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Alterations in regional myocardial deformation assessed by strain imaging in cardiac amyloidosis

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Abstract:

Background: Cardiac amyloidosis results in increased left ventricular (LV) wall thickness and diastolic dysfunction (DD). Strain measurements using velocity vector imaging (VVI) may further characterise myocardial dysfunction.

Methods: 43 AL amyloidosis patients were compared to age matched normals and hypertensive patients (HT). Subgroup analysis within the amyloid group was performed based on LV wall thickness ($\leq 14\text{mm}$, $> 14\text{ mm}$) and diastolic dysfunction (DD) (Group 1: Normal and impaired relaxation, Group 2: Pseudonormal, Group 3: Restrictive). LV strain (longitudinal, circumferential and radial strain (S) and strain rate (Sr)) were measured using velocity vector imaging (VVI).

Results: Increased LV wall thickness and DD were observed in the amyloid group. Global longitudinal ($-13.9 \pm 4.1\%$ vs $-16.7 \pm 3.8\%$; $p=0.002$) and radial ($27.4 \pm 13.4\%$ vs $38.8 \pm 15.7\%$; $p< 0.001$) strain were lower in the amyloid group vs normal controls whilst circumferential strain was similar. Segmental analysis demonstrated reduced mid and basal segmental strain with relative sparing of apical segments in the amyloid group. Reduced longitudinal and radial S, with preserved circumferential strain was observed in patients with wall thickness $>14\text{mm}$; however circumferential strain was also altered when severe DD (restrictive filling) was present.

Conclusion: Reduction in longitudinal and radial S and Sr were evident using VVI strain analysis in amyloidosis, with segmental heterogeneity in longitudinal S. There was relative preservation of circumferential strain, which was reduced only in patients with severe DD.

Keywords: strain, strain rate, velocity vector imaging, left ventricle, amyloidosis, hypertension

Introduction:

Cardiac amyloidosis is characterised by increased left ventricular (LV) wall thickness from extracellular deposition of fibril proteinaceous material ¹ with early impairment of diastolic

function. Systolic function is relatively preserved until late in the disease process². Cardiac involvement has poor prognosis, with heart failure occurring in ~ 25% of AL amyloid patients, with a median survival of 4 to 6 months after occurrence³. Hence early recognition of the cardiac disease is prognostically important for the patient and influences therapy, including proceeding with autologous stem cell transplant.

Strain (S) and strain rate (Sr), derived from tissue Doppler or 2-dimensional speckle tracking, measure myocardial deformation and rate of deformation respectively⁴. Systolic S detects subclinical myocardial dysfunction in various conditions with increased LV mass or wall thickness^{5,6}. Previous studies have demonstrated its utility for early detection of cardiac dysfunction in amyloid patients^{7,8}. Velocity vector imaging (VVI), a strain technique incorporating 2D speckle tracking and endocardial border tracking, also evaluates myocardial mechanics^{9,10}. The aims of this study were 1) to determine the feasibility of VVI derived S and Sr in identifying alterations of LV mechanics in cardiac amyloidosis compared with healthy controls, 2) to determine if alterations in myocardial mechanics in amyloid patients are related to increased LV wall thickness and mass by comparison to hypertensive patients (HT) and 3) to evaluate if alterations in strain occur based on severity of diastolic dysfunction (DD) in amyloid patients.

Methods:

The study population comprised of 46 amyloid patients (Westmead Hospital, Sydney (n=19) and Princess Alexandra Hospital, Brisbane (n=27)), recruited from April 2003 to September 2009. Both sites are tertiary referral centres, with specialised amyloid clinics receiving referrals from the states of New South Wales and Queensland respectively. 43 had AL amyloidosis while 3 had hereditary amyloidosis (ATTR). All patients had biopsy proven systemic amyloidosis, although cardiac biopsy (n=5) and/ or serum NT-pro BNP level were only available in 22 patients. In the remainder biopsy sites are as listed: cutaneous/adipose tissue n= 3, renal n=24, gastrointestinal n=7, peripheral nerve n=4, bone marrow n=1, laryngeal n=1, vitreous n=1. Detailed clinical and demographic information were obtained from all amyloid patients. 46 age matched normal subjects (no history of ischaemic heart disease, valvular disease, peripheral or cerebrovascular disease, hypertension or diabetes and on no cardioactive medications), and 46 age matched patients with HT were identified

from a departmental database. The HT patients had no other cardiac risk factor, had normal renal function and no symptoms or previous history of ischemic heart disease.

Transthoracic echocardiogram: Amyloid patients underwent a detailed echocardiogram according to a standardized study imaging protocol which was maintained across the referral sites (ie Westmead/ Princess Alexandra Hospital). A comprehensive transthoracic echocardiogram including 2- dimensional, Doppler and M-Mode echocardiography were performed using commercially available systems (Vivid 7 GE, IE33 Philips). Specific 2-dimensional images were obtained at a high frame rate with image optimization for strain and strain rate analysis.

LV wall thickness was the average of septal and posterior wall thickness; a cut off of 14mm was used to separate mild to moderate wall thickness vs moderate to severe wall thickness as per American Society of Echocardiography (ASE) guidelines ¹¹. Regional wall thickness (RWT) was calculated ¹¹; LV mass index (LVMI) was calculated from M-mode measurements by Devereux's method ¹¹ and indexed to body surface area. Patients were categorized into groups with normal diastolic function, impaired relaxation, pseudonormal or restrictive filling, as per ASE guidelines ¹².

Strain analysis: VVI software (VVI Syngo version 3.5, Siemens, Erlangen, Germany) was used to derive tissue velocity, strain and strain rate, with curves obtained after automated tissue tracking across the cardiac cycle ⁹. Longitudinal S and Sr were measured from the apical 4 chamber view from 6 LV segments to obtain regional strain; global longitudinal strain was the average of the 6 segments (Fig 1a & 1b). Radial and circumferential strain was measured from the parasternal short axis view at the level of the papillary muscles. Once again the LV was divided into 6 segments and global strain was the average from 6 segments (Fig 2 and Fig 3). An average of 3 measurements was used for the final analysis.

Statistical analysis: Data are reported as mean $\pm$ standard deviation. Differences among the 3 groups (amyloid vs normals vs HT) were examined by ANOVA with post hoc Bonferroni correction. Amyloid patients were categorised into groups on the basis of LV wall thickness (Group 1 $\leq$ 14mm and Group 2 $>$ 14mm). An independent samples t test examined differences between the subgroups. Three group comparisons based on grades of DD (Group 1: Normal and Impaired Relaxation, Group 2: Pseudonormal pattern and Group 3: Restrictive) was performed using ANOVA with post hoc Bonferroni correction for multiple

comparisons. Cox regression analysis was performed to evaluate univariate echocardiographic predictors of death with care taken to exclude variable with high collinearity. Statistical analysis was performed with SPSS 18 (IBM, Inc. Armonk, NY, USA).

Inter and intra observer variability:

10 randomly selected echocardiograms were reviewed by the same investigator, 4 weeks apart, blinded to previous measurements. Inter-observer variability was assessed by a second blinded investigator in the same 10 patients, and intra-class correlation (ICC) was evaluated.

Results:

Patient characteristics: Clinical and echocardiographic parameters for the Amyloid, HT and normal groups are presented in Table 1. The mean age of amyloid patients was 60 ± 12 years with 29 males (63%). As expected, blood pressure was higher in the HT group.

2D echocardiographic indices: LV septal and posterior wall thickness, LV mass index and relative wall thickness (RWT) were significantly increased in the amyloid group compared to both the HT and control groups. Mean LVEF was $53.3\% \pm 8.9$ in the amyloid group, and was reduced compared to the HT and normal groups. Diastolic function was altered in the amyloid group with increased E/A and E/E' ratio and reduced E' velocity (Table 1).

Strain parameters: Global longitudinal and radial strain was significantly reduced in the amyloid group compared to the normal group; although both global longitudinal and radial strain were higher in the HT group compared with the amyloid group, it failed to reach statistical significance. Interestingly, circumferential strain in the amyloid group was similar to both the normals and the HT group (Table 2a). Global longitudinal, radial and circumferential systolic strain rate (S-Sr) were significantly lower in the amyloid group compared to both the HT and normal group. Longitudinal S-Sr was also decreased in the HT group compared with normals. ICC for inter-observer variability of longitudinal strain was 0.875, whilst intra-observer ICC was 0.832. ICC for inter-observer variability of longitudinal strain rate was 0.94, whilst intra-observer ICC was 0.80. (data not shown)

Segmental analysis as an average of the basal, mid and apical segments demonstrated a reduction in strain and S-Sr in the basal and mid LV segments in the amyloid group compared to both the HT and normal groups. However a higher strain was observed in the apical segments in the amyloid group (Table 2b).

Global longitudinal early (E Sr) and late (A Sr) diastolic strain rate were reduced in the amyloid group compared to both the HT and normal group (Table 2a).

Strain parameters based on LV wall thickness: The amyloid patients were divided into subgroups based on LV wall thickness (group 1: LV wall thickness ≤ 14 mm, group 2: LV wall thickness > 14 mm). Subgroup analysis demonstrated a reduction in longitudinal and radial S and S-Sr in the group with LV wall thickness > 14 mm whilst circumferential S and Sr were relatively preserved (Table 3a). Segmental analysis demonstrated reduction in basal and mid segment strain in the group with wall thickness > 14 mm (Table 3a).

We further compared strain parameters between amyloid patients in group 1 versus normal controls and HT patients with wall thickness ≤ 14 mm. Longitudinal, radial and circumferential S were similar in all 3 groups while longitudinal and radial S-Sr were significantly lower in the amyloid group compared to normal controls. Interestingly, E-Sr and A-Sr were significantly lower in the amyloid group versus both normal and HT groups (Table 3b).

No patient in the amyloid group was hypertensive at recruitment into this study; however, 20/46 had a past history of HT. We performed a subgroup analysis of amyloid patients with HT (n=20) vs the remaining 23 (albeit acknowledging small group numbers) but demonstrated no significant differences between groups for longitudinal, radial or circumferential strain and strain rate parameters (data not shown).

Strain parameters within amyloid subgroups based on LVDD: Strain parameters within the amyloid group were analysed based on diastolic dysfunction (DD) (Table 4). Group 1 represented normal and impaired relaxation, group 2 pseudonormal and group 3 restrictive filling pattern. There was a significant reduction of longitudinal and radial S and Sr between group 1 and group 3 in keeping with the pattern observed with increasing wall thickness. However, in addition, we noted that with worsening DD, circumferential S was also significantly reduced. Thus with restrictive filling, a reduction in strain parameters in all three planes was observed in the amyloid group.

Relationship of strain parameters and diastolic dysfunction with mortality:

The median follow up period of the amyloid patients was 60 months [range 22- 68months]. There were 20 deaths out of the 43 patients (47%). Comparison of strain parameters showed that longitudinal and radial S and Sr were significantly lower in the amyloid patients who died than the patients who remained alive (Table 5a). Grade III diastolic dysfunction (restrictive filling pattern) was observed in a total of 17 study patients, 11 of whom died (65%). Patients with restrictive filling pattern had significantly lower longitudinal S, Sr, radial and circumferential S than those with lesser degree of DD (Table 5b).

We performed Cox regression for predictors of death using LVEF, indexed LVM, E' velocity and longitudinal and radial S- Sr (Longitudinal and radial systolic strain were not entered into this model given the collinearity between S and S-Sr); longitudinal Sr was the only independent predictor of death (HR= 26.6, p=0.048).

Discussion:

The present study demonstrates several alterations in myocardial mechanics in cardiac amyloidosis by VVI strain analysis; and additionally reinforces that cardiac involvement has poor prognosis with high mortality. A reduction in longitudinal and radial S and Sr parameters were observed in the amyloid group compared with normal, and a reduction in systolic Sr, E-Sr and A-Sr compared with the HT group. There was a differential reduction in the basal and mid segments with relatively preserved apical function in the amyloid group. Additionally, a differential reduction in longitudinal, radial and circumferential strain based on LV wall thickness and grade of DD were observed in the amyloid group.

Importance of early diagnosis of cardiac amyloidosis

Early diagnosis of amyloidosis is often difficult as presenting symptoms are broad and often unrelated; no single imaging, blood or urine test is diagnostic for the disorder. Cardiac involvement is a major determinant of outcome in amyloidosis^{3,13} and therefore its diagnosis is important in patient management. Although at present there are no disease-modifying therapies, the future development of specific treatments for amyloidosis will make early detection of cardiac involvement important. Moreover, knowledge of cardiac

involvement is important for the patient as it influences therapeutic options and has prognostic implications.

The increased LV wall thickness from infiltration can be misinterpreted as LV hypertrophy consequent to hypertension, particularly in early amyloidosis with a mild increase in wall thickness and preserved LV systolic function. Hypertrophic cardiomyopathy (HCM) is another differential; strain parameters are altered in HCM¹⁴ but is likely due to myocardial fibre disarray. Moreover, different patterns of strain alteration have been shown between HCM and cardiac amyloidosis¹⁴. Thus, accurate diagnosis of cardiac amyloidosis is important and we have demonstrated a reduction in S-Sr and diastolic Sr parameters even in the amyloid subgroup with wall thickness ≤ 14 mm compared to HT patients. Subgroup analysis of amyloid patients with a past history of HT versus those without, failed to demonstrate any differences in strain parameters suggesting that the observed differences in strain parameters relate primarily to the amyloid process.

Reduction in S and Sr parameters in amyloidosis

Despite the relative preservation of LVEF (mean $53.3 \pm 8.9\%$) in the amyloid group, there was significant reduction in systolic S and Sr compared to normal and the HT group.

Subclinical LV dysfunction, using both tissue Doppler⁷ and 2D strain¹⁵ have been reported despite normal conventional indices such as LVEF. This reflects the potential clinical utility of strain imaging for early diagnosis and for monitoring progress in cardiac amyloidosis.

Regional heterogeneity- Segmental variation in deformation pattern

In our study, longitudinal systolic S and Sr demonstrated a regional variation in the amyloid group; basal and mid segments were predominantly affected with relative sparing of apical segments. We further demonstrated that longitudinal strain in the basal and mid segments was significantly reduced with increased wall thickness > 14 mm. This pattern of regional heterogeneity was reported by Phelan et al¹⁶ and Bellavia et al¹⁷ using 2D and Doppler myocardial strain imaging respectively, and concluded that this may be a compensatory effect related to the functional impairment of the basal and mid LV segments. Similar regional heterogeneity has been reported in normal individuals and has also been corroborated in MRI studies¹⁸.

Differential alterations of longitudinal, radial and circumferential strain and Sr: possible mechanisms and determinants

We demonstrated a differential reduction in strain, with longitudinal and radial strain being affected earlier, whilst circumferential strain was preserved until the development of severe DD (restrictive filling pattern). This finding is similar to that reported by Wang et al¹⁹ in heart failure patients. A similar differential reduction in strain parameters (preservation of circumferential deformation with reduced longitudinal and radial deformation) was observed in patients with diastolic heart failure (DHF) and was distinct from patients with systolic HF (SHF) where strain parameters were reduced in all planes.

Subgroup analysis of amyloid patients by LV wall thickness showed preserved circumferential S and Sr even with wall thickness >14 mm, whilst longitudinal and radial parameters were reduced. A previous report using Doppler derived strain²⁰ in cardiac amyloidosis had shown that only longitudinal and radial systolic strain were reduced in amyloid patients with increased wall thickness whilst no significant differences were observed in circumferential strain.

Possible mechanisms:

2D strain analysis has demonstrated that regardless of the pathophysiology, initial ventricular injury affects the longitudinal function, whereas radial and circumferential function are preserved in the early phase^{21, 22}. The subendocardial fibres responsible for longitudinal function are often first affected by varying pathologies including ischaemia²³ and hypertrophy²⁴. Reduction in longitudinal function detected by strain imaging and confirmed by magnetic resonance imaging²⁵, was found to be an early and accurate indicator of LV dysfunction. With the progression of LV dysfunction, mid-wall fiber contraction is altered, leading to the deterioration of radial and circumferential deformation²⁶. Poulsen et al²⁷ had shown that reduced longitudinal strain is associated with increased collagen turnover and myocardial fibrosis in HT patients. A similar conclusion could be extrapolated to cardiac amyloidosis with increased LV wall thickness likely to occur from the combined effects of amyloid protein deposition and associated interstitial fibrosis.

Pathophysiology of cardiac amyloidosis and the likely relation to myocardial deformation abnormality:

Cardiac involvement in amyloidosis is characterised by proteinaceous deposits around myocytes with microvascular involvement ¹. Additional to the mechanical disruption to the myocardium, amyloid deposits induce oxidative stress ²⁸ with resultant endocardial foci of ischaemia, microinfarction and eventual fibrosis, all contributing to myocardial dysfunction. Magnetic resonance imaging (MRI) has demonstrated subendocardial infiltration by late gadolinium enhancement (LGE) in patients with cardiac amyloidosis ²⁹, and was associated with increased ventricular mass and impaired systolic function ³⁰. Anatomic pathology examination of autopsy specimens has supported this distinct pattern of LGE in cardiac amyloidosis and Becker et al ³¹ reported that cardiac amyloid deposits were predominantly located in the subendocardial region of the diseased hearts.

Prognostic value of strain parameters and diastolic dysfunction:

The influence of severe diastolic dysfunction on heart failure, development of arrhythmias, hospitalisation and mortality has been well documented in various disease states ^{32, 33}. Klein et al ³⁴ first demonstrated the prognostic significance of Doppler diastolic indices in prediction of outcomes in cardiac amyloidosis. Bellavia et al ¹⁷ followed up in their study with Doppler myocardial strain imaging to assess its additive value as a prognostic marker and found that regional peak longitudinal systolic strain could further define high-risk group of patients. The high prevalence of restrictive filling in our patients who died and their reduced strain parameters are similar to prior studies. Furthermore, multivariate analysis from our study showed that longitudinal S-Sr was the only independent predictors of death. 2D longitudinal strain parameters have demonstrated prognostic value in other disease states including heart failure ³⁵ and myocardial ischaemia ³⁶ and may have implications in the management of patients with cardiac amyloidosis.

Limitations: The present study involves a relatively small number of amyloid patients; however, significant differences in strain parameters were observed. Due to the small sample size, beta errors may occur with subgroups analysis. A study with a larger patient group comparing amyloid patients with and without cardiac involvement would further aid in characterisation of the disease process and the prognostic significance of these parameters.

The amyloid patients in this study were heterogenous in their disease stage and treatment received, making it difficult to extrapolate these results to specific amyloidosis treatment strategies. All patients had a tissue diagnosis of amyloid; similar to other published studies^{17, 20} cardiac biopsies were not performed in all patients. The HT group had increased wall thickness but was still significantly less than the amyloid group. However, indexed LV mass was similar between the two groups.

Conclusion: We examined longitudinal, radial and circumferential S and Sr in patients with amyloidosis using VVI. We demonstrated reduction in circumferential strain only in patients with severe diastolic dysfunction. Regional heterogeneity in longitudinal S and Sr was observed and basal and mid segment longitudinal S were reduced. Strain parameters were independent predictors of death and restrictive filling pattern. Strain parameters may be useful in the identification, monitoring and prognostication of patients with cardiac amyloidosis.

Author contributions:

Concept/design: Q. Lo, B. Haluska, E. Chia, M. Lin, D. Richards, T. Marwick, L. Thomas

Data analysis/interpretation: Q. Lo, T. Marwick, L. Thomas

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Critical revision of article: Q. Lo, B. Haluska, E. Chia, M. Lin, D. Richards, T. Marwick, L. Thomas

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Statistics: Q. Lo, L. Thomas

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Data collection: Q. Lo, B. Haluska, E. Chia, M. Lin

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Figure legends: *VVI based strain imaging of a patient with amyloidosis. Vectors and graphs of 6 segments of the left ventricle from the apical 4 chamber view demonstrating **Fig 1 a)** Longitudinal strain and **Fig 1b)** Longitudinal strain rate. Vectors and graphs of 6 segments of the left ventricle from the parasternal short axis view demonstrating **Fig2)** Radial strain and **Fig 3)** Circumferential strain.*

Table 1: Demographic and echocardiographic parameters

Parameters	Normal control	Amyloid group	Hypertensive	P
Number of patients	46	46	46	
Age (yrs)	59 ± 13	60 ± 12	59 ± 12	0.84
Weight (kg)	77.9± 15.3	76.9 ± 19	81.3 ± 14.7	0.43
Height (cm)	171.3± 11.0	170.1± 10.6	166.5 ± 10.8	0.095
BSA (m ²)	1.92± 0.2	1.88 ± 0.3	1.93 ± 0.2	0.6
SBP (mmHg)	120± 13 *	116 ±32 *	146 ± 19 §	<0.001
DBP(mmHg)	75± 9	69 ± 15 *	81 ± 11	<0.001
IVS (mm)	9.6±1.7 *	13.0±3.3 §*	11.8 ± 1.7 §	<0.0001
PW (mm)	9.4±1.9 *	13.3±3.6 §*	11.9 ± 1.3 §	<0.0001
LVEDV (ml)	89.1±21	81.9±33.3	107. 9 ± 43.2	0.15
LVESV (ml)	34.4±9.5	38.5 ± 18.6	41.3 ± 21.6	0.34
EF- Biplane (%)	61 ± 5	53 ± 9 §*	62 ± 4 §	<0.0001
LV mass index (g/m ²)	86.5±26.9 *	116.3 ± 40.8 §	126.5 ± 47.4 §	<0.001
RWT (mm)	0.39±0.08 *	0.63±0.25 §*	0.53 ± 0.04 §	<0.0001
MV-E (cm/s)	63.2±13.8	81.9±21.5 §	78.5± 9.3	<0.0001
MV- A (cm/s)	60.9±17.3	57.9±22.1	76 ± 15.6	0.20
E/A	1.1±0.4	1.9 ±1.5 §*	1.1 ±0.3	<0.003
MV Dec T (msec)	234.3±50.1	218.1 ±113.5	202.5 ± 38.7	0.58
E' (cm/s)	8.1±3.2	5.8±2.4 §	7.5 ± 2.9 §	<0.001
E/ E'	8.5±2.6	17.8±11.4§*	11.7 ± 4.7s	<0.0001

* $p < 0.05$ for ANOVA compared to Hypertensive

§ $p < 0.05$ for ANOVA compared to Normal

Table 2a: Comparison of global longitudinal, circumferential and radial strain and strain rate

Parameters	Normal control	Amyloid group	Hypertensive	P
Long Peak S strain (%)	-16.7±3.8	-13.9±4.1 §	-14.9±3.1	0.002
Long Peak S Sr (s^{-1})	-1.4±0.3 *	-1.0±0.3 §*	-1.2±0.3 §	<0.0001
Long Peak E Sr (s^{-1})	1.2±0.4	0.9±0.3 §*	1.2±0.3	<0.0001
Long Peak A Sr (s^{-1})	1.0±0.4	0.6±0.3 §*	1.0±0.3	<0.0001
Circum Peak S strain(%)	-24.9±9.7	-21.9 ± 5.2	-22.8±5.4	0.13
Circum Peak S Sr (s^{-1})	-2.0±0.5	-1.7±0.4 §*	-2.0±0.5	0.004
Radial Peak S strain(%)	38.8±15.7	26.9 ±13.4 §	33.5±10	<0.0001
Radial Peak S Sr (s^{-1})	2.4±0.6	1.7±0.9 §*	2.4±0.6	<0.0001

* $p < 0.05$ compared to Hypertensives

§ $p < 0.05$ compared to Normal

Table 2b: Comparison of longitudinal segmental peak systolic strain and strain rate

Segments	Parameter	Normal controls	Amyloid group	Hypertensive	P
Basal longitudinal	Strain (%)	-18.7±5.5	-11.1 ± 4.6§*	-16.4±4.4	<0.0001
	SR (s ⁻¹)	-1.6±0.5	-0.9±0.4§*	-1.4±0.4	<0.0001
Mid longitudinal	Strain (%)	-15.6±4.5	-12.5±5.9§*	-14.3±4.0	0.01
	SR (s ⁻¹)	-1.3±0.3 *	-0.9±0.3 §*	-1.1±0.3 §	<0.0001
Apical longitudinal	Strain (%)	-15.8±6.3	-18.1±5.7*	-14.1±4.2	0.003
	SR (s ⁻¹)	-1.4±0.5 *	-1.2±0.4	-1.1±0.4 §	0.01

*p< 0.05 compared to Hypertensives

§ p <0.05 compared to Normal

Table 3a: Longitudinal (global and segmental), circumferential and radial strain and strain rate in Amyloid group based on LV wall thickness

Parameter	Group 1($\leq 14\text{mm}$) n=29	Group 2($>14\text{mm}$) n=14	P
Global longitudinal S(%)	-15.3 $\pm$ 3.3	-11.6 $\pm$ 4.7	0.011
Global longitudinal systolic Sr (s^{-1})	-1.1 $\pm$ 0.2	-0.9 $\pm$ 0.3	0.012
Basal segment longitudinal S (%)	-12.5 $\pm$ 5.1	-9.1 $\pm$ 4.8	0.048
Basal segment longitudinal Sr (s^{-1})	-1.0 $\pm$ 0.4	-0.7 $\pm$ 0.4	0.05
Mid segment longitudinal S (%)	-14.2 $\pm$ 5.5	-9.7 $\pm$ 5.6	0.03
Mid segment longitudinal Sr (s^{-1})	-1.0 $\pm$ 0.2	-0.8 $\pm$ 0.4	0.16
Apical segment longitudinal S (%)	-19.0 $\pm$ 5.7	-16.2 $\pm$ 5.8	0.12
Apical segmental longitudinal Sr (s^{-1})	-1.3 $\pm$ 0.4	-1.1 $\pm$ 0.4	0.12
Global longitudinal E Sr (s^{-1})	1.0 $\pm$ 0.3	0.7 $\pm$ 0.3	0.0001
Global longitudinal A Sr (s^{-1})	0.7 $\pm$ 0.3	0.5 $\pm$ 0.3	0.09
Global circumferential S (%)	-22.8 $\pm$ 4.7	-20.3 $\pm$ 5.8	0.12
Global circumferential systolic Sr (s^{-1})	-1.8 $\pm$ 0.4	-1.6 $\pm$ 0.4	0.11
Global radial S (%)	31.9 $\pm$ 14.4	19.7 $\pm$ 6.3	0.002
Global radial systolic Sr (s^{-1})	1.9 $\pm$ 0.9	1.3 $\pm$ 0.5	0.025

Table 3b: Comparison of global longitudinal, circumferential and radial strain and strain rate in Amyloid group, hypertensive patients and normal controls, with wall thickness $\leq 14\text{mm}$

Parameter	Normal (n=45)	Amyloid(n=29)	Hypertension(n=43)	P
Longitudinal S(%)	-16.7±3.8	-15.3±3.3	-15.1±3.0	0.07
Longitudinal systolic Sr (s ⁻¹)	-1.4±0.3*	-1.1±0.2 §	-1.2±0.3 §	<0.001
Longitudinal E Sr (s ⁻¹)	1.2±0.4	1.0±0.3§*	1.2±0.3	0.012
Longitudinal A Sr (s ⁻¹)	1.0±0.4	0.7±0.3 §*	1.0±0.3	<0.001
Circumferential S (%)	-25.1±9.7	-22.8±4.7	-22.7±5.3	0.216
Circumferential systolic Sr (s ⁻¹)	-2.1±0.5	-1.8±0.4	-2.0±0.5	0.118
Radial S (%)	39.3±15.6	31.9±14.4	33.5±9.9	0.043
Radial systolic Sr (s ⁻¹)	2.4±0.6	1.9±0.9 §	2.4±0.6	0.027

*p< 0.05 compared to Hypertensives

§ p <0.05 compared to Normal

Table 4 : Strain and strain rates in Amyloid subgroups based on diastolic dysfunction

Parameter	Group 1 (normal + Impaired relaxation) n= 18	Group 2 (Pseudo- normal) n=8	Group 3 (Restrictive) n=17	P value
Longitudinal systolic S (%)	-16.8± 3.4 *	-12.7 ± 3.3	-11.4 ± 3.4	<0.0001

Longitudinal systolic Sr (s^{-1})	-1.2 $\pm$ 0.3 *	-0.9 $\pm$ 0.3	-0.9 $\pm$ 0.2	0.01
Circumferential S (%)	-22.9 $\pm$ 3.2 *	-24.7 $\pm$ 5.8 *	-19.5 $\pm$ 5.7	0.02
Circumferential systolic Sr (s^{-1})	-1.8 $\pm$ 0.4	-1.7 $\pm$ 0.5	-1.6 $\pm$ 0.5	0.57
Radial S (%)	31.1 $\pm$ 14.4 *	32.3 $\pm$ 12.5 *	19.9 $\pm$ 7.0	0.01
Radial systolic Sr (s^{-1})	1.9 $\pm$ 1.1	1.7 $\pm$ 0.5	1.4 $\pm$ 0.6	0.19

* p< 0.05 compared to Group 3

Table 5a: Comparison of strain parameters between amyloid patients who died and those who are alive

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Parameters	Dead (n= 20)	Alive (n=23)	P value
Longitudinal S (%)	-12.5±4.4	-15.1±3.5	0.04
Longitudinal Sr (s ⁻¹)	-0.9±0.3	-1.1±0.2	0.02
Circumferential S(%)	-20.4 ± 5.5	-23.3 ±4.5	0.06
Circumferential Sr (s ⁻¹)	-1.6±0.5	-1.8±0.4	0.14
Radial S (%)	20.9 ± 9.9	32.1±12.5	0.002
Radial Sr (s ⁻¹)	1.3±0.4	2.0 ± 0.9	0.004

Table 5 b: Comparison of strain parameters between patients with grade III diastolic dysfunction and those without

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Parameters	Grade III DD(n= 17)	Normal, Grade I or II DD(n=26)	P value
Longitudinal S (%)	-11.4±3.4	-15.5±3.8	0.001
Longitudinal Sr (s ⁻¹)	-0.9±0.2	-1.1±0.3	0.01
Circumferential S (%)	-19.5±5.7	-23.5±4.1	0.01
Circumferential Sr (s ⁻¹)	-1.6±0.5	-1.8±0.4	0.3
Radial S (%)	19.99±0.7	31.4±13.6	0.001

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