Myocardial constructive work and cardiac mortality in resynchronization therapy candidates

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Abstract Background

Recent studies have shown that myocardial constructive work (CW) assessed by pressure-strain loops (PSLs) is an independent predictor of a volumetric response to cardiac resynchronization therapy (CRT). The aim of this study was to evaluate the role of CW in predicting the cardiac outcome of heart failure patients undergoing CRT.

Methods

This is a retrospective study including 166 CRT candidates (ejection fraction [EF] ≤35%, QRS duration ≥120 milliseconds). Two-dimensional standard echocardiography and speckle-tracking echocardiography were performed before CRT and at 6-month follow-up. PSLs were used to assess myocardial CW.

Results

After a median follow-up of 4 years (range 1.3-5 years), cardiac death occurred in 14 patients (8%). A multivariable Cox regression analysis including age, coronary artery disease, and septal flash showed that CW≤888 mm Hg% was the only independent predictor of cardiac mortality (hazard ratio 4.23, 95% CI 1.08-16.5, $P = .03$). After 6 months of CRT, a 15% reduction in left ventricular end-systolic volume was observed in 118 (71%) patients, and a CRT volumetric response was identified. Among CRT responders, the concomitant presence of CW ≤888 mm Hg% identified a subgroup of patients at high risk of cardiac death ($P = .04$ in the log-rank test). The addition of CW ≤888 mm Hg% to a model including age, coronary artery disease, septal flash, and CRT response caused a significant increase in model power for the prediction of cardiac death (χ^2: 12.6 vs 25.7, $P = .02$).

Conclusions

The estimation of left ventricular CW by PSLs is a relatively novel tool that allows for the prediction of cardiac outcome in CRT candidates. (Am Heart J 2019;212:53-63.)

Cardiac resynchronization therapy (CRT) has been demonstrated to improve the left ventricular (LV) function and outcomes of patients with both systolic heart failure (HF) and wide QRS (>120 milliseconds)[1] who remain symptomatic despite optimized medical therapy.[2] Despite these striking results, approximately one-third of patients do not benefit and, in some cases, may even be harmed after CRT.[3] Several studies have shown that in HF patients with wide QRS and regional mechanical discoordination derived from the estimation of LV mechanical delay, CRT might alleviate the mechanical dyssynchrony caused by LV electrical activation delay.[4] Nevertheless, the routine use of mechanical discoordination as an adjunct to the electrocardiographic criteria for the selection of CRT candidates has not gained clinical acceptance[5] and has been shown to even be detrimental in patients with normal QRS.[6]

A potential explanation for these results is that the assessment of QRS duration and/or myocardial dyssynchrony does not take into account the role of residual myocardial contractility[7,8,9] as a potential source for LV functional restoration after CRT.

In recently published surveys[10,11] we demonstrated that the noninvasive estimation of global myocardial constructive work (CW) by pressure-strain loop (PSL) is a predictor of LV remodeling and response to CRT over common LV dyssynchrony parameters. The association between myocardial CW and outcome after CRT is, however, unknown. The aim of the present study was to assess the predictive role of myocardial CW on cardiac mortality in HF patients undergoing CRT.

Methods

Population

This is a retrospective, observational, monocentric study conducted on 166 patients with systolic HF undergoing CRT implantation according to current

guidelines.[1] All patients were in sinus rhythm and had a good acoustic window, allowing acquisition of 2-dimensional echocardiography and speckle tracking echocardiography with excellent image quality. At the time of CRT implantation, all patients were receiving optimized medical therapy. *Coronary artery disease* (CAD) was defined as a history of myocardial infarction and coronary revascularization or angiographic evidence of multiple-vessel disease or single-vessel disease with ≥75% stenosis of the left main or proximal left anterior descending artery.[12] CRT response was indicated by a decrease in LV end-systolic volume (ESV) >15% at the 6-month follow-up (FU).[5] A biventricular stimulation >90% after CRT implantation was mandatory for patient inclusion in the protocol. Clinical data including age, sex, and treatments were collected for each patient. The functional status was assessed by the estimation of the New York Heart Association (NYHA) functional class. Data on the vital status of patients were collected from hospital medical records or by interview with the patients' general practitioner or relatives.

The study was conducted in accordance with the "Good Clinical Practice" guidelines of the Declaration of Helsinki and reviewed by an independent ethics committee (Regional Ethic Committee validation number: 35RC14-9767). All patients gave their written informed consent for study participation. No extramural funding was used to support this work.

The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents

Echocardiography

All patients underwent standard transthoracic echocardiography using a Vivid 7 or Vivid E9 and E95 ultrasound system (GE Healthcare, Horten, Norway) equipped with a 3S or M5S 3.5-mHz transducer. Two-dimensional, color Doppler, pulsed-wave, and continuous-wave Doppler data were stored on a dedicated workstation for the offline analysis (EchoPAC, GE Healthcare, Horten, Norway). LV volumes and function were measured by the biplane method, as recommended.[13]

Assessment of septal flash

The presence of septal flash (SF) was visually assessed before CRT implantation. SF was defined by the presence of an early septal thickening/thinning within the isovolumic contraction period.[14,15]

## Myocardial work quantification

Myocardial work and related indices were estimated using a vendor-specific module (EchoPAC Version 202, GE Vingmed Ultrasound, Norway). Myocardial work was estimated as a function of time throughout the cardiac cycle by the combination of LV strain data obtained by speckle tracking echocardiography and a noninvasively estimated LV pressure curve, as previously described by Russel et al.[16] A 17-segment model was used for the estimation of segmental myocardial work.

The calculation of myocardial work followed several steps.

1. **LV strain analysis**. Two-dimensional grayscale images were acquired in the standard apical 4-, 3-, and 2-chamber views at a frame rate ≥60 frames/s, and the recordings were processed using an acoustic-tracking dedicated software (EchoPAC version 112.99, Research Release, GE Healthcare, Horten Norway) to estimate LV global longitudinal strain (GLS).[17] Image quality for the enrolled patients was optimal, and no LV segments were excluded from strain analysis.

2. **Noninvasive estimation of LV pressure (LVP)**. The profile of an empiric LVP waveform provided by the software was used for the prediction of LVP in each specific subject by the analysis of aortic and mitral valve events (mitral valve closure, aortic valve opening, aortic valve closure, mitral valve opening) during the cardiac cycle. The duration of time intervals of isovolumic contraction, LV ejection, and isovolumic relaxation was then determined by stretching or compressing the time axis of the averaged LVP curve to match the measured time intervals (Figure 1*A*, left side). The instantaneous systolic pressure value estimated by a brachial artery cuff was assumed to be equal to peak systolic LV pressure and to be uniform throughout the ventricle. This pressure value was then used to scale the normalized pressure signal in each patient (Figure 1*A*, right side). The reliability of this noninvasively estimated LV pressure curve was previously validated in a dog model,[16] in CRT candidates, in patients with dilated cardiomyopathy of ischemic and nonischemic etiology,[16,18,19] and in patients with arterial hypertension[19]

3. **Calculation of myocardial work**. Strain and pressure data were synchronized using the R wave on ECG as a common time reference (Figure 1*B*, left side). Myocardial work was then quantified by calculating the rate of segmental shortening by differentiating the strain curve and multiplying the resulting value by the instantaneous LV pressure (Figure 1*B*, right side). The result is a measure of instantaneous power, which was integrated over time to obtain myocardial work as a function of time. Work was calculated from mitral valve closure until mitral valve opening. During the isovolumic contraction and LV ejection period, segmental shortening contributes to the final LV ejection, whereas segmental stretch or lengthening does not contribute to LV ejection. As a result, the work performed by the myocardium during segmental

Figure 1
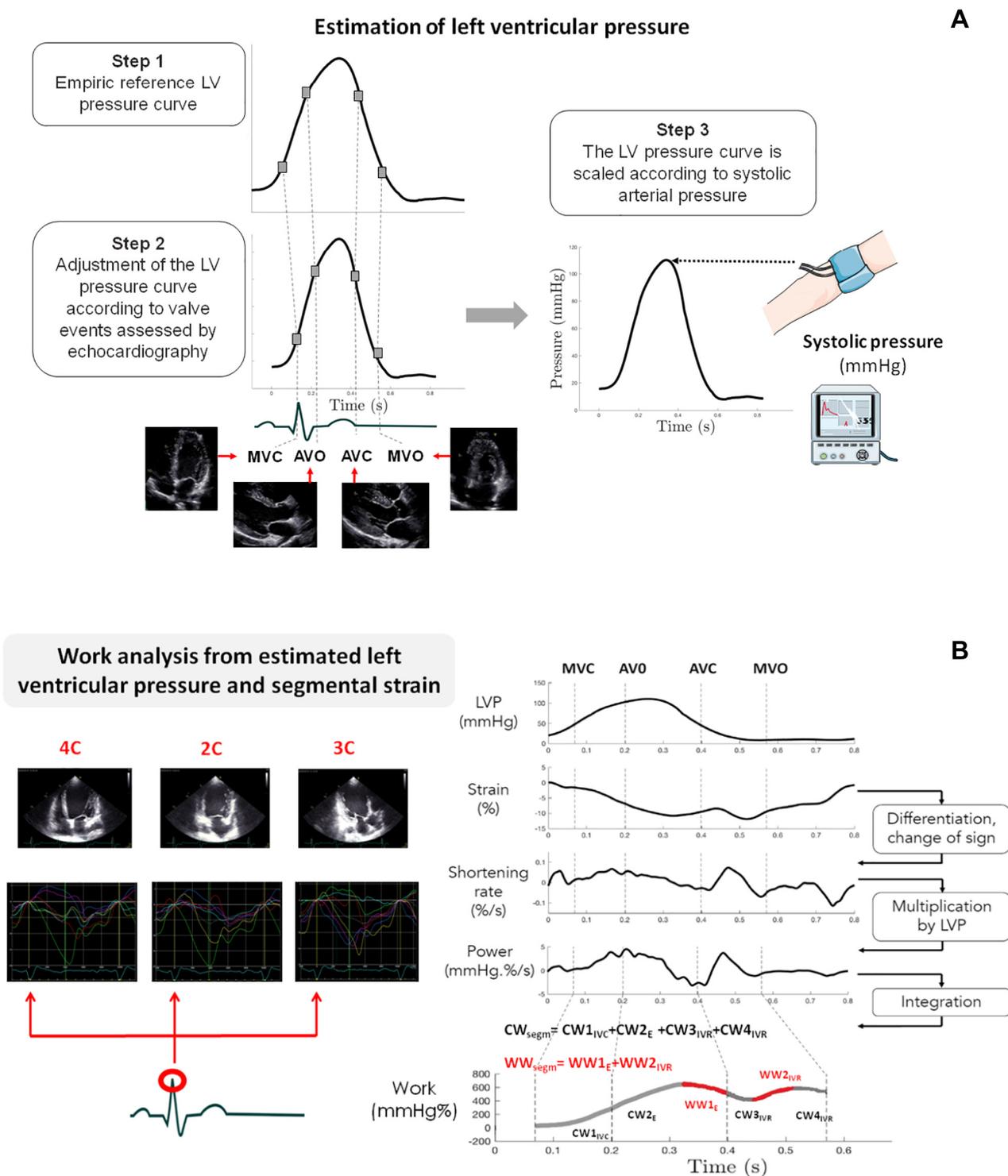
The noninvasive LV pressure curve was obtained using an empiric, normalized reference curve that was adjusted according to the duration of the isovolumetric and ejection phases of the left ventricle (A, left panel), and the systolic blood pressure estimated by a brachial artery cuff (A, right panel). Pressure data were then combined with left ventricular global longitudinal strain data using the R-wave onset in the electrocardiogram as a common time reference (**B**, left panel) and used for the estimation of myocardial work in each myocardial segment (**B**, right panel).

Table I. Baseline characteristics of the population

Variables	All patients (N = 166)	CW >888 mm Hg% (n = 99, 60%)	CW ≤888 mm Hg% (n = 67, 40%)	P value
Age, y	66±10	66±10	64±11	.19
Male, n	115 (69%)	61 (62%)	54 (81%)	.01
Ischemic disease, n	48 (29%)	27 (27%)	21 (31%)	.60
NYHA >II	70 (42%)	40 (40%)	30 (45%)	.52
Arterial hypertension	32 (19%)	18 (18%)	13 (19%)	.31
Diabetes	17 (10%)	6 (6%)	11 (16%)	.05
Dyslipidemia	63 (38%)	35 (35%)	28 (42%)	.40
Creatinine, µmol/L	99±31	95±30	104±31	.07
QRS widths, per ms	165±19	163±16	169±23	.07
QRS >150 ms	124 (75%)	75 (76%)	49 (73%)	.55
LBBB, n	136 (82%)	86 (87%)	50 (75%)	.14
LVEF, %	28±7	30±6	24±7	<.0001
LV-EDV, mL/m^2	120±42	105±31	143±45	<.0001
LV-ESV, mL/m^2	84±36	71±25	104±39	<.0001
LV-GLS, %	-9±3	-9±3	-6±2	<.0001
SF, n	105 (63%)	71 (72%)	34 (51%)	.01
Constructive work, per mm Hg%	1025±442	1288±329	636±171	<.0001
Wasted work, per mm Hg%	229±134	307±140	288±124	.39
CRT responders, n	118 (71%)	81 (82%)	37 (55%)	<.0001

EDV, End-diastolic volume.

shortening represents constructive work, whereas the work performed by the myocardium during stretch or segmental lengthening represents energy loss, which is defined as wasted work. During isovolumic relaxation, segmental lengthening contributes to LV relaxation, whereas segmental shortening does not. As a result, the work performed by the myocardium during segmental shortening, which does not promote LV relaxation, is considered wasted work, whereas the work performed by the myocardium during segmental lengthening is considered segmental constructive work. By averaging segmental constructive and wasted work for each segment, global constructive work (GCW) and global wasted work (GWW) were estimated for the entire LV.[16] The overall process of estimation of myocardial work was quite fast, taking no more than 2 minutes after LV strain assessment. The inter-observer and intraobserver concordances for the estimation of myocardial work have already been reported.[10,11]

Statistical analysis

Continuous variables are expressed as the mean and SD and were compared using Student *t* test. Categorical data are expressed as frequencies and percentages and were compared by the χ^2 test. Receiver operator characteristics curve (ROC) analysis and the Youden index were used to determine a CW cutoff that was able to predict events. Univariable Cox proportional hazards analysis of baseline clinical, electrocardiographic, and echocardiographic characteristics was performed using cardiac mortality as end

point. For each variable, the hazard ratio (HR) and 95% CIs were calculated. Only variables with a *P* value < .05 in the univariable analysis were inserted in the multivariable Cox analysis. Freedom cardiac death was plotted for both CW groups using Kaplan-Meier curves. Between-group differences in freedom from events were tested using the log-rank test. Finally, the merits of CW over different nested models including clinical variables, SF, and CRT response to predict mortality were assessed with Cox regression analysis, and the incremental value of each model was assessed by the χ^2 test at each step and by the Harrell *C*-concordance statistics. Intra- and interobserver reliability for the assessment of SF was estimated by the percentage of agreement and Cohen κ in 20 randomly selected patients.

All statistical analysis was performed using a standard statistical software program (SPSS Version 20.0, IBM, Chicago, IL, and R statistical software, version 3.4.4). A value of *P* < .05 was considered statistically significant.

Results

Baseline characteristics of the population are summarized in Table I. In the overall population, 48 (29%) patients had ischemic cardiomyopathy. Left bundle-branch block (LBBB) was present in 136 (82%) patients. SF was identified in 105 (63%) patients. Intra- and interobserver agreements for visual assessment of SF were 95% (κ = 0.90 [95% CI 0.71-1], *P* < .0001) and 90% (κ = 0.80 [95% CI 0.58-1], *P* = <0.0001), respectively.

ROC curve analysis showed that a cutoff value of 888 mm Hg% for CW was the best predictor of cardiac death (AUC 0.71, 95% CI 0.60-0.82, *P* = .007) (Figure 2). Patients with

Figure 2

Cardiac death

AUC 0.71 (0.60-0.82) *P* = .007
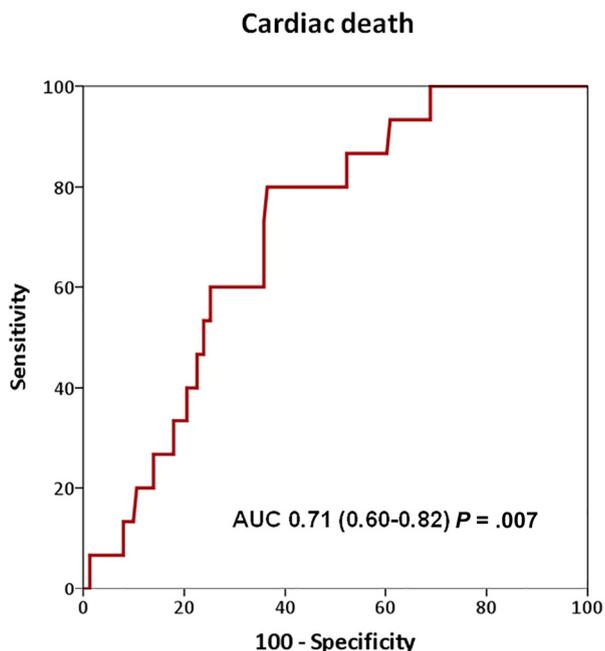
ROC curve analysis of left ventricular constructive work for the prediction of cardiac death.

Table II. Comparative data on left ventricular size, function, and myocardial work in CRT responders and nonresponders at baseline and at 6-month FU

	Responders n = 118 (71%)	Nonresponders n = 48 (29%)	P value
Baseline			
LV-EDV, mL/m^2	117±42	129±41	.037
LV-ESV, mL/m^2	83±35	89±36	.15
LV-EF, %	28±7	28±8	.62
LV-GLS, %	-9±3	-7±3	.0001
Constructive work, mm Hg%	1104±434	838±324	.0001
Wasted work, mm Hg%	325±137	245±114	.001
After 6 m of CRT			
LV-EDV, mL/m^2	80±28*	129±38	<.0001
LV-ESV, mL/m^2	45±21*	91±35†	<.0001
LV-EF, %	45±11*	28±9	<.0001
LV-GLS, %	-13±4*	-8±4	<.0001
Constructive work, mm Hg%	1452±420*	920±372	<.0001
Wasted work, mm Hg%	197±111*	197±102†	.99

* P < .0001 with respect to baseline.
† P<0.05 with respect to baseline.

CW≤888 mm Hg were more often male (*P* = .01) and had more dilated LV, lower LVEF and GLS (all *P* < .0001), and lower prevalence of SF (*P* = .01) than patients with CW>888 mm Hg. A significantly lower rate of CRT responders was observed in this group (*P* < .0001).

Clinical and echocardiographic data according to CRT response

At the 6-month FU, volumetric CRT response occurred in 118 (71%) patients. Nonresponders were more often male (81% vs 64%, *P* = .002) and had a lower prevalence of LBBB (29% vs 77%, *P* < .0001) and SF (67% vs 89%, *P* = .006) than responders. A significant difference in indexed LV end-diastolic volume, LV end-systolic volume, LVEF, and CW was observed between the 2 groups at baseline and at 6-month FU. A significant improvement in LV geometry and function was observed in CRT responders at the 6-month FU. On the contrary, a slight increase in the indexed LV end-systolic volume and decrease in WW were observed in nonresponders (Table II).

Follow-up

The median FU was 4 years (interquartile range 1.3-5 years). During this time span, cardiac death occurred in 14 patients (8%); 13 patients died of refractory HF, and 1 died 1 week after a heart transplant. In the multivariable Cox regression analysis, CW was an independent predictor of cardiac death (Table III, model A).

Kaplan-Meier survival curves (Figure 3) showed that CW≤888 mm Hg% was highly associated with a poor outcome (log-rank *P* = .008). Patients with CW≤888 mm Hg% had a higher risk of cardiac death (HR 4.76, 95% CI 1.33-17.12, *P* = .01) (Table III). When CW≤888 mm Hg% was used instead of the continuous variable to predict CRT response in the multivariable Cox regression analysis, it remained the only significant predictor of mortality (HR 4.23, 95% CI 1.08-16.5, *P* = .03).

Long-term outcome in relation to CRT response and SF

To compare the added value of CW over LV reverse remodeling for predicting the course of the disease, volumetric response to CRT was added to the Cox multivariable model (Table III, model B). In this model, CRT response was no longer a significant predictor of cardiac death, and it did not affect the HR of CW, which remained a significant predictor of cardiac mortality. Among responders, the presence of a CW≤888 mm Hg% resulted in increased cardiac mortality, as shown by the log-rank test. The concomitant absence of volumetric response to CRT and CW≤888 mm Hg identified a subgroup of patients with a particularly dismal prognosis (Figure 4).

The relationship between CW and outcome was independent from SF (Table II). In patients with SF, the presence of a CW≤888 mm Hg% was associated with a significantly increased CV and all-cause mortality (log-rank test: *P* = .001). Patients without SF and with CW≤888 mm Hg% presented the worst prognosis (Figure 5).

Finally, to evaluate the predictive value of CW≤888 mm Hg% over SF and CRT response for cardiac death, Cox regression analysis was used, and different nested models

Table III. Predictors of cardiac death at univariable and multivariable analysis

| | Univariable analysis | | | Multivariable analysis | | | | | |
| | | | | Model A | | | Model B | | |
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Age, per year	1.08	(1.01-1.15)	.02	1.07	(1.00-1.14)	.05	1.07	(1.00-1.15)	.04
Male sex	1.75	(0.49-6.27)	.39						
Ischemic disease	3.99	(1.34-11.94)	.01	2.99	(0.79-11.16)	.10	2.33	(0.71-1.15)	.16
NYHA >2	1.39	(0.46-4.24)	.56						
Arterial hypertension	0.81	(0.22-2.95)	.75						
Diabetes	2.56	(0.69-9.45)	.16						
Dyslipidemia	1.49	(0.49-4.56)	.49						
Creatinine, per μmol/L	1.01	(0.99-1.93)	.07						
QRS duration, per ms	0.99	(0.97-1.03)	.81						
QRS >150 ms	0.48	(0.17-0.40)	.18						
LBBB	0.87	(0.27-2.77)	.81						
LVEF, per %	0.99	(0.92-1.08)	.89						
LVEDV, per mL/m^2	1.01	(0.99-1.02)	.46						
LVESV, per mL/m^2	1.01	(0.99-1.02)	.69						
SF	0.19	(0.06-0.62)	.006	2.29	(0.54-9.71)	.26	0.48	(0.12-1.95)	.30
LV-GLS	1.21	(0.99-1.47)	.06						
Wasted work, per mm Hg%	0.99	(0.99-1.01)	.75						
Constructive work, per mm Hg%*	0.99	(0.99-1.00)	.04	0.99	(0.99-1.01)	.03	0.99	(0.99-1.00)	.04
Constructive work ≤888 mm Hg%	4.76	(1.33-17.12)	.01						
CRT response†	0.26	(0.09-0.78)	.02				0.68	(0.18-2.57)	.58

Two multivariate models were created: model A not including CRT response and model B including CRT response.

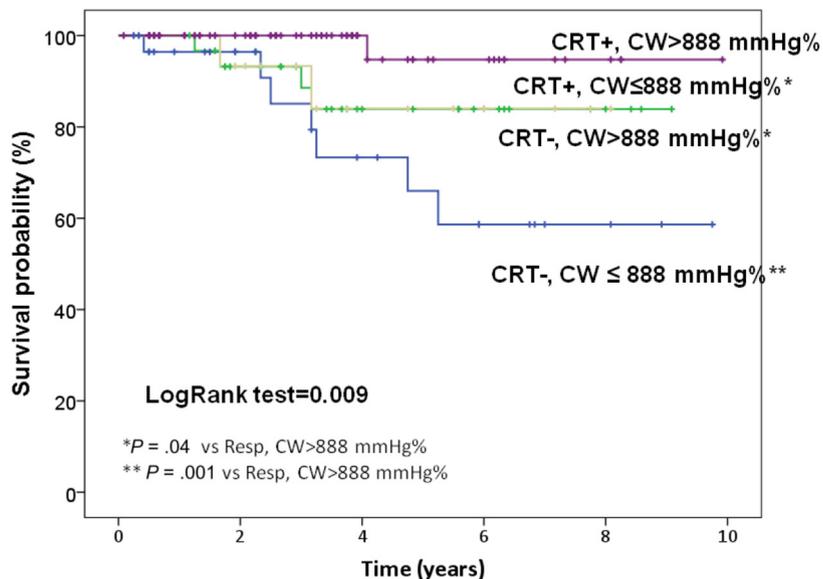* The continuous variable was inserted in the multivariate analysis.

† CRT response was added to multivariate analysis in model B but not in model A.

Figure 3

Freedom from cardiac death in all patients
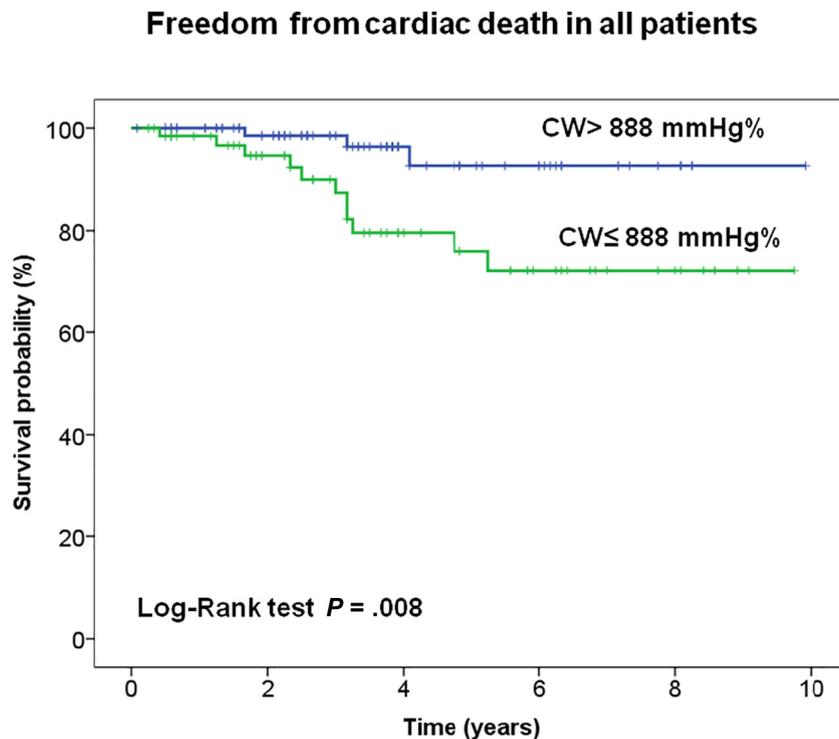
Kaplan-Meier estimates of the time to cardiac death displayed according to CW cutoffs.
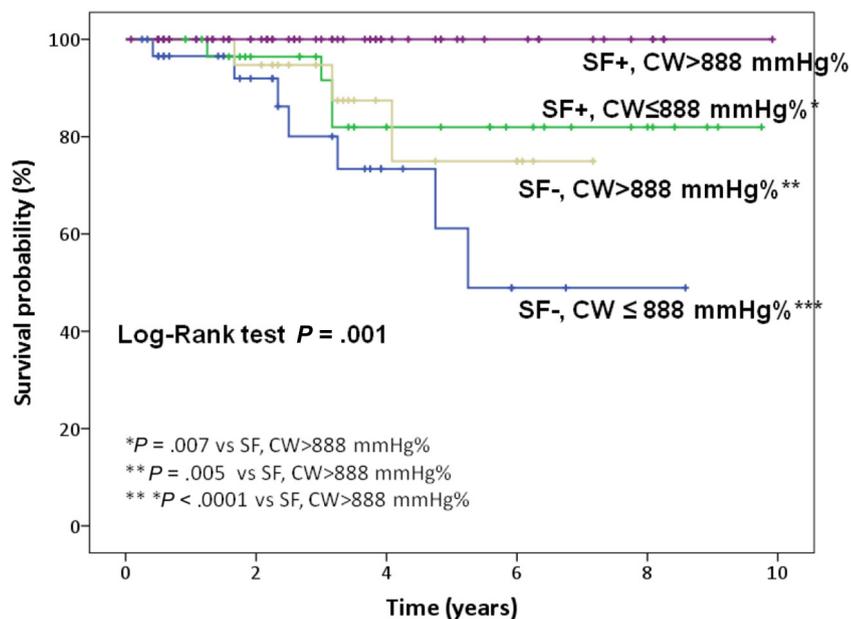
Figure 4

Freedom from cardiac death according to CW and CRT response

Kaplan-Meier estimates of the time to cardiac death in CRT responders (CRT+) and nonresponders (CRT−).
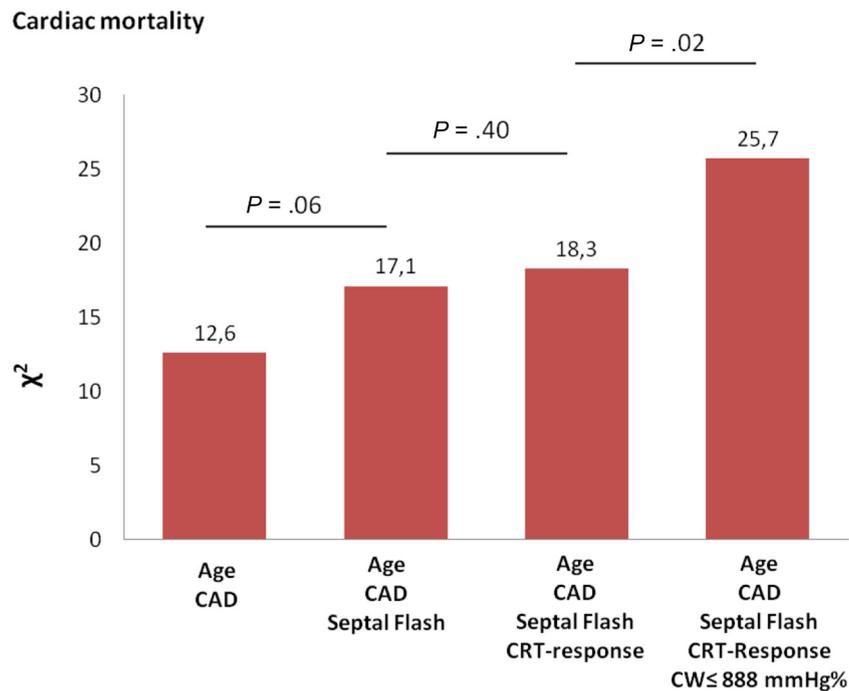
Figure 5

Freedom from cardiac death according to CW and SF

Kaplan-Meier estimates of the time to cardiac death in patients with SF (SF+) and without SF (SF−).

Figure 6

Incremental prognostic value of myocardial work on clinical variables, SF, and CRT response.

Table IV. Incremental prognostic value of clinical parameters, CRT response, and myocardial constructive work: discrimination index analysis

		Harrell C-concordance
Model 1	Age Ischemic disease	0.73
Model 2	Age Ischemic disease SF	0.75
Model 3	Age Ischemic disease SF CRT response	0.76
Model 4	Age Ischemic disease CRT response SF CW≤888 mm Hg	0.82

were created. The incremental value of each model was assessed by comparing the χ^2 value at each step. The accuracy of the Cox proportional hazards model in predicting cardiac mortality did not increase after adding SF and CRT response to clinical variables but was significantly increased by the addition of CW (Figure 6). Table IV shows the Harrell C-concordance statistic index for each model.

Discussion

In the present study, we showed that, in CRT candidates, the degree of global myocardial CW is a predictor of long-term survival independent of the presence of SF and the volumetric response to CRT.

Assessment of myocardial constructive work

PSL curves are a recently introduced tool that allows a noninvasive estimation of myocardial work. The reliability of this method with respect to the invasive estimation of myocardial work has been validated by experimental studies and mathematical models.[16,18,20] Regional differences in myocardial work assessed by PSLs have a strong correlation with the entity of myocardial glucose metabolism evaluated by FDG-PET.[16] These results support the hypothesis that the differences in CW detected by PSLs before CRT correspond to myocardial residual metabolic activity and contractile reserve and might, therefore, explain the role of baseline CW in predicting CRT response[10,11,16] and long-term survival after CRT.

Myocardial constructive work as a predictor of prognosis in CRT candidates

Although CRT has a pivotal role for the treatment of patients with HF and widened QRS, the lack of response to CRT remains an important clinical problem. From a

physiologic point of view, it seems reasonable to believe that the main effect of CRT might be observed when a delayed electrical activation is associated with significant LV mechanical delay.

Nevertheless, the origin of LV mechanical discoordination may arise from substrates—such as a regional myocardial scar or hypocontractility—that are unresponsive to the electrical stimulation of CRT.[9] In patients with HF undergoing CRT, Ciampi et al. demonstrated that the presence of contractile reserve assessed by dobutamine stress echocardiography was associated with a better prognosis independent of the presence of LV dyssynchrony.[21] In the present study, global CW was associated with CRT response and emerged as a predictor of long-term prognosis in CRT candidates; this result was independent of well-known predictors of CRT response, namely, QRS duration, LBBB, and SF.

The presence of LV dyssynchrony is traditionally considered a predictor of CRT response, and its correction by CRT is associated with good prognosis.[14,15]

In our observational study, patients with LV dyssynchrony identified by the presence of SF and CW>888 mm Hg% had the best outcomes, whereas the presence of CW<888 mm Hg% increased the risk of cardiac and all-cause death in patients with SF. The concomitant absence of SF and CW ≤888 mm Hg% was associated with a poor prognosis. These findings underscore the importance of the myocardial substrate of functional response beyond the assessment of LV dyssynchrony. Interestingly, the prognostic value of myocardial work persisted when CRT volumetric response is considered. In fact, the best prognosis was observed in CRT responders who also had a CW>888 mm Hg% before CRT implantation; the absence of response to CRT and a CW≤888 mm Hg were associated with the highest mortality.

Need for physiological understanding

The absence of myocardial viability is associated with the extent of LV remodeling before CRT and with the presence of extensive myocardial remodeling and fibrosis.[22]

In our population, CW≤888 mmH g% was associated with a greater LV size and reduced LVEF before CRT. This cutoff identified a subgroup of patients with a particularly dismal prognosis and limited positive remodeling after CRT implantation.

The possibility that LV stimulation might gradually recruit viable myocardium might, therefore, be the key to achieving significant LV reverse remodeling after CRT and improved survival. Myocardial viability can be assessed by several methods, including magnetic resonance imaging, stress echocardiography, and nuclear imaging. PSLs allow the assessment of myocardial performance in a rapid and effective manner and might, therefore, have a complementary role with respect to these costly investigations.

Speckle tracking echocardiography allows the simultaneous assessment of LV dyssynchrony, mechanical dispersion, and GLS. Previous studies have shown that the observation of LV mechanical dispersion in speckle tracking echocardiography is a predictor of ventricular arrhythmias in CRT candidates[23] and is related to LV fibrosis.[24] LV-GLS is also a well-known prognostic predictor in CRT candidates.[23,25] The assessment of myocardial work by PSLs can take into account the effect of afterload on LV function, which allows a comprehensive evaluation of LV performance.

Clinical perspectives

An increasing amount of data seems to underscore that the major benefits of CRT are observed when LV mechanical dyssynchrony is induced by an electrical activation delay. The results of the present study are not in opposition to this hypothesis but underscore the importance of the concomitant evaluation of the myocardial substrate of LV dysfunction in CRT candidates.

The existence of multiple independent mechanisms governing CRT response (eg, ECG patterns, electromechanical delay, and residual contractility) supports the hypothesis that a multimodal stepwise approach that combines clinical, electrocardiographic, and echocardiographic data might be more effective for the identification of CRT responders. Moving in that direction, the use of myocardial work seems very promising: it integrates the load, it is an automatic measurement with associated robustness, and it could be used as a global and a regional myocardial function parameter.

Limitations

This is a monocentric, retrospective study aimed at assessing the relationship between CW and mortality in CRT candidates. With respect to previous studies, which often include all-cause mortality and HF hospitalization in the primary end point, we focused specifically on the predictors of cardiac mortality. The overall cardiac mortality rate in our survey was relatively low (4%), which might be attributed to the high percentage of CRT responders (70%), the relatively low prevalence of ischemic cardiomyopathy (29%), and the significant increase in LVEF observed in responders (Table II). No validation cohort was created to replicate our findings on myocardial work, which currently limits its application in everyday clinical practice. Precise myocardial scar localization and extension by cardiac magnetic resonance imaging or nuclear imaging were not investigated in the current study, as far as the relationship between scar localization and LV lead position. Such investigations may be important to further understand the relationship between regional CW and LV function improvement in CRT candidates and should be the object of a future study.

As for many other echo parameters, the proper assessment of myocardial work requires a suitable

acoustic window and is not applicable to patients with poor echogenicity.

Until now, the validation of the noninvasive estimation of myocardial work by PSLs analysis has been restricted to patients to CRT candidates, patients with dilated cardiomyopathy of ischemic and nonischemic etiology, and patients with arterial hypertension,[16,18,19] which limits the reliable application of this method to these specific subsets of cardiac diseases.

Conclusions

CW assessed by PSLs is a recently introduced parameter that can predict long-term prognosis in CRT candidates. Patients with CW≤888 mm Hg% had a nearly 5-fold increased risk of cardiac death. CW assessment improves the prediction of mortality over the classical predictors of CRT prognosis, including LV dyssynchrony and CRT volumetric response, and allows the identification of a subset of patients with a significantly dismal prognosis.

Acknowledgments

Disclosures

Professor Smiseth is a co-inventor but no longer has ownership of the patent "Method for myocardial segment work analysis," which was used to calculate myocardial work. The other authors report that there are no conflicts of interest.

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