

Pulmonary Vein Antral Isolation Using an Open Irrigation Ablation Catheter for the Treatment of Atrial Fibrillation

A Randomized Pilot Study

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Objectives	We sought to test how catheter ablation using an open irrigation catheter (OIC) compares with standard catheters for pulmonary vein antrum isolation.
Background	Open irrigation catheters have the advantage of delivering greater power without increasing the temperature of the catheter tip, which enables deeper and wider lesions without the formation of coagulum on catheters.
Methods	Catheter ablation was performed using an 8-mm catheter (8MC) or an OIC. Patients were randomized to 3 groups: 8MC; OIC-1, OIC with a higher peak power (50 W); and OIC-2, OIC with lower peak power (35 W).
Results	A total of 180 patients were randomized to the 3 treatment strategies. Isolation of pulmonary vein antra was achieved in all patients. The freedom from atrial fibrillation was significantly greater in the 8MC and OIC-1 groups compared with the OIC-2 group (78%, 82%, and 68%, respectively, $p = 0.043$). Fluoroscopy time was lower in OIC-1 compared with OIC-2 and 8MC (28 ± 1 min, 53 ± 2 min, and 46 ± 2 min, respectively, $p = 0.001$). The mean left atrium instrumentation time was lower in the OIC-1 compared with the OIC-2 and 8MC groups (59 ± 3 min, 90 ± 5 min, and 88 ± 4 min, respectively, $p = 0.001$). However, there was a greater incidence of "pops" in the OIC-1 (100%, 0%, 0%, $p < 0.001$) along with higher incidences of pericardial effusion (20%, 0%, 0%, $p < 0.001$) and gastrointestinal complaints (17% in OIC-1, 3% in 8MC, and 5% in OIC-2, $p = 0.031$).
Conclusions	Although there was a decrease in fluoroscopy and left atrium instrumentation time with the use of OIC at higher power, this setting was associated with increased cardiovascular and gastrointestinal complications. (<i>J Am Coll Cardiol</i> 2007;49:1634–41) © 2007 by the American College of Cardiology Foundation

Radiofrequency (RF) catheter ablation has emerged in the past several years as an effective and curative approach for patients with symptomatic atrial fibrillation (AF) that is refractory to medical therapy (1–3). However, with current technology, this procedure is complex and time consuming, requiring delivery of many ablation lesions in the left and right atria. Although this procedure traditionally has been performed using a 4- or 8-mm RF catheter, such a catheter has many limitations, including coagulum formation and insufficient power delivery in areas of low blood flow.

Open irrigation catheters (OICs), however, are less likely to encounter these limitations and have been shown to result in larger lesion size and volume compared with traditional RF catheters (4–8), in part because of the prevention of coagulum and char formation at the catheter-tissue interface, which in turn prevents elevation in impedance. Additionally, with greater irrigation rates, the effect of blood flow on power delivery becomes minimal, making the OIC effective in both low and high blood flow areas (9). There are multiple preset power and irrigation-rate settings that are being used with OIC. These settings were mostly formed on the basis of in vivo and in vitro animal studies, and none was evaluated specifically for pulmonary vein (PV) isolation. We hypothesized that an OIC is superior to an 8-mm catheter (8MC) to achieve pulmonary vein antrum isolation (PVAI) for catheter ablation of AF.

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Methods

This study was in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines. It was performed with the subjects' written informed consent. The study protocol was approved by the institution board review committees in all centers involved.

Study population. This was a multicenter study that enrolled patients referred for PVAI. Patients between the ages of 18 to 80 years with symptomatic AF who had failed at least one antiarrhythmic medication were enrolled in the trial. Patients with previous PVAI procedure or history of esophageal or swallowing disorder were excluded from the study. Patients were randomized using a computer-generated program to either a dual-sensor 8-mm tip Celsius DS (Biosense Webster, Diamond Bar, California), a 3.5-mm ThermoCool open-irrigation tip catheter (Biosense Webster) using a higher power (50 W) and higher irrigation flow rate (30 ml/min; OIC-1) or a 3.5-mm ThermoCool open irrigation tip catheter using a lower power (35 W) and lower irrigation flow rate (17 to 30 ml/min; OIC-2). Crossovers were permitted at the end of the procedure if electrical isolation of the PV antra could not be achieved using the assigned catheter.

PVAI procedure. Four sheaths were placed: 1 in the right internal jugular vein, 1 in the left femoral vein, and 2 in the right femoral vein. A 20-polar catheter was placed from the right internal jugular vein into the coronary sinus with the 10 distal electrodes in the coronary sinus and 10 proximal electrodes positioned against the lateral wall of the right atrium. An Acunav intracardiac echocardiography (ICE) catheter (Siemens Acuson, Mountain View, California) was placed via the left femoral vein and was positioned in the right atrium. Via the right femoral vein, left atrial (LA) instrumentation was performed with double trans-septal puncture using ICE and fluoroscopic guidance. Systemic anticoagulation was initiated just before the first trans-septal puncture, using intravenous heparin with a target activated clotting time of approximately 400 s. A fixed-radius decapolar Biosense LASSO circular mapping catheter (Biosense Webster) was used for mapping the PV antra. Ablation along the PV antrum was performed until disappearance of local PV potential. The end point of the procedure was electrical isolation of all PV antra. Entry block generally was verified when no PV potentials could be recorded along the antrum or inside the PV by the circular mapping catheter. When present, electrical dissociation of the PV from the LA also was used to confirmed exit block. After isolation of all 4 PV antra, catheters were withdrawn to the right atrium. Potentials at the right atrium-superior vena cava junction were mapped and ablated if there was no phrenic nerve capture during high-output pacing from these sites. At the end of the procedure, systemic anticoagulation was discontinued and partially reversed with intravenous protamine before the removal of vascular sheaths.

Intraprocedure power titration.

In the OIC group, an esophageal temperature (ET) probe was inserted before the beginning of the procedure. In the power-control mode, RF power was initially set at either 30 W (OIC-1) or 10 W (OIC-2), with a maximum temperature limit of 45°C. Power was then titrated by a 5-W increase every few seconds up to a maximum of 50 W (OIC-1) or 35 W (OIC-2). The OIC was irrigated using heparinized saline infusion (2,000 IU/l) at a rate of 30 ml/min (OIC-1) or 17 to 30 ml/min (OIC-2) during RF delivery and at 2 ml/min when idle in both groups. In the OIC-2 group, the irrigation rate was increased from 17 to 30 ml once power delivery reached 30 W. The heparinized saline was infused using the Cool Flow pump (Biosense Webster). The power was titrated down when an elevation of ET occurred, and RF energy delivery was stopped if the ET reached 39°C or if the ET continued to increase despite down-titration of the RF generator power (Figs. 1A and 1B).

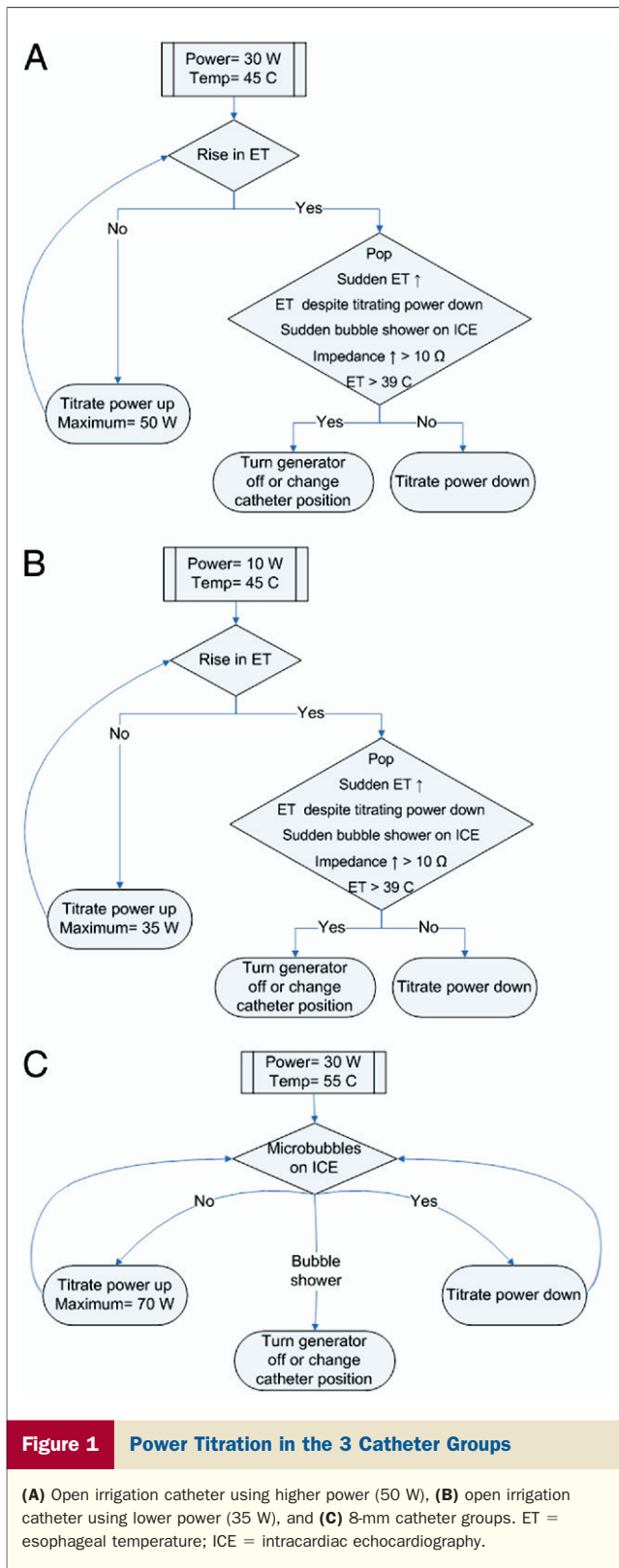
In the 8MC group, the initial RF power was set at 30 W and a maximum temperature limit of 55°C using the temperature control mode. The power was titrated up by increments of 5 W every few seconds to a maximum of 70 W, while we searched for microbubble formation caused by the ICE. Upon the detection of microbubbles, the power was titrated down. If a sudden shower of microbubbles was observed, RF energy delivery was immediately turned off. Patients in the 8MC group had their ET monitored during the PVAI procedure. Additionally, RF generator power was titrated in a similar fashion compared with the OIC groups as we searched for microbubble formation by ICE (Fig. 1C).

Follow-up. Oral anticoagulation therapy with warfarin was resumed on the evening of the procedure and was continued for at least 6 months. For some patients, warfarin was continued indefinitely, particularly for patients with risk factors who experienced recurrence of AF or if there was severe (~70%) PV stenosis demonstrated by cardiac computed tomography (CT) scan performed routinely at the 3-month follow-up evaluation after ablation. Antiarrhythmics, Singh Vaghan Williams classes IC and III (sotalol and dofetilide) were given and continued for a 2-month period. We used a 2-month blanking period in which episodes of AF within that time period were not considered procedure failures. Patients with recurrent AF during this 2-month period were offered electrical direct-current cardioversion. Patients with recurrent AF after the 2-month period were identified as procedural failure.

Patients were monitored with a 24-h ambulatory Holter recording before discharge. Upon discharge, an arrhythmia

Abbreviations and Acronyms

AF	= atrial fibrillation
ET	= esophageal temperature
ICE	= intracardiac echocardiography
LA	= left atrium
OIC	= open irrigation catheter
PV	= pulmonary vein
PVAI	= pulmonary vein antrum isolation
RF	= radiofrequency
8MC	= 8-mm catheter



transmitter was used to monitor events during the first 6 months. During the monitoring period, patients were asked to transmit when they experienced symptoms as well as at weekly intervals, even if they were asymptomatic.

Additional event recorder monitoring was obtained beyond the 6-month period to confirm freedom from AF. Additionally, information from implanted devices was used, when available, to document arrhythmia recurrence. Freedom from AF (procedural clinical success) was defined as absence of documented atrial arrhythmias off antiarrhythmics, excluding beta-blockers and calcium channel blockers.

Esophagoscopy. Patients who developed new symptoms of odynophagia or dysphagia underwent a chest CT and if the scan was normal they underwent an esophago-gastro-duodenoscopy (EGD).

Study end point. The primary end point of the study was freedom of atrial arrhythmias at 6 months. Secondary end points included: 1) Electrical isolation of all PV antra at the end of the procedure. 2) Fluoroscopy time, which was defined as the fluoroscopy time needed to perform the RF ablation portion of the procedure. This time excludes fluoroscopy time needed to perform the 2 trans-septal punctures. 3) Left atrial instrumentation time, defined as the total time during which there were catheters in the LA. 4) Duration of ablation along the esophagus, which was assessed and evaluated with ICE. 5) Complications, which could be in the form of cerebrovascular (thromboembolic or hemorrhagic), cardiovascular (cardiac perforation, tamponade), or gastrointestinal. 6) In patients who had their ET monitored, the maximum ET, incidences of ET elevation, postablation increase in ET and time needed for ET to return to within 1°C of baseline temperature were compared between the 3 groups.

Statistical analysis. Statistical analysis was performed using SPSS for Windows Version 13.0 (SPSS Inc., Chicago, Illinois). Continuous variables were expressed as mean ± standard error of the mean. Continuous variables of the 3 groups were compared using analysis of variance. Differences between each 2 groups were compared using post-hoc Bonferroni analysis. Categorical variables were expressed as percentages and were compared with the chi-square test. Comparisons between 2 groups were made with the Fisher exact test. Correlation coefficients between ET and catheter/generator parameters were performed by using simple linear regression analysis. A p value of <0.05 was considered statistically significant.

Results

The study was performed at 4 centers. A total of 180 patients were randomized to this study: 59 in the 8MC group, 61 in the OIC-1 group, and 60 in the OIC-2 group. All patients were followed for a period of at least 6 months, with a mean follow-up of 9 months. There was no statistically significant difference in patient characteristics or antiarrhythmic drug use between these groups (Table 1). There were no incidences of crossover between the groups.

Study outcomes. Procedural success, defined as PV antrum electrical isolation, was achieved in all of the patients at the

	8MC	OIC-1	OIC-2
Mean age (yrs)	59	59	62
Gender			
Male	45	51	49
Female	14	10	11
Mean LA size (cm)	4.3	4.0	4.4
Mean LVEF (%)	53	54	54
Cardiac surgery			
ASD repair	0	1	0
MVR or repair	4	3	2
ASD repair and MVR	0	1	1
Mean duration of AF (yrs)	6	6	6
Permanent AF	8	8	9
Prior typical atrial flutter ablation	3	4	2

8MC = 8-mm catheter; AF = atrial fibrillation; ASD = atrial septal defect; LA = left atrium; LVEF = left ventricular ejection fraction; MVR = mitral valve replacement; OIC-1 = open irrigation catheter with a higher peak power (50 W); OIC-2 = open irrigation catheter with a lower peak power (35 W).

end of the procedure using the assigned catheter. The freedom from AF or any other atrial arrhythmia at 6 months was significantly greater in the OIC-1 and 8MC groups compared with the OIC-2 group (78% in 8MC, 82% in OIC-1, and 68% in OIC-2 groups, respectively, $p = 0.043$) (Fig. 2).

Time intervals. The mean fluoroscopy time required for PVAI was significantly lower in the OIC-1 group compared with OIC-2 and 8MC groups (28 ± 1 min, 53 ± 2 min, 46 ± 2 min, $p = 0.001$). Additionally, the mean LA instrumentation time was significantly lower in the OIC-1 compared with OIC-2 and 8MC groups (59 ± 3 min, 90 ± 5 min, 88 ± 4 min, $p = 0.001$). Duration of ablation along the esophagus was significantly decreased in OIC-1 and OIC-2 groups compared with 8MC group (3.29, 3.31, and 6.29 min, respectively, $p = 0.001$) (Fig. 3).

Complications. There was one transient ischemic attack in the OIC-1 group; it occurred on the day of the procedure. There were no additional cerebrovascular events during follow-up any of the groups. In no patient was coagulum formation detected using either type of catheter. During ablation, pops were heard in all patients in the OIC-1 group. There was a mean of 1.3 pops heard per patient (Fig. 4A). Although OICs generate echogenic microbubbles as the result of saline infusion, there was a significant increase in microbubble density detected by ICE coinciding with pop formation. No pops were experienced in either the 8MC or OIC-2 groups ($p = 0.001$). After a pop was heard, we checked the cardiac silhouette by using fluoroscopy, and we screened the pericardial space by using ICE to look for pericardial effusions.

Pericardial effusion complicated 20% of the procedures performed in the OIC-1 and none of the OIC-2 and 8MC groups ($p = 0.001$). Screening for pericardial effusion was performed with ICE during the ablation procedure. Once noted, a more detailed examination was performed with transthoracic transducers if needed. All patients had a

thorough ICE procedure performed at the end of the ablation procedure. Two of the pericardial effusions were hemodynamically significant and required emergency pericardiocentesis (Fig. 4B). Small-to-moderate pericardial effusions with no hemodynamic significance were observed with a next day follow-up transthoracic echocardiogram. Warfarin was restarted if there is no increase in the size of the effusion. Two patients in the OIC-1 group developed periprocedural pulmonary edema requiring intravenous diuretic therapy (Fig. 4C).

Eleven patients (17%) in the OIC-1 group reported new symptoms of odynophagia or dysphagia within the first 3 weeks after the procedure; however, only 2 patients (3%) in the 8MC group and 3 patients (5%) in the OIC-2 developed these symptoms. ($p = 0.03$). Chest CT followed by an EGD was performed in all of these patients. Four patients in the OIC-1 group had evidence of focal areas of erythema along the anterior wall of the esophagus. None of the patients in the 8MC or the OIC-2 groups had any evidence of esophageal erythema. There were no signs of necrosis or bleeding in any group (Fig. 4D). None of the patients developed atrioesophageal fistula. A routine cardiac CT performed 3 months after the procedure demonstrated absence of significant ($>50\%$) pulmonary vein stenosis in all groups.

Esophageal temperature recordings. Patients in the OIC-1 group had a greater incidence of ET elevation compared with the OIC-2 and 8MC groups (94%, 60%,

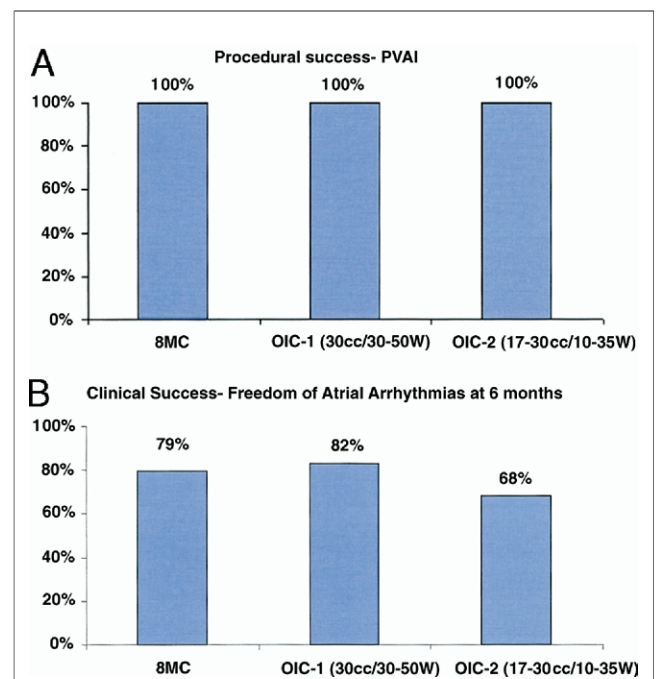
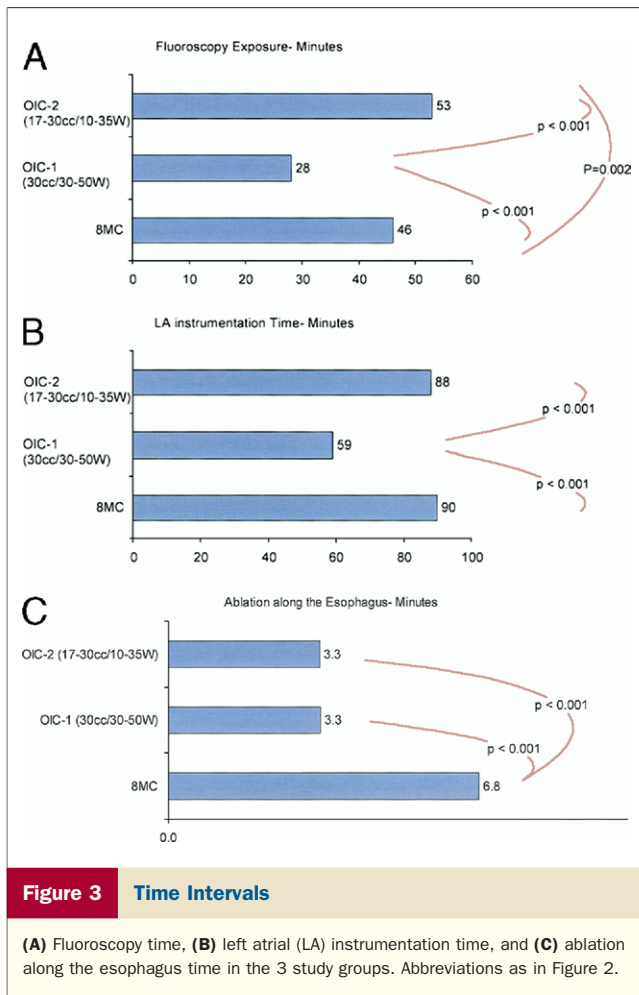


Figure 2 Short- and Long-Term Procedural Success

Success was defined as (A) pulmonary vein antrum isolation and (B) freedom of any atrial arrhythmias at 6 months. 8MC = 8-mm catheter; OIC-1 = 3.5-mm open irrigation tip catheter using a higher power and higher irrigation flow rate; OIC-2 = 3.5-mm ThermoCool open irrigation tip catheter using a lower power and lower irrigation flow rate; PVAI = pulmonary vein antrum isolation.



70%, respectively, $p = 0.02$). The maximal ET recorded also was greater in the OIC-1 group compared with OIC-2 and 8MC groups ($40.2 \pm 1^\circ\text{C}$, $38.3 \pm 1^\circ\text{C}$, and $38.6 \pm 1^\circ\text{C}$, respectively, $p = 0.001$). The continuation of temperature increase after termination of RF energy application was significantly greater in the OIC-1 and 8MC groups compared with the OIC-2 group (1.42°C , 1.24°C , 0.64°C , respectively, $p = 0.004$). In the OIC-1 group, the average time for the ET temperature to return to baseline after termination of RF power delivery was significantly longer in the OIC-1 compared with OIC-2 and 8MC groups (39 ± 3 s, 18 ± 2 s, 13 ± 1 s, $p = 0.001$) (Fig. 5).

In the OIC groups (OIC-1 and OIC-2), there was an average of 3 ET elevations per patient. This ET elevation occurred during isolation of the posterior aspect of the right and left posterior PV antrum. There was no correlation between ET and catheter tip temperature (mean = $38.2 \pm 0.3^\circ\text{C}$, $r^2 = 0.2$, $p = \text{NS}$), power (46 ± 1 W, $r^2 = 0.26$, $p = \text{NS}$), or impedance (93 ± 2 Ohms, $r^2 = 0.08$, $p = \text{NS}$).

In the OIC-1 group, titrating down the power was usually unsuccessful in promptly reducing the ET to $<38^\circ\text{C}$. However, in this group the ET elevation occurred when the generator settings were at a power of >35 W. Ninety percent of the ET elevation occurred with generator power >40 W.

Discussion

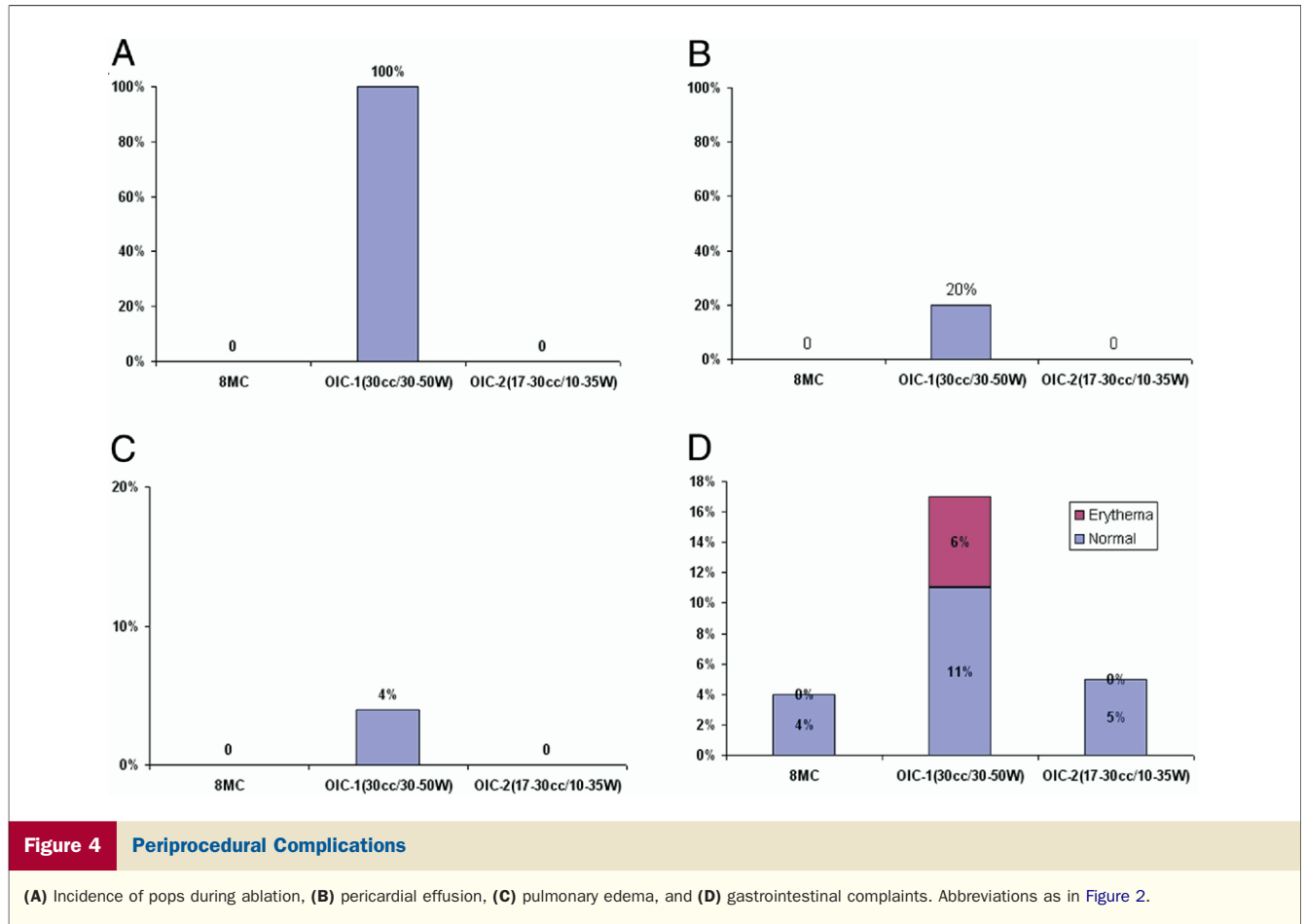
This study tested the 3 commonly used catheter/energy-delivery strategies of electrical isolation of the pulmonary vein antra: the 8MC and 2 power delivery settings for the OIC. We did not test the 4-mm standard catheter because of its significant limitation of power delivery in areas of low blood flow, although some centers reported an excellent success rate with its use (10).

Short-term follow up during a period of 6 months showed a lower success rate in the lower power-lower irrigation rate group (OIC-2). This result may imply that higher power delivery is needed for effective lesion formation and subsequently clinical success. However, there was no difference between higher power/higher irrigation rate group (OIC-1) and the 8MC group. Thus power may not be the only determinant of effective lesion formation; instead, other factors like catheter stability to insure adequate catheter-tissue contact may be important as well.

Although the PVAI procedure performed using either catheter was effective in isolating pulmonary vein antra, the higher power/higher irrigation group (OIC-1) had less radiation exposure to the patient and operator. On average, this would result in a saving of 60 rads to the patient. In addition, saving approximately 20 min of fluoroscopy per procedure could translate to a significant reduction in radiation exposure to the operator. Thus, the use of OIC at high power and irrigation rate could substantially impact radiation safety.

Left atrial instrumentation time, which was reduced in the higher power/higher irrigation rate group (OIC-1), may theoretically correlate with reduction of thrombotic and hemorrhagic complications. Thrombotic complications generally occur as a result of the presence of the ablation system in the LA, and hemorrhagic complications generally occur resulting from the use of systemic anticoagulation during the procedure. It is reasonable to consider that a decrease in LA instrumentation time may translate into favorable clinical outcomes with a reduction in these complications. Additionally, the decrease in the LA instrumentation time may translate into a decrease in total procedure time, which could lessen the risks of conscious sedation. However, a recent study by Dixit et al. (11) reported that 8-mm tip achieved PV isolation in lesser time as compared with a closed irrigated (cooled-tip) catheter. It was suggested that this effect was mitigated by the use of electro-anatomic mapping systems.

Despite the fact that the higher power/higher irrigation rate group (OIC-1) had a shorter duration of ablation along the esophagus, this did not translate into clinical benefit compared to the use of the 8MC. Indeed, there were more frequent and greater ET increases along with increased incidences of gastrointestinal symptoms and gross abnormalities detected by EGD. With the OIC, the depth of the direct resistive heating is significantly increased, which in turn increases the area of the effective heat source, resulting



in higher power and temperature delivery. These factors will not only result in a larger lesion but may potentially increase the likelihood of collateral damage to adjacent structures because of higher thermal latency (prolonged ET elevation after ablation) (Fig. 5E).

Additionally, because the peak tissue temperature while using an OIC is approximately 2 to 5 mm less than the endocardial surface, there is a risk of intramural supra-boiling temperatures and pops (4). All patients in the higher power/higher irrigation rate group (OIC-1) had at least one occurrence of pop. In 2 patients, pops were complicated by acute pericardial effusion with cardiac tamponade, necessitating emergency pericardiocentesis. The mechanism of the majority of the pericardial effusions remains unclear. The majority of effusions were mild, slowly accumulating, and not hemodynamically significant. Similarly, even the larger effusions requiring pericardiocentesis did not reaccumulate despite heparin and subsequent oral anticoagulation therapy. In this subgroup, the mechanism of effusion may be severe inflammation due tissue injury causing a diffuse inflammatory state.

The posterior wall of the LA represents a vulnerable area for possible complications during AF catheter ablation. Not only it is the thinnest part of the LA, but it lies in close proximity to the esophagus as well (12). The use of

higher-power delivery settings (OIC-1) in this area might have been the reason after the increased incidence of complications observed with OIC-1 group. It is possible that the use of lower-energy delivery settings in this area might have prevented both cardiac and esophageal complications.

The increased incidence of complications observed with the use of OIC at higher power and higher irrigation rate may be due to the limited effectiveness of ICE to monitor for excessive energy delivery to the tissue. It has been demonstrated that monitoring for intracardiac microbubble formation by ICE is an effective method to titrate energy delivery with the use of an 8-mm RF catheter for avoidance of excessive tissue heating (13,14). However, when using an OIC, the agitated saline droplets exiting the tiny catheter orifices at high velocity causes echogenic microbubble formation compromising the use of ICE for monitoring tissue overheating.

Two patients in OIC-1 group developed pulmonary edema requiring intravenous diuretic therapy. One patient had moderate left ventricular systolic dysfunction; however, the other patient had no history of structural heart disease. Both patients received more than 3 l of intravenous fluids during the procedure. Subsequently, during the course of this study with closer attention to fluid balance and with administration of

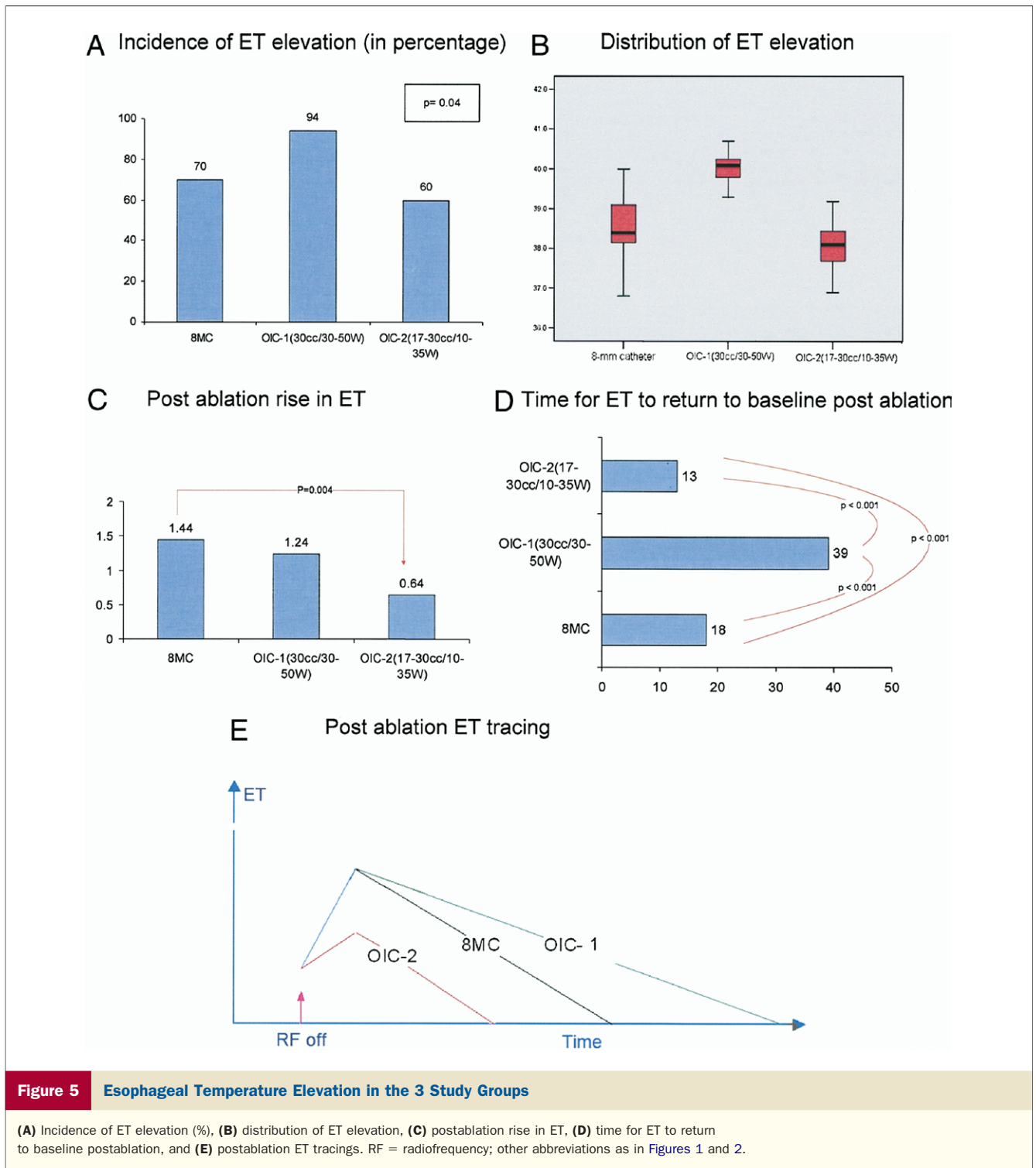


Figure 5 Esophageal Temperature Elevation in the 3 Study Groups

(A) Incidence of ET elevation (%), (B) distribution of ET elevation, (C) postablation rise in ET, (D) time for ET to return to baseline postablation, and (E) postablation ET tracings. RF = radiofrequency; other abbreviations as in Figures 1 and 2.

diuretics, particularly for patients with a history of systolic dysfunction, this complication was no longer encountered.

Study limitations. Our study is a randomized pilot one that was designed to study the safety and acute and subacute procedural success of PV antrum isolation performed using open irrigation catheters compared to 8-mm standard catheter. Thus, it has all the limitations

inherent to a pilot study, including smaller sample size and selection bias.

Conclusions

Despite evidence of improvement in LA instrumentation and fluoroscopy time, the use of OIC at a higher power and

higher irrigation rate was associated with increased rates of complications. However, because of the nonhomogeneous nature of the LA with respect to wall thickness, one could postulate that a modified approach using shorter RF pulsatile applications as well as lower power and lower irrigation rates at some LA locations, such as the posterior wall, and greater power and higher irrigation rates at other LA locations, such as the anterior, roof and septal structures might prove to be an effective alternative strategy.

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