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of disease-modifying therapy. During this study, these changes were less clear in women, and the impact of ERT was more pronounced. Although LV mass increased in women on ERT, T1 time increased, which could be consistent with either a sex-dependent response to therapy or a difference in myocardial response to storage. Limitations included the small sample size and lack of established prognostic T1 data, which made the relevance and importance of this parameter in disease progression unclear.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Cardiovascular Imaging* author instructions page.

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Regional Left Ventricular Myocardial Work Indices and Response to Cardiac Resynchronization Therapy

Cardiac resynchronization therapy (CRT) is a well-established heart failure (HF) treatment and exerts its effects through restoration of synchronous ventricular contraction. Myocardial work (MW) is a novel semiautomatic echocardiographic method which characterizes the efficacy of the left ventricular (LV) contraction by evaluating the amount of energy loss (wasted work [WW]) and the amount of work performed (constructive work [CW]) for each myocardial segment (1). We investigated regional differences in CW and WW between the septum and the lateral wall, its potential implications for CRT response, as well as the pattern of changes occurring early after CRT implantation. The review board of the Leiden University Medical Center approved this retrospective analysis of clinically acquired data and waived the need for patient written informed consent.

A total of 168 patients (71% men, mean age 65 $\pm$ 10 years) with HF and sinus rhythm were included. Speckle-tracking echocardiography was used to assess MW at baseline and early after CRT implantation (within the first 5 days). LV global longitudinal strain, noninvasive blood pressure measurements, and valves opening and closure times were integrated to construct pressure-strain loops. CW and WW of the septal and lateral walls were calculated as the average values of basal and mid-ventricular segments. CRT response was defined as a decrease in LV end-systolic volume $\geq$15 % at 6-month follow-up. The interobserver and intraobserver variability of MW indices was assessed calculating the intraclass correlation coefficient (ICC) on 35 randomly selected patients. Both interobserver and intraobserver variability was excellent for segmental CW (ICC >0.93) and acceptable for segmental WW (ICC >0.75).

Table 1 summarizes baseline characteristics and regional MW indices before and after CRT implantation in the overall population, CRT responders, and nonresponders. Nonischemic etiology of HF was significantly more frequent in CRT responders ($p = 0.027$). At baseline, CRT responders demonstrated significantly larger septal WW ($p = 0.038$) and lateral CW ($p = 0.005$) compared with nonresponders.

TABLE 1 Patient Characteristics at Baseline According to CRT Response and Changes in CW and WW of the Lateral Wall and Septum After CRT Implantation

	Overall Population (N = 168)	Responders (n = 99)	Nonresponders (n = 69)	p Value
Age at implantation, yrs	65 ± 10	65 ± 10	65 ± 11	0.980
Male	119 (71)	69 (70)	50 (73)	0.698
Etiology (nonischemic)	78 (46)	53 (54)	25 (36)	**0.027**
QRS morphology (LBBB)	91 (54)	59 (60)	32 (46)	0.091
Lateral lead position*	78 (57)	47 (55)	31 (59)	0.713
Quality of life, score	26.0 (11.5-44.0)	23.5 (11.0-42.5)	28.0 (14.0-45.0)	0.305
6MWT, m	347.5 ± 112.9	343.4 ± 108.4	353.9 ± 120.4	0.620
NYHA functional class				
II	54 (32)	32 (32)	22 (32)	0.952
III	101 (60)	60 (61)	41 (59)	0.877
IV	13 (8)	7 (7)	6 (9)	0.698
Medication				
Diuretic	137 (82)	78 (79)	59 (86)	0.269
ACE inhibitor	144 (86)	84 (85)	60 (87)	0.701
β-blocker	124 (74)	77 (78)	47 (68)	0.161
Digoxin	17 (10)	9 (9)	8 (12)	0.597
Diabetes	34 (20)	18 (18)	16 (23)	0.427
GFR, ml/min/1.73m^2	69.7 ± 29.3	69.2 ± 26.0	70.4 ± 33.6	0.818
QRS duration, ms	161.2 ± 23.2	162.8 ± 20.0	158.8 ± 27.0	0.298
LVEDV, ml	214.4 ± 76.6	208.9 ± 73.2	222.4 ± 81.1	0.263
LVESV, ml	161.8 ± 65.3	157.1 ± 62.6	168.5 ± 68.9	0.266
LVEF, %	25.3 ± 7.0	25.7 ± 7.1	24.8 ± 7.0	0.427
CW of the septum, mm Hg %	506.3 (253.8-826.1)	499.5 (253.0-804.5)	511.0 (241.5-953.8)	0.791
WW of the septum, mm Hg %	248.0 (136.4-425.5)	270.5 (160.0-451.5)	210.5 (106.3-336.5)	**0.038**
CW of the lateral wall, mm Hg %	866.0 (526.9-1,362.4)	989.5 (574.0-1,439.0)	689.0 (463.3-1,140.0)	**0.005**
WW of the lateral wall, mm Hg %	146.5 (71.3-284.5)	144.5 (85.0-271.5)	155.0 (43.5-292.3)	0.574

	Bl	Pi	p Value	Bl	Pi	p Value	Bl	Pi	p Value
CW of the septum†, mm Hg %	465.5 (222.0-826.5)	655.0 (412.5-954.5)	**<0.001**	433.0 (254.5-686.5)	664.5 (424.5-977.8)	**<0.001**	501.5 (192.3-976.6)	635.8 (393.8-898.0)	0.223
WW of the septum†, mm Hg %	255.0 (135.5-431.0)	164.5 (75.5-272.0)	**0.001**	305.0 (169.0-461.3)	145.0 (80.0-306.3)	**0.005**	202.8 (102.9-332.5)	168.5 (67.6-258.4)	**0.049**
CW of the lateral wall†, mm Hg %	840.5 (506.0-1,307.0)	676.0 (484.5-1,047.0)	**0.004**	1,036.5 (561.001,402.0)	818.0 (491.0-1,154.3)	**0.005**	566.5 (385.5-1,044.6)	658.0 (407.8-826.0)	0.282
WW of the lateral wall†, mm Hg %	133.0 (69.5-276.0)	206.5 (114.0-334.0)	**0.005**	132.5 (80.3-269.3)	198.5 (107.5-331.0)	**0.025**	142.3 (40.0-296.5)	208.5 (120.4-334.1)	0.076

Values are mean ± SD, n (%), or median (interquartile range). *Frequency of LV lead placed in the lateral wall was calculated for 138 patients with known LV lead position. †Values of CW and WW of the septum and lateral wall were compared in 115 patients (CRT responders n = 69, 60%) in which assessment of MW indices was feasible immediately after CRT implantation (within the first 5 days).

6MWT = 6-min walk test; Bl = baseline; CRT = cardiac resynchronization therapy; CW = constructive work; GFR = glomerular filtration rate; LBBB = left bundle branch block; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; NYHA = New York Heart Association; Pi = postimplantation; WW = wasted work.

To investigate the association between baseline regional MW and CRT response, a logistic regression analysis was performed. Among other baseline characteristics only nonischemic etiology (odds ratio [OR]: 2.028; 95% confidence interval [CI]: 1.08 to 3.808; p = 0.028), larger lateral wall CW (OR: 1.001; 95% CI: 1.000 to 1.001; p = 0.008), and larger septal WW (OR: 1.002; 95% CI: 1.000 to 1.003; p = 0.032) were associated with response to CRT. They were included in multivariate model (chi-square = 13.4; p = 0.004), where only CW of the lateral wall remained independently associated with CRT response (OR: 1.001; 95% CI: 1.000 to 1.001; p = 0.048).

On receiver-operating characteristic curve analysis, the area under the receiver-operating characteristic curve for CW of the lateral wall (0.628) and WW of the septum (0.594) was greater compared with the area under the receiver-operating characteristic curve of QRS duration (0.568), nonischemic etiology (0.587), and left bundle branch block morphology (0.566). A cutoff value of 332 mm Hg% for the septal WW and 881 mm Hg% for the lateral wall CW were best predictors for CRT response. On multivariate analysis (chi-square = 17.0; p = 0.001), lateral wall CW >881 mm Hg% remained independently associated with CRT response (OR: 2.237; 95% CI: 1.154 to 4.335; p = 0.017).

Within the first 5 days after CRT implantation, blood pressure measurements for pressure-strain loop analysis were available in 115 (69%) patients.

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Compared with nonresponders, CRT responders showed improvement in septal CW and WW, whereas the lateral wall demonstrated a significant decrease in CW and increase in WW (**Table 1**). Method of MW evaluation allows to detect different patterns of segmental changes in CW and WW between CRT responders and nonresponders with significant correction of unbalanced MW distribution in CRT responders, which can be observed already in the first days after CRT implantation.

In this retrospective study, we demonstrated differences in baseline segmental MW indices between CRT nonresponders and responders, the latter being characterized by larger WW of the septum and larger CW of the lateral wall. Importance of contractile reserve for CRT response has been previously reported (2). On multivariate analysis baseline CW of the lateral wall was independently associated with CRT response. Although the presented OR may indicate lack of discriminative value in clinical practice, similar findings for MW indices OR were reported in other studies (3). Considering the complexity of mechanisms involved in CRT response, these data suggest that CW of the lateral wall is 1 of the contributors to the reverse remodeling and should be further investigated in larger studies.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Cardiovascular Imaging* author instructions page.

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LETTERS TO THE EDITOR

"Quadruple Rule-Out" With Computed Tomography in a COVID-19 Patient With Equivocal Acute Coronary Syndrome Presentation

A 59-year-old man from an endemic area for coronavirus disease-2019 (COVID-19) in northern Italy presented to the hospital with dyspnea and chest pain. On physical examination, his temperature was 36.9°C and electrocardiogram showed ST-segment elevation in leads V_2 to V_3. The blood tests showed leukopenia (3,800 cells/μl) and troponin I increase (140 ng/l). Chest X-ray showed no pathological findings. Because of the COVID-19 emergency, a large-scale hub-and-spoke model was developed in the Lombardy region to select dedicated cardiology centers for management of acute coronary syndromes (ACS) to support other general hospitals that were converted to treat only patients with COVID-19 (1). In agreement with this model, the patient received a nasopharyngeal swab that tested positive for SARS-CoV-2 and subsequently underwent invasive coronary angiography (ICA) in a dedicated catheterization laboratory. ICA demonstrated normal coronary arteries with a diagnosis of myocardial injury with nonobstructive coronary artery disease. Although cardiac magnetic resonance (CMR) was considered for further evaluation, it was not performed because of equipment and room cleaning and disinfection issues. The day after admission, to evaluate for lung infection, pulmonary embolism, and myocardial injury, as suspected by biomarker elevation, a modified scan protocol including a nonenhanced acquisition followed by electrocardiogram-triggered contrast-enhanced computed tomography (CT) with delayed