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Patient-Specific Characteristics Determine Success of Surgical Atrial Fibrillation Ablation in Patients with Persistent Atrial Fibrillation

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ABSTRACT

Surgical atrial fibrillation ablation (SAFA) has not achieved the efficacy of Cox's original maze procedure, although technical improvements continue to be made. It is possible that biologic factors determine SAFA success. Therefore we examined how patient-specific characteristics affected SAFA success in 353 atrial fibrillation (AF) patients who underwent SAFA at a single institution. Among these, 257 (72.8%) had continuous AF and 96 (27.2%) had intermittent AF. For 297 patients (84.1%) postoperative follow-up was >3 months. We compared SAFA success in patients whose procedure involved only pulmonary vein isolation with those whose procedure involved extensive lesion sets. Multivariate analysis included AF duration, left atrial size, preoperative atrial flutter, concomitant procedures, lesion sets, and energy source. Early SAFA success was classified as freedom from AF between postoperative months 3 and 6, and intermediate success between postoperative months 6 and 12. Receiver-operating characteristic (ROC) curves and stratum-specific likelihood ratios (SSLR) were generated to compare intermediate failure by left atrial size (LAS) thresholds. SAFA was more successful in the intermittent than the continuous AF group (n = 66, 86% vs n = 165, 71%; $P = .014$). When pulmonary vein isolation was compared only to more extensive lesion sets, there was no difference in success in the intermittent (34, 91% vs 32, 81%; $P = .24$) or continuous groups (67, 73% vs. 98, 69%; $P = .603$). Success for intermittent AF patients was not correlated with variables considered; in continuous AF patients, predictors included presence of concomitant mitral valve repair/replacement ($P = .075$), decreasing LAS ($P = .025$) and absence of preoperative atrial flutter ($P = .001$). In the continuous AF group, ROC curves and corresponding areas under the curve (AUC) were 0.60 (0.50-0.71) for failure at 6 months to 1 year. SSLR analysis generated 2 strata for LAS: <8 cm with SSLR = 0.87 (0.74-1.0) and ≥8 cm SSLR = 2.98 (1.07-8.3). In patients with intermittent AF, SAFA achieved acceptable results regardless of tested preoperative and intraoperative variables. In continuous AF, patient-specific characteristics affected success more than intraoperative variables. Failure was more than 3-fold greater in continuous AF patients with an LAS ≥8 cm. In both patient types, more extensive lesion sets were not shown to improve outcomes. Future improvements in SAFA may depend on pharmacologic and/or surgical substrate modification.

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INTRODUCTION

The development of surgical atrial fibrillation ablation (SAFA) has been a significant advance in the treatment of atrial fibrillation (AF). SAFA is characterized by use of energy and simplified lesion sets to create conduction blocks [Spitzer 1999; Cox 2000; Gillinov 2002]. Although SAFA offers effective AF treatment in many cases, a subset of patients fail therapy regardless of the energy source, lesion set, or concomitant procedures [Handa 1999; Sie 2001; Mohr 2002].

Further elucidation of factors that determine SAFA success will be important in improving outcomes in the surgical treatment of AF. This study was undertaken to determine how patient-specific characteristics affect SAFA success. Because an increasing body of evidence suggests that AF results from multiple processes and that factors influencing outcome may be dependant on the underlying cause of AF, patients were stratified into 2 clinically distinct groups: intermittent and continuous AF [Haissaguerre 1998; Cox 2004a; Van Gelder 2004; Fuster 2006].

MATERIALS AND METHODS

Study Population

Data were prospectively collected on 353 consecutive AF patients older than 18 years who underwent SAFA at a single institution. Patients were classified into continuous (cAF) and intermittent (iAF) subgroups.

Data Collection

Preoperative and intraoperative variables were collected prospectively. Patients were followed at regular intervals by direct contact or referring physicians. Postoperative rhythms were recorded using a traditional 12-lead electrocardiograph (ECG) and transtelephonic cardiac monitoring. A transtelephonic ECG recorder (MicroER 4X, LifeWatch, Buffalo Grove, IL, USA) was available to all patients. Those who opted to use the device received the device at postoperative month 6 and 12 and were instructed to record their rhythms once daily, or in cases of symptomatic palpitations, for 30 consecutive days (n = 124, 35.1%) [Senatore 2005]. Patient rhythms were collected at the following time intervals: discharge, 6 weeks, 3 months, 6 months, and 1 year. A total of 3132 rhythm recordings were collected (Figure 1). Every patient had a minimum of 1 record available for analysis (range, 1 day to 56 months).

SAFA Procedure

The surgical approaches used were median sternotomy, right minithoractomy, bilateral thoracotomy, and thoracoscopy. In cases with concomitant procedures, ablation was generally completed first. Energy source and lesion sets were chosen at the discretion of the operating surgeon, but all included pulmonary vein isolating lesion (PVI) alone or in combination with mitral valve annulus lesion (ANNLS), left atrial appendage encircling lesion (LAA), or right-sided flutter lesion (Figure 2).

Definitions

Classifications of continuous and intermittent AF follow those proposed by [Cox 2004b]. Continuous AF was defined as AF that did not self terminate. Intermittent AF was defined as AF that self terminates but may be recurrent. Classifications of AF and preoperative atrial flutter were determined by ECG.

Left atrial size (LAS) was determined by intraoperative transesophageal echocardiography. Length of stay was defined as the number of days of inpatient stay, from on the day of the surgery to the day of discharge home or to a rehabilitation facility. Postoperative rhythm success was defined as freedom from AF and atrial flutter at the time point at which the patient was evaluated. Outcomes were separated into 2 separate cohorts, with short-term success classified as freedom from AF between postoperative months 3 to 6 and intermediate success as freedom from AF between postoperative month 6 and 12.

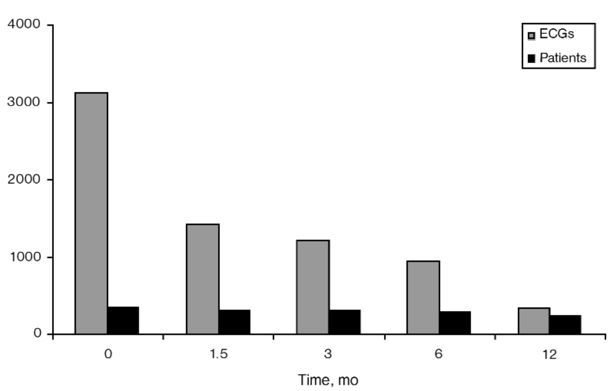

Figure 1. Number of patients with available electrocardiographic (EGC) follow-up and number of ECGs available at and beyond specified time points.

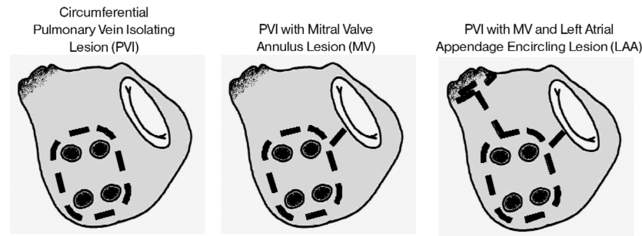

Figure 2. Lesion sets. Dashed line indicates ablation line. Shaded region represents the left atrial appendage, the white region the mitral valve annulus, and the black holes the pulmonary vein orifices.

Data Analysis

Data were analyzed using a standard statistical software package, Stata 9 (Stata Corp, College Station, TX, USA). Continuous variables were reported as means ± SD and compared using the Student *t*-test. To compare categorical variables, the χ^2 test was used. Although the impact of patient-specific characteristics on SAFA success was the primary focus of this study, the significance of intraoperative variables was also assessed. Multivariate analysis was used to determine the impact of patient specific characteristics and intraoperative variables on early and intermediate-term success. This analysis was performed with Cox logistic regression (forward, forward stepwise, and backward; enter $P < .10$, remove $P > .15$). The conventional P value of 0.05 or less was used to determine level of statistical significance. All reported P values are 2-sided.

Analyses of receiver operating characteristic (ROC) curves and stratum-specific likelihood ratios (SSLRs) were generated for variables with statistically significant associates for rhythm success. ROC curves were generated by plotting sensitivity on the ordinate and 1 – specificity on the abscissa, with the use of variable of interest as a continuous variable and success at 6 to 12 months as a binary outcome [Hanley 1982; Hanley 1983]. The area under the ROC curve was derived from Wilcoxon statistics. Threshold values for the variable were determined by combining adjacent strata with statistically indistinct SSLRs (ie, those with overlapping 95% confidence intervals [CI]), [Pierce 1993; Chen 1997].

RESULTS

Study Population

Among this patient group, 187 patients (53.0%) were females and 166 (47.0%) were males. Mean patient age was 67.2 ± 11.9 years. The median duration of AF was 4 years (mean = 6.7 years). Mean LAS was 6.1 ± 1.5 cm (range 3–12 cm). Our patient population consisted of 96 patients (27.2%) with intermittent AF and 257 patients (72.8%) with continuous AF, of which 77 of the total patients (21.8%) had preoperative atrial flutter. The 65.4 ± 12.4 year mean patient age in the iAF subgroup was less than the 67.2 ± 11.7 year mean patient age in the cAF subgroup

(*P* = .08). iAF subgroup LA size (5.5 ± 1.2 cm) and preoperative duration of AF (3.3 ± 4 years) were also significantly smaller (*P* = .003) and shorter (*P* = .0001) than in the cAF subgroup (6.1 ± 1.5 cm and 6.7 ± 7.7 years, respectively). Patient and operative characteristics are detailed in the Table.

Intraoperative Variables

Radiofrequency was used in 118 (33.4%) of patients, microwave was used in 174 (49.3%), and laser was used in 61 (17.3%); 174 (49.3%) of patients received PVI alone, 84 (23.8%) PVI with mitral valve and LAA, 77 (21.8%) PVI with ANNLS, 16 (4.5%) PVI with LAA, and the remaining 2 (0.6%) received PVI with flutter lesion. A right-sided flutter lesion was created in a total of 32 (11.2%) of patients. The LAA was amputated or occluded in 268 (75.9%) of patients.

Data Analysis

Compared with the cAF group, iAF patients achieved greater freedom from AF in early (3 to 6 months postoperative) (n = 73, 78.1% vs 175, 63.4%; *P* = .02) and intermediate (6 to 12 months postoperative) (68, 86.8% vs 163, 75.3%; *P* = .009) time periods.

In the iAF group, preoperative atrial flutter (*P* = .006) was predictive of inferior success in the early term (n = 18, 55.6% vs 55, 85.5%; *P* = .008). None of the analyzed variables were predictive of intermediate-term SAFA success. In the cAF group, multivariate analysis demonstrated that mitral valve repair/replacement (*P* = .003 and .09), smaller LAS (*P* = .056 and .041), and preoperative absence of atrial flutter (*P* = .047 and .001) were predictive of better early and intermediate freedom from AF. Notably, neither lesion set nor energy source selection was found to have an impact on early and intermediate SAFA success in either the cAF or iAF groups. However, when evaluating the effects of different lesion sets on AF resolution between 6 and 12 months, we found that isolating the pulmonary vein only was more successful (*P* = .05) in the intermittent group (89.2%, n = 37) than in the continuous group (73.3%, n = 75). No statistically significant differences were found in the effectiveness of other lesion sets in the 2 AF groups.

Table. Patient Descriptive Statistics*

	Persistent AF	Paroxysmal AF	Total	*P*	n = 255 (72.2%)	n = 98 (27.8%)	353
Patient-specific characteristics							
Male, n	132	56.1%	55	51.8%	187	53.0%	.463
Age, y	67.9 ± 11.3	65.4 ± 12.4	67.2 ± 11.7	.080			
Left atrial size, cm	6.1 ± 1.5	5.5 ± 1.2	6.0 ± 1.5	.003			
AF duration, y	7.8 ± 8.3	3.3 ± 4.0	6.7 ± 7.7	<.001			
Preoperative ejection fraction, %	49.9 ± 14.3	50.8 ± 13.5	50.2 ± 13.9	.717			
Preoperative atrial flutter, n	59	23.1%	18	18.4%	77	21.8%	.331
Intraoperative variables							
Epicardial lesions, n	46	18.0%	26	26.5%	72	20.4%	.076
Lone AF, n	11	5.0%	3	26.5%	14	3.8%	.660
Concomitant procedures, n							
MVR	192	75.3%	65	66.3%	257	72.8%	.090
AVR	31	18.8%	48	31.6%	79	22.4%	.010
TVR	29	11.4%	8	8.2%	37	10.5%	.378
CABG	66	25.9%	27	27.6%	93	26.4%	.750
ASD	13	5.1%	6	6.1%	19	5.4%	.703
Aortic Root	3	1.2%	1	1.0%	4	1.1%	.901
Approach, n							
Thoracotomy	53	20.8%	19	19.4%	69	19.6%	.920
Sternotomy	202	79.2%	78	79.6%	280	79.3%	.940
Energy source, n							
Laser	35	13.7%	36	26.5%	61	17.3%	.004
Radiofrequency	93	36.5%	25	25.2%	118	33.4%	.051
Microwave	127	49.8%	47	48.0%	174	49.3%	.756
Lesion set, n							
PV only	119	46.7%	55	56.1%	174	49.3%	.112
PVANNLAA	69	27.1%	15	15.3%	84	23.8%	.020
PVANNLS	54	21.2%	23	29.9%	77	21.8%	.640
PVLAA	11	4.3%	5	5.1%	16	4.5%	.750
FLUTTER	28	11.0%	8	8.2%	36	10.2%	.433

*ASD indicates atrial-septal defect; AVR, atrial valve repair/replace; CABG, coronary artery bypass graft; EF, ejection fraction; FLUTTER, right sided flutter lesions; MVR, mitral valve repair/replace; PV, pulmonary vein; PVANNLAA, pulmonary vein with mitral valve annulus and left atrial appendage encircling lesions; PVANNLS, pulmonary vein with mitral valve annulus lesions, PVLAA, pulmonary vein with left atrial encircling lesions, TVR, tricuspid valve repair/replace;.

In ROC/SSLR analysis, the corresponding area under the curve for LAS was 0.60 (0.50-0.70) for failure at 1 year in the cAF group. SSLR analysis generated 2 strata for LAS, <8 cm with an SSLR = 0.87 (CI: 0.74-1.0) and ≥8 cm with an SSLR = 2.98 (CI: 1.07-8.3). Only 47.1% (n = 17) of patients with LAS ≥8cm achieved freedom from AF in the intermediate 6-month to 1-year follow-up period. This result is in contrast to the 75.7% (n = 115) of patients with LAS <8 cm. Additionally, cAF patients with LAS ≥8cm (9.1%, n = 2) were also more likely than cAF patients with LAS <8 cm (1.9%, n = 3) to experience a postoperative thromboembolic event (*P* = .05).

DISCUSSION

In recent years, significant resources have been dedicated to further optimizing SAFA through the development of novel energy sources and variations in lesion sets. However, these efforts have offered only limited improvements in outcome. This analysis was unable to demonstrate any advantage across energy sources or with more extensive lesion sets within each individual AF classification. Although it is likely that certain energy sources or lesion sets are associated with a greater success rate in some patient populations [Gillinov 2006], these variables do not appear to be among the strongest predictors of success. Rather, our findings suggest that the tested biological variables may be a greater determinant of treatment success than intraoperative variables examined in this study.

In the iAF group, only history of atrial flutter was predictive of outcomes. None of the intraoperative variables collected affected intermediate success of the operation in the intermittent AF population. These findings are consistent with theories suggesting that left atrial remodeling occurs as a result of AF after prolonged periods of time [Wijffels 1997; Haissaguerre 1998; Cox 2004b; Van Gelder 2004; Fuster 2006]. In intermittent AF, it is reasonable to assume that isolation of pulmonary veins is sufficient, because chronic remodeling has not taken place and changes in atrial size and ejection fraction are less likely. The reported success rate of 89.2% in 6- to 12-month follow-up demonstrates that intermittent AF was effectively treated with PVI alone. This finding is consistent with Haissaguerre et al's seminal paper implicating the pulmonary veins as the site of initiation for paroxysmal AF [Haissaguerre 1998].

In contrast, in the continuous AF group, mitral valve repair/replacement, smaller LAS, and preoperative absence of atrial flutter were predictors of short-term and intermediate success. Each of these patient-specific variables is related to pathological processes that are not directly corrected by SAFA.

Our finding that lesion sets more extensive than the pulmonary vein-isolating lesion did not impact SAFA outcome may seem contradictory to macroreentrant theories of AF perpetuation [Cox 2004a] as well as clinical data presented elsewhere [Gillinov 2006]. This discrepancy may be due to smaller sample size and the associated reductions in statistical sensitivity. The mitral valve annulus and LAA lesions in the Cox-Maze III procedure are created to inhibit atrial fibrillation by limiting tissue in which macroreentrant circuits can form. It is also possible that the circumferential PVI lesion used in our institution achieves the same electrophysiological isolation of the left atrium as additional lesions (Figure 2).

We also found that energy source did not affect AF resolution. This lack of detected distinctions between energy sources may have occurred because the data were not analyzed by lesion location. The transmurality of epicardial lesions can be compromised by the convective cooling of endocardial blood as well as the impedance effect of fat on conductive heating. Although 20.4% (n = 72) of our study population received epicardial lesions, a majority of these were created with the microwave source (72.2%, n = 52). The small sample sizes for the remaining energy sources, as well as the uneven sampling distribution by energy sources prevented meaningful statistical analysis.

Study Limitations

This study was a retrospective analysis and not a randomized trial examining specific patient characteristics and intraoperative variables such as lesion set and energy source. As a result, these findings may be confounded by variations in patient population and surgeon preference in operative techniques. Such confounding seems less likely, however, because lesion set and energy source did not appear to influence outcome. In addition, although close follow-up was maintained on all patients, continuous cardiac monitoring was not part of the treatment protocol for all patients. Although a transtelephonic ECG device was made available to patients, only a subset of patients chose to use it (n = 122, 34.6%), a situation that introduces 2 sources of potential follow-up bias. The first is an overestimation of AF at later time points owing to the tendency of patients with symptomatic AF to have better follow-up. The second is that collected rhythms were available only for specific time points, making it possible that the prevalence of postoperative AF was underreported owing to episodes of paroxysmal AF. The capture of daily rhythms by the transtelephonic ECG devices was an attempt to correct for the latter issue and has been shown to be effective at capturing recurrences of atrial fibrillation [Senatore 2005].

Lastly, neither intraoperative assessment of electrical isolation of the ablated tissue nor pathological tissue analysis was performed. As a result, it is impossible to determine whether failure of SAFA can be attributed to technical error rather than the existence of pathological processes that cannot be corrected by SAFA. Without a prospective randomized controlled trial, the significance of different lesion sets and energy modalities cannot be established.

CONCLUSION

In the intermittent AF group, only history of atrial flutter was predictive of outcome, and only in short-term results. In the continuous AF group, mitral valve disease in need of surgical repair, smaller LAS, and absence of preoperative atrial flutter were predictors of short-term and intermediate-term success. The results of this study imply that preoperative patient-specific characteristics may have more influence on

SAFA outcome than the intraoperative variables we examined. Moreover, these findings suggest that biology may be a major determinant of SAFA success. Although intermittent-AF patients achieve acceptable SAFA success rates when only the pulmonary vein–isolating lesion is used, the lower resolution rate for continuous AF patients suggests that this population may not be amenable to this single therapeutic approach. Future work should stratify patients with continuous AF by risk and likelihood of AF resolution, with the intent of identifying patient selection criteria for the SAFA treatment option. Additionally, development of adjunctive treatments that modify the biological substrate, such as novel pharmacological treatment or parasympathetic denervation, may be necessary to improve the success of SAFA in patients with continuous AF [Barbuti 2002; Wirth 2003; Pappone 2004; Williams 2006; Kuo 2007].

REFERENCES

Barbuti A, Ishii S, Shimizu T, Robinson RB, Feinmark SJ. 2002. Block of the background K+ channel TASK-1 contributes to the arrhythmogenic effects of platelet-activating factor. Am J Physiol Heart Circ Physiol 282:H2024-30.

Chen JM, Levin HR, Michler RE, Prusmack CJ, Rose EA, Aaronson KD. 1997. Reevaluating the significance of pulmonary hypertension before cardiac transplantation: determination of optimal thresholds and quantification of the effect of reversibility on perioperative mortality. J Thorac Cardiovasc Surg 114:627-34.

Cox JL. 2004. Cardiac surgery for arrhythmias [Review]. J Cardiovasc Electrophysiol 15(2):250-62.

Cox JL. 2004. Surgical treatment of atrial fibrillation: a review. Europace. 5 Suppl 1:S20-9.

Cox JL, Ad N, Palazzo T, et al. 2000. Current status of the Maze procedure for the treatment of atrial fibrillation. Semin Thorac Cardiovasc Surg 12:15-9.

Fuster V, Ryden LE, Cannom DS, et al. 2006. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation) developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation. 114(7):e257-354.

Gillinov AM, Blackstone EH, McCarthy PM. 2002. Atrial fibrillation: current surgical options and their assessment [Review]. Ann Thorac Surg. 74(6):2210-7.

Gillinov AM, Bhavani S, Blackstone EH, et al. 2006. Surgery for permanent atrial fibrillation: impact of patient factors and lesion set. Ann Thorac Surg 82(2):502-13; discussion 513-4.

Haissaguerre M, Jais P, Shah DC, et al. 1998. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. New Engl J Med 3(339):659-66.

Handa N, Schaff HV, Morris JJ, Anderson BJ, Kopecky SL, Enriquez-Sarano M. 1999. Outcome of valve repair and the Cox maze procedure for mitral regurgitation and associated atrial fibrillation. J Thorac Cardiovasc Surg 118(4):628-35.

Hanley JA, McNeil BJ. 1982. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 143:29-36.

Hanley JA, McNeil BJ. 1983. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 148:839-43.

Kuo JY. Chen SA. 2007. Is vagal denervation a good alternative or just adjunctive to pulmonary vein isolation in catheter ablation of atrial fibrillation. J Am Coll Cardiol 49(12):1349-51.

Mohr FW, Fabricius AM, Falk V, et al. 2002. Curative treatment of atrial fibrillation with intraoperative radiofrequency ablation: short-term and midterm results. J Thorac Cardiovasc Surg 123:919-27.

Pappone C, Santinelli V, Manguso F, et al. 2004. Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation, Circulation 109:327-34.

Pierce JC, Cornell RG. 1993. Integrating stratum-specific likelihood ratios with the analysis of ROC curves. Med Decis Making 13:141-51.

Senatore G, Stabile G, Bertaglia E, et al. 2005. Role of transtelephonic electrocardiographic monitoring in detecting short-term arrhythmia recurrences after radiofrequency ablation in patients with atrial fibrillation. J Am Coll Cardiol 45:873-6.

Sie HT, Beukema WP, Ramdat Misier AR, Elvan A, Ennema JJ, Wellens HJ. 2001. The radiofrequency modified maze procedure: a less invasive surgical approach to atrial fibrillation during open-heart surgery. Eur J Cardiothorac Surg 19(4):443-7.

Spitzer G, Richter P, Knaut M, Schuler S. 1999. Treatment of atrial fibrillation in open heart surgery: the potential role of microwave energy. Thorac Cardiovasc Surg 47:374-8.

Van Gelder IC, Hemels ME. 2004. The progressive nature of atrial fibrillation: a rationale for early restoration and maintenance of sinus rhythm. Pacing Clin Electrophysiol 27(2):266-82.

Williams MR, Russo MJ, Oz MC, Argenziano M. Epicardial cardiac ablation using laser energy. Heart Surg Forum. 2006;9(2):E598-600.

Wijffels MC, Kirchhof CJ, Dorland R, Power J, Allessie MA. 1997. Electrical remodeling due to atrial fibrillation in chronically instrumented conscious goats: roles of neurohumoral changes, ischemia, atrial stretch, and high rate of electrical activation. Circulation. 96(10):3710-20.

Wirth KJ, Paehler T, Rosenstein B, et al. 2003. Atrial effects of the novel K(+)-channel-blocker AVE0118 in anesthetized pigs. Cardiovasc Res 60(2):298-306.