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CICLO 28°

LEFT BUNDLE BRANCH BLOCK DEFINITION PREDICTS RESPONSE TO CARDIAC RESYNCHRONIZATION THERAPY

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RIASSUNTO

Introduzione. La terapia di re sincronizzazione cardiaca (RCT) si è dimostrata efficace nel trattamento dei pazienti con scompenso cardiaco e blocco di branca sinistro (BBSn). Recentemente sono stati proposti nuovi criteri ECG per definire il BBSn. Questi criteri sono più restrittivi rispetto a quelli utilizzati nella definizione dell'American Heart Association (AHA), incrementando la specificità della diagnosi di BBSn. In questo studio abbiamo determinato la risposta alla RCT in termini ecocardiografici in pazienti che rispettvano (Strict-LBBB) o no (Traditional-LBBB) la nuova definizione di BBSn.
Metodi. Abbiamo arruolato pazienti consecutivi sottoposti ad impianto di RCT (pacemaker o defibrillatore) inclusi nel Regustro CRT MORE. Sono stati esclusi dall'analisi pazienti che non rispettavano i criteri di BBSn secondo la definzione dell'AHA, fibrillazione atriale, blocco di branca destro e già portatori di pacemaker. Strict-LBBB è stato definito come: QRS ≥140ms per I maschi e ≥130ms per le femmine, QS o rS in V1–V2, mid-QRS notching o slurring in ≥2 derivazioni contigue. I pazienti che hanno dimostrato una riduzione relativa ≥15% del volume telesistiolico ventricolare sinistro (VTS) a 12 mesi sono stati definiti "responder".

Results. Tra 335 pazienti con BBSn second la definizione LBBB, 131 (39%) presentavano Strict-LBBB. I pazienti com e senza Strict-LBBB presentavano caratteristiche cliniche ed elettrocardiografiche simili a parte la durata del QRS (166±20ms vs 152±25ms, p<0.001). Al controllo a 12 mesi sono risultati "responder" 205 (61%) pazienti: 85 (65%) pazienti con Strict-LBBB e 120 (59%) con Traditional-LBBB (p=0.267). All'analisi multivariata, la storia di fibrillazione atriale, il VTS più grande, e la presenza di mid-QRS notching in ≥1 derivazione (OR 1.96; 95%CI 1.04 to 3.70, p=0.038) sono risultati indipendentemente associati alla risposta ecocardiografica.

ConclusionI. La definizione più restrittiva di BBSn recentemente proposta non migliora l'identificazione dei pazienti responder" alla RCT rispetto alla definizone dell'AHA. Tra le variabili elettrocardiografiche, solo la presenza di mid-QRS notching in almeno una derivazione si correla alla risposta ecocardiografica alla CRT.

ABSTRACT

Background. Cardiac resynchronization therapy (CRT) was proved to be effective in patients with heart failure and left bundle branch block (LBBB). Recently, new ECG criteria have been proposed for the diagnosis of LBBB. These criteria are stricter than the current American Heart Association (AHA) criteria and thus increase the specificity of LBBB diagnosis. We assessed the rate of echocardiographic response to CRT in patients who did and did not meet new criteria (Strict-LBBB).

Methods. Consecutive patients who received CRT defibrillators were enrolled in the CRT MORE registry. Patients with no-LBBB QRS morphology according to AHA, atrial fibrillation, right bundle branch block and right ventricular pacing were excluded from the analysis. Strict-LBBB was defined as: QRS ≥140ms for men and ≥130ms for women, QS or rS in V1–V2, mid-QRS notching or slurring in ≥2 contiguous leads. Patients showing a relative decrease of ≥15% in left ventricular end systolic volume (LVESV) at 12 months were defined as responders.

Results. Among 335 patients with AHA LBBB, 131 (39%) had Strict-LBBB. Patients with and without Strict-LBBB showed comparable baseline characteristics except for QRS duration (166±20ms vs 152±25ms, p<0.001). At 12-month evaluation responders were 205 (61%). 85 (65%) patients had Strict-LBBB and 120 (59%) had no Strict-LBBB (p=0.267). On multivariate analysis, history of atrial fibrillation, larger LVESV, and presence of mid-QRS notching in ≥1 lead (OR 1.96; 95%CI 1.04 to 3.70, p=0.038) were independently associated with the echocardiographic response.

Conclusions. Recently proposed stricter criteria for LBBB diagnosis did not improve the identification of CRT responders. Among ECG variables, only the presence of mid-QRS notching in at least 1 lead was associated with the echocardiographic response.

INTRODUCTION

Epidemiology of heart failure

Approximately 2% of the adult population in developed countries has heart failure (HF); most patients will be aged >70 years and about half will have a left ventricular (LV) ejection fraction (EF) < 50%.[1] About 1% of emergency hospital admissions amongst adults are primarily due to heart failure, which contributes to a further 4%, although these may be underestimated due to issues with diagnosis and case definition.w81 In the EuroHeart Failure survey, 36% of those who had LV function assessed had an LVEF ≤ 35% and, of these, 41% had a QRS duration ≥120 ms; 7% had RBBB, 34% had LBBB or other intraventricular conduction delay (IVCD) and 17% had QRS ≥150 ms.[2] In the Italian Network on CHF (IN-CHF) registry, 1391 patients (25%) had complete LBBB, 336 (6%) had complete RBBB and 339 (6%) had other forms of IVCD.[3] The annual incidence of LBBB is about10% in ambulatory patients with LV systolic dysfunction and chronic HF.[4] Based on current guideline criteria,[5] only a small proportion of patients with HF (perhaps 5–10%) are indicated for cardiac resynchronization therapy (CRT) but this is still a large number of patients. Based on data from two EuroHeart Failure surveys and extrapolating from hospital discharge statistics,[2,6,7] it could be estimated that about 400 patients per million population per year might be suitable for CRT, or up to 400,000 patients per year in ESC countries.

The prognosis of HF is generally poor. Of patients admitted to hospital with HF, the one-year mortality is about 20% in those aged $\leq$ 75 years and > 40% if aged > 75 years, despite contemporary pharmacological therapy.[8-9] High-quality information on the prognosis of outpatient populations with HF is harder to find. Patients in clinical trials tend to be younger and with fewer co-morbidities than in clinical practice and consequently have a better prognosis, with an annual mortality of 5–10% in recent trials, even though

the trial protocols excluded very-low-risk patients.[10,11] However, treatment appears to have remarkably improved the prognosis of patients with chronic HF over the last 20 years. For example, the median life expectancy of patients enrolled in the Vasodilator in HEart Failure Trial V-HeFT-I trial (study period 1980–85), was just 3.5 years compared with more than 8 years for an age-equivalent population with moderately severe heart failure, treated with pharmacological therapy plus CRT, enrolled in CArdiac REsynchronization in Heart Failure (CARE-HF; study period 2001–2009).[12-14] An ESC survey found that patients who received a CRT device had a one-year mortality of ,10%.[15] Patients with a broad QRS complex have even a worse prognosis that may only be partially explained by having a lower LVEF.[2,3,17 –18] In the ICD arm of the Multicenter Automatic Defibrillator Trial (MADIT) CRT study, the patients with IVCD, RBBB and LBBB had 3-year mortality rates of 4, 7 and 8%, respectively.[19]

Atrial fibrillation (AF) is the most common arrhythmia in patients with HF. The EuroHeart Failure survey reported that up to 45% of patients with HF also presented with intermittent or permanent AF.[2] In chronic HF, the prevalence of AF is linked directly to disease severity, ranging from10–20% in mild-to-moderate CHF up to 50% in patients with advanced disease.[20] AF is a common cause of worsening HF and complicates management. Incident AF is associated with a worse prognosis but it is unclear whether patients with chronic AF have a worse prognosis than those in sinus rhythm, after correcting for age and co-morbidity.[21-26]w100–w105 AF may simply be a marker of more severe disease.

Cardiac dyssynchrony is complex and multifaceted. Prolongation of the atrio-ventricular (AV) interval delays systolic contraction, which might then encroach on early diastolic filling.[27] Atrial pressure falls as the atria relax. If ventricular contraction is delayed, then left ventricular (LV) diastolic pressures will exceed atrial pressure causing diastolic mitral regurgitation. The loss of ventricular pre-load then leads to a reduction in LV contractility,

due to loss of the Starling mechanism. Both inter- and intra-ventricular conduction delays lead to asynchronous contraction of LV wall regions (ventricular dyssynchrony), impairing cardiac efficiency and reducing stroke volume and systolic blood pressure. Poorly coordinated papillary muscle function may cause or aggravate functional systolic mitral regurgitation. Impaired performance promotes adverse LV remodelling. Cardiac resynchronization therapy helps to restore AV, inter- and intra-ventricular synchrony, improving LV function, reducing functional mitral regurgitation and inducing LV reverse remodelling, as evidenced by increases in LV filling time and LVEF, and decreases in LV end-diastolic- and end-systolic volumes, mitral regurgitation and septal dyskinesis.[28] The dominant mechanism of benefit is likely to vary from one patient to the next and within an individual patient over time. It is possible that no single measure will accurately predict the response to CRT, since the mechanism of benefit is so heterogeneous.[29-30]

History of CRT

CRT is an established treatment in patients with HF and ventricular conduction delay [31,32], especially in the form of left bundle branch block (LBBB) [33-37] in patients with New York Heart Association (NYHA) class III HF from a series of RCTs (**Figure 1**). This therapy aims to restore electrical and mechanical synchrony throughout the LV, thus improving cardiac function and reducing HF hospitalizations and death [33-36, 38].

The first randomized trials demonstrated the benefits of CRT on symptoms, exercise capacity and LV structure and function.[39-43] The CARE-HF and Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure (COMPANION) trials evaluated the effects of CRT-P on HF hospitalizations and all-cause mortality.[44-45] A recent meta-analysis showed that, in these patients, CRT improved symptoms and reduced all-cause mortality by 22% and HF hospitalizations by 35%[46] The evidence among NYHA class IV heart failure patients is limited, due to the low number of patients enrolled in RCTs (from 7 to 15%). In a sub-study of the COMPANION trial,w110 class IV patients who had had no

scheduled or unscheduled HF hospitalizations during the last month (termed ‘ambulatory’ class IV) showed a significant reduction in the combined primary endpoint of time to all-cause mortality and hospitalization, but only a trend for all-cause mortality and HF deaths. Four RCTs have demonstrated that CRT improves LV function, all cause mortality and HF hospitalizations of patients with mild HF symptoms (NYHA class I–II), sinus rhythm, LVEF ≤30–40% and QRS duration ≥120–130 ms.[47-50] However, improvement in functional status or quality of life among patients randomized to
CRT were modest and not robust. Most patients enrolled had NYHA class II HF symptoms; only 15% in Resynchronization reVErses Remodelling in Systolic left vEntricular dysfunction (REVERSE) and 18% in MADIT-CRT were in NYHA class I.[47,49] CRT did not reduce all-cause mortality or HF events among
NYHA class I patients. Therefore, the recommendation is restricted to patients in NYHA class II.

Pre-specified subgroup analyses of data collected in the MADIT-CRT, REVERSE and Resynchronization–Defibrillation for Ambulatory Heart Failure Trial (RAFT) trials demonstrated that patients with a QRS duration ≥150 ms benefited most from CRT.[47-49] Meta-analyses using aggregate data from randomized
trials showed that CRT was effective in reducing adverse clinical events in patients with baseline QRS duration ≥150 ms and suggested that CRT might not reduce events in patients with a QRS <150 ms.[51]

Indications to CRT

There is strong evidence that CRT reduces mortality and hospitalization, improves cardiac function and structure in symptomatic chronic HF patients with optimal medical treatment, severely depressed LVEF (i.e.
≤35%) and complete LBBB. In these patients, CRT was superior either to optimal medical therapy or to ICD alone. In these patients, further research is very unlikely to change our

confidence in the estimate of effect. Current European recommendations are displayed in **Figure 2.**

There is no evidence of benefit in patients with HF and QRS <120 ms. In the Cardiac REsynchronization THerapy IN Patients with Heart Failure and Narrow QRS (RethinQ) trial,[52] CRT did not improve peak oxygen consumption (primary endpoint) or quality of life in the subgroup of patients with QRS <120 ms and evidence of echocardiographic dyssynchrony. The study was of too short a duration to observe effects on morbidity and mortality. The recent randomized, double-blind Evaluation of Resynchronization Therapy for Heart Failure in Patients with a QRS Duration Lower Than 120 ms (LESSER-EARTH) trial,[53] which compared active vs. inactive CRT therapy, was prematurely interrupted due to futility and safety concerns after 85 patients were randomized. Indeed, CRT was associated with a significant reduction in the 6-minutewalk distance and a non-significant trend towards an increase in heart failure-related hospitalizations.

In conclusions, clinical factors influencing the likelihood to respond to CRT are presented in **Figure 3**.

CRT-D or CRT-P?

Previous randomized multicentre clinical studies evaluated the effect of CRT-D or CRT-P vs. medical therapy on all-cause mortality in patients with advanced HF (NYHA functional class III or IV symptoms).[45] The COMPANION trial investigated CRT-D implantation vs. optimal medical therapy and CRT-P implantation vs. optimal medical therapy; however, the trial was neither designed, nor powered to compare the effect of CRT-D vs. CRT-P implantation on all-cause mortality, and therefore does not provide conclusive data for the clinician.[44] The Cardiac Resynchronization Heart Failure (CARE-HF) trial compared CRT-P implantation with standard medical therapy and showed a significant mortality reduction in advanced heart failure patients with an implanted CRT-P. Furthermore, in the

extended follow-up of patients enrolled in CARE-HF, the authors demonstrated that patients implanted with a CRT-P alone derived a significant reduction in the risk for SCD.[14] Several other studies have shown that CRT alone reduces the risk of ventricular tachyarrhythmias and SCD due to LV reverse remodelling17 and as a result of the beneficial effects of CRT on the neurohormonal system.[54] This brings into question whether improvements in cardiac function and in the neurohormonal status resulting from CRT-P alone can sufficiently lower the risk of ventricular tachyarrhythmias such that the incremental benefit from CRT with defibrillator therapy would be of limited value. This may be the reason why several meta-analyses comparing the efficacy of CRT-D over CRT-P in patients with a primary indication for CRT have failed to show an incremental benefit of adding defibrillation therapy to CRT.[54-57] The risk of ventricular arrhythmias and SCD may be sufficiently reduced with CRT-P alone. Furthermore, CRT-D devices have a significantly higher cost and their widespread use remains limited especially in emerging countries that have fixed budgets for healthcare and where healthcare utilization is based on cost–benefit analysis. In addition, the complex design of defibrillator leads presents additional challenges including a higher risk of lead failure in the CRT-D systems.[58] Despite these great concerns, there is currently no consensus on in which patients CRT-P alone could be considered. The physician needs to estimate costs, benefit, and risks based on the individual patients. Clinicians in many countries face challenges in reimbursement of CRT devices, and expected future healthcare reforms will lead to additional scrutiny of expensive medical device therapies.[59]

Until clinical guidelines or consensus statements become available, our results may help clinicians identify patients in whom CRT-P alone may be sufficiently effective in reducing adverse outcomes.

Kutyifa et al. suggesteed that CRT-D does not have an incremental benefit over CRT-P in the reduction of all-cause mortality in non-ischaemic patients.[60] Only patients with

ischaemic aetiology of cardiomyopathy showed a significant reduction in mortality with an implanted CRT-D as compared with a CRT-P. The reason for this finding may be that patients with non-ischaemic cardiomyopathy are known to be at a lower risk for ventricular tachyarrhythmias particularly in the setting of CRT-induced reverse remodelling. They found a significantly higher risk of all-cause mortality in patients with ischaemic cardiomyopathy compared with non-ischaemic cardiomyopathy, and this difference in the mortality risk may be due to the higher risk of life-threatening ventricular arrhythmias and SCD in ischaemic patients. This might also explain the incremental benefit of CRT-D over CRT-P in ischaemic cardiomyopathy patients. CRT-D is providing incremental benefit by reducing the risk of SCD and all-cause mortality in patients with ischaemic cardiomyopathy. The European CRT survey evaluated baseline clinical characteristics[5] and outcome[15] of 2438 CRT patients with or without an ICD from 13 European countries between November 2008 and June 2009. In this survey, patients implanted with a CRT-D were younger, they were more often male, and they more often had ischaemic aetiology of cardiomyopathy and less often AF. The outcome data from the European CRT survey suggested that all CRT-D patients had better survival compared with CRT-P patients during short-term, 1-year (9–15 months) follow-up.[15] Differences in the clinical characteristics such as a higher percentage of ischaemic patients and an older age in the European CRT registry may explain the different findings between these studies. However, this needs further evaluation because currently older patients are more likely to be implanted with a CRT-P device. Another important observation is that there was a similar improvement in LV function in patients implanted with a CRT-D vs. a CRT-P.[60] This further underlines that since the improvement in cardiac function is the same in CRT-D and CRT-P, therefore the all-cause mortality in ischaemic and non-ischaemic patients may be equally related to heart failure-related death, but there is a difference in SCD-related death. However, patients with non-ischaemic cardiomyopathy had greater improvement in

LVEF than those with ischaemic cardiomyopathy. This phenomenon is well known and might be explained by the larger amount of scar tissue and lower contractile reserve in ischaemic patients that is not reversible by CRT.[61] Along this line, we might speculate that CRT-D may provide an incremental mortality benefit over CRT-P in those who are at a higher risk for SCD at implantation (e.g. ischaemic aetiology), or in those who have less pronounced LV reverse remodelling from CRT.

It is important to note that patients implanted with a CRT-P alone did not have an increased risk of mortality compared with those with a CRT-D. The mortality risk was equal to that of those with an implanted CRT-D, with HRs and *P*-value close to 1, indicating a neutral effect.

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Why do not patients respond to CRT?

Up to 30-50% of patients do not benefit significantly from this therapy [62]. Non-response may be due to underlying cardiomyopathy, type of ventricular conduction delay (LBBB *vs* non-LBBB), suboptimal medical therapy, ineffective biventricular pacing in atrial fibrillation, sub-optimal position of LV lead or device programming [63-66]. Duration of QRS interval ≥120 ms was the inclusion criterion used in most RCTs. Subgroup analysis, in a recent meta-analysis evaluating the impact of QRS duration on the efficacy of CRT, has shown that, in NYHA class III–IV HF patients, CRT significantly reduced all-cause mortality or hospitalization in patients with QRS duration ≥150 ms (data extracted from COMPANION and CARE-HF).[35] The magnitude of effect and certainty of benefit declined with shorter QRS duration. Furthermore, most patients in the RCTs had LBBB morphology, which was associated with a more pronounced benefit, compared with non-LBBB patients.[63] The relationship between QRS duration and morphology requires further exploration.

Sub-group analyses based on QRS morphology in the MADIT-CRT, RAFTand REVERSE trials,[33,47,50,67] and a meta-analysis of COMPANION, CARE-HF, MADIT-CRT and

RAFT,[36] suggested that patients with complete LBBB showed a greater benefit on the composite of morbidity/mortality from CRT, compared with patients with non-specific IVCD or RBBB. Whether this is also true when applied to the effect on mortality is uncertain. Also, patients with LBBB had longer QRS duration,and therefore analyses by morphology may be confounded by QRS duration. In particular, the MADIT-CRT trial showed that, in patients with LBBB, CRT-D reduced by 53% the risk of death or HF hospitalization, compared with ICD alone, whereas non-LBBB patients did not derive clinical benefit from CRT therapy (statistically not significant 24% increased risk).[33] With the exception of NYHA functional class I, all the pre-specified subgroups based on age, QRS duration ≥150 ms, LV volumes and LVEF showed consistent results that indicated a clinical benefit of CRT-D compared with ICD-only therapy in all subgroups of LBBB patients. In the non-LBBB patients, there was no evidence of clinical benefit from CRT-D, regardless of the subgroup evaluated. Similar results were observed in the RAFT and REVERSE trials.[50,67] Based on this evidence, current class I recommendations were restricted to patients with complete LBBB.

Aim of the study

Recently Strauss et al. [64-66,68-71] proposed new stricter criteria to define a “true-LBBB”, with the purpose of identifying more precisely patients responder to CRT.

Aim of the present study was to assess the rate of echocardiographic and clinical response to CRT in patients with LBBB according to AHA (traditional LBBB) and to Strauss’ criteria (strict LBBB).

METHODS

Study Population

This study is a sub-analysis of the CRT MORE study, an observational study aimed at identifying predictors of response to CRT, whose design has been published previously

[72]. The analysis focused on a group of consecutive patients who underwent CRT implantation according to 2010 ESC guidelines [73]. Patients with no-LBBB QRS morphology, atrial fibrillation, right bundle branch block and right ventricular pacing were excluded. Baseline clinical characteristics and 12-lead ECG were collected. Patients were classified into two groups: traditional LBBB and strict LBBB, as previously described [74]. The study was approved by the institutional review board, and all patients gave their written informed consent.

12-lead ECG

A standard ECG was performed in all subjects in the supine position during quiet respiration, at a paper speed of 25 mm/s and 50 mm/s and at a standard gain of 1 mV/cm. ECG parameters were independently analyzed and measured by 2 observers (F.M., A.B.): in case of disagreement a third observer (E.B.) was consulted. *Traditional LBBB* was defined according to the guidelines of American Heart Association (AHA)/American College of Cardiology Foundation (ACCF)/Heart Rhythm Society (HRS) published in 2009 [63]: 1) QRSd ≥120 msec; 2) delayed intrinsecoid deflection in leads I, V5, V6 ≥50 msec, 3) slurred R-waves in I, aVL, V5 and V6, 4) rS or QS waves in V1 through V2, 5) ST-T wave vectors opposite the main QRS vector, 6) absent Q in V5-V6. *Strict LBBB* was defined as QRSd ≥140 msec (men), QRSd ≥130 msec (women), QS or rS in V1-V2, mid-QRS notching or slurring in ≥ 2 contiguous leads (V1, V2, V5, V6, I and aVL) according to Strauss [64] (**Figure 4)**.

Echo

The echocardiographic evaluation included the assessment of left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), and LVEF assessed by Simpson's equation with the apical 4-chamber view and evaluation of the severity of mitral

regurgitation with color Doppler in the apical 4-chamber view.

Implantation procedure

In all patients enrolled in the Registry, devices and pacing leads were implanted by means of standard techniques and all devices were programmed in accordance with the clinical practice of each center. Transvenous LV pacing was obtained in all patients by positioning the lead in a coronary sinus branch. Coronary sinus branch selection and final LV lead positioning were left to the discretion of the implanting physician. The right appendage and RV apex or septum were suggested sites for atrial and RV stimulation.

Follow-up

All patients were routinely seen every 6 months up to 2 years after device implantation. The minimum follow-up duration was of 12 months. The following data were collected at the baseline and at scheduled visits: patient's history, medication use, physical examination results, ECG, device interrogation data and transthoracic echocardiographic measures.

End points

The primary end-points of the study were: 1) echocardiographic response to CRT, defined as a relative decrease of at least 15% in LVESV observed at 12-month follow-up for surviving patients, otherwise the last observation was carried forward [72]; 2) clinical response, defined as "improved" clinical composite score at 12-month follow-up [72]. In detail, on 12-month follow-up evaluation, patients were classified according to a score which assigns subjects to 1 of 3 response groups – improved, worsened, or unchanged. Patients were judged to have worsened if they died or were hospitalized because of worsening HF (at any time during the 12 months), or displayed worsening in New York

Heart Association (NYHA) functional class at their 12-month visit. Patients were judged to have improved if they had not worsened, and had displayed improvement in NYHA functional class at 12 months. Patients who had neither worsened nor improved were classified as unchanged [75].

Secondary end point was the cumulative survival from death or cardiovascular hospitalization.

Statistical analysis

Results are summarized as mean (±SD) or median (25%, 75% quartiles) for continuous variables, and as n (%) for categorical variables. Categorical differences between groups were evaluated by the $\chi 2$-test or the Fisher's exact test, as appropriate. Continuous variables were compared with the Student's t-test or Mann–Whitney test, as appropriate. Univariate and multivariate logistic regression analysis were performed to identify variables associated with the echocardiographic response to CRT. All variables associated with a statistical significance such as $P<0.1$ were considered for multivariate analysis. The cumulative probability of death or cardiovascular hospitalization was displayed by the method of Kaplan-Meier and using the log-rank test to compare cumulative events. A value of $P<0.05$ was considered significant. Statistics were analyzed with SPSS version 17 (SPSS Inc. Chicago, IL, USA).

RESULTS

A total of 335 patients met inclusion criteria for the analysis and had complete follow-up data for the assessment of the echocardiographic and clinical outcome. Patients were classified according to QRS morphology in 2 groups: traditional LBBB (204 patients, 61%) and strict LBBB (131 patients, 39%). Baseline clinical characteristics and echocardiographic findings of the overall population are summarized in Table 1. Baseline QRS duration resulted significantly larger in strict LBBB patients (166±20 msec vs 152±25

msec, p < <0.001). Mid-QRS notching in ≥ 2 leads was found in 51/204 (25%) traditional LBBB patients and in 122/131 (93%) strict LBBB patients (p<0.0001). Mid-QRS notching in ≥1 lead was present in 101/204 (49%) traditional LBBB patients and in 127/131 (97%) strict LBBB patients (p<0.0001). Mid-QRS notching was more frequently present in the following leads : 126 in V5 (38%), 124 in V6 (37%), 110 in D1 (34%), 58 in aVL (17%), 23 in V2 (7%), and 20 in V1 (6%).

Follow-up.

The length of follow-up was 365±83 days. Of the 335 patients included in analysis, 164 (49%) displayed an improvement in their HF clinical composite response at 12 months, 51 (15%) were classified as worsened and the remaining 120 (36%) as unchanged. At 12-month echocardiographic evaluation, 205 patients (61%) showed a decrease in LVESV ≥15% and were classified as responders. During the study period, 21 patients died and 28 were hospitalized for cardiovascular reasons. The combined end-point of death or cardiovascular hospitalization was reached by 46 (14%) patients.

Predictive value of QRS morphology.

The clinical composite response and the echocardiographic response were comparable at 12-month visit in the 2 groups (Table 2 and 3). The survival curves for death or cardiovascular hospitalization were calculated and no significant differences emerged between groups (log-rank test, p=0.827) (**Figure 5**).

Univariate and multivariate analysis of factors associated with echocardiographic response are listed in Table 4. At multivariate analysis history of atrial fibrillation (OR 0.424; 95% CI 0.216 to 0.833, p=0.001), larger end systolic left ventricular volume (OR 1.007; 95% CI 1.002 to 1.012, p=0.012) and presence of mid-QRS notching in at least 1 lead (OR 1.959; 95 % CI 1.039 to 3.695, p=0.038) were independently associated with the echocardiographic response.

DISCUSSION

Main finding. Recently proposed stricter criteria for LBBB diagnosis did not improve the identification of CRT responders. Among ECG variables, only the presence of mid-QRS notching in at least 1 lead was associated with the echocardiographic response.

Definition of LBBB: the "clinical problem"

Since LBBB morphology seems highly predictive of a positive CRT response, careful analysis of the baseline ECG is of great value to improve the selection of patients. However, identifying complete LBBB on the 12-lead ECG is not as straightforward as one might presume. In fact, definition of LBBB differs between current guidelines [31,32] and among clinical trials.[19,34,51] Recently, Strauss et al. suggested to include mid-QRS notch/slurring in ≥ 2 contiguous leads (V1, V2, V5, V6, I and aVL), which seems necessary to distinguish true complete LBBB from a combination of LV hypertrophy, LV dilatation and incomplete LBBB, regarded as LBBB using conventional criteria.[64]

These stricter criteria, if adopted, reduce the number of patients candidate to CRT. Among 158 patients diagnosed with LBBB according to the automated Glasgow criteria, the manual application of Strauss criteria confirmed the diagnosis of LBBB in 87% of the patients.[76] Our findings, that is a prevalence of strict LBBB in 39% of our population, are closer to the experience of Mascioli et al. [71]: among 111 patients with LVEF ≤ 35% and LBBB morphology who received a CRT device, only 55% presented with a "true" LBBB morphology. The choice to implant only this very selected population could exclude a significant number of potential responders to CRT.

Predictive value of QRS morphology

Published data showing that better response to CRT is associated with a "true" LBBB, derived from small studies. [70,71]. Mascioli et al.compared echocardiograpich and clinical outcome 816 ± 517 days after CRT implant of 111 patients with true LBBB (61 patients) and "false" LBBB (50 patients), according to the presence or not of the notch in ≥ 2 leads

among I, aVL, V1, V2, V5, V6. The “false” LBBB and a low dose of bisoprolol at the last follow-up correlated with a bad prognosis (death or hospitalization for heart failure), while only the “true” LBBB correlated with an increase ≥ 10% of left ventricular ejection fraction.[71] Tian et al. found that left ventricular ejection fraction increased significantly after CRT only in 22 patients with “true” LBBB, but not in 17 with “not true” LBBB, and in 19 patients with non-specific intraventricular delay.[70]

Our findings, obtained from a large cohort of patients enrolled in 31 different Centers, did not confirm previous results. CRT performed well in term of clinical composite response and echocardiographic response at 12-month both in patients with strict LBBB and in patients with traditional LBBB. At the multivariate analysis, along with sinus rhythm and a large end systolic left ventricular volume at enrollment, the presence of mid-QRS notching in at least 1 lead predicted a favorable outcome of CRT. In the vast majority of our patients, mid-QRS notching was recorded in the leads which explored the lateral wall of the left ventricle (I, aVL, V5 and V6). The presence of mid-QRS notching in these leads might be sufficient to identify patients with a delayed conduction along the left lateral ventricular wall who could benefit from CRT.

Conclusions

The presence of mid-QRS notching in at least 1 lead identifies patients with an echocardiographic response to CRT.

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TABLES

Table 1. Demographic data, baseline clinical parameters and pharmacological treatment.

Parameter	Traditional LBBB (n=204)	Strict LBBB (n=131)	*p*
Male gender, n (%)	153 (75)	88 (67)	0.120
Age, years	69±10	70±9	0.364
Body Mass Index	26±6	26±7	0.677
Ischemic etiology, n (%)	86 (42)	56 (43)	0.915
History of atrial fibrillation, n (%)	53 (26)	33 (25)	0.872
QRS duration, ms	152±25	166±20	<0.001
PR duration, ms	189±50	187±44	0.732
NYHA class - Class II, n (%) - Class III/IV, n (%)	 75 (37) 129 (63)	 48 (37) 83 (63)	0.982
Diabetes, n (%)	62 (30)	43 (33)	0.640
COPD, n (%)	38 (19)	29 (22)	0.433
Chronic kidney disease, n (%)	49 (24)	39 (30)	0.243
Hypertension, n (%)	119 (58)	82 (63)	0.437
LV ejection fraction, %	28±6	29±6	0.297
LVEDV, ml	195±87	198±71	0.813
LVESV, ml	143±74	143±58	0.982
Moderate to severe mitral regurgitation, n (%)	170 (83)	98 (75)	0.057
CRT-D device, n (%)	184 (90)	114 (87)	0.366
β-Blocker use, n (%)	163 (80)	109 (83)	0.450
ACE-inhibitor use, n (%)	111 (54)	72 (55)	0.921
Diuretic use, n (%)	171 (84)	110 (84)	0.972
Class III antiarrhythmic use, n (%)	44 (22)	24 (18)	0.471
Ivabradine, n (%)	18 (9)	7 (5)	0.237
LV lead position: Basal	42 (21)	30 (23)	0.615
LV lead position: Mid	143 (70)	88 (67)	0.573
LV lead position: Apical	18 (9)	13 (40)	0.735
LV lead position: Anterior	10 (5)	3 (2)	0.227
LV lead position: Lateral	192 (94)	125 (96)	0.606
LV lead position: Posterior	2 (1)	3 (2)	0.335

NYHA = New York Heart Association; COPD = Chronic obstructive pulmonary disease; LV = Left ventricular; LVEDV = Left ventricular end-diastolic volume; LVESV = Left ventricular end-systolic volume; CRT-D = Cardiac resynchronization therapy defibrillator; ACE = Angiotensin-converting-enzyme.

Table 2. Classification of study population according to HF clinical composite response at 12-month visit.

	Traditional LBBB (n=204)	**Strauss LBBB (n=131)**	***p***
Improved, n (%)	93 (46)	71 (54)	0.124
Unchanged, n (%)	78 (38)	42 (32)	0.250
Worsened, n (%)	33 (16)	18 (14)	0.545

Table 3. Classification of study population according to echocardiographic response at 12-month visit.

	Traditional LBBB (n=204)	**Strauss LBBB (n=131)**	***p***
Responder, n (%)	120 (59)	85 (65)	0.267
Non responder, n (%)	84 (41)	46 (35)	

Table 4. Univariate and multivariate analyses of factors associated with the echocardiographic end-point.

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*P*
Age	0.985	0.956 to 1.015	0.319	-	-	-
Male gender	**0.569**	**0.297 to 1.088**	**0.082**	0.604	0.296 to 1.221	0.160
Ischemic aetiology	0.673	0.384 to 1.180	0.167	-	-	-
History of AF	**0.327**	**0.172 to 0.621**	**0.001**	**0.424**	**0.216 to 0.833**	**0.013**
QRS duration	1.003	0.992 to 1.015	0.542	-	-	-
PR duration	1.000	0.993 to 1.007	0.940	-	-	-
NYHA Class (II)	1.403	0.792 to 2.484	0.244	-	-	-
Hypertension	0.856	0.490 to 1.496	0.585	-	-	-
Diabetes	0.842	0.463 to 1.534	0.575	-	-	-
COPD	0.902	0.445 to 1.826	0.774	-	-	-
Chronic kidney disease	0.678	0.361 to 1.273	0.228	-	-	-
Echocardiographic findings				-	-	-
LVEF	0.975	0.935 to 1.018	0.247	-	-	-
LVEDV	**1.004**	**1.000 to 1.008**	**0.024**	-	-	-
LVESV	**1.006**	**1.001 to 1.011**	**0.011**	**1.007**	**1.002 to 1.012**	**0.012**
LVEDD	0.991	0.960 to 1.023	0.573	-	-	-
LVESD	0.999	0.972 to 1.027	0.951	-	-	-

Severe MR	0.678	0.390 to 1.177	0.167	-	-	-
Pharmacologic treatment				-	-	-
ACE/ARB	**1.715**	**0.910 to 3.231**	**0.096**	1.332	0.662 to 2.682	0.422
Diuretics	0.943	0.455 to 1.954	0.874	-	-	-
Statin	0.889	0.510 to 1.549	0.677	-	-	-
Beta-blockers	**1.967**	**0.923 to 4.187**	**0.079**	1.726	0.747 to 3.986	0.201
Ivabradyn	1.301	0.429 to 3.947	0.638	-	-	-
Antiarrhythmics	1.068	0.249 to 4.588	0.930	-	-	-
Notch _1 lead (at least)	**2.104**	**1.168 to 3.790**	**0.013**	**1.959**	**1.039 to 3.695**	**0.038**
Notch_2 lead (at least)	1.599	0.925 to 2.767	0.092	-	-	-
Notch_2 contiguous lead	1.391	0.802 to 2.415	0.239	-	-	-
Apical lead positioning	1.417	0.552 to 3.632	0.462	-	-	-
Lateral lead positioning	1.046	0.359 to 3.053	0.934	-	-	-

AF = atrial fibrillation; COPD = Chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; LVEDV = left ventricular end diastolic volume; LVESV= left ventricular end sistolic volume; LVEDD = left ventricular end diastolic diameter; LVESD = left ventricular end sistolic diameter; MR = mitral regurgitation.

FIGURES

Figure 1: Inclusion criteria, design, endpoints, and main findings of the randomized clinical trials evaluating CRT in HF patients in sinus rhythm.[32]

Trial (ref)	No.	Design	NYHA	LVEF	QRS	Primary endpoints	Secondary endpoints	Main Findings
MUSTIC-SR[52]	58	Single-blinded, crossover, randomized CRT vs. OMT, 6 months	III	<35%	≥150	6MWD	NYHA class, QoL, peak VO_2 LV volumes, MR hospitalizations, mortality	CRT-P improved 6MWD, NYHA class, QoL, peak VO_2, reduced LV volumes and MR and reduced hospitalizations
PATH-CHF[51]	41	Single-blinded, crossover, randomized RV vs. LV vs. BiV, 12 months	III–IV	NA	≥150	Peak VO_2, 6MWD	NYHA class, QoL hospitalizations	CRT-P improved NYHA class, QoL and 6MWD and reduced hospitalizations
MIRACLE[49]	453	Double-blinded, randomized CRT vs. OMT, 6 months	III–IV	≤35%	≥130	NYHA class, 6MWD , QoL	Peak VO_2 LVEDD, LVEF, MR clinical composite response	CRT-P improved NYHA class, QoL and 6MWD and reduced LVEDD, MR and increased LVEF
MIRACLE-ICD[54]	369	Double-blinded, randomized CRT-D vs. ICD, 6 months	III–IV	≤35%	≥130	NYHA class, 6MWD , QoL	Peak VO_2 LVEDD, LVEF, MR clinical composite response	CRT-D improved NYHA class, QoL, peak VO_2
CONTAK-CD[53]	490	Double-blinded randomized CRT-D vs. ICD, 6 months	II–III–IV	≤35%	≥120	NYHA class, 6MWD , QoL	LV volume, LVEF composite of mortality, VT/VF, hospitalizations	CRT-D improved 6MWD, NYHA class, QoL, reduced LV volume and increased LVEF
MIRACLE-ICD II[60]	186	Double-blinded, randomized CRT-D vs. ICD, 6 months	II	≤35%	≥130	Peak VO_2	VE/VCO_2, NYHA, QoL, 6MWD, LV volumes and EF, composite clinical endpoint	CRT-D improved NYHA, VE/CO_2 and reduced LV volumes and improved LVEF
COMPANION[55]	1520	Double-blinded randomized OMT vs. CRT-P / or vs. CRT-D, 15 months	III–IV	≤35%	≥120	All-cause mortality or hospitalization	All-cause mortality, cardiac mortality	CRT-P and CRT-D reduced all-cause mortality or hospitalization
CARE-HF[56]	813	Double-blinded randomized OMT vs. CRT-P 29.4 months	III–IV	≤35%	≥120	All-cause mortality or hospitalization	All-cause mortality, NYHA class, QoL	CRT-P reduced all-cause mortality and hospitalization and improved NYHA class and QoL
REVERSE[61]	610	Double-blinded, randomized CRT-ON vs. CRT-OFF, 12 months	I–II	≤40%	≥120	% worsened by clinical composite endpoint	LVESV index, heart failure hospitalizations and all-cause mortality	CRT-P/CRT-D did not change the primary endpoint and did not reduce all-cause mortality but reduced LVESV index and heart failure hospitalizations.
MADIT-CRT[50]	1820	Single-blinded, randomized CRT-D vs. ICD, 12 months	I–II	≤30%	≥130	All-cause mortality or heart failure hospitalizations	All-cause mortality and LVESV	CRT-D reduced the endpoint heart failure hospitalizations or all-cause mortality and LVESV. CRT-D did not reduced all-cause mortality
RAFT[62]	1798	Double-blinded, randomized CRT-D vs. ICD 40 months	II–III	≤30%	≥120	All-cause mortality or heart failure hospitalizations	All-cause mortality and cardiovascular death	CRT-D reduced the endpoint all-cause mortality or heart failure hospitalizations. In NYHA III, CRT-D only reduced significantly all-cause mortality

Figure 2: Indications to CRT in patients in sinus rhythm.[32]

Recommendations	Class [a]	Level [b]
1) LBBB with QRS duration >150 ms. CRT is recommended in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. [d]	I	A
2) LBBB with QRS duration 120–150 ms. CRT is recommended in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. [d]	I	B
3) Non-LBBB with QRS duration >150 ms. CRT should be considered in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. [d]	IIa	B
4) Non-LBBB with QRS duration 120–150 ms. CRT may be considered in chronic HF patients and LVEF ≤35% who remain in NYHA functional class II, III and ambulatory IV despite adequate medical treatment. [d]	IIb	B
5) CRT in patients with chronic HF with QRS duration <120 ms is not recommended.	III	B

Figure 3: clinical factors influencing the likelihood to respond to CRT.[32]

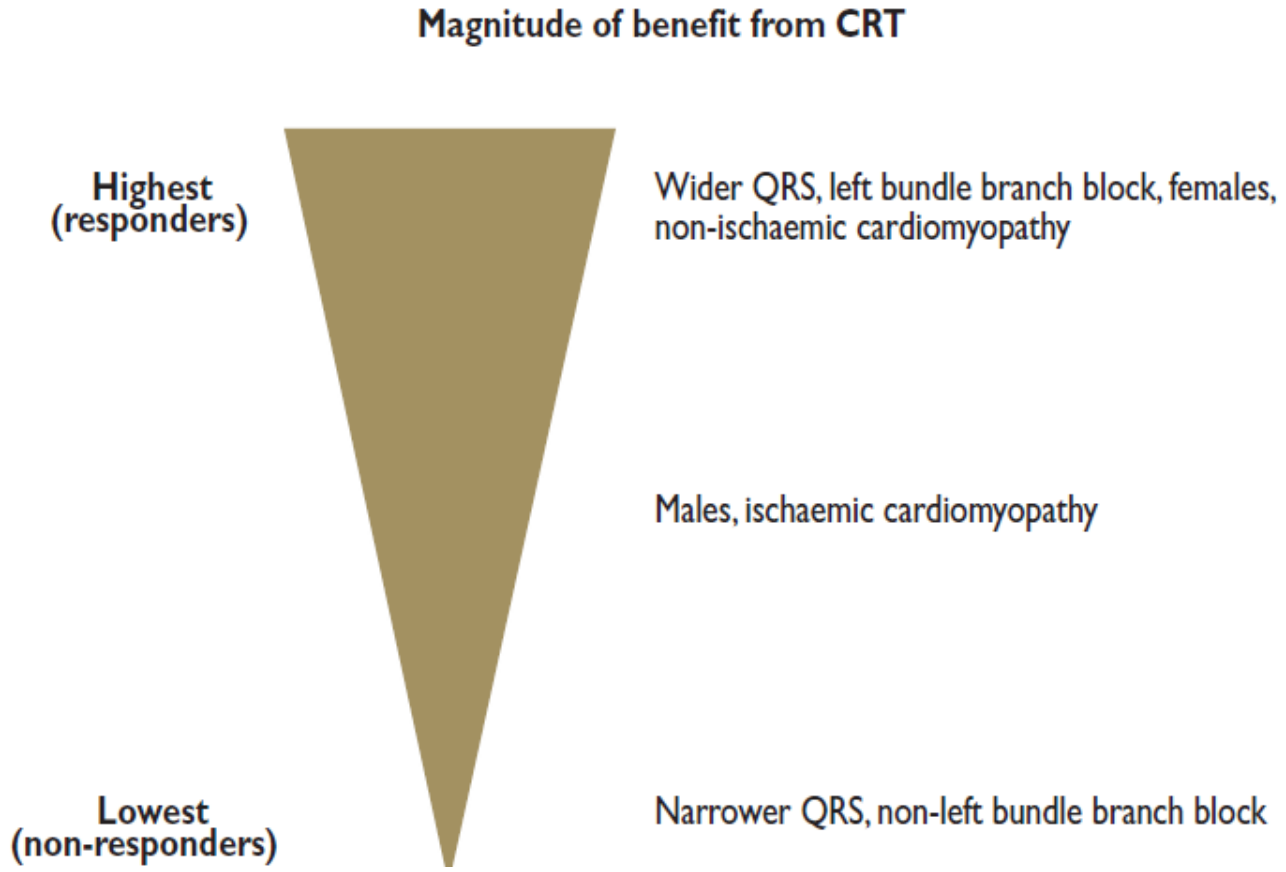


Figure 4: Typical ECG features of Traditional LBBB according to AHA definition (a) and Strict LBBB according to Strauss (b). Of note, the presence of mid-QRS notching in lateral leads (circles) in LBBB according to Strauss, lacking in traditional LBBB.

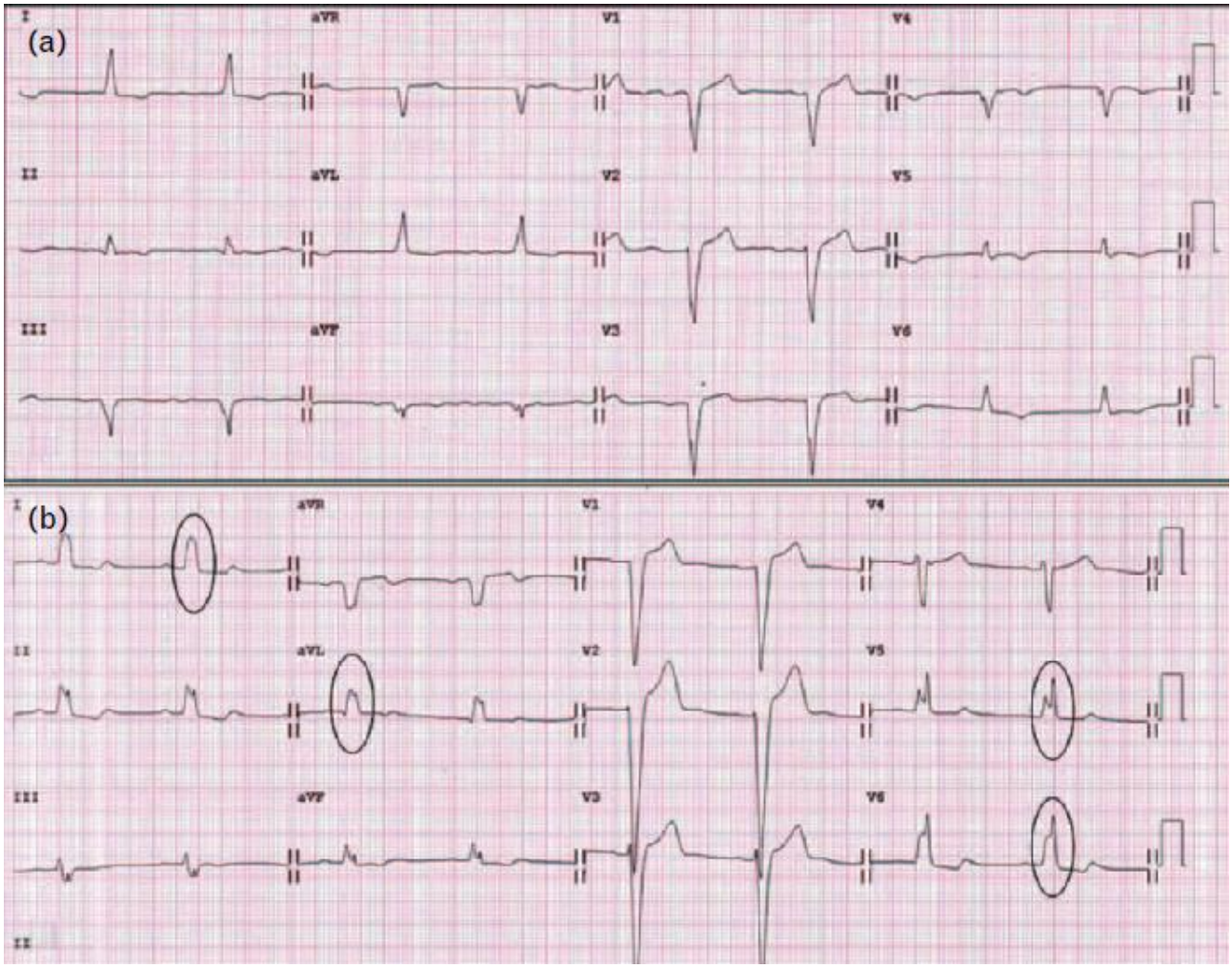
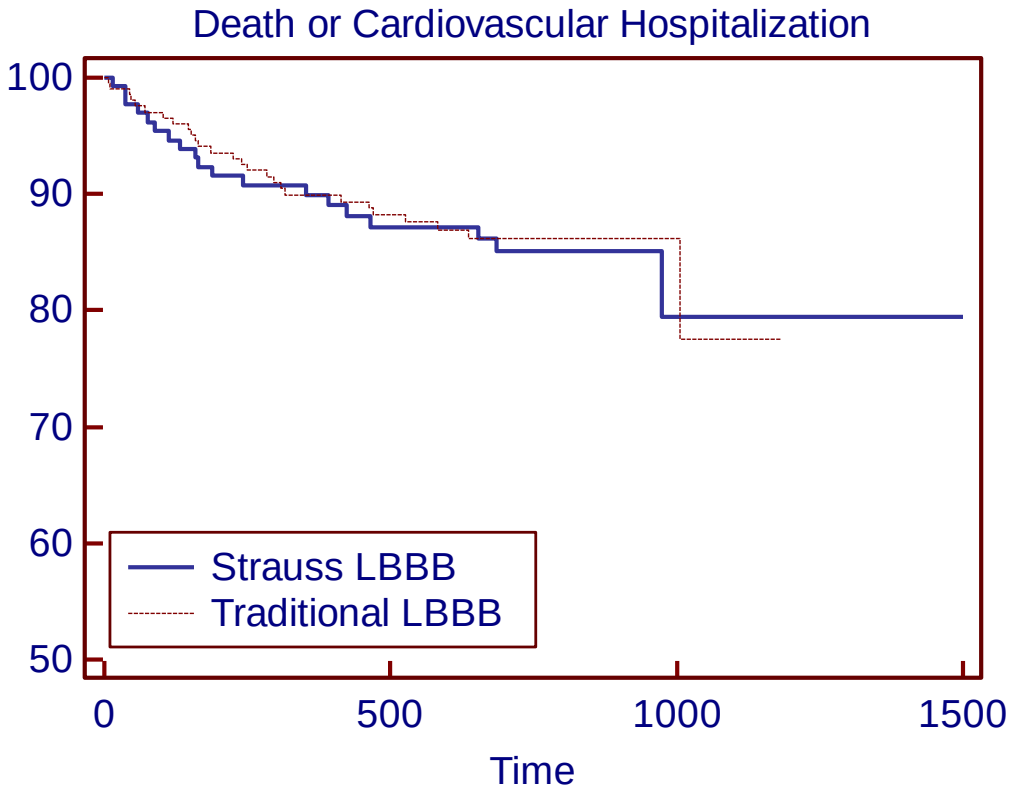


Figure 5: survival curves for death or cardiovascular hospitalization.



Overall long-rank test: *p=0. 8273*

ATTIVITA' SVOLTA DAL DOTTORANDO

PUBBLICAZIONI

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PARTECIPAZIONE A CONGRESSI

a) XV International Symposium on Progress in Clinical Pacing, Rome December 4-7 2013

b) Anatomia per l'Aritmologo: fibrillazione atriale, Padova 2 febbraio 2013

c) 10° Congresso Nazionale AIAC, 14-16 marzo 2013

d) La prevenzione dell'ictus nei pazienti con FA: nuove opzioni terapeutiche, Padova 18 aprile 2013

e) Forum Triveneto di Aritmologia, Padova 3 maggio 2013

f) Heart Rhythm Society 2013, Denver May 8-11 2013

g) Nuovi anticoagulanti orali: dagli eccellenti risultati degli studi clinici alla progressive introduzione nel mondo reale, Padova 24 maggio 2013

h) 44° Congresso Nazionale di Cardiologia ANMCO, Firenze 30 maggio-1 giugno 2013

i) XIV incontro scientifico progressi in Aritmologia Clinica, Capo Vaticano, 6-8 giugno 2013

j) Luci in Aritmologia, Pisa 14 giugno 2013

k) ESC Congress 2013, Amsterdam August 31 2013

l) XVI Congresso nazionale SICSPORT, Padova 12-14 settembre 2013

m) Innovazione e progresso nella fibrillazione atriale, Milano 19 ottobre 2013

n) 21^ Brixen Conference sulla Prevenzione Cardiovascolare, Bressanone 24-26 ottobre 2013

o) Venice Arrhythmias 2013, Venice October 27-29 2013

p) Autumn School, 26 novembre 2013

q) La rete delle Neurocardiologie italiane per la prevenzione secondaria dell'ictus cardioembolico, Roma 31 gennaio 2014

r) Anatomia per l'Aritmologo, Padova 1 febbraio 2014

s) Novità in terapia intensiva cardiologica: competenze del cardiologo intensivista nelle moderne UTIC, Padova 14 febbraio 2014

t) Ipertensione arteriosa. Cause, patologie d'organo e terapia, Padova 21-22 febbraio 2014

u) Universo trombosi. Rompere il legame tra fibrillazione atriale & ictus. Consigli d'autore, Mestre 25 febbraio 2014.

v) 11° Congresso Nazionale AIAC, 13-15 marzo 2014

w) Update in arrythmogenic cardiomyopathy and sudden cardiac death in the young: novel technologies, genetics, and pathology, Padova, March 20-21 2014

x) Congresso regionale ANMCO Veneto, Rovigo 3 maggio 2014

y) Il profilo del nuovo presente, Capo Taormina 11-13 maggio 2014

z) Venice Interventional Cardiology 2014, Venice May 15-17 2014

aa) Xformance. Percorso di training formativo e analisi dei casi clinici sui Nuovi Anticoagulanti Orali, Mestre 16-17 maggio 2014

bb) L’atleta master e lo sport: quando il cuore non regge la passione, Treviso 23 maggio 2014

cc) 45° Congresso Nazionale di Cardiologia ANMCO, Firenze 29-31 maggio 2014

dd) XV incontro scientifico progressi in Aritmologia Clinica, Capo Vaticano, 5-7 giugno 2014

ee) Luci e ombre in Aritmologia, Pisa 26-27 giugno 2014

ff) ESC Congress 2014, Barcellona August 30 to September 3 2014

gg)Cesena Aritmologia Clinica, Cesena 12 settembre 2014

hh)Summer School, Padova 29 settembre – 3 ottobre 2014

ii) La fibrillazione atriale come non l’avete mai conosciuta, Padova 17 ottobre 2014

jj) 22^ Brixen Conference sulla Prevenzione Cardiovascolare, Bressanone 23-25 ottobre 2014

kk) Le ragioni del cuore…e del cervello, Ospedaletto di Pescantina (VR) 7-8 novembre 2014

ll) Atrial Fibrillation Ablation 2014, Ivrea 12-13 novembre 2014

mm) La fibrillazione atriale nel 2015: vecchie terapie e nuove prospettive, Negrar (VR) 17 gennaio 2015

nn)Stroke criptogenico: cuore di tenebra, Padova 23 gennaio 2015

oo)La terapia anticoagulante nella fibrillazione atriale: implicazioni nefrologiche, Padova 31 gennaio 2015

pp) L'anatomia per l'aritmologo: aritmie dagli efflussi ventricolari, Padova 31 gennaio 2015

qq) Dabigatran. La sicurezza di due anni di pratica clinica in Italia, Siena 6-8 febbraio 2015

rr) Focus sullo scompenso cardiaco, Porto Viro (RO) 28 febbraio 2015

ss) 12° Congresso nazionale AIAC, Bologna 12-14 marzo 2015

tt) State of heart, Milano 18 marzo 2015

uu) Attualità in Cardiologia dello Sport, Bardolino (VR) 28 marzo 2015

vv) XXXIV corso di aggiornamento in Cardiologia Pediatrica, Padova 1-2 aprile 2015

ww) Consenso di Neurocardiologia sui NAO, Mestre (VE), 9-10 aprile 2015

xx) State of the art in electrical management of cardiac diseases, Bordeaux (FRA) 14-15 aprile 2015

yy) Terapia della resincronizzazione cardiac: "stato dell'arte", Mestre (VE) 18 aprile 2015

zz) Novità in terapia intensiva cardiologica: le sfide cardiologiche del nuovo millennio, Padova 8 maggio 2015

aaa) Congresso regionale ANMCO: Qui noi facciamo così, Padova 9 maggio 2015

bbb) L'ictus cerebrale oltre la trombolisi, Portogruaro 22 maggio 2015

ccc) Forum triveneto di Elettrofisiologia: Nervi e Aritmie, Padova 22 maggio 2015

ddd) Spring School, Bressanone 29-30 maggio 2015

eee) 46° Congresso nazionale ANMCO, Milano 4-6 giugno 2015

fff) Luci in Arimologia 2015, Pisa 10-11 settembre 2015

ggg) Fibrillazione atriale e terapia anticoagulante: come, quando e perché, Monastier (TV) 18-19 settembre 2015

FORMATO EUROPEO PER IL CURRICULUM VITAE

INFORMAZIONI PERSONALI

Nome	**BERTAGLIA EMANUELE**
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Nazionalità	ITALIANA
Data di nascita	11 GIUGNO 1966

ESPERIENZA LAVORATIVA

• Date	01 settembre 2012 ad oggi
• Nome e indirizzo del datore di lavoro	Regione Veneto Azienda Ospedaliera di Padova
• Tipo di azienda o settore	Azienda Ospedaliera
• Tipo di impiego	Dirigente Medico di I livello
• Principali mansioni e responsabilità	Responsabile UOS di Aritmologia Interventistica dal 01 gennaio 2013

• Date	06 agosto 1997-31 agosto 2012
• Nome e indirizzo del datore di lavoro	ULSS 13 MIRANO – REGIONE VENETO
• Tipo di azienda o settore	Azienda ULSS
• Tipo di impiego	Dirigente Medico I livello
• Principali mansioni e responsabilità	Responsabile UOS Dipartimentale di Elettrofisiologia, Elettrostimolazione e Scompenso Cardiaco dal 01 aprile 2009 al 31 agosto 2012 Direttore f.f. della UOC di Cardiologia dal 01 giugno 2007 al 30 aprile 2008 Responsabile UOS di Elettrofisiologia, Elettrostimolazione dal 25 maggio 2007 al 31 marzo 2009

• Date	Dal 3 gennaio 1995 al 9 gennaio 1996
• Nome e indirizzo del datore di lavoro	OSPEDALE MILITARE DI PADOVA
• Tipo di azienda o settore	Ospedale militare tipo A
• Tipo di impiego	Assistente
• Principali mansioni e responsabilità	Aiuto Reparto di Anestesia e Rianimazione

ISTRUZIONE E FORMAZIONE

• Date	1991-1997
• Nome e tipo di istituto di istruzione o formazione	Università degli Studi di Padova
• Principali materie / abilità professionali oggetto dello studio	
• Qualifica conseguita	Specializzazione in Cardiologia
• Date	1991
• Nome e tipo di istituto di istruzione o formazione	Università degli Studi di Padova
• Principali materie / abilità professionali oggetto dello studio	
• Qualifica conseguita	Abilitazione alla professione di Medico Chirurgo
• Date	1985-1991
• Nome e tipo di istituto di istruzione o formazione	Università degli Studi di Padova
• Principali materie / abilità professionali oggetto dello studio	
• Qualifica conseguita	Laurea in Medicina e Chirurgia

CAPACITÀ E COMPETENZE PERSONALI

PRIMA LINGUA **ITALIANO**

ALTRE LINGUE

INGLESE

• Capacità di lettura	Eccellente
• Capacità di scrittura	Eccellente
• Capacità di espressione orale	Buono

PRODUZIONE SCIENTIFICA

- **PER EXTENSO** **79**
  - Riviste con IF 54
  - Riviste senza IF 25
- CAPITOLI DI LIBRO E ATTI CONGRESSUALI 8
- LETTURE SU INVITO A RIUNIONI E CONGRESSI 88
  - Internazionali 20
  - Nazionali 58

CAPACITÀ E COMPETENZE ORGANIZZATIVE

- Dirigente medico di I livello di Cardiologia dal 6 agosto 1997, nel corso degli anni ha sviluppato, oltre a competenze generali nell'ambito della disciplina di Cardiologia, competenze specifiche nel campo dell'Aritmologia, in particolar modo dell'elettrofisiologia, dell'ablazione trans catetere delle aritmie, della cardiostimolazione, della gestione del paziente con scompenso cardiaco cronico.
- In qualita' di direttore f.f. dell'U.O.C. di Cardiologia del P.O. di Mirano nel corso del 2007 ha partecipato all'istituzione della rete cardiologica regionale veneta

per la gestione dell'infarto miocardico acuto, e ha gestito l'organizzazione di questa attivita' per le ULSS 13 e 14.

- in qualita' di responsabile dell'U.O.S. a valenza dipartimentale di elettrofisiologia, elettrostimolazione e scompenso cardiaco, ha gestito in prima persona l'ambulatorio per lo scompenso cardiaco del P.O. di Mirano dal 1 aprile 2009 al 31 agosto 2012, ponendo particolare attenzione all'organizzazione delle cure per il paziente affetto da scompenso cardiaco cronico, creando un sistema integrato con l'U.O.C. di Medicina e la rete dei medici di Medicina Generale. Ha favorito, tra i primi all'interno della regione veneto, l'introduzione di sistemi di telemedicina per la gestione domiciliare del paziente con aritmie e del paziente con scompenso cardiaco cronico, mediante la rilevazione a distanza di elettrocardiogramma, pressione arteriosa e peso corporeo. (vedi allegati 17, 82, 83, 94, 100) Ha validato l'efficacia della telemedicina nel paziente con scompenso cardiaco cronico partecipando alla Ricerca Finalizzata della Regione Veneto 2006 per la "Realizzazione di un modello di integrazione tra Ospedale e territorio con utilizzo di strumentazioni informatiche e reti telematiche per il monitoraggio a domicilio dello scompenso cardiaco; Cluster 7 del progetto Renewing Health".
- Dal 25 maggio 2007, come responsabile prima dell'U.O.S. di elettrofisiologia ed elettrostimolazione e poi dell'U.O.S. a valenza dipartimentale di elettrofisiologia, elettrostimolazione e scompenso cardiaco, ha introdotto all'interno del P.O. di Mirano l'utilizzo del controllo remoto dei dispositivi impiantabili, diventando un punto di riferimento nazionale su tale materia, come testimoniato dalle numerose partecipazioni a congressi in qualita' di relatore sull'argomento (vedi allegati 81, 85, 87, 89, 106).
- In qualita' di direttore f.f. dell'U.O.C. di Cardiologia del P.O. di Mirano, ha gestito dal 1 giugno 2007 al 30 aprile 2008 un reparto dotato di 44 posti letto, di cui 8 di utic, 32 di degenza ordinaria, e 4 di day-hospital:
    - Acquisendo esperienza nella gestione del personale;
    - Delegando i colleghi nella conduzione delle varie attivita' di reparto (emodinamica, elettrofisiologia, terapia intensiva cardiologica, imaging cardiovascolare);
    - Consentendone l'aggiornamento professionale costante;
    - Favorendo l'autonomia tecnico-professionale del personale infermieristico e tecnico;
    - Creando un buon clima lavorativo cercando di appianare i conflitti interni.
- In qualita' di Presidente del Consiglio Direttivo Veneto dell'Associazione Italiana di Aritmologia e Cardiostimolazione ha favorito la creazione di sistemi "hub & spoke" per la gestione delle urgenze aritmologiche (trattamento dello storm artimico ed estrazione di elettrocateteri impiantati infetti o malfunzionanti). (vedi allegato 84). A tal proposito, nel corso del 2014 e' stato chiamato dall'area sanita' e sociale della regione veneto a far parte del gruppo tecnico per la realizzazione del "modello assistenziale di rete cardiologica per la diagnosi e terapia nei confronti di pazienti affetti da aritmia e scompenso cardiaco" (vedi allegato 107).
- In qualita' di Presidente del Consiglio Direttivo Veneto dell'Associazione Italiana di Aritmologia e Cardiostimolazione ha partecipato alla realizzazione del documento di "Health Techonolgy Assessment AIAC sull'ablazione della fibrillazione atriale" (vedi allegato 64).

CAPACITÀ E COMPETENZE TECNICHE

.

- Ablazione trans catetere di fibrillazione atriale, aritmie reciprocanti SV e ventricolari come primo operatore: 1228
- Studio elettrofisiologico di aritmie sopraventricolari e ventricolari come primo operatore: 152
- Applicazione di pacemaker e/o defibrillatore impiantabile con o senza sistema

di resincronizzazione come primo operatore: 891
- Applicazione di ICD sottocutaneo come primo operatore: 2
- Sostituzione di pacemaker e/o defibrillatore impiantabile come primo operatore: 239
- Riposizionamento di elettrocateteri cronicamente impiantati per stimolazione e/o defibrillazione e/o revisione tasca come primo operatore: 29
- Estrazione di elettrocateteri cronicamente impiantati per stimolazione e/o defibrillazione come primo operatore: 36
- Controllo elettronico di pacemaker e/o defibrillatore impiantabile come primo operatore:1399

Accanto all'attività assistenziale, nel campo dell'Aritmologia e in particolare dell'Aritmologia Interventistica, ha condotto numerose ricerche cliniche su:

- Modificazioni cardiovascolari indotte dall'ipossia d'alta quota (vedi allegato 1)
- Basi morfologiche delle aritmie sopraventricolari e ventricolari (vedi allegato 2, 5, 9, 42, 55)
- Prevenzione della morte improvvisa (vedi allegato 54)
- Trattamento farmacologico della fibrillazione atriale (vedi allegato 7, 11, 20, 21)
- Effetti clinici della terapia di resincronizzazione cardiaca (vedi allegato 36, 38, 69, 70, 72, 78,)
- Ablazione della fibrillazione atriale (vedi allegati 12, 18, 26, 35, 37, 39, 41, 68, 73, 74, 75, 79, 91)
- Investigatore principale del registro multicentrico triveneto sull'ablazione del flutter atriale (vedi allegato 15, 16)
- Membro dello Steering Committee dello studio multicentrico nazionale "A prospective, randomised, controlled study on effect of catheter ablation for the cure of atrial fibrillation (Catheter Ablation for the Cure of Atrial Fibrillation Study)" (vedi allegato 21)
- Investigatore Principale dello studio multicentrico internazionale "A Clinical and Health-Economic Evaluation of Pulmonary Vein Encirculation Compared to Antiarrhythmic Drug Treatment in Patients with Persistent Atrial Fibrillation (Catheter Ablation for the Cure of Atrial Fibrillation – 2 Study)" (vedi allegato 27)
- Membro dello Steering Committee dello studio multicentrico nazionale EPASS (cardiostimolazione) (vedi allegato 42)
- Investigatore principale del registro multicentrico nazionale CARTOMERGE (ablazione della fibrillazione atriale) (vedi allegato 34)
- Membro dello Steering Committee dello studio multicentrico nazionale CRT_MORE (re sincronizzazione cardiaca) (vedi allegato 72)

Ha iniziato dal 2005 ad utilizzare il sofisticato sistema di integrazione delle immagini nel sistema di mappaggio elettroanatomico Carto-Merge, diventandone uno dei maggiori esperti a livello europeo (vedi allegati 32, 34).

Ha fatto parte della Task-force che ha redatto le Linee guida AIAC 2010 per la gestione e il trattamento della fibrillazione atriale (vedi allegati 63, 65)

In qualità di responsabile dell'U.O.S. di Aritmologia Interventistica dell'Azienda Ospedaliera di Padova ha favorito la realizzazione di interventi ibridi in collaborazione con i Cardiochirurghi per il trattamento della fibrillazione atriale, delle aritmie ventricolari maligne, e per l'estrazione degli elettrocateteri cronicamente impiantati (vedi allegati 71, 88).

SOGGIORNI PER STUDIO E ADDESTRAMENTO PROFESSIONALE ALL'ESTERO

Spedizione scientifica Ev-K2-CNR organizzata dall'Università di Padova in collaborazione con il CNR al campo base del monte Everest (Nepal), per studiare le modificazioni cardiovascolari indotte dall'ipossia d'alta quota. Set

Department of Cardiological Sciences,
St.George's Hospital Medical School, University of London
(Prof. A.J.Camm & Prof.W.J.McKenna) Nov
Laboratoire d'Electrophysiologie,
Hopital Cardiologique Haut-Leveque, Pessac, Bordeaux (France) Ma

ATTIVITA' DIDATTICA

Insegnamento di Semeiotica delle valvulopatie al 1° anno della Scuola di Specializzazione in Malattie dell'apparato cardiovascolare dell'Università degli Studi di Padova (vedi allegato 117)

ASSOCIAZIONI

- Presidente del Consiglio Direttivo Regionale Veneto della Associazione Italiana Cardiologia ed Elettrostimolazione dall'aprile 2010 a marzo 2014
- Segretario del Consiglio Direttivo Nazionale della Associazione Italiana Cardiologia ed Elettrostimolazione da marzo 2014

Autorizzo il trattamento dei miei dati personali ai sensi del D.lgs. 196 del 30 giugno 2003.

30 gennaio 2016 *Emanuele Bertaglia*