Predictive role of left atrial and ventricular mechanical function in postoperative atrial fibrillation: a two-dimensional speckle-tracking echocardiography study

Ameliyat sonrası atriyum fibrilasyonunu öngörmede sol atriyum ve ventrikülün mekanik fonksiyonlarının rolü: İki boyutlu speckle-tracking ekokardiyografi çalışması

Özcan Başaran, M.D., Kürşat Tigen, M.D.,[#] Gökhan Gözübüyük, M.D.,[*] Cihan Dündar, M.D.,[†] Ahmet Güler, M.D.,[‡] Onur Taşar, M.D.,[§] Murat Biteker, M.D., Can Yücel Karabay, M.D.,[‡] Mustafa Bulut, M.D.,[‡] Tansu Karaahmet, M.D.,[||] Cevat Kırma, M.D.[‡]

Dept. of Cardiology, Muğla Sıtkı Koçman University Faculty of Medicine, Muğla, Turkey; [#]Dept. of Cardiology, Marmara University Faculty of Medicine, İstanbul, Turkey; [*]Dept. of Cardiology, Malatya State Hospital, Malatya, Turkey; [†]Dept. of Cardiology, Büyük Meydan Hospital, Samsun, Turkey; [‡]Dept. of Cardiology, Kartal Koşuyolu Heart Training and Research Hospital, İstanbul, Turkey; [§]Dept. of Cardiology, Elazığ Training and Research Hospital, Elazığ, Turkey; [||]Dept. of Cardiology, Acıbadem University Faculty of Medicine, İstanbul, Turkey

ABSTRACT

Objective: The aim of this study was to determine the role of left-sided mechanical parameters in postoperative atrial fibrillation (POAF) in patients undergoing coronary artery bypass grafting (CABG).

Methods: Ninety patients with coronary artery disease and normal left ventricular (LV) function in sinus rhythm were enrolled in the study. Preoperative LV and left atrial (LA) mechanics were evaluated by two-dimensional (2D) speckle-tracking echocardiography (STE), including strain and rotation parameters, and volume indices. Patients were monitored in order to detect POAF during the postoperative period.

Results: Twenty-three of 90 patients (25.6%) developed POAF. Age (p<0.001) and preoperative beta blocker usage (p=0.001) were the clinical parameters associated with POAF. Left atrial maximum volume index (LAV[max]i) increased, and peak left atrial longitudinal strain (PALS) was impaired in POAF patients (p=0.001, p<0.001, respectively). Left ventricular twist (LVtw) and left ventricular peak untwisting velocity (UntwV) were augmented in POAF patients (p=0.013, p=0.009, respectively). Receiver operating characteristic analysis showed N-terminal pro-brain natriuretic peptide (NT-proBNP) levels above 70 pg/ml and predicted POAF with a sensitivity of 74% and specificity of 78% (area under curve: 0.758, 95% confidence interval [CI] 0.631–0.894, p<0.001). Logistic regression analysis demonstrated that age (odds ratio [OR] 1.1, CI 1.01–1.20, p=0.034), preoperative beta blocker usage (OR 8.84, CI 1.36–57.28, p=0.022), NT-proBNP (values >70 pg/ml, OR 22.377, CI 3.286–152.381, p<0.001), PALS (OR 0.86, CI 0.75–0.98, p=0.023), and UntwV (OR 1.02, CI 1.00–1.04, p=0.029) were the independent predictors of POAF.

Conclusion: The combination of 2D STE, clinical, and biochemical parameters may help predict POAF.

ÖZET

Amaç: Bu çalışmada koroner arter baypas cerrahisi (KABG) uygulanacak hastalarda, ameliyat sonrası atriyum fibrilasyonu (AF) gelişmesini öngörmede sol kalbe ait mekanik parametrelerin rolünü değerlendirmeyi planladık.

Yöntemler: Çalışmaya koroner arter hastalığı olan, normal sol ventrikül sistolik fonksiyonuna sahip, sinüs ritminde 90 hasta alındı. Hastaların ameliyat öncesi sol atriyum ve sol ventrikülün mekanik fonksiyonları (strain, rotasyonal parametreler ve hacim indeksleri) iki boyutlu speckle-tracking ekokardiyografisi ile değerlendirildi. Hastalar ameliyat sonrası dönemde AF gelişimini değerlendirmek için monitorize edildiler.

Bulgular: Doksan hastanın 23'ünde (%25.6) AF gelişti. Yaş (p<0.001), ameliyat öncesi beta bloker kullanımı (p<0.001) AF ile ilişkili klinik parametreler olarak saptandı. Sol atriyum hacim indeksi AF gelişen hastalarda artmış olarak bulundu (p<0.001). Sol atriyumun strain (SAS) değerleri ise AF gelişen hastalarda azalmış olarak bulundu (p<0.001). Sol ventrikül twist ve pik untwisting hız (PUH) ise artmış olarak saptandı (sırasıyla, p=0.013 ve p=0.009). ROC analizinde 70 pg/ml üzerindeki NT-proBNP düzeylerinin AF'yi %74 duyarlılık ve %78 özgüllük (AUC: 0.758, %95 GA=0.631–0.894, p<0.001) ile gösterdiği bulundu. Lojistik regresyon analizi sonucunda yaş (her bir yıllık artış OO: 1.133 GA: 1.029–1.247 p=0.011), beta bloker kullanımı (kullanmayanlarda kullananlara göre OO: 18.558 GA: 2.098-164.145 p=0.009), NT-proBNP (70 pg/ml üzerindeki değerler altındakilere göre OO: 22.377 GA: 3.286–152.381 p<0.001), SAS (OO: 0.839 GA: 0.730-0.963 p=0.013) ve PUH (OO: 1.032 GA: 1.009–1.055 p=0.005) AF için bağımsız değişkenler olarak saptandı.

Sonuç: İki boyutlu speckle-tracking ekokardiyografisi, klinik ve laboratuvar verilerin birlikte kullanımı ameliyat sonrası atriyum fibrilasyonu gelişiminin öngörülmesinde yardımcı olur.

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Correspondence: Dr. Özcan Başaran. Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, Muğla.
Tel: +90 252 - 214 13 26 e-mail: basaran_ozcan@yahoo.com

Postoperative atrial fibrillation (POAF) is a risk factor for short-term morbidity and decreased long-term survival.[1] The incidence of POAF after isolated coronary artery bypass graft surgery (CABG) may be as high as 30%.[2] Furthermore, the occurrence of POAF increases when the patient has 1 or more cardiovascular risk factors.[3] POAF has 2 major pathophysiological mechanisms: degenerative changes in atrial myocardium and preoperative electrophysiological changes. Atria with preoperative mechanical dysfunction may develop atrial fibrillation (AF) during surgery. Enlarged left atrium and poor left atrial (LA) mechanical functions have been found to be predictors of POAF.[4]

Impaired left ventricular (LV) mechanical function assessed by echocardiography (LV ejection fraction) was associated with POAF.[5] However, the role of subclinical LV mechanical function assessed by two-dimensional (2D) speckle-tracking imaging is less clear. Lower values of LV global longitudinal strain, measured by speckle-tracking echocardiography (STE), were associated with POAF in patients with aortic stenosis.[6] LV diastolic dysfunction is another risk factor for developing POAF.[7] LV rotational mechanics such as torsion, twist, and untwisting rate have not yet been investigated. There is a correlation between LV diastolic dysfunction, LA pressure, high B-type natriuretic peptide (BNP) levels and recurrence of AF.[8,9]

The aim of this study was to evaluate the association between POAF, LA and LV mechanical functions, and natriuretic peptides in patients having CABG.

METHODS

A prospective study was performed in 90 patients attending Kartal Koşuyolu Education and Research Hospital for CABG between March 2009 and December 2010. All included patients were in sinus rhythm and were without significant valvular disease. Exclusion criteria were thyroid function abnormality, chronic kidney disease, redo CABG, and a history of previous AF. Patients were monitored for 4 days in the intensive care unit and step-down unit. Postoperatively, 12 lead electrocardiograms were obtained daily. Postoperative AF was defined as any episode of AF lasting at least 15 minutes.[5] The study population was divided into 2 groups according to POAF development. Blood samples were obtained the day before surgery to measure N-terminal pro-brain natriuretic peptide (NT-proBNP) concentrations.

The investigation conformed to the principles outlined in the Declaration of Helsinki. The study was approved by the local ethical committee. All participants gave written informed consent.

Abbreviations:

2D	*Two-dimensional*
AF	*Atrial fibrillation*
BNP	*B-type natriuretic peptide*
CABG	*Coronary artery bypass grafting*
CI	*Confidence interval*
LA	*Left atrial*
LAV	*Left atrial volume*
LAV(max)	*Left atrial maximum volume*
LAV(max)i	*Left atrial maximum volume index*
LAV(min)	*Left atrial minimum volume*
LV	*Left ventricular*
LVtw	*Left ventricle twist*
NT-proBNP	*N-terminal pro-brain natriuretic peptide*
OR	*Odds ratio*
PALS	*Peak LA longitudinal strain*
POAF	*Postoperative atrial fibrillation*
STE	*Speckle-tracking echocardiography*
UntwV	*Left ventricle peak untwisting velocity*

Echocardiography

Twenty-four hours before surgery, a baseline echocardiograph was obtained using conventional 2D echocardiography (Vivid 7, GE Vingmed Ultrasound AS, Horten, Norway) with a 3.5-MHz multiphase array probe in the left lateral decubitus position. Digital cineloop images were acquired from parasternal and apical views (standard parasternal short-axis from mid-ventricular level, apical long-axis, 2-chamber, and 4-chamber images). All examinations were performed by a single experienced cardiologist. Standard M-mode, 2D, and color coded tissue Doppler images were obtained and stored in cineloop format from 3 consecutive beats and transferred to a workstation for further offline analysis (EchoPAC 6.1, GE Vingmed Ultrasound AS, Horten, Norway). To optimize color saturation, the gain settings, filters, and pulse repetitive frequency were adjusted. A color Doppler frame scanning rate of 100–140 Hz was used for color tissue Doppler images.

Cardiac dimensions were measured according to the guidelines of the American Society of Echocardiography, and LV ejection fraction was calculated by biplane Simpson's method.[10]

Left atrial volume (LAV) was calculated from the apical 4- and 2-chamber views by area-length formula and indexed to the body surface area.[10] The left atrial minimum volume (LAV[min]) was measured at the ventricular end diastole, left atrial maximum volume

(LAV[max]) at the end systole, and LAV(p) at the atrial contraction (P wave on electrocardiogram).[11] The left atrial stroke fraction was calculated as (LAV[max]−LAV[min])÷LAV(max). The LA active emptying fraction was calculated as (LAV[p]−LAV[min])÷LAV(p). The LA passive emptying fraction was calculated as (LAV[max]−LAV[p])÷LAV(max).

2D STE

LA-focused images, in apical 4-chamber view, were obtained for LA speckle-tracking analysis. A minimum frame rate of 40 frames/sec was required for reliable operation of the program. For 2D speckle-tracking strain analysis, a line was manually drawn along the LA endocardial contour of the apical 4-chamber view after contraction, when the LA was at its minimum volume, using the point-and-click approach.[12] The software automatically generated additional lines close to the atrial epicardium and mid-myocardial line, with the narrowest region of interest.[12] The region of interest included the entire LA myocardial wall, and a click feature increased or decreased the widths between endocardial and epicardial lines for thicker or thinner walls. Strain curves for each atrial segment were generated, and peak LA longitudinal strain (PALS) was used for LA mechanical function (Figure 1a).

Circumferential and longitudinal directional analysis of LV strain was performed by 2D speckle-tracking imaging technique.[13,14]

Assessment of longitudinal peak systolic strain was performed by applying 2D speckle-tracking imaging to the apical 2- and 4-chamber views of the LV. The LV was divided into 6 segments in each apical

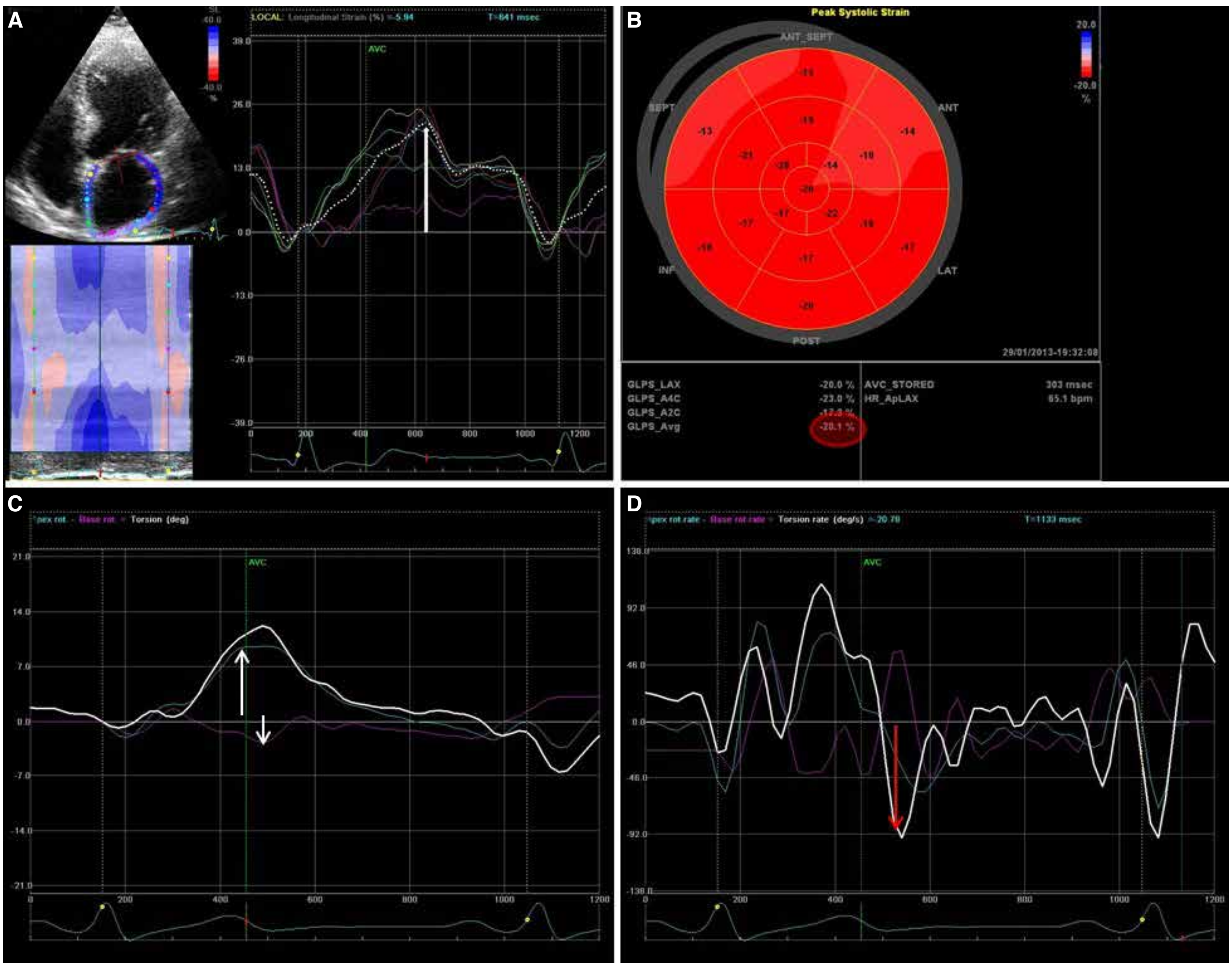

Figure 1. 2D STE **(A)** PALS (white arrow), **(B)** LVGLS (red circle), **(C)** LV basal and apical rotation (white arrows), **(D)** UntwV (red arrow).

view. The values of LV global longitudinal strain were derived from the average value of the 6 segmental peak systolic longitudinal strain values (Figure 1b).

Assessment of global radial strain and global circumferential strain was performed by applying 2D speckle-tracking imaging to the parasternal short-axis views of the LV. The basal level, midventricular level, and apical short-axis of the LV were divided into 6 segments. The values of global radial strain and global circumferential strain were derived from the average of the 6 segmental peak systolic strain values.

LV rotation parameters were assessed from parasternal short axis views at the basal level (mitral valve) and at the apical level. LV basal rotation, LV apical rotation, LV twist (LVtw), and LV peak untwisting velocity (UntwV) were calculated (Figures 1c, d). LVtw was defined as the net difference between the LV rotation angles at the basal level and apical level.

Statistical methods

"SPSS for Windows 17.0" software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Continuous variables were given as mean±SD, and categorical variables were given as percentages. Continuous variables were analyzed by independent sample t-test. Differences in the median values between groups were analyzed using Mann-Whitney U test. Categorical variables were analyzed by chi-square test or Fisher's exact test. A logistic regression model was used for determining POAF predictors. Receiver operating characteristic analysis was performed to find a cut-off value for prediction. A p value <0.05 was considered significant.

RESULTS

The clinical, demographic, and echocardiographic parameters of the patients are summarized in Table 1. Comparing non-POAF patients to POAF patients, age (58.7±10.1 years, 64.3±7.4 years, respectively, p<0.001), LAV(max)i (26.4±8.4 ml/m^2, 34±11.3 ml/m^2, respectively, p<0.001), and NT-proBNP levels (56.0, 4.9153.2 pg/dl; 96.4, 10.0–195.0 pg/dl, respectively, p<0.001) were higher in POAF patients, while beta blocker usage (91%, 60%, respectively, p<0.001) was lower in POAF patients.

Among 2D strain parameters, PALS was lower in AF patients than non-AF patients (24.2±5.8, 31.7±9.6, respectively, p<0.001). Left ventricular global longitudinal strain, left ventricular global radial strain, and left ventricular global circumferential strain values were not different between the 2 groups (-16.1°±3.9°, -14.8°±3.6°, respectively, p=0.188; -20.4°±7.9°, -20.2°±6.5°, respectively, p=0.926; 44.4°±7.6°,

Table 1. Baseline demographic, clinical, and echocardiographic properties

Variable	Non-POAF (n=67)	POAF (n=23)	*p*
Age (years)	58.7±10.1	64.3±7.4	<0.001
Gender (male %)	82	69	0.241
Hypertension (%)	37	43	0.601
Diabetes mellitus (%)	25	26	0.946
Beta blocker usage (%)	91	60	<0.001
BNP median, range (pg/dl)	56.0, (4.9–153.2)	96.4, (10.0–195.0)	<0.001
LVEF (%) median, range	63.0, (50.1–72.2)	62.0, (55.4–70.5)	0.978
LAV(max)i (ml/m^2)	26.4±8.4	34±11.3	<0.001
LAV(min)i (ml/m^2)	11.9±4.8	15.8±6.3	0.003
LAV(p)i (ml/m^2)	19.8±7.0	25.9±9.7	0.002
LA stroke F (%)	55.7±10.6	53.6±8.0	0.386
LA active emptying F (%)	40.3±12.0	38.6±10.0	0.618
LA passive emptying F (%)	25.6±11.5	24.1±9.3	0.558

POAF: Postoperative atrial fibrillation; BNP: Preoperative N-terminal pro-brain natriuretic peptide; LVEF: Left ventricular ejection fraction; LAV(max)i: Left atrial maximal volume index; LAV(min)i: Left atrial minimum volume index; LAV(p)i: Left atrial precontraction volume index; LA stroke F: Left atrial stroke fraction; LA active emptying F: Left atrial active emptying fraction; LA passive emptying F: Left atrial active emptying fraction. P values are given for the differences between non-POAF and POAF.

Table 2. **Logistic regression model**

	Univariate			Multivariate		
	p	OR	95% CI	*p*	OR	95% CI
Age (every 1 year increase)	0.003	1.085	1.028–1.146	0.011	1.133	1.029–1.247
Non-beta blocker usage	0.002	6.536	1.998–21.378	0.009	18.558	2.098–164.145
NT-proBNP	<0.001	9.822	3.290–29.322	0.001	22.377	3.286–152.381
LAV(max)i	0.003	1.087	1.030–1.148	0.212	1.064	0.965–1.172
PALS (every 1% increase)	0.002	0.874	0.804–0.950	0.013	0.839	0.730–0.963
UntwV	0.002	1.022	1.008–1.037	0.005	1.032	1.009–1.055
LVtw	0.028	0.915	0.845–0.991	0.353	0.934	0.810–1.078

POAF: Postoperative atrial fibrillation; NT-proBNP: N-terminal pro-brain natriuretic peptide; LAV(max)i: Left atrial maximum volume index; LASs: Left atrial peak strain; UntwV: Left ventricular peak untwisting velocity; LVtw: Left ventricular twist; OR: Odds ratio; CI: Confidence interval. Bold figures indicate independent predictors of POAF.

44.8°±6.3°, respectively, p=0.549). LVtw and UntwV were significantly lower in AF patients than in non-AF patients (16.3°±5.6°, 20.5°±8.1°, respectively, p=0.009; -122.9°/sec±38.0°/sec, -147.7°/sec±43.8°/sec, respectively, p=0.013) (Figure 2).

Receiver operating characteristic analysis was performed, and NT-proBNP level above 70 pg/ml predicted POAF with a sensitivity of 74% and specificity of 78% (area under curve=0.758, 95% CI 0.631–0.894, p<0.001). Univariate logistic regression

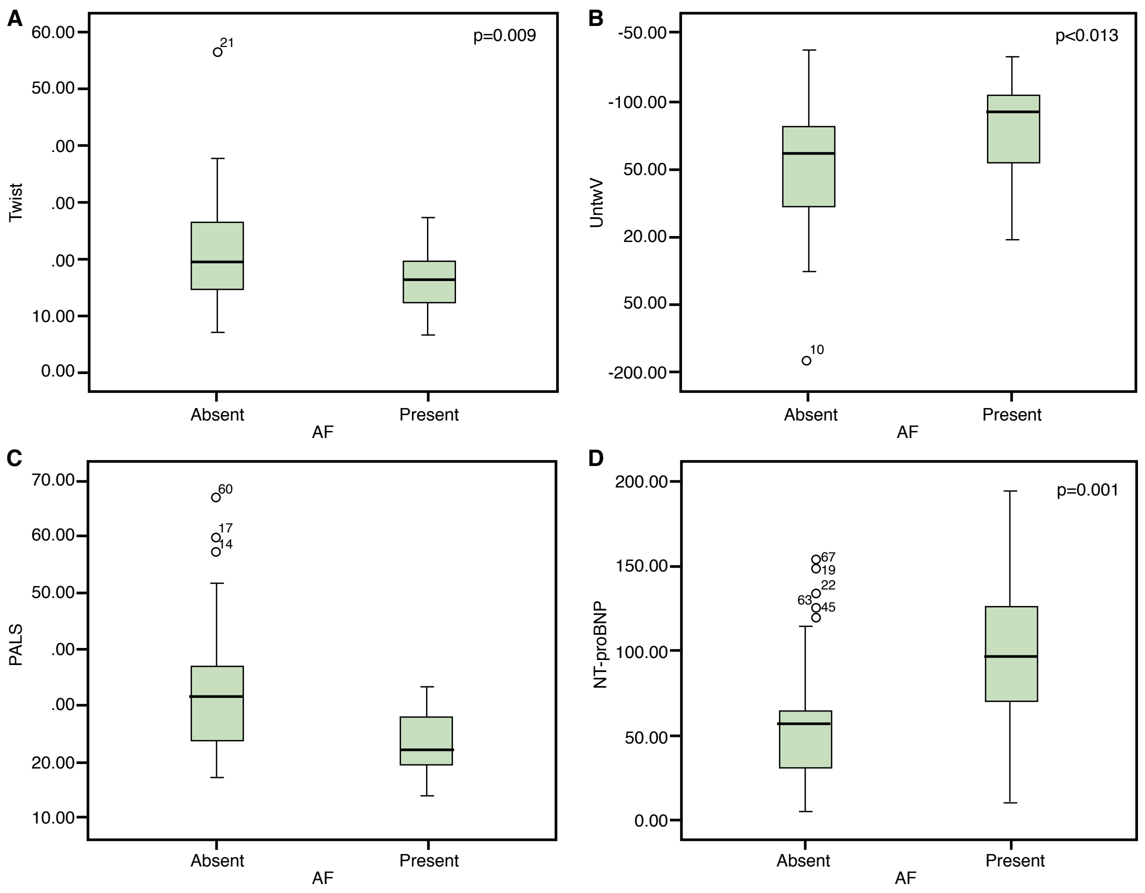

Figure 2. **(A-D)** LVtw, untwisting velocity, PALS, and NT-proBNP values of POAF and non-POAF patients.

analysis showed an association among POAF and the following variables: age, beta blocker usage, NT-proBNP, LAV(max)i, PALS, LVtw, and UntwV. Multivariate logistic regression analysis was performed to find independent predictors of POAF. Age (every 1 year increase: OR 1.133, CI 1.029–1.247, p=0.011), preoperative beta blocker usage (non-users to users: OR 18.558, CI 2.098–164.145, p=0.009), NT-proBNP (values >70 pg/ml: OR 22.377, CI 3.286–152.381, p<0.001), PALS (every 1% increase: OR 0.839, CI 0.730–0.963, p=0.013), and UntwV (every 1°/sec increase: OR 1.032, CI 1.009–1.055, p=0.005) were independent risk factors for POAF (Table 2).

DISCUSSION

Our findings indicate that age, non-usage of beta blocker, NT-proBNP, LAV(max)i, and PALS are associated with POAF development. In addition, age, non-usage of beta blocker, NT-proBNP, PALS, and UntwV were found to be independent predictors of POAF.

AF is the most common arrhythmia and complicating factor in cardiac surgery, prolonging intensive care unit and total hospital stay.[3,15–18] Older age appears to be the most important clinical risk factor for development of POAF.[17,19] Aging causes cardiac structural changes such as fibrosis and cardiac myocyte enlargement. Consequently, LV hypertrophy and decreased early-to-late diastolic filling ratio occur with aging.[20] Furthermore, aging was the major determinant of early-to-late ratio in the Framingham Heart Study.[21] As early diastolic filling rate decreases, late diastolic atrial contraction increases in compensation, leading to atrial hypertrophy and enlargement. As a consequence of increased age and impaired LA functions, POAF might develop more frequently in older patients.[19]

LA function is closely related with AF and can be estimated by LA volume measurements, Doppler analysis of transmitral and pulmonary venous flow, and by tissue Doppler echocardiography. While 2D LA volume measurements are affected by geometric assumptions, Doppler analysis is an indirect parameter that is influenced by loading conditions. Tissue Doppler techniques are useful for the assessment of atrial function, but they are angle dependent.[22] Two-dimensional STE is a novel technique for detecting myocardial deformation.[23] In a recent study, LA strain was found to be impaired before LA enlargement in patients with paroxysmal AF.[24] LA strain was also associated with AF recurrence after AF ablation procedures.[25] Previous studies have shown a predictive value of LA strain in POAF.[26–29] In our study, PALS, LAV, and volume indices were all associated with POAF development. However, in contrast to previous studies, the LA functions assessed by volume index had no effect on POAF.[30] Moreover, the multivariate logistic regression analysis revealed that PALS acts as an independent risk factor.

STE is a new and promising tool for the evaluation of myocardial function.[31] LV mechanical dysfunction was shown to be an independent risk factor for POAF development in patients with aortic stenosis.[6] However, we were not able to show an impact of LV longitudinal strain assessed by STE on POAF development. LV untwisting velocity is a good indicator of LV active relaxation, making it an important marker of isovolumic relaxation.[32] LVtw and UntwV were significantly lower in POAF patients (p=0.009, p=0.013, respectively). Untwisting velocity was also an independent predictor of POAF development (every 1°/sec increase: OR 1.032, CI 1.009–1.055, p=0.005). The difference in ventricular twist suggests a dysfunction in subepicardial fibers, while maintenance of longitudinal strain may be associated with spared subendocardial fiber function. Early dysfunction in subepicardial fibers may be related with POAF. Our study demonstrates impaired LV rotational dynamics, but no longitudinal strain was associated with POAF development.

BNP is a good surrogate of LV systolic and diastolic functions. It has been found to be an independent predictor of LV filling pressure.[33] Increased BNP and NT-proBNP levels were associated with AF after thoracic and cardiac surgery.[19,34,35] Similar to previous studies, our study demonstrated that high plasma NT-proBNP levels were associated with a higher risk of developing POAF. In addition, we showed that impaired LA strain, LV untwisting velocity, advanced age, high plasma NT-proBNP levels, and beta blocker usage were independent risk factors for developing POAF.

Limitations

This is a limited single-center study. Prospective large cohort studies are needed to evaluate the prognostic value of LA strain, LV twist, and NT-proBNP levels in POAF prediction. STE is a novel, easily applicable, and useful technique in the evaluation of myocardial function. However, it depends on the image quality, and the software was not primarily developed to evaluate atrial strain and strain rate.

Conclusion

Postoperative AF is a major arrhythmia which complicates cardiac surgery. A combination of 2D STE, as well as clinical and biochemical parameters might help to predict the probability of a given patient developing POAF.

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