

Impact of catheter-tissue contact force on lesion size during right ventricular outflow tract ablation in a swine model

Jing-Bo Jiang¹, Jin-Yi Li², Zhi-Yuan Jiang², An Wang², Zheng Huang², Hong-Yuan Xu², Cheng-Lin Shu², Gui-Juan Li², Yi-Sheng Zheng², Yan He², Guo-Qiang Zhong²

¹Department of Cardiology, Guilin People's Hospital, Guilin Medical University, Guilin, Guangxi 541002, China;

²Department of Cardiology, The First Affiliated Hospital, Guangxi Medical University, Nanning, Guangxi 530021, China.

Abstract

Background: The catheter-tissue contact force (CF) is one of the significant determinants of lesion size and thus has a considerable impact on the effectiveness of ablation procedures. This study aimed to evaluate the impact of CF on the lesion size during right ventricular outflow tract (RVOT) ablation in a swine model.

Methods: Twelve Guangxi Bama miniature male pigs weighing 40 to 50 kg were studied. After general anesthesia, a ThermoCool SmartTouch contact-sensing ablation catheter was introduced to the RVOT via the femoral vein under the guidance of the CARTO 3 system. The local ventricular voltage amplitude and impedance were measured using different CF levels. We randomly divided the animals into the following four groups according to the different CF levels: group A (3–9 g); group B (10–19 g); group C (20–29 g); and group D (30–39 g). Radiofrequency ablations were performed at three points in the free wall and septum of the RVOT in power control mode at 30 W for 30 s while maintaining the saline irrigation rate at 17 mL/min. At the end of the procedures, the maximum depth, surface diameter, and lesion volume were measured and recorded. A linear regression analysis was performed to determine the relationship between continuous variables.

Results: A total of 72 ablation lesions were created in the RVOT of the 12 Bama pigs. The maximum depth, surface diameter, and volume of the lesions measured were well correlated with the CF (free wall: $\beta = 0.105$, $\beta = 0.162$, $\beta = 3.355$, respectively, $P < 0.001$; septum: $\beta = 0.093$, $\beta = 0.150$, $\beta = 3.712$, respectively, $P < 0.001$). The regional ventricular bipolar voltage amplitude, unipolar voltage amplitude, and impedance were weakly positively associated with the CF ($\beta = 0.065$, $\beta = 0.125$, and $\beta = 1.054$, respectively, $P < 0.001$). There was a significant difference in the incidence of steam pops among groups A, B, C, and D (free wall: $F = 7.3$, $P = 0.032$; septum: $F = 10.5$, $P = 0.009$); and steam pops occurred only when the CF exceeded 20 g. Trans-mural lesions were observed when the CF exceeded 10 g in the free wall, while the lesions in the septum were non-trans-mural even though the CF reached 30 g.

Conclusions: CF seems to be a leading predictive factor for the size of formed lesions in RVOT ablation. Maintaining the CF value between 3 and 10 g may be reasonable and effective for creating the necessary lesion size and reducing the risk of complications, such as steam pops and perforations.

Keywords: Catheter ablation; Ventricular Premature Complexes; Tachycardia, Ventricular; Animal Experimentation

Introduction

Radiofrequency catheter ablation (RFCA) has been widely accepted as an effective non-pharmacological treatment in patients with idiopathic ventricular arrhythmias (VAs), including frequent premature ventricular contractions and ventricular tachycardia. The most common candidate ablation focus for idiopathic VAs is located in the outflow tract, especially the right ventricular outflow tract (RVOT).^[1,2] However, according to previous studies, 7% to 20% of cases of VAs originating from the RVOT fail

to achieve successful acute catheter ablation or experience subsequent recurrences.^[1-4]

The contact force (CF) between the catheter tip and myocardial tissue has been shown to be one of the major determinants of lesion size in experimental studies and thus has a significant impact on the effectiveness of VAs ablation procedures.^[5,6] On the contrary, excessive CF may lead to an increased risk of severe procedural complications, such as cardiac tamponade and steam pops.^[6-8] Unfortunately, the range of effective and safe CF

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.1097/CM9.0000000000000859

Jing-Bo Jiang and Jin-Yi Li contributed equally to the work.

Correspondence to: Dr. Guo-Qiang Zhong, Department of Cardiology, The First Affiliated Hospital, Guangxi Medical University, Nanning, Guangxi 530021, China
E-Mail: zhongggqxmu@163.com

Copyright © 2020 The Chinese Medical Association, produced by Wolters Kluwer, Inc. under the CC-BY-NC-ND license. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Chinese Medical Journal 2020;133(14)

Received: 04-03-2020 Edited by: Yuan-Yuan Ji

values that need to be maintained during ablation in RVOT remains unclear. Our study aimed to evaluate the impact of the catheter-tissue CF on the lesion size during RVOT ablation in an experimental swine model using a novel CF-sensing ablation catheter. The heart size of a pig that weighs 40 to 50 kg is comparable to that of a normal human adult, and the hemodynamic condition of a pig heart is similar to that of a normal human adult heart.^[9,10] Therefore, Guangxi Bama miniature pigs weighing 40 to 50 kg were selected as experimental animals in our study.

Methods

Animals and ethical approval

Twelve Guangxi Bama miniature male pigs provided by the Experimental Animal Center of Guangxi Medical University weighing 44.8 ± 2.4 kg (range 40–50 kg) were studied. The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (No. 2016 KY-E-069). All procedures used in this study were in accordance with our institutional guidelines that complied with the international ethics and humane standards for animal use. Every effort was made to minimize the number of animals and reduce their suffering. All experiments were performed in the Animal Imaging Laboratory of Guangxi Medical University from August 2015 to February 2016. We estimated the sample size by reviewing the relevant animal experiment literature reporting radiofrequency ablation lesions in animal atria or ventricles,^[11–14] and we believed that 12 swine might meet the design requirements of this study.

Animal preparation

After an intra-muscular injection of a mixed solution of ketamine hydrochloride (10 mg/kg; Zhejiang Jiuxu Pharmaceutical Co., Ltd., Zhejiang, China) and midazolam (0.5 mg/kg; Jiangsu Enhua Pharmaceutical Co., Ltd., Jiangsu, China) for sedation, basic anesthesia was administered with an intra-muscular injection of sodium pentobarbital (15 mg/kg; Beijing Borking Technology Co., Ltd., China). Then, general anesthesia was maintained by using a continuous intravenous infusion of propofol (50–100 mg/h; Sichuan Guorui Pharmaceutical Co., Ltd., Sichuan, China). All the pigs were intubated and then mechanically ventilated with oxygen. A continuous infusion of amiodarone (Hangzhou Sanofi Pharmaceutical Co., Ltd., Zhejiang, China) at a rate of 1 mg/min throughout the procedure and an intravenous bolus of lidocaine (1 mg/kg; Hebei Tiancheng Pharmaceutical Co., Ltd., Hebei, China) just before ablation were used to prevent the occurrence of radiofrequency-induced malignant VAs.

Establishment of a three-dimensional geometric model of the RVOT

A ThermoCool SmartTouch Ablation Catheter (Biosense Webster Inc., Irvine, CA, USA), which is a novel CF-sensing quadripolar ablation catheter with a 3.5-mm external irrigation tip electrode, was used in our study. The ablation catheter was inserted into the right femoral vein

and advanced into the right atrium under the guidance of the CARTO 3 electroanatomic mapping system (Biosense Webster Inc.). When the catheter was suspended in the right atrial cavity without endocardial contact, the CF value was calibrated to 0 g (the non-contact baseline value). Then, real-time CF data and the direction of the force vector were shown to the operators. We reconstructed the three-dimensional geometric model of the right atrium and the RVOT under the guidance of the CARTO 3 mapping system in fast anatomical mapping mode.

Measurements of the local ventricular voltage amplitude and impedance

Three to four points were selected and manually marked in the free wall and septum of the RVOT under the guidance of the CARTO 3 mapping system. The operator attempted to manipulate the distal end of the ablation catheter to sequentially contact the ventricular endocardium at each point under four different levels of CFs (3–9, 10–19, 20–29, and 30–39 g). When the location of the catheter and the CF range remained stable for more than 5 s, the ventricular bipolar voltage amplitude, the unipolar ventricular voltage amplitude, and the real-time impedance obtained from the distal electrodes were measured with the help of the measurement software provided by the CARTO 3 system.

Ablation protocol

Through the random number table method, we randomly divided the 12 animals into the following four groups according to the different CF ranges: group A (CF 3–9 g); group B (CF 10–19 g); group C (CF 20–29 g); and group D (CF 30–39 g). Three Bama pigs were included in each group. The radiofrequency signals were administered at three different sites in the free wall and septum of the RVOT in each group, and the distance between those sites was required to be greater than 7 mm. Before administering the radiofrequency signals, the catheter tip was kept stable at the selected ablation sites for longer than 5 s, while the CF value was maintained within a preset range. Then, the radiofrequency signals were delivered between the distal electrode of the ablation catheter and an adhesive patch (Biosense Webster Inc.) that was placed on the back skin of the pig. A Stockert Radiofrequency Power Generator (Biosense Webster Inc.) was set to the power-controlled irrigation mode for radiofrequency energy delivery. During ablation discharge, the ablation parameters were monitored and kept constant. The radiofrequency signals were delivered at 30 W for 30 s while maintaining the saline irrigation rate at 17 mL/min.

Measurement and pathologic study

At the end of the ablation procedure, 20 mL of 2% triphenyl tetrazolium chloride solution (Shanghai Tongyuan Biotechnology, Co., Ltd., Shanghai, China) was intravenously administered. The experimental animals were humanely euthanized by an intravenous injection of 20 mL of 10% potassium chloride solution 30 min after the triphenyl tetrazolium chloride injection. Thoracotomies were performed to remove the hearts from the

experimental animals. The gross anatomy of the ablation lesions in the RVOT region was visually observed, and the presence or absence of trans-mural injuries and steam pops were recorded. Radiofrequency lesions that formed over the myocardium were measured macroscopically with a high-precision digital caliper (Shanghai Minnet Industrial Co., Ltd., Shanghai, China). The maximum depth, maximum diameter, depth at the maximum diameter, and surface diameter were measured and recorded, and the lesion dimensions and lesion volume were determined using a previously reported formula,^[6] as shown in Figure 1. Sections from the lesions were obtained and fixed in 10% neutral-buffered formalin (Nanchang Yulu Experimental Equipment Co., Ltd., Nanchang, China). The tissue was dehydrated, embedded in paraffin, sectioned at a thickness of 5 μm , and stained with hematoxylin and eosin. The specimens were examined under light microscopy (Olympus Inc., Tokyo, Japan).

Statistical analysis

Data analysis was performed using IBM SPSS Statistics for Windows version 17 (IBM Corp., Chicago, IL, USA). The lesion size parameters (including the maximum depth, maximum diameter, depth at the maximum diameter, and surface diameter) and the electrophysiology parameters (including the ventricular bipolar voltage amplitude, the ventricular unipolar voltage amplitude, and the real-time impedance) conform to normal distribution since none of the normality of the distribution test was found to be significant at $\alpha = 0.05$ level using the Kolmogorov-Smirnov test. Simple descriptive statistics (mean \pm standard deviation) of continuous variables were calculated. An independent t test was used to compare the means of variables between the two groups. Comparisons of independently measured variables among four groups were performed using one-way analysis of variance, and Tukey test was performed for multiple comparisons. A

linear regression analysis was performed to determine the relationship between continuous variables. Categorical variables (including the incidence rate of steam pops and trans-mural lesions) were described as proportion and compared with Fisher exact test. Two-tailed P values of $P < 0.05$ were considered statistically significant.

Results

In this study, 72 ablation lesions were created in the RVOTs of 12 Bama pigs. Thirty-six of the lesions were distributed in the free walls, and the other 36 lesions were distributed in the septums. The thicknesses of the free wall and septum of the RVOT were 5.0 ± 0.7 mm and 11.3 ± 1.8 mm, respectively ($t = 19.33$, $P < 0.001$). The effect of contact pressure applied during ablation therapy on the effects of ablation is as follows.

Relationship between CF value and ventricular voltage amplitude and impedance

Linear regression analysis showed that the ventricular bipolar voltage amplitude, unipolar voltage amplitude, and impedance values obtained from the distal electrodes of the catheters were positively correlated with the CF value (bipolar voltage amplitude: $\beta = 0.065$, $R^2 = 0.141$, $P < 0.001$; unipolar voltage amplitude: $\beta = 0.125$, $R^2 = 0.113$, $P < 0.001$; impedance: $\beta = 1.054$, $R^2 = 0.166$, $P < 0.001$). However, the correlation coefficient was low. A comparison between the groups with different CF ranges showed that the mean bipolar voltage amplitude, unipolar voltage amplitude, and impedance in the CF 10 to 19 g and CF 20 to 29 g groups were significantly higher than those in the CF 3 to 9 g and CF 10 to 19 g groups, respectively. However, those values in the CF 30 to 39 g and CF 20 to 29 g groups were not statistically significantly different. The details of these results are shown in Table 1.

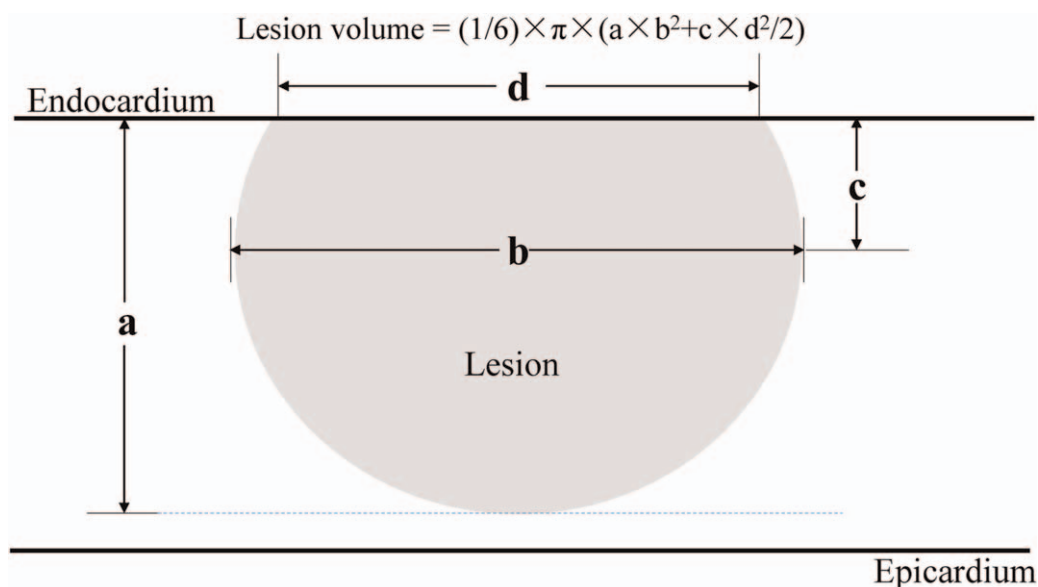


Figure 1: A schematic of the formula for calculating the ablation lesion volume. a: maximum depth; b: maximum diameter; c: depth at the maximum diameter; d: surface diameter.

Table 1: Comparison of local ventricular voltage amplitude and impedance among groups with different CF ranges.

Variables	Group A (n = 45)	Group B (n = 45)	Group C (n = 45)	Group D (n = 45)	F	P
CF (g)	6.67 ± 1.98	15.53 ± 2.37*	25.16 ± 2.33 [†]	35.36 ± 2.70 [‡]	2273.00	<0.001
Bipolar voltage amplitude (mV)	1.71 ± 1.57	2.84 ± 2.09*	3.71 ± 2.92 [§]	3.50 ± 1.60	21.50	<0.001
Uipolar voltage amplitude (mV)	8.34 ± 3.78	10.00 ± 3.60	11.76 ± 5.02 [§]	12.22 ± 3.81	6.43	<0.001
Impedance (Ω)	185.60 ± 26.35	193.70 ± 26.52	209.90 ± 29.54 [†]	210.00 ± 21.74	15.72	<0.001

Values are shown as mean ± standard deviation. Data were compared with one-way analysis of variance among the four groups. The four groups were divided according to the different CF levels: group A (3–9 g), group B (10–19 g), group C (20–29 g), and group D (30–39 g). Comparison between group B and group A: $P < 0.001$, ^{||} $P < 0.01$; comparison between group C and group B: [†] $P < 0.001$, [§] $P < 0.05$; comparison between group D and group C: [‡] $P < 0.001$. CF: Contact force.

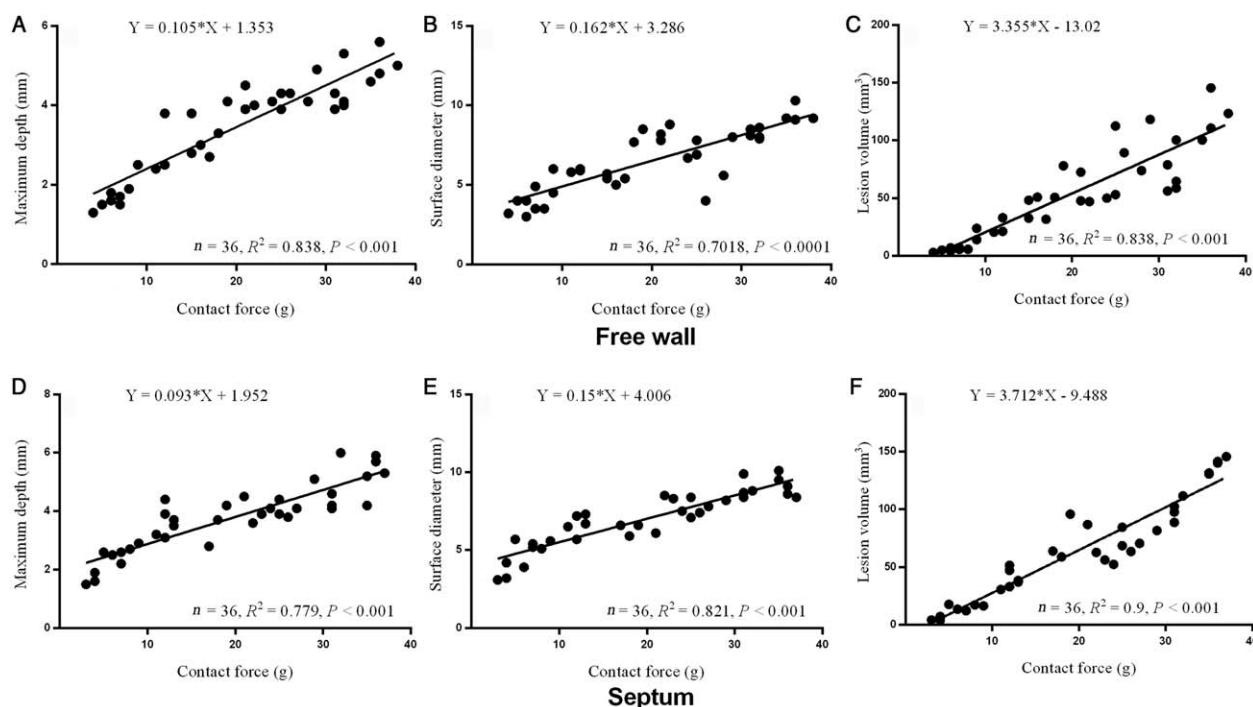


Figure 2: Linear regression analysis of the CF and ablation lesion size in the RVOT. (A–C) Linear regression analysis of the CF and ablation lesion size in the free wall of the RVOTL: (A) maximum depth, (B) surface diameter, (C) lesion volume. (D–F) Linear regression analysis of the CF and ablation lesion size in the septum of the RVOT: (D) maximum depth, (E) surface diameter, (F) lesion volume. CF: Contact force; RVOT: Right ventricular outflow tract.

Lesion size as measured by maximum depth, surface diameter, and lesion volume

Linear regression analysis showed that the maximum depth, surface diameter, and volume of the lesions in the RVOT were well correlated with the CF when the radiofrequency power, time, and irrigation rate remained constant [Figure 2]. The comparison results of the mean maximum depth, surface diameter, and volume of the ablation lesions between groups A, B, C, and D are shown in Table 2. Figure 3A–3C shows gross pathological specimens of the ablation lesions, and Figure 3D shows histological changes in an ablation lesion created in the free wall of the RVOT.

Steam pops and trans-mural lesions as possible indicators of complication from treatment

As shown in Table 3, there was a significant difference in the incidence rate of steam pops among groups A, B, C and

D (free wall: $F = 7.3$, $P = 0.032$; septum: $F = 10.5$, $P = 0.009$). The average CF value when the steam pops occurred was 30.8 ± 4.5 g in the free wall and 31.5 ± 5.2 g in the septum. There was no significant difference between these two CF values ($t = -0.249$, $P = 0.808$). A difference in the incidence of trans-mural lesions in the free wall of the RVOT on gross inspection among the four groups was significant ($F = 17.2$, $P = 0.001$). Nevertheless, trans-mural lesions were not observed in the septum of the RVOT in all the groups.

Discussion

The most notable findings observed in our study were as follows: (1) The lesion size in the RVOT was well correlated with the CF when the radiofrequency power, time, and irrigation rate remained constant; (2) The lesion depth and volume stopped increasing when the CF reached 20 to 29 g in the free wall, but those values constantly increased as the CF increased in the septum; (3) Steam pops

Table 2: Comparison of lesion size among groups with different CF ranges.

Variables	Group A (n=9)	Group B (n=9)	Group C (n=9)	Group D (n=9)	F	P
Free wall						
CF (g)	6.78 ± 1.72	15.00 ± 2.83*	24.44 ± 2.70 [†]	33.56 ± 2.74 [‡]	188.00	<0.001
Thickness of ventricular wall (mm)	4.91 ± 0.60	4.81 ± 0.85	4.51 ± 0.12	4.89 ± 0.19	0.81	0.500
Maximum depth (mm)	1.81 ± 0.43	3.16 ± 0.62*	4.22 ± 0.32 [†]	4.62 ± 0.60	54.98	<0.001
Surface diameter (mm)	4.07 ± 0.95	6.16 ± 1.16 [§]	7.09 ± 1.50	8.77 ± 0.77	27.24	<0.001
Lesion volume (mm ³)	8.42 ± 6.61	40.83 ± 18.17 [¶]	73.84 ± 27.63 ^{**}	93.22 ± 30.89	24.00	<0.001
Septum						
CF (g)	5.89 ± 2.03	13.89 ± 3.26*	24.33 ± 2.35 [†]	33.56 ± 2.79 [‡]	187.60	<0.001
Thickness of ventricular wall (mm)	11.33 ± 1.86	11.89 ± 2.26	10.94 ± 1.62	10.97 ± 1.69	0.50	0.685
Maximum depth (mm)	2.28 ± 0.50	3.61 ± 0.52*	4.16 ± 0.45	5.02 ± 0.76	36.21	<0.001
Surface diameter (mm)	4.60 ± 1.02	6.47 ± 0.59*	7.70 ± 0.77 ^{**}	9.06 ± 0.64 ^{††}	53.75	<0.001
Lesion volume (mm ³)	11.62 ± 5.37	50.73 ± 20.47*	69.71 ± 12.41	121.2 ± 21.26 [‡]	70.82	<0.001

Values are shown as mean ± standard deviation. Data were compared with one-way analysis of variance among the four groups. The four groups were divided according to the different CF levels: group A (3–9 g), group B (10–19 g), group C (20–29 g), and group D (30–39 g). Comparison between group B and group A: *P < 0.001, §P < 0.01, ¶P < 0.05; comparison between group C and group B: †P < 0.001, **P < 0.05; comparison between group D and group C: ‡P < 0.001, ||P < 0.05, ††P < 0.01. CF: Contact force.

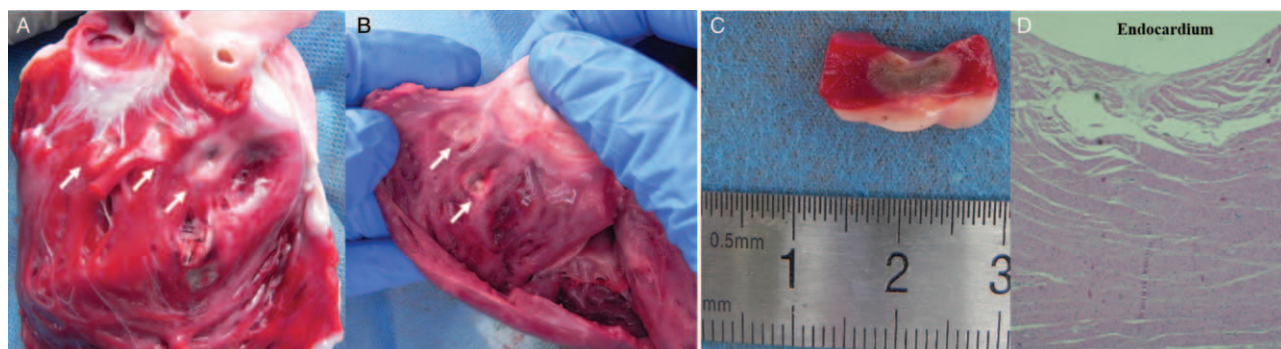


Figure 3: Pathological specimens of ablation lesions from the RVOT. (A) Examples of three endocardial lesions on the septum of the RVOT are indicated by white arrows. (B) Examples of two endocardial lesions on the free wall of the RVOT are indicated by white arrows. (C) Examples of a trans-mural lesion section at a CF of 32 g on the free wall of the RVOT. (D) Representative microscopic images (hematoxylin and eosin staining, original magnification ×40) of a lesion section from the free wall of the RVOT shows corrugated, arranged and broken myocardial fibers, substantial swelling, and necrosis of myocardial fibers, which is consistent with the pathological presentation of electrical current damage. CF: Contact force; RVOT: Right ventricular outflow tract.

Table 3: Comparison of the incidence rate of steam pop and trans-mural lesion among groups with different CF ranges.

Variables	Group A (n=9)	Group B (n=9)	Group C (n=9)	Group D (n=9)	Fisher exact test	P
Free wall						
Trans-mural lesions	0	2	5	8	17.2	0.001
Steam pops	0	0	2	4	7.3	0.032
Septum						
Trans-mural lesions	0	0	0	0	–	–
Steam pops	0	0	3	5	10.5	0.009

Values are shown as n. The four groups were divided according to the different CF levels: group A (3–9 g), group B (10–19 g), group C (20–29 g), and group D (30–39 g). CF: Contact force.

occurred only when the CF exceeded 20 g; and (4) Trans-mural lesions were observed when the CF exceeded 10 g in the free wall, while trans-mural lesions were not observed in the septum.

The factors that influence lesion size during ablation include the distal diameter of the ablation catheter, local

blood flow velocity, irrigation rate of saline, and the CF between the tip of the ablation catheter and myocardial tissue; among these factors, the CF plays the most important role.^[5,6,8,11] However, ablations were performed on the atrial endocardium or epicardium in most previous studies, and ablations were performed on animal skeletal muscle or ventricular muscle in a few *in vitro*

studies.^[11-14] So we performed this *in vivo* experimental study to evaluate the effect of CF on the size of ablation lesions when using CF-sensing catheters to perform an ablation procedure in the RVOT.

Shah *et al*^[11] found lesion size correlates linearly with measured CF-time integral. Constant contact produced the largest, and intermittent contact produced the smallest lesions despite constant RF power and identical peak CFs. Study from Matia Frances *et al*^[15] showed that lesions were never trans-mural with average forces <10 g and the mean depth was very low (0.75 mm). CFs of at least 20 g were required to achieve trans-mural lesions. Besides, the lesions were positively correlated to the average force during the applications. Di Biase *et al*^[16] evaluated lesions in the left atrium at six settings by using a robotic navigation system with a constant duration (40 s) and flow rate of either 17 or 30 mL/min with an open irrigated catheter. They concluded lower power settings (≤ 35 W) and lower/medium contact pressure were more likely to show a “relative” spared endocardial surface. Contact pressure between 20 and 30 g and a power setting of 40 W appeared to achieve trans-murality by preserving safety. In our study, the CF between the distal end of the ablation catheter and myocardial tissue was positively correlated with the maximum depth, surface diameter, and volume of the ablation lesion. The results are consistent with those of previous studies.^[5,6,8,14] In addition, we found when the CF was 10 g or greater; a trans-mural lesion might appear on the free wall of the RVOT. If the lesion became a trans-mural lesion, the maximum depth, and volume of the lesion stopped increasing as the CF increased. These results are significantly different from the results of previous experimental studies, in which thick skeletal muscle or left ventricular muscle was ablated.^[17-19]

Furthermore, excessive CF could result in severe cardiac complications, such as mechanical perforations and steam pops.^[6-8] Our study also showed that the incidence of steam pops increased as the CF increased. When the CF reached 30 to 39 g, the incidence of steam pops was as high as 50%, and all the steam pops occurred only when the CF exceeded 20 g. In our study, the mean CF that led to steam pops was 30.8 ± 4.5 g on the free wall and 31.5 ± 5.2 g on the septum of the RVOT, which were lower than the CF reported by Nazeri *et al*^[7] and Perna *et al*.^[20] These results may be due to the following: (1) In contrast to the research conducted by Nazeri *et al* and Perna *et al*, we performed ablation in the RVOT instead of the left atrium, and the local blood flow conditions and the myocardial thickness were significantly different; and (2) In the study conducted by Nazeri *et al*, the radiofrequency power was 40 W, and the saline irrigation flow rate was 30 mL/min. In comparison, the radiofrequency power in our study was 30 W, and the saline perfusion flow rate was 17 mL/min.

Our study also suggested a low possibility of mechanical perforation and pericardial effusion when the CF is less than 40 g during the mapping and ablation procedure. Since we did not attempt to perform a mapping and ablation procedure with CF levels greater than 40 g, we could not further assess the minimum CF that leads to mechanical perforations. Steam pops may lead to acute

perforations and cardiac tamponades when ablating the free walls of the RVOT. We found the occurrence of steam pops was very likely during ablation when the CF exceeded 20 g, and the occurrence of steam pops was especially more likely when the CF was greater than 30 g. Therefore, operators should pay close attention to the real-time change in the CF and attempt to maintain the CF at a level that does not exceed 20 g during ablation.

The mechanism of idiopathic VAs originating from the RVOT is mostly focal triggering activity or an autonomic abnormality.^[2] Most of the origins are located just under the endocardium instead of the epicardium. This result is greatly different from the ablation of atrial fibrillation or atrial flutter,^[21-24] which causes trans-mural injury at the time of circumferential pulmonary vein isolation or linear blocking. Therefore, when performing the ablation procedure in the RVOT, achieving trans-mural injury may not be as necessary. When performing ablation on patients with idiopathic RVOT-VAs, maintaining the CF value between 3 and 10 g or performing the ablation with lower energy may be reasonable and effective. Considering that the origin of VAs is located deep under the septal endocardium of the RVOT, increasing the CF from 10 to 20 g during ablation should be considered; however, CF levels greater than 20 g should be avoided.

Before administering CF-sensing catheters, the contact condition between the distal end of the ablation catheter and myocardial tissue was evaluated by operators using indirect indicators, including the local voltage amplitude, the temperature recorded from the distal end of the ablation catheter, the change in impedance, and the swing condition of the ablation catheter observed under fluoroscopy.^[25-27] However, many studies have shown that these alternative indicators are not sufficiently reliable to reflect the real-time contact condition.^[27-29] Therefore, the direct measurement of the CF is the only reliable indicator.

In this study, the ventricular bipolar voltage amplitude, unipolar voltage amplitude, and initial impedance showed weak positive correlations with the real-time CF shown by the CARTO 3 system. However, these indicators overlapped substantially; therefore, it could be difficult for operators to assess CFs accurately according to these indicators in clinical practice. Theoretically, the reduction in the local ventricular voltage is related not only to poor contact but also to pathological factors, such as local ventricular muscle fibrosis, ventricular low voltage area, past ablation injury, and temporary tissue congestion. Although high ventricular voltage can be used to predict a good contact condition, excessive CF cannot be excluded. Therefore, the clinical application value of predicting the real-time CF by measuring the local ventricular voltage amplitude before ablation is very limited.

The limitations of this study are as follows: (1) Although Guangxi Bama miniature pigs are good animal models for cardiac studies, anatomical differences undoubtedly exist between pigs and humans; therefore, the clinical applicability of the results could be limited; (2) The number of experimental animals and ablation lesions in this study was

limited, which might lead to statistical bias; (3) Intracardiac echocardiography, trans-esophageal echocardiography, and digital subtraction angiography, which might affect the precise positioning of the catheters, were not used in our study; (4) Due to the influence of the heartbeat and respiratory movement, the relative displacement of the ablation catheters could not be avoided entirely during the mapping and ablation procedure, and the slight fluctuation of the CF, which might affect the lesion size, could also not be avoided; and (5) The optimal CF range when ablating the RVOT of humans remains uncertain, and further basic experiments and clinical studies are required for evaluating and validating the effectiveness and safety of CF-sensing catheters in patients with RVOT-VAs.

In conclusion, the CF seems to be the leading predictive factor of lesion size in RVOT ablation. Maintaining the CF value between 3 and 10 g may be reasonable and effective for creating the necessary lesion size and reducing the risk of complications, such as steam pops and perforations.

Funding

This study was supported by a grant of the Major Research and Development Project of Guangxi (No. AB16380231).

Conflicts of interest

None.

References

- Hayashi T, Liang JJ, Shirai Y, Kuo L, Muser D, Kubala M, *et al.* Trends in successful ablation sites and outcomes of ablation for idiopathic outflow tract ventricular arrhythmias. *JACC Clin Electrophysiol* 2020;6:221–230. doi: 10.1016/j.jacep.2019.10.004.
- Cronin EM, Bogun FM, Maury P, Peichl P, Chen M, Namboodiri N, *et al.* 2019 HRS/EHRA/APHR/LAHR expert consensus statement on catheter ablation of ventricular arrhythmias. *Europace* 2019;21:1143–1144. doi: 10.1093/europace/euz132.
- Latchamsetty R, Yokokawa M, Morady F, Kim HM, Mathew S, Tilz R, *et al.* Multicenter outcomes for catheter ablation of idiopathic premature ventricular complexes. *JACC Clin Electrophysiol* 2015;1:116–123. doi: 10.1016/j.jacep.2015.04.005.
- Saba MM, Li A. Mapping and ablation of ventricular outflow tract arrhythmias. *Card Electrophysiol Clin* 2019;11:597–607. doi: 10.1016/j.ccep.2019.08.003.
- Calzolari V, De Mattia L, Indiani S, Crosato M, Furlanetto A, Licciardello C, *et al.* In vitro validation of the lesion size index to predict lesion width and depth after irrigated radiofrequency ablation in a porcine model. *JACC Clin Electrophysiol* 2017;3:1126–1135. doi: 10.1016/j.jacep.2017.08.016.
- Mori H, Kato R, Sumitomo N, Ikeda Y, Goto K, Tanaka S, *et al.* Relationship between the ablation index, lesion formation, and incidence of steam pops. *J Arrhythmia* 2019;35:636–644. doi: 10.1002/joa3.12195.
- Nazeri A, Ganapathy A, Massumi A, Massumi M, Constantine G, Raz S, *et al.* Contact-force recovery can predict cardiac perforation during radiofrequency ablation. *Pacing Clin Electrophysiol* 2014;37:1129–1132. doi: 10.1111/pace.12409.
- Franco E, Rodriguez Munoz D, Matia R, Hernandez-Madrid A, Sanchez Perez I, Zamorano JL, *et al.* Contact force-sensing catheters: performance in an ex vivo porcine heart model. *J Interv Card Electrophysiol* 2018;53:141–150. doi: 10.1007/s10840-018-0435-y.
- Crick SJ, Sheppard MN, Ho SY, Gebstein L, Anderson RH. Anatomy of the pig heart: comparisons with normal human cardiac structure. *J Anat* 1998;193 (Pt 1):105–119. doi: 10.1046/j.1469-7580.1998.19310105.x.
- Douglas WR. Of pigs and men and research: a review of applications and analogies of the pig, *sus scrofa*, in human medical research. *Space Life Sci* 1972;3:226–234. doi: 10.1007/BF00928167.
- Shah DC, Lambert H, Nakagawa H, Langenkamp A, Aeby N, Leo G. Area under the real-time contact force curve (force-time integral) predicts radiofrequency lesion size in an in vitro contractile model. *J Cardiovasc Electrophysiol* 2010;21:1038–1043. doi: 10.1111/j.1540-8167.2010.01750.x.
- Leshem E, Tschabrunn CM, Contreras-Valdes FM, Zilberman I, Anter E. Evaluation of ablation catheter technology: comparison between thigh preparation model and an in vivo beating heart. *Heart Rhythm* 2017;14:1234–1240. doi: 10.1016/j.hrthm.2017.04.035.
- Casella M, Gasperetti A, Gianni C, Zucchelli G, Notarstefano P, Al-Ahmad A, *et al.* Ablation Index as a predictor of long-term efficacy in premature ventricular complex ablation: a regional target value analysis. *Heart Rhythm* 2019;16:888–895. doi: 10.1016/j.hrthm.2019.01.005.
- Tofiq BJ, Lukac P, Nielsen JM, Hansen ESS, Tougaard RS, Jensen HK, *et al.* Radiofrequency ablation lesions in low-, intermediate-, and normal-voltage myocardium: an in vivo study in a porcine heart model. *Europace* 2019;21:1919–1927. doi: 10.1093/europace/euz247.
- Matia Frances R, Hernandez Madrid A, Delgado A, Carrizo L, Pindado C, Moro Serrano C, *et al.* Characterization of the impact of catheter-tissue contact force in lesion formation during cavo-tricuspid isthmus ablation in an experimental swine model. *Europace* 2014;16:1679–1683. doi: 10.1093/europace/eut351.
- Di Biase L, Natale A, Barrett C, Tan C, Elayi CS, Ching CK, *et al.* Relationship between catheter forces, lesion characteristics, “popping,” and char formation: experience with robotic navigation system. *J Cardiovasc Electrophysiol* 2009;20:436–440. doi: 10.1111/j.1540-8167.2008.01355.x.
- Yokoyama K, Nakagawa H, Shah DC, Lambert H, Leo G, Aeby N, *et al.* Novel contact force sensor incorporated in irrigated radiofrequency ablation catheter predicts lesion size and incidence of steam pop and thrombus. *Circ Arrhythm Electrophysiol* 2008;1:354–362. doi: 10.1161/CIRCEP.108.803650.
- Thiagalangam A, D’Avila A, McPherson C, Malchano Z, Ruskin J, Reddy VY. Impedance and temperature monitoring improve the safety of closed-loop irrigated-tip radiofrequency ablation. *J Cardiovasc Electrophysiol* 2007;18:318–325. doi: 10.1111/j.1540-8167.2006.00745.x.
- Weiss C, Antz M, Eick O, Eshagzai K, Meinertz T, Willems S. Radiofrequency catheter ablation using cooled electrodes: impact of irrigation flow rate and catheter contact pressure on lesion dimensions. *Pacing Clin Electrophysiol* 2002;25 (Pt 1):463–469. doi: 10.1046/j.1460-9592.2002.00463.x.
- Perna F, Heist EK, Danik SB, Barrett CD, Ruskin JN, Mansour M. Assessment of catheter tip contact force resulting in cardiac perforation in swine atria using force sensing technology. *Circ Arrhythm Electrophysiol* 2011;4:218–224. doi: 10.1161/CIRCEP.110.959429.
- Reddy VY, Shah D, Kautzner J, Schmidt B, Saoudi N, Herrera C, *et al.* The relationship between contact force and clinical outcome during radiofrequency catheter ablation of atrial fibrillation in the TOCCATA study. *Heart Rhythm* 2012;9:1789–1795. doi: 10.1016/j.hrthm.2012.07.016.
- Guo XY, Ma CS. Atrial fibrillation ablation: indications, outcomes, complications, and future directions. *Chin Med J* 2017;130:1891–1893. doi: 10.4103/0366-6999.211900.
- Baccillieri MS, Rizzo S, De Gaspari M, Paradiso B, Thiene G, Verlato R, *et al.* Anatomy of the cavotricuspid isthmus for radiofrequency ablation in typical atrial flutter. *Heart Rhythm* 2019;16:1611–1618. doi: 10.1016/j.hrthm.2019.05.030.
- Sun YJ, Yin XM, Cong T, Gao LJ, Chang D, Xiao XJ, *et al.* Comparison of cryoballoon ablation for atrial fibrillation guided by real-time three-dimensional transesophageal echocardiography vs. contrast agent injection. *Chin Med J* 2019;132:285–293. doi: 10.1097/CM9.0000000000000076.
- Rozen G, Praszek L, Zilberman I, Cordaro K, Heist EK, Beeckler C, *et al.* Prediction of radiofrequency ablation lesion formation using a novel temperature sensing technology incorporated in a force sensing catheter. *Heart Rhythm* 2017;14:248–254. doi: 10.1016/j.hrthm.2016.11.013.
- De Bortoli A, Sun LZ, Solheim E, Hoff PI, Schuster P, Ohm OJ, *et al.* Ablation effect indicated by impedance fall is correlated with contact

- force level during ablation for atrial fibrillation. *J Cardiovasc Electrophysiol* 2013;24:1210–1215. doi: 10.1111/jce.12215.
27. Ikeda A, Nakagawa H, Lambert H, Shah DC, Fonck E, Yulzari A, *et al.* Relationship between catheter contact force and radiofrequency lesion size and incidence of steam pop in the beating canine heart: electrogram amplitude, impedance, and electrode temperature are poor predictors of electrode-tissue contact force and lesion size. *Circ Arrhythm Electrophysiol* 2014;7:1174–1180. doi: 10.1161/CIRCEP.113.001094.
28. Barrio-Lopez T, Ortiz M, Castellanos E, Lazaro C, Salas J, Madero S, *et al.* Relationship between left atrium catheter contact force and pacing threshold. *J Interv Card Electrophysiol* 2017;49:147–155. doi: 10.1007/s10840-017-0253-7.
29. Sasaki N, Okumura Y, Watanabe I, Sonoda K, Kogawa R, Takahashi K, *et al.* Relations between contact force, bipolar voltage amplitude, and mapping point distance from the left atrial surfaces of 3D ultrasound- and merged 3D CT-derived images: Implication for atrial fibrillation mapping and ablation. *Heart Rhythm* 2015;12:36–43. doi: 10.1016/j.hrthm.2014.09.007.

How to cite this article: Jiang JB, Li JY, Jiang ZY, Wang A, Huang Z, Xu HY, Shu CL, Li GJ, Zheng YS, He Y, Zhong GQ. Impact of catheter-tissue contact force on lesion size during right ventricular outflow tract ablation in a swine model. *Chin Med J* 2020;133:1680–1687. doi: 10.1097/CM9.0000000000000859