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Preoperative Angiotensin Blocking Drug Therapy Is not Associated with Atrial Fibrillation after Cardiac Surgery

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Abstract

Background—Preoperative use of angiotensin blocking drug therapy (ABDT) with ACE-inhibitors or Angiotensin II receptor blockers (ARBs) and its link to occurrence of postoperative atrial fibrillation (POAF), a common marker of poor outcomes after cardiac surgery, remains controversial.

Methods—From 1997-2003 10,552 patients underwent coronary artery bypass grafting (CABG) with or without valve surgery. To adjust for differences of clinical characteristics between patients receiving ABDT within 24 hours prior to surgery compared to those who did not, propensity score analyses were conducted.

Results—ABDT was prescribed in 4,795 (45%) prior to surgery of which 1,725 (36%) developed POAF prior to discharge vs. 1908 (33%) of 5,757 patients who have not received ABDT (unadjusted odds ratio [OR] of 1.13 (95% Confidence Interval [CI] 1.05-1.25, $p < 0.01$). In 6744 propensity score matched patients with well balanced co-morbidity profiles, ABDT was not associated with POAF (OR 1.05, CI 0.95-1.16, $p = 0.38$). Stratified analysis within quintiles of propensity score and propensity-adjusted logistic multivariable regression confirmed these findings.

Conclusions—In this large observational study we found no evidence of an association between preoperative angiotensin blockade and the occurrence of postoperative atrial fibrillation. Adequately powered randomized studies are needed to clarify the best strategy of perioperative angiotensin blocking drug therapy in patients with and without guideline-based indications.

Postoperative atrial fibrillation (POAF) is a common complication after cardiac surgery. Its occurrence can be reduced by prophylactic medications, such as beta blockers(1) and

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Disclosures
None

amiodarone(2). However, effects of preoperative use of angiotensin blocking drug therapy (ABDT) with angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) on occurrence of POAF remains controversial. There is new evidence that preoperative use of ABDT may even be harmful(3).

Elevated plasma angiotensin II levels promote vascular oxidant stress and hypertension(4). Increased atrial pressures and elevated angiotensin II levels accelerate the development of atrial interstitial fibrosis(5). ABDT reduces cardiac myocyte remodeling and atrial fibrosis in animal models(6), and has protective hemodynamic and electrophysiological effects by blocking the effects of angiotensin II and reducing inflammation(7). These findings suggest that preoperative use of ABDT might reduce POAF by inducing reverse structural and electrical remodelling. A few small studies have investigated the association of ABDT with POAF, but had discordant results(3,8-10). There have been safety concerns of perioperative use of such therapy(3,11). Therefore the primary objective of this study was to examine the association of preoperative use of ABDT with POAF in the setting of its pre-surgical withdrawal.

Methods

Patients

From 1997 to 2003, 10920 Cleveland Clinic patients underwent coronary artery bypass graft surgery with or without valve surgery. Of these, 4,795 patients were prescribed ABDT and 5,759 were not. Patients were identified from the prospective Cardiovascular Information Registry (CVIR) at Cleveland Clinic, in which more than 450 variables are entered by trained abstractors with 10% random independently 100% audited quality assessment. Patients in AF or having a paced rhythm on preoperative ECG were excluded, the latter because quantitative ECG measurements were uninterpretable, leaving 10552 patients in the study cohort (Figure 1).

Medication use

Recording in our database of preoperative use of ABDT was in accordance with Society of Thoracic Surgeons (STS) reporting model defined as an active prescription for an ACE inhibitor or ARB within 30 days of cardiac surgery with the last dose given within 24 hours prior to surgery. ABDT was typically stopped immediately prior to surgery to prevent postoperative vasoplegia and restarted postoperatively at the treating physician's discretion. No chemical prophylaxis to prevent POAF was used in the study population. Beta blockers were typically given the morning of surgery in patients who have been receiving such therapy preoperatively. Their perioperative continuation was inconsistent, which may have contributed to the increased risk of POAF in patients who were on these drugs preoperatively.

Data

1. Patient, Procedure, and Outcome data—Demographics, cardiac and non-cardiac comorbidities, preoperative medication use, laboratory data, procedural details, and postoperative in-hospital morbidities were obtained from the CVIR (E-Appendix A). All data has been approved by our Institutional Review Board for use in research with patient consent waived.

2. Echocardiographic data—Estimates of left atrial diameter, left ventricular ejection fraction and valvular regurgitation and stenosis were extracted from our IRB approved echocardiography database. Estimate of left ventricular ejection fraction was collected from the last available study. If ejection fraction was not obtained during last echocardiogram it

was averaged from prior studies within 6 months. Severity of valvular regurgitation was graded 0-4, with 0 indicating absence and 4 severe and valvular stenosis was graded 1-5 with 1 indicating absence and 5 severe.

3. Quantitative ECG data—Quantitative electrocardiographic measurements were obtained from the last preoperative resting 12-lead ECG using commercially available Magellan Marquette software (©General Electronics, Milwaukee, Wisconsin). Heart rate, PR interval, P wave dispersion, QRS duration and voltage criteria of left ventricular hypertrophy (LVH) by Sokolow-Lyon and Cornell were analyzed as known predictors of POAF(12). P wave dispersion was defined as the maximum P wave duration minus the minimum P wave duration in any of the 12 ECG leads. Sokolow-Lyon voltage criteria for LVH were defined as the sum of amplitudes of the S wave in lead V1 and the maximum R wave in lead V5 or V6. Cornell voltage criteria for LVH were defined as the sum of amplitudes of the R wave in lead aVL and the S wave in lead V3.

Outcome

The primary study outcome was development of POAF prior to discharge, requiring therapy with rate controlling or anti-arrhythmic medication or electrical cardioversion. This definition is in accordance with Society of Thoracic Surgeons National Adult Cardiac Database, with the exception that we allowed patients with history of AF, but in normal sinus rhythm at time of surgery, into the study (see: http://www.ctsnet.org/file/rptDataSpecifications252_1_ForVendorsPGS.pdf, page 126). POAF was detected by continuous telemetry monitoring during the entire hospital stay and/or 12-lead ECG.

Statistical analysis

Continuous variables are summarized by means and standard deviations and categorical variables are summarized by frequencies and percentages (Table 1). Patient variables were compared with two-tailed student's t-test for continuous variables and χ^2 statistics for categorical variables. Between patients treated with ABDT and those not treated with ABDT some variables had clinically important differences. Therefore propensity score techniques were used to make fair comparisons.

Modeling of the propensity score

Logistic regression analysis with ABDT as the outcome variable was used to construct a propensity model with the inclusion of 74 demographic and clinical variables (see E-Appendix). Non-linear relationships were relaxed with restricted cubic splines. Interaction terms were included if considered clinically meaningful. A parsimonious regression model was first created by stepwise backwards elimination to identify the most influential variables predicting ABDT (Table 2). A non-parsimonious logistic regression model was then created with the inclusion of all patient characteristics and interaction terms to obtain the propensity of ABDT for each patient as a score ranging from 0 to 1 (i.e. propensity score)(13). The C-statistic (area under ROC curve) of the non-parsimonious propensity model averaged 0.73, indicating fair ability to discriminate treatment groups (Figure 2). Hosmer-Lemeshow test statistic indicated goodness of fit ($p=0.7$). The propensity score was logit transformed (i.e. linear propensity score) and used for propensity score matching, stratification and regression.

Propensity score matching

A greedy matching algorithm formed patient pairs, whose linear propensity scores fell within 60% of the standard error. Matching was done in a 1:1 fashion without replacement,

which resulted in 6744 matched patients (70% of possible matches). As a measure of covariate balance between matched treatment groups, standardized differences (percentage of pooled standard deviation) of covariates that confound comparisons between treatment groups were calculated and plotted. A lack of balance was defined as a standardized difference in excess of 10%.

Propensity score stratification and adjusted regression

In a second analytical step, patients were analyzed within quintiles of their linear propensity scores. This method allowed analysis of all patients without exclusion of poorly matched patients. Comparisons of treatment effect within quintiles, oftentimes representing different stages of diseases underlying ABDT, can detect inhomogeneities and may be more generalizable than propensity score matching. Odds ratios of each quintile were calculated and averaged as they were found to be homogenous. Third, linear propensity score adjusted logistic regression was performed.

Occurrence of POAF as well as secondary outcomes between treatment groups were compared with a paired McNemar χ^2 -test in the propensity score matched and the stratified analysis and reported as odds ratios (OR) with 95% confidence intervals (CI).

Subgroup analysis

We applied identical analytical steps to investigate the association of POAF with ABDT in four subgroups. The first was 3227 propensity score-matched patients who underwent isolated valve surgery in the same time frame. The second was propensity score-matched patients undergoing isolated CABG. The third was an analysis of propensity score matched patients with exclusion of those with atrial fibrillation in their past and the fourth patients undergoing off-pump CABG.

SAS version 9.1 (©SAS Institute Inc., Cary, NC) and R version 2.6.1 (©The R Foundation for Statistical Computing, www.r-project.org), were used for all analyses.

The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

Missing data

The exposure variable (ABDT) and outcome variable (POAF) were complete. Missing values of left ventricular ejection fraction by echo were imputed using a non-linear regression equation derived from ejection fraction measured from ventriculogram during heart catheterization. Missingness of other variables did not exceed 14% and was handled with informed 5-fold multiple imputation using the MCMC algorithm of PROC MI in SAS version 9.1 (©SAS Institute Inc., Cary, NC).

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Results

Occurrence and treatment of POAF

Occurrence of POAF peaked on postoperative day 2 (E-Figure 1). As expected, patients with isolated CABG surgery were less likely to develop POAF than were patients undergoing CABG with valve surgery. Patients undergoing CABG with mitral valve replacement and any kind of combined valve surgery had markedly higher rates of POAF, ranging between 62% and 67% (Figure 3). Of patients who developed POAF, 22% underwent electrical cardioversion. All other patients were treated medically with rate controlling or anti-arrhythmic drugs.

ABDT and POAF

Univariate analysis indicated that ABDT was associated with an increased risk of POAF (OR 1.13 [CI 1.05-1.23]). Evidence-based indications of ABDT, such as hypertension, congestive heart failure and prior myocardial infarction are major risk factors of POAF and confound unadjusted comparisons of patients with and without preoperative ABDT (Table 2). By propensity score matching, important predictors of POAF were similar in both treatment groups (Figure 4). Analysis of the propensity score matched cohort did not find this association (OR 1.02 [CI 0.93-1.13]). To examine whether exclusion of 3808 (36%) unmatched patients introduced a selection bias a stratified analysis by quintiles of all patients' propensity scores was conducted. These results were similar and validated those of the propensity score matched analysis. Propensity score adjusted multivariable logistic regression confirmed absence of an association of ABDT with POAF (Table 3). We found no procedural subgroups that benefited from preoperative use of ABDT. Specifically, propensity matched patients who underwent isolated CABG had an OR 1.02 [CI 0.9-1.17]), indicating no benefit from preoperative ABDT use. Similarly, propensity matched analysis of 3227 patients who underwent isolated valve surgery also demonstrated no statistically significant association of preoperative ABDT and POAF (OR 0.91, CI 0.74-1.09, data not shown). We excluded patients with prior episodes of AF in a secondary analysis, after we found that those patients were more likely to have POAF (65% vs. 32%, $p<0.0001$) and were more likely to have used ABDT prior to surgery (52% vs. 45%, $p<0.0001$). After exclusion of patients with prior episodes of AF, results were similar: 1023 (33%) of 3131 patients with preoperative ABDT use and 992 (32%) of 3131 patients without ABDT use developed POAF ($p=0.4$). In propensity-adjusted analysis of patients, who underwent off-pump CABG, 131 (25%) of 459 patients with ABDT and 126 (29%) of 507 patients without ABDT developed POAF ($p=0.2$).

Secondary outcomes and in-hospital mortality

Unadjusted analysis showed that patients, who were preoperatively treated with ABDT, had a significantly higher occurrence of postoperative ventricular tachycardia, ventricular fibrillation and cardiac arrest. Univariate comparison of treatment groups also showed an increased use of inotropic support after surgery as well as in-hospital mortality in patients exposed to preoperative ABDT. Propensity score matching, however, eliminated these associations suggesting confounding of the unadjusted results. There was a trend of patients with preoperative ABDT use to stay in the hospital longer (Table 4),

Discussion

Our study did not find an association of preoperative use of Angiotensin blocking drug therapy with the development of postoperative atrial fibrillation in patients undergoing cardiac surgery. Although beta-blockers and Amiodarone(1,2) amongst others have shown to be effective as prophylactic medication, preoperative Angiotensin blockade with pre-

surgical withdrawal does not seem to be a feasible strategy to prevent such arrhythmias. However, our data also suggest that Angiotensin blocking drug therapy does not increase postsurgical complications if given within 24 hours of surgery.

Burden of disease

AF after cardiac surgery occurs in about 35% of patients(14). The associated increases in morbidity, mortality and health care costs have been well documented(15) and although preventable with prophylactic medications in some patients, up to 24% develop POAF despite prophylactic therapy(2) demonstrating the need for additional preventative strategies.

Pathophysiology of POAF

The pathophysiology of POAF remains an enigma. Experiments in clinical and basic science suggest a multifactorial causality. Age has been repeatedly shown to be the strongest predictor of POAF. History of hypertension, and obesity are additional clinical predictors of POAF(16). POAF has been associated with left atrial enlargement(17), elevated postoperative pulmonary capillary wedge pressure(18), postoperative sympathetic activation(19), increased Interleukin-6 and CRP, as well as Angiotensin II levels(20,21).

Atrial fibrosis and P wave duration prior to cardiac surgery, suggested a role for altered atrial conduction as arrhythmia substrate(22,23) and NADPH oxidase activity in the atrial appendage, suggested a role for oxidant stress(23). Angiotensin II signaling via its G-protein coupled receptors promotes NADPH oxidase activity. Blockade of Angiotensin II receptors with candesartan decreased intra-atrial conduction time and shortened duration of AF in dogs(24). Infusion of Angiotensin decreased atrial effective refractory period, an effect that could be reversed with Angiotensin II receptor blockade and ACE inhibition(25). These studies suggest that Angiotensin may be a contributing pathway to development of POAF and that ACE-inhibitors and ARBs may decrease occurrence of POAF by altering structural and electrical remodeling and oxidative stress.

Previous studies

Ozaydin and colleagues(8) randomized patients undergoing cardiac surgery and treated with ACE inhibitors to candesartan (an ARB) or placebo. Those treatment groups were compared to a non-randomized control group without any ABDT and showed a significant relative risk reduction of 72% (ACE-inhibitor plus candesartan) and 66% (ACE-inhibitor and placebo). Addition of candesartan to ACE inhibitors did not further reduce POAF. Because ACE-inhibitor use was not randomized and multivariable adjustment found age to be the only independent predictor of POAF, one has to suspect selection bias.

White et al.(9) presented an observational study including patients from AFIST (Atrial Fibrillation Suppression Trial) II and III of preoperative ACE inhibitors and their association with POAF. In the original trials patients were randomized to amiodarone and atrial pacing in a factorial design and patients..ACE-inhibitor use was associated with a non-significant OR of 0.72 (95% CI 0.42–1.20). A post-hoc power analysis suggested that the study fell 260 patients short to detect a significant difference for the observed treatment effect.

Coleman et al.(10) also found no statistically significant association of ABDT and POAF in a propensity score analysis of 376 patients undergoing cardiothoracic surgery. However, the matching algorithm excluded 74% of patients, and the propensity of ABDT was obtained with a parsimonious propensity model, which may not have sufficiently adjusted for hidden bias.

A recent study by Miceli and colleagues(3) suggested in a propensity score matched analysis that preoperative use of ABDT increases the risk of POAF, renal failure, inotrope use and death after cardiac surgery. Coleman and Miceli's study used methods similar to ours to adjust for confounding patient characteristics. However, propensity score methods only adjust for confounders that are considered in the propensity score regression model. Miceli and colleagues did not consider left atrial size, race (this was a study from England with uncertain racial diversity), preoperative blood pressure measurements, preoperative beta blocker, calcium channel blocker or inotrope use, and valvular disorders, associated with ischemic heart disease (but uncorrected at operation), all of which may have confounded their results. Interestingly we found higher occurrence of POAF, renal failure, inotrope use, and in-hospital mortality in our unadjusted analyses, but not in propensity-matched analyses, suggesting that these findings were related to confounders for which we were able to adjust. Although one previous study suggested that withdrawal of ABDT may predispose to POAF(14), we did not observe such association. Because ABDT is being withheld at our institution prior to cardiac surgery our study suggests that discontinuation of ABDT prior to surgery does not increase the odds of POAF, although in theory, annihilation of positive effects of ABDT and negative effects of its withdrawal should be considered.

Other observations

Patients, who were treated with ABDT prior to surgery, did not differ from untreated patients with respect to the occurrence of acute myocardial infarction, stroke, ventricular arrhythmias, cardiac arrest or in-hospital mortality benefit (Table 4). This observation suggests that short term benefits from ABDT in the surgical setting may be limited and that withdrawal does not increase the propensity of any of these adverse outcomes. Whether rapid restoration of ABDT after cardiac surgery has a positive effect on outcomes has yet to be determined.

Postoperative vasoplegia and inotrope resistance have been reported in some studies(11). We did not find evidence for an increased need for new inotropic support after surgery in patients who used ABDT preoperatively. However, as ABDT was typically stopped prior to surgery we cannot comment on the impact of perioperative continuation of therapy.

Strengths and limitations

One of the primary strengths of our study is the size of the patient cohort under investigation, and the extensiveness of variables available to adjust for confounding. The statistical methods based on propensity score adjustment were used to reduce selection bias and make fair comparisons. The observed associations of preoperative ABDT use were assessed not only with respect to POAF, but also other clinically important secondary outcomes and in-hospital mortality. The observational design of our study as a single center experience of a tertiary referral center and the inability to account for adherence, duration and time of restoration of ABDT after surgery limit our results. Further, because ABDT was recorded in our database in accordance to the STS reporting model, we were unable to separate ACE-inhibitors from ARBs. However, given the time frame of our study (1997-2003), we speculate that results are likely to be driven by ACE-inhibitors rather than ARBs, because most ARBs were marketed in the late 1990s, making them relative newcomers in our patient cohort. Another limitation is current practice of withholding ABDT in the early perioperative period and consequentially not being able to investigate their immediate hemodynamic effects on the development of POAF. However, because evidence suggests that these effects potentially are harmful(3,11), our results are applicable to many institutions. Our study provides the best evidence of preoperative use of angiotensin blocking drug therapy's feasibility as prophylaxis against postoperative atrial fibrillation in patients undergoing cardiac surgery to-date. Given current available data and existing

indications of ABDT in many patients undergoing cardiac surgery, it is unlikely that a well designed and adequately powered randomized trial investigating the effects of ABDT on POAF will be initiated at present time.

Conclusion

In propensity score adjusted analyses, we found no significant association of preoperative angiotensin blocking drug therapy with postoperative atrial fibrillation after cardiac surgery. In our study, ABDT did not increase occurrence of POAF, renal failure, inotrope use or in-hospital mortality when adjusted for confounding patient characteristics. These results provide no rationale to recommend preoperative prescription of ABDT prior to cardiac surgery in patients who do not have other compelling indications for such treatment, because established beneficial effects on cardiac remodeling do not appear to be associated with lower occurrence of POAF. Although adequately powered clinical trials should be designed to confirm our results and define the optimal time of ABDT restoration after cardiac surgery, they are at present unlikely to occur.

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Electronic APPENDIX A

Patient and Procedure Data used for Propensity Adjustment

Demography:	Gender, age at operation (years), race, body mass index ($\text{kg}\cdot\text{m}^2$), preoperative systolic and diastolic blood pressure (mmHg)
Preoperative symptoms:	New York Heart Association functional class (I-IV, categorized), Canadian Angina class (0-4), emergency operation
Cardiac comorbidity:	History of atrial fibrillation or flutter, history of ventricular arrhythmia, history of heart failure, previous cardiac operation, history of endocarditis, history of hypertension
Noncardiac comorbidity:	History of smoking, history of peripheral arterial disease, previous stroke, history of chronic obstructive pulmonary disease, history of renal disease (creatinine $>2 \text{ mg}\cdot\text{dL}^{-1}$), history of diabetes mellitus
Valve pathology:	Aortic valve regurgitation (grade 0-4), aortic valve stenosis (grade 1-5), mitral valve regurgitation (grade 0-4), mitral valve stenosis (grade 1-5), tricuspid valve regurgitation (grade 0-4), presence of aortic regurgitation/stenosis, presence of mitral regurgitation/stenosis, presence of tricuspid regurgitation
Echocardiography:	Left ventricular ejection fraction (%), left atrial diameter (cm)
Angiography:	extend of left anterior descending coronary artery disease (% stenosis), left circumflex artery disease (% stenosis), left main trunk disease (% stenosis), right coronary artery disease (% stenosis)
Electrocardiography:	Heart rate (bpm), PR interval, P-wave dispersion, QRS duration (ms), left ventricular hypertrophy: index by Sokolow-Lyon and Cornell (μV)
Electrocardiographic diagnoses:	Myocardial infarction (anterior, septal, inferior), LV hypertrophy, presence of left bundle branch block, presence of normal sinus rhythm, presence of sinus bradycardia, presence of sinus tachycardia

Medication use:	Preoperative ACE-inhibitor/angiotensin II receptor blocker (outcome variable of propensity score model), preoperative calcium channel blocker, preoperative beta blocker, preoperative inotrope
Laboratory data:	Creatinine clearance ($\text{mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$), preoperative blood urea nitrogen ($\text{mg} \cdot \text{dL}^{-1}$), preoperative hematocrit (%)
Operative Data	
Support:	Cardiopulmonary bypass time (min), aortic clamp time (min), off-pump coronary artery bypass grafting
Surgery type:	Coronary artery bypass grafting, number of internal thoracic artery grafts, aortic valve repair/replacement, mitral valve repair/replacement, tricuspid valve repair/replacement
Experience:	Date of operation as interval to a fixed date before cohort surgeries
Interaction terms:	Presence of diabetes and hypertension, diabetes and congestive heart failure, age and diabetes, age and hypertension, age and congestive heart failure, age and left ventricular ejection fraction, age and renal disease, hypertension and beta blocker use, hypertension and congestive heart failure, chronic obstructive pulmonary disease and hypertension, age and body mass index

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Figure 1.
Patient flow diagram
AF indicates atrial fibrillation; CABG, coronary artery bypass grafting; ECG, electrocardiogram.

Figure 2. Density plot of propensity scores of patients with (dotted line) and without (solid line) Angiotensin blocking drug therapy. The overlapping area represents patients with similar propensity scores available for close matches.

Figure 3.

Occurrence of postoperative atrial fibrillation by surgery type AVR indicates aortic valve replacement; CABG, coronary artery bypass grafting; Combined surgery, CABG with any combined valve surgery; MV, mitral valve; MVR, mitral valve replacement.

Figure 4. Standardized difference plot: Standardized differences in percent of patient characteristics between patients with and without preoperative Angiotensin blocking drug therapy before matching (dots) and after matching (squares). AV indicates Aortic Valve; BUN, blood urea nitrogen; ECG, electrocardiogram; LV, Left Ventricular; MI, myocardial infarction; MV, Mitral Valve; NYHA, New York Heart Association.

E-Figure 1.

Table 1
Patient Characteristics

Variable	ABDT (n=4,795)	No ABDT (n=5,757)	P value
Demographics			
Age, years *	66 ± 11	66 ± 11	.2
Female gender	1322 (28)	1448 (25)	.005
Race Caucasian	3980 (83)	4720 (82)	<.0001
Black	306 (6.4)	255 (4.4)	<.0001
Clinical characteristics			
BMI, kg/m ² *	29 ± 5.6	28 ± 5	<.0001
Hypertension	4037 (86)	3916 (70)	<.0001
BP systolic, mmHg *	134 ± 24	135 ± 22	<.0001
BP diastolic, mmHg *	73 ± 14	74 ± 13	.0003
Pulse pressure, mmHg *	62 ± 20	61 ± 19	<.0001
Paroxysmal AF	424 (8.8)	472 (6.9)	<.0001
Diabetes Mellitus	2152 (45)	1722 (30)	<.0001
Smoking	3138 (66)	3702 (65)	.4
COPD	1144 (24)	1165 (20)	<.0001
Congestive heart failure	1885 (39)	1018 (18)	<.0001
Prior stroke	434 (9.1)	393 (6.8)	<.0001
Creatinine clearance, mg/dl *	83 ± 43	86 ± 39	<.0001
Peripheral vascular disease	2446 (51)	2363 (41)	<.0001
NYHA class I	443 (9.2)	580 (10)	.2
II	2363 (49)	2930 (51)	.1
III	1036 (22)	939 (16)	<.0001
IV	953 (20)	1306 (23)	.0005
Beta Blockers	3260 (68)	3795 (66)	<.0001
Calcium Channel blockers	1168 (24)	1647 (29)	<.0001
Inotropes	149 (3.1)	108 (1.9)	<.0001
Cardiac characteristics			
Left atrial diameter, cm *	4.3 ± 0.7	4.2 ± 0.7	.8
LV-ejection fraction, % *	44 ± 13	49 ± 11	<.0001
Mitral valvular stenosis	43 (1.2)	68 (0.9)	.2
Mitral valvular regurgitation	2295 (48)	2070 (36)	<.0001
Aortic valvular stenosis	599 (13)	840 (15)	.002
Aortic valvular regurgitation	986 (21)	1050 (18)	.003
EKG characteristics			
Ventricular rate, bpm *	70 ± 14	67 ± 13	.0001
PR interval, ms *	174 ± 34	170 ± 31	<.0001

Variable	ABDT (n=4,795)	No ABDT (n=5,757)	P value
P-wave dispersion, iV*	73 ± 20	72 ± 20	.8
QRS duration, ms*	102 ± 20	98 ± 18	<.0001
Cornell voltage, iV*	1700 ± 830	1600 ± 760	<.0001
Sokolow-Lyon voltage, iV*	2100 ± 1100	2100 ± 960	<.0001
Surgical characteristics			
Internal thoracic artery graft	3876 (81)	4701 (82)	.3
Mitral valve repair	575 (12)	358 (6)	<.0001
Mitral valve replacement	158 (3.3)	142 (2.5)	.01
Aortic valve replacement	622 (13)	796 (14)	.2

* Data is presented as number (%) or mean ± standard deviation where indicated; AF indicates atrial fibrillation; BMI, body mass index; BP, resting blood pressure; LV, left ventricular; NYHA, New York Heart Association class

Table 2
Variables Associated with Preoperative ABDT Use

Variable	Coefficient Standard Error	P value
Body mass index	0.011 ± 0.0043	0.009
Race other than white or black	0.11 ± 0.2	0.05
Angina class	−0.073 ± 0.023	0.0014
NYHA class III	0.12 ± 0.058	0.03
CHF	0.59 ± 0.057	<.0001
Hypertension	0.89 ± 0.055	<.0001
Diabetes mellitus	0.42 ± 0.046	<.0001
Peripheral vascular disease	0.11 ± 0.045	0.01
Preoperative hematocrit	−0.014 ± 0.0044	0.002
Preoperative blood urea nitrogen	0.0042 ± 0.0021	0.05
Calcium channel blockers	−0.28 ± 0.049	<.0001
LV ejection fraction	−0.019 ± 0.002	<.0001
Left atrial diameter	0.14 ± 0.035	<.0001
Severity of aortic valve stenosis	−0.17 ± 0.02	<.0001
Severity of aortic valve regurgitation	0.095 ± 0.062	0.04
Severity of mitral valve regurgitation	0.071 ± 0.019	0.0003
QRS duration	0.0042 ± 0.0012	0.0003
Septal infarct on ECG	0.36 ± 0.096	0.0002
Anterior infarct on ECG	0.39 ± 0.11	0.0006
Emergency surgery	−0.69 ± 0.17	<.0001
Later cardiac surgery date	0.19 ± 0.013	<.0001

Table 3
Results of Different Statistical Methods

Method of Analysis	OR	95% CI
Unadjusted	1.13	1.05-1.23
PS-matched	1.05	0.95-1.16
PS, stratified by quintiles	0.99	0.9-1.08
PS-adjusted multivariable regression	1.03	0.94-1.13

CI indicates confidence interval; OR, odds ratio; PS, propensity score;

Table 4
Secondary Outcomes in Propensity-Matched Cohort

Complication No. of events (%)	ABDT (n=3,437)	No ABDT (n=3,437)	P value
Electrical Cardioversion	276 (8.0)	256 (7.4)	0.4
Pulmonary embolism	6 (0.2)	5 (0.1)	1 *
Renal failure (Cr >2 mg/dl)	244 (7.1)	243 (7.1)	0.6
Myocardial infarction	29 (0.8)	25 (0.7)	0.6
New inotropic support	227 (6.6)	240 (7.0)	0.2
Stroke	46 (1.3)	61 (1.8)	0.1
Ventricular tachycardia	169 (4.9)	144 (4.2)	0.2
Ventricular fibrillation	36 (1.0)	38 (1.1)	0.8
Cardiac arrest	55 (1.6)	45 (1.3)	0.3
In-hospital death	47 (1.4)	51 (1.5)	0.7
Length of hospital stay [†]	11 (9)	11 (9.6)	0.07 [‡]

ABDT indicates Angiotensin blocking drug therapy; Cr, Creatinine; No., number; POAF, postoperative atrial fibrillation;

* Fisher's exact test

[†] Presented as mean (standard deviation)

[‡] Wilcoxon-Mann-Whitney test