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Early and Late Outcome after Microwave Ablation for Chronic Valvular Atrial Fibrillation

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ABSTRACT

Background: Microwave energy ablation is one of the newer therapeutic options for surgically treating patients with chronic atrial fibrillation (AF) concomitant with mitral valve disease. The aim of this study was to retrospectively evaluate potential risk factors that may have influenced early as well as remote outcome in a set of patients undergoing microwave energy ablation for chronic AF.

Methods: Patients (n = 42) underwent ablation on an arrested heart concomitant with mitral valve surgery. Twelve patients also underwent tricuspid valve repair or replacement. Logistic regression analyses were performed to evaluate effect of potential risk factors on postablation rhythm status at discharge and at latest follow-up examination.

Results: With control for age, patients with recurrent AF at discharge (10/42 [24%]) tended to have preoperative AF of significantly longer duration (odds ratio [OR], 1.64; 95% confidence interval [CI], 1.15-2.35; *P* = .01) and greater left atrial diameter (OR, 1.14; 95% CI, 1.03-1.26, *P* = .01) than patients in sinus rhythm (32/42 [76%]). At latest follow-up examination, risk of AF was significantly heightened with longer duration of preoperative AF (OR, 1.47; 95% CI, 1.09-1.96; *P* = .01) and larger left atrium (OR, 1.12; 95% CI, 1.02-1.23; P = .02) after adjustment for age, length of follow-up time, and presence of early arrhythmia recurrence.

Conclusions: Results for this consecutive series of patients indicated that early and late success after surgical energy ablation may be associated with discrete patient characteristics. Longer arrhythmia duration and greater left atrial diameter seem to be factors independently influencing early and remote success, and there seems to be a self-protective effect of the presence of sinus rhythm at discharge. Further study would be valuable to confirm our findings.

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INTRODUCTION

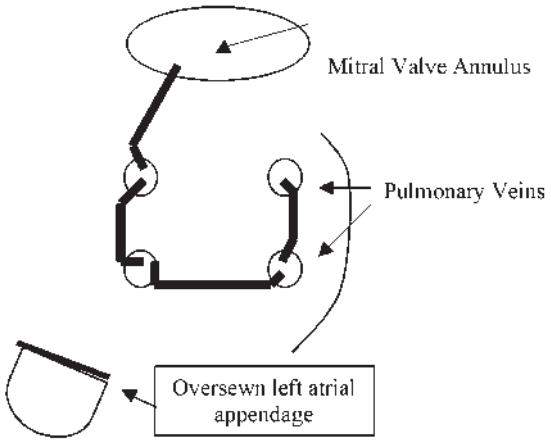
Mitral valve disease is commonly associated with atrial cardiomyopathy and atrial fibrillation (AF) [Sueda 1997, Kalil 1999]. After a routine mitral valve procedure, there is little likelihood of spontaneous restoration of sinus rhythm in patients with concomitant AF. Past investigation has demonstrated 20% to 30% probability of success without some other form of intervention [Sueda 1997, Gaita 2000]. With adjunctive drug and electrical cardioversion, this proportion may improve to 40% or 50% [Coplen 1990, Vigano 1996]. Such discouraging results have promoted the development of surgical therapies, namely tissue ablation techniques, for treating patients with concomitant AF.

The maze cut-and-sew procedure, developed by James Cox, is considered the gold standard regarding potential for achieving good clinical success in this patient population [Cox 2000]. However, because the maze procedure can be difficult to perform, prolongs cardiopulmonary bypass time, and may not be appropriate for some patients, use of energy ablation to emulate the maze cut-and-sew technique has been under rapid development. Our clinical site has recently adopted microwave energy for treating AF in our mitral valve patients. We have been satisfied overall with our clinical results after microwave energy ablation; however, we have had patients who experienced early recurrence of AF after the procedure. Results of past investigations have indicated that selected patient characteristics, or risk factors, may affect clinical outcome after cardiac ablation [Haïssaguerre 2000, Pasic 2001]. The aim of this study was to evaluate the effect of important demographic and clinical variables on early rhythm status and on late outcome in a set of patients with chronic AF who presented normally for mitral valve surgery and underwent surgical microwave energy ablation.

MATERIAL AND METHODS

Patients

Forty-two consecutive patients who underwent mitral valve repair or replacement and received microwave energy ablation were included in this study. Mitral pathology was rheumatic in all patients but 1, in whom it was due to infective endocarditis. Twelve (28%) of the 42 patients underwent additional tricuspid valve repair or replacement. All patients had chronic AF for 6 months or longer and documented 2 or



Lesion pattern used for surgical treatment of chronic atrial fibrillation in patients undergoing a concomitant mitral valve procedure.

more times with standard electrocardiography (ECG). Informed written consent for study participation was obtained from the patients.

Surgical Ablation Procedure

Energy ablation was performed with the Microwave Ablation System (AFx, Fremont, CA, USA) and the Flex 2 ablation probe (AFx). The system emits modulated microwaves at 2.45 GHz; power application for each lesion was 40 W over 25 seconds. The ablation portion of the procedure was conducted on the arrested heart on cardiopulmonary bypass immediately prior to valve replacement or reconstruction.

The objective of the ablation procedure was to create continuous ablation lines linking the mitral valve annulus to the region of the ostia of the pulmonary veins. Ablation lines were made under direct view of the surgeon, beginning from the mitral annulus, directed up to the ostium of the left inferior vein, and then to the left superior, right superior, and right inferior pulmonary vein ostia, respectively (Figure). Pulmonary vein lesions were extended 10 mm into the interior of each pulmonary vein. All lesions were placed in the left atrium. The lesion set has been previously described [Knaut 1999]. The left atrial appendage was oversewn.

Postoperative Care

Patients received 80 to 120 mg sotalol daily, unless it was contraindicated, until 90 days postoperatively if stable sinus rhythm was demonstrated. One patient, who showed signs of sotalol intolerance, received amiodarone (200 mg/day). In patients who presented with AF recurrence in the postoperative period, or in patients who did not spontaneously convert to sinus rhythm after the ablation procedure, increasing doses of sotalol up to 240 mg/day were administered. Electrical cardioversion was carried out in patients in whom pharmacological attempts to convert the rhythm were unsuccessful. Cardioversion was performed after the patient was stabilized and demonstrated remission of pleural and/or pericardial effusion, normal blood pressure, and electrolyte and hematocrit levels. If the initial cardioversion was unsuccessful or AF recurred, a second cardioversion was performed 5 days later. Rhythm status was monitored during the hospital stay with standard 12-lead ECG, which was performed daily until discharge. A 24-hour Holter monitor ECG was captured just prior to discharge.

After hospital discharge, patients' cases were followed as usual and customary for a mitral valve procedure. Holter monitor ECG data were collected at specified postoperative time points. For patients with persisting postoperative AF, prophylactic therapy was administered according to the discretion of the attending physician.

Statistical Analysis

Logistic regression analyses were performed to evaluate the effect of risk factors on rhythm status, determined with 24-hour Holter-monitoring, at 2 different postoperative time points—hospital discharge and most recent follow-up evaluation. Patients were retrospectively classified into 1 of 2 outcome groups at each time point. The sinus rhythm group consisted of patients who showed stable sinus rhythm over the 24-hour monitoring period; the AF group demonstrated evidence of AF.

Risk factor variables were entered into each multivariate model on the basis of statistical significance ($P \leq .10$) revealed in univariate analyses or if they were considered to have potential clinical relation to other factors. Factors examined included sex, age, AF duration, left atrial diameter measured with echocardiography, etiology of mitral pathology (rheumatic, endocarditic), type of mitral lesion (mitral insufficiency, mitral stenosis, or complex lesion), type of surgical procedure (mitral valve, mitral valve and tricuspid valve), and surgical order (initial 15 cases, subsequent 27 cases). Presence of stable sinus rhythm at discharge and incidence of early AF recurrence were additionally evaluated as factors influencing late outcome. The effect of length of follow-up time was considered in the model evaluation of rhythm status at most recent follow-up examination.

RESULTS

At discharge, 32 (76.2%) of 42 patients demonstrated stable sinus rhythm, and 10 (23.8%) of 42 patients showed evidence of AF. There were no in-hospital complications or deaths. Three patients needed permanent pacemaker implantation because of symptomatic bradycardia. In 26 (61.9%) of 42 patients, AF recurred during the early postoperative period (6.7 ± 6.9 day; range, 0-33 days). Sixteen (61.5%) of the patients converted successfully to SR: 4 after increased doses of sotalol were administrated, 10 by means of cardioversion, and 2 spontaneously. Ten patients, in whom pharmacological attempts and subsequent first and second attempts at cardioversion failed to restore stable sinus rhythm, were discharged in AF. One patient (female, 60 years old) who was discharged in AF, died 8 months postoperatively because of a fatal cerebral thromboembolic event. Postoperative follow-up (7.3 ± 3.7 months; range, 1-14 months) was uneventful for all other patients. The 10 patients who demonstrated AF at discharge remained in AF at last follow-up

Table 1. Surgical Procedure and Indications for Surgery*

	All (n = 42)	AF at discharge (n = 10)	AF at last follow-up examination (n = 14)
Mitral pathology			
Rheumatic	41 (97.6%)	10 (100%)	14 (100%)
Endocarditic	1 (2.4%)		
Mitral disease			
Mitral regurgitation	11 (26.2%)	3 (30.0%)	4 (28.6%)
Complex lesion	26 (61.9%)	6 (60.0%)	9 (64.3%)
Mitral stenosis	5 (11.9%)	1 (10.0%)	1 (7.1%)
Surgical procedure			
Mitral valve replacement	36 (85.7%)	10 (100%)	13 (92.9%)
+Tricuspid valve replace	1 (2.4%)	0	1 (7.1%)
+Tricuspid valve repair	10 (23.8%)	3 (30.0%)	3 (21.4%)
Mitral valve repair	6 (14.3%)	0	1 (7.1%)
+Tricuspid valve repair	1 (2.4%)	0	0

*AF indicates atrial fibrillation.

examination (2-14 months) and received postoperative therapy at the discretion of their attending physicians. Three patients, who were in sinus rhythm at discharge, had AF recurrence at the most recent follow-up examination (4, 12, and 13 months, respectively). In 1 patient, who was discharged in sinus rhythm, atypical atrial flutter recurred 3 months after the procedure. For this particular patient, invasive electrophysiological study was performed, and arrhythmia, which was shown to involve the left atrium, was cured by percutaneous ablation with radiofrequency (RF) current.

Distribution of mitral pathology, mitral disease, and surgical procedure in outcome groups is presented in Table 1. Most patients received mitral valve replacement, 28% of them undergoing an additional tricuspid valve procedure.

Left atrial diameter and AF duration were significantly associated with AF at discharge (Table 2). It was interesting that male sex showed a protective effect against AF; however, this finding was not statistically significant. Results were similar in univariate analyses of risk factors for recurrence of AF at the most recent follow-up examination (Table 3). Patients in the AF group were more likely to be older (but the difference did not reach statistical significance) and have significantly larger left atrial diameter and preoperative AF of longer duration than those in the sinus rhythm group. Average follow-up time did not differ significantly between rhythm status groups ($P = .41$).

Multivariate analyses were performed for simultaneous assessment of risk factors (Table 4). Although age was constant, risk of having AF at hospital discharge was heightened significantly with larger left atrial diameter (model 1) and with longer AF duration (model 2). In simultaneous evaluation of left atrial diameter and AF duration, both factors were significantly associated with probability of sinus rhythm at discharge (model 3).

Age, left atrial diameter, AF duration, length of follow-up time, and in-hospital arrhythmia recurrence were included in the multivariate analysis for evaluation of risk factors for AF at the most recent follow-up examination (model 4). With simultaneous control for these 5 important factors, preoperative AF duration and left atrial diameter emerged as the only variables in the set that significantly heightened risk of AF recurrence. The odds ratios suggested that risk of recurrent AF in the postoperative period following the ablation procedure approximately doubled for every additional year of preoperative AF duration and rose by 21% for every additional millimeter of left atrial diameter in this mitral valve population. Presence of stable sinus rhythm at discharge could not be successfully combined into logistic models predicting AF

Table 2. Univariate Analysis of Risk Factors for Atrial Fibrillation Recurrence at Hospital Discharge*

	Sinus Rhythm (n = 32)	Atrial Fibrillation (n = 10)	Unadjusted Odds Ratio [±95% CI]
Sex			1.59 ($P = .55$) [0.33, 7.69]
Male	13 (55%)	3 (30%)	
Female	19 (45%)	7 (70%)	
Age, y	55.5 ± 8.5	57.4 ± 7.8	1.03 ($P = .52$) [0.94, 1.13]
Median, range	58.0, 39-68	58.5, 47-73	
Atrial fibrillation duration, y	3.6 ± 2.3	7.4 ± 3.5	1.64 ($P = .01$) [1.15, 2.35]
Median, range	3.0, 0.50-8.0	7.0, 2.0-13.0	
Left atrial diameter, cm	54.9 ± 7.5	65.4 ± 9.9	1.14 ($P = .01$) [1.03, 1.26]
Median, range	55.0, 43.0-80.0	64.0, 53.0-83.0	
Surgery order			1.27 ($P = .75$) [0.28, 5.73]
Initial cases (n = 15)	11 (34.4%)	4 (40.0%)	
Remainder of cases (n = 27)	21 (65.6%)	6 (60.0%)	
Procedure type			1.09 ($P = .91$) [0.22, 5.45]
Mitral only	23 (71.8%)	7 (70.0%)	
Mitral + tricuspid	9 (28.1%)	3 (30.0%)	

*CI indicates confidence interval.

Table 3. Univariate Analysis of Risk Factors for Atrial Fibrillation at Most Recent Follow-up Examination*

	Sinus Rhythm (n = 28)	Atrial Fibrillation (n = 14)	Unadjusted Odds Ratio [±95% CI]
Sex			1.16 (*P* = .82) [0.29, 4.59]
Male	11 (39.3%)	5 (35.7%)	
Female	17 (60.7%)	9 (64.3%)	
Age, y	54.7 ± 8.4	58.3 ± 7.7	1.06 (*P* = .19) [0.97, 1.15]
Median, range	55.5, 39-68	59.0, 47-73	
Duration of atrial fibrillation, y	3.5 ± 2.4	6.5 ± 3.3	1.47(*P* = .01) [1.09, 1.96]
Median, range	2.5, 0.5-8.0	5.5, 2.0-13.0	
Left atrial diameter, mm	54.6 ± 7.8	63.0 ± 9.4	1.12 (*P* = .02) [1.02, 1.23]
Median, range	54.5, 43.0-80.0	60.0, 51.0-83.0	
Follow-up time, mo	7.0 ± 3.6	8.1 ± 4.1	1.08 (*P* = .40) [0.89, 1.31]
Median, range	7.0, 1.0-14.0	8.0, 2.0-14.0	
Surgery order			1.58 (*P* = .49) [0.40, 6.19]
Initial (n = 15)	9 (32.1%)	6 (42.8%)	
Remainder (n = 27)	19 (67.8%)	8 (57.1%)	
Procedure type			1.00 [0.23, 4.32]
Mitral only	20 (71.4%)	10 (71.4%)	
Mitral + tricuspid	8 (28.6%)	4 (28.6%)	
Early recurrence of atrial fibrillation	15 (53.6%)	11 (78.6%)	3.17 (*P* = .13) [0.69, 14.57]

*CI indicates confidence interval.

at the follow-up examination, most likely because of effects of the well-known intercorrelation between the variables (multicollinearity) and/or the fact that all the patients who were discharged in AF remained in arrhythmia at the last follow-up examination. However, 28 (100%) of the patients who were in sinus rhythm at follow-up and only 4 (28.6%) of 14 patients demonstrating late AF were discharged in stable sinus rhythm ($P < .001$).

COMMENT

Atrial fibrillation, one of the most common cardiac arrhythmias, is associated with excess morbidity, decreased quality of life, and early mortality. Basic research over the last 20 years has supported the hypothesis proposed by Moe in the late 1950s that AF, in most cases, is a result of propagating multiple reentrant wavelets, which manifest as rapid and irregular myocardial electrical activity [Moe 1959, 1962]. As a consequence of this wavelet activity, atrial systolic function is diminished, and this effect can reduce stroke volume up to 25%. The result is the symptoms and health risks observed with AF.

Our finding that clinical success following surgical ablation may be affected by the presence of risk factors related to myocardial health gives biologic plausibility to previous experimental study of the relationship between AF and atrial cardiomyopathy. Atrial cardiomyopathy is associated with anatomic and electrophysiological remodeling, most notably changes in substrate refractory period, amplitude and duration of action potential, and conduction velocity. These modifications appear to establish an environment that facilitates multiple reentry activity [Wijffels 1995]. Experimental animal model studies have shown that when AF is maintained over time it tends to recur more frequently and finally becomes sustained [Wijffels 1995]. The progressive self-perpetuating nature of this arrhythmia, aptly described as "AF begets AF," occurs simultaneously with electrophysiological atrial substrate remodeling [Wijffels 1995]. Atrial enlargement is a well-known precipitating factor of AF and has been shown to be associated with myocardial fibrosis as well as nonhomogeneous conduction, unidirectional block, and reentry. These

Table 4. Multivariate Analysis of Risk Factors for Atrial Fibrillation (AF) at Hospital Discharge and at Latest Follow-up Examination*

	Adjusted Odds Ratio	95% CI (*P* Value)
At hospital discharge		
Model 1		
Age	1.09	0.98, 1.20 (.12)
LA diameter	1.13	1.03, 1.25 (.01)
Model 2		
Age	1.03	0.93, 1.13 (.58)
AF duration	1.44	1.07, 1.94 (.02)
Model 3		
AF duration	2.33	1.19, 4.56 (.01)
LA diameter	1.25	1.06, 1.48 (.01)
Most recent follow-up examination		
Model 4		
Age	1.11	0.94, 1.33 (.21)
LA diameter	1.21	1.01, 1.46 (.04)
Follow-up time	1.15	0.83, 1.60 (.38)
AF duration	2.14	1.09, 4.19 (.03)
Early AF recurrence	0.50	0.04, 6.50 (.59)

*CI indicates confidence interval; LA, left atrial.

changes are a potential milieu for perpetuation of multiple reentry circuits. Moreover, it is well known that a critical mass of circulating wavelets must be present for AF to occur. Increased atrial size would permit the coexistence of many reentrant circuits and thus facilitate arrhythmia recurrence and stability. On the basis of results of the present study we concluded that patients who were unable to maintain stable sinus rhythm in the perioperative as well as the postoperative period following microwave energy ablation tended to have longer preoperative AF duration and relatively larger atrial diameter. Both parameters are associated with cardiomyopathy and appear likely to increase "resistance" to surgical ablation treatment of chronic AF.

The literature is mixed in terms of effects of patient characteristics on postoperative outcome following atrial ablation. Our observations are consistent with reports by Haïssaguerre and colleagues [2000], who showed that identification of multiple (as opposed to 1) arrhythmogenic pulmonary veins was associated with older age, longer AF duration, and larger atrial dimension. Pasic [2001] evaluated a large number of factors for associated risk of predisposition to postoperative AF recurrence in patients who underwent concomitant valve or coronary artery bypass surgery. After univariate analyses, these authors reported significantly increased risk of recurrence for patients who appeared to be "sicker," in particular those with mitral stenosis or coronary artery disease, and in patients who had lengthier coronary artery bypass or operative times. Pasic et al found no association between AF duration or left atrial diameter and AF recurrence; however, the difference in their findings from ours may have been a result of confounding by inclusion of both coronary artery bypass and valve patients in the same analysis set. Oral and associates compared postoperative rhythm status outcome for patients with paroxysmal AF and patients with persistent AF [Oral 2002]. Recurrence was significantly more frequent in patients with more persistent AF, but the investigators found no differences between populations in other potential clinical predictors, including left atrial size and duration of AF. It would be valuable to confirm our findings with a larger set of patients to fully characterize relationships between risk factors and to define effects on outcome.

Use of microwave energy surgical ablation is a relatively new approach for treating rheumatic AF. Surgical energy ablation has been designed to emulate the maze procedure, in which the aim is to compartmentalize the atrial walls into electrically isolated areas by placing linear lesions to interrupt propagation of reentrant wavelets. Clinical results for our patient set demonstrated a success rate similar to those previously described for atrial ablation with mitral valve surgery. Sueda and colleagues [1997], after using a left atrial approach in the arrested heart as we did but using the maze cut-and-sew procedure, reported a success rate of 86% at hospital discharge. Gaita and colleagues [2000] reported 74% success at discharge after use of a left atrial approach with cryoablation. With RF ablation, Pasic et al [2001] reported 25% success at 1 week and 59% at 1 month. Williams and his group reported 64% success at hospital discharge. In our study group, 76% of patients were in sinus rhythm at discharge [Williams 2001].

Short-term postoperative results for our group after microwave energy ablation were encouraging. Our 66% success rate at an average follow-up time of 7.3 ± 3.7 months compares similarly with other literature reports. The Sueda cohort demonstrated a success rate of 78% 3 months after surgical ablation [Sueda 1997]. Gaita reported 68% success following surgical cryoablation alone and 87% success with additional postablation intervention, including RF ablation and antiarrhythmic drugs [Gaita 2000]. Cox et al suggested that in the first 3 months AF recurrence rate may be expected to be between 30% and 40% in patients surgically treated for chronic AF with the classic maze procedure [Cox 2000]. However, although more than 60% of patients presented with AF recurrence in the early postoperative period, this factor alone showed no influence on late results. Similar results were found by others [Cox 2000]. On the other hand, in our study presence of sinus rhythm at discharge showed a self-protecting effect during follow-up, a finding that may suggest that sinus rhythm begets sinus rhythm in this group of patients. These intriguing phenomena probably can be attributed to time dependency, which determines resolution of atrial remodeling after long-lasting AF [Wijffels 1995]. Self-perpetuation of sinus rhythm highlights the value of aggressive prophylactic treatment in the early postoperative period in an attempt to maintain physiological rhythm.

Surgical ablation with microwave energy is moderately invasive but prolongs the routine arrested heart operation by only 15 to 20 minutes. Microwave energy surgical ablation used in this way, like the maze procedure, has a significant limitation—it is impossible to verify effectiveness of electrical block during the operation. Success rate seems to depend on uninterrupted continuity of ablation lines, which at present can be confirmed only macroscopically by the operator. Development of capability to objectively verify lesion continuity or immediate success intraoperatively, which in our opinion could improve the success rate of microwave energy surgical ablation, would be beneficial.

The question of what lesion set provides the highest efficiency and effectiveness, combined with minimal risk to the patient, remains debatable. For mitral valve patients, we prefer to use a left atrial approach. The pattern we have selected, an unclosed square shape to isolate the region around the pulmonary veins, protects the posterior wall of the atrium from electrical isolation, a condition that could lead to rhythm asynchrony or dyssynchrony and increased risk of thrombosis. Our decision to extend ablation into the ostia was based on results of this previous study. It has been demonstrated that 90% or more of focal reentrant is initiated within the pulmonary vein ostia. Recent evidence of pulmonary hypertension and pulmonary vein stenosis attributed to RF catheter ablation of the pulmonary vein ostia has been reported, the incidence being between 10% and 15% [Haïssaguerre 2000]. The mechanism by which this phenomenon occurs is not clear, but results of animal studies have indicated that hemodynamic and pathologic changes can be significant in the first 3 months following focal RF catheter ablation. Yu et al showed that focal pulmonary vein stenosis probably occurs frequently after RF catheter ablation. These authors,

however, reported that in most cases stenosis is not clinically significant, although risk of symptomatic pulmonary hypertension rose when ablation was performed over 2 or more veins [Yu 2001]. We observed no cases of either pulmonary hypertension or pulmonary vein stenosis in up to 14 months of follow-up. Our observation is supported by more than 2 years of clinical experience in Dresden, Germany, after performance of approximately 200 procedures with no complications arising from pulmonary vein stenosis [M. Knaut, personal communication]. Haïssaguerre and colleagues suggested the incidence of pulmonary vein stenosis was related to RF exposure, 45 W appearing to be the critical level [Haïssaguerre 2000]. Without direct experimental comparative work, it is difficult to define the critical boundary for microwave energy. However, microwave energy heats tissue differently from RF and requires less intense direct tissue exposure to create a lesion of the same depth. This difference in tissue heating may result in differences in tissue healing response over time.

Results of this limited retrospective study suggested that selected patient characteristics may affect early outcome following surgical ablation. Furthermore, large-scale investigation is necessary to fully define the impact of these potential risk factors. Microwave energy appears to provide a good treatment alternative for patients with chronic AF concomitant with mitral valve disease, although further characterization of clinical experience would be beneficial for determining long-term efficacy over a broader-based patient population.

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