Age –Related Changes in Cardiovascular Structure: Insights from population-Based Echo Studies

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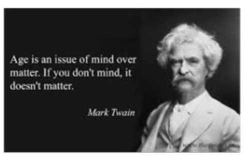
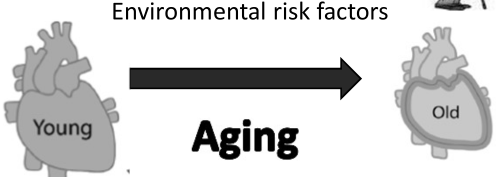
Age is BUT a Number



Environmental risk factors



Aging

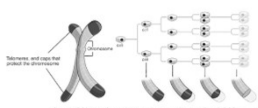
Genetic influence on human lifespan and longevity

Danish, Finnish, Swedish twins
1870-1910
20,502 individuals
Followed up till 2003-2004

- Genetic influence 25% - More important age> 65 years
- Environmental factors 50%

vB Hjelmborg J et al. Hum Genet 2006;119:312

Molecular Basis of Aging



- Shortening of the Telomere
  (nucleoprotein and caps on the chromosomes)
- Increases vulnerability of aging cells to DNA damage and dysregulation
- Inadequate replacement of damaged or dead cells from precursor cell populations

Age-associated Physiologic Changes

Hematopoietic system
Bone marrow mass decreases
Functional reserves

Liver
Reduction in Mass

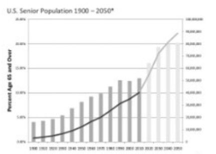
Kidneys
Decrease renal mass
Reduce creatinine clearance

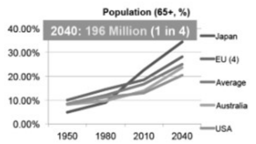
Immune function
Decrease in immune function

Lungs
Reduction in surface area
Increase in anatomic dead space

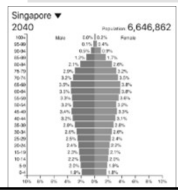
Muscle
Reduction in Muscle mass

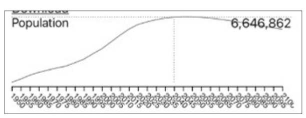
By 2040, US and Europe 1 in 4 individuals ≥ 65yrs



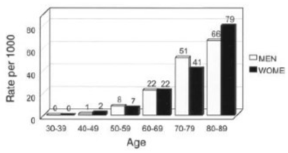


By 2040, Singapore 1 in 3 individuals ≥ 65 years

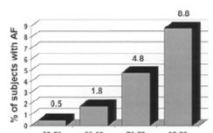




Prevalence of HF by Age in Framingham



Prevalence of AF by Age in Framingham



CHA2DS2-VASc score

C	CCF
H	Hypertension
A	**>75 years**
D	Diabetes Mellitus
S	Stroke/TIA/Systemic Embolism
V	Vascular Disease
A	**65-74 years**
Sc	Female

Age –Related Changes in Cardiovascular Structure:

LV function (LVEF, Longitudinal, Circumferential function, Torsion
LV remodeling (LV size, LV wall thickness, LV mass, /Volume)

Normal Population Studies
Asklepios,
CARDIA5,
Flemehgho,
Padua
NORRE- 734 participants.

Community / Cross-sectional and Longitudinal studies . Hypertension, DM.
Framingham Longitudinal Study – 4062 with 4 serial Echoes
HUNT study in Norway – 1980, 49827 participants, Echo in 2006-2008, 1296 participants
MESA- CMR. Cross-sectional/Longitudinal(2935)
ARIC- 1105 participants (Age 67-89years)

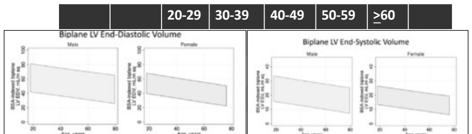
Age –Related Changes in Cardiovascular Structure:

1. LV size increases with age
2. LVEF decreases with age
3. Longitudinal function and torsion increase
4. Mass/ Volume ratio increases

LV Size and LVEF by Age and Gender

Asklepios, CARDIA5, Flemehgho, Padua

Lang RM et al. J Am Soc Echocardiogr 2015;28:1-39



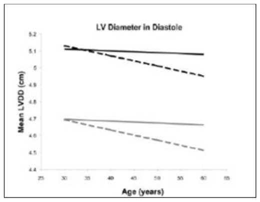
		20-29	30-39	40-49	50-59	≥60	
SV	M	73	69	66	64	62	↓
	F	55	52	49	46	44	↓
EF	M	62	61	62	63	63	↔
	F	63	63	64	64	65	↑

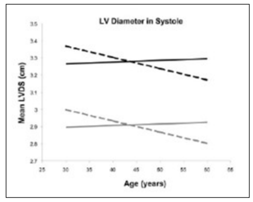
Age- and Sex-Related Influences on Left Ventricular Mechanics in Elderly Individuals Free of Prevalent Heart Failure

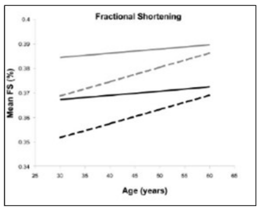
The ARIC Study (Atherosclerosis Risk in Communities)

Chung-Lieh Hung, MD, MSc*; Alexandra Gonçalves, MD, PhD, MMSc*; Amil M. Shah, MD, MPH; Susan Cheng, MD, MPH; Dalane Kitzman, MD; Scott D. Solomon, MD

	67-70 221	71-73 220	73-76 222	76-80 221	80-89 221	p
EDV	84.3	82.7	81.9	82.0	79.1	0.029
ESV	28.3	27.4	26.9	27.7	26.1	0.03
SV	56.1	55.3	55	54.1	53	0.032
LVEF	66.7	67.3	67.6	66.7	67.5	0.34







Men with RF
Men without RF
Women with RF
Women without RF

Framingham
Longitudinal follow up
4 serial Echo studies over 16 years

Cheng S. Circulation 2010;122:570-578

LVEF
2D Biplane
3D

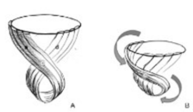
LV systolic function

- longitudinal atrial–ventricular motion may account for nearly 60% of cardiac SV,
- remaining part contributed by circumferential function and wringing motion.(Carlsson et al)

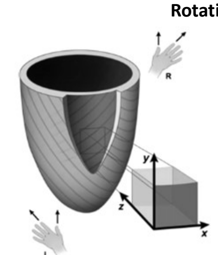
LV Longitudinal function
S' velocity
Global Longitudinal Strain

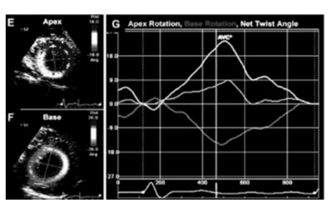
Circumferential
Radial

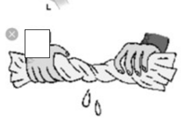
Twist
Torsion



Rotation, Twist, Torsion





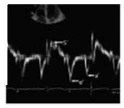


Rotation- rotation of the cross sectional plan
(LV Base and Apex)
Twist- Net rotation of the base and Apex
Torsion- Twist/Distance between the base and apex

Longitudinal Function of the LV – s’

Reference Values and Distribution of Conventional Echocardiographic Doppler Measures and Longitudinal Tissue Doppler Velocities in a Population Free From Cardiovascular Disease

Havard Dalen, MD; Anders Thorstensen, MD; Lars J. Vatten, MD, PhD; Svein A. Aase, MSc, PhD; Asbjorn Stoylen, MD, PhD



HUNT study of Norway

Age and Sex Specific of S’, Mean Annular Systolic Velocities by pw TDI

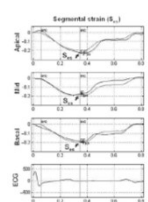
	Females	Males
Feasibility, no. (%)	652 (%)	590 (98%)
<40 yrs cm/s	8.9+1.1	9.4+1.4
40-60 yrs cm/s	8.1+1.2	8.6+1.3
> 60 yrs cm/s	7.2+1.2	8.0+1.4
All	8.2+1.3	8.6+1.4

Cir Cardiovasc Imaging. 2010;3:614-622

Longitudinal Function of the LV- Longitudinal strain by Tissue Doppler

Segmental and global longitudinal strain and strain rate based on echocardiography of 1266 healthy individuals: the HUNT study in Norway

	Female[3]	Male[3]
<40 years[4] (208 women/126 men)		
S_{es}^1 (%), mean (SD)	−17.9 (2.1)	−16.8 (2.0)
SR_s^2 (s^{-1}), mean (SD)	−1.09 (0.12)	−1.06 (0.13)
40–60 years[4] (336 women/327 men)		
S_{es}^1 (%), mean (SD)	−17.6 (2.1)	−15.8 (2.2)
SR_s^2 (s^{-1}), mean (SD)	−1.06 (0.13)	−1.01 (0.12)
>60 years (119 women/150 men)		
S_{es}^1 (%), mean (SD)	−15.9 (2.4)	−15.4 (2.4)
SR_s^2 (s^{-1}), mean (SD)	−0.97 (0.14)	−0.97 (0.14)
Mean[5]		
S_{es}^1 (%), mean (SD)	−17.4 (2.3)	−15.9 (2.3)
SR_s^2 (s^{-1}), mean (SD)	−1.05 (0.13)	−1.01 (0.13)



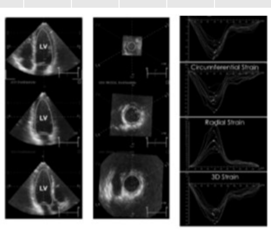
Strain and Strain deceases with age.

European Journal of Echocardiography (2010) **11**, 176–183

Age-Related Normal Range of Left Ventricular Strain and Torsion Using Three-Dimensional Speckle-Tracking Echocardiography

	1-3	4-9	10-19	20-29	30-39	40-49	50-59	>60	p
GLS	-22.7	-21.9	-21.4	-19.8	-19.1	-19.6	-19.9	-19.9	**<0.001**
GCS	-29.3	-29.4	-28.4	-28.4	-28.5	-27.4	-28.6	92.5	0.3542
GRS	88.6	92.7	90.4	86.3	83.4	82.9	84.5	92.5	0.1599
3D	-38.5	-38.8	-37.9	-36.3	-36.3	-36.2	-37.1	-39.0	**0.0188**

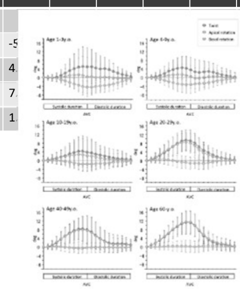
3D STE
335 participants
170 males
Age 1-88



Kaku K. et al. J Am Soc Echocrdiogr 2014;27:55-64

Age-Related Normal Range of Left Ventricular Strain and Torsion Using Three-Dimensional Speckle-Tracking Echocardiography

Age(Yrs)	1-3	4-9	10-19	20-29	30-39	40-49	50-59	>60	p
Rotation									
Basal	-5.35	-5					22	-1.70	<0.0001
Apical	5.05	4.					22	12.79	<0.0001
Twist	8.49	7.					45	12.70	**<0.0001**
Torsion	1.78	1					6	1.75	**<0.0001**



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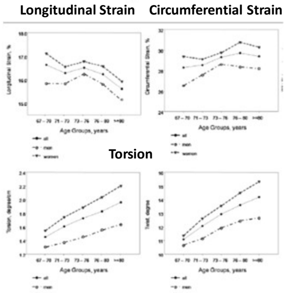
Longitudinal Strain **Circumferential Strain**

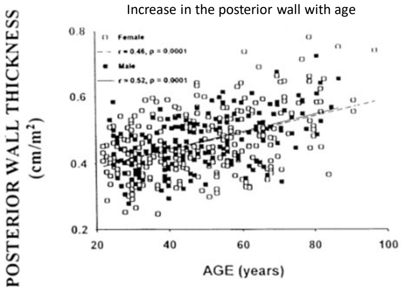


Postulated that myocardial twist may increase as a response to loss of longitudinal function → help to preserve LVEF

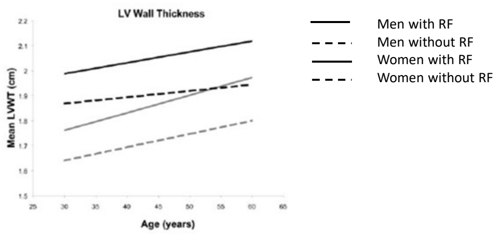
Circ Cardiovasc Imaging. 2017

LV posterior wall thickness in Healthy subjects by M-Mode
Without hypertension and cardiovascular disease

Increase in the posterior wall with age



Gerstenblitg G et aaaaal. Circ 1977;56:273-278
Benjamin EJ et al. Am J Cardiol. 1992; 70: 508-515
Swinne CJ et al. Am J Cardiol 69;69:823-826



Framingham
Longitudinal follow up
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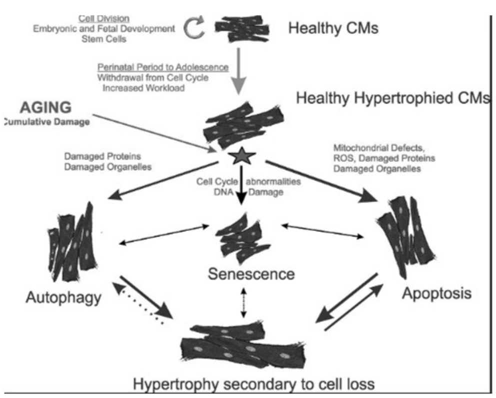
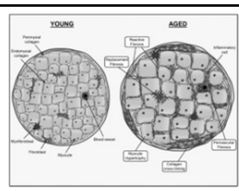


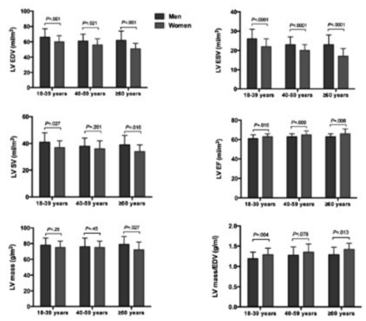


Older hospitalized patients **without apparent cardiovascular disease** –Autopsy findings
Aging rats
CMR studies

No increase in LV mass
Decrease in number of myocytes
Increase in Cardiomyocyte size (greater in males than in females)
Focal increase in collagen

Olivetti G et al. Cir Res 1991;68:1560-1568
Anversa et al. Cir Res 1990;67:671
Venkatesh et al. Hypertension 2014;64:508
Donekal et al. Circ Cardiovas c Imaging. 2014;7:292

Comprehensive Analysis of Left Ventricular Geometry and Function by Three-Dimensional Echocardiography in Healthy Adults



Age association
LV size decrease
LV mass – no change
LV mass/ Volume increase
No change in sphericity
(Increase in concentricity)

? Physiologic response to increased arterial pressure and afterload with age.

(J Am Soc Echocardiogr 2013;26:618-28.)

Age- and Sex-Related Influences on Left Ventricular Mechanics in Elderly Individuals Free of Prevalent Heart Failure

The ARIC Study (Atherosclerosis Risk in Communities)

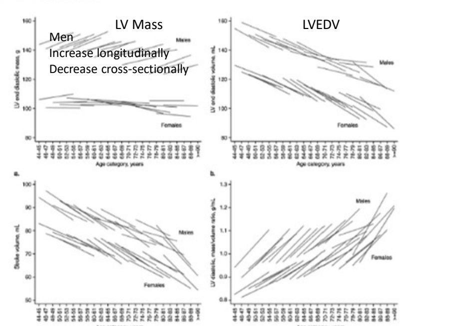
1105- Free of HF, Hypertensive, DM, CAD

Concentric Remodeling of the LV with Age
Increasing LV mass and Decreasing LV volume

Age	67-70	71-73	73-76	76-80	80-89	P value
Females%	62	63.2	63.1	57	57.9	
IVS cm	1.03	1.05	1.04	1.07	1.10	<0.001
LPW cm	0.88	0.88	0.88	0.92	0.90	0.003
LV mass I Gm/m2	74.3	76	75.7	80.3	80.2	<0.001
LV mass I 3D Gm/m2	67.3	68.4	69.4	70.5	71.5	<0.001
MV ratio	1.70	1.75	1.77	1.85	1.88	<0.001
MV ratio 3D	1.64	1.70	1.74	1.76	1.83	<0.001

Adverse Left Ventricular Remodeling and Age Assessed with Cardiac MR Imaging: The Multi-Ethnic Study of Atherosclerosis[1]

Age –related Longitudinal and cross-sectional changes of LV mass and volume in Women and Men
Baseline CMR 5004, FU CMR 2984 (9.4 years later)



Age –Related Changes in Cardiovascular Structure
LV mass/Volume

	MESA		Framingham		ARIC		3D Echo Muraru JASE 2013	
	Women	Men	Women	Men	Women	Men	Women	Men
LVM	↓	↑	WT⇧	WT↑	↑	↑	⇩	⇔
LVEDV	↓	↓	↓	↓	↓	↓	↓	↓
M/V	↑	↑	↑	↑	↑	↑	↑	↑

With increasing age, the LV becomes smaller, increase in concentricity (M/V ratio)

Gender Differences in Cardiac Remodeling, Mechanics and Torsion

	Sex, Female (vs Male) Univariable Analysis Coefficient (95% CI)	P Value	Multivariable Analysis Coefficient (95% CI)	P Value
Conventional echocardiography				
EDV, mL	−27.4 (−29.6, −25.2)	<0.001	−26.6 (−28.9, −24.3)	<0.001
ESV, mL			−10.69 (111.79, 19.58)	<0.001
SV, mL			−15.93 (−17.4, −14.46)	<0.001
LVEF, %			2.35 (1.65, 3.06)	<0.001
Longitudinal strain, %			−0.76 (−1.13, −0.38)	<0.001*
Circumferential strain, %			−2.00 (−2.71, −1.29)	<0.001
Twist, degree			1.74 (1.22, 2.26)	<0.001*†
Male				
Female				
Torsion, degree/cm			0.42 (0.35, 0.49)	<0.001*†
Male				
Female				
TCR, degree×%/cm			−1.07 (−1.32, −0.82)	<0.001*†
Male				
Female				

Women

Women
- Smaller Volumes in women
- Higher LV function and greater Torsion
- Provide adequate CO to meet tissue demands

Men
- Greater chamber size, higher mass and
- lower intrinsic contractile function

Higher rate of cardiomyocyte turnover, apoptosis, and fibrosis.

Piro M. JACC 2010, Olivetti G. JACC 1995
Mallat Z. J Gerontol A Biol Sci 2001

Smaller LVEDV and LVESV

Higher LVEF

Higher LS

Greater Torsion

Circ Cardiovasc Imaging. 2017. J Am Soc Echocardiogr 2013

Gender Differences in Cardiac Remodeling, Mechanics and Torsion

	Sex, Female (vs Male) Univariable Analysis Coefficient (95% CI)	P Value	Multivariable Analysis Coefficient (95% CI)	P Value
Conventional echocardiography				
EDV, mL	−27.4 (−29.6, −25.2)	<0.001	−26.6 (−28.9, −24.3)	<0.001
ESV, mL	−10.83 (−11.83, −9.84)	<0.001	−10.69 (111.79, 19.58)	<0.001
SV, mL	−16.57 (−18.01, −15.13)	<0.001	−15.93 (−17.4, −14.46)	<0.001
LVEF, %	2.13 (1.52, 2.74)	<0.001	2.35 (1.65, 3.06)	<0.001
IVS, cm	−0.07 (−0.09, −0.05)	<0.001	−0.07 (−0.09, −0.05)	<0.001*
LVPW, cm	−0.07 (−0.08, −0.05)	<0.001	−0.07 (−0.09, −0.05)	<0.001*
LV mass index, gm/m²	−8.56 (−10.78, −6.34)	<0.001	−7.26 (−9.58, −4.94)	<0.001*
LV mass index, 3D, gm/m²	−8.80 (−10.32, −7.28)	<0.001	−7.88 (−9.56, −6.21)	<0.001*
MV ratio	0.15 (0.10, 0.21)	<0.001	0.17 (0.11, 0.23)	<0.001*
MV ratio, 3D	0.07 (0.03, 0.11)	0.001	0.05 (0.01, 0.10)	0.018*

LV wall thickness
Men > Women

LV Mass Index
Men > Women

Mass to Volume ratio
Women > Men

Cardiac Adaptions, Mechanics and torsion in Hypertension

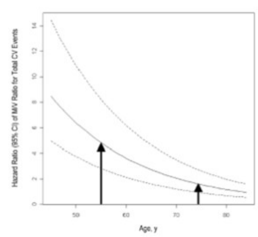
- Thicker IVS and LVPW
- Higher LV mass index
- Worse Longitudinal function
  (attenuated with adjustment for LV geometry)
- Greater torsion indices

Fibrosis, Extracellular matrix deposition,
Concentric remodelling, Subclinical ischaemia

Hung Clet al. Circ Cardiovasc Imaging.2017;10
Cheng S et al. Circulation;122:570

Age-Related Left Ventricular Remodeling and Associated Risk for Cardiovascular Outcomes: The Multi-Ethnic Study of Atherosclerosis

Increasing Mass / Volume Ratio
associated with
Increased risk of CV events

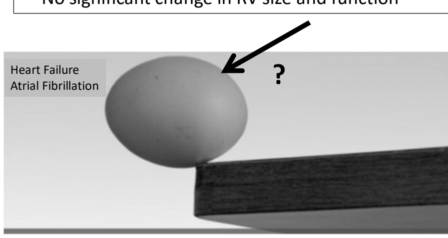


Fitted curves represent hazard ratios (95% CI) of M/V ratio with respect to total CV events across increasing age while adjusting for age, sex, race/ethnicity, height, weight, hypertension status, LDL cholesterol, diabetes, and smoking. As shown, the risk is greater for those individuals who develop the "typical" age-associated LV remodeling phenotype at a younger compared to older age (arrows).

Circ Cardiovasc Imaging. 2009 May ; 2(3): 191–198.

Age –Related Changes in Cardiovascular Structure

- Maintain LVEF, Decrease LS, Increase Torsion
- Decrease in LVEDV, increase Mass/Volume ratio (Concentricity)
- LV diastolic function, LA size
- No significant change in RV size and function



Thank you