The Effect of Contact Force in Atrial Radiofrequency Ablation

Electroanatomical, Cardiovascular Magnetic Resonance, and Histological Assessment in a Chronic Porcine Model

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ABSTRACT

OBJECTIVES This study sought to determine the effect of contact force (CF) on atrial lesion size, quality, and transmurality by using a chronic porcine model of radiofrequency ablation.

BACKGROUND CF is a major determinant of ventricular lesion formation, but uncertainty exists regarding the most appropriate CF parameters to safely achieve permanent, transmural lesions in the atria.

METHODS Intercaval linear ablation (30 W, 42°C, 17 ml/min irrigation) was performed in 8 Göttingen minipigs by using a force-sensing catheter with CF > 20 g (high force) or < 10 g (low force) at alternate ends of the line, separated by an intentional gap. Voltage mapping and cardiovascular magnetic resonance (CMR) imaging were performed pre-ablation, immediately after ablation, and at 2 months' post-procedure. Lesions were sectioned orthogonal to the axis of ablation to assess transmurality.

RESULTS Mean CF was 22.6 ± 11.4 g and 7.8 ± 4.0 g in the high and low CF regions. Acute tissue edema was greater with high CF, both caudally (7.0 mm vs. 4.6 mm; p = 0.016) and cranially (6.9 mm vs. 4.6 mm; p = 0.038). There was no difference in chronic lesion size (voltage mapping) or volume (late gadolinium enhancement CMR) between high and low CF regions. There was no difference in scar density (assessed by low-voltage criteria and late gadolinium enhancement signal intensity) or histological transmurality between high and low CF regions.

CONCLUSIONS Although high CF (>20 g) resulted in more acute tissue edema than low CF (<10 g), chronically there was no difference in lesion size, quality, or transmurality. Appropriate CF targets for atrial ablation may be lower than previously thought. (J Am Coll Cardiol EP 2015;1:421–31) © 2015 by the American College of Cardiology Foundation.

Catheter-tissue contact force (CF) is a key determinant of radiofrequency (RF) ablation lesion formation in both ex vivo ventricular (1–4) and in vivo nonmyocardial (5–7) ablation models. Similarly, increasing CF leads to increased lesion depth and diameter in vivo in the canine ventricle (8). Although high CF has been associated with increased ventricular lesion size, whether the

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same is true of the thin-walled left atrium is not known.

Procedural safety profiles are also affected by CF. Risk of tamponade is directly related to applied CF, with a minimum force of 38 g being sufficient for perforation in ex vivo human atrial tissue (9). In a study of porcine atrial ablation, application of RF energy reduced the perforating force by 23% (10), and perforating forces were significantly lower through previously ablated tissue (11). Furthermore, CF itself is an independent predictor of steam pops and thrombus formation (6). Ideal CF targets for atrial ablation must therefore balance both lesion effectiveness and safety of application.

In the present study, we explored the relationship between catheter myocardium CF in an in vivo chronic porcine atrial ablation model. The model was designed to replicate human atrial ablation and used standard clinical-grade ablation equipment throughout. By controlling for all ablation-related parameters, including catheter stability, the effect of CF on ablation lesion creation is determined in isolation.

METHODS

ANIMAL MODEL AND PROTOCOL. Animal studies complied fully with Danish law on animal experiments. Eight male Göttlingen minipigs (41.2 ± 7.2 kg) were pre-sedated with intramuscular azaperone (4 mg/kg) and midazolam (0.5 mg/kg). General anesthesia was induced with intravenous ketamine (5 mg/kg) and midazolam (0.5 mg/kg), and the animals were intubated and mechanically ventilated. Anesthesia was maintained with a continuous intravenous infusion of propofol (3 mg/kg/h) and fentanyl (15 μg/kg/h).

Two of the 8 minipigs underwent pre-ablation cardiovascular magnetic resonance (CMR) imaging, and all 8 minipigs subsequently underwent electroanatomic mapping (EAM) and ablation according to the protocols described in the following sections. Immediately post-ablation, all animals were transferred for CMR imaging before being recovered from anesthesia and returned to the farm for 2 months. Minipigs were used to ensure minimal growth during the recovery period. After 2 months, the animals were anesthetized according to the same protocol and underwent chronic CMR imaging followed by EAM. Subsequently, a midline sternotomy was performed in all animals, and the hearts were removed en bloc and perfusion-fixed, ready for subsequent analysis.

ELECTROANATOMICAL MAPS AND ABLATION. Two 8-F sheaths were placed percutaneously into the right femoral vein, followed by an intravenous injection of 100 IU/kg of heparin. A 6-F decapolar reference catheter was positioned in the coronary sinus (CS). An 8-F ablation catheter (ThermoCool SmartTouch, D curve; Biosense Webster, Diamond Bar, California) was advanced to the right atrium (RA). A 3-dimensional geometric model of the RA was created by using the Carto 3 MEM system (Biosense Webster), and a high-density, pre-ablation peak-to-peak bipolar voltage map was constructed during proximal CS pacing.

Linear RF ablation (42°C, 30 W, 17 ml/min irrigation) was performed from the superior vena cava (SVC) to the inferior vena cava (IVC) along the posterior wall of the RA. The intercaval region of the RA was selected for ablation. Ablation was performed as a continuous drag with the catheter moved every 30 s. After completion of the intercaval linear lesion, a second high-density voltage map was immediately acquired during proximal CS pacing. Delivery of effective ablation was confirmed by the absence of pace capture (3-mA output, 2-ms pulse width) along the ablation line and the presence of a new activation detour during CS pacing. After recovery (2 months’) post-ablation, chronic voltage maps were created by adhering to the same protocol.

CARDIOVASCULAR MAGNETIC RESONANCE. CMR was performed on a 1.5-T magnetic resonance system (Achieva, Philips Medical Systems, Best, the Netherlands) equipped with a 5-element cardiac phased-array coil. First, survey and sensitivity encoding reference scans were obtained, followed by a 2-dimensional multi-cardiac phase cine scan acquired in a 4-chamber orientation. From this scan, the trigger delay was determined for all subsequent scans to minimize artifacts from atrial wall motion.
3 mm). The respiratory navigator was used to minimize motion artifacts and to ensure acquisition at end-expiration for all slices.

Thirty minutes after administration of 0.2 ml/kg of Gadovist (Bayer HealthCare Pharmaceuticals, Berlin, Germany), axial 3-dimensional late gadolinium enhancement (LGE) imaging was performed (respiratory-navigated, electrocardiogram-triggered inversion recovery turbo field echo acquisition; spatial resolution 1.3 × 1.3 × 4 mm³ [reconstructed to 0.6 × 0.6 × 2 mm³]; echo time/repetition time 3.0 ms/6.2 ms; flip angle 25°). The inversion time was determined by using a preceding Look-Locker sequence to achieve optimal suppression of the atrial blood pool signal.

MACROSCOPIC AND MICROSCOPIC EXAMINATION. After the animals were killed, the hearts were explanted and suspended in cold normal saline. The aorta and main pulmonary artery were cannulated, and the pulmonary veins, IVC, and SVC were cross-clamped. Retrograde perfusion fixation of the heart was performed by using 1-l of Karnovsky’s fixative (Solmedia Ltd., Shrewsbury, United Kingdom) per heart. The ablation line and surrounding tissue were excised en bloc and mounted in plastic frames, allowing 5-mm sections to be removed from the caudal and cranial ends of the ablation line. Each section was photographed and then dehydrated, embedded in paraffin, sectioned (5-µm sections), and stained with Masson’s trichrome for microscopic examination.

DATA ANALYSIS. Catheter stability. Catheter stability at each end of the ablation line was determined by using the Carto 3 VisiTag module, with stability filters set to 2.5 mm/10 s. The number of VisiTags created during ablation per unit length of ablation line was taken to represent catheter stability within that ablation region.

Electroanatomical mapping. Chronic voltage maps were registered to immediate post-ablation maps by 3-dimensional translation and rotation using the SVC, IVC, RA appendage, and azygos veins as registration landmarks. Short-axis clipping planes were applied to remove the SVC above the right atrial appendage, to remove the IVC below the CS, and to divide the chamber through the center of the ablation gap. Low-voltage area arising from ablation was quantified by using the ablation index (AI). For each half of the chamber, AI was defined as the post-ablation low-voltage area minus the pre-ablation low-voltage area divided by the ablation area. Pre- and post-ablation low-voltage areas were defined as the area of the caudal or cranial ends of the shell <0.5 mV. Ablation area was defined as the area of the shell indicated by the Carto ablation tags. AI was calculated for post-ablation acute and chronic voltage maps. Scar density and mean ablation region voltage were then calculated. First, 3-dimensional scar regions were removed from the Carto 3 geometric model by using a box-clipping function (Kitware Inc., New York, New York). The resulting 3-dimensional posterior RA regions were resolved to 2 dimensions by using a surface parameterization technique (13). Ablation regions were thereby determined by projecting the ablation region (determined by intraprocedural ablation tags) onto the post-ablation acute and chronic patches to allow quantification of the voltage within the ablation region.

Cardiovascular magnetic resonance. Acute and chronic wall thickness was measured manually on axial T2W images. Chronic LGE enhancement was quantified by 2 metrics. Ablation volume at each end of the ablation line was determined as follows: First, a region of interest encompassing the entire posterior wall of the RA was manually created on the axial LGE images. Next, enhancement within the region of interest was identified by applying automatic signal intensity thresholds at a range of SDs above the mean atrial blood pool signal intensity. Finally, the image slice representing the center of the ablation gap was identified as the middle slice on the isosurface threshold level at which the distance of the apparent gap was minimized. From this standardized reference a 1-cm region was taken of either side of the central ablation gap, thereby allowing relative ablation volumes to be compared between the animals at 3 SDs above the blood pool mean for chronic LGE images. Fibrosis intensity was quantified as the maximum and mean LGE signal intensity found within the posterior RA region of interest. Intensities are presented as the image intensity ratio (IIR), the ratio of ablation region signal intensity divided by the mean right atrial blood pool signal intensity. Mean IIR was simply defined as the mean of the IIRs for each voxel in the 1-cm region of interest defined earlier. Peak IIR was determined by manually drawing a 2-dimensional region of interest in the posterior wall of the RA for each slice of the axial LGE image. The maximal intensity within these regions for each imaging slice was plotted against distance along the ablation line, thereby allowing peak IIR to be determined for caudal and cranial ends of the ablation line.

Microscopic examination. An ablation scar was defined as transmural where a contiguous region of scar was evident from the endocardial to the epicardial aspects on the transverse sections. Fibrosis scoring of the ablation scar was determined as follows. Whole sections were digitized (10× magnification).
by using a scanning brightfield microscope (Leica Microsystems, Milton Keynes, United Kingdom). The ratio of blue to red staining of 3 rectangular zones within the ablation scar was quantified by using an ImageJ macro as previously described (14).

**STATISTICAL ANALYSIS.** Data analysis was performed by using GraphPad Prism version 6.0c (GraphPad Software, San Diego, California). Results are presented as mean ± SD. The Student paired t test was used to compare group means between high- and low-force regions. A significance level of \( p < 0.05 \) was considered statistically significant.

**RESULTS**

**PROCEDURAL AND ABLATION PARAMETERS.** All 8 animals survived until the end of the protocol, and no animals were excluded from analysis due to premature death. No procedural complications occurred. Mean applied CF was 22.6 ± 11.4 g in high-force zones and 7.8 ± 4.0 g in low-force zones \( (p < 0.0001) \) (Figures 1A and 1B), resulting in average force-time integrals of 1,170 ± 509 gs (high-force) and 272 ± 94 gs (low-force). There was no difference in ablation times (high-force 6.7 ± 1.9 min vs. low-force 6.8 ± 1.9 min; \( p = 0.9197 \)) or ablation line dimensions (high-force 4.3 ± 0.6 cm vs. low-force 3.7 ± 0.6 cm; \( p = 0.1687 \)). Correspondingly, there was no significant difference in ablation time per unit length between regions (high-force 1.64 ± 0.57 min/cm vs. low-force 1.84 ± 0.51 min/cm; \( p = 0.5300 \)). Catheter stability was identical between high- and low-force zones, with mean VisiTag densities of 3.87 ± 0.65 tags/cm and 3.84 ± 0.94 tags/cm, respectively \( (p = 0.9932) \). CF resulted in a significant increase in impedance (measured mid-chamber) from baseline, up to 25 g, with a plateau thereafter (Figure 1C). Overall, a significantly greater proportion of ablation lesions was delivered at maximum power output at regions of

![Figure 1](https://example.com/figure1.png)

(A, B) Contact force distribution during low- and high-force ablation. (C) Change in impedance with catheter–myocardium contact force. (D) Maximal power output (30 W) during ablation for low- and high-force ablation regions.
low-force compared with regions of high-force ablation (Figure 1D), and this difference was observed in every animal. Mean power during ablation was $24.8 \pm 6.6$ W versus $28.7 \pm 4.0$ W in the high- and low-force zones ($p < 0.0001$).

**ELECTROANATOMIC MAPPING.** Pre-ablation, post-ablation, and chronic mapping was performed in all animals, resulting in a total of 24 electroanatomic maps with an average of 1,161 points per map. Achieved ablation size was quantified for acute and chronic post-ablation maps using the AI, which represents the area of new low voltage on post-ablation voltage maps indexed to the area of RF energy application. There was no difference in post-ablation acute AI or chronic AI voltage maps between the high- and low-force ablation regions (Figure 2). Scar density was quantified on EAM as the proportion of the ablation zone $<0.5$ mV. There was no excess reduction in scar density between acute and chronic time points for scarring created with low-force ablation compared with high-force ablation (Figure 3). Similarly, there was no increase in ablation region voltage between acute and chronic time points for either high- or low-force ablation.

**CARDIAC MAGNETIC RESONANCE.** Consistent with our previous experience, no appreciable pre-ablation T2W or LGE enhancement was seen in any pig.

Compared with pre-ablation voltage distributions, post-ablation voltage distributions exhibit a leftward skew that is similar for both the HF and LF ablation regions. Comparing acute versus chronic time points, there is no excess increase in voltage recovery for LF compared with HF regions. Abbreviations as in Figure 2.
undergoing pre-ablation imaging (12). Acute T2W wall thickness was significantly greater for high-force ablation compared with low-force ablation, and this difference persisted when cranial and caudal ends of the ablation line were considered separately (Figure 4). In contrast, there was no difference in chronic LGE scar volume between high- and low-force ablation regions (Figure 5). Similarly, there was no difference in mean (Figure 6A) or peak (Figure 6B) LGE IIR between the 2 ablation regions.

**MACROSCOPIC AND MICROSCOPIC EXAMINATION.** Macroscopic photographs of chronic ablation lesions after perfusion fixation are shown in Figure 7. The mid-chamber ablation gaps measured 5.3 ± 1.5 mm. The ablation line was sectioned perpendicular to the axis of ablation through the high- and low-force regions, resulting in 16 sections. In all 16 sections, replacement of normal atrial wall with fibrous scar tissue was identified. Transmural scar was seen in 14 of the 16 sections, with both nontransmural ablation scars occurring in high-force ablation zones. There was no significant difference in quantified fibrosis density between the high- and low-force regions (59.1% vs. 68.1%, respectively; p = 0.2961).

**DISCUSSION**

The main findings of the present study are as follows: 1) low-force ablation (<10 g) resulted in RF ablation lesion size, quality, and transmurality equivalent to those of high-force ablation in an atrial ablation model; 2) catheter–myocardium–blood pool interface impedance was proportional to CF within the range of 0 to 25 g and reached a plateau thereafter; and 3) during temperature-controlled RF energy delivery, higher generator power output appeared to compensate for reduced catheter–myocardium energy transfer at low CF.

With the advent of intraprocedural CF-monitoring catheters, it has become possible not only to confirm contact of the catheter tip with a physical barrier (i.e., myocardium) but also to directly measure the force (magnitude and direction) exerted by that barrier on the catheter tip. In clinical studies, the use...
of CF monitoring has been associated with improved procedural outcomes, regardless of the CF applied (15), and low CF has been associated both with procedural failure (16) and with sites of pulmonary venous reconnection (17). Despite these findings, use of CF-sensing technology does not universally lead to improved procedural outcomes (18), raising the possibility that other confounding factors may at least partially explain the relationship between CF and outcome in clinical studies.

Examining lesion sizes created in the ex vivo studies further supports this argument. As shown in Figure 8, most studies display a linear relationship between CF and lesion depth at low CFs before reaching a plateau between 10 and 20 g. Of particular importance is that even at minimal CF, the shortest duration applications achieved a lesion depth of almost 4 mm. Considering the typical thickness of the human left atrial wall ranging up to 3 to 4 mm (19,20), it follows that low-force ablation could achieve transmural scarring in atrial ablation. This hypothesis is supported by in vivo studies of ventricular radiofrequency ablation (demonstrating 5.0- to 5.9-mm lesion depth even at low CF) but has not been tested in an in vivo atrial model.

Based on these observations, the present study aimed to assess the size, quality, and transmurality of atrial ablation lesions created at low force (<10 g; mean 7.8 g) compared with lesions created at high force (>20 g; mean 22.6 g). We used a previously validated porcine right atrial ablation model representing an ablation site that is similar in morphology and thickness to the human left atrium (12). The low- and high-force targets were selected based on previous research demonstrating consistent contact at 9.9 ± 8.6 g and tissue tenting at 25.0 ± 14.0 g of CF (21). Crucially, equal stability was ensured between low- and high-force regions by using the VisiTag module in the Carto 3 mapping system, and any effect of regional variation in tissue characteristics was
negated by performing ablation in counterbalanced order with both high and low force being used at the caudal and cranial ends of the ablation line. Under these controlled conditions, there were no differences in lesion size, quality, or transmurality either acutely or at 2 months’ post-ablation between the low- and high-force strategies. Therefore, equivalent procedural success should be achievable with low-force ablation, whenever consistent catheter–myocardium contact can be established.

Although our study was not powered to detect procedural complications, increased CF may be associated with complications, especially cardiac perforation, tamponade, and damage to extracardiac structures. Studies examining perforating forces have generally identified higher minimum perforating forces than those used in our study; however, it is still desirable to use the minimum CF required to increase the margin of safety. Of note in our study, T2W wall thickness was significantly greater at regions of high force than low force. Two possible hypotheses support this finding. First, even though low force achieved transmurality, high force may have resulted in greater (unnecessary) energy transfer, leading to more atrial wall edema. Because increased edema (T2W enhancement) has been associated with AF recurrence after pulmonary vein isolation (22), it is conceivable that high CF may actually be counterproductive by causing edema-related functional block and underestimation of the size of any ablation gaps. Second, because tissue tenting has been identified on intracardiac ultrasound with forces of approximately 25 g (21), high-force ablation in the present study may have resulted in heating and edema of extracardiac structures. This finding is consistent with previous research identifying an independent role for catheter–myocardium CF in esophageal injury during left atrial ablation (23), as well as CMR studies identifying increased aortic and esophageal LGE post–left atrial ablation (24,25).

**STUDY LIMITATIONS.** The results presented here describe the effect of CF on linear ablation in an animal model. Given the similarity of wall thickness and profile of the porcine RA to the human left atrium, we
would, however, expect similar findings in the human left atrium but acknowledge this limitation of any animal model of human cardiac tissue. Also, to most closely resemble clinical practice, drag lesions rather than point lesions were created. It is possible that the lesions will therefore overlap, resulting in a cumulative effect on tissue heating. By performing ablation solely at the posterior RA, the range of CF vectors is limited. Although this action is necessary to isolate the effect of CF on lesion formation, we acknowledge this limitation when extrapolating the findings to human left atrial ablation with a larger range of force vectors.

**CONCLUSIONS**

By using a combined EAM, imaging, and histological examination approach, we demonstrated equivalent chronic atrial ablation lesion formation at low and...
high catheter-myocardium CF. Appropriate CF targets for left atrial ablation may be lower than previously described, especially with concomitant use of novel stability-sensing technologies, and adoption of lower force targets may lead to improved procedure safety.

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