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Echocardiography

Atrial Function Assessed by Speckle Tracking Echocardiography Is a Good Predictor of Postoperative Atrial Fibrillation in Elderly Patients

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Objective: Advanced age is an independent predictor of postoperative atrial fibrillation (POAF) in patients undergoing coronary artery bypass surgery. We evaluated whether left atrial (LA) dysfunction assessed by strain contributes to identifying elderly patients prone to POAF. Methods: Case–control study of 70 subjects undergoing coronary artery bypass surgery. Clinical and laboratory characteristics were recorded at baseline and 72 hours after surgery. Echocardiography was performed during the preoperative period; LA dimensions and deformation by strain (systolic wave [LASs]) as well as strain rate (systolic wave [LASRs] and atrial contraction wave [LASRa]) were assessed. Results: Postoperative atrial fibrillation occurred in 38.5% of patients within the first 72 hours after surgery (28.5% of the younger vs. 48.6% of the older group). Baseline and postoperative inflammatory markers as well as total surgical and aortic clamp time were similar between groups. LA function was markedly impaired in subjects with POAF. Age correlated with LASs, LASRs, and LASRa. These associations remained consistent when subjects 75 years or older were considered separately. Both LASs and LASRa for patients with or without POAF, respectively, were significantly impaired in elderly subjects with POAF. Multivariate analysis provided further evidence that both LASs and age are independent predictors for POAF. Conclusion: Age-related changes in atrial function preceding atrial dilation are evident only upon LA strain analysis. LA strain impairment is an independent predictor of POAF irrespective of age and may serve as a surrogate marker for biological processes involved in establishing the substrate for POAF. (Echocardiography 2016;33:242–248)

Key words: atrial fibrillation, aging, atrial function, echocardiography, speckle tracking

Postoperative atrial fibrillation (POAF) is a common complication after cardiac surgery, with incidences of 10–65% reported in different series.[1] Although POAF was previously considered a benign condition, current consensus is that it is associated with a long-term increase in morbidity and mortality, mostly due to stroke and heart failure.[2]

Advanced age is the most commonly identified predictor of POAF. It has been proposed that elderly patients are susceptible to POAF due to preexisting comorbidities that promote a pro-arrhythmic substrate through increased left atrial (LA) fibrosis and left ventricular (LV) diastolic dysfunction.[3] Left atrial function assessment by 2D speckle tracking echocardiography can be used to identify early functional changes in the left atria associated with the occurrence of paroxysmal atrial fibrillation and POAF.[4] In this study, we evaluated whether LA dysfunction assessed by strain contributes beyond traditional risk factors

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to the increased POAF burden among elderly patients.

Materials and Methods:

Patients:

Subjects in normal sinus rhythm undergoing elective coronary artery bypass graft (CABG) at a university hospital (Hospital Clinico de la Pontificia Universidad Catolica de Chile, Santiago) between January 2008 and May 2011 were included. Baseline clinical characteristics, 2D echocardiogram, and basic laboratory tests were obtained at admission. All patients underwent cardiopulmonary bypass (CPB) using a roller pump and a membrane oxygenator with a standard cardiotomy suction setup. Hypothermia was used in all cases, cooling patients to a core temperature of 30°C. Myocardial protection was provided with antegrade and retrograde crystalloid cardioplegic solution (St. Thomas Hospital solution) infused alternately every 10–15 minutes. Aprotinin was not used at any time. Venous drainage was achieved with a single double-stage cannula introduced through right atrial appendage amputation and directed toward the inferior vena cava. Patients were monitored continuously for 72 hours postoperatively using a telemetry system with automated arrhythmia detection (IntelliVue MP70; Philips Healthcare, Andover, MA, USA). In every patient with a suspected arrhythmic event, a standard 12-lead ECG was recorded and reviewed by a trained cardiologist. Atrial fibrillation (AF) episodes longer than 15 minutes were considered POAF episodes for the purpose of this study.

To minimize the impact of other comorbidities on the analysis, the following exclusion criteria were applied: (1) need for urgent revascularization or preoperative cardiogenic shock, (2) history of myocardial infarction within the previous 2 months, (3) need for associated heart valve surgery, (4) history of malignancy, autoimmune disorder, or chronic inflammatory disease, (5) chronic steroid treatment, (6) thyroid dysfunction, or (7) evidence of active infection.

Our institutional ethics review board approved the study protocol. All patients gave written informed consent. This study was registered as FONDECYT 1100801 and funded by the Chilean National Commission of Scientific Investigation (http://www.conicyt.cl).

Clinical and Biochemical Measurements:

Neutrophil count, white blood cell (WBC), and high-sensitivity C-reactive protein (hs-CRP) were used as inflammatory markers. Neutrophil count and WBC were quantified with an automated cell detector, and hs-CRP was determined using a high-sensitivity immunoreagent (Dade Behring, Deerfield, IL, USA).

Echocardiography:

Baseline 2D echocardiography including apical four- and two-chamber views obtained with the patient in the left lateral decubitus position was performed by a trained operator using a 2.5–5 MHz phased array transducer (VIVID 7; GE Medical Systems, Horten, Norway). LA volume was calculated from apical four- and two-chamber views of the LA using the biplane method of disks. Diastolic function was evaluated by mitral inflow velocities assessed by standard pulsed-wave Doppler at the tips of the mitral valve leaflets in an apical four-chamber view and by tissue Doppler velocities of the medial and lateral mitral annulus. For speckle tracking analysis, the images were acquired at a frame rate of at least 60 Hz. Images were analyzed offline using commercial software for LA strain and LA strain rate assessment (EchoPAC; GE Medical Systems). The endocardial border was manually traced using a point-and-click technique. LA strain was calculated with the reference point set at the onset of the P-wave of the surface ECG to identify the peak of the positive strain wave (LASs) during ventricular systole. Similarly, we identified the peak positive strain rate (LASRs) in the LA strain rate curve during ventricular systole and the peak negative strain rate (LASRa) during active atrial contraction. LASs and LASRs were used as surrogates of LA reservoir function, and LASRa was used as a surrogate of LA active contractile function. The software divided the atrial wall into six segments, and the average was used for analysis (Fig. 1). A trained operator performed all measurements on two separate occasions to rule out significant operator-related variation, as reported elsewhere.[4]

Statistical Analysis:

Continuous variables were expressed as mean ± standard deviation; for categorical variables, n (%) was used. Continuous variables were tested for normality using the Kolmogorov–Smirnov test. For normally distributed variables, univariate comparisons between groups were performed with Student's *t*-test; otherwise, the Mann–Whitney U-test was used. Categorical variables were analyzed using chi-square. The Bland–Altman method was used to assess the intraoperator variability of repeated LA strain measures. Variables with significant differences between groups were included in a multivariate logistic regression to evaluate their utility as independent predictors of POAF. Statistical analysis was performed with SPSS 16.0 (SPSS Inc., Chicago, IL, USA).

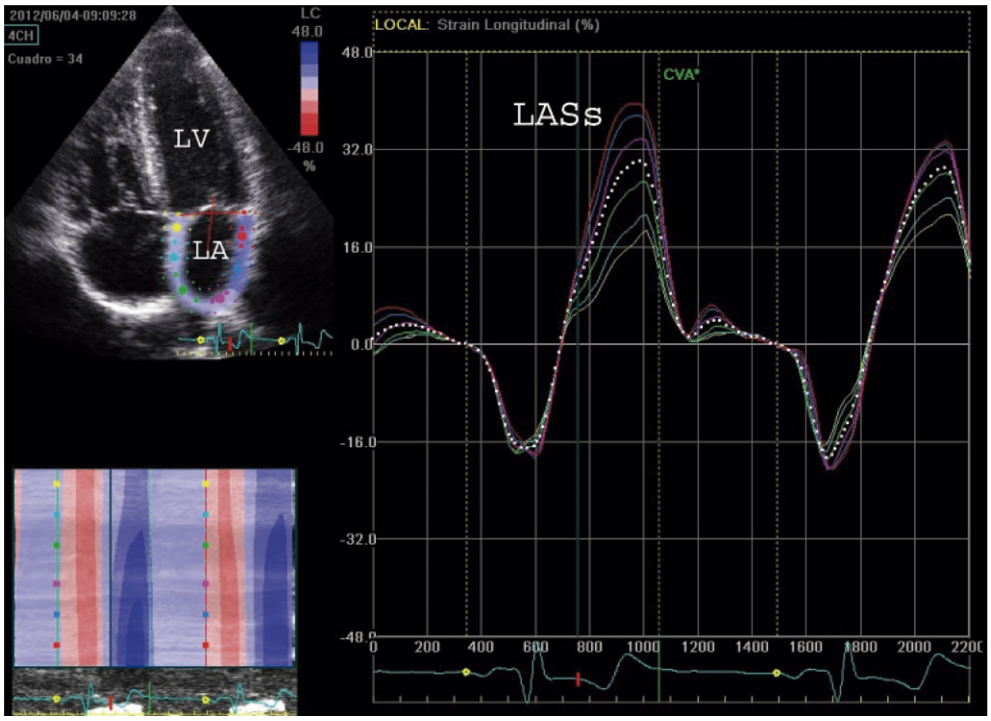

Figure 1. Representative image of normal left atrial strain curve measured by speckle tracking echocardiography.

Results:

Clinical Characteristics:

Case–control study. Seventy patients were included (35 subjects below 75 and 35 subjects 75 years or older), 31.2% female. The older subjects had a slightly higher prevalence of hypertension and diabetes mellitus, but the difference was not statistically significant (85.7 vs. 65.7% and 37.1 vs. 28.5%, respectively). Conversely, hyperlipidemia was more common in younger subjects (54.2 vs. 45.7%, P = 0.02). Both groups had similar morbidity profiles and preoperative medications. Clinical characteristics are summarized in Table I.

The average number of conduits was 2.7 ± 0.9 in elderly patients and 3.0 ± 1.2 in younger patients, P = 0.54. There were no significant differences in CPB time (104.1 ± 46.4 vs. 101 ± 35.8 min for younger vs. older subjects, P = 0.37), aortic clamp time (76.2 ± 44 vs. 66.5 ± 34.6 min, P = 0.35), or postoperative balance (2155 ± 1073 vs. 2255 ± 1185, P = 0.76). As expected, the EuroSCORE risk index was slightly higher in the elderly population (3.06 ± 2.48 vs. 3.29 ± 2.39, P = 0.42) (Table I).

Postoperative atrial fibrillation incidence was significantly higher in the elderly cohort (48.6 vs. 28.5%, P = 0.03). There were no differences between groups in the timing of POAF onset (12.3 ± 20.6 vs. 14.1 ± 26.2 h after surgery for younger vs. elderly subjects, P = 0.22) or POAF duration (12.4 ± 6 vs. 9.8 ± 6.8 h, P = 0.27). The majority of patients converted to sinus rhythm spontaneously (16.2%) or after amiodarone infusion (62.6%). Electrical cardioversion was required in two subjects due to hemodynamic instability associated with the onset of the arrhythmia. All subjects were in normal sinus rhythm at discharge (Table I).

Laboratory Data:

Baseline laboratory tests were evaluated both at admission and 72 hours after surgery, summarized in Table II. Baseline hs-CRP levels were above normal limits in both groups and were slightly higher in elderly patients, although the difference did not reach statistical significance (6.3 ± 11.1 vs. 8.6 ± 16.2, P = 0.76). Other inflammatory parameters, such as WBC, neutrophil absolute count, and erythrocyte sedimentation rate (ESR), were similar in both groups. Routine baseline laboratory test results did not differ significantly between younger versus older patients. After surgery, all subjects showed increased inflammatory parameters, irrespective of age.

Echocardiography Data:

Echocardiographic characteristics of both groups are listed in Table III. LA strain variability within repeated measures was assessed using the Bland–Altman method, which showed excellent reproducibility for all parameters analyzed (Figure S1).

TABLE I

Clinical Characteristics

Variable n (%)	Age <75 Years (n = 35)	Age ≥75 Years (n = 35)	P-Value
Clinical characteristics			
Age	61.8 ± 7.7	80.6 ± 2.8	<0.01
Hypertension	23 (65.7)	30 (85.7)	0.08
Diabetes mellitus	48 (28.5)	13 (37.1)	0.57
Hyperlipidemia	19 (54.2)	16 (45.7)	0.28
Stroke	3 (8.5)	2 (5.7)	0.24
COPD	2 (5.7)	1 (2.8)	0.28
CKD	2 (5.7)	0 (0)	0.16
Therapy			
ACEi/ARA	19 (54.3)	22 (62.8)	0.42
β-blockers	17 (48.6)	18 (51.4)	0.54
CCB	5 (14.2)	6 (17.1)	0.55
Statins	18 (51.4)	22 (62.8)	0.44
Amiodarone	2 (5.7)	0 (0)	0.69
Surgical procedure			
Average no. of bridges	2.7 ± 0.9	3.0 ± 1.2	0.54
CPB time	104.1 ± 46.4	101 ± 35.8	0.37
Aortic clamp time	76.2 ± 44	66.5 ± 34.6	0.35
Postoperative balance	2155 ± 1073	2255 ± 1185	0.76
EuroSCORE risk index	3.04 ± 2.35	3.29 ± 2.39	0.32
POAF			
Incidence of POAF	10 (28.5)	17 (48.6)	0.01
Onset of POAF (h)	16.2 ± 22.6	14.1 ± 26.2	0.54
POAF duration (h)	11.6 ± 7.4	9.8 ± 6.8	0.52

ACEi = angiotensin-converting enzyme inhibitors; ARA = angiotensin II receptor antagonists; CCB = calcium channel blockers; CKD = chronic kidney disease; CPB = cardiopulmonary bypass; COPD = chronic obstructive pulmonary disease; POAF = postoperative atrial fibrillation.

Routine echocardiographic measures did not differ between older and younger subjects, but elderly patients exhibited less deformation during the LA reservoir and contractile phases than younger patients, with a significant correlation between impaired LA reservoir function and age (LASs $r = -0.389$ $P < 0.01$; LASRs $r = 0.409$, $P = 0.03$) as well as impaired contractile function and age (LASRa $r = 0.6$, $P < 0.01$) (Fig. 2).

Left atrial reservoir and contractile function, assessed by LA strain and LA strain rate, was markedly reduced in subjects who developed POAF: LASs (10.0 ± 1.1% vs. 24.0 ± 1.2% for subjects with vs. without POAF, $P < 0.001$), LASRa (−0.6 ± 0.1/s vs. 1.8 ± 0.12/s for subjects with vs. without POAF, $P < 0.001$), and LASRs (0.6 ± 0.01 vs. 1.2 ± 0.01 for subjects with vs. without POAF, $P < 0.001$). Interestingly, younger patients with POAF exhibited changes in LA contractile function and reservoir function similar to those observed in elderly patients, as is shown in Figure 3. When elderly subjects were considered separately, both LASs and LASRa were significantly impaired in those with POAF (10.9 ± 4.6% vs. 22.6 ± 2.5%, $P < 0.01$; −0.71 ± 0.4/s vs. −1.3 ± 0.3/s, $P = 0.03$, for older patients with vs. without POAF, respectively).

As this mechanical impairment may provide a substrate for POAF, we tested the utility of LA strain and LA strain rate analysis in detecting subjects at elevated risk for POAF, using a multivariate analysis including age, sex, comorbidities, LA dimensions, and LV function and dimensions. Age (OR 1.09, 95% CI, 1.01–1.16) and LASs (OR 1.63, 95% CI, 1.19–2.22) were both independent predictors of POAF, suggesting that atrial function assessed by echocardiographic deformation parameters may enhance the clinical profile for identifying subjects at high risk for POAF (Fig. 4). When elderly patients were evaluated separately, the only significant predictor of POAF was LASs (OR 1.48, 95% CI 1.01–2.02).

Discussion:

POAF is a common complication after heart surgery, accounting for prolonged inpatient stays, increased hospitalization costs, and significantly higher morbidity and mortality.[5] Despite an incidence as high as 30% according to most clinical series,[6–8] its pathophysiology is poorly understood and effective prophylaxis approaches are still lacking.[9]

Advanced age is the most prominent and consistent risk factor for POAF. Our study shows that

TABLE II

Laboratory Results

Variable	Age <75 Years (n = 35)	Age ≥75 Years (n = 35)	P-Value
Preoperative			
Creatinine (mg/dL)	0.9 ± 0.3	1.1 ± 0.4	0.20
BUN (mg/dL)	20.5 ± 8.7	20.8 ± 7.2	0.79
Potassium (mEq/L)	4.1 ± 0.9	3.8 ± 0.8	0.34
hs-CRP (mg/dL)	6.3 ± 11.1	8.6 ± 16.2	0.76
Hb (g/L)	14.1 ± 3.6	13.4 ± 1.2	0.37
WBC (10^3/mL)	7.2 ± 1.6	7.3 ± 1.8	0.80
ESR (mm/h)	17.2 ± 17.6	17.2 ± 11.0	0.90
Postoperative			
Creatinine (mg/dL)	1.0 ± 0.5	1.1 ± 0.5	0.41
BUN (mg/dL)	19.5 ± 9.8	21.8 ± 8.7	0.67
Potassium (mEq/L)	3.8 ± 0.4	4.1 ± 0.6	0.32
hs-CRP (mg/dL)	16.1 ± 14.7	14.7 ± 8.1	0.68
Hb (g/L)	9.7 ± 3.2	10.1 ± 1.9	0.06
WBC (10^3/mL)	9.1 ± 4.4	9.2 ± 5.8	0.09
ESR (mm/h)	40.7 ± 25.3	46.7 ± 26.8	0.54

BUN = blood ureic nitrogen; hs-CRP = high-sensitivity C-reactive protein; Hb = hemoglobin; WBC = white blood cell count; ESR = erythrocyte sedimentation rate.

TABLE III

Echocardiography Results

Variable	Age <75 Years (n = 35)	Age ≥75 Years (n = 35)	P-Value
LAD (mm)	34 ± 18	37 ± 16	0.54
LVEF (%)	40 ± 29	35 ± 26	0.42
E-wave (cm/s)	54 ± 36	61 ± 48	0.47
A-wave (cm/s)	55 ± 36	67 ± 40	0.17
LASs (%)	20 ± 10.7	16 ± 5	0.25
LASRa (1/s)	−1.4 ± 0.8	−0.9 ± 0.4	0.03
LASRs (1/s)	1.1 ± 0.5	1.0 ± 0.3	0.21

LAD = Left atrial diameter; LVEF = left ventricular ejection fraction; LASs = peak of the positive strain wave; LASRs = peak positive strain rate; LASRa = peak negative strain rate.

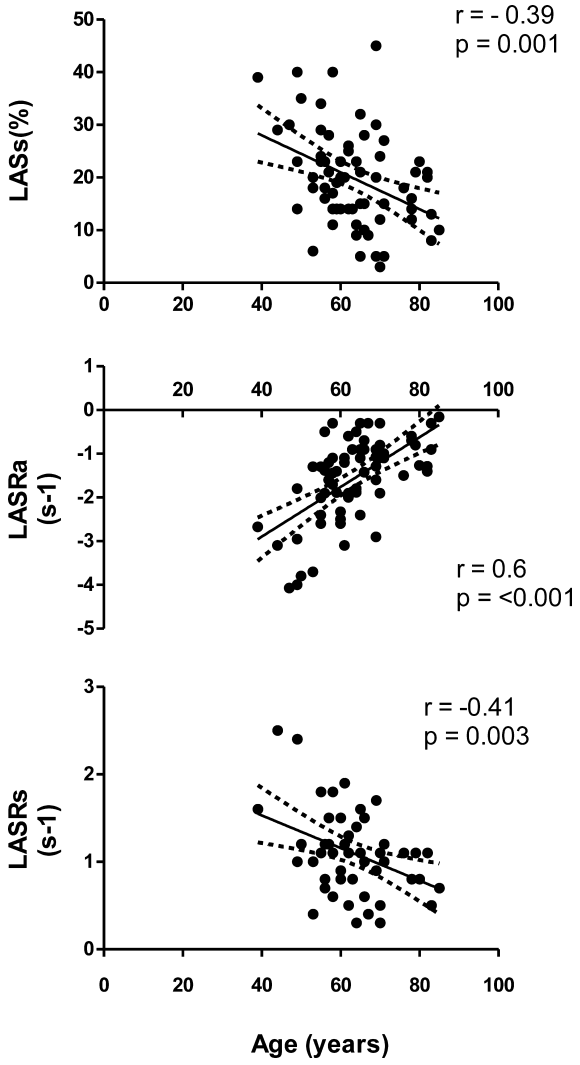

Figure 2. Correlation between atrial function parameters and aging. As age increases, left atrial (LA) reservoir function (LASs, LASRs) and contractile function (LASRa) worsen. This decreased mechanical LA function likely represents increased atrial fibrosis secondary to the aging process, which may explain, at least partially, the increased incidence of postoperative atrial fibrillation in the elderly.

the incidence of POAF among elderly patients is significantly higher than in younger subjects (48.6% vs. 28.5%). It has been proposed that aging is associated with left ventricular filling abnormalities[10] which in turn contribute to LA enlargement, impairing both reservoir and pump function during atrial systole. This is consistent with epidemiologic data showing that AF is more common in elderly subjects with heart failure and preserved ejection fraction than in patients with impaired ejection fraction,[11] reflecting the importance of left ventricular filling in the pathogenesis of the arrhythmia.

Several groups have proposed that atrial enlargement is a predictor for developing AF in the general population, particularly among those over 65 years old.[12] In fact, atrial enlargement is a surrogate measure of the complex cellular changes usually denominated "atrial remodeling."[13,14] In our study, neither LA volume or LA diameter were independent predictors of POAF, probably because the inclusion of atrial function in the model gives a more comprehensive description of LA performance, given the links between chamber size, deformation, and con-

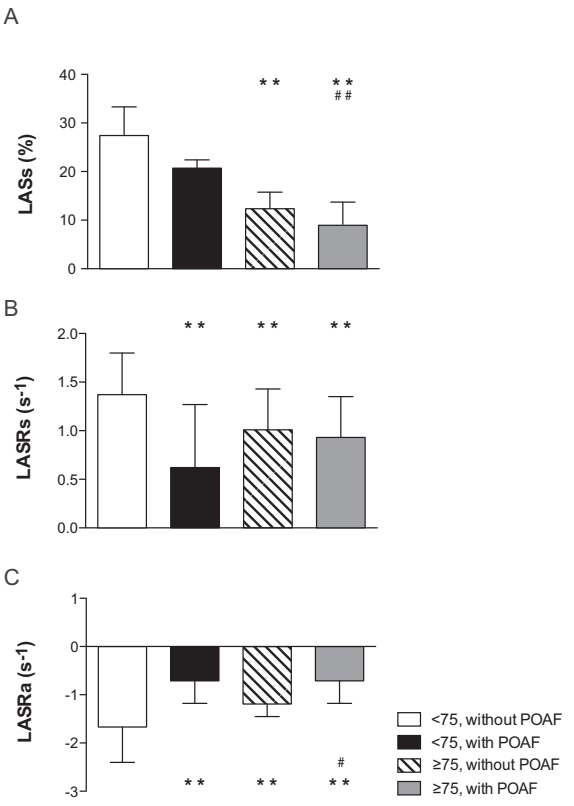

Figure 3. Young subjects with postoperative atrial fibrillation (POAF) showed impaired atrial function. The level of contractile and reservoir atrial function impairment observed in young subjects with POAF was similar to that observed in the elderly population. Elderly subjects with POAF showed significant differences in LASs and LASRa versus age-matched individuals without POAF. **A.** Left atrial strain (LASs). **B.** Left atrial peak negative strain rate (LASRa). **C.** Left atrial peak positive strain rate (LASRs). $^{**}P < 0.01$ versus reference population (young subjects without POAF). $^{\#}P < 0.05$ versus older subjects without POAF. $^{\#\#}P < 0.01$ versus older subjects without POAF.

tractile performance.[15] Atrial enlargement represents an advanced stage of this process, and due to its poor sensitivity, it is unsuitable for screening candidates susceptible to developing AF among a high-risk population, as is the case with patients undergoing coronary artery bypass surgery.

LA strain and strain rate enhance traditional echocardiography by evaluating the three components of atrial function: reservoir, conduit, and pump function.[12,16,17] In the aging heart, an increasingly stiff ventricular myocardium promotes progressive atrial stretching, upregulation of local renin–angiotensin system, increased synthesis of angiotensin II, and atrial autophagy, ultimately leading to atrial dysfunction and dilation.[9,18] Impaired atrial strain reflects an early stage of this process and has been shown to predict new-onset AF in the elderly population.[9,18]

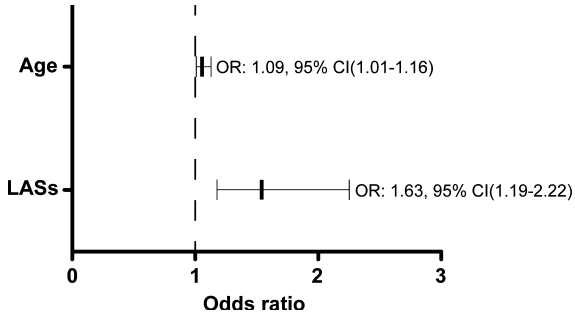

Figure 4. Independent predictors of atrial fibrillation (AF) after multivariate analysis.

The inclusion of a younger cohort in our study allows us to better contextualize the findings in LA strain. While strain parameters seem to gradually deteriorate with advancing age, there were no significant differences between younger and older subjects beyond LASRa measurements; however, patients who develop POAF, irrespective of age, exhibited marked differences in LA strain, reinforcing the concept that POAF occurs on top of a previously altered substrate which can be identified using more accurate tools for assessing LA function. We also found that LA dysfunction is a predictor of POAF in patients undergoing coronary bypass surgery.[4] In our study, LA strain and strain rate values in older POAF subjects were approximately 50% lower than in age-matched healthy subjects.[19,20] To our knowledge, this is the first study to show that assessing LA myocardial deformation may improve clinical prediction of POAF in the elderly. In fact, LASs impairment was able to predict POAF after adjusting for age, sex, and comorbidities.

Limitations:

The main limitations of this study were the small sample size, as the study was designed to test whether LA strain could identify subjects prone to POAF in an elderly population. The inclusion of younger patients was necessary to provide a reference framework for strain measurements, but a larger study focused strictly on the elderly population would be desirable. A major limitation of echocardiography is its highly operator-dependent nature. Because all measurements were performed by a trained operator, interoperator agreement was not assessed in this study. Thus, the results reflect the expertise of one university center, which may limit the reproducibility of the results.

Conclusions:

Advanced age is associated with significant changes in atrial function as assessed by LA deformation imaging. Recognizing these changes will

allow the clinician to identify patients at higher risk for POAF development beyond traditional risk factors. Further studies are warranted to evaluate the utility of this bedside tool in identifying patients who would benefit from POAF prophylaxis.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Bland–Altman analysis for repeated LA strain measurements.