

No Difference in Passive LV Stiffness in Chronic Early Compares to Late LV Afterload in Early Diastolic Dysfunction in Porcine Model at 8th Week

Dr. Popevska Sofija*

Institution Imaging and dynamics, Department of Cardiovascular Sciences, Medical faculty, Katholieke Universiteit Leuven, Belgium.

*Correspondence:

Dr. Popevska Sofija, Institution Imaging and dynamics, Department of Cardiovascular Sciences, Medical faculty, Katholieke Universiteit Leuven, Belgium

Received: 14 Aug 2026; **Accepted:** 18 Sep 2026; **Published:** 30 Sep 2026

Citation: Popevska Sofija. No Difference in Passive LV Stiffness in Chronic Early Compares to Late LV Afterload in Early Diastolic Dysfunction in Porcine Model at 8th Week. *Cardiol Vasc Res.* 2026; 10(2): 1-7.

ABSTRACT

Background: passive LV stiffness in chronic LL compares to EL, in early systolic with diastolic LV pump dysfunction, as result from impaired LV filling has not been defined wheatear is associated with early development reduced LV stiffness with SD. Earlier increased passive LV stiffness, in development systolic with diastolic LV dysfunction is not defined in the P-V loop's assessment of LV DD.

Objective: was to assess passive LV stiffness constant β , using bi-exponential regression analysis of EDPVR and the LVH remodeling. How it relates to early DD in HF development between 4th vs. 8th week in comparative assessment of LL and EL was measured from LV P-V loops` in a pig model.

Methods: Single mono and bi-exponential regression were used to assess the passive LV stiffness constants (α and β), so to assess relation between early development diastolic with systolic LV pump dysfunction in LL vs. EL at 4th vs. 8th week. Also how this relates to early SD having DD was assessed in the porcine model from P-V loops. Fourteen male pigs (28 ± 3 kg) having ascending aorta stenosis with early LV afterload (EL=6), vs. descending thoracic aorta stenosis, with late LV afterload (LL=8) underwent invasive LV P-V loops` measurements, during LV load reduction at 4th vs. 8th week. Single nonlinear mono and bi-exponential regression of EDPVR were performed for calculating passive LV stiffness and constants (β_1 and β_2), using special software from maximal end-diastolic LV pressure and volume. Two-way repeated measures ANOVA, post-hoc Tukey test and were used for statistical data analysis. Results are means $\pm$ SEM or median (quartiles) for significant level at $p < 0.05$.

Results: Bi-exponential regression model, showed difference in β , with reduction in EL vs. LL at 8th weeks. α stiffness constants was also not different in LL vs. EL, though bi-exponential β_2 constant was early reduced at 4th week significantly in LL vs. EL (0.07 ± 0.015 mmHg/ml in EL vs. 0.04 ± 0.007 mmHg/ml in LL) that was different from shift to the right in EL vs. leftwards in LL at 8th week. Increased β_2 was found in EL that did not shifted rightwards at 8th week. It showed DD at 8th week. Increased LV stiffness shows early SD present in EL at 4th and in LL at 8th week. Increased β is earlier pathologic in EL at 4th vs. 8th week, being reduced as in LL at 8th week, due to change in compliance from rightwards EDPVR shift, indicating adverse LVH remodeling.

Conclusion: β_1 as well as α are not different as found in mono-exponential regression assessment of DD in SD. Due to rightward shift of EDPVR in bi-exponential regression, as found in DD there is early systolic LV dysfunction in EL vs. LL. This shows how early SD having increased EDPVR, as LV systolic dysfunctional parameter in LL and EL in porcine mode, in absolute LV volumes.

Keywords

Pressure-volume loops, Passive stiffness, Left ventricular remodeling, Systolic dysfunction, Afterload, Systolic-diastolic interaction, Systolic load.

Abbreviations

LV- left ventricle, ESPVR – end-systolic pressure-volume relation, Elv – end-systolic LV elastance, EDPVR - end-diastolic pressure-volume relation.

Introduction

Increased chronic late vs. early LV afterload, as found in arterial hypertension (HTA) has been relevant for earlier development diastolic LV dysfunction (DD), in chronic systolic HF as result of reduced LV filling from impaired LV passive stiffness. Changes in LV stiffness are being difficult to be described between LL and EL, where LL results with early reduced passive LV stiffness in P-V assessment compares to simple LV volumes assessing LVH [1-3]. Increased LV stiffness has been related with reduced coronary flow at rest, in increased LV preload, due to reduced diastolic coronary perfusion pressure in LVH that results with shift of EDPVR upwards. The coupling between systolic and diastolic LV dysfunction, as result from increased end-systolic LV load has been determined in acute setting previously, having increased end-systolic LV load relevant for early reduced systolic LV pump function from diastolic LV dysfunction. However, it has been showed that EL can also result with diastolic LV dysfunction in LVH remodeling with consequent reduction in systolic LV pump function and adverse LVH remodelling from EDPVR assessment. This could result with early reduced end-systolic LV stiffness in moderate afterload [4]. How does changes in LV load and passive LV stiffness are related, in order to assess early SD in LVH remodeling and has not been previously studied in prospective study, using large animal model compatible to human pathophysiology. There is relation between systolic and diastolic LV dysfunction, where VA coupling can indicate present diastolic with systolic LV dysfunction, though reduced LV load. Late LV load (LL) has been related to development of early LV relaxation abnormality, as in DD, adverse LVH remodelling, with systolic dysfunction, and development early HFrEF [2-8]. EL has been relevant for early developing increased LV stiffness, resulting with systolic LV dysfunction, related to reduced LV compliance resulting with increased cPP, and concentric LVH remodeling [9]. Both EL and LL associate with development of DD with LVH, and earlier systolic dysfunction in HTA, HF, having increased risk of MACE and mortality among hypertensive and/or CAD patients. They associate with development of increased stiffness in diastolic LV dysfunction having prolonged LV relaxation rate [2-12]. LVH is factor for earlier development CAD, and systolic HF, having increased LV afterload [13-16]. Early adverse structural and functional changes within LVH are not precisely defined concerning progression towards developing systolic LV dysfunction with diastolic impairment, resulting from arterial hypertension, aortic stenosis, or coarctation, having subclinical HF, representing B stage in late compares to early LV afterload in

early SD assessment.

How this relates to adverse LVH remodeling with early HF was assessed at 4th vs. 8th week in prospective experimental randomized study. The purpose of this study was [5] to assess DD from passive LV stiffness assessment in invasive pressure-volume loops' assessment, using relevant porcine model of late vs. early LV load, representing stage B diastolic dysfunction in systolic HF. It shows early [4] analysis of LVH remodeling and the relation to early development DD with SD between 4th vs. 8th week. The hypothesis tested earlier occurrence stage b systolic with diastolic LV dysfunction within increased stiffness between 4th vs. 8th week in model of aortic banding from assessment of passive LV stiffness from EDPVR in late vs. early LV afterload. This was a prospective experimental study to assess DD for adverse LVH remodeling in relation to preload and early systolic LV pump dysfunction between LL and EL, in a large animal model and also to assess how these parameters are related to early HF and DD occurrence, being relevant for developing congestive symptoms. Reduced LV stiffness is found in early systolic HF that can be early assessed from right shift of EDPVR curve. How this relates to LV afterload has been assessed in P-V loops in relation to elastance changes [1-5,13,14].

Methods

In fourteen domestic male pigs (28±2.4 kg weight) LV stiffness was assessed from invasive P-V loops' measurements of maximum LV preload at 4th vs. 8th week. Descending thoracic aorta banding for moderate chronic late LV afterload (LL=8) was compared to ascending aorta stenosis, that was created for chronic early LV load (EL=6). Pig-tailed conductance catheter was used for P-V measurements, being calibrated at zero pressure at room temperature, and using manometer calibrator within LabChart7. The experiments were performed in the animals being kept at 37C. A 5Fr fluid-filled pig-tailed Millar catheter was used, with synchronized ECG DII lead, for recording LV P-V loops at sampling rate of 200Hz. LV pressure-volume loops were recorded for analysis having respiration preserved, during mechanical ventilation suspended, during preload with afterload reduction with plastic balloon catheter (10Fr) in LabChart 7 (AD Instruments, Houston, Texas, USA). After being heparinized (100 IU/kg), through the common carotid artery, the catheter was position in the LV apex and P-V loops' measurements were obtained during balloon catheter inflation in the inferior caval vein, above the diaphragm. LVESVs and LVEDVs from MRI were used for calibrating LV volume channel at post-hoc. End-diastolic LV pressure-volume relation from LV P-V loops' were exported from measurements during steady state and preload reduction in LabChart 8, so to assess maximal passive LV stiffness constant, using nonlinear regression and was compared to bi-exponential regression assessment with special software. LV passive stiffness constant (β) was analyzed from bi-exponential with mono-exponential regression analysis, using special software, as well as the LV capacitance for LVP 30mmHg (V30) with α stiffness constant at 4th and 8th week. Further, novel early diastolic LV

volume constant assessing from the EDPVR curve assessed LV volume over pressure change (v) was used to determine the LV early-diastolic stiffness from LV volume change. For statistical data analysis we used two-way repeated measures ANOVA, post-hoc Tukey test and Levene normality test. Variance analysis of aligned rank transformed data was performed for not normally distributed data as nonlinear non-parametrical testing and results are shown as means $\pm$ se or medians (with quartiles), with significant level at $p < 0.05$.

Results

The results from passive LV stiffness assessment of diastolic with systolic LV dysfunction from pressure-volume relation, both β_1 (early) and β_2 (late) stiffness with α constants showed early rightwards shift in bi-exponential regression, from LV loop's being measured in the 4th vs. 8th week in LL vs. EL. The results are being presented in the table. In figure is shown the mathematical regression used for assessment of passive LV stiffness, using nonlinear EDPVR assessment in bi-exponential with monoexponential regression for calculating β stiffness constant. Reduced LV passive stiffness in LL vs. EL from pressure-volume loop's measurements was present in the 4th vs. 8th weeks. Bi-exponential EDPVR analysis showed that early and late β stiffness constants were not different between groups in the 8th week, but at 4th week showing increased passive LV stiffness in EL group. However β_2 was different between groups and at 4th week was increased in EL compares to LL (group $p = 0.03$), as resulted

from the LV afterload type ($p=0.069$), that was not significant at 8th week. This was from shift in right with EL compares to upwards in LL. Mono-exponential β was not different in LL vs. EL in the 4th vs. 8th week. Bi-exponential V30 was different being increased in LL, though insignificant right and upward shift in EL at 8th week, and in LL at 4th week of LVH remodeling. This resulted with no difference in passive β_1 and α LV stiffness constants in LL vs. EL in the 8th week, with β_2 tending to have significant shift within passive stiffness in EL vs. LL in the 8th week as result from reduced passive stiffness in moderate early LV afterload. Further, early-diastolic LV volume change (v_1 , v_2) constants and v_2/v_1 ratio from bi-exponential EDPVR fit were also not different neither changed in LL and EL between 4th vs. 8th week measurements. This is indicating on the effects of change in passive LV stiffness being reduced with EL vs. LL at 8th week. Mono vs. bi-exponential regression showed early LV diastolic dysfunction with adverse LVH in LL at 4th vs 8th week, with SD and reduced LV stiffness in EL. This can indicate on early systolic dysfunction in EL at 4th vs. 8th week, as to no difference in β_1 found in bi-exponential nonlinear assessment that was significantly different from monoexponential at 4th vs.8th week. This shows how SD usually occurs in presence of relative increased passive LV stiffness in LVH that was reduced in EL and was relevant for systolic dysfunction from LV pump dysfunction and impaired LV filling with preload reserve at 8th week. This is in not line with cMRI showing concentric LVH remodeling in EL and LL at 4th weeks and reduced relative wall thickness of LV in LVH remodeling in LL at 8th week.

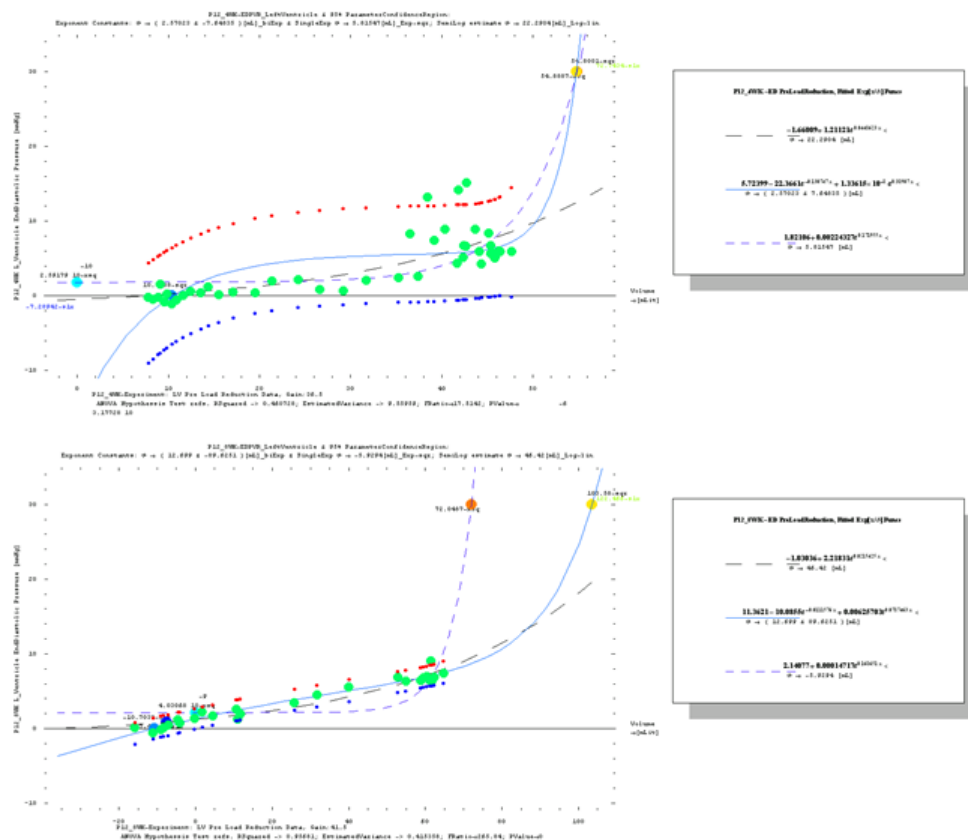


Figure 1: Central figure presenting mono with bi-exponential EDPVR assessment in EL at 4th vs. 8th week using special software for nonlinear regression assessment of DD with SD in early HF.

Pressure-Volume loops parameters	LL 4 th week (8)	EL 4 th week (6)	LL 8 th week (8)	EL 8 th week (6)	p interaction
β mmHg/ml	0.12±0.06	0.15±0.05	0.09±0.04	0.14±0.06	Ns
V30 biex (mL)	112 ± 11	75.5 ± 7	131 ± 26	94 ± 8	Ns
α biex(Alfa) mmHg/mL	-14 ± 6	-41±12	-37±12.4	-52 ±12.4	0.6
β ₁ mmHg/ml	0.11± 0.02	0.15±0.05	0.12±0.02	0.12±0.015	0.4
β ₂ mmHg/mL	0.04 ± 0.007	0.07±0.015	0.05 ± 0.005	0.045 ±0.01 ¥	0.07
v1 constant (mL/mmHg)	15± 5	13± 7	11 ± 3	9 ±1.4	Ns
v2 constant (mL/mmHg)	39 ± 11	15± 9	24 ± 4	24 ± 15	0.25
v2/ v1 ratio	3 ± 0.4	1± 1.25	2.5 ± 0.35	2.3 ± 1.35	0.27

Table - bi-exponential LV stiffness regression parameters in LL and EL at 4th vs. 8th week of aorta banding. * for significant change between 4th vs. 8th week in both groups; ¥ for group difference (§ posthoc p in 4th week); ¶ for change in LL and EL between 4th vs. 8th week.

The increased LV stiffness shows early systolic LV dysfunction present earlier in EL at 4th vs 8th weeks, as result from reduced elastance. There was no relation found between EDPVR shifts with change in nonlinear ELV in LL or EL group at 8th week. It is indicating on early detecting systolic LV dysfunction from nonlinear LV EDPVR assessment, using bi-exponential regression where β₁ has been found to be reduced in LL at 4th week and insignificantly in the 8th week in EL group that was not different from LL at 8th week. Reduced nonlinear maxELV between 4th vs. 8th week in LL tended to be reduced from EL group (8 vs. 4th week in LL -0.5±1 mmHg/mL, EL 0.75±0.3 mmHg/mL p<0.05 one-way ANOVA). This was result of reduced ELV from nonlinear ESPVR fit in LL, being shifted towards LV volume axis in the 8th week. However, in EL shift of bi-exponential β₁ constant towards right with V30 indicated that there is systolic LV dysfunction though biexpβ is reduced, being under investigated in presence of increased passive LV stiffness in early systolic HF development. Passive bi-exponential LV stiffness between 4th vs. 8th week (Δβ₂) changes that was little increased in LL compares to EL where it was reduced significantly. This was different, though being decreased within LL earlier at 4th week and in EL at 8th week. It is indicating on systolic LV dysfunction present at 4th and 8th week (4-8 week Δβ₂ LL 0.012 ± 0.007 mmHg/mL vs. EL -0.013(-0.023-0.0055 mmHg/mL) p=0.1). The bi-exponential regression method of EDPVR assessment compares to mono-exponential regression assessment can be also used to earlier assess systolic LV dysfunction being found in EL, with increased passive LV stiffness at rest. This was not different, but also present in mono-exponential assessment of passive LV stiffness. No difference in β₁ indicated present diastolic LV dysfunction though different LV afterload at 4th vs 8th week. In this porcine model having chronic LL to compare with EL between 4th vs. 8th week, it presented with early reduced β₂ in bi-exponential assessment of passive LV stiffness constant at 4th vs. 8th. β₁ was not different at 4th or 8th week for DD and SD. There was significant difference in the 4th vs. 8th week being increased in EL and early reduced with LL at 4th week, but not in the 8th week. As result of rightward shift and downwards within EL, in bi-exponential assessment it (passive LV stiffness) was not different from LL at

8th week, being earlier reduced within LL compares to EL in the 4th week, in similar peak LV afterload. Increased passive LV stiffness indicates systolic and diastolic LV dysfunction are both present in parallel earlier in chronic EL vs. LL group between 4th vs. 8th week.

Discussion

This study showed that due to the increased LV afterload, nonlinear regression assessment of EDPVR was performed to assess the LV stiffness vs. pressures, did not show difference in terms of LV pump dysfunction in relation to absolute LV volumes and LV afterload at 8th week, but in the 4th weeks. This can relate to reduced passive LV stiffness that can be used to differentiate early development of systolic LV pump dysfunction with HF though difference in LV load and heart rate, being higher at rest in EL group. Early DD occurrence and increased LV rate were somehow related to systolic pump dysfunction in increased LV preload in EDPVR assessment in EL vs. LL at 4th vs. 8th week. ESPVR tended to be reduced within LL compares to the EL where it increased in the 8th week (Popevska S). This is relevant for association found between systolic LV load and nonlinear VAC ratio that increased in LL and was reduced with EL at 4th week. It indicated that there is systolic with diastolic LV dysfunction in LV afterload increase. However, this also shows how LVH remodeling is related to early SD having adverse LVH and HF in chronic late LV afterload at 4th weeks vs. early LV load at 8th week. Assessing the interaction of LV systolic–diastolic dysfunction is relevant, in order to determine how passive LV stiffness is being affected in LVH remodeling characterize the development of LV systolic dysfunction and to further assess their relation to changes in LV stiffness in LL compared to EL between 4th vs. 8th week periods. Reduced LV stiffness is relevant for early development systolic LV dysfunction, but not presence of increased passive LV stiffness. However, deviations outside from normal range in DD, correlating with LV stiffness are both relevant whether it is increased or reduced in LV afterloads increase. Increased LV passive stiffness is relevant for development of symptoms in early systolic HF from worsening of DD. This study is important because it shows how LL compares to EL has early reduced passive LV stiffness indicate differences and change in LVH remodeling, relevant for developing early systolic LV dysfunction present in both groups in the 4th vs. 8th week of the increased LV afterload. In this porcine model having LL and EL, impaired LV contractility developed in LL earlier than EL, though being more increased than physiologic limits, reported previously in stress [3]. There is potential relevance of LV stiffness as found in Ves0 with Elv when is assessed in nonlinear ESPVR fit that can

assess early contractile LV dysfunction with diastolic impairment in LL and EL group, between 4th vs. 8th week. Moreover, correlation between ELV and passive stiffness in EL was not present neither in LL, that characterized LV ESPVR fit, when being nonlinear in LL in the 8th week, as found previously. Small changes in diastole can have great impact on LV contractile function from reduced LV elastance that can affect myocardial end-diastolic function. Change of the shape of the LV contractility curve usually reflects early adverse change of LV torsion and twist in early systolic LV dysfunction, as well as, β_2 being either increased as in EL or reduced as in LL at 4th vs. 8th week. Invasive P-V assessment in end-systolic load of LV stiffness is accurate for defining presence of systolic and diastolic LV dysfunction in subclinical systolic HF. Though late vs. early LV afterload can have increased preload as from afterload having relative increased absolute EDV, this is in presence of altered and affected Frank-Starling mechanism, as found in the 8th week. In healthy LVs that is unchanged structurally, LV stiffness may be affected by change in LV preload resulting from reduced coronary perfusion and mean arterial pressure in increased LV load. It has been previously discussed how SD may have effect on EDPVR in presence of LV ischemia [5]. In AS early diastolic LV dysfunction is related to reduced LVEF when global LV longitudinal strain is more that -15%. In presence of HTA DD has been seen when lateral e' is less that 9 m/s). The main finding of this study is that SD and DD are assessed from EDPVR bi-exponential regression being more accurate method compares to mono-exponential regression method in early LVH remodeling. In previous noninvasive-single beat assessment of LV end-systolic load and stiffness, ELV was reduced and EaELV coupling increased, in LL compares to EL. Having increased ELV with reduced coupling in EL between 4 vs. 8 week showed early DD [12]. Invasive LV pressure-volume relation assessment of passive LV stiffness constant compares to maximal ELV and EaELV from P-V loop did show difference in developing early systolic LV pump dysfunction between LL and EL, between 4th vs. 8th week. Rightwards shifting of EDPVR in EL between 4 vs. 8 weeks that occurred in LL, showed early reduced β_2 stiffness constant in. LL compares to EL that is not different between groups, as result from myocardial ischemia present at 8th week. This indicates early adverse LVH remodeling in chronic LL and in EL, different from the changes being described between LL and EL group in the rat model in the 8th. Having shift of EDPVR to the right towards increased LV end-diastolic volumes with preload in EL was present in this model in the 8th week [3]. However, the most important finding in the study is that increased LV stiffness is found in SD in LVH that results with DD in the 8th week from reduced systolic pump function in LV stiffness assessment. This is not in line with previous model showing early increased end-systolic LV stiffness in severe aortic stenosis with EDPVR shift to the right at 5th week and reduced systolic LV function in DD [3,13]. β_1 was not different at 4th or 8th week as found in previous invasive tau assessment that indicates early DD in both groups being more severe in EL. LV stiffness can correlate positively, with LV effective work with peak oxygen demand and with the extent of both systolic and diastolic LV dysfunction as found from LVEF in previous studies, being

both afterload and preload dependent (Starling et al). This is being improved with reduced LV end-systolic afterload, but not with peak systolic pressure resulting from present early systolic with diastolic LV dysfunction though reduced LV afterload in LL. However, previous study did not assess neither compare LV end-systolic load and systolic LV dysfunction between chronic LL and EL group in the 8th week from P-V assessment in bi-exponential regression. These findings relate to difference found in β_2 stiffness constant that tended to be result from systolic LV load, as well as LV dysfunction, with no difference in passive LV stiffness in bi-exponential regression assessment at 8th week. Dependent reduction in systolic LV function in LL compares to. EL was present and significant in the 8th week, but not in the 4th week. In EL compares to LL there is different myofilaments orientation having more parallel and even orientation without disorganized filaments orientation with more preserved parallel orientation and increased RWT ratio with posterior LV wall thickness, suggesting on increased LV afterload. In LL reduced RWT in hypertrophic response, presented with increased LV volume, is related with reduced LV systolic function presented from ELV compared to the EL. β and EDPVR increased while developing reduced LV systolic function compared to its asymptomatic stage showing that the LL subgroup is more sensitive to reduced LV preload [9,15]. It was reported that greater concentric hypertrophy developed within LL having leftwards shift in EDPVR compared to rightward shift of EDPVR in EL, created by suprarenal abdominal compares to aortic arch banding with stenosis in the 4th week [3]. Increased passive LV stiffness contributes to systolic LV dysfunction that has been related to increased LV fibrosis in previous hypertensive rat model [13,14]. Increased passive LV stiffness is related to presence of LV fibrosis in arterial hypertension; aortic coarctation or aortic valve stenosis [12,15,17]. However, its impact of early LV systolic dysfunction has been seen as result of reduced LV filing and SVs to maintain adequate coronary perfusion in LL early compares to the EL being seen in the 4th vs. 8th week. LV afterload increase resulted with significant differences in LV stiffness, in EDPVR, Elv, LVEF and hydroxyproline concentrations [1,8,14]. This results from LV response with relativity in progressing towards developing of systolic with diastolic LV pump dysfunction, in increased LV afterload, as found in LVH remodeling with HTA. This presents with either systolic or diastolic LV dysfunction [1,9]. In LL EDPVR early shifted to the right at the 4th week, having progressive increase in β compares to EL where it reduced with reduction of LV afterload at 8th week. Present systolic LV dysfunction within increased LV afterload and/or preload is afterload dependent and sensitive to change in LV loading conditions and heart rate can affect LV elastance [6-20]. However, passive LV stiffness could be affected by heart rate at rest or stress that affects LV end-systolic elastance and afterload. Changes in passive LV stiffness but not as in ELV are found when drugs as ACE and Ca²⁺ channels inhibitors with hronotropic and inotropic effects are used to improve systolic dysfunction and impaired rate of LV relaxation. This not affects passive LV stiffness acutely, being related to LV structural changes rather that change in pressures. However, their effect on passive LV stiffness are being

result from improved systolic LV dysfunction, with normal EF. Changes are present when change in LV microstructure affecting the myofilaments with its orientation and the extracellular matrix composition are being found. Assessing early development of stage b HF in pulsatile vs. nonpulsatile LV load at systole, as in HTA, or AS with AoC this shows how early HF is present in LL vs. EL at 4th vs. 8th weeks and indicated the need of reassessing LV preload and afterload with reserves in LVH. Increased afterload results with severe systolic pump dysfunction that can be improved with LV load reduction. In this as in previous study, nonlinear EDPVR fit showed that can easier relate to change in LV contractility, especially when being reduced (Popevska S.1). Herein, reduced LV contractility was presented within EDPVR curve more towards the volume axis and reduced LV elastance with more nonlinear regression that depends on the LV afterload profile [8,21]. Increased LV stiffness is relevant in development of systolic LV dysfunction that is improved with normalizing LV load. There is variability in load and ventricular coupling within hypertensive patients, being related with reduced end-systolic LV elastance [9,18]. It differentiates early systolic LV dysfunction in increased systolic LV load, as in hypertensive and AS population [5,7,12,18]. This found no difference in LL vs. EL in passive LV stiffness at 8th weeks, being earlier reduced between 4th vs. 8th week in increased LV load. Increased ELV in ascending aortic stenosis has been related to impaired LV filling and contractile reserve and greater reduction after MI in previous models [13]. Increased LV stiffness affects adversely contractile LV function that reduces with LL compares to EL where it is relatively unchanged at 8th week. Rightward EDPVR shift between LL and EL may indicate on supply ischemia being present with EL, whilst in LL there is greater demand ischemia and could be predominant in development earlier diastolic LV dysfunction resulting with SD [9]. The bi-exponential EDPVR nonlinear regression method for assessment can be used to see whether there is early systolic LV dysfunction and adverse LVH remodeling from rightwards shift, if outside limits are affected when using the confidence interval. Systolic and diastolic LV dysfunction in LL compares to EL are characterized by late vs. early associated interaction between myocardial contractile elements and LV relaxation [16]. Different myocardial and/or LV chamber contractility affects diastolic LV function in afterload associated development of SD [9]. Increased LV stiffness was found in presence of reduced helical myofibrillar orientation that contributes to increased LV stiffness [13]. This study found reduced end-systolic LV stiffness and afterload with increased ventricular-aorta coupling, in LL compared to EL group in line to increased passive LV stiffness indicating early diastolic and systolic LV dysfunction in LL and EL group with different β_2 , being reduced within EL between 4th vs. 8th week. Also noninvasive assessment of stiffness may not correlate with invasive measurement of passive stiffness, as showed in previous reports aiming to implement this type of diastolic LV assessment in SD so to assess early adverse LVH remodeling [9,11]. This is regulated by Beta adrenergic response having late Ca²⁺ channel antagonists relevant for improving end-systolic stiffness, but not diastolic stiffness and relaxation such as nifedipime However, previous

assessment showed that ELV was earlier reduced in LL compares to EL at 4th vs. 8th week, suggesting more needed Ca²⁺ late channel blockage so to improve SD in DD within LVH remodeling in porcine model of moderate HTA. It is of interest to assess the systolic-diastolic ventricular dysfunction in early detection of systolic LV dysfunction in LL and EL that was assessed in this experiment study and is being discussed in previous report [5]. It showed that there is early adverse LVH with SD in response to LL and EL at 4th vs. 8th week of LV afterload increase. The findings in this report show how LVH progresses towards SD in chronic LL and EL, but still there is SD in EL as result from increased thickness of LV wall in response at 4th week. This results with reduced coronary flow at rest and stress in this porcine model. In previous study was assessed the ELV with myocardial LV works for early SD in HTA population and still the relative effects from changes in LV stiffness in early SD have not been assessed in early HF but in HTA [6-11,18,19]. Lack of previous invasive LV P-V assessment to determine early SD from EDPVR assessment as one performed in this study from dedicated regression, showed SD when assessing early shift in DD development having increased afterload. This aim to assess EDPVR shift from single-beat bi-exponential regression so can be use in early SD that show its relative similarity to biexponential tau regression in SD with DD assessment in increased LV afterload. In this porcine model comparing LL to EL as found in HTA, aortic stenosis, coarctation, with stage B with systolic dysfunction, there is early DD and associated defect, indicating early diastolic and systolic LV dysfunction in reduced end-diastolic LV stiffness, in nonlinear assessment in LL at 4th week and in EL at 8th week in LVH remodeling. This is increased at 4th week within EL vs. LL that reduced between 4th vs. 8th week in bi-exponential regression. Reduced β_2 constant, and LV afterload, was found in EL and differences in LV load (late vs. early) in rightward EDPVR shift between 4th vs. 8th week. This study showed how maximum elastance correlates with passive stiffness in early SD with DD assessment in LVH remodeling.

References

1. Norton GR, Woodiwiss AJ, Gaasch WH, et al. Heart failure in pressure overload hypertrophy. *JACC*. 2002; 39: 664-671.
2. Russo C, Jin Z, Takei Y, et al. Arterial wave reflection and subclinical left ventricular systolic dysfunction. *Journal of Hypertension*. 2011; 29: 574-582.
3. Kobayashi S, Yano M, Kohno M, et al. Influence of Aortic Impedance on the Development of Pressure-Overload Left Ventricular Hypertrophy in Rats. *Circulation*. 1996; 94: 3362-3368.
4. Zile MR, Izzi G, Gaasch WH. Left Ventricular Diastolic Dysfunction Limits Use of Maximum Systolic Elastance as an Index of Contractile Function. *Circulation*. 1991; 2; 674-680.
5. Popevska S. Shorten τ_1 in chronic early vs. late systolic LV load for systolic dysfunction in ascending vs. descending thoracic aortic stenosis. *International J Cardiovascular and Thor Surg*. 2024; 10: 19-28.
6. Cohen-Solal A, Caviezel B, Himbert D, et al. Left ventricular-

- arterial coupling in systemic hypertension: analysis by means of arterial effective and left ventricular elastances. *Journal of Hypertension*. 1994; 12: 591-600.
7. Kuznetsova T, D'hooge J, Kloch-Badelek M, et al. Impact of hypertension on ventricular-arterial coupling and regional myocardial work at rest and during isometric exercise. *JASE*. 2012; 25: 882-890.
 8. Popevska S. Adverse left ventricular hypertrophy in descending thoracic vs. ascending aorta banding in novel porcine model. cMRI study. *EHJ Supp*. 2019; 40: 911.
 9. Aurigemma GP, Zile MR, Gaasch WH. Contractile behavior of the left ventricle in diastolic heart failure: With emphasis on regional systolic function. *Circulation*. 2006; 113: 296-304.
 10. Galderisi M. Diagnosis and management of left ventricular diastolic dysfunction in the hypertensive patient. *Am J Hypertens*. 2011; 24: 507-517.
 11. Kamimura D, Hans S, Suzuki T, et al. Delayed Time to Peak Velocity Is Useful for Detecting Severe Aortic Stenosis. *JAHA*. 2016; 5: e003907.
 12. Lam CSP, Shah AM, Bourlaug B, et al. Effect of antihypertensive therapy on VA mechanics, coupling and efficiency. *EHJ*. 2013; 34: 676-683.
 13. Ishikawa K, Aguero J, Oh JG, et al. Increased stiffness is the major early abnormality in a pig model of severe aortic stenosis and predisposes to congestive heart failure in the absence of systolic dysfunction. *Journal of the American Heart Association*. 2015; 4.
 14. Yamamoto K, Masuyama T, Sakata, Y, et al. Myocardial stiffness is determined by ventricular fibrosis, but not by compensatory or excessive hypertrophy in hypertensive heart. *Cardiovascular research*. 2002; 55: 76-82.
 15. Aurigemma GP, Silver KH, Priest MA, et al. Geometric changes allow normal ejection fraction despite depressed myocardial shortening in hypertensive left ventricular hypertrophy. *JACC*. 1995; 26: 195-202.
 16. Borlaug BA, Melenovsky V, Redfield MM, et al. Impact of Arterial Load and Loading Sequence on Left Ventricular Tissue Velocities in Humans. *JACC*. 2007; 50: 1570-1577.
 17. Ganau A, Devereux RB, Pickering TG, et al. Relation of left ventricular hemodynamic load and contractile performance to left ventricular mass in hypertension. *Circulation*. 1990; 81: 25-36.
 18. Roman MJ, Ganau A, Saba PS, et al. Impact of Arterial Stiffening on Left Ventricular Structure. *Hypertension*. 2000; 36: 489-494.
 19. Junichiro Hashimoto, Berend E Westerhof, Nico Westerhof, et al. Different role of wave reflection magnitude and timing on left ventricular mass reduction during antihypertensive treatment. *Hypertension*. 2008; 26: 1017-1024.
 20. Chirinos JA, Phan TS, Syed AA, et al. Late systolic myocardial load is associated with left atrial dysfunction in hypertension. *Circ Cardiovasc Imag*. 2017; 10: e006023.
 21. Gillebert TC, Lew WY. Influence of systolic pressure profile on rate of left ventricular pressure fall. *The American Journal of Physiology*. 1991; 261: 805-813.
 22. Zamani P, Bluemke DA, Jacobs DR, et al. Resistive and Pulsatile Arterial Load as Predictors of Left Ventricular Mass and Geometry Novelty and Significance. *Hypertension*. 2015; 65: 85-92.