

#ASEchoJC Twitter Chat

Tuesday, September 15 – 8 PM ET

Similarities and Differences in Left Ventricular Size and Function among Races and Nationalities:

Results of the World Alliance Societies of Echocardiography Normal Values Study, Asch, Federico M. et al., *Journal of the American Society of Echocardiography*, Volume 32, Issue 11, 1396-1406.e2.

Introduction & Welcome: Ritu Thamman (@iamritu) & Enrique Garcia-Sayan (@EGarciaSayan) – Moderators

Welcome everyone to tonight's #ASEchoJC on WASE study- a groundbreaking observational study by @robertomlang & @FedericoAsch who are our guests tonite done around Globe to define WHAT IS NORMAL for LV size&fxn

Tweetorial: <https://twitter.com/iamritu/status/1305234224203681792?s=20>

Q1: What was the impetus to conduct the #WASE study?

A1 Notable Responses:

Roberto Lang (@robertomlang): Reference limits in current guidelines used globally are based on European and American individuals. But its apparent that different ethnicities may have different normal values. WASE was created from 15 countries to reflect the diversity of populations around world

Enrique Garcia-Sayan (@EGarciaSayan): Key basis for WASE normal values study:

- Not all Red heartare the same
- Prior studies mainly performed in United States/EU
- Measurements not done the same way as today
- Not always utilizing a core lab

Ritu Thamman (@iamritu): Perhaps one of the reasons is that prior studies were not uniformly conducted @ASE360 Foundation sponsored #WASE to get a uniform assessment of LV size & function

Ritu Thamman (@iamritu): 15 countries & 18 centers around the world!! This is a major accomplishment



WASE world map depicting countries that completed enrollment in the WASE Normal Values Study.

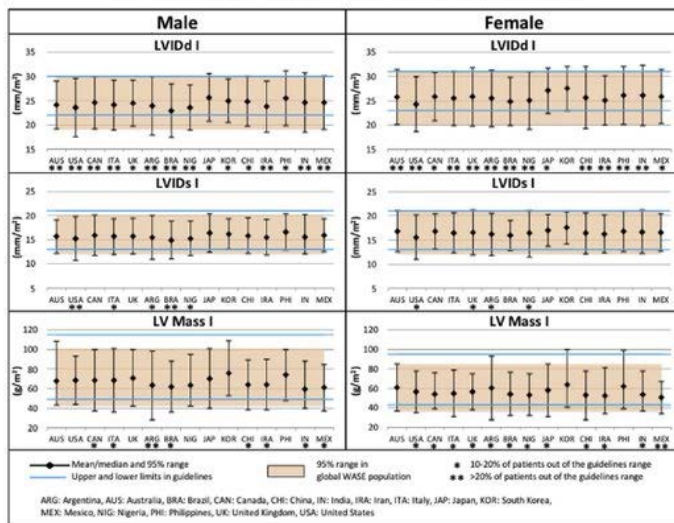
Roberto Lang (@robertomlang): Each of the papers published from the WASE study will have over 2000 subjects, both males and females, representing all continents and divided equally into 3 age groups

Q2: How did the WASE results differ from the @ASE360 #EACVI guidelines?

A2 Notable Responses:

Enrique Garcia-Sayan (@EGarciaSayan): some key differences were noted with guidelines. WASE study found smaller LV linear dimensions, and larger volumes. Authors @robertomlang & @FedericoAsch mention technique may play a role. M-mode overestimates, and suboptimal biplane MoD underestimates measurements.

Left Ventricular Linear Measurements in WASE vs ASE Guidelines



J Am Soc Echocardiogr. 2019;32(11):1396-1406.e2.

#ASEchoJC @EGarciaSayan

Roberto Lang (@robertomlang): Large countries, such as Brazil, China, and India, may represent different ethnic groups. These differences will unfortunately not be elucidated in the #WASE study

Raj Janardhanan (@rajdoc2005): Was the data equally distributed amongst these larger countries? Or did any particular country dominate - to create a bias?

Federico Asch (@federicoasch): Each center enrolled 100 subjects. a few countries had 2 centers, but equally distributes by age and gender

Q3: How do the WASE values of LVEDV & LVESV impact stroke volume criteria for Low flow aortic stenosis (Svi <35ml/m2)

A3 Notable Responses:

Federico Asch (@FedericoAsch): #WASE only help distinguish normal YES/NO. Abnormals were not studied. LFLG in AS different from Normal values. LFLG <35 tested specifically in AS population towards outcomes. WASE does not challenge this notion

Roberto Lang (@robertomlang): In clinical medicine, the criteria used to define low vs high output cardiac states are arbitrary, and do not account for ethnic diversity. We are currently studying this, and anticipate that normal reference values will change according to ethnicity, BSA, and height.


Ezequiel Guzzetti MD (@E_Guzzetti): Excellent point. Sex differences should also be accounted (women have smaller LV volumes) In a recent paper we published with @PPibarot and @ClavelLabo in @JACCJournals optimal cut-points for low-flow were <32 ml/m2 for women vs <40 ml/m2 for men

Q4: What is the significance of the WASE finding that Women have higher GLS?

A4 Notable Responses:

Federico Asch (@FedericoAsch): Women have better indices of function: no news. While GLS is novel, higher EF was news with 2015 CQ Guidelines. Likely just a reflection of smaller ventricles, but the strain difference questions the concept.

Ritu Thamman (@iamritu): Are you looking into LV GLS in other cohorts of females by age?

GLS slightly Higher in Females #ASEchoJC  **ASE** AMERICAN SOCIETY OF ECHOCARDIOGRAPHY
Sound Saves Lives

Female	GLS, %	Country	Male	GLS, %
ARG	-17 to -26	ARG	ARG	-18 to -25
AUS	-17 to -25	AUS	AUS	-17 to -24
BRA	-18 to -26	BRA	BRA	-17 to -25
CAN	-17 to -25	CAN	CAN	-17 to -23
CHI	-18 to -25	CHI	CHI	-17 to -25
IN	-18 to -26	IN	IN	-17 to -25
IRA	-19 to -26	IRA	IRA	-17 to -24
ITA	-18 to -27	ITA	ITA	-18 to -24
JAP	-18 to -27	JAP	JAP	-17 to -24
KOR	-17 to -26	KOR	KOR	-16 to -23
MEX	-19 to -26	MEX	MEX	-19 to -24
NIG	-18 to -26	NIG	NIG	-17 to -24
PHI	-17 to -24	PHI	PHI	-17 to -23
UK	-18 to -26	UK	UK	-17 to -25
USA	-18 to -26	USA	USA	-17 to -24
% of variation	4.78	% of variation	6.04	
P	.026	P	.020	

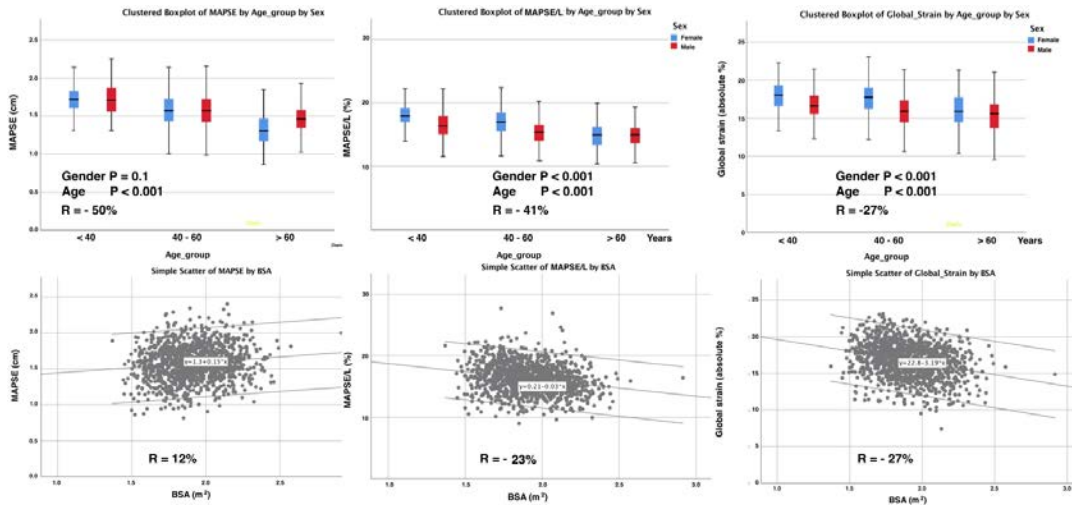
Federico Asch (@FedericoAsch): Not yet, but strain 3D will be coming and plenty of opportunities with it

Asbjørn Støylen (@strain_rate): 1/ In the HUNT3 study, EF and GLS was highest in women, S' in men, while MAPSE showed no sex difference. The effect was present in all age groups.

<https://pubmed.ncbi.nlm.nih.gov/29399886/>

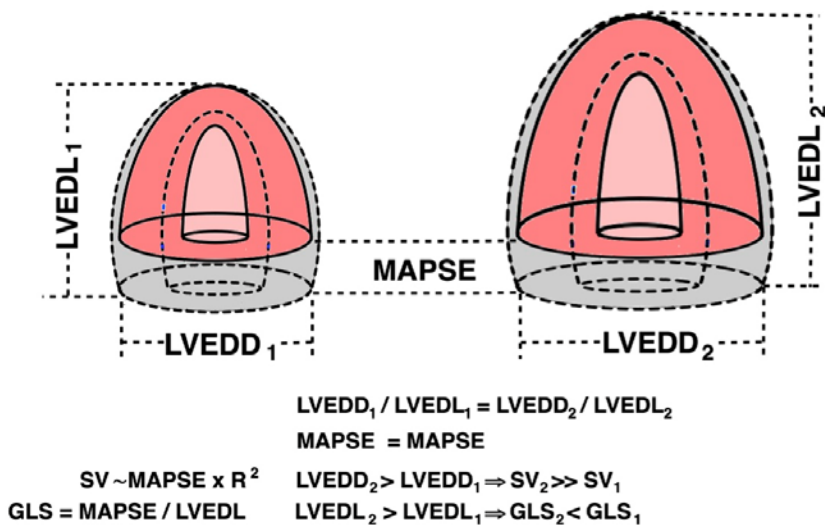
2/ Sex difference was also independent of method for GLS. But it was a simple effect of body (heart) size, while MAPSE was BSA and sex independent.

http://folk.ntnu.no/stoylen/strainrate/What_does.html#Why_is_GLS_normalised_MAPSE_more_BSA



3/ Why is this? We also found in the HUNT study that the LV length/external diameter ratio was BSA independent, so bigger LVs were both longer AND wider.

4/ about 70% of stroke volume is due to long axis shortening. Thus, the MAPSE part of SV dominates, and = long axis shortening x mitral annular external area. With a larger diameter of a larger heart, SV is larger even with unchanged MAPSE.



5/ GLS is MAPSE corrected for LV (or wall) length, but not for diameter, so it DECREASES by increasing body and heart size, a systematic error that carries over to sex differences. MAPSE had a weak positive correlation with BSA, but not enough for significant sex differences

Erin Michos (@ErinMichos): Did you know that women have higher #GLS ? #ASEchoJC #WASE Normal Values Study

Q5: How should the finding of lower abnormality cutoff of LVEF be adjusted upward? By what % ?

A5 Notable Responses:

Federico Asch (@FedericoAsch): BREAKING NEWS: CRITICAL FINDING!!! #WASE: EF>57%(M), >58%(F) should be Normal cutoff, small variations among nationalities and gender, opposed to 52% and 54% in Guidelines. #WASE consistent with CMR data

Enrique Garcia-Sayan (@EGarciaSayan): LLN of LVEF must be adjusted based on #WASE study findings. Will affect common practice of referring to 50-55% as "low normal" (embedded in software too). How about LLN of 53% for cardio-oncology?

In both genders, average LVEF values were similar among races and countries, with small variations of the order of magnitude of 1% to 2%. Similar to the guidelines, normal LVEF values were slightly higher in women than in men. Of note, however, the entire normal range of LVEF was considerably narrower in both genders, across races and countries. This is likely a result of the uniformity in data acquisition and interpretation methodology, as well as the larger sample size. These results suggest that the LLN of LVEF should be adjusted upward from the previously recommended cutoff values.

Jose Donato Magno (@doc_jdam): I think one way to approach the dilemma is to consider the individual as his or her own "reference standard." This stresses the value of a good baseline echo most especially in medical conditions that require monitoring of LV size and systolic function. #WASE

Harriet Van Spall (@hvanspall): All things consid'd, 55-60% is likely where N #EF sits, closer to 55 for 🧑 & 60 for 🧑. #EF may not be the ideal classific'n scheme in #HF (we have related work under review) but remains a practical approach to guide Tx until other approaches are used to test Tx effic'y

Q6: How should we adjust LV indexed dimensions and LV mass based on your WASE results?

A6 Notable Responses:

Federico Asch (@FedericoAsch): So far we have only explored indexing by BSA in #WASE. Further comparisons indexing by height, weight or BSA are being evaluated. More to come, stay tuned!

David Wiener (@DavidWienerMD): This is a huge issue, given the obesity epidemic; where indexing by BSA introduces a whole new source of error

Shaden Khalaf (@ShadenKhalaf): Indexing to BSA is problematic in my opinion. We often drop a patients weight > 10lbs pounds in a couple of days of CHF admission with diuresis. Or than if ur pregnant. The numbers will be all over the place

Jordan Strom (@DocStrom): Good point. Lots of variation here too. Some recommend indexing to height or height² for this reason. Important that #WASE will be including height in future study.

Q7: What are some pitfalls in measuring LV dimensions?

A7 Notable Responses:

Roberto Lang (@robertomlang): LV dimensions should be measured from 2D PLAX view, making sure that measurements are made perpendicular to the long axis of the LV at the tip of the mitral valve leaflets

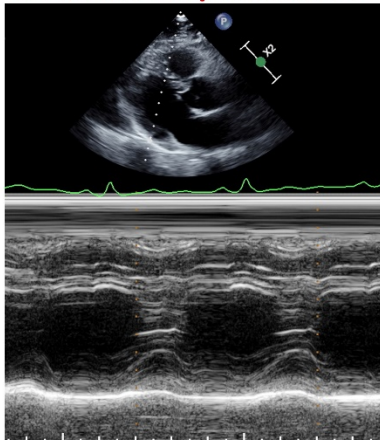
Jordan Strom (@DocStrom): How do you handle basal septal hypertrophy in LV measurement? Lots of variation in what is done in practice - would love to hear what Il Maestro has to say.

Roberto M Lang (@robertomlang): Good question - we usually measure immediately distal to the upper septal thickening. Not many of the #WASE subjects had this finding

Enrique Garcia-Sayan (@EGarciaSayan): importance of proper 2-D measurement of LV to avoid overestimating size, volume and mass. Major difference between #WASE study and older data!

Why are LV linear measurements and LV mass index lower in WASE?

M-mode Perpendicular?



than previously reported. As a result, in all countries, $\geq 10\%$ of the study subjects, and in most countries $>20\%$, fell below the guidelines recommended ranges. This finding was more pronounced for end-diastolic compared with end-systolic dimensions. A possible explanation for these findings is that the guideline-recommended normal values of linear dimensions were obtained from a mix of parasternal short- and long-axis views, as well as M-mode images, in which oblique cross-sections might have resulted in overestimated dimensions. In contrast, in our study, all linear dimensions were obtained from 2D parasternal long-axis views, in which particular care was taken to identify the dimension perpendicular to the long axis of the ventricle at the tip of the mitral valve leaflets. Such differences between WASE results and the guidelines propagated into LV mass measurements, which resulted in lower normal ranges. As a result, for both genders and most races and countries, $\geq 10\%$ of the study subjects fell below the guideline-recommended ranges of LV mass. Despite the small differ-

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Tatsuya Miyoshi (@Tatsu_Miyoshi): Some elderly had septal hypertrophy, but most of all middle and young age subjects didn't have it.

Federico Asch (@federicoasch): Foreshortening, oblique measurements, etc. #WASE Instructed acquisition avoiding LV foreshortening, similar length in A2C and A4C views. May explain why WASE volumes are higher than those in guidelines.

Ritu Thamman (@iamritu): signs your #LV Is Foreshortened

- 1.apex will move rapidly rather than appear stationary compared to other segments
2. Globular rather than bullet/tapering shape
- 3.Apical 4 & 2 chamber view have different apex lengths/size
4. apex looks thick(should look thin)

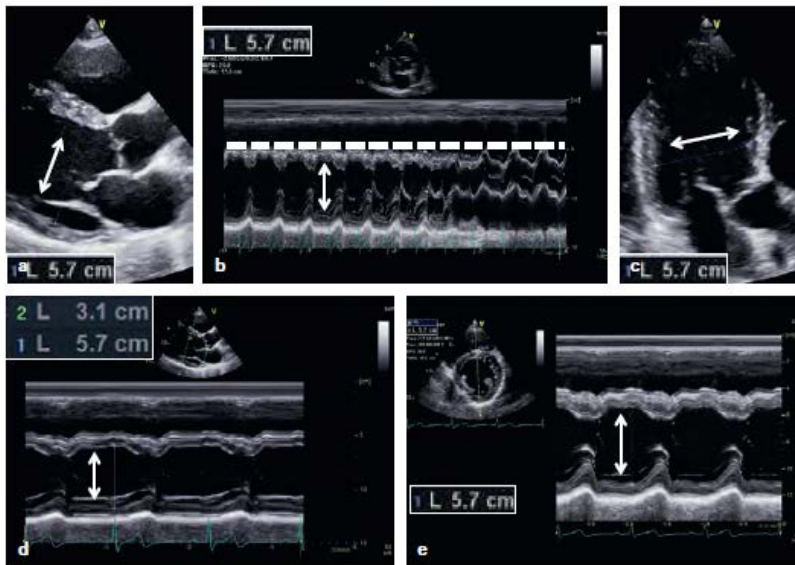
Left Heart Interrogation – Foreshortening



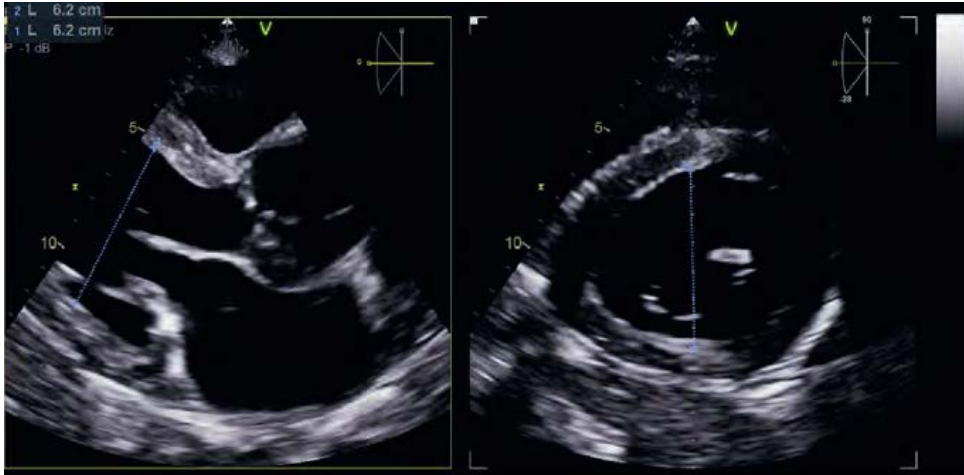
Vincent Sorrell: (@VLSorrellImages): Non-alignment May create pseudo-dilation which has the downstream potential to lead to mismanagement (eg. Unnecessary VHD surgery).

Sorrell motto: "LV measures are like echo vital signs!"

Echocardiography sbs (@echo_stepbystep): Testing of LV cavum diameters with different measuring methods:

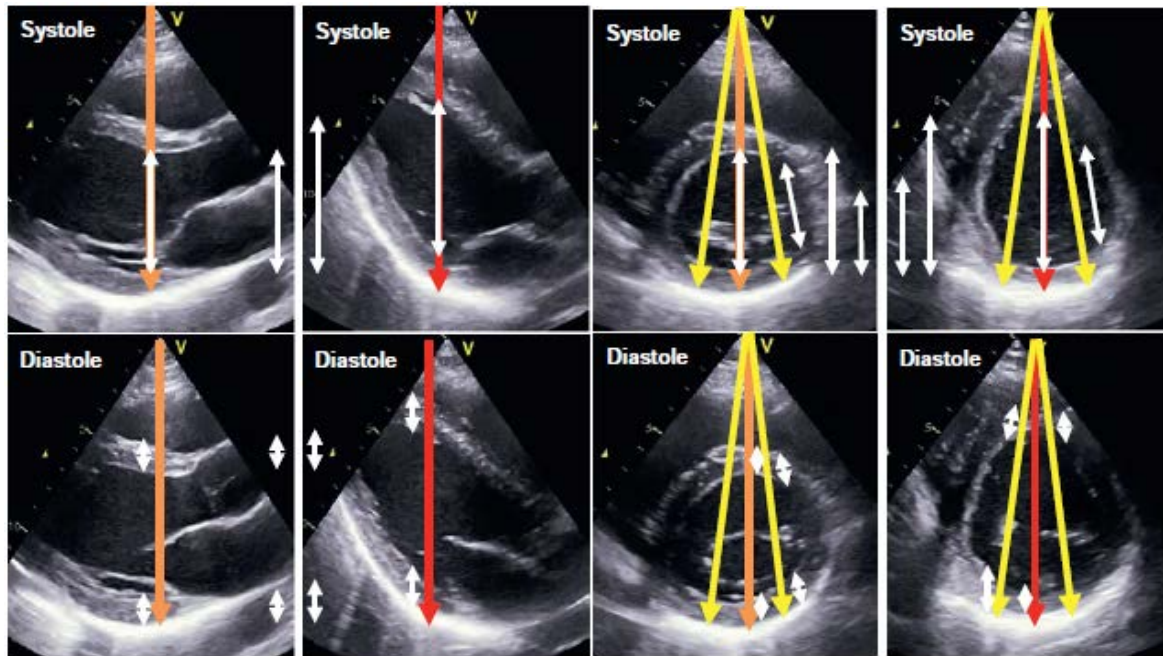


Echocardiography sbs (@echo_stepbystep): Illustration of the misdetermination of diameters and wall thicknesses of the LV in M-mode due to lack of standardization:



Echocardiography sbs (@echo_stepbystep): Above in the picture (a) is a biplane representation of the parasternal long axis with simultaneous derivation of the corresponding perpendicular short. Despite chord threads, this long axis is centrally set, so that the cavum with one. Diameter of 62 mm can be measured correctly

Echocardiography sbs (@echo_stepbystep): Illustration of the misdetermination of diameters and wall thicknesses of the LV in M-mode due to lack of standardization:



Laurent Quiqueree (@lquiquer): work hard on it and take your time you can get perpendicular with M-Mode in 95% cases, don't give up, move your patient, correlate with 2-d ... M-Mode still should be 1st choice. Better temporal resolution, 2-d lazy way out and not as accurate

Roberto Lang (@robertomlang): Measurements should not be obtained from 2D targeted M-Mode, and care should be taken to avoid foreshortening of the LV

Roberto Lang (@robertomlang): When establishing normal values, each country should strictly follow the ASE/EACVI quantification guideline

Q8: How was the statistical analysis done for #WASE

A8 Notable Responses:

Roberto Lang (@robertomang): Statisticians from @FedericoAsch's MedStar corelab analyzed the data. Complicated given the GIGANTIC excel database

Federico Asch (@FedericoAsch): Important improvement from previous studies: Normal ranges defined per standards, as the values that would include 95% of the normal population, excluding 2.5% on each extreme. Stats methods depending on normality of data distribution for each category

Laurey (@su_dar_shan): This would be assuming LVEF has normal distribution. Was it so or skewed to one side on the #WASE data?

Tatsuya Miyoshi (@Tatsu_Miyoshi): LVEF in both gender has normal distribution in #WASE study.

Sharon Mulvagh (@HeartDocSharon): Have we addressed normal values with UEA (contrast agents)? This is really needed! Is there a subset?

Ritu Thamman (@iamritu): No #UEA subset in WASE