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ORIGINAL RESEARCH

LA Mechanics in Decompensated Heart Failure

Insights From Strain Echocardiography With Invasive Hemodynamics

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ABSTRACT

OBJECTIVES The aim of this study was to assess the effect of congestion and decongestive therapy on left atrial (LA) mechanics and to determine the relationship between LA improvement after decongestive therapy and clinical outcome in immediate or chronic heart failure with reduced ejection fraction (HFrEF).

BACKGROUND LA mechanics are affected by volume/pressure overload in decompensated HFrEF.

METHODS A total of 31 patients with HFrEF and immediate heart failure (age 64 ± 15 years, 74% male, left ventricular ejection fraction 20 ± 12%) underwent serial echocardiography during decongestive therapy with simultaneous hemodynamic monitoring. LA function was assessed by strain (rate) imaging. Patients were re-evaluated 6 weeks after discharge and prospectively followed up for the composite endpoint of heart failure readmission and all-cause mortality.

RESULTS LA reservoir function was markedly reduced at baseline and improved with decongestion (peak atrial longitudinal strain from 6.4 ± 2.2% to 8.8 ± 3.0% and strain rate from 0.29 ± 0.11 s^{-1} to 0.38 ± 0.13 s^{-1}), independent of changes in left ventricular global longitudinal strain, LA end-diastolic volume, and mitral regurgitation severity ($p < 0.001$). Both measures continued to rise at 6 weeks (up to 13.4 ± 6.1% and 0.50 ± 0.19 s^{-1}, respectively; $p < 0.001$). LA pump strain rate only increased 6 weeks after discharge (-0.25 ± 0.12 s^{-1} to -0.55 ± 0.29 s^{-1}; $p < 0.010$). Changes in LA mechanics correlated with changes in wedge pressure ($r = -0.61$; $p < 0.001$). Lower peak atrial longitudinal strain values after decongestion were associated with increased risk for the composite endpoint of heart failure and mortality ($p < 0.019$).

CONCLUSIONS LA reservoir and booster function, while severely impaired during immediate decompensation, significantly improve during and after decongestive therapy. Poor LA reservoir function after decongestion is associated with worse outcome. (J Am Coll Cardiol Img 2020;■:■-■) © 2020 by the American College of Cardiology Foundation.

The pathophysiological contribution and prognostic impact of left atrial (LA) mechanics in heart failure are often underappreciated. More than solely being a passive extension of the left ventricle, the left atrium can be regarded as a dynamic continuum of the left ventricle with a principal role of ensuring left ventricular (LV) filling and cardiac performance by its reservoir, conduit, and booster pump function (1). This 3-phase role depends not only on LV diastolic and systolic function but also

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ABBREVIATIONS AND ACRONYMS

2D = two-dimensional

HFrEF = heart failure with reduced ejection fraction

LA = left atrial

LV = left ventricular

LVEF = left ventricular ejection fraction

PALS = peak atrial longitudinal reservoir strain

PAWP = pulmonary artery wedge pressure

on intrinsic LA properties (1-3). As such, any alteration in ventricular performance or loading condition may affect the interdependence between the left atrium and the left ventricle. To date, few studies have assessed the effect of congestion and decongestive therapy on LA mechanics. The current study sought to determine the effects of hemodynamic congestion and decongestive therapy on LA mechanics in acutely decompensated chronic heart failure with reduced ejection fraction (HFrEF). Furthermore, the relation between changes in LA function, LV filling pressures, responsiveness to decongestive therapy, and clinical outcome was assessed.

METHODS

STUDY DESIGN. Patients with acutely decompensated HFrEF admitted in the heart failure intensive care unit of a single tertiary care center (Ziekenhuis Oost-Limburg, Genk, Belgium) were prospectively included between 2011 and 2013 to undergo invasive hemodynamic monitoring and simultaneous echocardiography (4). Comprehensive echocardiographic data, laboratory data, and hemodynamic measurements were always obtained simultaneously in a congestive state (at admission in resting conditions on average 1 h after pulmonary artery catheter placement) and after optimization of cardiac filling pressures (pulmonary artery wedge pressure [PAWP] <18 mm Hg and central venous pressure <8 mm Hg), through decongestive therapy with diuretic agents and intravenous sodium nitroprusside switched to oral hydralazine and neurohumoral blockers per protocol (4). Six weeks after hospital discharge, patients were evaluated at the outpatient clinic with repeat echocardiography. In addition, the initial study cohort was followed up prospectively for the development of heart failure readmission and all-cause mortality.

The study complied with the Declaration of Helsinki, and the locally appointed ethics committee approved the research protocol. Written informed consent was obtained from every patient before any study-specific procedure was performed.

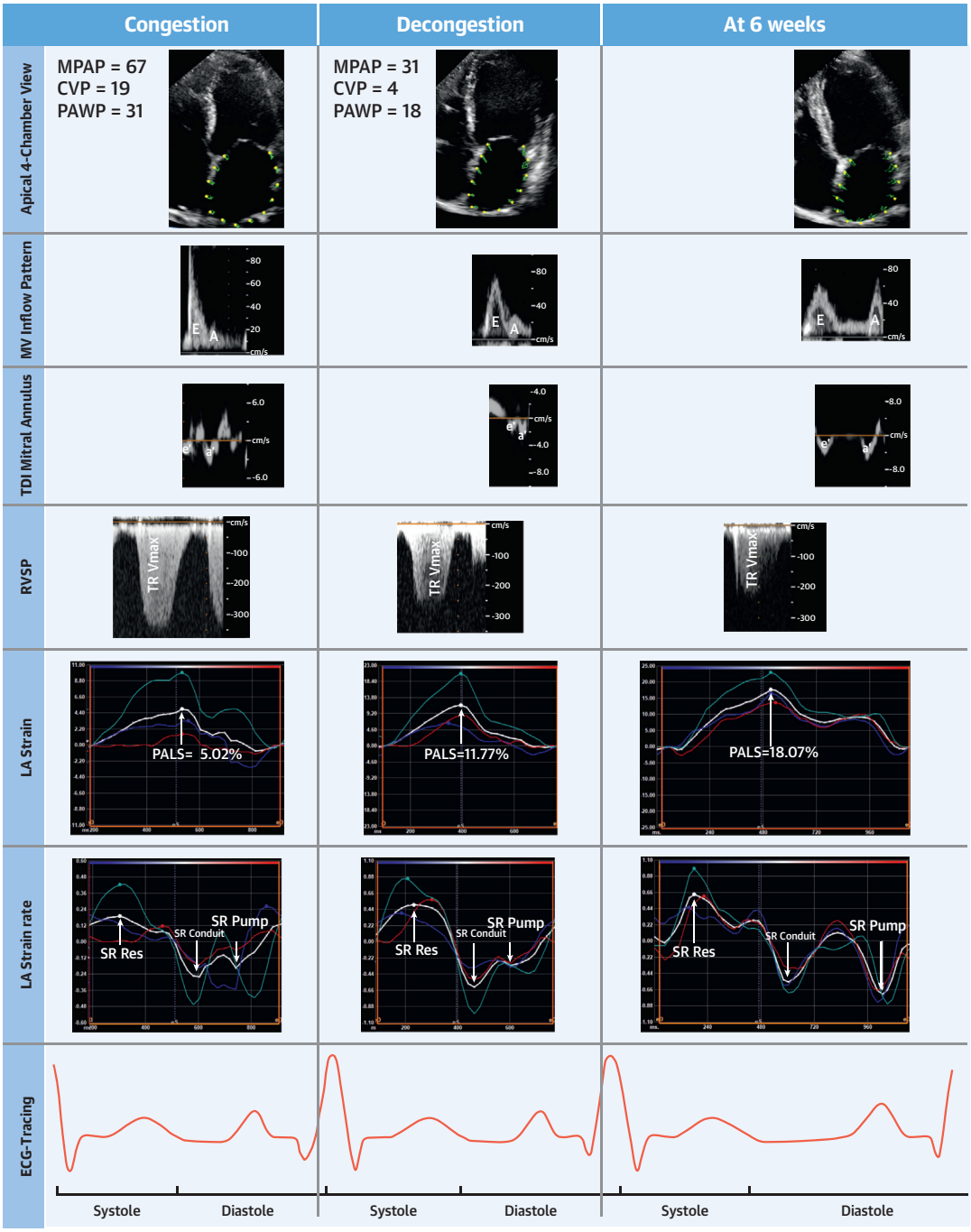
STUDY POPULATION. Patients were eligible if they were ≥18 years of age and presented with symptomatic decompensated HFrEF warranting invasive hemodynamic-guided therapy according to their treating cardiologist. Additional inclusion criteria were: 1) left ventricular ejection fraction (LVEF) ≤40%, restrictive LV filling pattern on echocardiography in addition to a right ventricular systolic pressure ≥40 mm Hg; and 2) agreement of the patient with the placement of a radial and pulmonary artery catheter (Swan-Ganz Continuous Cardiac Output Thermodilution Catheter 744HF75, Edwards Lifesciences, Irvine, California) for study purposes. Exclusion criteria after obtaining baseline hemodynamic measurements were: 1) PAWP <15 mm Hg; 2) mean pulmonary arterial pressure <25 mm Hg; 3) cardiac index ≥2.6 l/min/m^2; 4) need for inotropic support or ventricular assist devices; 5) previous mitral valve intervention; and 6) insufficient imaging quality to allow adequate speckle-tracking echocardiography.

BASELINE HEMODYNAMIC MEASUREMENTS. At inclusion, the pulmonary artery catheter was placed with fluoroscopic guidance in the catheterization laboratory. Baseline hemodynamic measurements were performed in the supine position at end-expiration with the balloon-tipped pulmonary artery catheter at steady state 1 h after placement. During hemodynamic and echocardiographic measurements, an arterial and mixed venous blood sample was collected for blood gas analysis, used for the calculation of cardiac output/index according to the Fick equation (4).

IMAGE ACQUISITION AND STORAGE. Comprehensive two-dimensional (2D) echocardiographic examinations were performed with a commercially available system (IE33 Philips Medical Systems, Andover, Massachusetts) during stable electrocardiography recording at the same moment invasive hemodynamic assessments were performed. Standard 2D and Doppler echocardiographic images were acquired by experienced cardiac sonographers. Echocardiographic images were stored as DICOM files on a secured server and analyzed off-line, using third-party software Image arena version 4.6 (TomTec Imaging Systems GmbH, Unterschleissheim, Germany). All echocardiographic parameters were measured according to the American Society of Echocardiography guidelines (5). LV volumes and LVEF were measured by using the modified Simpson rule. Mitral regurgitation was graded as trace, mild, moderate, or severe by using an integrated approach, as recommended (6).

ASSESSMENT OF LA MECHANICS. LA maximum volume (at the end of ventricular systole) and LA minimum volume (at the end of LV diastole) were measured by using the modified Simpson rule. Furthermore, the 3-fold action of the left atrium (reservoir, conduit, and booster pump function) was assessed by using strain and strain rate imaging derived from 2D speckle-tracking echocardiography

CENTRAL ILLUSTRATION **Evolution of Left Atrial Strain (Rate) and Conventional Echocardiographic Parameters of Diastolic Function After Decongestion and at 6-Week Follow-up**



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During immediate congestion, a restrictive mitral inflow pattern is found along a depressed mitral annulus septal e′ and severely depressed left atrial (LA) reservoir and booster pump function. After decongestion and further follow-up until 6 weeks after hospital discharge, significant increments in LA reservoir function (peak atrial longitudinal reservoir strain [PALS]) appear. Booster pump strain rate (SR), a measure of LA contractile function, only increases significantly as of 6 weeks.
CVP = central venous pressure; ECG = echocardiography; MPAP = mean pulmonary artery pressure; MV = mitral valve; PAWP = pulmonary artery wedge pressure; RVSP = right ventricular systolic pressure; SR Res = strain rate reservoir; TDI = tissue Doppler-derived imaging; TR Vmax = maximum velocity of the tricuspid regurgitant velocity jet.

according to the EACVI/ASE/Industry Task Force recommendations to standardize deformation imaging (7). Offline speckle-tracking analysis of the phasic LA function was performed by using a commercially available software package (2D cardiac performance analysis, Image arena version 4.6). Peak atrial longitudinal strain (PALS) was determined as the peak positive strain value during late systole on the averaged longitudinal strain curve. In addition, the (positive) reservoir strain rate in late systole, the (negative) conduit strain rate in early diastole, and the (negative) pump strain rate were determined from the averaged LA longitudinal strain rate curve.

The **Central Illustration** summarizes the evolution of LA strain parameters in addition to conventional echocardiographic indices of diastolic function. Supplemental Table 1 presents the interobserver variability of LA functional measurements, illustrating overall excellent agreement (intraclass correlation coefficient >0.9 for strain [rate] measurements both in a congestive state and after decongestive therapy).

CLINICAL FOLLOW-UP. All patients were followed up prospectively for the development of heart failure readmissions or all-cause mortality. Heart failure readmissions were defined as unscheduled hospitalizations during which intravenous diuretic agents were administered because of signs and symptoms of congestion. Censoring occurred when the final patient had completed 1 year of follow-up.

STATISTICAL ANALYSIS. Categorical data are expressed as numbers and proportions and compared by using the chi-square test. Continuous variables are expressed as mean ± SD if normally distributed or median [interquartile range] if not. Normality was assessed by using the Shapiro-Wilk statistic. Repeated measurements were compared by using the paired Student's *t*-test. To account for between-subject differences and adjust for co-variates (in-subject differences), an analysis of covariance model was built assessing changes in between-subject factors and within-subject factors. Pearson's correlation was used to assess the relation between 2 or more continuous variables if parametric assumptions were met. Kaplan-Meier curves were constructed, with the log-rank test used to test differences in event rate for the combined endpoint of all-cause mortality and heart failure readmission. Statistical significance was always set at a 2-tailed probability level of <0.05. Statistics were performed by using SPSS version 22 (IBM SPSS Statistics, IBM Corporation, Armonk, New York).

RESULTS

STUDY POPULATION. A total of 37 patients were initially included in the prospective protocol; 6 patients were excluded from LA strain analysis due to insufficient quality of the LA image acquisition. Baseline characteristics of the patient population (N = 31) are summarized in **Table 1**. Patients were on average 64 ± 15 years of age; 77.4% were male with a mean LVEF of 20 ± 12%. There was an equal proportion of patients with an ischemic and a nonischemic etiology of heart failure. At the time of admission, patients were "cold and wet," as reflected by a PAWP of 26 ± 7 mm Hg, a central venous pressure of 14 ± 7 mm Hg, and a cardiac index of 1.8 ± 0.5 l/min/m^2. Ten patients presented with atrial fibrillation at admission and remained in atrial fibrillation even after decongestion. Of the patients in sinus rhythm at study entry, none developed atrial arrhythmias thereafter. The use and doses of neurohumoral blocker therapy were similar for all patients after discharge.

Hemodynamic changes before and after decongestive therapy are summarized in **Table 2**. PAWP decreased to 15 ± 7 mm Hg ($p < 0.001$) and central venous pressure to 6 ± 5 mm Hg ($p < 0.001$). The median N-terminal pro-B-type natriuretic peptide level was 3,901 pg/ml (1,825 to 8,231 pg/ml) (**Table 1**) and 2,288 pg/ml (1,059 to 3,364 pg/ml) at admission and discharge, respectively. N-terminal pro-B-type natriuretic peptide levels at admission were comparable between patients with PALS after decongestion above the mean versus below the mean, although there was a trend toward lower values at discharge in the latter subgroup ($p = 0.316$ and $p = 0.060$, respectively).

LA FUNCTION BEFORE AND AFTER DECONGESTIVE THERAPY. At baseline, LA volume index was 69 ± 26 ml/m^2. Reservoir function was markedly reduced as assessed by PALS (6.42 ± 2.21%) and reservoir strain rate (0.29 ± 0.11 s^{-1}). Pump strain rate was -0.25 ± 0.12 s^{-1} (**Table 3**). Baseline PALS and LV global longitudinal strain were moderately correlated ($r = -0.58$; $p = 0.002$). Patients with PALS below the sample mean exhibited significantly larger LA end-diastolic and end-systolic volumes ($p < 0.001$).

After decongestion, both PALS and reservoir strain rate increased significantly (6.42 ± 2.21% to 8.80 ± 3.00% and 0.29 ± 0.11 s^{-1} to 0.38 ± 0.13 s^{-1}, respectively; $p < 0.001$ for both). The improvement in LA reservoir function was independent of changes in LV global longitudinal strain ($p < 0.001$), changes in

TABLE 1 Baseline Characteristics of the Study Population (N = 31)

Demographic characteristics and comorbidities	
Age, yrs	64 ± 15
Male sex	24 (77.4)
Ischemic cardiomyopathy	15 (48.4)
NYHA functional class III/IV	16 (51.6)/9 (29.0)
Obesity	11 (35.5)
Hypertension	15 (48.4)
Diabetes	9 (29.0)
Dyslipidemia	19 (61.3)
History of atrial fibrillation	10 (32.3)
Clinical characteristics	
BMI, kg/m^2	28.1 ± 6.0
Sinus rhythm	22 (71.0)
eGFR, ml/min/1.73 m^2	62.4 ± 21.5
NT-proBNP, pg/ml	3,901 (1,825-8,231)
Heart failure medication	
ACE inhibitor or ARB	16 (51.6)
Hydralazine	8 (25.8)
Beta-blocker	23 (74.2)
MRA	13 (41.9)
Loop diuretic	18 (58.1)
Baseline echocardiographic parameters	
LVEDV, ml	229 ± 79
LVESV, ml	182 ± 74
LVEF, %	20 ± 12
LV endoGLS, %	-7.3 ± 3.5
E, m/s	0.9 ± 0.2
A, m/s (if sinus rhythm)	0.4 ± 0.1
E/A (if sinus rhythm)	2.6 ± 0.7
MV deceleration time, ms	139.7 ± 42.1
Mean E/e′ (septal and lateral)	16.8 ± 6.6
Moderate or higher MR	16 (51.6)

Values are mean ± SD or n (%), unless otherwise indicated.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BMI = body mass index; BSA = body surface area; eGFR = estimated glomerular filtration rate; LV endoGLS = left ventricular endocardial global longitudinal strain; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; MR = mitral regurgitation; MRA = mineralocorticoid receptor antagonist; MV = mitral valve; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association.

TABLE 2 Resting Hemodynamic Variables at Admission and After Decongestive Therapy

	Admission	After Decongestive Therapy	p Value
Heart rate, beats/min	84 ± 20	78 ± 12	0.013*
SBP, mm Hg	126 ± 23	112 ± 19	<0.001*
DBP, mm Hg	76 ± 15	59 ± 10	<0.001*
MAP, mm Hg	93 ± 14	77 ± 10	<0.001*
CVP, mm Hg	14 ± 7	6 ± 5	<0.001*
SPAP, mm Hg	58 ± 11	40 ± 16	<0.001*
DPAP, mm Hg	28 ± 8	18 ± 8	<0.001*
MPAP, mm Hg	38 ± 8	26 ± 10	<0.001*
PAWP, mm Hg	26 ± 7	15 ± 7	<0.001*
Cardiac index, l/min/m^2	1.8 ± 0.5	2.2 ± 0.7	0.002*

Values are mean ± SD. *Significant longitudinal change from baseline to follow-up.

CVP = central venous pressure; DBP = diastolic blood pressure; DPAP = diastolic pulmonary artery pressure; MAP = mean arterial pressure; MPAP = mean pulmonary artery pressure; PAC = pulmonary artery compliance; PAWP = pulmonary artery wedge pressure; SBP = systolic blood pressure; SPAP = systolic pulmonary artery pressure.

MR/LA severity ($p < 0.001$), changes in LA end-diastolic volume ($p < 0.001$), or baseline LA end-diastolic volume ($p = 0.001$). As illustrated in Figures 1A and 1B, both PALS and reservoir strain rate continued to increase at 6 weeks after discharge (up to 13.44 ± 6.08% and 0.50 ± 0.19 s^{-1}; $p < 0.001$ for both compared with either baseline or discharge). Conversely, conduit and pump strain rate did not improve promptly after decongestion ($p = 0.071$ and $p = 0.103$). Only after 6 weeks, a significant improvement in LA contractility-assessed by booster pump strain rate-was assessed by booster pump strain rate, found (-0.25 ± 0.12 s^{-1} at baseline to -0.55 ± 0.29 s^{-1} at 6 weeks; $p < 0.010$) (Figure 1C).

At baseline, no significant correlation was found between PALS and PAWP ($p = 0.269$) (Figure 2A). After decongestive therapy, there was a moderate correlation between PALS and PAWP ($r = -0.50$; $p = 0.006$) (Figure 2B). Larger decreases in PAWP during decongestion correlated with larger increases in PALS ($r = -0.61$; $p < 0.001$) (Figure 2C). Adjusted for LV end-diastolic volume, LV end-systolic volume, LV global longitudinal strain, and LA volume index, PALS after decongestion remained an independent predictor for PAWP (forward multivariate linear regression model; $p = 0.033$).

PROGNOSTIC VALUE OF RESERVOIR FUNCTION ON HEART FAILURE HOSPITALIZATION AND ALL-CAUSE MORTALITY. Mean follow-up was 655 ± 289 days. Thirteen patients were readmitted for immediate decompensated heart failure (n = 10 vs. n = 3 PALS after decongestion below and above the mean, respectively; log-rank test; $p = 0.030$). Five patients

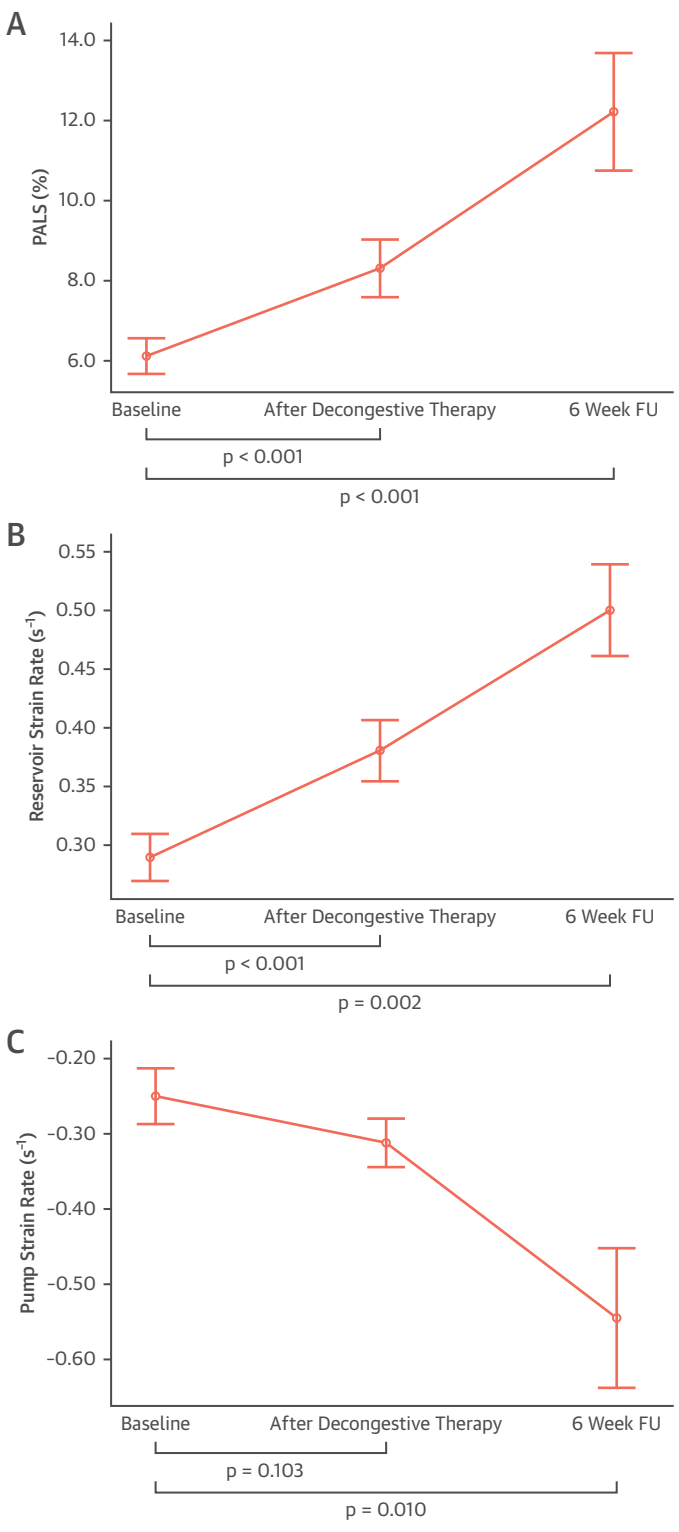
TABLE 3 Functional and Mechanical LA Parameters at Baseline and After Decongestion and at 6 Weeks

	Baseline	After Decongestion	6-Week Follow-up
LA EDV, ml	108 ± 42	93 ± 43*†	78 ± 34*,†
LAVI, ml/m^2	69 ± 26	64 ± 25*	59 ± 18‡
LA endoGLS, %	6.04 ± 2.35	8.25 ± 3.27*	13.5 ± 5.90*,†
PALS, %	6.42 ± 2.21	8.80 ± 3.0*	13.44 ± 6.08*,†
SR reservoir, s^{-1}	0.29 ± 0.11	0.38 ± 0.13*	0.50 ± 0.19*,†
SR conduit, s^{-1}	-0.40 ± 0.21	-0.47 ± 0.21	-0.52 ± 0.31
SR pump, s^{-1} (if sinus rhythm)	-0.25 ± 0.12	-0.31 ± 0.10	-0.55 ± 0.29†,‡

Values are mean ± SD. *$p < 0.001$ compared with baseline. †$p < 0.05$ compared with value after decongestion. ‡$p < 0.01$ compared with baseline.

endoGLS = endocardial global longitudinal strain; EDV = end-diastolic volume; LA = left atrial; LAVI = left atrial volume index; PALS = peak atrial longitudinal reservoir strain; SR = strain rate.

FIGURE 1 Longitudinal Changes in PALS, Reservoir Strain Rate, and Booster Pump Strain Rate After Decongestive Therapy



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died in the subgroup with lower decongested PALS, opposed to 1 in the other subgroup (log-rank test; p = 0.140). Figure 3 shows the Kaplan-Meier curve for the combined endpoint of heart failure recurrence and all-cause mortality. Baseline PALS was not predictive (p = 0.471). Lower PALS values after decongestion (i.e., below the sample mean) were associated with a higher event rate (log-rank test; p < 0.019). In a forward conditional multivariable model incorporating LA volume index, LV end-diastolic volume, and LV global longitudinal strain, PALS after decongestion remained independently associated with the composite endpoint (hazard ratio: 0.78; 95% confidence interval: 0.62 to 0.97; p = 0.030). These differences in outcome were despite largely comparable baseline patient characteristics, resting hemodynamic values, and echocardiographic features (Supplemental Table 2). Similarly, less recovery of PALS after decongestive therapy (ratio of delta PALS/PALS after decongestion below a median value of 33%) was associated with higher event rates (log-rank test; p < 0.038) (Supplemental Figure 1). In contrast, conventional parameters such as mean E/e′ or LA volume index after decongestion were not predictive of the combined endpoint (log-rank test; p = 0.091 and p = 0.067).

DISCUSSION

This study adds novel information about the effects of decongestive therapy on alterations in LA mechanical function and its association with outcomes in advanced decompensated HFrEF. Key findings of this study are, first, decongestive therapy and afterload reduction acutely improved LA reservoir function, assessed by PALS and reservoir strain rate. Second, while immediate changes in PAWP during decongestive therapy correlated with immediate

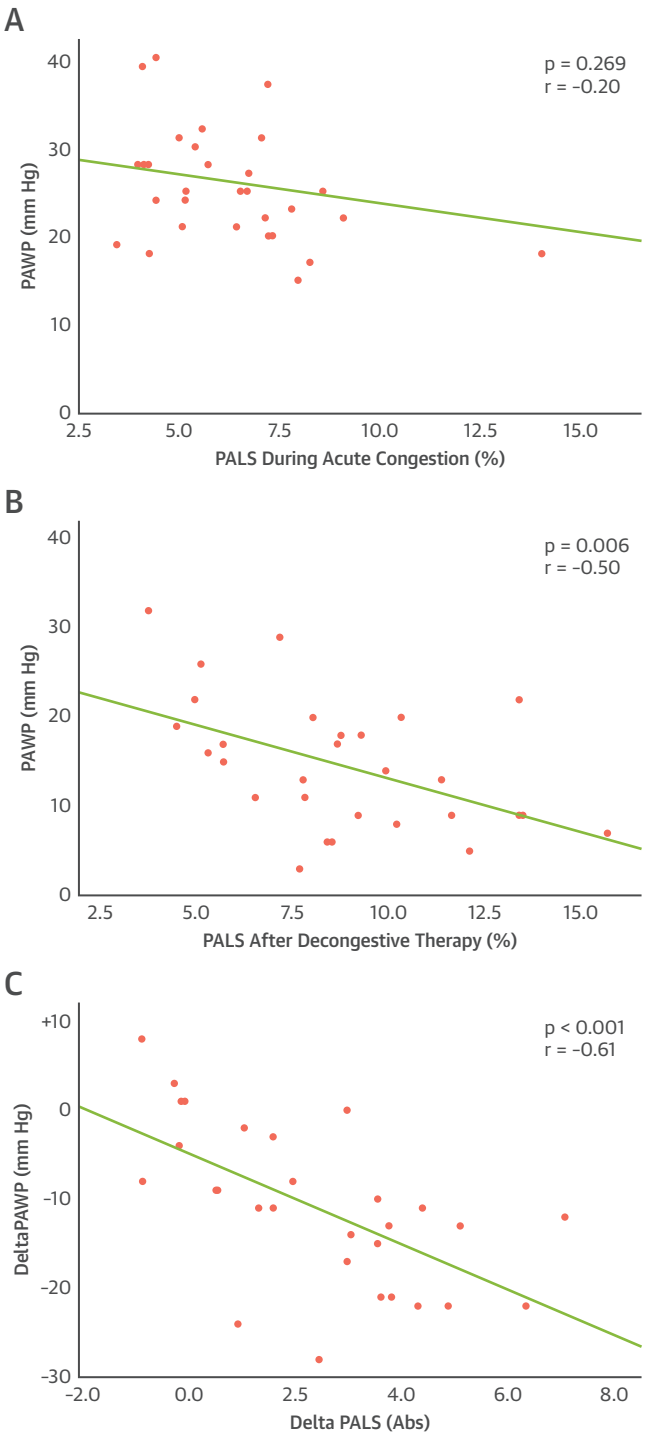
FIGURE 1 Continued

(A and B) In advanced heart failure with reduced ejection fraction with high filling pressures and low cardiac output, peak atrial longitudinal reservoir strain (PALS) and reservoir strain rate, both measures of left atrial (LA) reservoir function, are markedly declined. PALS and reservoir strain rate significantly improve immediately after decongestive therapy and a further 6 weeks after hospital discharge. **(C)** Opposed to PALS and reservoir strain rate, pump strain rate (a measure of LA booster pump activity) only improves significantly 6 weeks after hospital discharge. Presumably, recovery of intrinsic atrial booster pump function requires time to be effective. Of note, a more negative value coincides with a higher booster pump function. Error bars represent SEM. FU = follow-up.

changes in LA reservoir function, intrinsic LA mechanics (including contractile function) improved incrementally up to 6 weeks after appropriate decongestion, even in advanced heart failure states. Third, PALS after decongestion was associated with PAWP, independent of LV and LA volumes. Lastly, greater improvement in PALS and a higher absolute PALS value after decongestion were independently associated with a lower risk for the composite endpoint of all-cause death or immediate heart failure recurrence. Thus, our data show that LA reservoir function is strongly impaired in immediate decompensated HFrEF but has the potential to recover in a subset of patients in the weeks after decongestive therapy, which is related to improved outcomes. These data indicate that effective decongestion is a prerequisite, yet no guarantee, to restore LA function.

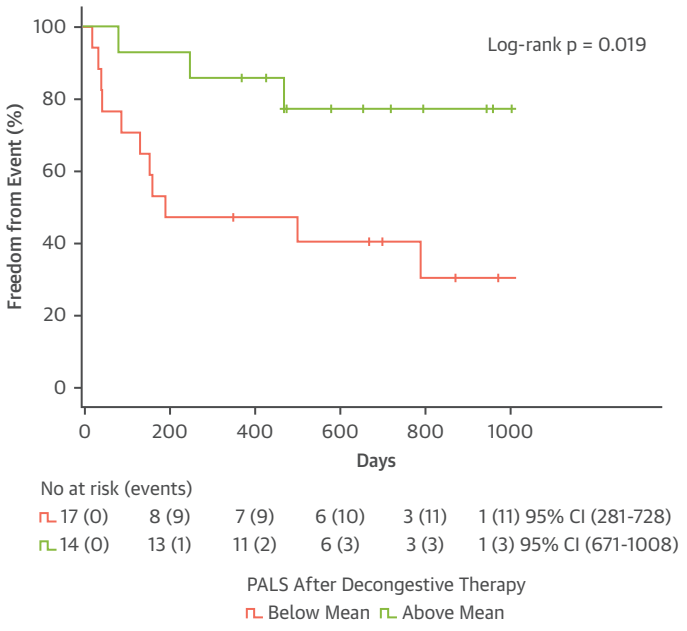
PATHOPHYSIOLOGY OF LA MECHANICAL FAILURE IN HFrEF. Far beyond being a small transport chamber passively emptying into the left ventricle during diastole, the left atrium exerts a 3-phase function (reservoir, conduit, and booster pump) during the cardiac cycle to maintain cardiac performance (2,3) (Supplemental Figure 2, left-sided panel). In this regard, it is important to underscore the continuous dynamic interplay between LA and LV mechanics. The left atrium is excessively prone to volume and/or pressure overload in the context of increased LV filling pressures (8). As such, LA failure in the context of global heart failure may be the result of intrinsic atrial myopathy (9), altered loading forces (i.e., hypertension, immediate congestion), or maladaptive compensatory mechanisms (3). The latter refers to a short-term rise in contractile shortening when LA size increases following exposure to high filling volume (LA preload) or pressure (LA afterload) (Frank-Starling law at the atrial level) (Supplemental Figure 2, center panel). Ultimately, LA contractile function declines when the optimal threshold fiber length is exceeded (10,11) (Supplemental Figure 2, right-sided panel). Few studies have assessed LA mechanics by deformation imaging in HFrEF. PALS outperformed E/e′ as a predictor for LV end-diastolic pressure in advanced HFrEF (12) and proved to be a powerful prognosticator for the composite endpoint of heart failure rehospitalization and all-cause death in these subjects (13). Moreover, LA reservoir function at rest correlated strongly with impaired functional capacity during exercise (14). Importantly, all of these studies have focused on LA function in stable, compensated HFrEF. Instead, LA adaptation to pressure and volume overload has not been studied extensively.

FIGURE 2 Correlations Between PALS and PAWP



(A) No significant correlation was found between peak atrial longitudinal reservoir strain (PALS) and pulmonary artery wedge pressure (PAWP) during congestion. **(B)** A modest significant correlation was found between PALS and PAWP after decongestive therapy. **(C)** Differences between PALS and PAWP at baseline (wet) and after decongestive therapy correlate significantly. Abs = absolute.

FIGURE 3 Freedom for Heart Failure Recurrence or All-Cause Mortality



Kaplan-Meier estimate showing a significant lower event rate of the composed endpoint of heart failure recurrence or all-cause mortality in decongested patients with peak atrial longitudinal reservoir strain (PALS) above the mean of 8.80%. CI = confidence interval.

This study offers novel information on LA mechanics measured simultaneously with invasive hemodynamic values in immediate heart failure, while evaluating the effect of decongestive therapy. LA reservoir function (according to PALS and reservoir strain rate) and booster pump function (booster pump strain rate) were markedly declined at baseline in a state of congestion, along with a restrictive mitral valve inflow pattern and increased cardiac filling pressures. Adequate decongestion led to a significant increase in reservoir function (both PALS and reservoir strain rate). Importantly, this improvement was independent of changes in LV global longitudinal strain and LA end-diastolic volume (considering both are key drivers for LA expansion as well) (13,15,16). Six weeks after hospital discharge, an additional increase in mean LA reservoir function was found, advocating additional LA mechanical function improvement. Booster pump strain rate improved significantly only after 6 weeks.

Of note, PALS during hospitalization (both before and after decongestive therapy) was considerably lower in this study compared with previous studies reporting PALS in chronic HFrEF (13,14). These differences may relate to the additional insult (i.e., immediate decompensation warranting hemodynamic-guided therapy) to which the diseased left atrium is exposed. Previously, LA pressure-area relations illustrate reduced LA compliance in congestive heart failure with major effects on LA passive mechanical properties (V-loop) (17). In progressive heart failure with a restrictive filling pattern, the left atrium transitions from a storage and contractile chamber to a basic conduit (i.e., conduit function predominates, as illustrated by the pressure-volume loop in Supplemental Figure 2, right-sided panel) (8,18). Also, increased LV filling pressures (during immediate congestion) may act as a "second-hit" for LA booster pump mechanics already functioning at the tipping point of the Frank-Starling mechanism (8).

Heart failure therapy is able to decrease LV wall tension and LA afterload mismatch, which seems to relieve LA booster pump function in the failing heart (19,20). In addition to restoring LA preload reserve, arterial vasodilators have been shown to improve operative atrial distensibility in congestive heart failure (20). These data are consistent with the findings in our study, showing a significant rebound of LA reservoir and booster pump function. Most probably, LA mechanical recovery requires time. Booster pump strain rate only improved significantly after 6 weeks. PALS improved steadily to previously reported values in stable HFrEF after an event-free interval of 6 weeks.

Finally, our study found a significant relation between LA reservoir function after decongestion and the composite endpoint of all-cause mortality or immediate exacerbated heart failure. This effect may in part be explained by the contribution of impaired LA mechanics to circulatory failure, sodium retention, and possibly the facilitation or maintenance of atrial fibrillation (2,15).

STUDY LIMITATIONS. This single-center study is limited by the relatively small sample size, which hampers generalization of the effect of LA mechanics on hard clinical endpoints and possibly may explain the lack of significance of conventional echocardiographic parameters on these end points. Echocardiography-based LA strain measurements demand sufficient image quality to track the thin-walled left atrium in the far field and was therefore not feasible in all of the initially included patients. Third, measuring LA (dys)function by using deformation imaging has yet to achieve widespread acceptance. As such, intervendor variability and consensus on the normal reference values are currently not clearly defined. Interpretation of atrial

functional indices can be challenging, caused by the continuous interplay with the left ventricle and sensitivity to loading changes. However, assessing LA mechanics longitudinally during various loading conditions in HFrEF was the primary objective of this study.

CONCLUSIONS

This study assessed LA mechanics with simultaneous invasive hemodynamic variables in acutely decompensated HFrEF and evaluated the effect of decongestive therapy and afterload reduction. Immediate decompensated heart failure resulted in a markedly compromised reservoir and booster pump function. Adequate decongestive therapy was able to unload the left atrium, reflected by a significantly increased reservoir and pump function over time. Worse reservoir strain after decongestion was associated with a higher risk for the composite endpoint of heart failure recurrence or all-cause death.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE LA mechanics are affected by loading conditions in heart failure and might contribute to ongoing sodium retention and circulatory failure. LA reservoir and booster pump function are markedly declined during congestion but can recover. Worse LA reservoir function after decongestion associates with adverse outcomes.

TRANSLATIONAL OUTLOOK: Future research studying LA failure in the context of global heart failure and its pathophysiological contribution to worse clinical outcome is needed.

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KEY WORDS acute heart failure, heart failure with reduced ejection fraction, left atrial function, speckle-tracking echocardiography

APPENDIX For supplemental tables and figures, please see the online version of this paper.