LV Diastolic Function (LVDF) In the Young and Old

- Introduction
- How does age affect LVDF?
- When does LVDF become abnormal? Transition to HFPEF?
- Can we prevent LVDD?

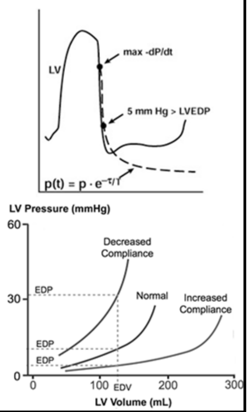
LV Diastolic Dysfunction (LVDD)

- Abnormality of LV relaxation, distensibility and filling irrespective of LVEF or symptoms
- Propensity of LV to develop ↑ filling pressure (LVFP or LVEDP)
- LVFP ≠ LVDD

  ≠ LAP or PCWP

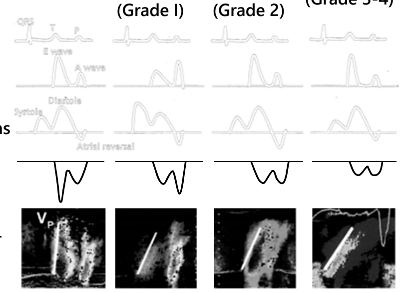
Assessing LVDF

- Active LV relaxation: Analysis of pressure decline (tau)
- Passive LV filling/chamber stiffness (effective operating compliance): Analysis of pressure-volume curves (stiffness constant)

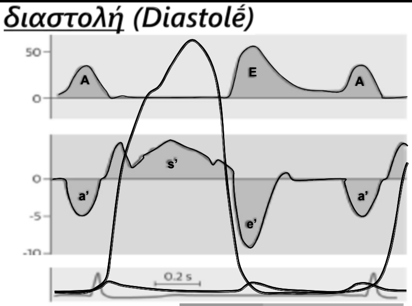


LVDF Assessment by Echo

	Normal	Abnormal Relaxation (Grade I)	Pseudo-normal (Grade 2)	Restrictive (Grade 3-4)
ECG				
Mitral Inflow				
Pulm Veins				
Tissue Doppler				
Color M-mode				



διαστολή (Diastolḗ)

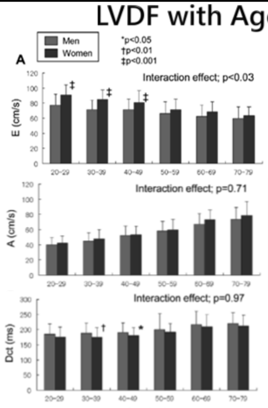


LV relaxation	+++	++	+	—
LV elastic recoil	+++	+++	—	—
LV compliance	—	++	++	+++
LA pressure	—	+++	++	++

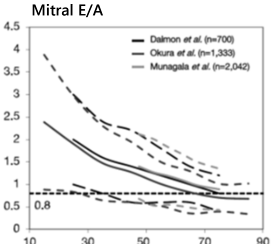
LVDF by Echo: “Post-Truth”?

- Indicates ↑ LVFP, not myocardial abnormality or LVEDPVR: E, E/A
- Load dependence: nearly all pseudonormalize
- Composite indexes ↑ measurement error: E/e’

LVDF with Age: Mitral Inflow



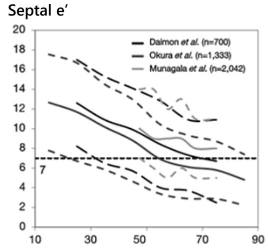
Mitral E/A



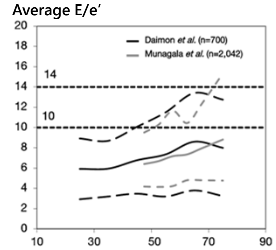
Popovic. Cardiovasc Diagn Ther 2018

Tissue Doppler

Septal e’



Average E/e’



Age (years)

Diastolic dysfunction starts from adolescence!

Popovic. Cardiovasc Diagn Ther 2018;8:18

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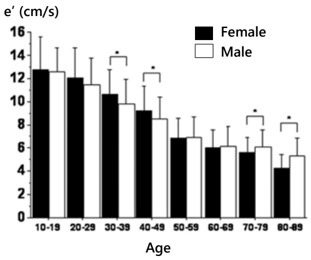
Tissue Doppler

- 1333 healthy individuals (mean age, 55 yrs; range, 10-89) without known heart disease or HTN



Age 30-49: e′ in F > M
Age 70-89: e′ in F < M
*P<0.01

Okura. Circ Cardiovasc Imaging. 2009;2:41

10

LVDF in Elderly: ARIC

- LVDF assessed in 5801 elderly subjects (mean age 76, range 67–90 yrs; 42% male)
- 10th and 90th percentile limits for "normal LVDF" determined in 401 subjects free of CVD and CVRF
- Outcome: incident HF hosp or death

	10th percentile	90th percentile
e′ septal	4.6	8.1
e′ lateral	5.2	9.9
E/e′ septal	7.2	14.4
E/e′ lateral	6.1	12.7
LAVI	15.2	30.2

Shah. Circulation. 2017

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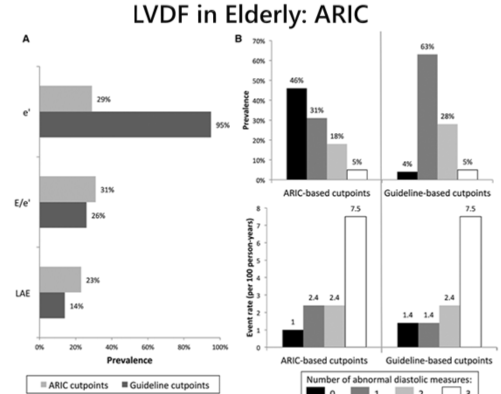
LVDF in Elderly: ARIC



Shah. Circulation. 2017

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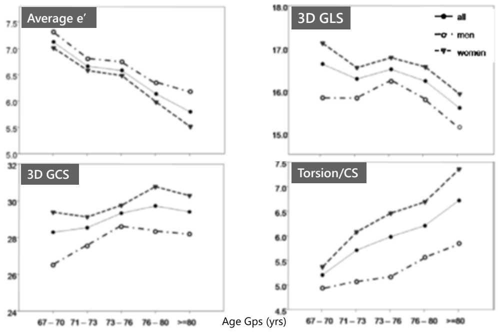
Ageing and LV Mechanics

- 1105 subjects (76±5 yrs, 61% women) without prevalent HF in ARIC
- Ageing → worse longitudinal and LVDF, with greater ↑ torsion in women



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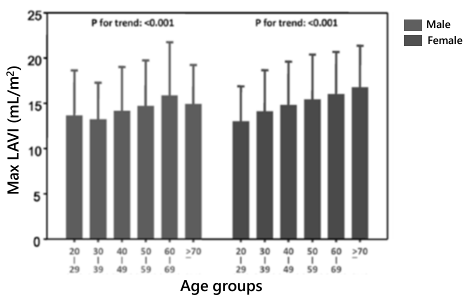
Hung. Circ Cardiovasc Imaging. 2017

LA Volume Index with Ageing

- LAV index measured in 2812 healthy subjects (65% men; age 47±10 yrs)



Liao. Circ Cardiovasc Imaging. 2017

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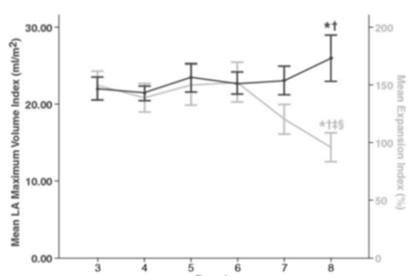
LAVI and Function with Ageing

- 220 normal subjects (mean age 45±17 yrs, range 20-80)
- LAVI remain nearly stable until 8th decade
- Predated by changes in LA phasic volumes



Boyd. J Am Coll Cardiol Img 2011

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How to Diagnose HFPEF: 2016 ESC Guidelines

Symptoms signs

+

LVEF ≥50%

+

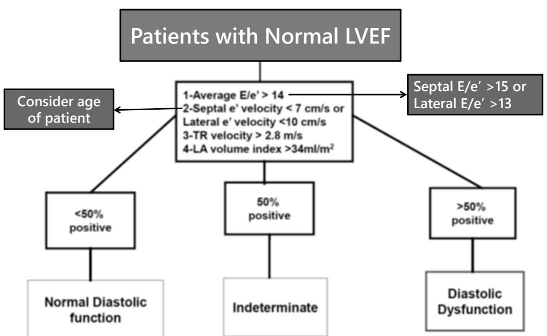
↑ BNP
BNP >35 pg/mL
NT-proBNP >125

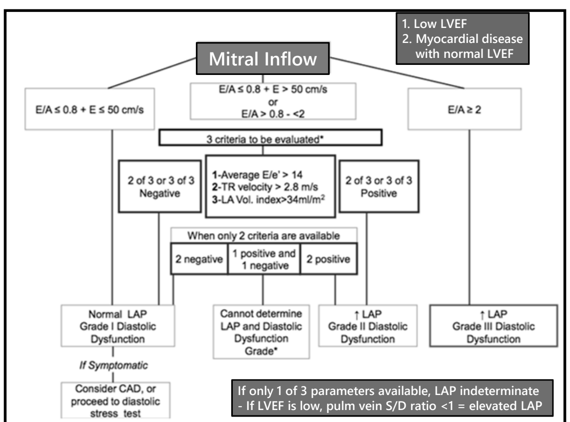
+ 1 of

Structural abnormality
- LAVI) >34 mL/m²
- LVMI ≥115 g/m² (males) ≥95 g/m2 (females)

Functional abnormality
- E/e' ≥13
- mean e' <9 cm/s

2016 ASE Diastolic Function Guidelines





2016 ASE Diastolic Function Guidelines

Table 4 LV relaxation, filling pressures and 2D and Doppler findings according to LV diastolic function

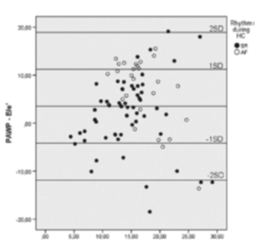
	Normal	Grade I	Grade II	Grade III
LV relaxation	Normal	Impaired	Impaired	Impaired
LAP	Normal	Low or normal	Elevated	Elevated
Mitral E/A ratio	≥0.8	≤0.8	>0.8 to <2	>2
Average E/e′ ratio	<10	<10	10–14	>14
Peak TR velocity (m/sec)	<2.8	<2.8	>2.8	>2.8
LA volume index	Normal	Normal or increased	Increased	Increased

2016 ASE Guidelines: Caveats

- Expert consensus, not fully validated
- Confusion as to which algorithm to use
- Indexes often provide conflicting "indeterminate" info
- Not pure diastolic index: LAVI, PASP
- Affected by non-diastolic factors: PASP, LAVI
- Not routinely applicable in many situations: AF, VHD, etc

Pitfalls of e′ and E/e′

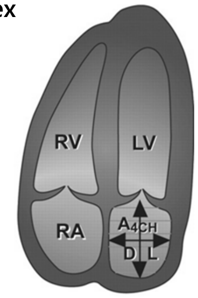
- E/e′ derived from empiric observations
- Unreliable in
  - Spherical LV, hyperdynamic state
  - RWMA: AMI/scar, paced, LBBB
  - MV disease: MS, MR >moderate, MVR/repair
  - MAC, Constriction
  - Others: LVAD, RV disease (lateral vs. septal e′)
- Measurement error



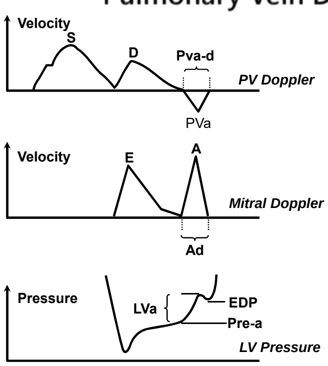
Hummel. Eur J Heart Fail. 2017

Left Atrial Volume

- LA enlargement is not index of instantaneous pressure
  - takes time to occur
  - persists long after LAP ↓
- LAE may be present in
  - athletes
  - bradycardia
  - anemia
  - atrial arrhythmias
  - MV disease



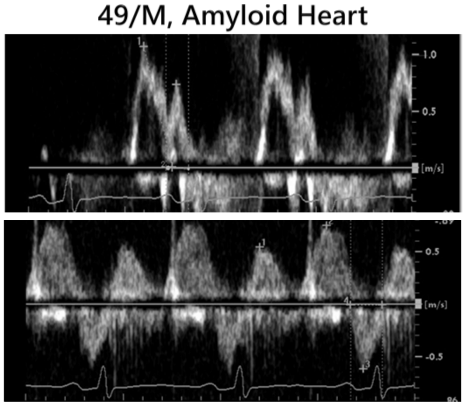
Pulmonary Vein Doppler



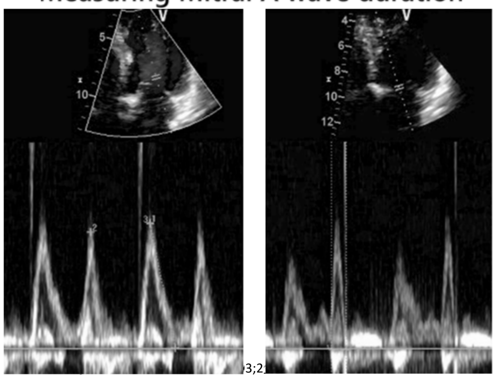
Mean LAP high if
- S/D ratio <1
- systolic filling fraction <40%

Rossvoll and Hatle. J Am Coll Cardiol 1993

49/M, Amyloid Heart

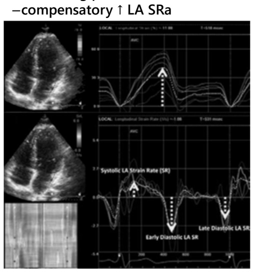


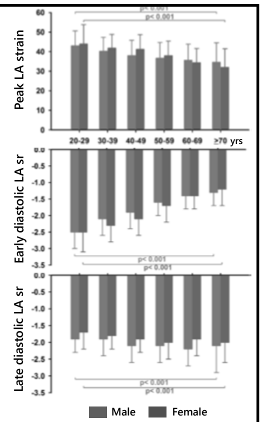
Measuring Mitral A wave duration



LA Strain and Age

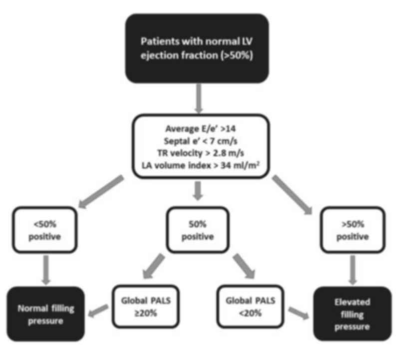
- LA speckle-tracking in 2812 healthy subjects (65% men; age 47±10 yrs)
- women had higher peak strain but also ↑ functional decay with ageing than men
- ↑ age and BP independently a/w
  - worsening peak strain
  - compensatory ↑ LA SRa





26 Liao. Circ Cardiovasc Imaging. 2017

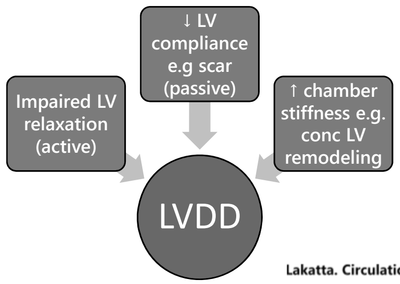
LA Strain in the LVDF Algorithm



27 Cameli. Heart Fail Rev. 2017

What Causes LVDD/↑ LVEDP?

Normal aging → myocardial fibrosis, altered collagen properties and abnormal calcium handling → reduced LV compliance and relaxation



Lakatta. Circulation 2003

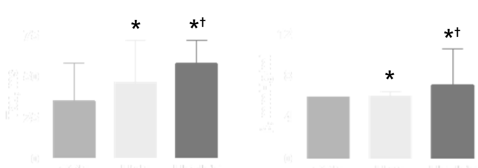
LV Diastolic Pressure (mmHg)

Table 1. **Left Ventricular Pressure, Volume, Relaxation, and Passive Stiffness.***

Variable	Patients with Diastolic Heart Failure (N=47)	Controls (N=10)	P Value
Body-surface area (m^2)	2.2±0.25	2.1±0.18	0.31
Heart rate (beats/min)	71±11	73±13	0.81
Volume at P_{min} (ml)	51±13	55±7	0.31
Volume at P_{preA} (ml)	75±15	88±8	0.03
End-diastolic volume (ml)	103±22	115±9	0.01
P_{min} (mm Hg)	12±6	4±1	<0.001
P_{preA} (mm Hg)	16±5	6±2	<0.001
End-diastolic pressure (mm Hg)	25±6	8±2	<0.001
τ (msec)	59±14	35±10	0.01
P_{sr} (mm Hg)	7±5	0	<0.001
Corrected minimal diastolic pressure (mm Hg)	5±2	4±1	0.10
Measured stiffness			
Curve-fitting constant	6.5±4.3	2.3±0.8	0.003
Stiffness constant	0.02±0.01	0.01±0.01	0.01
Corrected stiffness			
Curve-fitting constant	1.5±1.1	2.3±0.8	0.03
Stiffness constant	0.03±0.01	0.01±0.01	<0.001

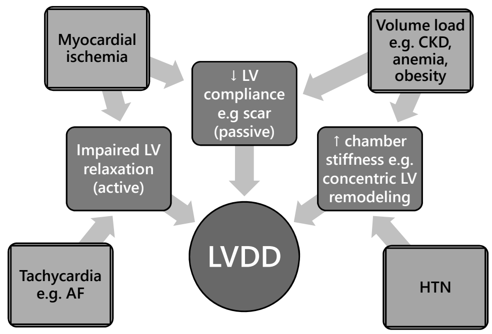
Zile, N Engl J Med 2004;350:1953-9

LVDF: Control (n=617) vs HTN (719) vs HFPEF (244)
LV Relaxation & Diastolic Stiffness

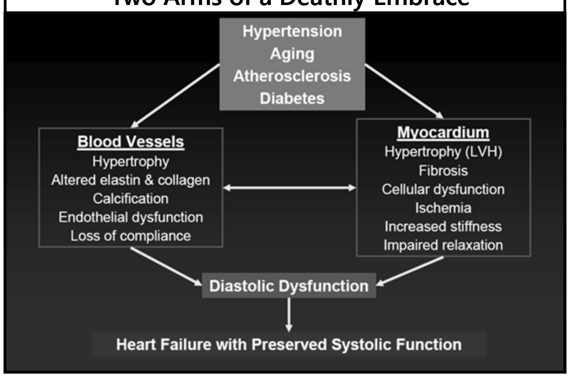


Adjusted p *<0.05 vs CON; †<0.05 vs HTN

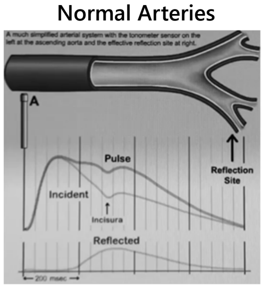
What Causes LVDD/↑ LVEDP?



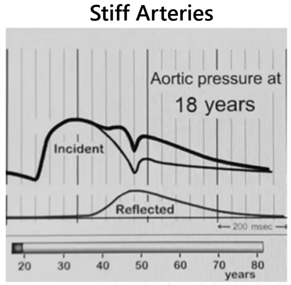
HTN and LVDD: Two Arms of a Deathly Embrace



Normal Arteries



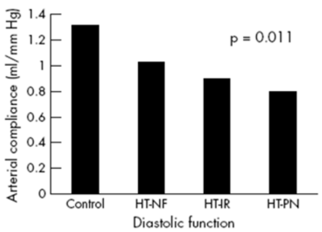
Stiff Arteries



Animation from AtCor Medical

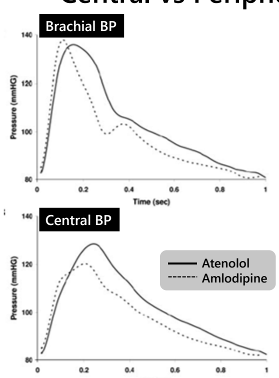
Consequences of Arterial Stiffening

- ↑ LV load → LVH, HFPEF
- ↑ central pulse pressure → CVA, renal failure
- ↓ diastolic coronary perfusion pressure → ischemia



Mottram. Heart 2005

Central vs Peripheral BP in ASCOT

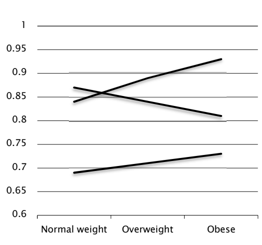


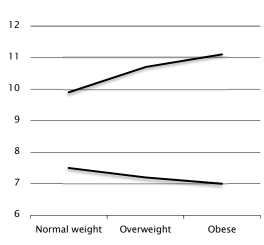
- CAFÉ substudy (n=
  - Amlodipine ↓ CASP 4mmHg vs. atenolol
  - central PP significantly a/w composite outcome of total CV events & procedures + onset of renal impairment
- LVDF substudy (n=563)
  - LVMI and LAV ↓ in both gps
  - E/e' unchanged in amlodipine gp but ↑ in atenolol gp

Williams. Circulation 2006
Barron. Hypertension. 2014

Diastolic Function by BMI

LVDF measured in 950 subjects in community-based CABL (Cardiovascular Abnormalities and Brain Lesions) study





Values adjusted for age, sex, LVMI, HR, HTN, DM

Russo. J Am Coll Cardiol 2011;57:1368-74

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Background. Heart failure with preserved ejection fraction (HFpEF), traditionally considered a disease of the elderly, may also affect younger patients. However, little is known about HFpEF in the young.

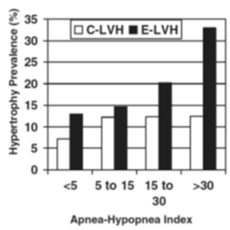
Methods. We prospectively enrolled 1203 patients with HFpEF (LVEF≥50%) from 11 Asian regions. We grouped patients into very young (<55 years; N=157), young (55-64 years; N=284), older (65-74 years; N=355), and elderly (≥75 years; N=407) HFpEF, and compared clinical and echocardiographic characteristics, quality of life and outcomes across age groups and between very young HFpEF and age- and sex-matched controls without HF.

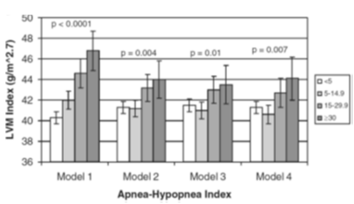
Results. Thirty seven percent (37%) of our HFpEF population was under 65 years of age. Younger age was associated with male preponderance, a higher prevalence of obesity (BMI≥30 kg/m^2; 36% in very young HFpEF vs 16% in elderly) together with less renal impairment, atrial fibrillation and hypertension (all p<0.001). Left ventricular filling pressures and prevalence of LV hypertrophy were similar in very young and elderly HFpEF. Quality of life was better, and death and HF hospitalization at 1 year occurred less frequently (p<0.001) in the very young (7%) compared to elderly (21%) HFpEF. Compared to controls, very young HFpEF had three-fold higher death rate and twice the prevalence of hypertrophy.

Conclusion. Young and very young patients with HFpEF display similar adverse cardiac remodeling as their older counterparts, and very poor outcomes compared to controls without HF. Obesity may be a major driver of HFpEF in a high proportion of HFpEF in the young and very young.

Sleep Apnea and LV Mass

Sleep Heart Health Study
- 2058 community-based participants (mean age 65±12 yrs; 58% women)
- SDB associated with ↑ echo LV mass





Association of LVM index with AHI
- Model 1: age, sex, race, and parent cohort
- Model 2: +BMI
- model 3: +SBP, antiHTN meds, Hx AMI
- model 4: +DM, smoking, EtOH

Chami. Circulation. 2008;117:2599

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Conclusions

- LVDF is a continuum, with evolution from early age
- Despite authoritative guidelines, distinction between normal and abnormal LVDF is often unclear
- Pitfalls and limitations of LVDF indexes should be recognized; newer ones e.g. PALS may be useful in resolving "indeterminate" LVDF
- Prevention of LVDD seems possible by risk factor intervention but needs verification in larger studies.

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