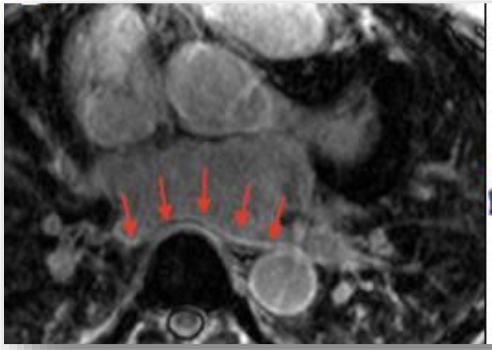
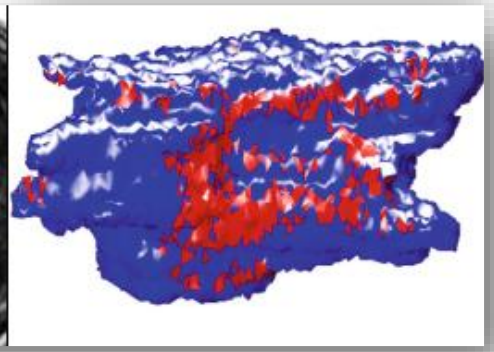
INDICAZIONE DEI NUOVI ANTICOAGULANTI ORALI
IN TEMA DI FIBRILLAZIONE ATRIALE

Roma, 8-9 Marzo 2019



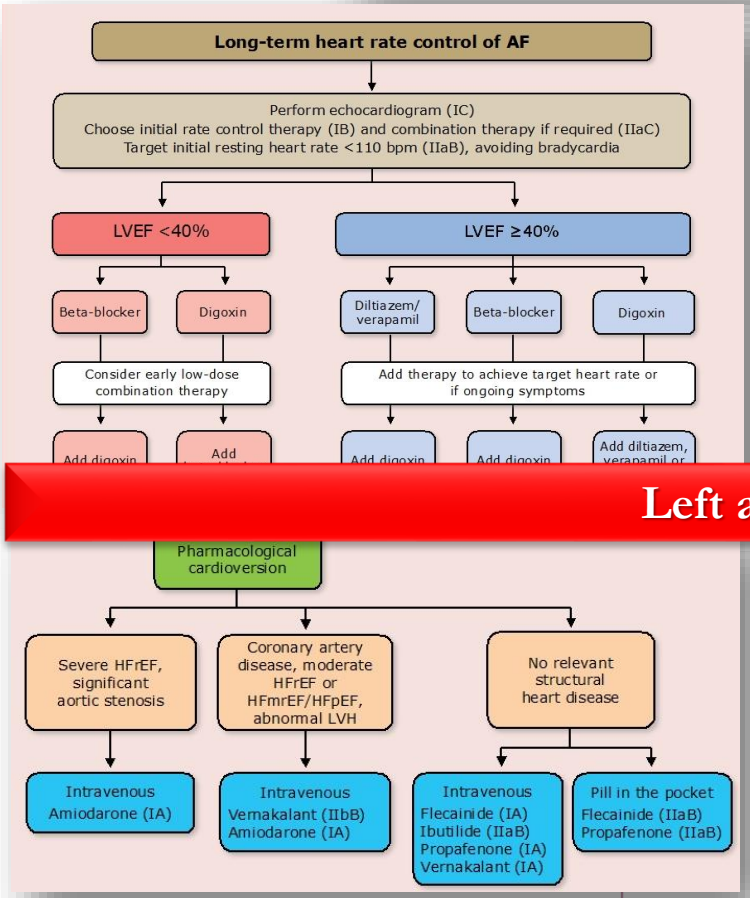


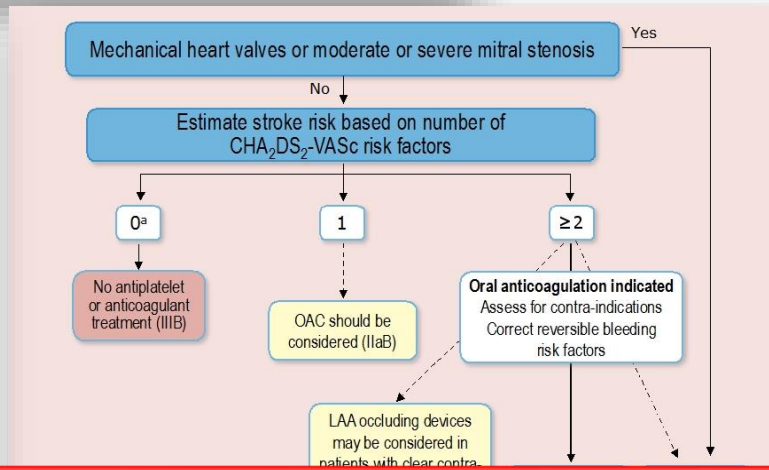
# *Imaging del danno d'organo della fibrillazione atriale*

**Gabriella Locorotondo, MD PhD**
**U.O. Diagnostica Cardiologica Non Invasiva**
**Fondazione Policlinico Universitario A. Gemelli IRCCS Roma**

# Role of imaging in current ESC guidelines

| Recommendations | Class | Level |
|---|---|---|
| ECG documentation is required to establish the diagnosis of AF. | I | B |
| A full cardiovascular evaluation, including an accurate history, careful clinical examination, and assessment of concomitant conditions, is recommended in all AF patients. | I | C |
| Transthoracic echocardiography is recommended in all AF patients to guide management. | I | C |
| Long-term ECG monitoring should be considered in selected patients to assess the adequacy of rate control in symptomatic patients and to relate symptoms with AF episodes. | IIa | C |



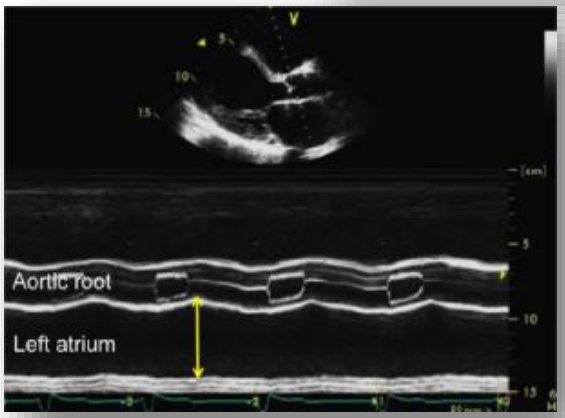

**Left atrial size**

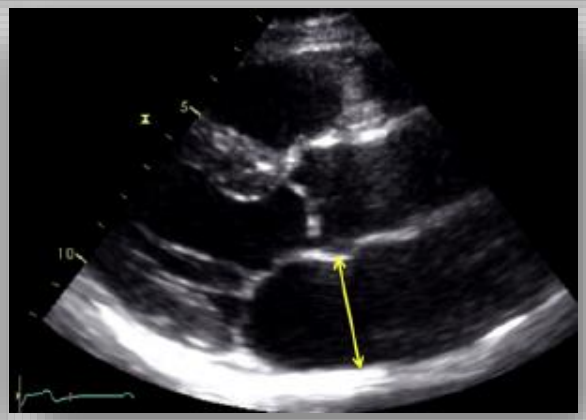
| Recommendations | Class[a] | Level[b] | Ref[c] |
|---|---|---|---|
| Early mitral valve surgery should be considered in severe mitral regurgitation, preserved LV function, and new-onset AF, even in the absence of symptoms, particularly when valve repair is feasible. | IIa | C | 276 |
| Mitral valvulotomy should be considered for asymptomatic patients with severe mitral stenosis and suitable valve anatomy who have new-onset AF. | IIa | C | |


European Heart Journal - doi:10.1093/eurheartj/ehw210

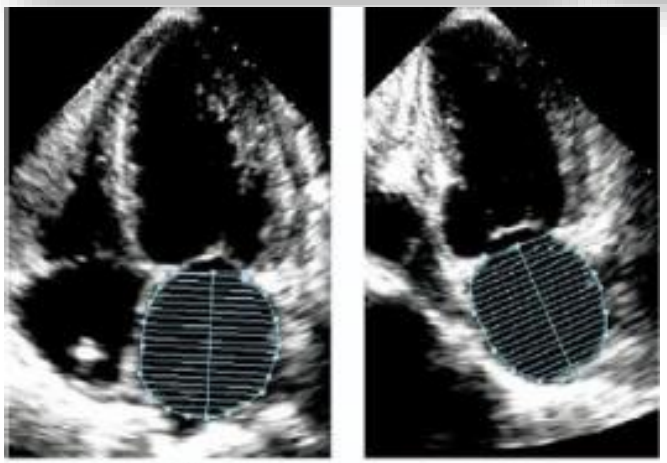
GUIDELINES AND STANDARDS

# Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging



AP linear dimension should not be used as the sole measure of LA size




When assessing the LA size and remodeling, the measurement of LA volume is recommended

Care should be taken to avoid foreshortening of the LA, because the longitudinal axes of the LV and LA frequently lie in different planes

Single-plane apical 4CH indexed LA volumes are 1 to 2 mL/m2 smaller than apical 2CH volumes

# Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

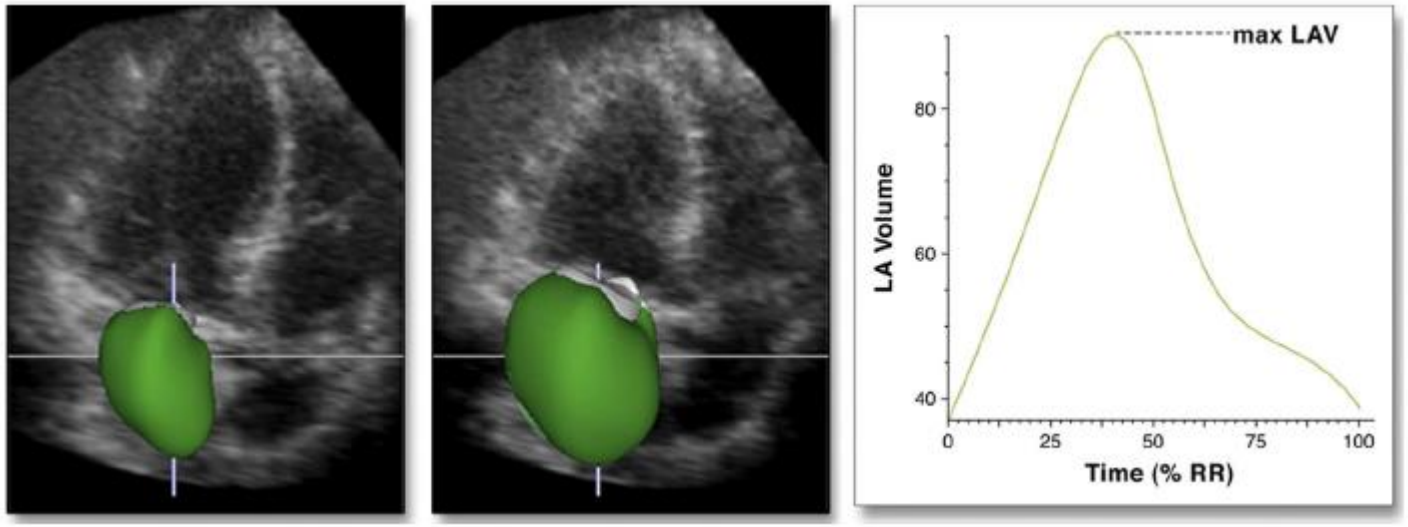



Table 4 Normal ranges and severity partition cutoff values for 2DE-derived LV EF and LA volume

| | Male | | | | Female | | | |
|---|---|---|---|---|---|---|---|---|
| | Normal range | Mildly abnormal | Moderately abnormal | Severely abnormal | Normal range | Mildly abnormal | Moderately abnormal | Severely abnormal |
| Maximum LA volume/BSA (mL/m$^2$) | 16–34 | 35–41 | 42–48 | >48 | 16–34 | 35–41 | 42–48 | >48 |

Kawel-Boehm et al. Journal of Cardiovascular Magnetic Resonance (2015) 17:29
DOI 10.1186/s12968-015-0111-7

Journal of Cardiovascular Magnetic Resonance

# Normal values for cardiovascular magnetic resonance in adults and children

Nadine Kawel-Boehm[1], Alicia Maceira[2], Emanuela R Valsangiacomo-Buechel[3], Jens Vogel-Claussen[4], Evrim B Turkbey[5], Rupert Williams[6], Sven Plein[7], Michael Tee[8], John Eng[9] and David A Bluemke[8*]

**Table 10 Left atrial volume and function in the adult for the SSFP technique based on the biplane area-length method according to reference [4]**

| Parameter | Men | | | Women | | |
|---|---|---|---|---|---|---|
| | mean | SD | Lower/ upper limits* | mean | SD | Lower/ upper limits* |
| Max. LA volume (ml) | 103 | 30 | 43-163 | 89 | 21 | 47-131 |
| Min. LA volume (ml) | 46 | 14 | 18-74 | 41 | 11 | 19-63 |

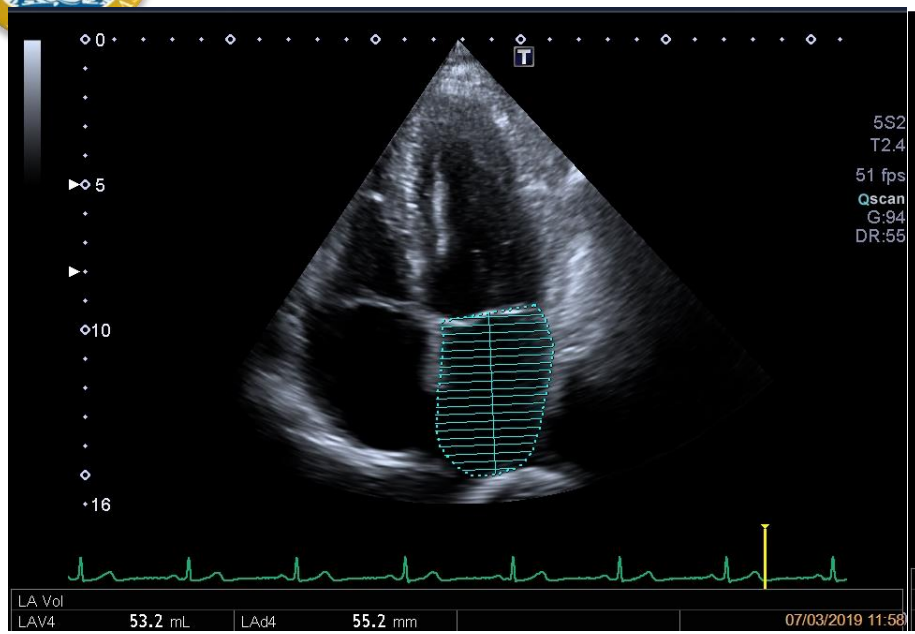
**Table 11 Left atrial maximal volume in the adult for the SSFP technique based on 3D modeling methods, according to reference [17]**

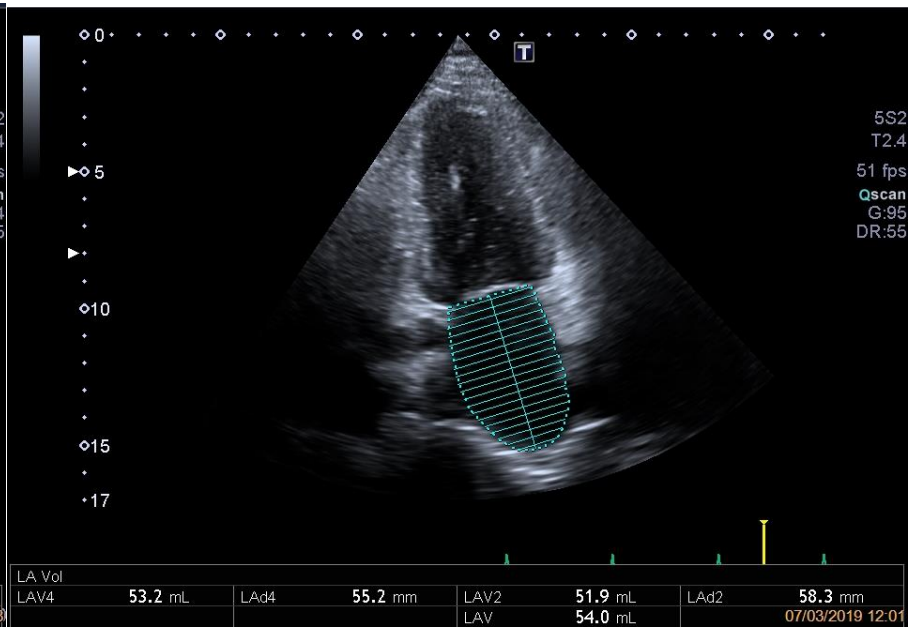
| Parameter | Men | | | Women | | |
|---|---|---|---|---|---|---|
| | mean | SD | Lower/ upper limits* | mean | SD | Lower/ upper limits* |
| Max. LA volume (ml) | 77 | 14.9 | 47-107 | 68 | 14.9 | 38-98 |
| Max. LA volume/BSA (ml/m$^2$) | 39 | 6.7 | 26-52 | 40 | 6.7 | 27-53 |

**Table 12 Left atrial maximal area in the adult for the SSFP technique, according to reference [17]**

| Parameter | Men | | | Women | | |
|---|---|---|---|---|---|---|
| | mean | SD | Lower/ upper limits* | mean | SD | Lower/ upper limits* |
| Area (cm$^2$) 4ch | 22 | 3.7 | 15-29 | 20 | 3.7 | 13-27 |
| Area/BSA (cm$^2$/ m$^2$) 4ch | 11 | 1.8 | 7-15 | 12 | 1.8 | 8-16 |
| Area (cm$^2$) 2ch | 21 | 4.7 | 12-30 | 19 | 4.7 | 10-28 |
| Area/BSA (cm$^2$/ m$^2$) 2ch | 11 | 2.4 | 6-16 | 11 | 2.4 | 6-16 |
| Area (cm$^2$) 3ch | 19 | 3.6 | 12-26 | 17 | 3.6 | 10-24 |
| Area/BSA (cm$^2$/ m$^2$) 3ch | 10 | 1.8 | 6-14 | 10 | 1.8 | 6-14 |

# Is left atrial size the sole hallmark of AF?




***A large proportion of patients who develop AF do not have an enlarged LA by the LAVmax***

**[Pagola J, González-Alujas T, Flores A, et al. Left atria strain is a surrogate marker for detection of atrial fibrillation in cryptogenic strokes. Stroke 2014;45:e164–6]**

***More than one-third of AF patients do not have enlarged LA, and for paroxysmal AF, this proportion is even higher (52%).***

**[ENGAGE AF-TIMI 48, Echocardiographic Study Investigators. Left atrial structure and function in atrial fibrillation: ENGAGE AF-TIMI 48. Eur Heart J 2014;35:1457–65]**

EDITORIAL COMMENT

# Incremental Predictive Value of Left Atrial Parameters Over Clinical Risk Scores for Subsequent Atrial Fibrillation

## Function Beyond Size*

Kazuaki Negishi, MD, PhD

JACC: CARDIOVASCULAR IMAGING

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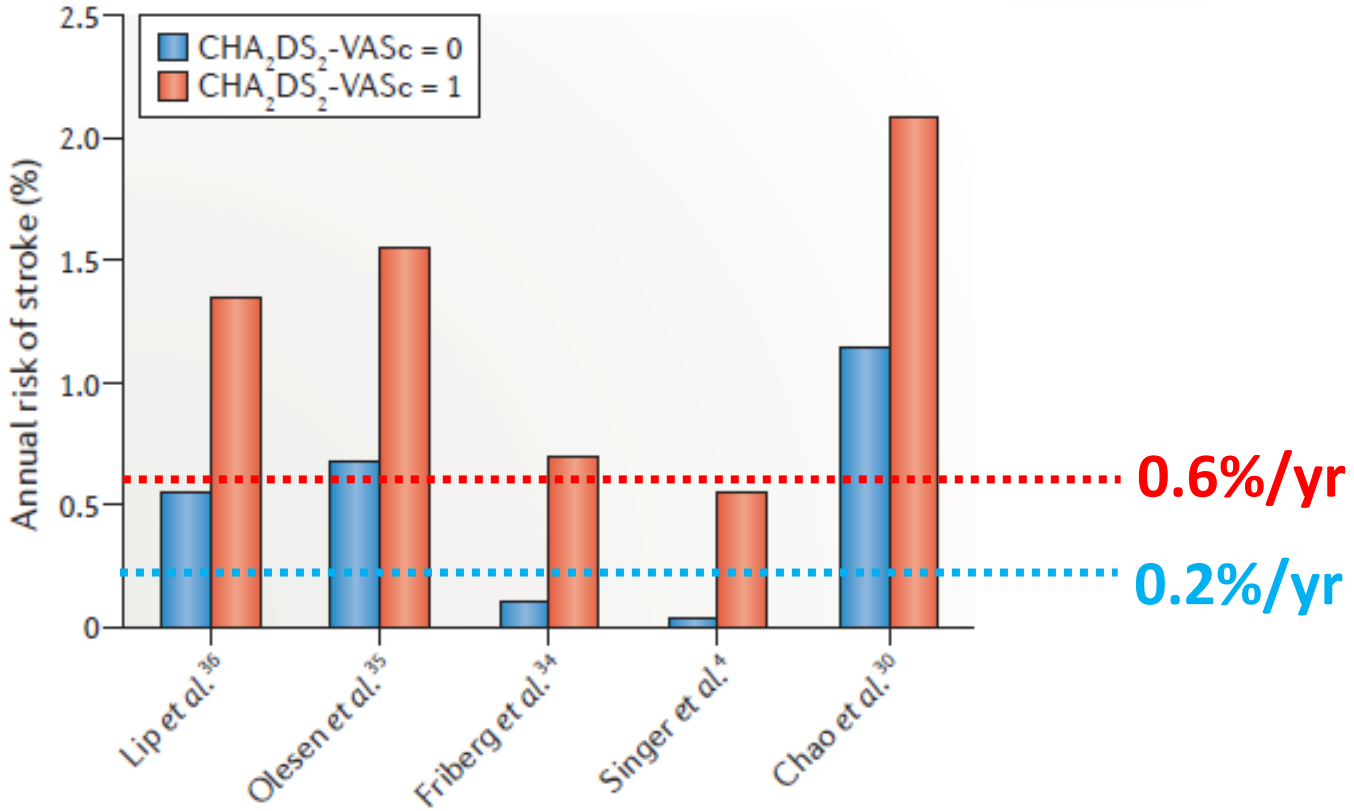
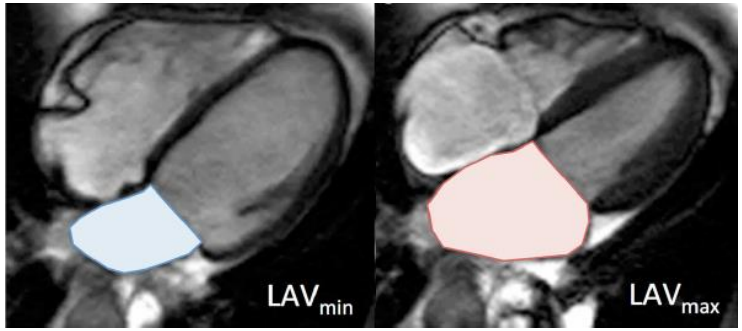


**Can risk of new-onset AF be predicted by imaging features of organ damage?**

**Can risk of stroke in AF patients be better predicted by imaging features of organ damage?**

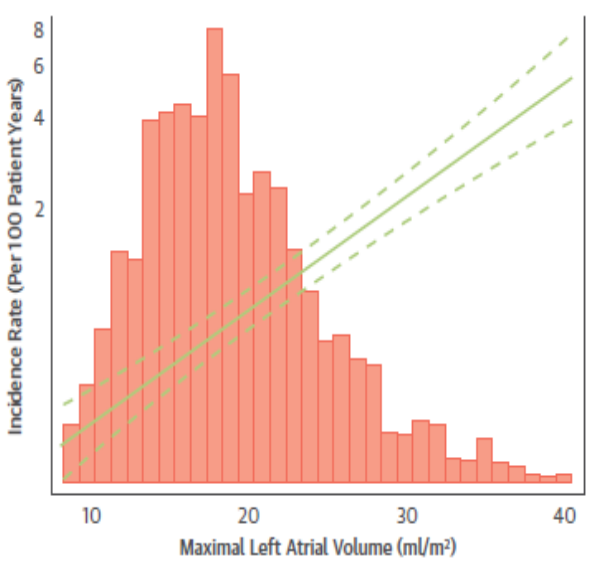
**Can imaging features of organ damage better clarify cause of criptogenetic stroke?**

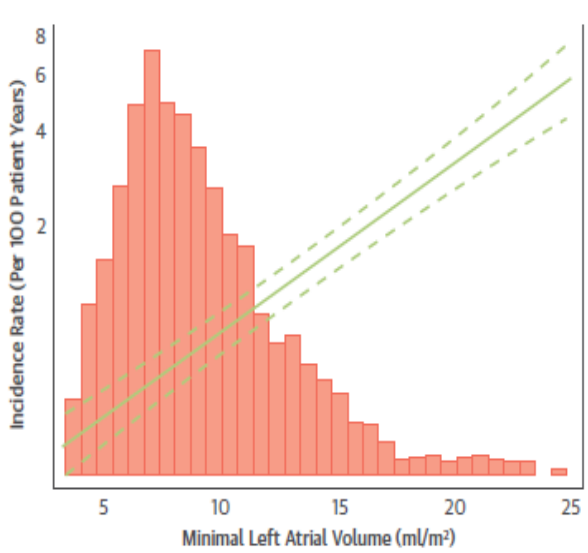
# The Copenhagen City Heart Study

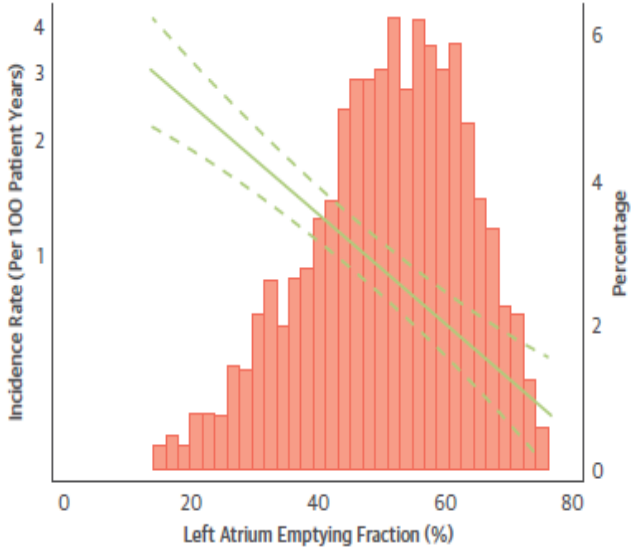



1951 pts
Median follow-up 11 yrs
184 (9.5%) new-onset AF

$$(LAV_{max} - LAV_{min})/LAV_{max} \times 100\%$$




*Olsen FJ, JACC Cardiovasc Imag 2018*

# The Copenhagen City Heart Study

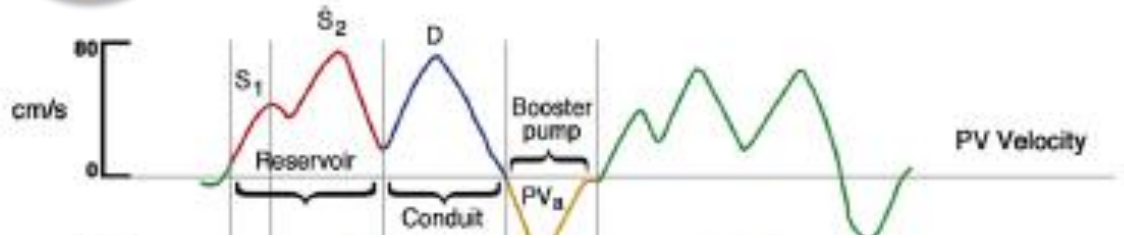
**TABLE 4** Cox Regression for LA Measures Stratified According to Hypertension

| | Normotensive (n = 1,092; Events = 53) | | Hypertensive (n = 852; Events = 131) | |
|---|---|---|---|---|
| | HR (95% CI) | p Value | HR (95% CI) | p Value |
| Univariable model | | | | |
| Maximal LA volume, per 1-ml/m$^2$ increase | 1.10 (1.06-1.15) | <0.001 | 1.07 (1.05-1.09) | <0.001 |
| Minimal LA volume, per 1-ml/m$^2$ increase | 1.24 (1.18-1.30) | <0.001 | 1.10 (1.07-1.12) | <0.001 |
| LA emptying fraction, per 1% decrease | 1.05 (1.03-1.06) | <0.001 | 1.02 (1.01-1.03) | 0.001 |
| Multivariable model 1 | | | | |
| Maximal LA volume, per 1-ml/m$^2$ increase | 1.10 (1.05-1.14) | <0.001 | 1.06 (1.04-1.08) | <0.001 |
| Minimal LA volume, per 1-ml/m$^2$ increase | 1.22 (1.16-1.28) | <0.001 | 1.08 (1.05-1.10) | <0.001 |
| LA emptying fraction, per 1% decrease | 1.04 (1.02-1.06) | <0.001 | 1.02 (1.00-1.03) | 0.031 |
| Multivariable model 2 | | | | |
| Maximal LA volume, per 1-ml/m$^2$ increase | 1.08 (1.04-1.12) | <0.001 | 1.05 (1.02-1.07) | <0.001 |
| Minimal LA volume, per 1-ml/m$^2$ increase | 1.15 (1.10-1.21) | <0.001 | 1.07 (1.03-1.09) | <0.001 |
| LA emptying fraction, per 1% decrease | 1.03 (1.01-1.05) | 0.003 | 1.01 (0.99-1.02) | 0.26 |
| Multivariable model 3 | | | | |
| Maximal LA volume, per 1-ml/m$^2$ increase | 1.04 (0.97-1.10) | 0.25 | 1.02 (0.99-1.06) | 0.15 |
| Minimal LA volume, per 1-ml/m$^2$ increase | 1.13 (1.03-1.25) | 0.010 | 1.01 (0.96-1.06) | 0.66 |

In the subgroup of normotensive pts, LA functional measures can even predict AF in individuals with structurally normal LA (defined as LAVmax<34 ml/m2)

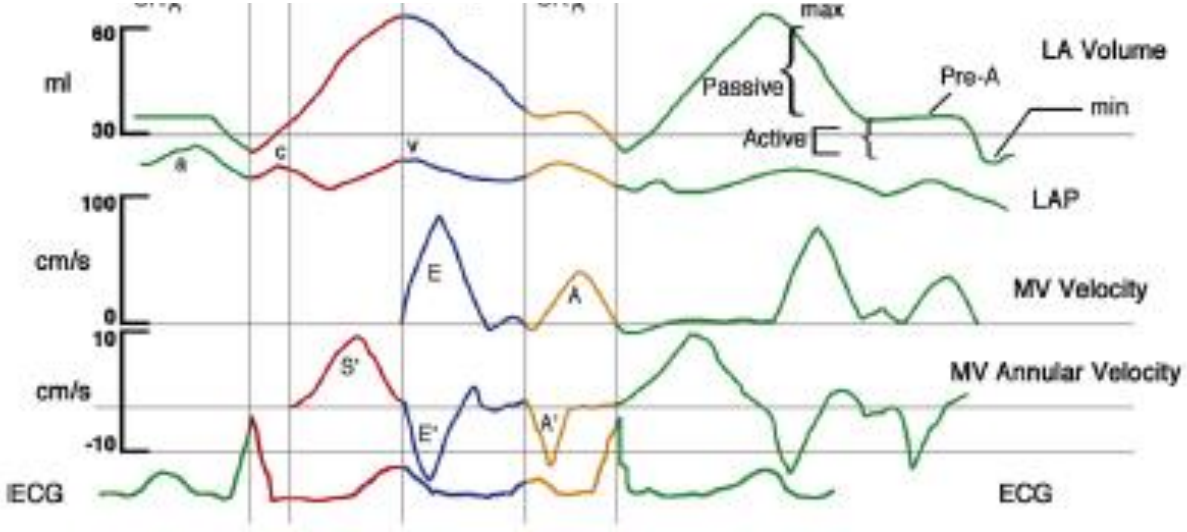
*Olsen FJ, JACC Cardiovasc Imag 2018*

# Function beyond size




**Reservoir for pulmonary venous return during ventricular systole**

**Conduit for pulmonary venous return during early ventricular diastole**



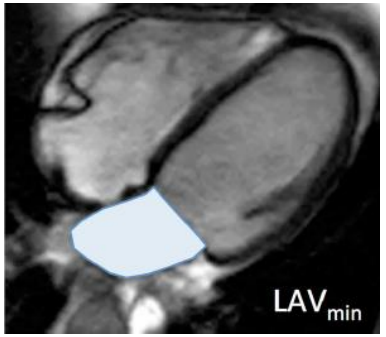

**Reservoir function is influenced by descent of the LV base during systole and by LV end-systolic volume.**

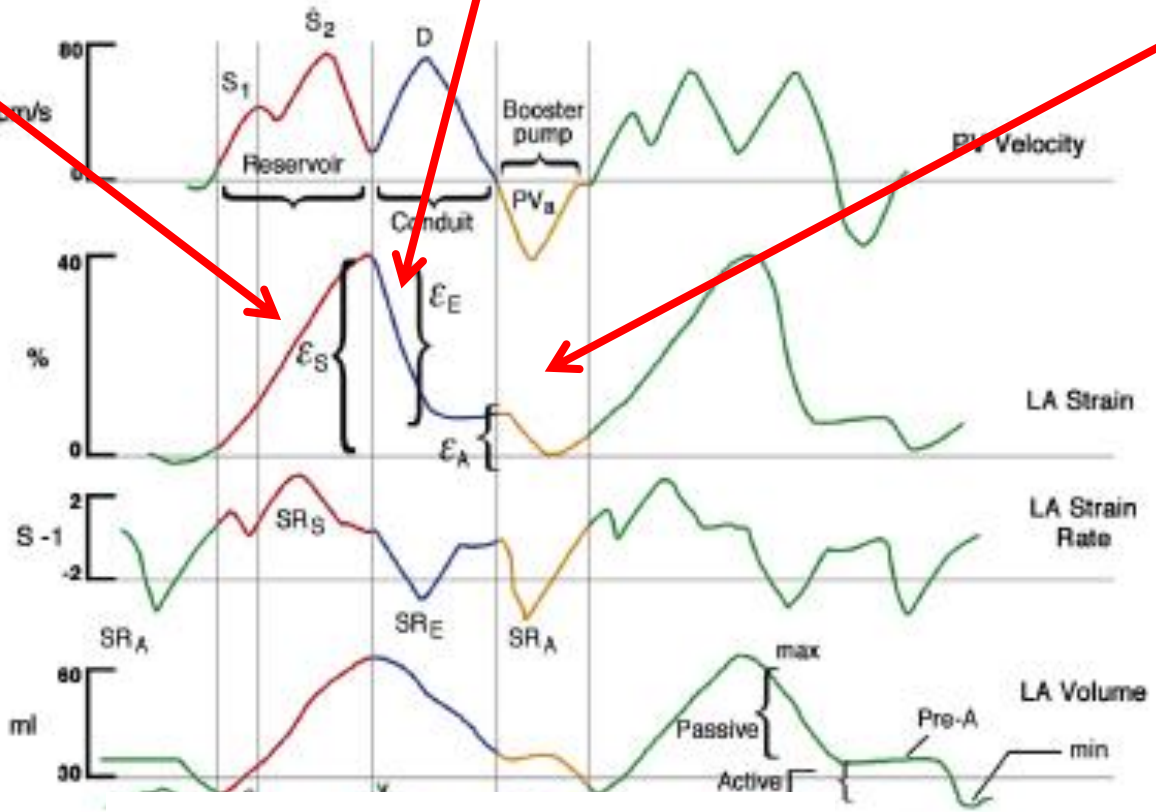
**Conduit function is closely related to LV relaxation and compliance.**

**Atrial booster pump function is dependent on the degree of venous return (atrial pre-load) and LV end-diastolic pressures (atrial afterload)**

**Frank-Starling law**

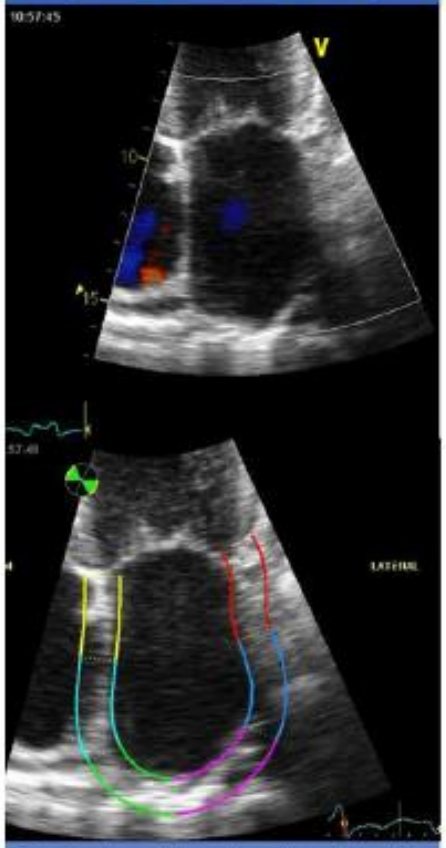
# Function beyond size



# Left atrial strain

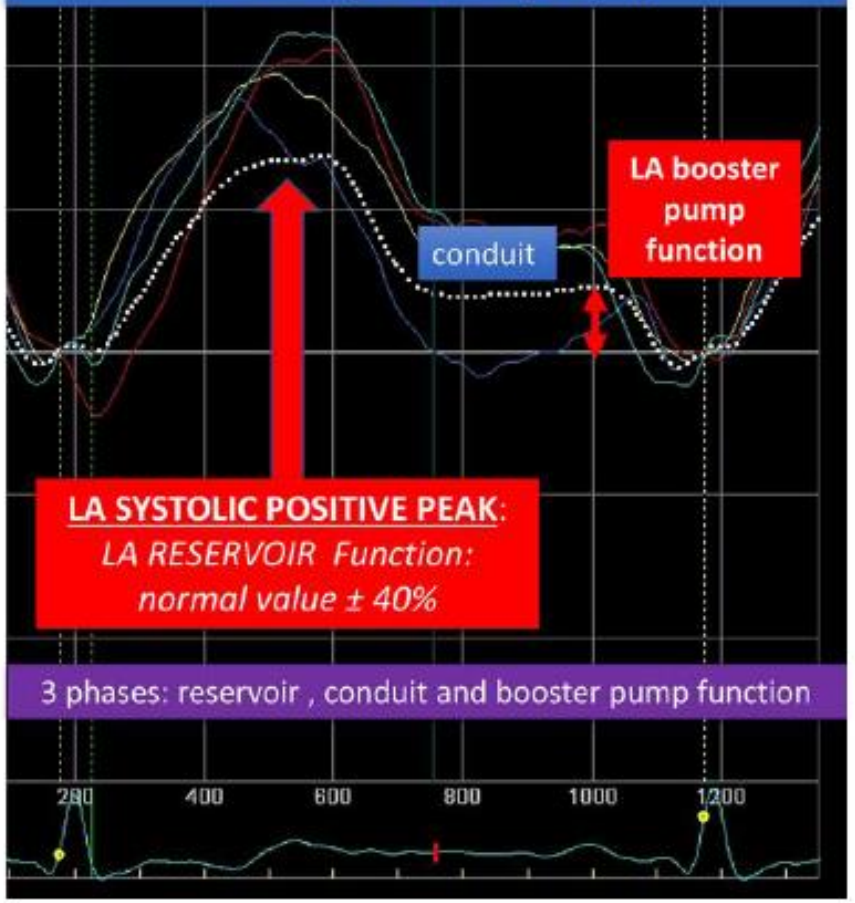
Zoom on the left atrium in apical 2 and 4 chambers views



Semi-automatic contouring of the left atrial borders for speckle tracking

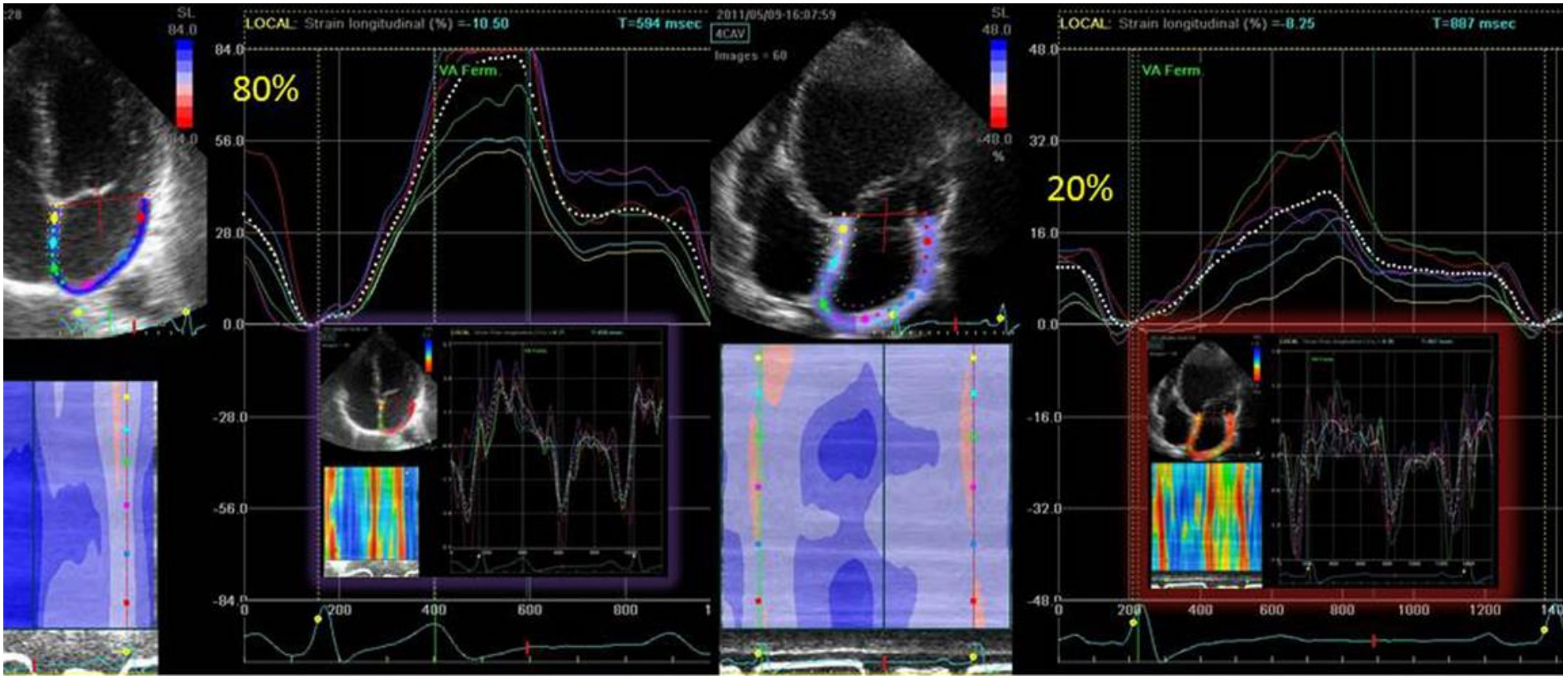
Parametric imaging for checking the quality of the tracking

Display of the left atrial deformation over a cardiac cycle, starting in this example at the QRS (following the settings made for the left ventricular speckle tracking analysis)




3 phases: reservoir , conduit and booster pump function

# Left atrial strain in Atrial Fibrillation




Normal

Atrial fibrillation

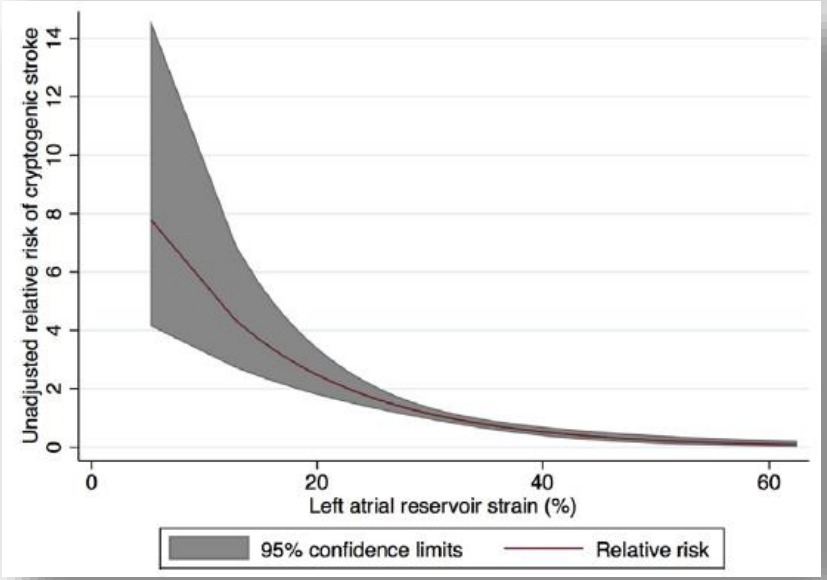
# Left Atrial Dysfunction in the Pathogenesis of Cryptogenic Stroke: Novel Insights from Speckle-Tracking Echo

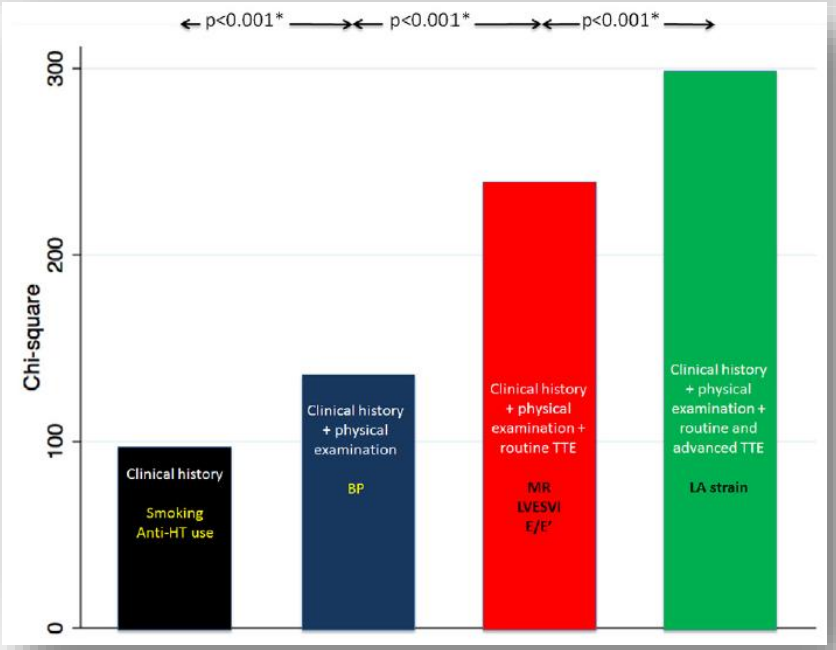
**Table 1** Characteristics of patients with CS and control subjects

| | Patients with CS ($n$ = 371) | Control subjects ($n$ = 371) | $P$ |
|---|---|---|---|
| LAVI (mL/m$^2$) | 25 ± 9 | 25 ± 8 | .70 |
| LA reservoir strain (%) | 30 ± 7 | 34 ± 7 | **<.001** |

**Table 2** Model for the identification of CS

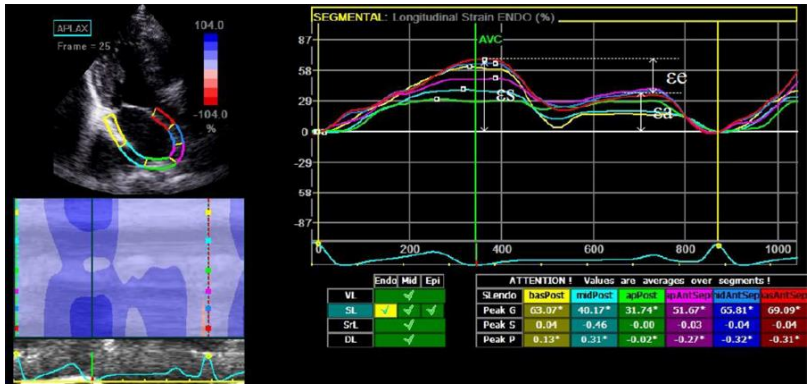
| | Univariate | | Multivariate | |
|---|---|---|---|---|
| Parameter | OR (95% CI) | $P$ | OR (95% CI) | $P$ |
| LA reservoir strain, per 1% reduction | 1.08 (1.06–1.11) | <.001 | **1.07 (1.05–1.10)** | **<.001** |

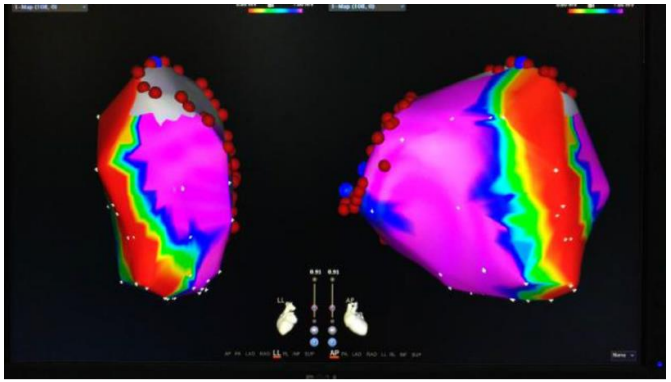



*Leong DP, J Am Soc Echo 2016*

# Mechanical remodeling correlates with electrical remodeling of LA



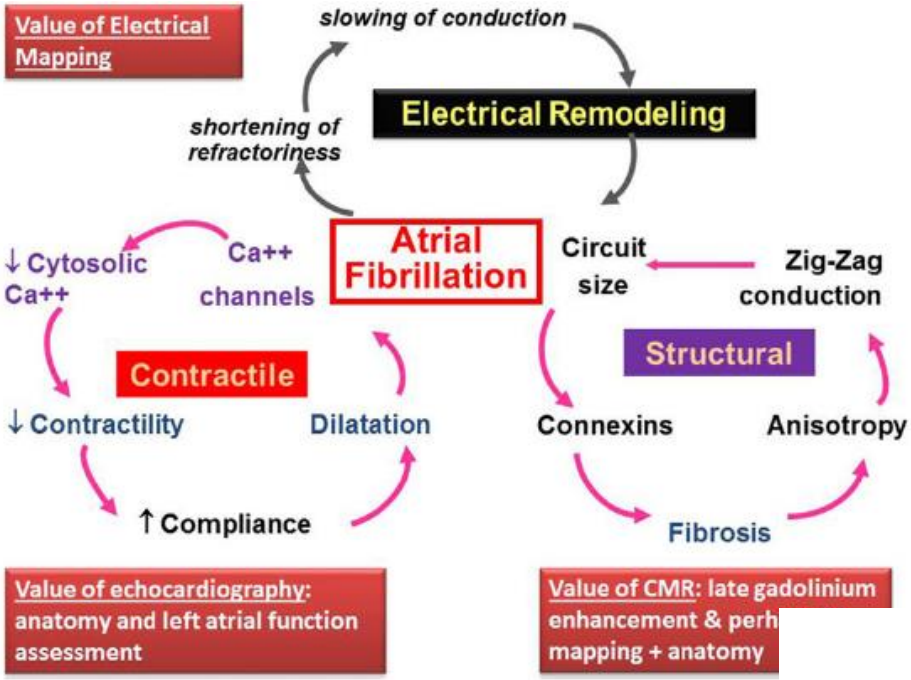
40 pts with paroxysmal AF

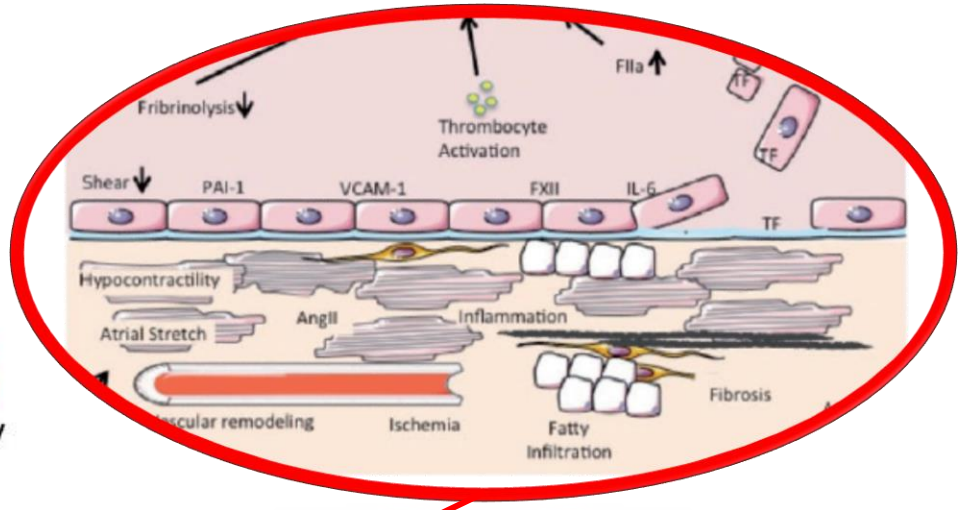
LV group (bipolar voltage < 0.5 mV)

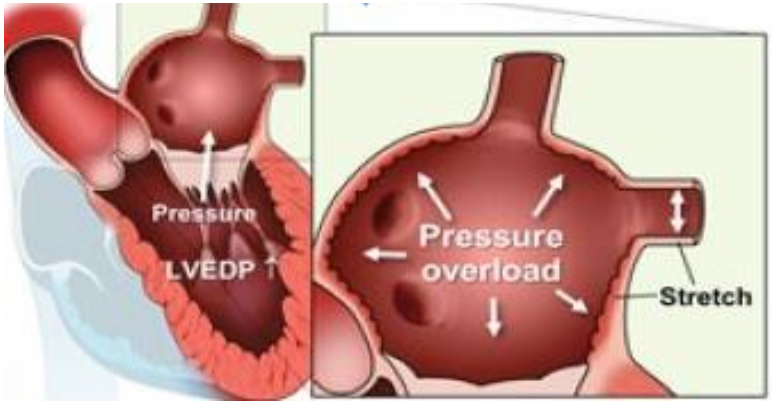
Non-LV group (bipolar voltage > 0.5 mV)

| Variables | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | *P* value | OR | 95% CI | *P* value |
| Age | 1.049 | 0.972–1.131 | 0.217 | | | |
| LVEF | 1.012 | 0.886–1.155 | 0.863 | | | |
| LA diameter | 1.117 | 0.953–1.310 | 0.171 | | | |
| LA Vmax | 0.996 | 0.960–1.033 | 0.831 | | | |
| LA Vmin | 1.046 | 0.984–1.112 | 0.148 | | | |
| LAEF | 0.891 | 0.822–0.966 | 0.005 | 0.864 | 0.704–1.057 | 0.154 |
| LA stroke | 1.001 | 0.512–1.955 | 0.999 | | | |
| LAVi | 1.002 | 0.940–1.069 | 0.946 | | | |
| E/A | 1.839 | 0.554–6.108 | 0.320 | | | |
| Global strain | 0.890 | 0.808–0.979 | 0.017 | 1.347 | 1.005–1.807 | 0.046 |

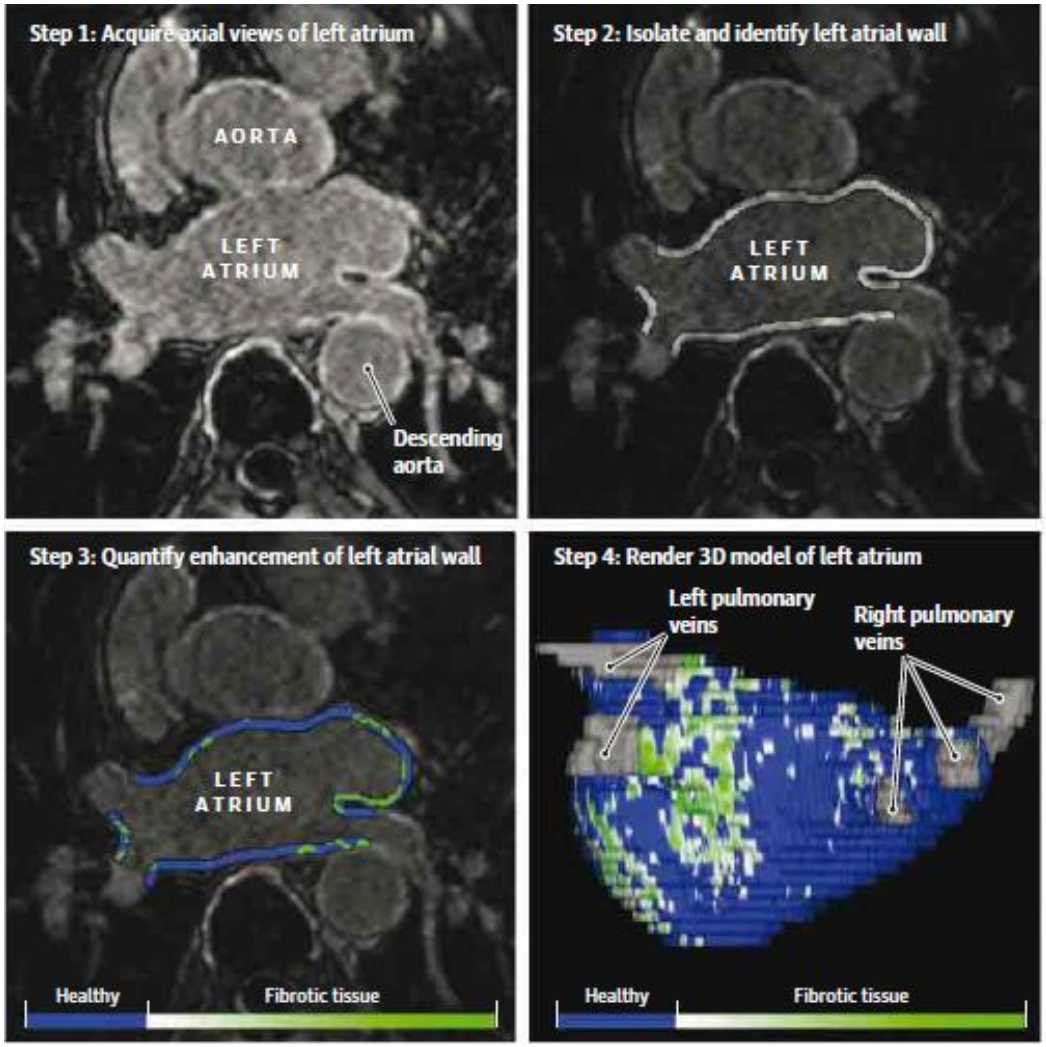
# A paradigm shift in the pathophysiology of AF: the atrial cardiomyopathy

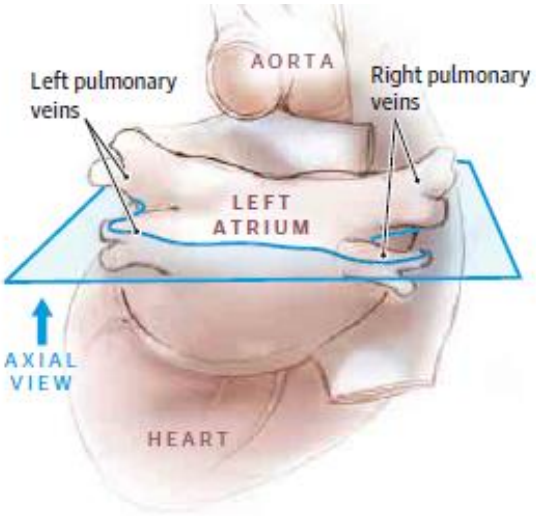


# Atrial fibrosis is the hallmark of structural LA remodeling in AF



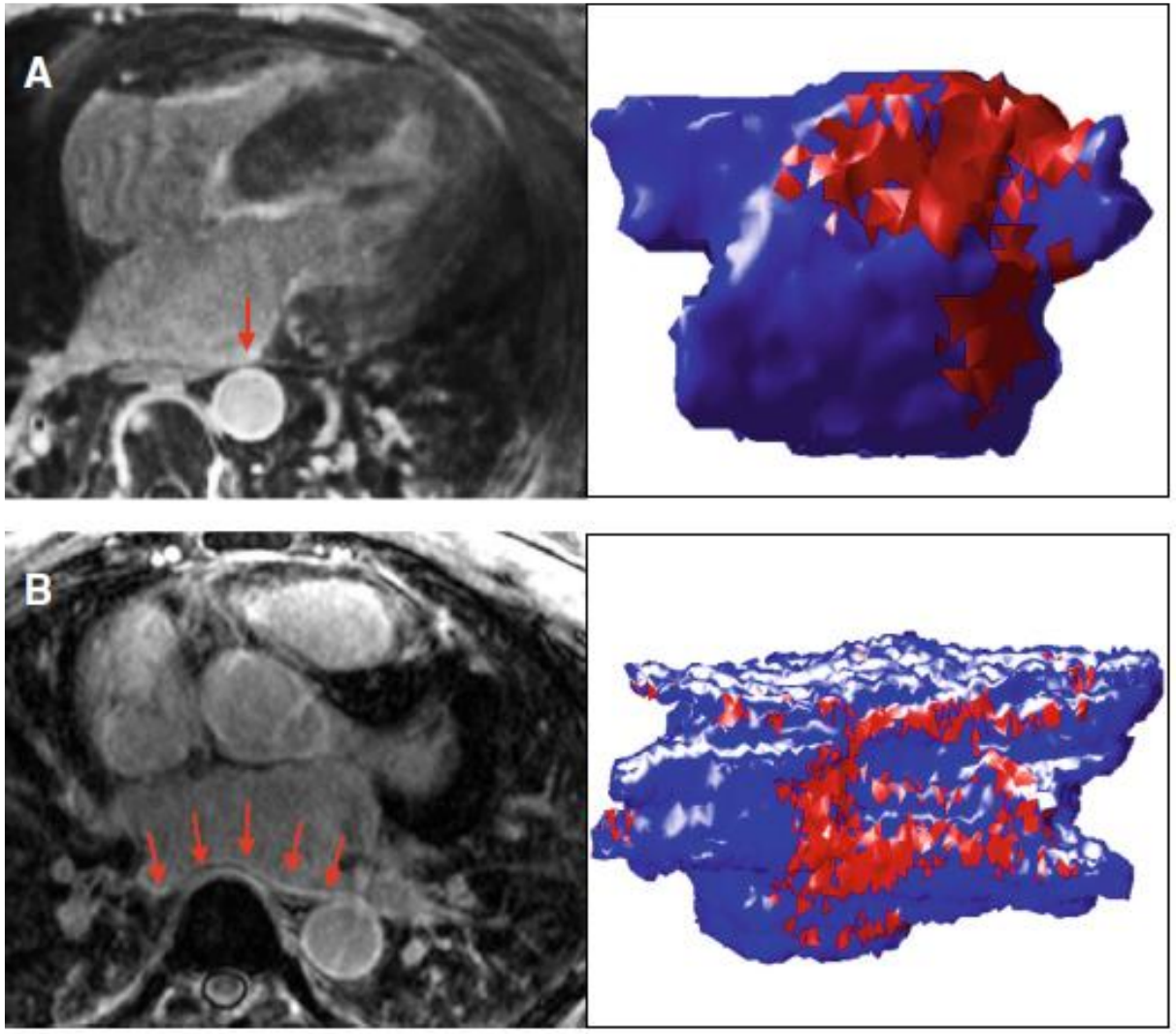



*Marrouche NF, JAMA 2014*

# Atrial fibrosis is the hallmark of structural LA remodeling in AF

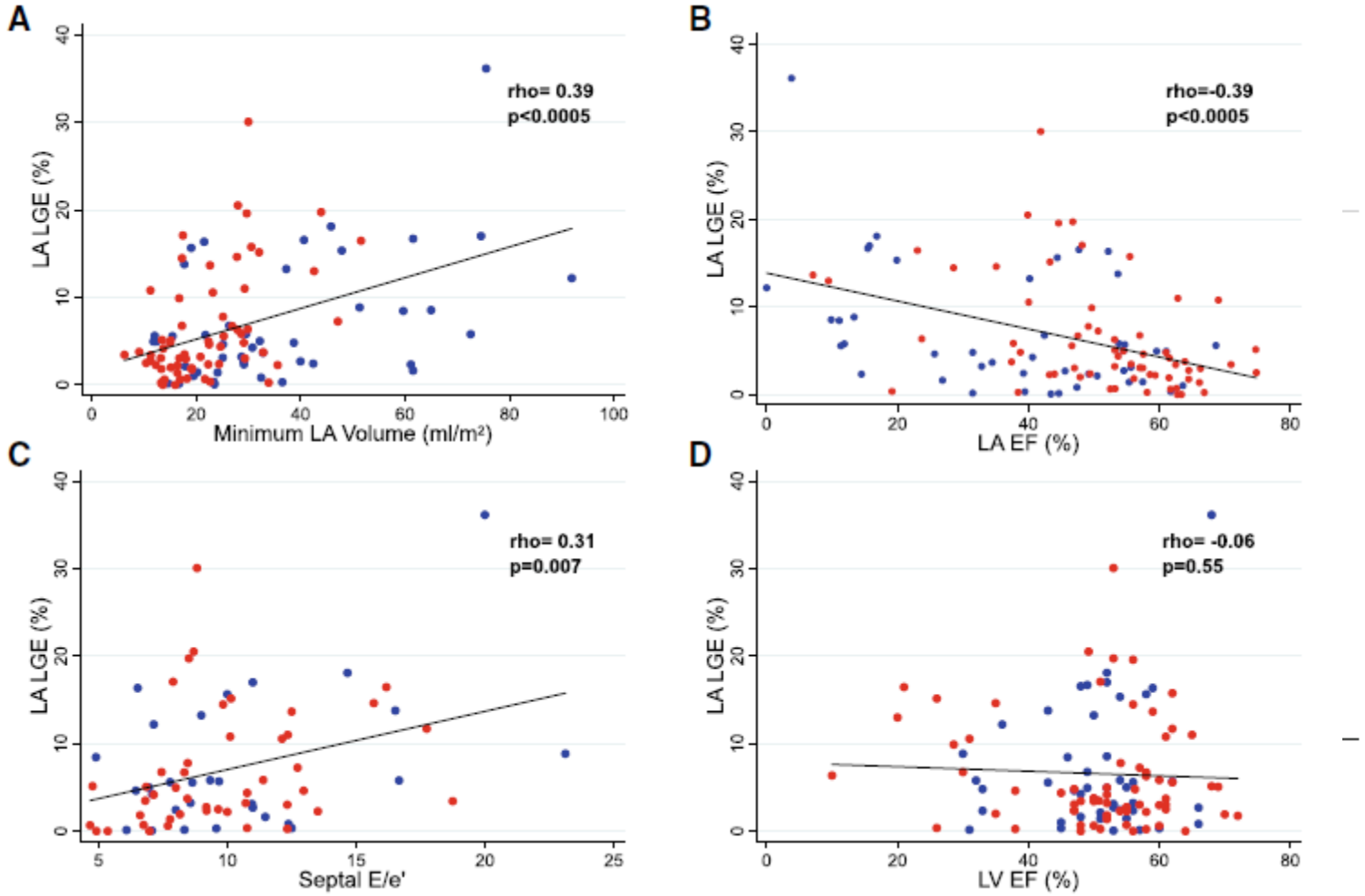
Hypertrophic cardiomyopathy

Ischemic heart disease



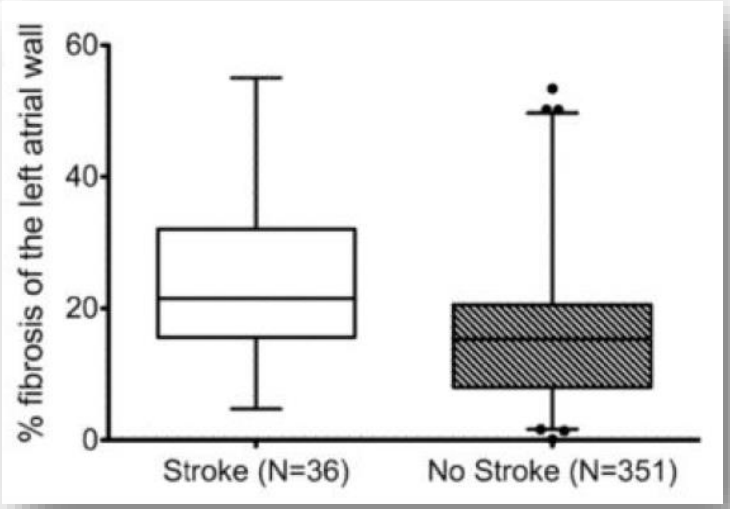

*Marrouche NF, JAMA 2014*

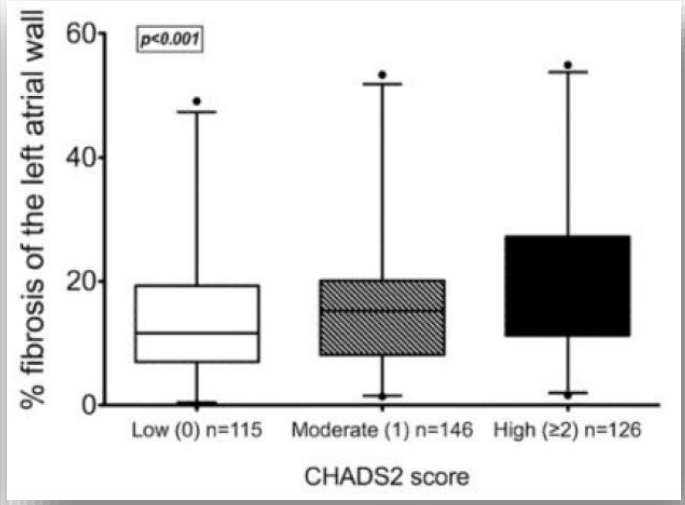
# Atrial fibrosis predicts new-onset AF

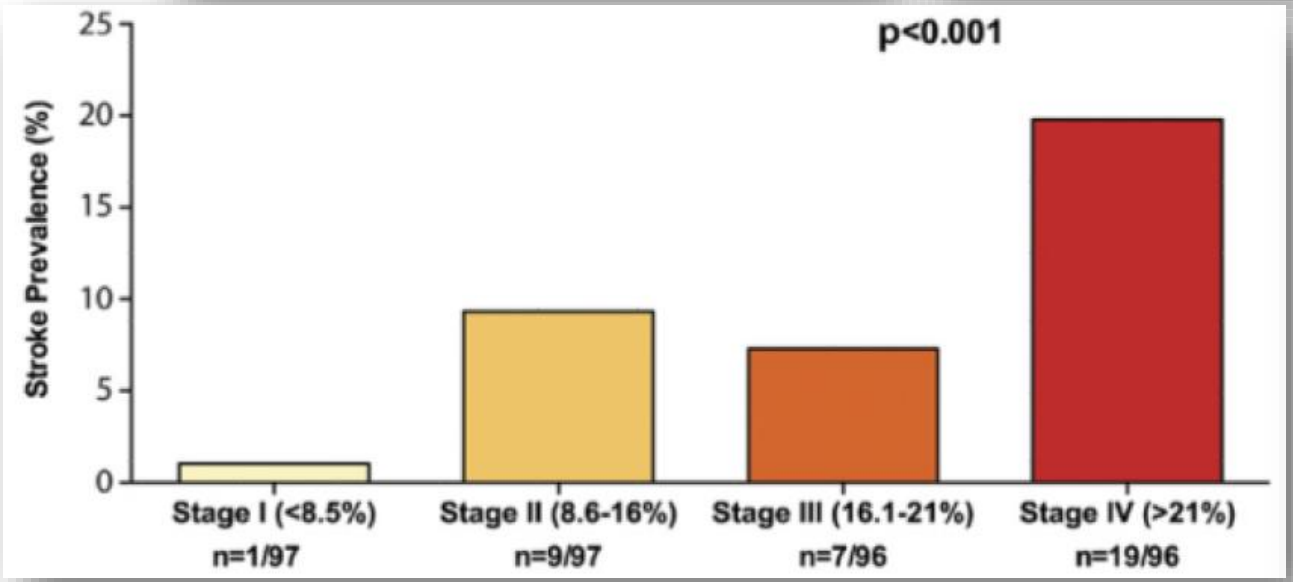



*Quail M, J Cardiovasc Magn Res 2019*

# Association of LA Fibrosis Detected by DE-CMR and the Risk of Stroke in Patients With AF



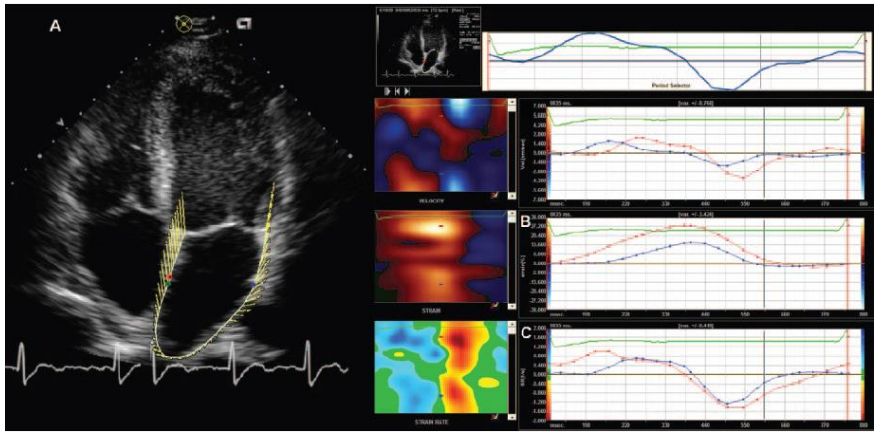

**Multivariate**

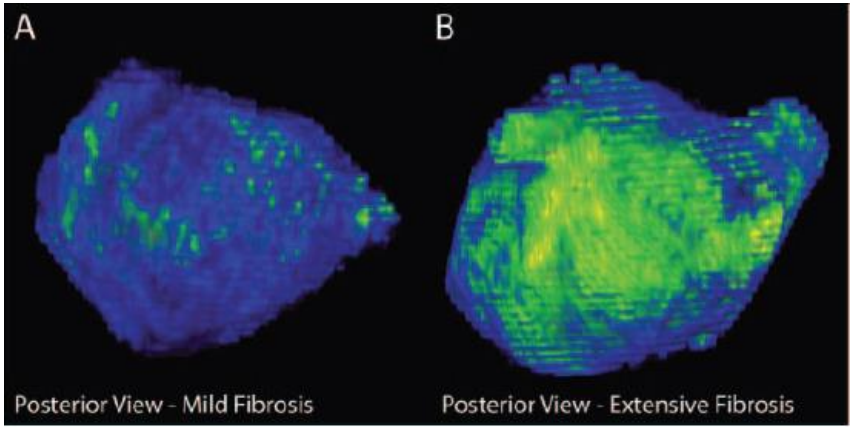
| Variable | OR | p Value |
|---|---|---|
| Persistent vs. paroxysmal AF | 1.02 | 0.98 |
| Warfarin use | 0.58 | 0.14 |
| Female vs. male | 3.11 | 0.003 |
| Diabetes mellitus | 0.43 | 0.21 |
| Hypertension | 1.35 | 0.51 |
| Congestive heart failure | 0.36 | 0.19 |
| Age >75 yrs | 1.18 | 0.58 |
| LA remodeling stage | 2.91 | 0.027 |

*Daccarett M, JACC 2011*

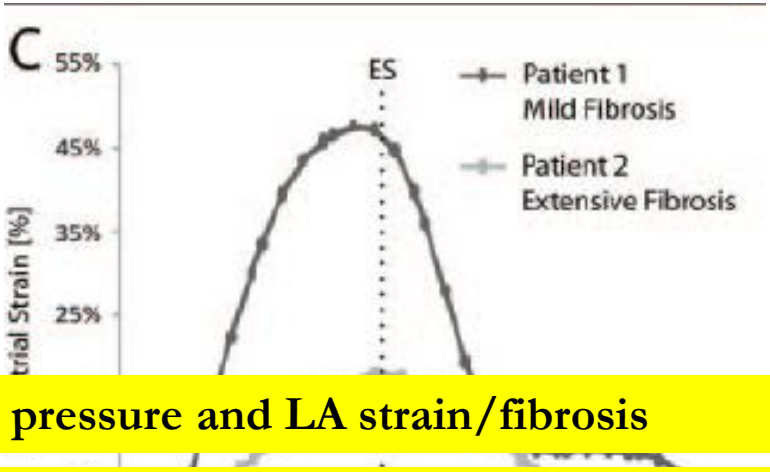
# LA strain in patients with paroxysmal and persistent AF relates to LA fibrosis detected at MR

**55 pts with paroxysmal or persistent AF. 16 (29%) were on AF during Echo and MR**



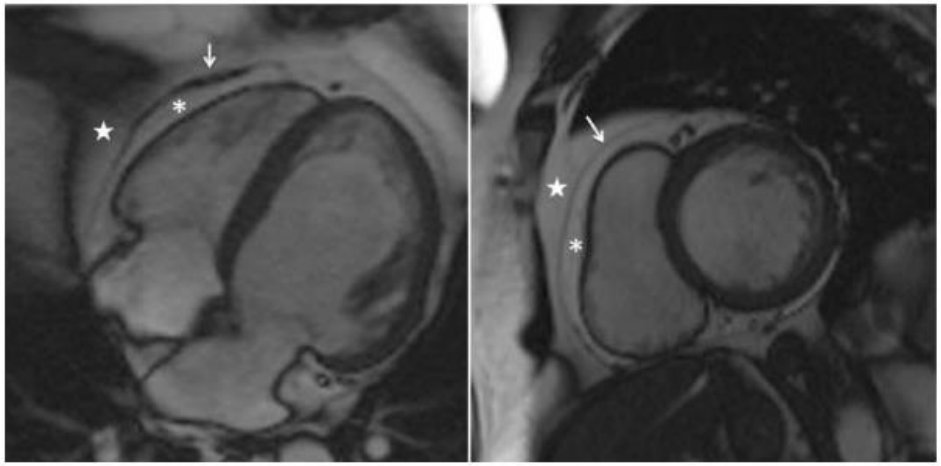

| | Total (n=55) | Paroxysmal AF (n=24) | Persistent AF (n=31) | *P* Value |
|---|---|---|---|---|
| LA wall fibrosis, % | 19±15 | 14±9 | 22±18 | 0.04 |
| LA biplane volume index, mL/m$^2$ | 35±11 | 31±11 | 37±10 | 0.04 |

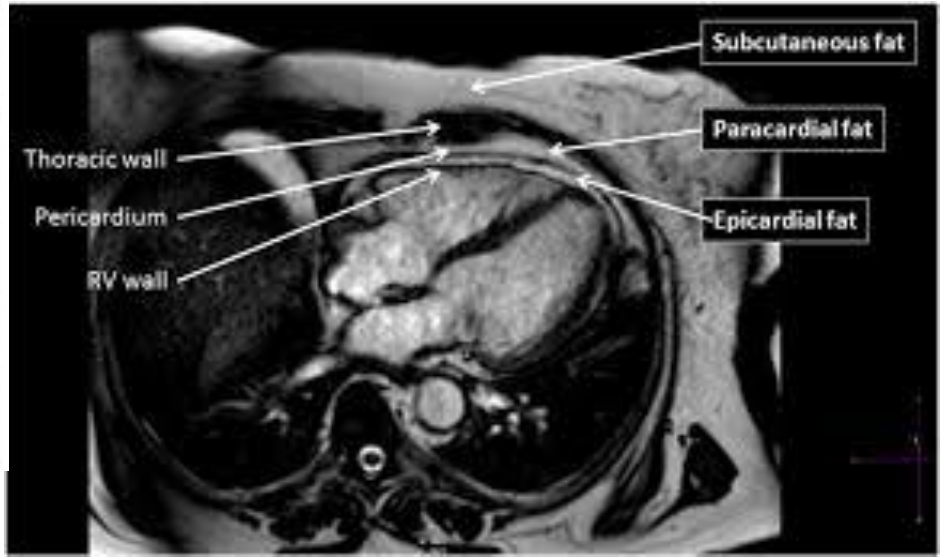


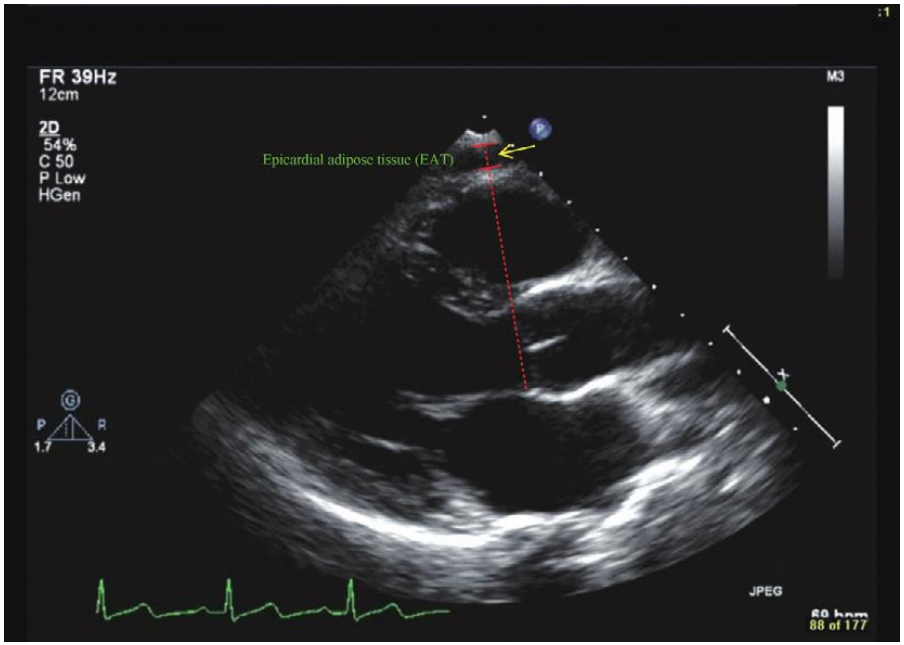

**No correlation between E/E' LV filling pressure and LA strain/fibrosis**

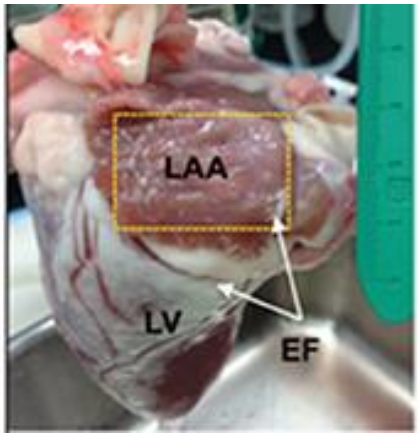
**Neither the extent of fibrosis nor the degree of reduction in strain was influenced by age, sex, severity of mitral regurgitation, or history of hypertension, suggesting that the changes may be primarily due to AF.**

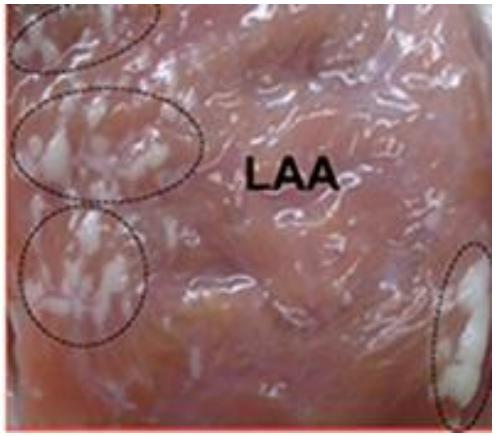
# Increased epicardial fat thickness in AF



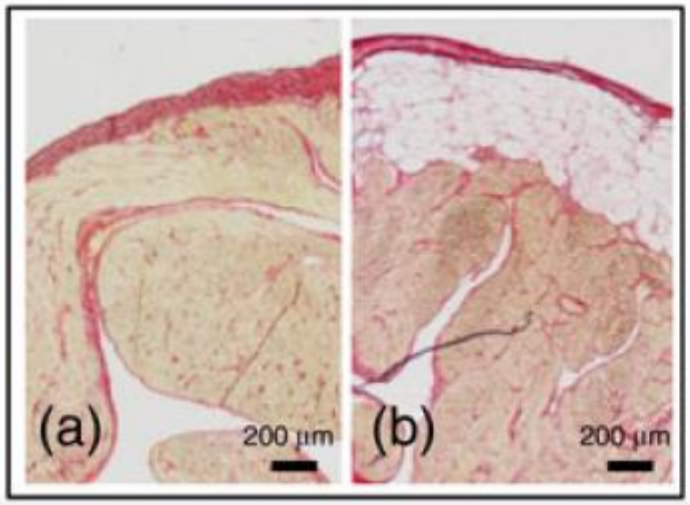


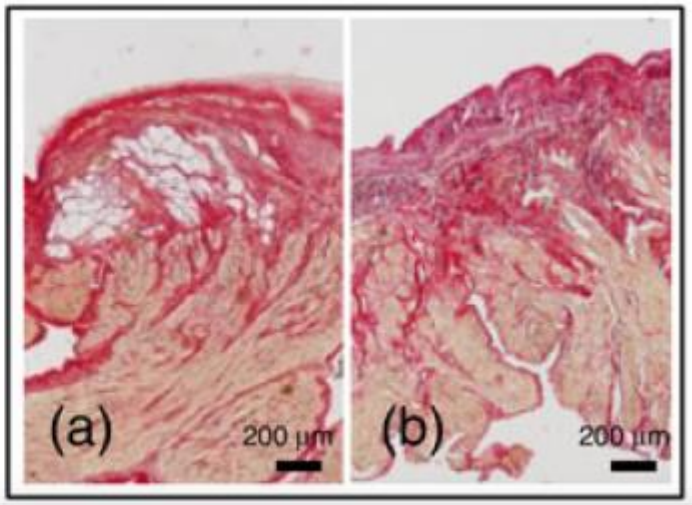



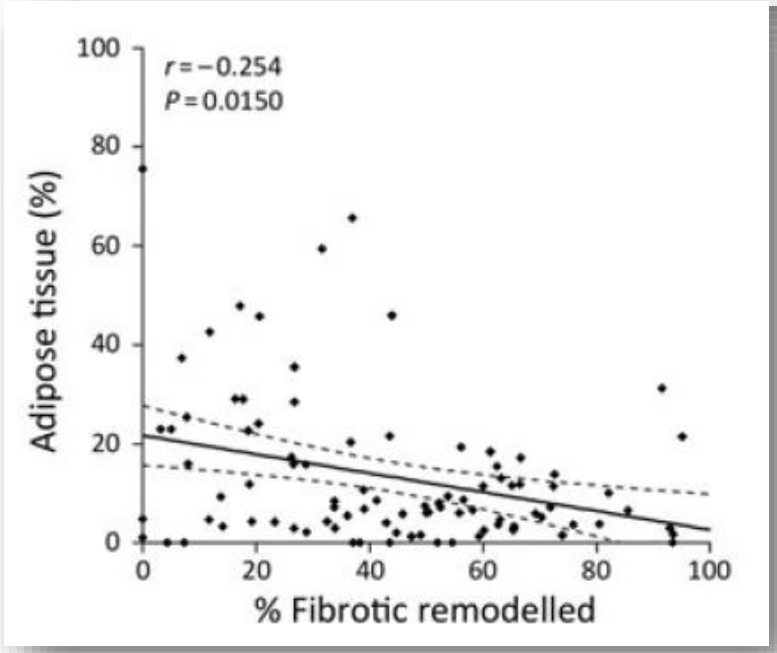



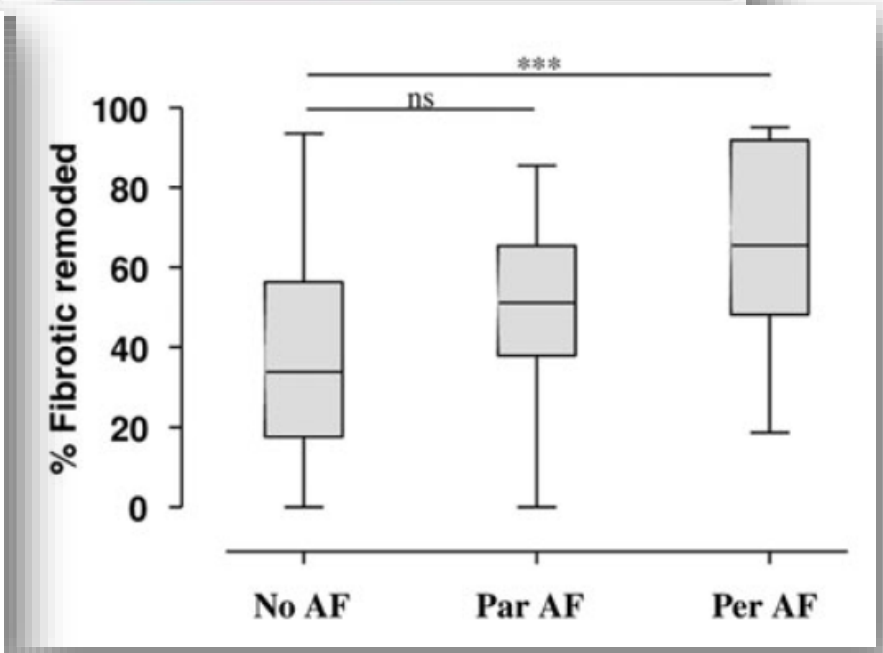



# AF is associated with the fibrotic remodelling of adipose tissue in the subepicardium of human and sheep atria



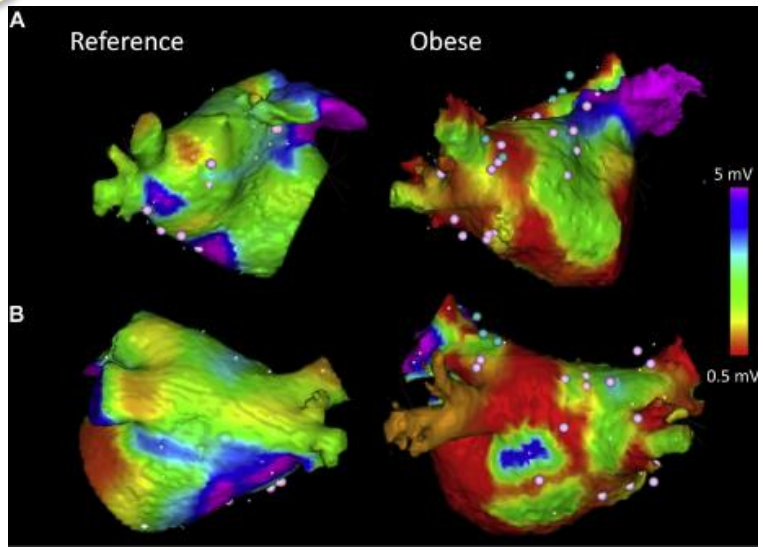



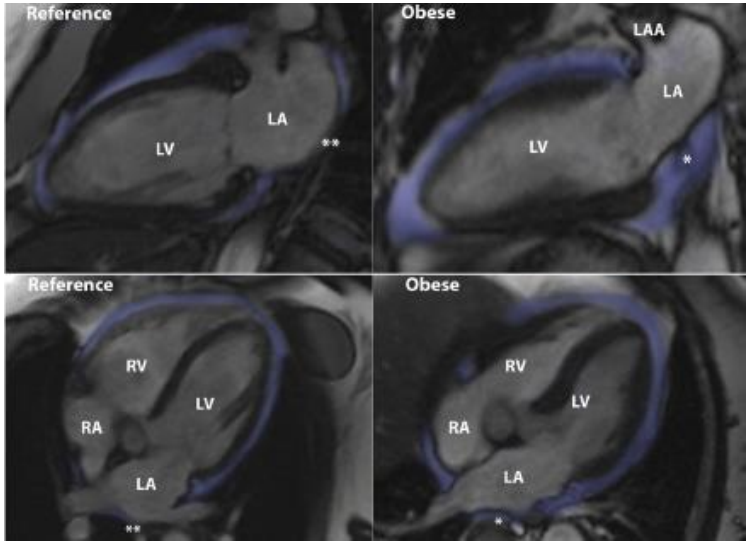



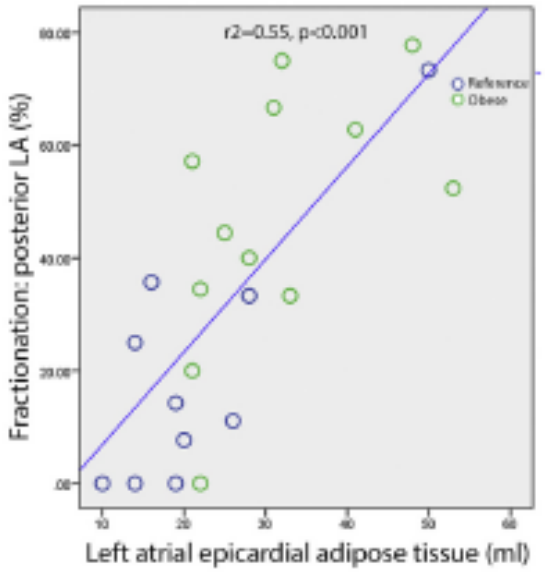



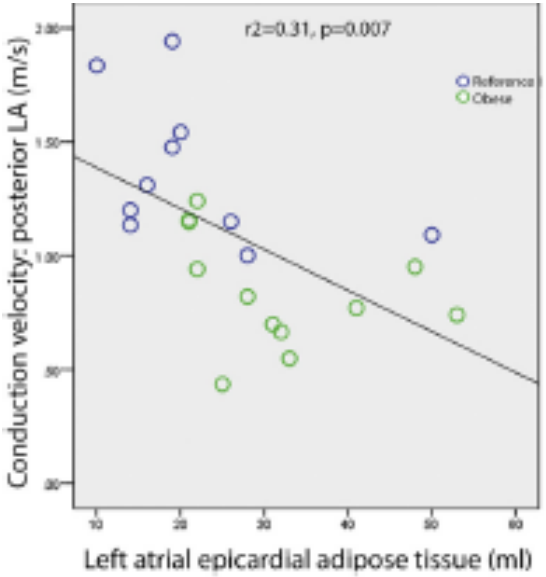

*Haemers P, Eur Heart J 2017*

# Electroanatomical Remodeling of the Atria in Obesity



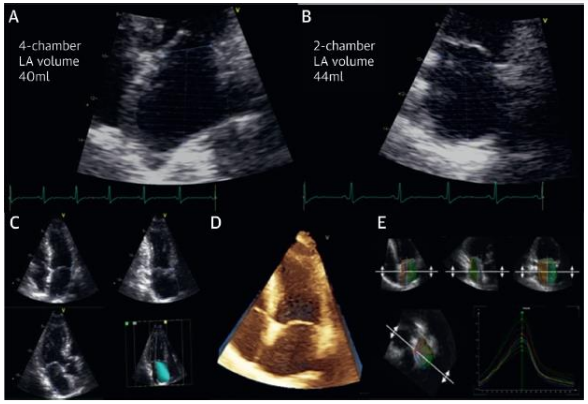

*Mahajan R, JACC Clin Electrophysiology 2018*

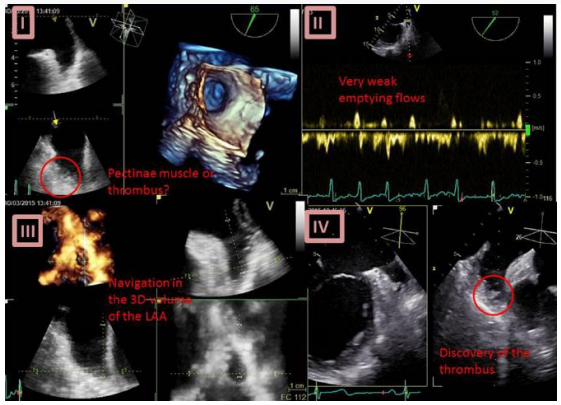
# *Take-home messages*

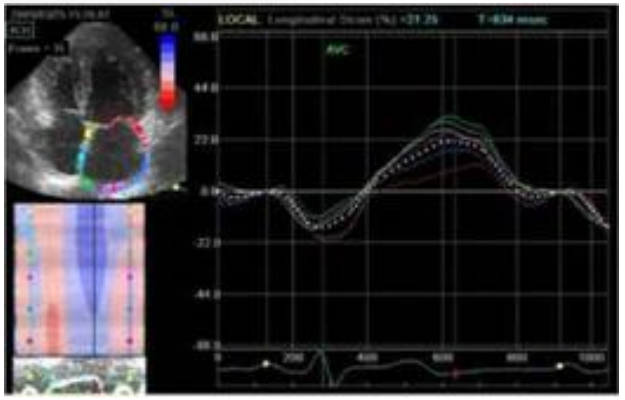
European Heart Journal – Cardiovascular Imaging (2016) **17**, 355–383
doi:10.1093/ehjci/jev354

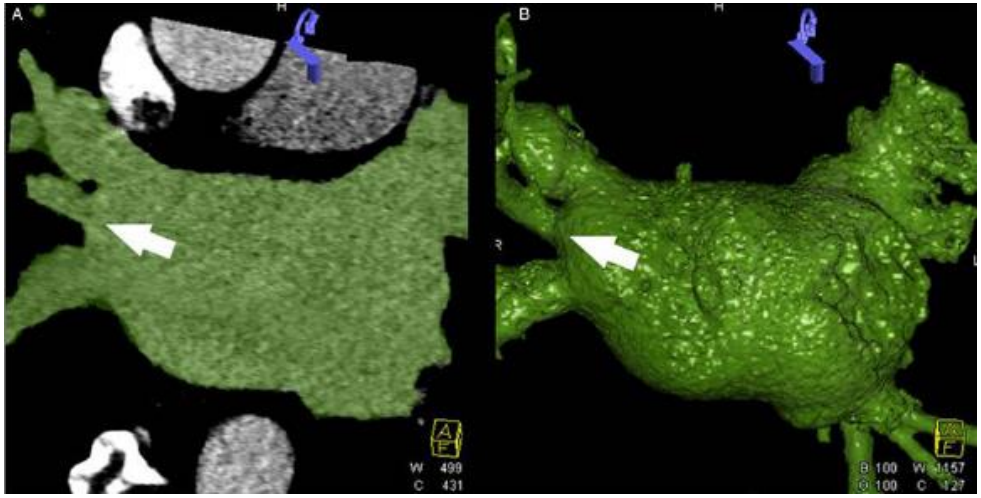
REVIEW

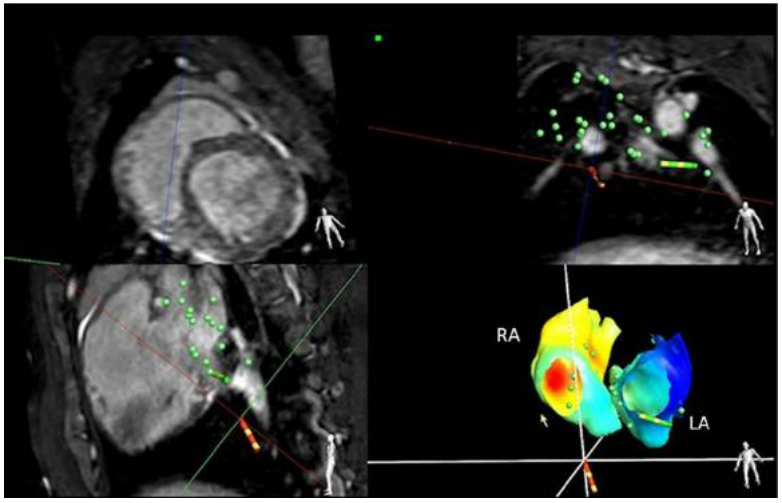
# EACVI/EHRA Expert Consensus Document on the role of multi-modality imaging for the evaluation of patients with atrial fibrillation



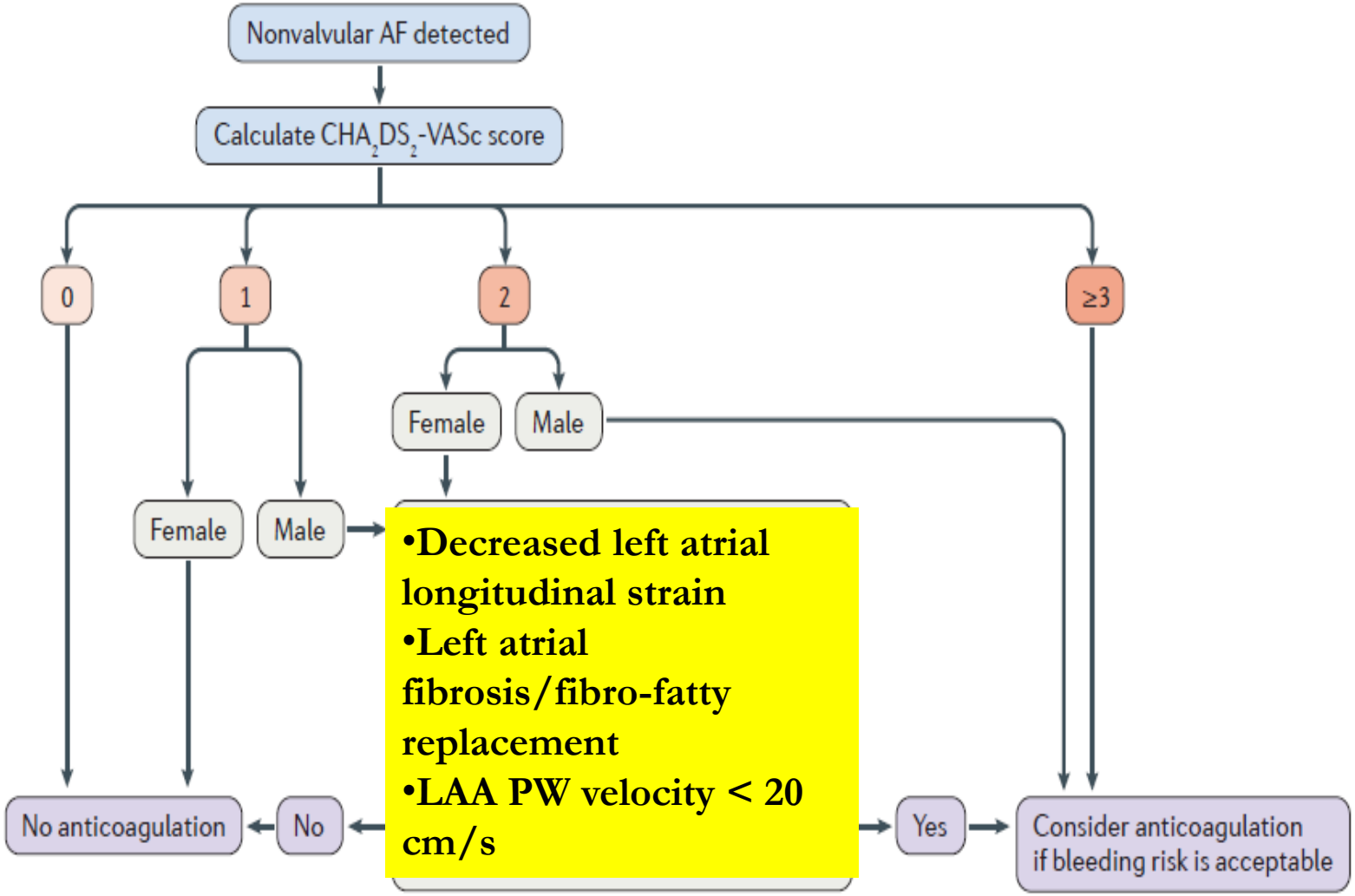





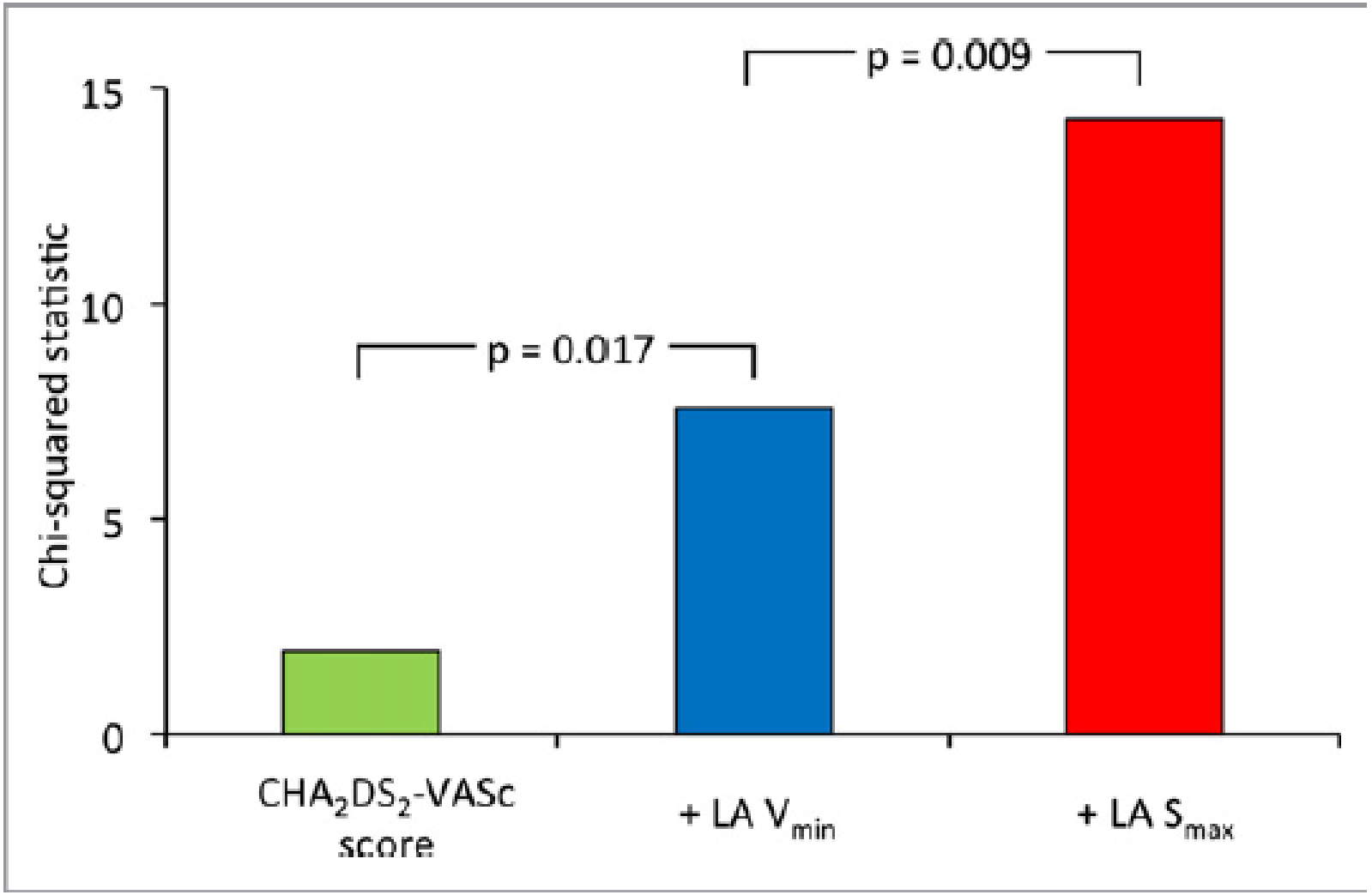



# How can imaging enter AF work-flow?




*Modified from Calenda BW, Nature Reviews/Cardiology 2016*

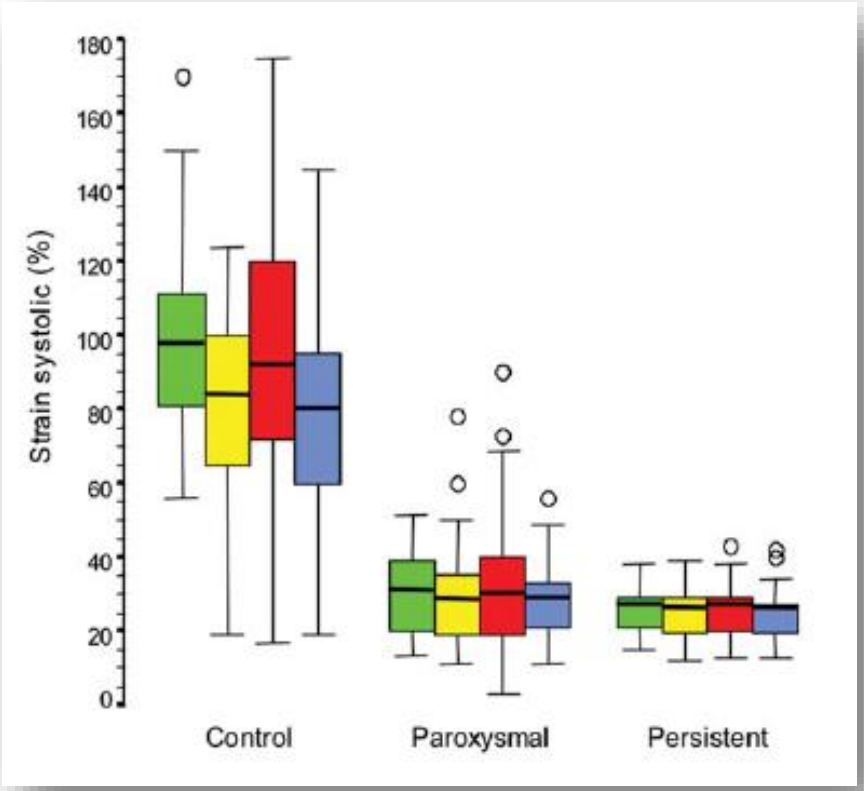
# Quantitative Tissue-Tracking CMR of Left Atrial Deformation and the Risk of Stroke in Patients With AF

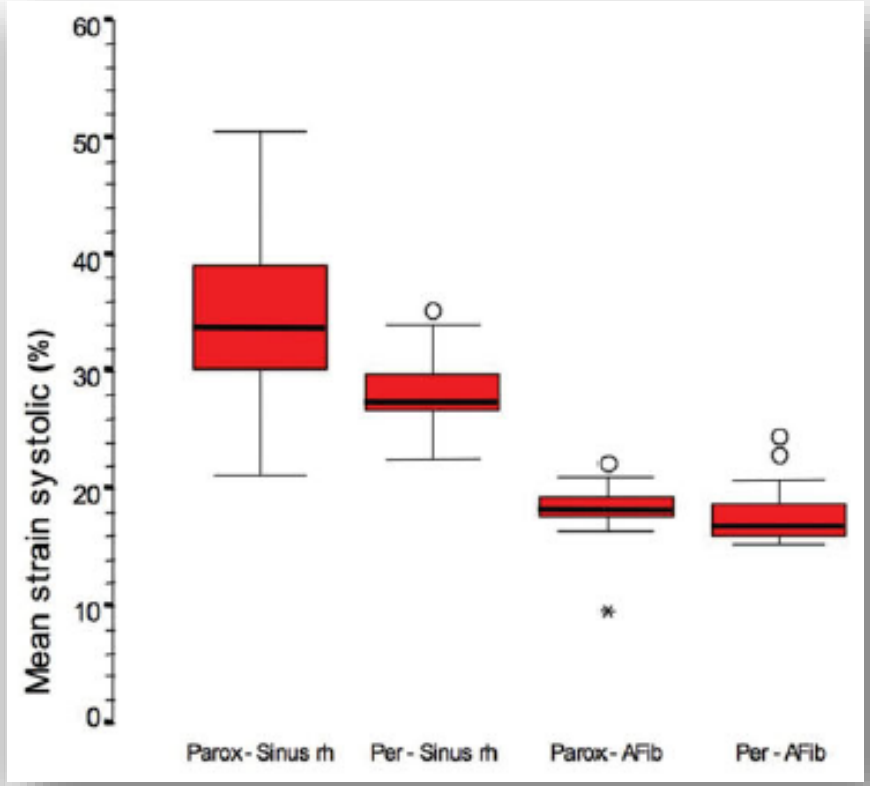



*Inoue YY, J Am Heart Assoc 2015*

# Atrial deformation predicts the maintenance of sinus rhythm after catheter ablation of AF

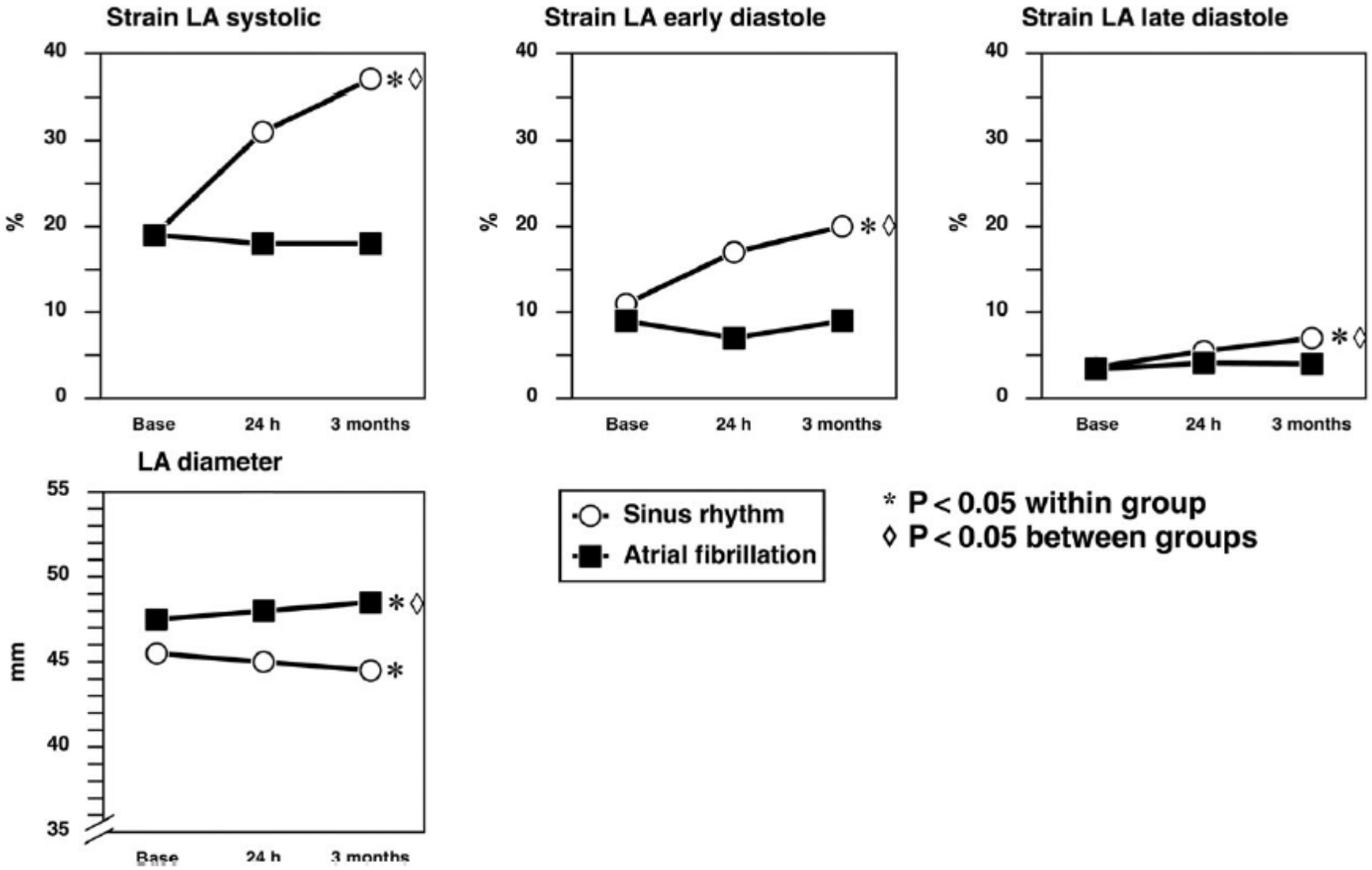
| | Controls ($n$ = 25) | Paroxysmal AF patients ($n$ = 74) | Persistent AF patients ($n$ = 44) | $P$-value (paroxymal AF vs. persistent AF) |
|---|---|---|---|---|
| Mean strain LAs (%) | $88 \pm 23^{a,b}$ | $20 \pm 3$ | $16 \pm 3$ | 3.1E−09 |
| Mean strain LAe (%) | $22 \pm 6^{a,b}$ | $12 \pm 4$ | $8 \pm 3$ | 3.1E−09 |
| Mean strain LAa (%) | 7.5 (6.3;9.9)[a,b] | 5.2 (2.7;6.1) | 0.9 (0;2.9) | 9.0E−10 |




*Schneider C, Eur Heart J 2008*

# Atrial deformation predicts the maintenance of sinus rhythm after catheter ablation of AF

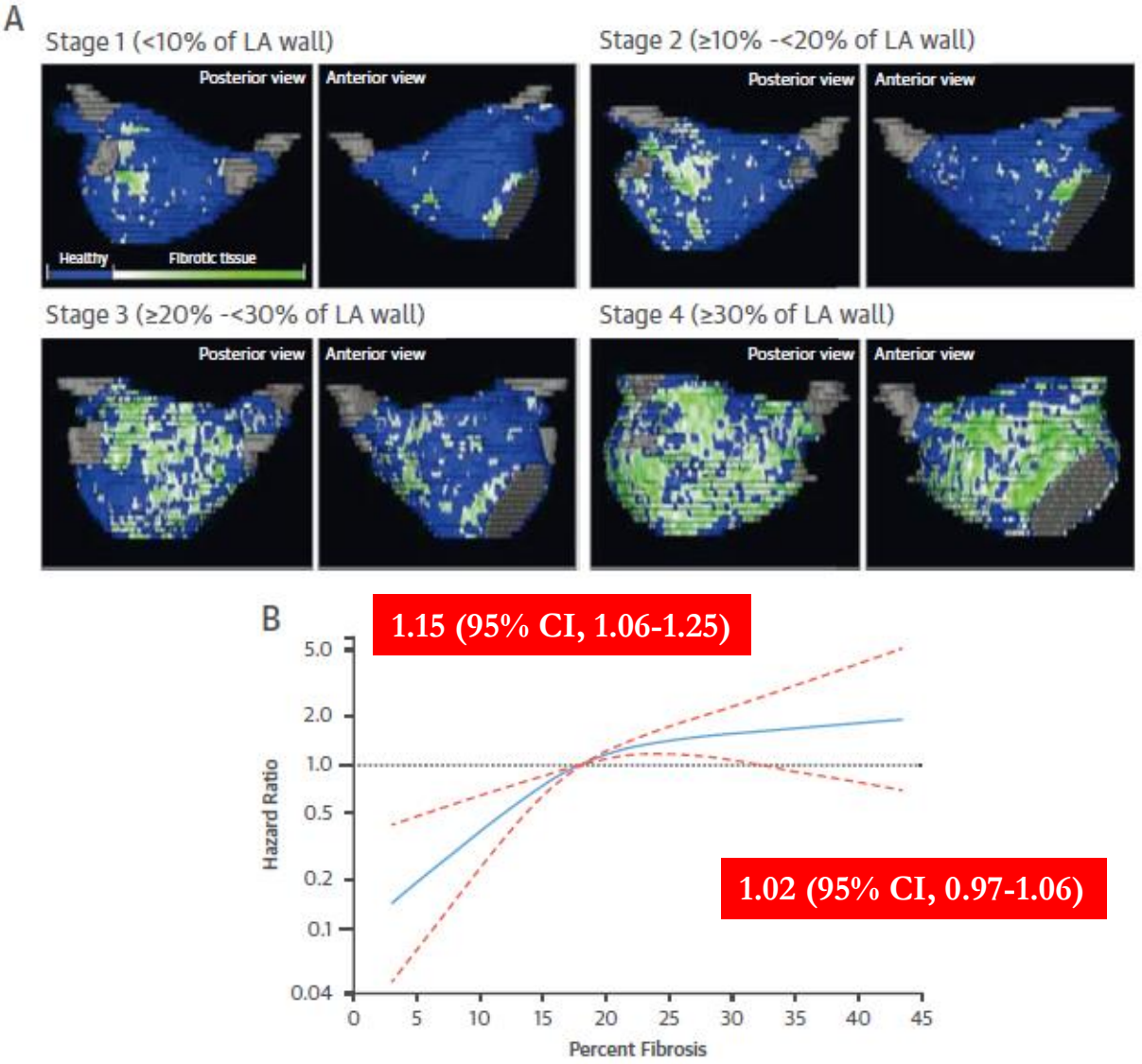



*Schneider C, Eur Heart J 2008*

# Association of Atrial Tissue Fibrosis Identified by DE-MRI with AF Catheter Ablation The DECAAF Study

The overall HR was 1.06 (95%CI, 1.03-1.09; p<.001) per 1% increase in atrial fibrosis*

*[adjusted for age, sex, hypertension, congestive HF, mitral valve disease, diabetes, type of AF (paroxysmal vs persistent), LA volume, LV EF, and participating center]




*Marrouche NF, JAMA 2014*

**Editorial**

# Left Atrial Strain

## A Must or a Plus for Routine Clinical Practice?

Erwan Donal, MD, PhD; Elena Galli, MD, PhD; Frederic Schnell, MD, PhD

- **LA strain is load dependent and influenced by LV function. It has been proposed that instead of focusing on the reservoir function, authors should look more carefully at the booster pump function.**

- **The reduction in LV filling pressures reduces but rarely normalizes LA volumes. There seems to be a strong association between reduction in LV filling pressure and improvement in LA function as indicated by the improvement in LA strain**

- **LA strain is a predictor of atrial fibrillation occurrence and recurrence, and its value seems to be associated with thromboembolic risk. Larger randomized studies are needed to confirm the association with thromboembolic risk and to assess whether LA strain can be used to risk-stratify patients**

*Circ Cardiovasc Imaging*. 2017

Gemelli

Fondazione Policlinico Universitario A. Gemelli
Università Cattolica del Sacro Cuore

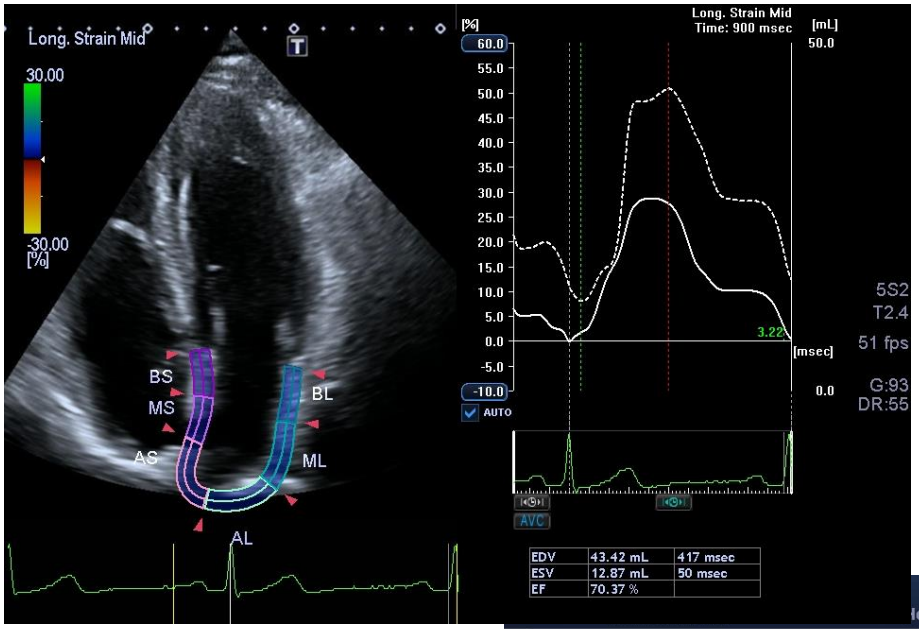
*We must remember to treat the patient and not the disease or the echocardiogram*

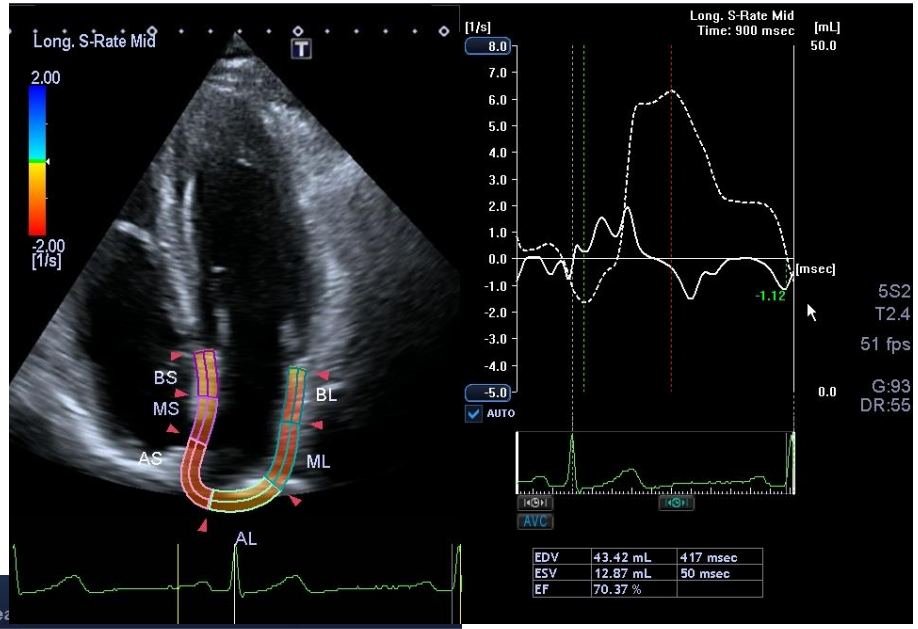
# Grazie per l'attenzione

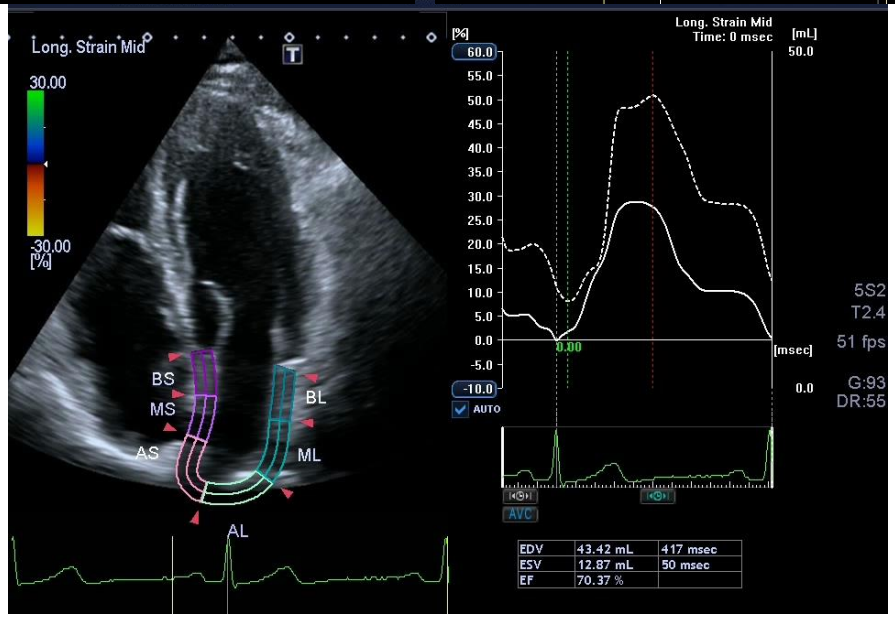
**Gabriella Locorotondo, MD PhD**
**U.O. Diagnostica Cardiologica Non Invasiva**

**gabriella.locorotondo@policlinicogemelli.it**

# Male, 59 yrs old, hypertensive



# Male, 60 yrs old, significant LVH due to untreated systemic arterial hypertension

## Aprile 2017

| VOLUMI VENTRICOLO SIN. | FC | kg | cm | SCm² |
|---|---|---|---|---|
| Ritmo sinusale | 56 | 85 | 167 | 1.94 |
| Simpson Monoplano Proiezioni | 2C | 4C | Med | Vind |
| Ventricolo Sin V.Diastolico(ml) | 152 | 141 | **147** | (126) |
| Ventricolo Sin V.Sistolico(ml) | 83 | 86 | **85** | (58) |
| Frazione di Eiezione(%) | 45 | 39 | **42** | |

| Funzione Diastolica V.Sin | E | A | Dt | E/E' |
|---|---|---|---|---|
| Picco A di Strain rate atriale sin: -0.43 media disfunzione diastolica (pseudonorm.) | 69 | 66 | 163 | 12 |

MASSA Vsin in 2D g 398 L_Strain -5,5
PEP/LVET 0,46 PLStrain msec Lat-Set 168

| | Vind |
|---|---|
| Vol.s ATRIO SIN (ml) BIPL 94 | (62) |

| Ventricolo DESTRO (mm) | Tapse | LL/2 |
|---|---|---|
| | 18 | 24 |

EF media 2c+4c/2 in Speckle Tracking: 41%

completo collasso inspiratorio della cava inferiore

| VOLUMI VENTRICOLO SIN. | FC | kg | cm | SCm² |
|---|---|---|---|---|
| Ritmo sinusale | 55 | 82 | 170 | 1.94 |
| Simpson Monoplano Proiezioni | 2C | 4C | Med | Vind |
| Ventricolo Sin V.Diastolico(ml) | 85 | 91 | **88** | (126) |
| Ventricolo Sin V.Sistolico(ml) | 35 | 43 | **39** | (58) |
| Frazione di Eiezione(%) | 59 | 53 | **56** | |

| Funzione Diastolica V.Sin | E | A | Dt | E/E' |
|---|---|---|---|---|
| lieve disfunzione diastolica (alt. rilasciamento) | 37 | 51 | 271 | 9 |

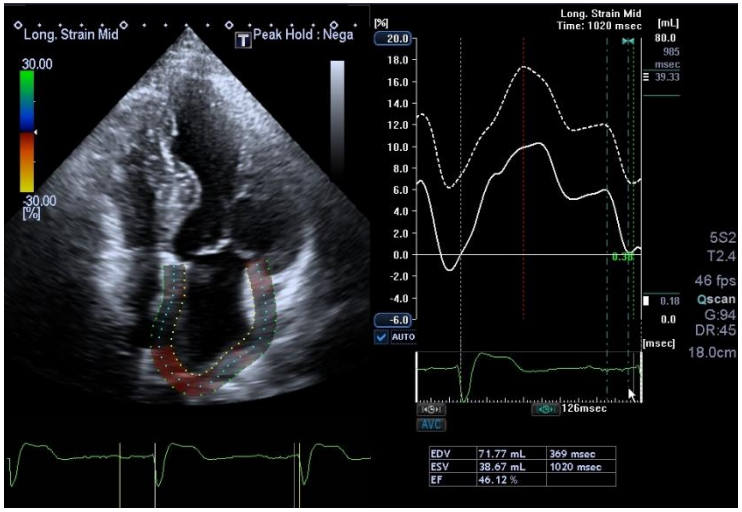
IRT Vsin msec 108 PTStrain msec Lat-Set 0
PEP/LVET 0.51 PLStrain msec Lat-Set 260

| | Vind |
|---|---|
| Vol.s ATRIO SIN (ml) BIPL 65 | (62) |

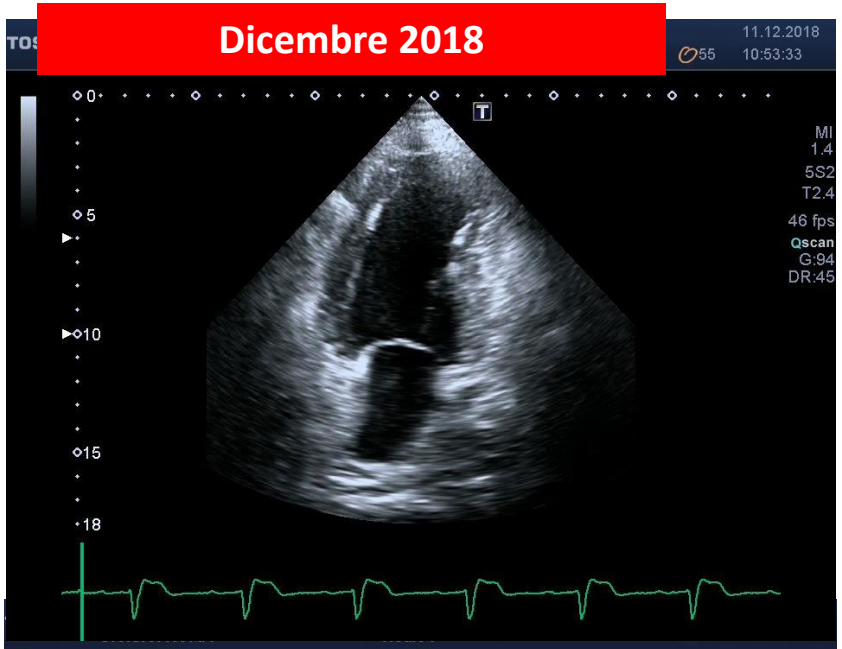
| Ventricolo DESTRO (mm) | Tapse |
|---|---|
| | 16 |

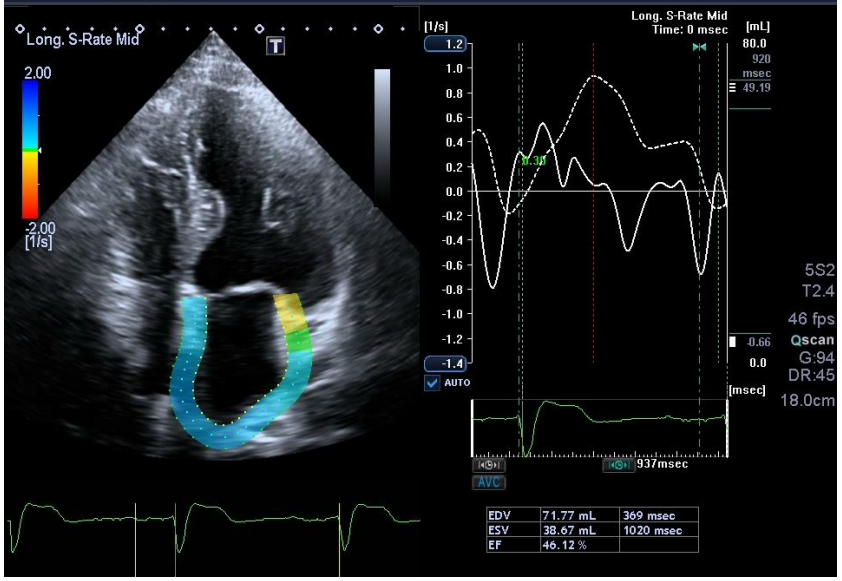
EF media 2c+4c/2 in ST: 56% L_Strain: -6 ; Strain rate atriale 0.66

completo collasso inspiratorio della cava inferiore



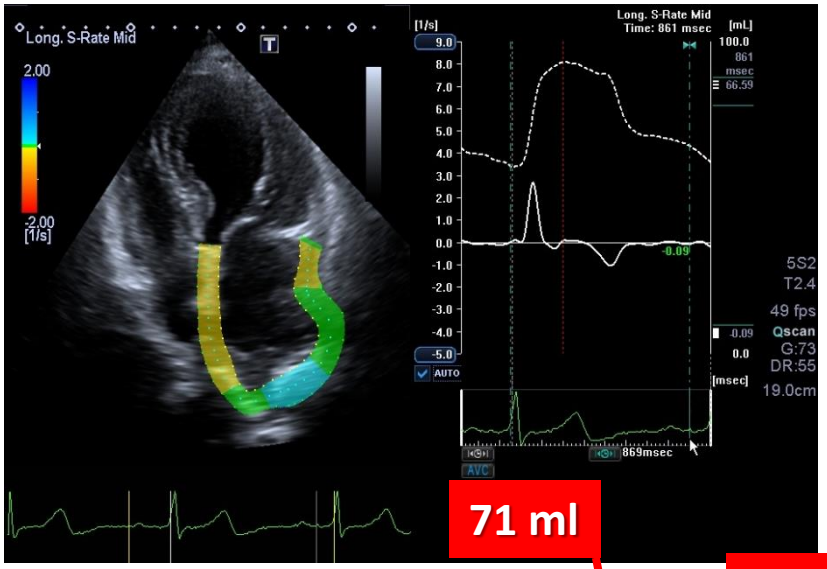

## Dicembre 2018

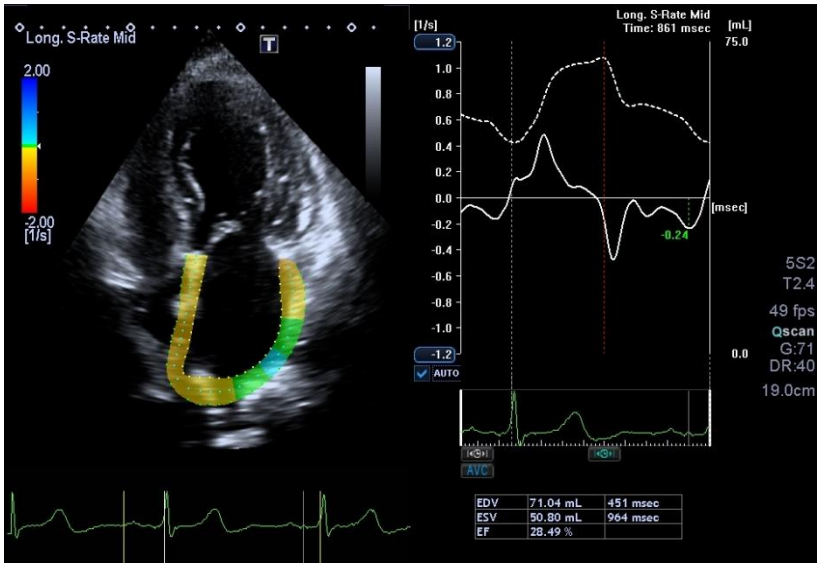


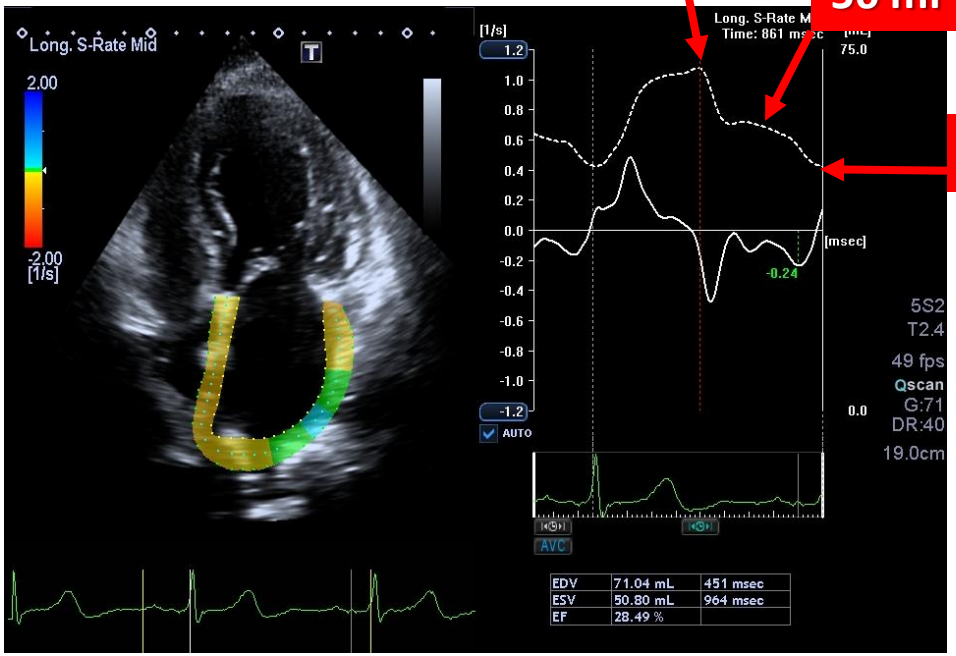

*Courtesy of dott. F. Pennestri*

# Female, 82 yrs old, Non-ST elevation MI (sept.2017), 3 vessel disease, hypertension, dyslipidemia

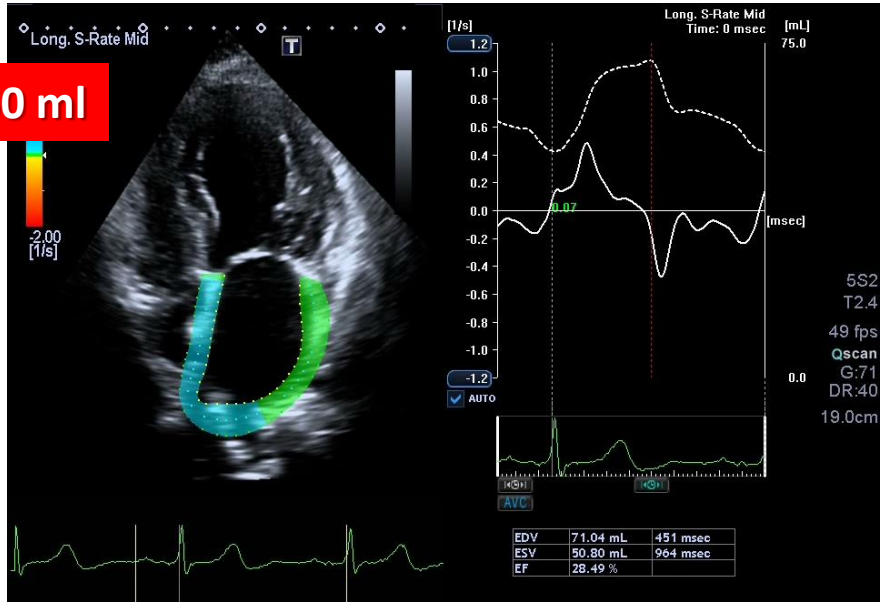



56 ml

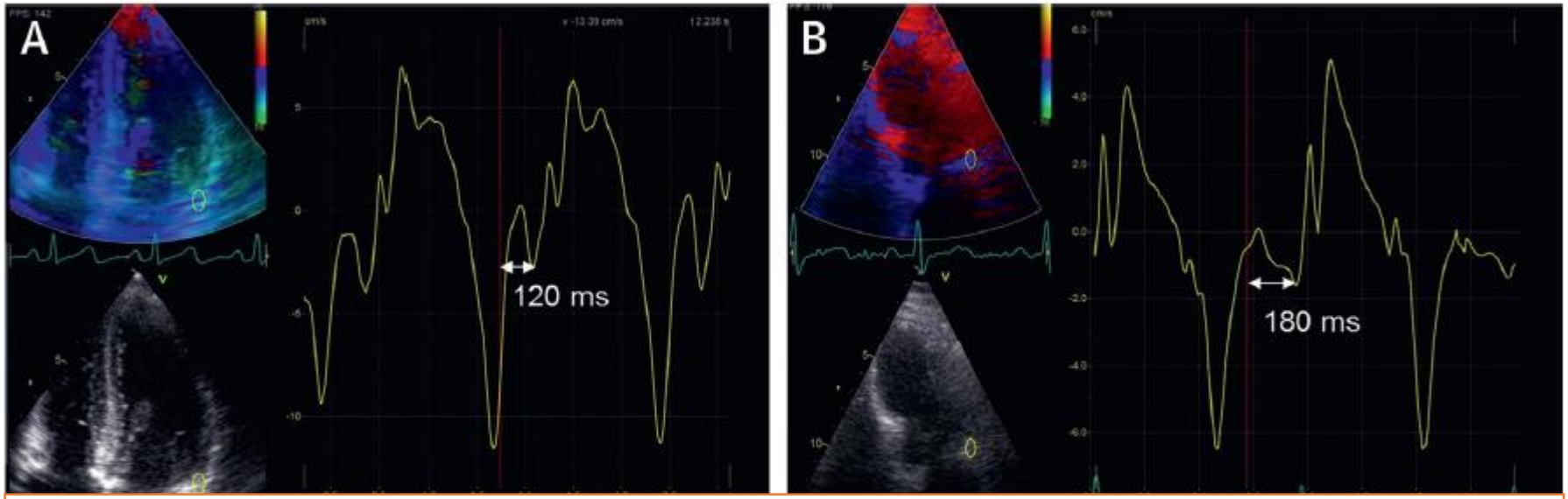



50 ml




*Courtesy of dott. F. Pennestri*

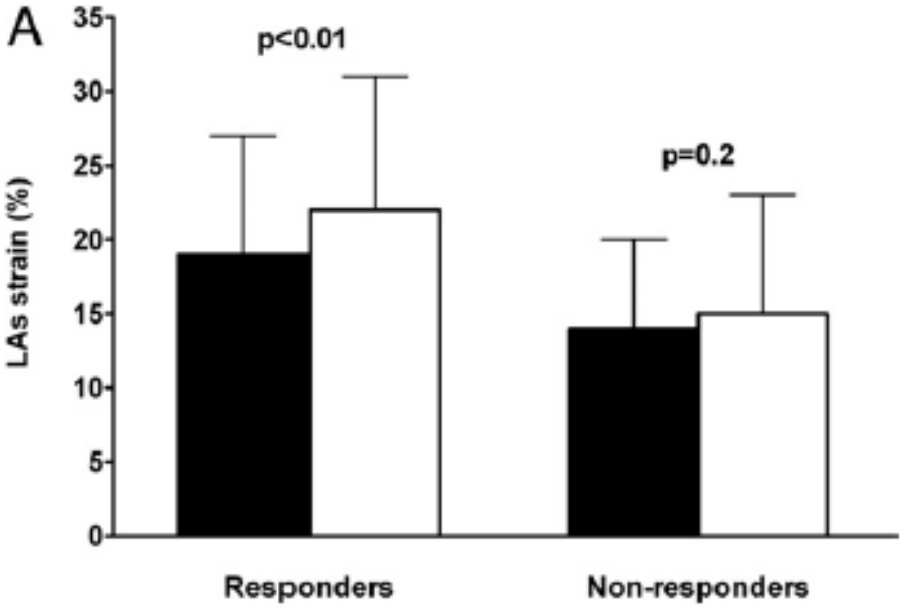
# Time Delay Between Electrical and Mechanical Activation of the LA (PA-TDI) predicts new-onset AF and Ablation Efficacy

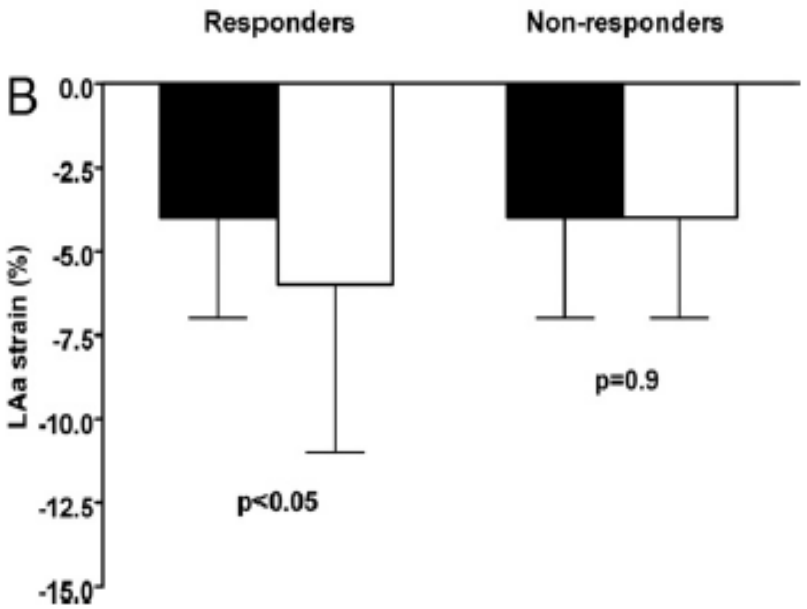



- Patients who presented with AF during follow-up had longer PA-TDI duration than patients who remained in sinus rhythm (172 ± 25 ms vs. 150 ± 20 ms; p <0.001). Prolonged PA-TDI was independently associated with new-onset AF (odds ratio: 1.37; p < 0.027).

- PA-TDI has also been correlated with the efficacy of radiofrequency catheter ablation: patients with longer PA-TDI had higher risk of AF recurrences at follow-up (odds ratio: 1.04; p < 0.001)

# Left Atrial Strain Predicts Reverse Remodeling After Catheter Ablation for Atrial Fibrillation




*Tops LF, JACC 2011*

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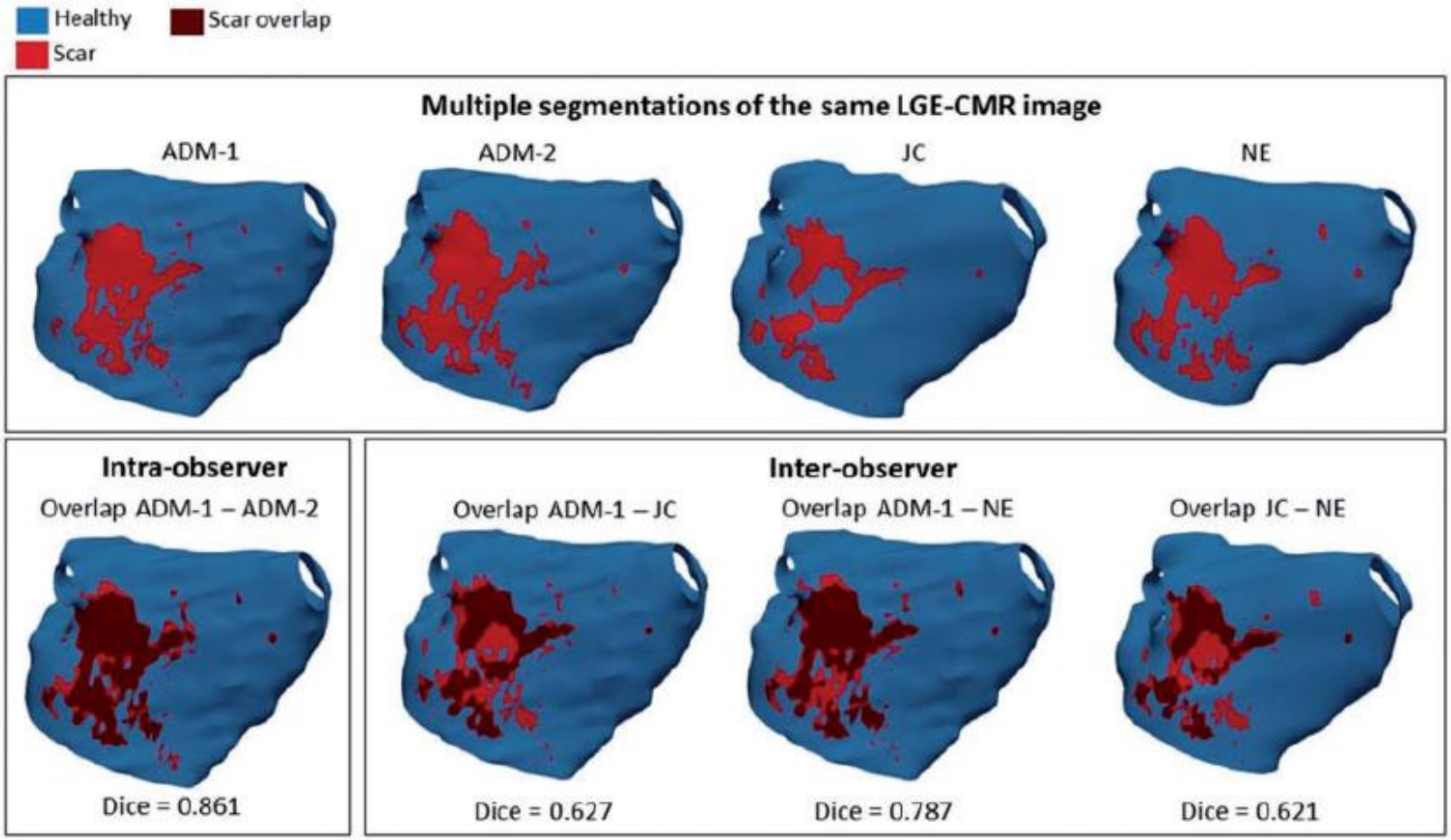
# Reproducibility and accuracy of late gadolinium enhancement cardiac magnetic resonance measurements for the detection of left atrial fibrosis in patients undergoing atrial fibrillation ablation procedures

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