Cardiac resynchronization therapy improves ejection fraction and cardiac remodelling regardless of patients' age

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Aims	Cardiac resynchronization therapy (CRT) improves symptoms and reduces mortality in heart failure (HF) patients, but little data exist on the efficacy of CRT in the elderly. The aim of our study is to define CRT-related benefits in terms of left ventricular ejection fraction (LVEF) improvement in two subgroups of patients (<75 and ≥ 75 years old) and test possible differences between these two groups.
Methods and results	Single-centre prospective observational study including 65 patients with optimally treated, advanced HF and indication to CRT. All patients were investigated with clinical evaluation, Minnesota Living with Heart Failure Questionnaire (MLHFQ), 12-lead electrocardiogram, and full echocardiographical study before CRT implant and 3 and 12 months after. Left ventricular ejection fraction showed a time-related improvement in the whole population ($+10.6\%$ over 12 months) as well as in each subgroup. The magnitude of LVEF improvement was similar in elderly and non-elderly patients ($+13.6$ vs. $+7.9\%$; $P = $ ns). Left ventricular diameters, pulmonary artery systolic pressure, New York Heart Association class, MLHFQ score, and QRS width all showed a time-related improvement in the whole population as well as in each subgroup. End-diastolic left ventricular diameter remodelling and QRS width reduction were significantly more pronounced in the elderly, whereas other clinical and instrumental secondary endpoints showed a similar improvement between ≥ 75 and <75 years old patients. There was no significant difference regarding mortality between elderly and non-elderly patients.
Conclusion	Cardiac resynchronization therapy is as effective in improving LVEF in elderly as in non-elderly patients. Age alone should not be a determinant to restrict resynchronization therapy in HF patients.
Keywords	CRT • Echocardiography • Pacing • Congestive heart failure • Elderly

Introduction

Heart failure (HF) is the most important cause of morbidity, mortality, and hospitalization in the elderly.[1,2] Several randomized controlled trials have shown an improvement of outcome with cardiac resynchronization therapy (CRT) in appropriately selected patients with systolic HF and/or evidence of electrical dyssynchrony. Potential beneficial mechanisms include improved contractile function and reverse ventricular remodelling.[3–7]

Despite the relevant increase in the prevalence and incidence of chronic HF in older individuals,[8] the mean age of patients enrolled

in clinical trials of CRT is often <70 years.[3–7] In literature, there are few data about the effectiveness of CRT in older people. As a result, it is still not completely clear whether CRT benefits apply to older patients as well as younger patients. This is an important issue since HF has a dramatic impact on aged people and impairs their quality-of-life together with age-associated co-morbidities.

The aim of our study was to define CRT-related benefits in terms of left ventricular ejection fraction (LVEF) improvement in two subgroups of patients (<75 and ≥ 75 years old) and test whether elderly patients' echocardiographical recovery could be similar to the one expected in a younger population.

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What's new?

- Elderly patients are currently under-represented in modern clinical trials regarding cardiac resynchronization therapy (CRT). The present paper provides some useful insight regarding resynchronization therapy in patients over 75 years.
- A patient over 75 years old undergoing CRT implantation could expect the same magnitude in improvement of systolic performance and ventricular remodelling as non-elderly, despite an higher prevalence of co-morbidities.
- Potential benefits of CRT in elderly patients are evident even 3 months after device implant, and are steadily present after 1 year follow-up.
- Life expectancy, and not mere age alone should be a determinant when considering CRT in an elderly patient.

Methods

Study endpoints

The primary endpoint of the present study was to assess differences in LVEF improvement between CRT recipients <75 and ≥75 years old during a 12-month follow-up.

Secondary endpoints of the study were to assess differences in improvements of the following variables between older and younger CRT patients during a 12-month follow-up: left ventricular (LV) diameters (both diastolic and systolic), systolic pulmonary artery pressure (sPAP), New York Heart Association (NYHA) class, Minnesota Living with Heart Failure Questionnaire (MLHFQ) score, and QRS duration.

Inclusion criteria and study protocol

This is a single-centre prospective observational study (Cardiology Clinic, Ospedali Riuniti di Ancona, Marche Polytechnic University). Enrolment started in July 2009 and ended in December 2011. The study population originally included 130 patients with advanced HF and successfully implanted with biventricular pacing (CRT-P) with or without an implantable cardioverter-defibrillator (CRT-D). Patients were consecutively screened for inclusion and divided accordingly into two age groups: <75 years old (69 screened patients) and ≥75 years old (61 screened patients). All included patients fulfilled current European recommendations for CRT implantation (NYHA class III or IV, LVEF ≤ 35% and QRS duration >120 ms or NYHA class II, LVEF ≤ 35%, QRS duration >150 ms).[9] According to the protocol, CRT-P or CRT-D were added to optimal medical therapy which included four main classes of drugs: beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and aldosterone antagonists. Patients were excluded if they had a life expectancy <1 year, if they had an acute coronary syndrome or stroke in the last 3 months, if they were admitted for acute HF decompensation, or if they had severe aortic stenosis. At the end of the screening process (*Figure 1*), 65 patients were enrolled: 32 of those were ≥75 years old and 33 were <75 years old. The present study was performed according to the Declaration of Helsinki. At the time of enrolment, all patients gave their written informed consent. For each patient, demographic data, history, and clinical variables were collected at baseline, at 3 and at 12 months after device implantation. The presence of chronic obstructive pulmonary disease (COPD), diabetes, hypertension, dyslipidaemia, obesity (defined as body mass index ≥30 kg/m^2), and renal failure (creatinine clearance <60 mL/min/1.73 m^2, calculated with the Cockcroft–Gault formula) was ascertained according to current guidelines.[10–13] At baseline and 3 and 12 months after device implantation, clinical evaluation, as well as a 12-lead electrocardiogram (ECG), and a complete echocardiographical study were performed. Symptoms of HF were classified according to the NYHA classification, and the decision between NYHA class II or III was taken by consensus by three authors (M.B., M.V.M., and L.C.). For further assessment of clinical status, the self-administered 'MLHFQ' was used for scoring the quality-of-life on a scale from 0 (best) to 105 (worst).[14] Moreover, time to first HF episode and history of atrial fibrillation were reported in the database.
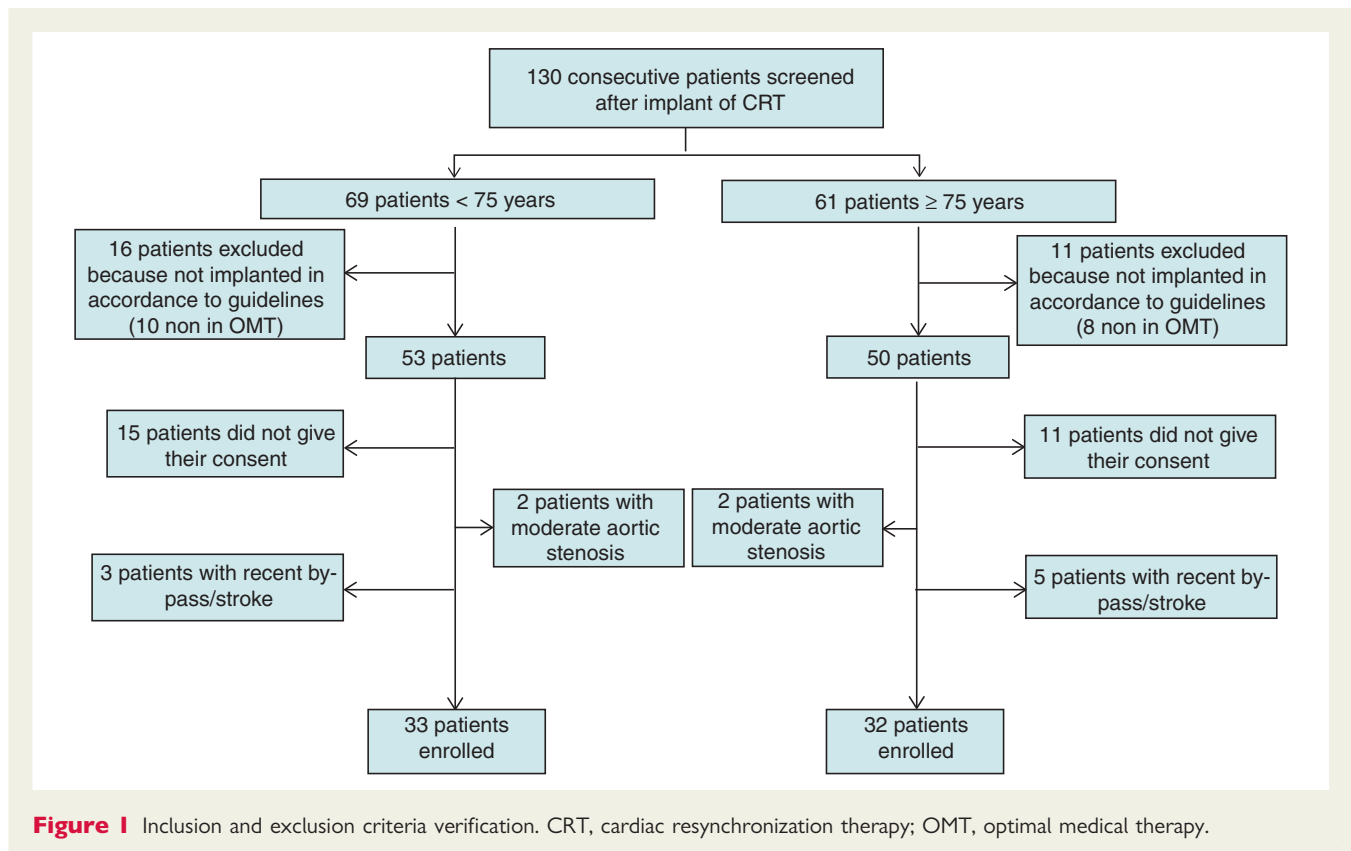
Electrocardiogram

The ECG, performed at baseline and at each follow-up visit, was recorded on an electrocardiographic recording system (Cardioline Delta 60 Plus). Standard 12-lead ECGs were acquired at a paper speed of 25 mm/s and a scale of 10 mm/mV. The assessment of spontaneous and paced QRS duration (recorded in the largest QRS from the surface leads) and morphology were performed by two independent observers (M.B., M.V.M.).

Echocardiographic protocol

All patients underwent echocardiography before device implantation and at 3 and 12 months follow-up. Studies were performed with the subjects at rest in the left lateral decubitus position with commercially available ultrasound transducer and equipment (M4S probe, Vivid 7 PRO, GE-Vingmed Ultrasound). Complete two-dimensional, colour and continuous-wave Doppler echocardiographic images were acquired. Left ventricular end-diastolic diameter (LVEDD) and LV end-systolic diameter (LVESD) were based on the criteria proposed by the American Society of Echocardiography.[15] Global LV function was assessed by modified biplane Simpson's method. In each patient, the sPAP was estimated according to Guidelines for the Echocardiographic Assessment of the Right Heart.[16] One single operator (M.B.) performed all echocardiographical evaluations to avoid inter-individual variability.

Cardiac resynchronization therapy implantation

All patients were implanted with a biventricular pacemaker (Cognis P106 or 107, Boston Scientific; Consulta CRT-D or Syncra CRT-P, Medtronic Inc.; Promote Accel RF, St Jude Medical; Lumax HF-T, Biotronik). Several types of LV leads were used (Easytrack 3 IS, Easytrack 2, Acuity, Boston Scientific; 4196, Attain ability, Medtronic; Corox OTW, Biotronik; Quickflex 1258, St Jude Medical). The right atrium and right ventricle were stimulated by positioning standard bipolar barbed leads in the right atrial appendage and right ventricular apex, respectively. A combined device (CRT plus internal defibrillator) was implanted in 61 patients (94.1%). Device implantation was successful in all cases without any major complications (death, pneumothorax, subclavian thrombosis, coronary sinus dissection, and intraoperative haemorrhage). The standard settings included atrioventricular (AV) delays of 100 ms (sensed) and 120 ms (paced), DDD or DDDR mode (VVI or VVIR if permanent atrial fibrillation was present), a lower pacing rate of 50 b.p.m., and an upper pacing rate of 130 b.p.m. The AV interval was adjusted for optimal diastolic filling by Doppler echocardiographic assessment of mitral inflow and the interventricular interval was adjusted by Doppler echocardiographic assessment of LV outflow at 8 ± 1 days after implantation.[17] The lower rate was adjusted to overcome the spontaneous heart rate and grant >90% of paced beats before patient's discharge.

Figure 1 Inclusion and exclusion criteria verification. CRT, cardiac resynchronization therapy; OMT, optimal medical therapy.

Device interrogation

At each follow-up visit, device interrogation was performed. Device interrogation included evaluation of the integrity of the system and leads information (amplitude, impedance, and thresholds).

Statistical analysis

Sample size calculation showed that a population of ≥ 32 subjects in each group would have a $> 80\%$ power to detect a mean LVEF difference $\geq 5\%$ between elderly and non-elderly patients (with $\alpha = 0.05$), assuming a standard deviation of 7%, using a general linear model for repeated measures. Quantitative variables were checked for normality by the Kolmogorov–Smirnov test. Analysis of variance (ANOVA) adjusted by age and sex was used to compare normally distributed quantitative variables. Kruskal–Wallis ANOVA was used to compare non-normally distributed quantitative variables. Categorical variables were assessed by using χ^2 analysis. General linear model for repeated measures was used to assess time-dependent changes between 0, 3, and 12 months follow-up. SPSS 13.0 for Windows (SPSS Inc.) was used for statistical analysis. Values of $P < 0.05$ were taken as statistically significant.

Results

Study population and baseline characteristics

In the overall population there were 52 male (80%) and 13 female (20%) patients. The mean age was 71.5 ± 9.0 years. Heart failure was mainly due to ischaemic cardiomyopathy (34 patients, 52.3%)

with a mean LVEF of $26.4 \pm 4.8\%$ in the whole population. Forty-nine patients (75.4%) had NYHA functional class III at the time of implant. Baseline characteristics of the study population, also divided by subgroups, are summarized in *Table 1*. The study subgroups were composed by 33 (50.7%) non-elderly patients (aged < 75 years old) with a mean age 64.7 ± 7.7 years and 32 (49.3%) elderly patients with a mean age of 78.5 ± 2.6. There was no significant difference regarding HF aetiology between elderly and non-elderly patients. Elderly patients had a wider baseline QRS duration (157.5 ± 20.5 vs. 149.1 ± 30.3 ms; $P = 0.023$). Both groups were optimally treated with beta-blockers (90.6% of elderly patients, 91% of non-elderly patients), ACEIs or ARBs (93.7% of elderly patients, 84.9% of non-elderly patients), and aldosterone antagonists (56.2% of elderly patients, 63.6% of non-elderly patients).

Primary endpoint: cardiac resynchronization therapy effects on left ventricular ejection fraction

Left ventricular ejection fraction showed a time-related improvement in the whole population ($+10.6\%$ over 12 months) as well as in each subgroup as shown in *Table 2* and *Figure 2* (P within subjects < 0.001). There was no interaction between time and elderly condition and the magnitude of LVEF improvement was similar in elderly when compared with non-elderly people ($+13.6$ vs. $+7.9\%$; P between subjects $=$ ns). There was no difference regarding CRT-related LVEF improvements between ischaemic and non-ischaemic patients ($+9.8$ vs. $+11.3\%$; P between subjects $=$ ns),

Table 1 General characteristics of the whole population, also divided between elderly and non-elderly patients

	Total population (n = 65)	≥75 years (n = 32)	<75 years (n = 33)	P value
Age (years)	71.5 ± 9.0	78.5 ± 2.6	64.7 ± 7.7	<0.001
Male sex (n, %)	52 (80.0)	25 (78.1)	27 (81.8)	0.321
SBP (mmHg)	118.5 ± 16.0	118.5 ± 16.1	118.6 ± 16.1	0.982
HR (b.p.m.)	72.8 ± 8.9	72.7 ± 12.9	72.8 ± 9.1	0.990
COPD (n, %)	18 (27.7)	13 (40)	5 (15)	0.090
CRF (n, %)	45 (65.2)	26 (81)	19 (59)	0.055
Ischaemic aetiology (n, %)	34 (52.3)	13 (40)	21 (64)	0.063
Hypertension (n, %)	51 (78.5)	25 (71.4)	26 (78.8)	0.948
Diabetes mellitus (n, %)	22 (33.8)	10 (31.2)	12 (36.7)	0.663
Atrial fibrillation (n, %)	25 (38.4)	11 (34.4)	14 (42.4)	0.558
NYHA IV (n, %)	8 (12.3)	2 (6.2)	6 (18.2)	0.017
NYHA III (n, %)	49 (75.4)	29 (90.6)	20 (60.6)	0.012
NYHA II (n, %)	8 (12.3)	1 (3.2)	7 (21.2)	0.032
MLHFQ score (n, %)	39.6 ± 17.2	40.1 ± 18.4	39.4 ± 17.1	0.887
QRS duration (ms)	150.0 ± 23.2	157.5 ± 20.5	149.1 ± 30.3	0.023
LBBB (n, %)	53 (81.5)	26 (81.2)	27 (81.2)	0.979
LVEF (%)	26.4 ± 4.8	27.2 ± 4.8	25.7 ± 4.7	0.185
LVEDV (mL)	229.1 ± 86.5	211.2 ± 56	249.9 ± 75.3	0.070
LVESV (mL)	164.5 ± 49.7	145.2 ± 41.9	193.7 ± 49.9	0.013
Beta-blockers (n, %)	59 (90.8)	29 (90.6)	30 (91)	0.963
ACEI/ARB (n, %)	58 (89.2)	30 (93.7)	28 (84.9)	0.515
AA (n, %)	39 (60.0)	18 (56.2)	21 (63.6)	0.390

Continuous variables are expressed as mean ± standard deviation. Categorical variables are expressed as total number (%).
SBP, systolic blood pressure; HR, heart rhythm; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; NYHA, New York Heart Association; MLHFQ, Minnesota Living With Heart Failure Questionnaire; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; AA, aldosterone antagonists.

and there was no interaction between time and ischaemic aetiology over 12 months.

Secondary endpoint: cardiac resynchronization therapy effects on other echocardiographical parameters

Regarding other echocardiographical parameters, LVEDD, LVESD, and sPAP all showed a time-related improvement in the whole population as well as in each subgroup (Table 2). Left ventricular end-systolic diameter improvement was more pronounced in the elderly (−9.4 vs. −4.0 mm; P between subjects = 0.011), whereas LVEDD and sPAP benefits were of similar magnitude when ≥75 and <75 years old were compared.

Secondary endpoint: cardiac resynchronization therapy effects on clinical variables

New York Heart Association class and MLHFQ showed a similar trend with a significant improvement over the 12-month follow-up (P within subjects < 0.001 for both NYHA class and MLHFQ). There was no interaction between time and age class (all P = ns) and elderly patients experienced improvements of the same magnitude as non-elderly (NYHA class: +1.9 vs. 2.2; MLHFQ: −16.5 vs. −23; all P between subjects = ns).

Secondary endpoint: cardiac resynchronization therapy effects on 12-lead electrocardiogram

Elderly patients also had a much greater reduction of QRS width when compared with non-elderly patients (−42.8 vs. −33.3 ms; P between subjects = 0.041) even if both subgroups showed a progressive shortening of QRS width over time (Figure 3).

Safety assessment

There was no significant difference regarding mortality between elderly and non-elderly patients, with seven deaths for cardiovascular events (five elderly and two non-elderly; P = ns). One patient in the non-elderly group underwent cardiac transplantation after 6 months, and was therefore lost to follow-up.

Device implantation complications were observed in 14 patients (21%). The most frequent event was the dislodgement of at least one of the leads (n = 10; 15.4%), which however always occurred during the length of the hospitalization (mean time to dislodgement 1.4 ± 0.3 days), and were promptly treated by repositioning, with no further dislodgements reported after 3 months. Pocket haematomas were observed in 2 elderly patients and in one non-elderly patient, and were treated conservatively. One pocket infection was observed in an elderly patient between the 3- and

Table 2 Echocardiographical and clinical changes at 3- and 12-month follow-up

	Baseline (n = 65)	Three months (n = 63)	Twelve months (n = 57)	P value	P for interaction
LVEF (%)	25.4 ± 4.1	33.2 ± 6.5	36.0 ± 7.0		
<75 years	25.3 ± 4.8	31.6 ± 5.5	33.2 ± 5.1		
≥75 years	25.4 ± 3.6	34.4 ± 7.3	39.0 ± 7.7		
Within-subjects				<0.001	0.132
Between-subjects				0.163	
LVEDD (mm)	70.5 ± 8.4	64.9 ± 8.8	64.2 ± 10.4		
<75 years	73.9 ± 8.2	70.9 ± 7.6	69.4 ± 11.4		
≥75 years	68.6 ± 8.1	61.6 ± 7.8	61.3 ± 8.9		
Within-subjects				0.002	0.465
Between-subjects				0.134	
LVESD (mm)	59.1 ± 9.5	51.5 ± 10.5	51.2 ± 11.7		
<75 years	66.7 ± 7.9	62.0 ± 8.5	62.7 ± 7.9		
≥75 years	56.4 ± 9.5	47.7 ± 8.5	47.0 ± 10.1		
Within-subjects				0.015	0.426
Between-subjects				0.011	
sPAP (mmHg)	40.9 ± 14.5	33.7 ± 11.8	32.3 ± 12.7		
<75 years	38.8 ± 11.4	35.8 ± 14.8	33.8 ± 14.8		
≥75 years	42.5 ± 17.1	32.1 ± 9.7	31.1 ± 11.8		
Within-subjects				0.031	0.442
Between-subjects				0.888	
NYHA class	3.0 ± 0.5	1.3 ± 1.1	1.0 ± 1.0		
<75 years	3.0 ± 0.7	1.4 ± 1.0	0.8 ± 1.0		
≥75 years	3.0 ± 0.3	1.3 ± 1.1	1.1 ± 1.0		
Within-subjects				<0.001	0.324
Between-subjects				0.680	
MLHFQ score	41.5 ± 20.7	26.2 ± 16.0	21.7 ± 10.6		
<75 years	40.9 ± 18.6	22.9 ± 16.2	17.9 ± 11.1		
≥75 years	41.2 ± 22.2	28.9 ± 16.0	24.7 ± 9.4		
Within-subjects				<0.001	0.662
Between-subjects				0.308	
QRS duration (ms)	152.7 ± 24.3	117.3 ± 19.1	114.2 ± 17.7		
<75 years	143.3 ± 23.9	110.0 ± 19.5	110.0 ± 17.1		
≥75 years	160.7 ± 22.3	123.4 ± 16.9	117.9 ± 19.1		
Within-subjects				<0.001	0.474
Between-subjects				0.041	
HR (b.p.m.)	74.5 ± 9.6	70.3 ± 9.8	70.4 ± 7.9		
<75 years	74.2 ± 10.5	69.8 ± 11.3	70.4 ± 8.2		
≥75 years	74.8 ± 9.8	70.8 ± 9.4	70.4 ± 8.5		
Within-subjects				0.087	0.969
Between-subjects				0.927	

Continuous variables are expressed as mean ± standard deviation. Categorical variables are expressed as total number (%).
LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; sPAP, systolic pulmonary artery pressure; NYHA, New York Heart Association; MLHFQ, Minnesota Living With Heart Failure Questionnaire; HR, heart rate.

the 12-month follow-up visit. The patient died shortly thereafter for unrelated concomitant causes and was therefore lost to follow-up. A cumulative rate of biventricular pacing >90% was confirmed in all patients performing each follow-up. No significant difference was found in time to first HF recurrence between elderly and non-elderly patients (3.5 vs. 4.5 months; *P* = ns).

Discussion

Current knowledge about CRT benefits shows interesting results in treatment of advanced HF,[3–7] but this evidence is currently demonstrated only in selected patients with a mean age <70 years and without significant co-morbidities. Such patients do
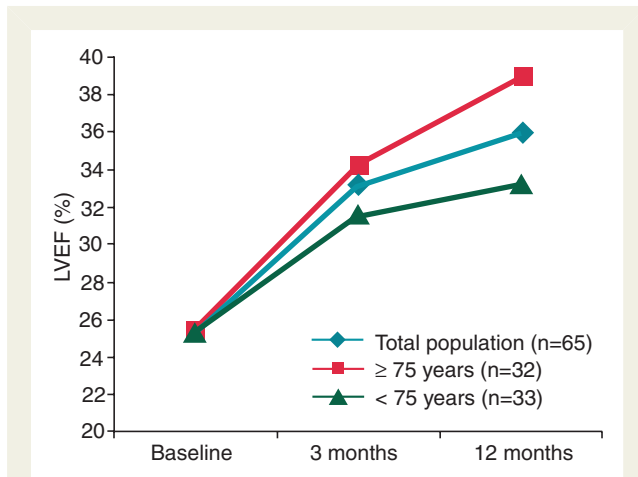
Figure 2 Temporal trend of LVEF pre-CRT implant and during the 12-month follow-up.
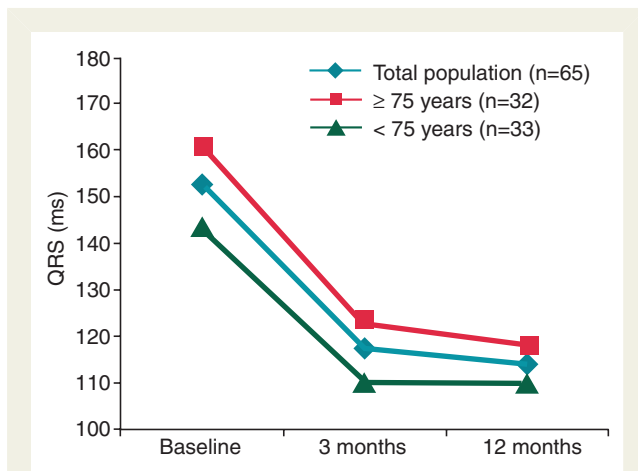

Figure 3 Temporal trend of QRS width during the 12-month follow-up.

not reflect the spectrum of real-world population with severe HF, whose mean age is often much higher.[8] Moreover, the prevalence of HF in the whole population is between 2 and 3%, but rises sharply at 75 years of age reaching 10–20% between the eighth and ninth decades.[2] Our study shows that elderly patients can benefit greatly from biventricular pacing in terms of LVEF improvements, as well as other echocardiographical and clinical parameters. Moreover, these improvements seem similar to the ones experienced by the non-elderly subjects, and are consistent for the entire 1 year follow-up. In common practice, the advanced age often represents an argument to restrict the use of biventricular pacing to younger patients, even if it is well-known that CRT-related reduction of mortality and morbidity is not dependent on age. For example, in the Cardiac Resynchronization-Heart Failure (CARE-HF) trial, a pre-specified subgroup analysis showed no difference in the primary endpoint of death from any cause or hospitalization for major cardiovascular events between patients <66.4 years old and patients ≥66.4 years old.[6] Similar results were obtained in a subgroup analysis of the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial.[5] A substudy of the Multicenter Automatic Defibrillator Implantation Trial with CRT (MADIT-CRT)[18] trial even showed that CRT-D was associated with a significant 41% risk-reduction of HF or death compared with ICD-only therapy, risk reduction that was not present in patients <60 years. In this kind of setting, our data support the hypothesis that older patients can benefit from CRT even in terms of ejection fraction improvement and cardiac remodelling, and that the expected outcome is similar to the non-elderly one. All these echocardiographical improvements could partially explain the reduced risk of HF and death showed by the elderly population in the clinical trials mentioned above.[5,6,18] A recently published subgroup analysis by age of the MIRACLE and MIRACLE-ICD trials was in line with our data and showed that elderly patients who receive CRT have comparable improvements in NYHA class and LVEF as younger patients.[19] Similar results are also demonstrated in other observational experiences, in which, however, the probability of a type II error has never been elucidated by aimed sample size calculation.[20–25] Conversely, our study provides good, albeit observational evidence of similar improvements in LVEF with an 80% statistical power. Echocardiographical improvements in the elderly are, however, not limited to LVEF but include also favourable cardiac ventricular remodelling and sPAP reduction, and all of those are of similar magnitude to the ones expected in younger patients. QRS duration, the first and perhaps most studied index of cardiac dyssynchrony, was significantly wider in the elderly when compared with non-elderly patients in our population before CRT implant. However, by the end of the 12-month follow-up, both groups showed a mean QRS < 120 ms, which obviously translates into a significant greater reduction of QRS width in elderly patients at 1 year. Together with echocardiographical and electrocardiographical changes, the whole population as well as each subgroup experienced a significant improvement in health-related quality-of-life after CRT implant. This finding is consistent with previous literature on quality-of-life following CRT.[3,4,22] Our study did not note any age effects on perceived improvement of physical, social, and mental functions as reported[26] in a small sample size study which, however, differed in quality-of-life evaluation methods and follow-up duration.

These data, along with a higher reduction of LVESD, although non-primary endpoints of our study, provide solid evidence against restricting resynchronization therapy because of advanced age.

Another interesting aspect emerging from our study is the good adherence to maximum tolerated medical therapy regardless of the age of patients. The treatment goal is hardly reached in the current clinical practice as underlined in the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting.[27] Indeed, ACEIs, ARBs, and beta-blockers are commonly underused because of the co-morbidities intrinsic to geriatric populations or physicians' fear of side effects.

Nonetheless, an optimal medical therapy before CRT implant is indeed mandatory, and could have contributed to the significant clinical and instrumental improvements found in our elderly

patients, improvements which are already significant 3 months after CRT implant.

In conclusion, our study shows that CRT is as effective in improving LVEF in an aged population as in non-elderly patients and represents a valid therapy to achieve echocardiographical as well as clinical benefits in advanced HF.

The present study adds evidences against the notion that age alone should be a determinant to deny resynchronization therapy to elderly patients.

Conflict of interest: none declared.

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