [25th–75th percentile: 10–97%]. Baseline parameters and ventricular pacing percentage were evaluated by means of univariate analysis to assess their ability to predict the occurrence of the endpoints during follow-up. The factors that showed a significant association with all-cause death were: older age, lower BMI, presence of RBBB and LBBB, history of atrial fibrillation, diabetes, chronic obstructive pulmonary disease, chronic kidney disease, LVEF of <50%, NYHA class, higher CHA2DS2-VASc score and the percentage of ventricular pacing (Table 2). The factors that were associated with the combined endpoint of cardiovascular death and HF hospitalization were: older age, presence of LBBB, history of atrial fibrillation, coronary artery disease, chronic obstructive pulmonary disease, chronic kidney disease, LVEF of <50%, NYHA class, higher CHA2DS2-VASc score and the percentage of ventricular pacing. In particular, a percentage of ventricular pacing of >40% was associated with death with a hazard ratio of 1.27 [95% confidence interval (CI): 1.08–1.48, $P = 0.004$], and with the combined endpoint of cardiovascular death and HF hospitalization with a hazard ratio of 1.94 (95% CI: 1.37–2.74, $P < 0.001$). The results of the multivariate analyses are reported in Table 3.

Discussion

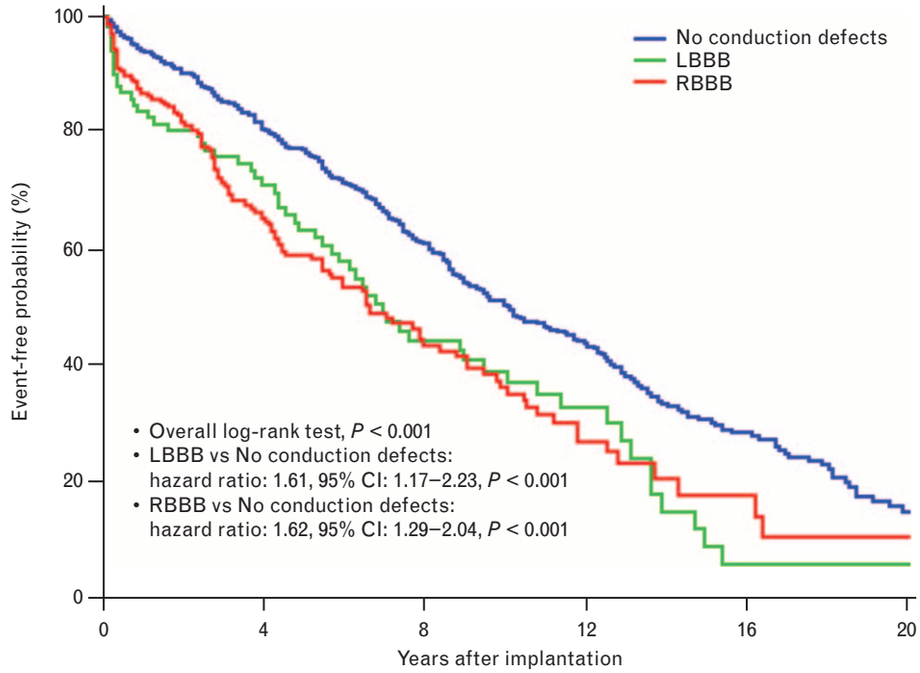
Main findings

In this study, we investigated the risk of all-cause mortality in patients with a standard indication for permanent single- or dual-chamber pacing and normal or moderately depressed LV function when RBBB was detected at the time of implantation. Our findings revealed that in these patients, the presence of basal RBBB was an independent predictor of mortality.

Right bundle branch block and prognosis

Right bundle branch block is characterized by either a significant delay or lack of electrical conduction through the right bundle branch and distal Purkinje fibers, resulting in ventricular activation primarily occurring via the left bundle branch.[12] The block can be a signal of underlying cardiac conditions, including ischemic, inflammatory, or infiltrative heart diseases, as well as pulmonary embolism.[12–15] In patients with established cardiovascular disease, RBBB is recognized as a predictor of adverse

Fig. 1



Number at risk

No conduction defects	825	526	292	140	53	15
LBBB	98	56	28	13	1	1
RBBB	241	116	46	16	5	3

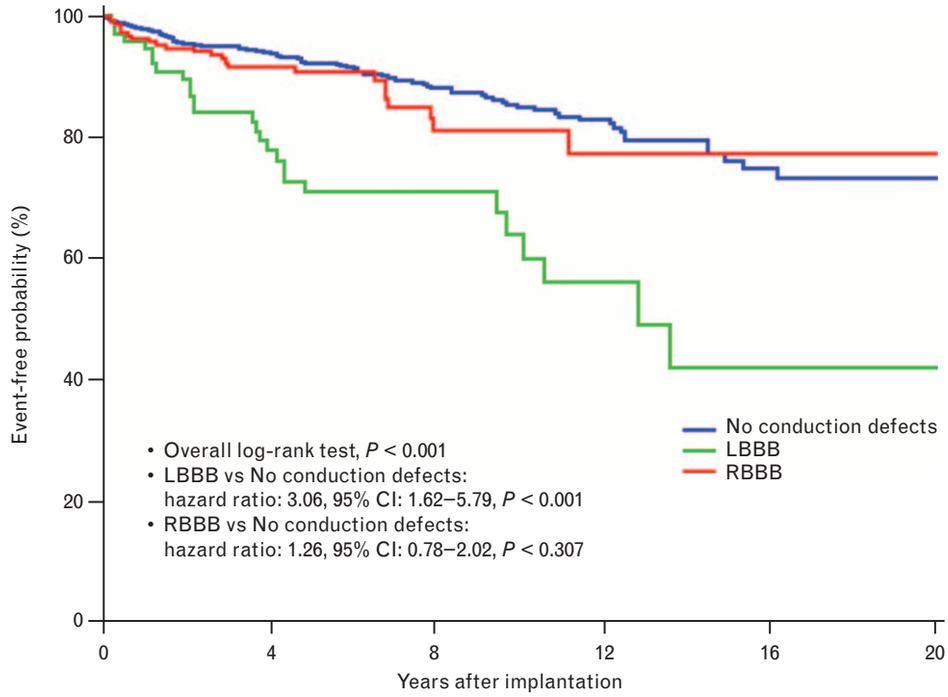
Kaplan–Meier estimates of time to all-cause death, stratified by presence or absence of RBBB and LBBB. LBBB, left bundle branch block; RBBB, right bundle branch block.

outcomes, particularly mortality.[4–6,16] Nevertheless, the evidence regarding the association between RBBB and mortality in patients without cardiovascular disease is conflicting. A large-scale study involving over 18 000 participants without a history of myocardial infarction or HF found that RBBB was predictive of death,[17] while a study conducted exclusively in women did not confirm this finding.[18]

In our analysis of long-term survival in patients eligible for antibradycardia pacing with preserved or mildly reduced LVEF, we documented a survival rate of approximately 70% at 5 years and 50% at 10 years. In the REPACE registry,[19] the authors reported a survival rate of approximately 60% for patients aged between 75 and 84 years at 5 years and approximately 30% at 10 years. Similarly, Pérez-Díaz *et al.*[20] reported an all-cause mortality rate of 21% at 3.5 years in elderly patients with pacemakers. In our study, mortality due to cardiovascular causes was relatively low (7%), and only 10% of patients were hospitalized for HF during the follow-up period. In the present analysis, the presence of RBBB was associated with an unfavorable prognosis, similar to that associated with LBBB, with a hazard ratio of 1.62 in Kaplan–Meier analysis. However, when considering the combined endpoint of cardiovascular death and HF hospitalization, this endpoint was associated with LBBB (with a hazard ratio of 3.06), but not with RBBB.

Right bundle branch block has been linked to various comorbidities, including pulmonary hypertension, chronic obstructive pulmonary disease, hypertension, and diabetes.[21–23] In our population of patients with indications for pacemaker placement, RBBB may signify a more compromised overall clinical condition rather than a cardiac disease signal. Patients with baseline RBBB tended to be older, more frequently male, with chronic kidney disease, but less frequently had a history of atrial fibrillation compared with patients without conduction blocks. Additionally, while RBBB patients reported a slightly worse functional class, their systolic function was comparable to that of patients without conduction blocks, unlike patients with LBBB, among whom mildly reduced LVEF was more frequently observed. Alongside older age and other

Fig. 2



Number at risk

No conduction defects	825	513	277	128	47	15
LBBB	98	46	26	10	1	1
RBBB	241	112	41	15	5	3

Kaplan–Meier estimates of time to the combined endpoint of cardiovascular death and HF hospitalization, stratified by presence or absence of RBBB and LBBB. LBBB, left bundle branch block; RBBB, right bundle branch block.

Table 2 Univariate and multivariate analysis of factors predicting all-cause death in the study population

	Univariate analysis			Multivariate analysis		
	HR	**95% CI**	*P*	**HR**	**95% CI**	*P*
Male gender	0.99	0.85–1.15	0.885	–	–	–
Age	1.09	1.08–1.10	<0.001	1.09	1.08–1.10	<0.001
Body mass index	0.96	0.95–0.98	<0.001	0.99	0.97–1.01	0.260
Right bundle branch block	1.56	1.28–1.89	<0.001	1.33	1.09–1.63	0.005
Left bundle branch block	1.47	1.13–1.91	0.004	1.27	0.97–1.66	0.081
History of atrial fibrillation	1.32	1.14–1.53	<0.001	1.20	1.03–1.40	0.019
Coronary artery disease	0.97	0.79–1.18	0.737	–	–	–
Hypertension	1.05	0.88–1.24	0.597	–	–	–
Diabetes mellitus	1.27	1.07–1.51	0.006	1.36	1.12–1.66	0.002
COPD	1.59	1.33–1.91	<0.001	1.20	0.99–1.45	0.068
Chronic kidney disease	2.29	1.91–2.74	<0.001	1.55	1.27–1.90	<0.001
Peripheral arterial disease	1.20	0.93–1.52	0.094	–	–	–
LV ejection fraction <50%	1.87	1.52–2.29	<0.001	1.25	0.99–1.58	0.061
NYHA class	2.05	1.82–2.32	<0.001	1.28	1.10–1.50	0.002
CHA2DS2-VASc score	1.23	1.17–1.30	<0.001	0.95	0.89–1.01	0.127
% of ventricular pacing >40%	1.27	1.08–1.48	0.004	0.97	0.82–1.14	0.679

COPD, chronic obstructive pulmonary disease; HR, hazard ratio; LV, left ventricular; NYHA, New York Heart Association.

Table 3 Univariate and multivariate analysis of factors predicting the combined endpoint of cardiovascular death and HF hospitalization in the study population

	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P*	HR	95% CI	*P*
Male gender	1.18	0.87–1.60	0.292	–	–	–
Age	1.03	1.01–1.05	<0.001	1.02	1.00–1.05	0.036
Body mass index	0.97	0.93–1.01	0.097	–	–	–
Right bundle branch block	1.07	0.70–1.63	0.765	–	–	–
Left bundle branch block	2.89	1.92–4.35	<0.001	2.13	1.38–3.29	<0.001
History of atrial fibrillation	1.42	1.06–1.92	0.021	1.31	0.96–1.78	0.092
Coronary artery disease	2.24	1.62–3.09	<0.001	1.32	0.88–1.99	0.179
Hypertension	1.13	0.80–1.61	0.490	–	–	–
Diabetes mellitus	1.31	0.94–1.85	0.115	–	–	–
COPD	2.20	1.57–3.08	<0.001	1.22	0.83–1.78	0.310
Chronic kidney disease	3.41	2.46–4.73	<0.001	1.80	1.23–2.63	0.003
Peripheral arterial disease	1.52	0.99–2.33	0.058	–	–	–
LV ejection fraction <50%	5.82	4.24–7.97	<0.001	3.00	1.98–4.55	<0.001
NYHA class	2.56	2.01–3.25	<0.001	1.16	0.85–1.59	0.338
CHA2DS2-VASc score	1.30	1.17–1.45	<0.001	1.04	0.91–1.20	0.552
% of ventricular pacing >40%	1.94	1.37–2.74	<0.001	1.62	1.14–2.31	0.007

COPD, chronic obstructive pulmonary disease; HR, hazard ratio; LV, left ventricular; NYHA, New York Heart Association.

comorbidities, the presence of RBBB emerged as an independent predictor of mortality in multivariable analysis. However, it was not associated with the combined endpoint of cardiovascular death and HF hospitalization, which was instead predicted by LBBB, as previously shown,[7] and by the extent of right ventricular pacing.

In a previous analysis of patients without cardiovascular disease, the adverse prognostic value of RBBB was also observed.[24] Among over 22 000 patients referred for stress testing, RBBB was detected in approximately 1%. Over a mean follow-up of 12 years, 8% of patients died, with 3% of deaths attributed to cardiovascular causes. Even after adjusting for multiple confounders, RBBB remained independently associated with increased all-cause mortality, with a hazard ratio similar to that measured in our study (hazard ratio: 1.5). It is worth noting that our population of pacemaker recipients was substantially older (78 versus 52 years), explaining the higher observed mortality. In both studies, survival curves for patients with and without RBBB began to diverge relatively early during follow-up. In the study by Gaba *et al.*, the presence of RBBB led to an increased rate of cardiovascular death approximately 7 years after the observation commenced. Conversely, in our population of older patients with shorter life expectancies due to competing noncardiovascular causes of death, RBBB did not result in more frequent events.

The prevalence of RBBB has been reported to range from 0.2% to 1.3%.[12] In the HF population, the incidence of non-LBBB is lower than that of typical LBBB but is still frequently encountered. In a cohort study of patients with NYHA class II–IV symptoms, 7.6% exhibited RBBB.[25] Some studies have reported higher mortality in patients with non-LBBB compared with those with LBBB. One study showed a 29% increase in mortality at the 4-year follow-up for patients with RBBB when compared with those with LBBB, with the risk ratio further increasing in those with LVEF of <30%.[16] In our study, RBBB was relatively prevalent in patients indicated for permanent pacing with preserved LVEF, and it served as a negative prognostic factor, although it was not specifically associated with cardiovascular events.

Possible pacing strategies for right bundle branch block

Our study identified a substantial amount of right ventricular pacing, i.e. >40% ventricular pacing rate, as an independent predictor of cardiovascular death and HF hospitalization in patients with RBBB and this could be the background for exploring alternative pacing strategies for this specific subset of patients.

Cardiac resynchronization therapy has demonstrated beneficial effects in correcting ventricular dyssynchrony induced by LBBB, with significant clinical and prognostic benefits in eligible patients.[26] Not only biventricular but also left-ventricular-only pacing appears beneficial in patients with low LVEF and a wide QRS.[27] Recently, the randomized–controlled BUDAPEST trial successfully tested the hypothesis that upgrading to CRT would be associated with improved clinical outcomes in patients

with a prior pacemaker or defibrillator and consistent right ventricular pacing.[28] However, the efficacy of biventricular pacing in patients with non-LBBB remains uncertain and unpredictable. In an observational study[29] involving 99 patients with RBBB or other conduction defects and LVEF <35%, the average LVEF increased by 4% with biventricular pacing during a mean follow-up of 13 months. Less certainty exists regarding the evidence supporting the use of conduction system pacing for patients with non-LBBB morphology.[30–33] Some small observational studies[34,35] have shown that QRS duration can be narrowed with His-bundle pacing in patients with RBBB and advanced HF. Moreover, a study[36] demonstrated that LBB area pacing can improve cardiac function in patients with RBBB and LVEF of <50% with bradycardia pacing indications. Targeted studies would be required to evaluate the efficacy of alternative pacing strategies in the subgroup of patients with RBBB.[10,37,38] However, due to the relatively low weight of cardiovascular events on total mortality, the impact on the outcome of novel stimulation techniques might be limited in elderly patients with RBBB, such as those included in the present study.

Limitations

The main limitation of the present study is the retrospective design of the analysis and the risk of residual confounding related to the many factors affecting outcome in patients implanted with a pacemaker.[39] Indeed, some variability in the selection or management of patients during the inclusion period may have influenced the results– specifically, the evolution of cardiac pacing recommendations that has taken place. For instance, contemporary guidelines advocate for considering physiologic pacing in patients with LVEF of between 36% and 50%, whereas during the study period, RV pacing was the sole option employed. Additionally, current guidelines suggest that a septal RV lead position might be preferable for patients at higher risk of perforation, whereas in our series, an apical position was utilized for all patients. Nonetheless, the incidence of periprocedural complications remained within acceptable limits. Moreover, the study was carried out in a single center, the operators in charge of patient selection, device implantation and clinical management did not change during the study period and all the patients included were consecutive.

Conclusions

In patients with standard pacemaker indications and normal or moderately depressed LV function, the presence of basal RBBB was an independent predictor of mortality. However, it was not associated with the combined endpoint of cardiovascular death and HF hospitalization.

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Conflicts of interest

There are no conflicts of interest.

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