Clinical Utility of Tissue Doppler Imaging in Prediction of Atrial Fibrillation After Coronary Artery Bypass Grafting

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Background. Atrial systolic dysfunction in patients with coronary artery disease might influence the development of atrial fibrillation after coronary artery bypass grafting (CABG). Tissue Doppler imaging of the mitral annulus during atrial systole has proved to quantify, accurately, left atrial contractile function. Therefore, the aim of the present study was to investigate the correlation between preoperative left atrial dysfunction assessed by tissue Doppler and postoperative atrial fibrillation after CABG.

Methods. We studied a total of 96 patients (mean age 67 ± 6 years; range, 55 to 81) undergoing CABG who were preoperatively in sinus rhythm. All patients underwent a preoperative transthoracic echocardiography with tissue Doppler evaluation. Until the day of discharge, all patients were monitored with continuous electrocardiographic telemetry.

Results. There were no hospital deaths. Postoperative atrial fibrillation was recorded in 24 of 96 patients (25%). Patients with postoperative atrial fibrillation were signif-

Postoperative atrial fibrillation (AF) is one of the most frequent complications after coronary artery bypass grafting (CABG), and it is associated with a higher incidence of thromboembolic complications, length of intensive care unit and hospital stay, and significantly increased costs [1]. Much attention has focused on postoperative AF but its determinants are not completely understood.

Atrial systolic dysfunction has been observed in patients with coronary artery disease [2, 3]. Atrial contractile dysfunction may predict the development of postoperative AF in patients undergoing CABG, therefore a reliable measurement of preoperative atrial function may be useful to identify patients with increased risk of AF after CABG.

Doppler echocardiographic measurements of left atrium systolic function such as transmitral atrial filling velocity and atrial filling fraction [4-6] or the

icantly older (70 ± 6 vs 65 ± 8 years; p = 0.006), had a preoperative larger left atrium diameter (38 ± 5 vs 36 ± 4 mm; p = 0.045), a larger left atrium area (13.2 ± 3.4 vs 11.5 ± 2.3 cm²; p = 0.007), and a lower peak atrial systolic mitral annular tissue Doppler velocity (10 ± 3 vs 13 ± 5 cm/second; p = 0.01). Stepwise logistic regression analysis showed that age 70 years or greater (p = 0.02; odds ratio [OR] 2.0), preoperative medication with β -blockers (p = 0.04; OR 0.7), left atrium area 13 cm² or greater (p = 0.02; OR 2.5), and peak atrial systolic mitral annular tissue Doppler velocity 9 cm/second or less (p =0.03; OR 1.8) were independently related with the incidence of postoperative atrial fibrillation.

Conclusions. Tissue Doppler is useful for assessing preoperative atrial dysfunction and predicting atrial fibrillation after CABG. Further studies are needed to confirm this finding.

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measurement of left atrium area changes by planimetry [4] failed to predict postoperative AF. However, these methods have some drawbacks that may partially explain these results. In fact, transmitral atrial velocity is more dependent on the atrioventricular pressure gradient rather than atrial contractility per se [7] and it is highly sensitive to changes in loading condition while far-field artifacts may affect the accuracy of atrial area calculation.

Tissue Doppler imaging (TDI) is a relatively new technology that allows direct noninvasive measurements of myocardial velocities [3, 8]. Direct assessment of the mitral annulus velocity during atrial systole by TDI analysis has proved to be a sensitive and reproducible tool for quantifying left atrial contractile function [8] and it reflects atrial contractile function better than transmitral atrial filling velocity (Fig 1), disregarding the severity of diastolic dysfunction [3].

Therefore, the aim of the present study was to investigate the correlation between left atrial dysfunction assessed preoperatively by TDI analysis and the incidence of postoperative atrial fibrillation in patients undergoing CABG.

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Fig 1. Comparison of peak atrial filling velocity (A) from transmitral Doppler flow (TMDF) velocity spectra and peak atrial systolic mitral annular velocity at tissue Doppler imaging (TDI) analysis (*) in two patients with delayed early diastolic relaxation. The TDI peak atrial systolic mitral annular velocity in patient B shows an impaired atrial systolic function which is normal in patient A. However, in patient B transmitral atrial filling velocity appears to be normal or paradoxically increased even in presence of atrial contractile dysfunction. This example clearly shows that TMDF velocity may fail to detect atrial contractile dysfunction in the presence of delayed early diastolic relaxation.



Material and Methods

Study Patients

The Ethics Committee of our institution approved this retrospective study by Chairman's action and waived patient's consent. During the study period (from May 2005 to December 2005) a total of 236 surgical revascularization procedures were performed in our institution.

For the present, investigation inclusion criteria were isolated elective CABG with cardiopulmonary bypass and preoperative sinus rhythm. We excluded patients with a preoperative history of AF, significant mitral or tricuspid lesions, left ventricular ejection fraction less than 0.35 and requirement for class I or III antiarrhythmic drugs for at least one week before surgery. We finally studied a total of 96 patients (mean age 67 \pm 6 years; range, 55 to 81).

All patients underwent a preoperative transthoracic echocardiography with TDI analysis during the week before surgery. Until the day of discharge, all patients were monitored with continuous electrocardiographic (ECG) telemetry. A standard 12-lead ECG was recorded on the day of discharge for each patient.

Echocardiographic Analysis

Transthoracic echocardiography Doppler echocardiography was performed using an Accuson Sequoia with a multifrequency transducer (Mountain View, CA). All recordings were performed by a single investigator (G.M.C). Left ventricular dimensions and wall thickness measurements were made in the parasternal long axis view with m-mode cursor positioned just beyond the mitral leaflet tips, perpendicular to the long axis of the ventricle according to the recommendations of the American Society of Echocardiography (ASE) [9]. If the mmode recordings were technically inadequate, twodimensional measurements were used. Left ventricular mass (LVM) was calculated with the corrected ASE formula [10]:

$$LVM = 0.8 \left[1.04(IVS_d + LVID_d + PWT_d)^3 - LVID_d \right) - LVID_d^3 - 13.6$$

where IVS_d is the end-diastolic interventricular septum thickness, $LVID_d$ is the LV end-diastolic internal diameter, and PWT_d is the LV end-diastolic posterior wall thickness. The LVM was indexed (LVMi) to the body surface area. The left atrial anterior-to-posterior diameter was measured in the parasternal view at end-systole from the m-mode trace at the level of the aortic root. The left atrial area was determined by tracing the endocardium from the four-chamber view at maximal atrial dimension. Left ventricular ejection fraction by twodimensional echocardiography was obtained by the modified biplane Simpson method from apical four- and two-chamber views.

Mitral inflow was recorded as previously described [11]. From transmitral Doppler spectra of 3 to 5 consecutive cardiac cycles, average values were calculated for the following parameters: peak early (E) and late (A) filling velocities, deceleration time. Myocardial velocities obtained with tissue Doppler were recorded using a standard pulse-wave Doppler technique with the sample volume placed at the junction of the left ventricle lateral wall with the mitral lateral annulus from the four-chamber view. Peak velocities during systole (S_m), early

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diastole (E_m), and atrial systole (A_m) were measured. The final value represented the average of at least four cardiac cycles.

Operative Procedure

A median sternotomy was performed in all patients. Cardiopulmonary bypass was established in a standard fashion by ascending aortic cannulation and with a single two-stage venous cannulation of the right atrium. Myocardial protection was achieved by antegrade intermittent warm blood cardioplegia every 15 minutes. All patients received a left internal mammary artery to the left anterior descending coronary artery and a saphenous vein was used as conduit to complete surgical revascularization. Proximal anastomoses of vein grafts were performed during a single aortic cross-clamp time.

Clinical Predictors

According to previous studies, we selected 12 clinical variables associated with AF after CABG [12, 13]. The covariates analyzed included patients demographic data (such as age, gender, body mass index, body surface area, heart rate), coexisting medical condition (such as hypertension, diabetes mellitus, and chronic obstructive pulmonary disease), and preoperative medications such as β -blockers that were continued postoperatively to avoid withdrawal; surgical factors such as aortic cross-clamp and bypass times, and number of grafts performed.

Statistical Analysis

The statistical analysis was performed using SPSS software (version 12.1; SPSS, Inc, Chicago, IL). Continuous variables are expressed as mean \pm standard deviation. The unpaired Student *t* test was used to compare continuous variables, and categoric data were analyzed using the χ^2 test or Fisher exact test as appropriate. To assess the influence of other preoperative covariates on preop-

 Table 1. Demographic and Operative Characteristics

Characteristics	Yes AF $(n = 24)$	No AF (n = 72)	p Value
Mean age (years)	70 ± 6	65 ± 8	0.006
Male/Female	14/24	45/72	0.8
BSA (m ²)	1.8 ± 0.4	1.7 ± 0.4	0.5
BMI	29 ± 5	27 ± 7	0.2
HR (beats/min)	74 ± 12	70 ± 11	0.1
Hypertension (n)	13/24 (54%)	45/72 (62%)	0.48
COPD (n)	13/24 (54%)	23/72 (32%)	0.08
Diabetes (n)	12/24 (50%)	25/72 (34%)	0.15
β -blockers (n)	7/24 (29%)	43/72 (60%)	0.01
No. of distal anastomoses/patient	$\textbf{2.7} \pm \textbf{0.5}$	$\textbf{2.6} \pm \textbf{0.4}$	0.3
ACC time (min)	90 ± 31	85 ± 23	0.4
CPB time (min)	111 ± 35	105 ± 27	0.4

ACC = aortic cross clamp; AF = atrial fibrillation; BMI = body mass index; BSA = body surface area; COPD = chronic obstructive pulmonary disease; CPB = cardiopulmonary bypass; HR = heart rate.

Table 2. Preoperative Echocardiographic Parameters	reoperative Echocardiographic Pa	Parameters
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Parameters	Yes AF ($n = 24$)	No AF $(n = 72)$	Value
LVID _d (mm)	56 ± 4	54 ± 05	0.07
LVEF (%)	0.53 ± 0.09	0.57 ± 0.11	0.11
LAD (mm)	0.38 ± 0.05	36 ± 4	0.04
LAA (cm ²)	13.2 ± 3.4	11.5 ± 2.3	0.007
LVMi (g/m²)	135 ± 11	132 ± 12	0.28
E wave (m/sec)	0.67 ± 9	0.72 ± 12	0.06
A wave (m/sec)	0.52 ± 13	0.49 ± 12	0.30
DT (msec)	201 ± 29	195 ± 31	0.4
S _m (cm/sec)	13 ± 3	13 ± 4	0.06
E _m (cm/sec)	16 ± 3	17 ± 2	0.06
A _m (cm/sec)	10 ± 3	13 ± 5	0.01

A = peak atrial filling velocity from transmitral Doppler spectra; AF = \bar{A}_m = peak atrial systolic mitral annular velocity; DT = atrial fibrillation; deceleration time from transmitral Doppler spectra; E = peak earlyfilling velocity from transmitral Doppler spectra; $E_m = diastolic mitral annular velocity; LAA = left atrium area;$ $E_m = peak early$ LAD = LVEF = left ventricular ejection fraction; left atrium diameter: $LVID_d = left$ ventricular end-diastolic internal diameter; LVMi = left S_m = peak systolic mitral annular velocity. ventricular mass index;

erative TDI peak atrial systolic mitral annular velocity (A_m) , linear regression analysis was used including other preoperative echocardiographic parameters and variables found to be significantly related with A_m at univariate analysis were entered into a stepwise multiple regression analysis to investigate the independent effect on A_m . Multivariable stepwise logistic regression analysis



Fig 2. Regression plot of correlation between preoperative peak atrial systolic mitral annular velocity (A_m) at tissue Doppler analysis and preoperative left atrial area (LAA) (p = 0.02, r = -0.25; regression equation: y = 16.1-0.3*x). (Postoperative atrial fibrillation: $\bigcirc = no$; $\blacktriangle = yes$; — = fit line for total.)

sis was used to identify the independent predictors of postoperative AF. Only variables found to be significantly associated with postoperative AF were included into the model. A variable was entered into the model if its associated significance level was less than 0.05 and it was removed from the model if its associated significance level was greater than 0.1. The fit of the model was assessed using the Hosmer-Lemeshow goodness-of-fit test. A p value and odds ratio with 95% confidence interval are reported. Statistical significance was set at the 0.05 level.

Results

Hospital mortality (\leq 30 days) was 0 of 96 (0%). During the period of observation, postoperative AF was recorded in 24 of 96 patients (25%) and none of them experienced thromboembolic complications. Postoperative AF occurred 3.2 \pm 2.0 days after surgery (range, 0 to 7). The median hospital stay for the group without postoperative AF was 7 days versus 8 days in those with postoperative AF (p = not significant [ns]). Sinus rhythm was restored in all patients with antiarrhythmic medical therapy: 21 patients required class III and 3 patients class II antiarrhythmic drugs. Demographic and operative characteristics of the study patients are listed in Table 1. Patients with postoperative AF were significantly older (mean age 70 \pm 6 vs 65 \pm 8 years; p = 0.006) and less often had preoperative medication with β -blockers (7 of 24 vs 43 of 72 patients; p = 0.01). Preoperative echocardiographic parameters are listed in Table 2. Postoperative AF was associated with a larger left atrium diameter $(38 \pm 5 \text{ vs } 36 \pm 4 \text{ mm}, p = 0.045)$, a larger left atrium area $(13.2 \pm 3.4 \text{ vs } 11.5 \pm 2.3 \text{ cm}^2, p = 0.007)$, and a lower peak atrial systolic A_m detected by TDI (10 \pm 3 vs 13 \pm 5 cm/second; *p* = 0.01). At linear regression analysis preoperative A_m was only modestly associated with preoperative left atrium area (p = 0.02, r = -0.25; Fig 2), left atrium diameter (p = 0.04, r = -0.15) and TDI peak E_m (p = 0.02, r = 0.21) At stepwise multivariate analysis no covariate was found as an independent predictor preoperative A_m.

To be included into multivariate model, continuous variables found to be significantly associated with postoperative AF at univariate analysis were dichotomized by

Table 3. Predictors of Postoperative AF at Stepwise Logistic Regression Analysis^{a,b}

Predictors	OR	95% CI	p Value
Age \geq 70 years	2.0	1.2-4.5	0.02
Preoperative β-blockers	0.7	0.5-0.9	0.04
Left atrial area $\geq 13 \text{ cm}^2$	2.5	1.6-5.1	0.02
Peak atrial systolic mitral annular velocity $(A_m) \le 9 \text{ cm/sec}$	1.8	1.1–3.5	0.03

^a Nagelkerke adjusted R²: 0.49. ^b Hosmer-Lemeshow goodness-of-fit test: p = 0.95; DF = 8; $\chi^2 = 2.7$.

CI = confidence interval; DF = Doppler flow; OR = odds ratio.

means of receiver operating characteristic curves (ROC) analysis. The ROC curves analyses showed the following: that age 70 years or greater predicted postoperative AF with a sensitivity of 63% and a specificity of 55%; left atrium diameter 38 mm or greater predicted postoperative AF with a sensitivity of 41% and a specificity of 52%; left atrium area 13 cm² or greater predicted postoperative AF with a sensitivity of 54% and a specificity of 61%; and finally, peak atrial systolic mitral annular velocity 9 cm/second or less predicted postoperative AF with a sensitivity of 51% and a specificity of 58%.

As shown in Table 3, stepwise logistic regression analysis showed that age 70 or greater, preoperative medication with β -blocker, left atrium area 13 cm² or greater, and peak atrial systolic mitral annular velocity 9 cm/second or less were independently associated with postoperative AF. The Nagelkerke-adjusted R-squared was 0.49. The Hosmer-Lemeshow goodness-of-fit test was not significant for lack of fit.

Comment

This study showed that atrial systolic dysfunction in patients with coronary artery disease undergoing CABG represents a risk factor for postoperative AF. Previous investigations failed to show a correlation between preoperative atrial systolic function and AF after CABG but they used Doppler echocardiography [4–6] or left atrial area changes by planimetry [4] to assess atrial contractile function and none of them evaluated it by TDI analysis.

Quantitative assessment of atrial function remains limited because it requires invasive pressure-volume loops, thus precluding its routine clinical use [14]. Doppler echocardiography is routinely used to assess atrial function by estimating the hemodynamic difference between the atrium and the ventricle. However, atrial systolic function is not assessed directly by this method, which may be consequently affected by changes in loading condition [14, 15]. In fact, in patients with delayed early diastolic relaxation, an increased atrial preload in late diastole may result in increased filling during late diastolic phase even in the presence of atrial contractile dysfunction [3]. Therefore, transmitral atrial velocity could appear to be normal or even paradoxically increased (Fig 1), failing to detect atrial systolic dysfunction. On the other hand, the assessment of LA area changes by planimetry [4] is technically complex, time consuming, and it may be not accurate.

Tissue Doppler imaging is a recently developed technique for quantification of myocardial velocity using low velocity pulsed wave Doppler interrogation of the myocardium [16, 17]. The TDI of the mitral annulus during atrial systole has proved to be a highly sensitive and reproducible tool for quantifying left atrial contractile function [8] and it has been shown to reflect atrial contractile function better than transmitral atrial velocity [3], even in patients with diastolic dysfunction (Fig 1).

In the present study we were able to show that preoperative left atrial dysfunction assessed by A_m negatively influenced the incidence of postoperative AF. We found

also that ageing and left atrial enlargement related with postoperative AF. In healthy subjects, ageing and left atrial enlargement have been proved to have a direct effect on left atrial contractile function assessed by TDI [18]. On the other hand, recent investigations [3, 8] have shown that in patients with coronary artery disease, ageing and left atrial dimension do not directly affect left atrial systolic function assessed by TDI. Our results confirmed these findings. In fact, we only found a weak correlation between A_m and LA dimension but not with ageing, and multivariate analysis failed to show an independent effect of LA enlargement on A_m. It is possible that in patients with coronary artery disease, atrial systolic dysfunction may directly be caused by atrial myocyte ischemia or infarction [3] even in the absence of LA enlargement.

Only impaired left ventricular systolic function has previously been proved to independently influence A_m [3] in patients with coronary artery disease and, as a consequence, we excluded patients with impaired left ventricular ejection fraction from our analysis. The present study was not intended to analyze the mechanism of producing postoperative AF with preexisting atrial dysfunction in patients undergoing CABG. However, it is possible that left atrial dysfunction may lead to a higher risk of postoperative AF through an increased atrial electrical vulnerability and neurohormonal activation. In fact, impaired atrial systolic function is associated with increased atrial pressure at the end diastole that may lead to electrical remodeling, with a shortening of the atrial effective refractory period or an increase in dispersion of refractoriness, resulting in vulnerability to AF [19, 20]. In addition, an increased atrial pressure has proved to stimulate the release of atrial natriuretic factor [21, 22], which has been shown to be a predictor of paroxysmal atrial fibrillation [23].

In conclusion, our findings suggest that atrial dysfunction likely precedes the development of postoperative atrial fibrillation. The TDI analysis is a useful tool to assess atrial function accurately, it is highly reproducible, and these aspects favor the application of TDI technology in the evaluation of atrial function in patients undergoing CABG. In addition we found that an increased left atrial area was associated with postoperative AF. Given the link between left atrial size and function and atrial fibrillation in the general population [24], these findings support the hypothesis that postoperative AF may be partially explained by the same pathogenesis. A selective therapeutic approach involving risk prediction should be investigated as a possible strategy of prophylaxis in patients undergoing CABG.

The multivariate model obtained in this study explains only 49% of the variance in the incidence of AF after CABG and this suggests that other factors may be implicated.

In our analysis, we included clinical variables that were reported in large studies [12, 13]. However, in patients undergoing CABG surgery, several intraoperative factors not easily detectable (such as adequacy of atrial protection during CPB) may influence the occurrence of postoperative AF. Also, postoperative hypokalemia and hypomagnesemia could be related with the occurrence of postoperative AF not explained by our model.

In addition, the sample size of this study is a limitation in light of the small differences for many of the operative data between patients with and without postoperative AF. Consequently, we cannot exclude a type II error for failing to distinguish these two groups with our preoperative assessments. Finally, our study only investigated AF that occurred during hospitalization. As a result, we might have underestimated the incidence of postoperative AF that may have occurred postdischarge.

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Requirements for Recertification/Maintenance of Certification in 2007

Diplomates of the American Board of Thoracic Surgery who plan to participate in the Recertification/ Maintenance of Certification process in 2007 must hold an active medical license and must hold clinical privileges in thoracic surgery. In addition, a valid certificate is an absolute requirement for entrance into the recertification/maintenance of certification process. If your certificate has expired, the only pathway for renewal of a certificate is to take and pass the Part I (written) and the Part II (oral) certifying examinations.

The American Board of Thoracic Surgery will no longer publish the names of individuals who have not recertified in the American Board of Medical Specialties directories. The Diplomate's name will be published upon successful completion of the recertification/maintenance of certification process.

The CME requirements are 70 Category I credits earned during the 2 years prior to application. At least 35 CME hours need to be in thoracic surgery. Category II credits are not allowed. The Physicians Recognition Award for recertifying in general surgery is not allowed in fulfillment of the CME requirements. Interested individuals should refer to the *Booklet of Information* for a complete description of acceptable CME credits.

Diplomates should maintain a documented list of their major cases performed during the year prior to application for recertification. This practice review should consist of 1 year's consecutive major operative experiences. If more than 100 cases occur in 1 year, only 100 should be listed.

Candidates for recertification/maintenance of certification will be required to complete all sections of the SESATS self-assessment examination. It is not necessary for candidates to purchase SESATS individually because it will be sent to candidates after their application has been approved.

Diplomates may recertify the year their certificate expires, or if they wish to do so, they may recertify up to two years before it expires. However, the new certificate will be dated 10 years from the date of expiration of their original certificate or most recent recertification certificate. In other words, recertifying early does not alter the 10-year validation.

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The deadline for submission of applications for the recertification/maintenance of certification process is May 10 each year. A brochure outlining the rules and requirements for recertification/maintenance of certification in thoracic surgery is available upon request from the American Board of Thoracic Surgery, 633 N St. Clair St, Suite 2320, Chicago, IL 60611; telephone: (312) 202-5900; fax: (312) 202-5960; e-mail: info@abts.org. This booklet is also published on the website: www.abts.org.