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# Conversion of Atrial Fibrillation after Cardiosurgical Procedures by Vernakalant® as an Atrial Repolarization Delaying Agent (ARDA)

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## ABSTRACT

**Background:** Postoperative, new-onset atrial fibrillation (POAF) is one of the most common complications after cardiosurgical procedures. Vernakalant has been reported to be effective in the conversion of POAF. The aim of this study was to evaluate the efficacy and safety of vernakalant for atrial fibrillation after cardiac operations, and to investigate predictors for the success of vernakalant treatment.

**Patients and Methods:** Post-cardiac surgery patients with new-onset of atrial fibrillation (AF) were consecutively enrolled in this study. Demographic data as well as intraoperative and postoperative parameters were analyzed. Vernakalant administration was primarily started 5.5 hours after new-onset POAF: 3 mg/kg intravenously over 10 min, and in case of non-conversion, a second dose of 2 mg/kg intravenously over 10 min.

**Results:** 129 consecutive patients (70.2 ± 9.1 years) were included: 61 patients with coronary artery bypass graft (CABG) surgery, 49 patients with isolated valve procedures, and 19 patients with combined procedures (CABG and valve). Conversion in sinus rhythm was achieved after the first vernakalant dose in 57 patients (44%), and after the second dose in 41 patients (32%). The mean time to conversion was 13.7 ± 14.1 min. The patients receiving valve procedures depicted a significantly lower conversion rate. The following variables lowered conversion rate: no preoperative beta blocker, postoperative troponin levels >500 ng/L, and systolic blood pressure >140 mmHg. At the first follow-up, 92% of the converted patients showed sinus rhythm, while 80% of the non-responders showed sinus rhythm ($P < .01$).

**Conclusions:** The POAF was effectively converted by vernakalant. The conversion rate of POAF after valve surgery was lower when compared to isolated CABG.

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## INTRODUCTION

Postoperative atrial fibrillation (POAF) is the most frequently encountered complication following cardiac surgery [Peretto 2014]. Although often self-limited, stroke, cardiac failure, hemodynamic instability, and death are not uncommon [Ahlsson 2009; Almassi 1997]. To date, the etiology and pathophysiology of POAF have not yet been fully elucidated. Postoperative autonomic activation due to heart manipulations, hypovolemia, anemia, pain or infection, perioperatively administered catecholamines, inflammation with or without pericarditis, metabolic alterations such as hypoglycemia, and electrolyte imbalance have been proposed as major potential contributing factors [Chelazzi 2011].

Prophylaxis and treatment options vary depending on the severity, comorbidities, duration, and etiology. Besides electric cardioversion, different medical therapies exist to terminate atrial fibrillation and maintain sinus rhythm. Beta blockers and Amiodarone are the two most commonly used medications for prophylaxis [Omae 2012; Mayson 2007]. For acute measures, the administration of beta blockers, calcium channel blockers, and amiodarone or electrical cardioversion must be considered [Peretto 2014; Omae 2012]. Other antiarrhythmic drugs (AAD) can also be used, depending on the hemodynamic condition. Furthermore, studies evaluating the perioperative use of statins and anti-inflammatory drugs have shown promising results [Winchester 2010; Mariscalco 2007; Halonen 2007].

Nevertheless, all these therapeutic options have their drawbacks, such as the potential side effects of amiodarone on the lungs and thyroid, the drug-drug interactions of beta blockers, and the cardiodepressive effects of AADs [Bash 2012]. Vernakalant is a novel antiarrhythmic agent used for rapid cardioversion of a recent onset atrial fibrillation (AF) via the blocking of early-activating potassium atrial channels and frequency-dependent atrial sodium channels [Helgadottir 2012; Camm 2011; Kowey 2009]. Vernakalant has low cardiodepressive effects, and a fast conversion in sinus rhythm can be expected [Helgadottir 2012; Camm 2011; Kowey 2009]. However, its efficacy and safety of use after cardiac surgery remains to be clarified.

Therefore, the aim of the present study is to evaluate the efficacy and safety of vernakalant for AF after cardiac

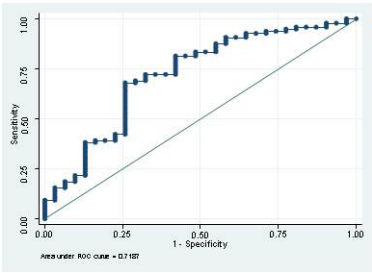


Figure 1. Predictive behavior of the model checked by the ROC curve.

operations and to investigate predictors for the success of vernakalant treatment.

## MATERIALS AND METHODS

We retrospectively analyzed 129 patients that were operated on between 2011 and 2015. All patients suffered from AF after cardiosurgical procedures, predominantly coronary artery bypass grafting (CABG) or valve procedures, and were treated with vernakalant.

In the patients with postoperative AF, we analyzed preoperative and perioperative parameters, such as demographic, procedural, and outcome data. All patients with new occurrences of postoperative AF were treated with vernakalant in order to convert the AF to sinus rhythm. The administration of vernakalant was conducted as follows: vernakalant hydrochloride 3mg/kg was given intravenously over 10 minutes. If AF persisted, additional vernakalant hydrochloride (2mg/kg over 15 minutes) was administered. The primary endpoints analyzed were the two conversion rates (after the first, and cumulative after the second dose). The time to conversion was analyzed as a secondary endpoint.

### *Statistical Analysis*

The data were analyzed according to established standards of descriptive statistics. Categorical variables were compared using a $\chi 2$ test. Continuous variables are reported as medians with interquartile range, or mean ± SD. For comparisons, the t test (based on testing for normal distribution) or the 2-tailed Mann–Whitney U test were used as appropriate. Location differences of k > 2 groups were tested using the nonparametric Kruskal-Wallis H test. Odds ratios and 95% confidence intervals were provided where appropriate. A P value of less than .05 was considered significant. In a multivariate approach, the variables influencing the probability of conversion were analyzed using a logistic regression model. The goodness of the resulting predictive model was assessed with an ROC curve. Bootstrapping with 1,000 replications was employed to estimate the confidence interval of the area under curve statistic. Statistical analyses were performed using STATA V.13 (Stata Corp, College Station, Texas, USA).

### *Correlations of Endpoint Variables with Potential Influencing Factors*

We focused on the following parameters to investigate their correlation with our defined endpoint variables: age, sex, diagnosis prior to surgery (i.e. coronary artery disease [CAD], AF), surgical procedure (CABG, valve procedure, combined procedures), on pump/off pump surgery, duration of surgery, left ventricular ejection fraction, time between surgery and onset of AF, and time between onset of AF and first dose of vernakalant.

For these variables, the zero hypothesis of missing correlation with the endpoint variables was tested (conversion after

Table 1. Clinical Data and Perioperative Parameters

| | Mean + sd/Proportion (n) n=129 |
|---|---|
| Age (years) | 70.2 ± 9.1 |
| Sex ( % male) | 69.8 (90) |
| Body Height (cm) | 172.4 ± 9.1 |
| Body Weight (kg) | 81.7 ± 16.5 |
| BMI | 27.04 ± 4.9 |
| Medical history | |
| Diabetes (% IDDM and NIDDM) | 28.7 (37) |
| Hypertension (%) | 84.5 (109) |
| Cholesterol above 200 mg/dl (%) | 54.3 (70) |
| CABG vessel involved | |
| One vessel disease (%) | 18.1 (15) |
| Two vessel disease (%) | 16.9 (14) |
| Three vessel disease (%) | 65.1 (54) |
| Left main stem stenosis (%) | 33.3 (41) |
| LVEF (Angio) <50% (%) | 16.3 (21) |
| Wall motion abnormalities (%) | 24.0 (31) |
| Surgery | |
| CABG (%) | 47.3 (61) |
| - pump on (% of CABG) (%) | 52.5 (32) |
| - pump off (% of CABG) (%) | 47.5 (29) |
| Isolated Valve procedures (%) | 38.0 (49) |
| Combined CABG and valve procedures (%) | 16.0 (19) |
| - Mitral replacement/reconst. (%) | 25.0 (3) |
| - Atrial replacement/reconst. (%) | 73.5 (16) |
| Combined Aortic and Mitral (%) | 1.5 (1) |
| Duration of surgery (min) | 235.8 ± 72.5 |
| Extracorporal circulation. (min) | 139.4 ± 63.7 |
| Cross-clamp time (min) | 87.3 ± 40.5 |
| Use of catecholamines* (%) | 89.9 |

Sd indicates standard deviation; BMI, body mass index; IDDM, Insulin-Dependent Diabetes Mellitus; NIDDM, Non-Insulin-Dependent Diabetes Mellitus; LVEF, left ventricular ejection fraction; CABG, coronary artery bypass graft surgery.
*except from low dose dobutamine

Table 2. Baseline Statistics by Type of Procedure

| | CABG | CABG and valve | Valve procedures | *P* |
|---|---|---|---|---|
| Patients | 61 | 19 | 49 | |
| Age (years) | 70.3 | 72.4 | 69.6 | ns |
| Sex (% male) | 73.8 | 73.7 | 63.3 | ns |
| High cholesterol level (>200mg/dl) (%) | 75.4 | 52.6 | 28.6 | < .001 |
| Wall motion abnormalities (%) | 39.3 | 10.5 | 10.2 | < .001 |
| Surgery | | | | |
| Use of catecholamines* (%) | 82.0% | 94.7% | 98.0% | < .001 |
| Duration of surgery (min) | 234.2 | 238.8 | 236.8 | ns |
| Extracorporeal circulation (min) | 115.1 | 137.5 | 155.9 | < .025 |
| Cross clamp time (min) | 71.3 | 86.1 | 98.2 | < .001 |
| Post surgery | | | | |
| Time to onset of AF (h) | 80.7 | 97.2 | 105.0 | < .025† |

*Except from low dose dobutamine

†Non-parametric ANOVA (Kruskal-Wallis test) indicated a significant difference ($p<0.025$)

CABG indicates coronary artery bypass graft; AF, atrial fibrillation.

first dose, conversion after second dose, time to conversion below 15 min).

### *Ethics Committee Approval*

This study was approved by the ethics committee of the medical faculty of the Heinrich-Heine University, complying with the principles outlined in the Declaration of Helsinki.

## RESULTS

### *Patient Population*

Table 1 summarizes the baseline statistics for the entire study population (n=129). The majority of patients were male (70%) with a mean age of 70 years. Of all the patients, 47% underwent CABG surgery, 37% isolated valve, and 16% combined CABG and valve procedures. The mean time between surgery and onset of AF was 92 hours (± 77 hours, median 70 hours, interquartile range 54-97 hours). Certain baseline parameters varied significantly by type of procedure (Table 2, test results based on ANOVA mean comparison).

### *Conversion After First Dose*

For 57 out of 129 patients (44%), conversion after the first dose of vernakalant was observed. The elapsed time between the onset of AF and the first dose of vernakalant was 5.5 ± 9.8 hours. In 5% of the patients, the first vernakalant dose was not administrated before 24 hours after onset of atrial fibrillation.

Table 3a depicts the rate of the incidence of conversion after the first dose of vernakalant with regard to perioperative parameters. We found several parameters that are not demonstrated in table 3a, as they did not correlate significantly with successful conversion after the first vernakalant dose. However, these clinical settings were associated with a more frequent rate of conversion by trend: body height ≤160 cm (females only), preoperative use of beta blockers, peak troponin T level after onset of AF <500 ng/L. These additional findings should be considered exploratory, as they were not based on prior hypotheses.

### *Conversion After Second Dose*

For the additional 41 patients (32%), conversion was achieved after the second dose. For 98 patients (76%), cumulative conversion after the first or second dose of vernakalant was observed. The cumulative conversion after the first or second dose was significantly correlated with the type of surgery. Mitral valve procedures and combined procedures show decreased conversion rates. A smaller, slightly non-significant correlation was found between the time between postoperative onset of AF and administration of the first vernakalant dose (Table 3b).

Additionally, several variables showed a non-significant correlation with conversion after the second dose. Conversion was significantly more frequent for men with body height ≤ 170 cm. Conversion was also more frequent for patients with preoperative beta blocker administration. Patients with surgeries ≤3.5 hours had a lower conversion rate (65%). Those with peak creatinkinase (CK) levels <100 U/L after onset of AF had less frequent conversion. Again, these additional findings must be considered exploratory, as they were not based on prior hypotheses.

### *Time to Conversion*

Mean time to conversion was 13.7 ± 14.1 min. No significant predictors were found in the predefined group of potential predictors. The data indicate that age and some diagnostic

Table 3a. Conversion After the First Dose of Vernakalant by Demographic/Treatment Groups

| | | n | Conversion after 1st dose (percen-tage within group) (n) | Conversion after 1st dose (count) | *P* |
|---|---|---|---|---|---|
| Age (years) | ≤70 years | 56 | 51.79% | 29 | |
| | 71+ years | 73 | 38.36% | 28 | ns |
| Sex | Male | 90 | 41.11% | 37 | |
| | Female | 39 | 51.28% | 20 | ns |
| Body height (cm) (male patients, n = 90) | ≤ 170 cm | 17 | 47.06% | 8 | |
| | > 170 cm | 73 | 39.73% | 29 | ns |
| Body height (cm) (female patients, n = 39) | ≤ 160 cm | 17 | 64.71% | 11 | |
| | > 160 cm | 22 | 42.86% | 9 | ns* |
| Left ventricular ejection function (Angio) (%) | < 50 | 21 | 52.38% | 11 | |
| | ≥ 50 | 108 | 42.59% | 46 | ns |
| Surgery (broad categories) | CABG | 61 | 47.54% | 29 | |
| | Valve procedures† | 48 | 45.83% | 22 | |
| | CABG and valve procedures | 20 | 30.00% | 6 | ns |
| Surgery (fine categories) | Bypass TAR | 20 | 40.00% | 8 | |
| | Bypass ACVB | 41 | 51.22% | 21 | |
| | Valve AV | 34 | 50.00% | 17 | |
| | Valve MV | 14 | 35.71% | 5 | |
| | Valve AV/MV | 20 | 30.00% | 6 | ns |
| Bypass Surgery (including mix bypass/valve) | Y | 80 | 42.50% | 34 | |
| | N | 49 | 46.94% | 23 | ns |
| Bypass Surgery | off pump | 29 | 44.83% | 13 | |
| | on pump | 51 | 41.18% | 21 | ns |
| Valve surgery (including mix bypass/valve) | Y | 68 | 41.18% | 28 | |
| | N | 61 | 47.54% | 29 | ns |
| Time Surgery to onset of AF (hours) | ≤ 70 h | 65 | 43.08% | 28 | |
| | > 70 h | 64 | 45.31% | 29 | ns |
| Time Onset of AF to first dose (h) | ≤ 2.0 h | 70 | 47.14% | 33 | |
| | > 2.0 h | 59 | 40.68% | 24 | ns |

CABG indicates coronary artery bypass graft; TAR, thrombocytopenia absent radius; ACVB, aortocoronary venous bypass; AV, atrioventricular; MV, mitral valve; AF, atrial fibrillation.

*The initially differences in body height are significant. With the fourfold test, there is no significance

†Two surgeries involving tricuspidal valves

data (cholesterol level, insulin-dependent diabetes mellitus [IDDM], wall motion abnormalities) might influence the time to conversion.

### *Multivariate Approach*

In a multivariate logistic model, the cumulative conversion after the first or second dose of vernakalant was explained by type of surgical procedure, duration of surgery, and time between the onset of POAF and the administration of the first vernakalant dose. The explanatory variables (with the exception of duration) proved to be significant, although the level of significance tends to be unsatisfactory for a retrospective study (Table 4).

Goodness of fit was tested with the Hosmer-Lemeshow test. The test showed no significant departure in the distributions of actual events and the predicted event counts.

The constant (intercept) term in the logistic regression represents a baseline probability of conversion.

Table 3b. Conversion After the First or Second Dose of Vernakalant by Demographic/Treatment Groups

| | | n | Conversion after 1st or 2nd dose (within group percentage) | Conversion after 1st or 2nd dose (count) | *P* |
|---|---|---|---|---|---|
| Age (years) | ≤ 70 years | 56 | 85.70% | 48 | |
| | 71+ years | 73 | 69.86% | 51 | < .05 |
| Sex | Male | 90 | 73.33% | 66 | |
| | Female | 39 | 82.05% | 32 | ns |
| Body height (cm) (male patients, n=90) | ≤ 170 cm | 17 | 88.24% | 15 | |
| | > 170 cm | 73 | 69.86% | 51 | ns |
| Body height (cm) (female patients, n=39) | ≤ 160 cm | 17 | 82.35% | 14 | |
| | > 160 cm | 22 | 81.82% | 18 | ns* |
| Left ventricular ejection function (Angio) (%) | < 50 | 21 | 80.95% | 17 | |
| | ≥ 50 | 108 | 75.00% | 81 | ns |
| Surgery (broad categories) | CABG | 61 | 83.61% | 51 | |
| | Valve procedures† | 48 | 75.00% | 36 | |
| | CABG and valve procedures | 20 | 55.00% | 11 | < .05 |
| Surgery (fine categories) | Bypass TAR | 20 | 70.00% | 14 | |
| | Bypass ACVB | 41 | 90.24% | 37 | |
| | Valve AV | 34 | 79.41% | 27 | |
| | Valve MV | 14 | 64.29% | 9 | |
| | Valve AV/MV | 20 | 55.00% | 11 | < .05 |
| Bypass Surgery (including mix bypass/valve) | Y | 80 | 76.25% | 61 | |
| | N | 49 | 75.51% | 37 | ns |
| Bypass Surgery | off pump | 29 | 79.31% | 23 | |
| | on pump | 51 | 74.51% | 38 | ns |
| Valve surgery (including mix bypass/valve) | Y | 68 | 69.12% | 47 | |
| | N | 61 | 83.61% | 51 | ns |
| Time Surgery to onset of AF (h) | ≤ 70 h | 65 | 81.54% | 53 | |
| | > 70 h | 64 | 70.31% | 45 | ns |
| Time Onset of AF to first dose (h) | ≤ 2.0 h | 70 | 81.43% | 57 | ns |
| | > 2.0 h | 59 | 69.49% | 41 | .064 |

CABG indicates coronary artery bypass graft; TAR, thrombocytopenia absent radius; ACVB, aortocoronary venous bypass; AV, atrioventricular; MV, mitral valve; AF, atrial fibrillation.

*The initially differences in body height are significant. With the fourfold test there are no significancy

†2 surgeries involving tricuspidal valves

The predictive behavior of this model was checked using the ROC curve (Figure 1). The area under curve (also referenced as q statistic) was 0.72, with a 95% confidence interval ranging from 0.614 to 0.823 (CI estimated by bootstrapping).

Furthermore, the deviance residuals resulting from the logistic model were calculated. For most observations, the deviance residuals were in an acceptable range. However, four patients showed a high deviation between the actual observation (no conversion) and the predicted probability of conversion, which turned out to be very high (>0.85) for these patients.

### *Follow-Up*

Table 5 compares the follow-up results of the group with successful vernakalant administration (conversion after the first or second dose, "group A") with the complementary group that showed no conversion after the second dose ("group B").

Table 4. Results of a Logistic Regression Explaining the Cumulative Conversion Rate Dose 1 or 2

| Type of surgery | Odds ratio | Standard deviation | *P* |
|---|---|---|---|
| CABG | 1 = base | | |
| Valve replacement | 0.150 | 0.092 | |
| CABG and valve replacement | 0.555 | 0.279 | .008 (joint test) |
| Duration of surgery (min) | 1.006 | 0.0035 | .084 |
| Time from onset to dose 1 (hours) | 0.956 | 0.192 | .024 |
| Constant * | 1.817 | | |

CABG indicates coronary artery bypass graft.
*the constant (intercept) term in the logistic regression represents a baseline probability of conversion.

Table 5. Follow-Up Results

| | Cumulative conversion after 1st or 2nd dose % (n) | | *P* |
|---|---|---|---|
| | yes | no | |
| Patients | 98 | 31 | |
| Days until discharge | 11.0 (±8.8) | 11.7 (±6.6) | ns |
| First follow-up (early post-operative) | | | |
| ECG with Sinus Rhythm | 95.9% | 80.6% | < .01 |
| LVEF < 50 % | 16.3% (16) | 12.9% (4) | |
| LVEF ≥ 50 % | 83.7% (82) | 87.1% (27) | ns |
| Abnormal wall motion | 30.6% (30) | 19.3% (6) | |
| No irregular wall motion | 69.4% (68) | 80.7% (25) | ns |
| NYHA I | 56.1% (55) | 58.1% (18) | |
| NYHA II-IV | 43.9% (43) | 41.9% (13) | ns |
| Second follow-up (late post-operative) | | | |
| ECG with Sinus Rhythm | 98.0% | 96.7% | ns |
| NYHA I | 93.9% (92) | 77.4% (24) | |
| NYHA II-IV | 6.1% (6) | 22.6% (6) | < .01 |

ECG indicates electrocardiogram; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Patients were discharged 11.2 ± 8.3 days after surgical procedure. Successful administration of vernakalant did not influence the length of stay. The patient's electrocardiograms (ECG) were re-assessed close to the discharge day, and were typically assessed again three months after discharge in the outpatient clinic (during the first two registry years and up to 36 months after discharge). At the first follow-up (postoperative 9.0 ± 2.4 days), 92% of the patients maintained sinus rhythm. This proportion was significantly higher in group A. However, 30 patients (31%) in group A showed a lower left ventricular ejection fraction (LVEF), compared to 13 patients (19%) in group B. At the second follow-up (5.2 ± 1.2 months postoperatively), the ECG assessment showed sinus rhythm for 98% of the patients. No differences between the groups were observed.

The New York Heart Association (NYHA) classification substantially improved compared to the preoperative and early postoperative status (90% NYHA class I, compared to 7% preoperative and 56% early postoperative). However, there was a significant difference in the proportions between group A and B. In group A, the late postoperative proportion of NYHA I patients was 94%, compared to 77% in the complementary group. It must be kept in mind that the allocation into NYHA classes was based on the subjective acknowledgment of resident physicians, as well as ambulatory and long-term care.

### *Complications During Vernakalant Administration*

We observed events of clinical interest occurring within 1, 2, 12 and 24 hours after vernakalant administration with blood pressure monitoring and ECG registration. No clinically important changes in laboratory parameters or vital signs occurred after first or second administration of vernakalant. Vernakalant was well tolerated in our population of post-operative patients. Overall, the blood pressure values did not drop significantly 10, 30, 60, or 120 minutes after vernakalant infusion. Minimal changes in blood pressure were transient, and no patient was harmed thereby. No ventricular tachycardia or torsades de pointes occurred during and after vernakalant infusion. Additionally, we neither observed any neurologic complications nor any relevant bradycardia.

## DISCUSSION

The currently available antiarrhythmic agents for pharmacologic cardioversion of AF in cardiac surgery are limited by their negative side effects, such as delayed onset of action, slow metabolism, proarrhythmic potential [Camm 2011; Kowey 2009]. Because of this fact, new strategies for treatment must be investigated. Particularly in cardiac surgery, the need for a rapidly acting, efficacious, and well-tolerated AAD is obvious [Kowey 2009]. As shown by Roy et al in placebo-controlled phase II and III clinical trials, intravenous vernakalant application effectively converted recent-onset AF, and was well tolerated [Kowey 2009; Roy 2008; Roy 2004].

This retrospective study was designed to evaluate the predictive factors of conversion with vernakalant administration in clinical practice in patients with recent-onset AF after cardiac surgery.

In 57 patients (44%), conversion in sinus rhythm was achieved after the first dose of vernakalant. For 41 patients (32%), conversion was achieved after the second dose. The overall success rate was 76%. In 5% of the cases, the time to the first dose was over 24 hours. The descriptive statistics indicate a high proportion of outliers. No correlation was

detected for our presumed variables. The cumulative conversion after the first or second dose was significantly correlated with the type of surgery. Mitral valve procedures and combined procedures revealed a decreased conversion rate. A smaller, slightly non-significant correlation was found for the time between postoperative onset of AF and the administration of the first vernakalant dose.

However, our results correspond with previous reports in which proarrhythmic side effects could not be observed after vernakalant [Pratt 2010]. In the ACT trials I-IV, the most common side effects were bradycardia and hypotension, however, no deaths or proarrhythmic effects, including torsades de pointes, were reported in these studies [Philip 2014; Pratt 2010; Kowey 2009; Roy 2005].

Despite these results, close hemodynamic monitoring during vernakalant infusion and within the following two hours should be performed. In 2009, Kowey et al reported episodes of hypotension or bradycardia in 9.3% and 13.1% of vernakalant-treated cardiosurgical patients, respectively [Kowey 2009]. In their 2011 ARVO study, Camm et al reported severe adverse effects, such as bradycardia <40/min and hypotension <85 mmHg, during the two-hour observation period in 2.6 % of the patients [Bash 2012]. Based on the findings in the literature, we recommend monitoring blood pressure and heart rate during the vernakalant infusion, and for 120 minutes afterwards.

Previous research on AF after cardiac surgery was limited to the use of single therapy with either vernakalant, other antiarrhythmic drugs, and/or electrical cardioversion. The effect of vernakalant on the treatment of recent-onset AF has been widely debated in previous research [Bash 2012; Pratt 2010; Kowey 2009; Roy 2008; Roy 2004].

With our analysis we aimed to clarify predictors for success of isolated vernakalant treatment in cardiosurgical patients with new-onset AF. Our primary endpoints consisted of the two conversion rates, after the first and cumulatively after the second dose of vernakalant. We could not confirm our suggested predictors for a successful conversion by comparing converted and non-converted patients. However, our data indicate that age and some clinical parameters, such as cholesterol level, IDDM, and wall motion abnormalities might negatively influence the time to conversion. The time to conversion has decreased over the years: in 2014 and 2015, time to conversion was below 15 minutes for all 46 (out of 61) patients who could be converted to sinus rhythm; this fact may be explained by the learning curve and the routine use.

The above-mentioned parameters that may reduce the incidence of conversion were also described by Eltheni in 2012 [Eltheni 2012]. Helgadottir et al reported in recent studies that the incidence of postoperative AF was higher in patients with aortic valve replacement [Helgadottir 2012]. This is generally consistent with our results, as patients with severe aortic stenosis usually display a hypertrophied interventricular septum (IVS). The type of surgery was identified as the main factor influencing the conversion rate. The conversion rate was significantly higher for isolated CABG procedures compared to valve and combined CABG/valve procedures. In our present study, the conversion rate of 76% after isolated vernakalant therapy was slightly higher compared to previous results by Kowey et al, detailing the rapid conversion of AF after cardiac surgery [Kowey 2009]. Regarding the fact that currently, a significant number of postoperative patients still need electrical cardioversion (EC) with sedation, and the presence of possible complications like embolism, our results could prove vernakalant as a good option for medical cardioversion [Kowey 2009].

Antiarrhythmic drugs such as amiodaron or beta-blockers represent an effective treatment in postcardiotomy patients [Khanderia 2008]. Compared to a high conversion rate, rare adverse events and fast onset of effect were shown in previous investigations and our study. Philip et al reported amiodarone to be less effective for recent-onset AF, with a conversion rate of only 5% within the first 90 min in postcardiotomy patients [Philip 2014].

Furthermore, long-term treatment with amiodarone can cause serious complications such as non-cardiac toxicity, including pulmonary, hepatic, thyroid, and neurologic side-effects. Moreover, its intravenous administration could be associated with hypotension, bradycardia, and thrombophlebitis, and this agent should be used with caution in patients with severe pulmonary disease and low pulmonary resistance [Khanderia 2008]. In contrast, vernakalant is the first marketed drug with relative atrial selectivity and a low rate of adverse events reported, indicating a higher safety profile. Beta-blockers are also relatively safe in terms of adverse events, however, they are mainly used to control ventricular rate rather than ventricular rhythm [Khanderia 2008].

Vernakalant is a novel antiarrhythmic agent used for rapid cardioversion of a recent onset atrial fibrillation via the blocking of early-activating potassium atrial channels and frequency-dependent atrial sodium channels. Recent studies showed that intravenous application of vernakalant in patients with structural heart disease is safe and effective [Bash 2012]. Our data support these findings, confirming a safe administration of vernakalant for acute AF after cardiac surgery and a high conversion rate to sinus rhythm.

Our study has several limitations. The main limitations are the retrospective design and the limited number of patients in a single institution. Due to this retrospective design, the significance levels should be interpreted with caution. Furthermore, none of the previous usual therapy strategies with other antiarrhythmic drugs, such as beta-blockers or electrolyte substitution, were quantified. Randomized, clinical trials are necessary to fundamentally confirm the quality, safety, and efficacy of vernakalant use in cardiac surgery.

## CONCLUSION

Our results show that administration of vernakalant was highly effective for the treatment of AF in postoperative cardiosurgical patients, with a high conversion rate of 76%. It appears to be a safe and promising option compared to current methods. It permits a medical conversion with a low side-effect profile, and provides a rapidly acting therapeutic alternative for the conversion of AF.

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