High incidence of Low Catheter-Tissue Contact Force at the Cavotricuspid Isthmus During Catheter Ablation of Atrial Flutter: Implications for achieving isthmus block

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\textit{Short title: Contact force during cavotricuspid isthmus ablation}

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Abstract

Background: Recurrent atrial flutter following cavo-tricuspid isthmus (CTI) ablation remains a significant problem. The prevalence of low contact force (CF) during CTI ablation using standard tools is unknown. Our aim was to characterize the prevalence of low CF applications when experienced operators performed CTI ablation using “traditional” markers of contact blinded to CF measurements.

Methods and Results: Average CF (grams, g) and force-time integral (FTI) was analyzed in 458 lesions in 17 patients undergoing CTI ablation. The isthmus was divided into the annular, mid and caval segments for region-specific analysis. Despite “good” contact using traditional markers, there was significant variability in CF within each isthmus segment (e.g. annular CTI 1-57g). A high proportion of lesions had a CF <10g (40%). Lowest CF was the annular (median 9 g), followed by the mid (12g) and the caval CTI (18 g, P<0.001). Sites of acute CTI re-connection had a lower average CF and FTI than non-reconnected sites (P<0.05). Each 1g increase in CF was associated with a 16% reduction in risk of recovered CTI conduction (95% confidence interval: 4-27%, P=0.01)

Conclusions: Use of surrogate markers of “good contact” during ablation by experienced operators in the absence of real-time CF sensing resulted in nearly half of all lesions being delivered with low CF with marked region-specific variability in CF. Low CF was implicated in longer time to achieve conduction block and increased
risk of acute reconnection. These findings underscore the importance of real-time CF measurements for optimizing ablation of typical atrial flutter.

**Keywords:** atrial flutter; cavo-tricuspid isthmus; contact-force sensing; reconnection; catheter ablation.
Introduction

Recent studies have reported the utility of CF-sensing during catheter ablation of atrial fibrillation (AF) in reducing ablation time to achieve pulmonary vein isolation (PVI),\(^1\) acute pulmonary vein reconnection\(^1,2\) and risk of AF recurrence.\(^3\) These studies have also demonstrated the anatomic regions in which contact force is most often poor.\(^1,4,5\) Cavotricuspid isthmus (CTI) ablation for atrial flutter (AFl) is one of the most common RF ablation procedures performed worldwide yet comparable contact data is lacking. Although complete CTI block can be readily achieved in almost all patients acutely, the recurrence rate of isthmus dependent flutter remains considerable even in experienced hands.\(^6,7\) In this study, we characterize real-time CF recordings during CTI ablation in humans performed by experienced operators using traditional markers of contact, yet blinded to real-CF readings in order to determine the prevalence of low contact lesions. Second, we sought to determine the relationship between CF parameters, time to achieve conduction block and subsequent risk of acute CTI re-conduction.

Methods

Consecutive patients with paroxysmal or persistent AFl undergoing CTI ablation under general anesthesia were prospectively recruited. The procedure was performed by two operators who had procedural experience of >200 previous AFl ablations with a minimum of 50 procedures/year. The study protocol was approved by the Melbourne Health Human Research Ethics Committee. The present study includes and expands on the patient population recruited and reported on previously.\(^8\)
**Catheter setup**

Intra-cardiac catheters were positioned as follows: (1) 10-pole coronary sinus catheter, (2) 20-pole catheter positioned along either the right atrial free wall or the tricuspid annulus, (3) His-bundle catheter, and (4) mapping and ablation catheter delivered through an 8.5-Fr SRO sheath (St. Jude Medical, Minneapolis, MN). At the start of the procedure, CTI geometry was constructed using non-fluoroscopic mapping system (Ensite NavX, St. Jude Medical). Bipolar intracardiac EGMs and 12-lead surface ECG were recorded simultaneously on a computerized digital amplifier system. Intracardiac electrograms (EGMs) were filtered between 30 and 500 Hertz.

In patients presenting with AFl, the tachycardia mechanism was identified to be CTI-dependent using a combination of activation mapping along multipolar catheters, entrainment mapping, and activation mapping. Patients presenting in sinus rhythm had AFl induced with burst and programmed atrial stimulation with infusion of isoprenaline when required. Ablation was either performed in AFl or fixed proximal coronary sinus pacing at 600 milliseconds when in sinus rhythm. In all patients, the CTI was the only site of radiofrequency (RF) ablation; no adjunctive left atrial ablation was performed.

**Ablation**

Point-by-point ablation of the CTI was performed commencing from the annular to the caval end of the CTI with the endpoint of sustained bidirectional CTI block. Operators used only traditional markers of “good” catheter-tissue contact such as catheter-tip motion on fluoroscopy and the 3D mapping system, EGM quality, in
addition to EGM abatement and impedance fall with ablation. Operators were blinded to real CF measurements throughout the procedure. Each RF lesion was delivered aiming for one or more of the following: minimum 5 ohm (Ω) impedance fall, >50% attenuation in EGM amplitude, and/or development of local split potentials at the RF site. During ablation, power was limited to 40 Watts, irrigation set at 17 mL/minute, and temperature limited to 48° Celsius. At the discretion of the operator, RF could be terminated prematurely (before 30 seconds) if it were judged that contact was poor based on the absence of one of the aforementioned factors. Lesions where subjectively “good” contact could not be obtained resulting in premature RF termination were excluded from the analysis. Care was taken to ensure that the anatomic line was completed even after demonstration of bidirectional CTI block. The presence of bidirectional block was assessed at baseline, upon abrupt termination of atrial flutter, immediately upon evidence of unidirectional block during ablation in sinus rhythm, and repeatedly at 5-minute intervals during a 30 minute waiting period.

Ablation catheter

A novel CF-sensing catheter were used as described previously (TactiCath; St. Jude Medical). Briefly, it is an open-irrigation catheter that contains a triaxial sensor located between the second and third electrodes, which measures the force (amplitude and direction) of the contact between the tissue and the catheter-tip electrode. The CF sensor has a resolution and sensitivity of 1 gram (g) in a bench test.
Each RF lesion was logged for average CF (in g) and force-time integral (FTI = real-time force x ablation time, g*s).\textsuperscript{9} The average CF, FTI, lesion location on the CTI and the duration of RF were recorded. The CTI was divided into equal length segments (annular, mid, and caval) for the purpose of region-specific analysis of CF.\textsuperscript{11} RF time required to achieve bidirectional block for the first time during the procedure, the site of the last lesion that resulted in bidirectional block, and site of acute conduction recurrence were recorded.

**Endpoints**

The primary aim was to describe the average CF and FTI, and number of lesions delivered with low CF (<10g) or low FTI (<400g*s) during CTI ablation in a region-specific manner. The secondary aims were to: (1) determine the relationship between low CF lesions (<10g) or low FTI lesions (<400g*s) and the RF time needed to achieve acute bidirectional CTI block and; (2) determine the relationship between CF parameters and lesions that produced sustained bidirectional CTI block (no return of conduction after 30 minutes of waiting) versus lesions that produced transient CTI block (return of conduction after 30 minutes of waiting).

**Statistical Analysis**

The Statistical Package for the Social Sciences for Windows (release 22, IBM, Armonk, New York, USA) was used for analysis. Continuous variables were expressed as mean ± standard deviation, if normally distributed. Where normal distribution was not present, log transformation of the raw values was performed to meet the assumption of homogeneity of variance. Median and interquartile range
representing 25-75% of the sample (Q25-Q75) was used if the data was not normally distributed. To account for operator variability, multiple lesions within each patient, and the resulting correlation within patients, we applied linear mixed regression models to compare the difference in log-transformed average CF and FTI between different CTI regions. A generalized linear mixed model was fitted to compare the frequency of low average CF and low FTI lesions between each CTI region. CF data on lesions that produced sustained bidirectional CTI block (no return of conduction after 30 minutes of waiting) were compared with CF data on lesions that showed transient CTI block (return of conduction after 30 minutes of waiting). Univariable linear regression analysis was performed to determine the relationship between CF and RF time to achieve bidirectional CTI block. A two-tailed \( P<0.05 \) was considered statistically significant. Graphs were constructed using Prism version 5.0d (GraphPad Software Inc, La Jolla, CA, USA).

**Results**

**Baseline characteristics**

Seventeen patients undergoing ablation of drug-refractory CTI-dependent AF were included. Mean age was 60 ± 10 years (18% females) with median arrhythmia duration of 2 years (Q25-Q75: 1-3 years), and failure of a median 2 anti-arrhythmic drugs (Q25-Q75: 1-3). Mean left ventricular ejection fraction, mean right atrial area and mean CTI length were 64 ± 4%, 18 ± 3 cm\(^2\) and 38 ± 6.4 mm, respectively. Analysis was performed on 458 lesions (median 20 lesions per patients, Q25-Q75: 15-37 lesions) after exclusion of 62 lesions with premature RF termination (<10 seconds), abrupt catheter displacement or adjudged as “poor” contact by the
operator. Mean RF duration was 26 ± 7 seconds with median impedance fall of 12 Ω (Q25-Q75: 9-16 Ω). All lesions had an impedance fall of >5 Ω and the median CF was 12g (Q25-Q75: 6-23g) in the study population.

The number of lesions delivered at the annular, mid and caval CTI were 107 (23%), 213 (46%) and 139 (30%). There was no significant difference in the region-specific average CF (overall P=0.75) nor the FTI (overall P=0.8) between the two operators.

**Anatomic variation of CF parameters at the CTI**

Using traditional markers of contact, there was wide variation in CF during ablation within each CTI region (Figure 1A). For example, CF varied from 1-57 g at the annular CTI. There was also significant variability in CF during ablation between different CTI regions; highest CFs were observed at the caval CTI, followed by mid and annular CTI (Figure 1A, P<0.001 between all groups). This relationship remained preserved if analysis was restricted to only those lesions with an impedance fall ≥10 (median CF [Q25-Q75] for annular, mid and caval CTI of 9g [5-15g], 13g [7-19g] and 18g [12-26g] respectively, P<0.001 between all 3 groups).

Overall, 40% of lesions were delivered with a low average CF (<10g) and 63% were delivered with a low FTI (<400 g*s). When analysis was restricted to only those lesions with an impedance fall ≥10 Ω, 36% of lesions were still delivered with a low average CF and 60% were delivered with a low FTI. Incidence of lesions with low CF were highest at the caval, followed by the mid and annular CTI (Figure 1B, P<0.001), a relationship that remained preserved when restricting the analysis to include only those lesions with an impedance fall of ≥10 Ω (53%, 40%, 19%,
respectively, \( P<0.001 \)).

There was also wide variation in the FTI during ablation within and between each CTI region (Figure 2A), with the highest FTI at the caval, followed by the mid and annular CTI respectively (\( P<0.001 \) between all 3 groups). The relationship remained preserved when analysis was restricted to only those lesions with an impedance fall of \( \geq 10 \, \Omega \) (median FTI, Q25-Q75 for annular, mid and caval CTI of 220 g*s [126-413 g*s], 297 g*s [167-514 g*s], and 471 g*s [289-745 g*s], \( P<0.001 \) between all 3 groups). The frequency of lesions with a low FTI also followed the same pattern (Figure 2B, \( P<0.001 \) between all 3 groups), even if analysis was restricted to only those lesions with an impedance fall of \( \geq 10 \, \Omega \) (75%, 65%, 41%; \( P<0.001 \) respectively).

**Relationship between CF parameters and ablation time required to achieve acute bidirectional CTI block**

There was a strong, linear, positive correlation between number of lesions with low average CF and low FTI and total ablation time to achieve acute bidirectional CTI block (CF: \( r^2=0.6, \, P<0.001 \); FTI: \( r^2=0.8, \, P<0.001 \), Figure 3A, B). No other clinical parameter (age \( [P=0.7] \), gender \( [P=0.9] \), duration of AF \( [P=0.7] \), number of failed anti-arrhythmic drugs \( [P=0.2] \), right atrial area \( [P=0.2] \), CTI length \( [P=0.4] \), left ventricular ejection fraction \( [P=0.8] \)) predicted total ablation time required to achieve acute bidirectional CTI block.

**Relationship between CF parameters and CTI re-conduction in the waiting period**
Acute bidirectional CTI block was achieved in all patients. The CTI line was anatomically complete in all patients. CTI conduction, however, recovered in 8/17 patients (47%) during the waiting period at 26 lesion sites. All reconnection sites occurred over sites of prior ablation. After ablation of the recovered region, acute bidirectional block was achieved in all patients and did not recover in the following 30 minutes. Patients with evidence of CTI reconnection had significantly lower mean procedural CF and FTI than patients without reconnection (CF: 13±5g vs. 18±5g, P=0.04; FTI: 311±163 g*s vs. 487±138 g*s, P=0.03). Furthermore, original RF lesions at sites that recovered conduction had lower CF (median 8g [Q25-Q75: 5-9g] vs. 22g [Q25-Q75: 14-28g], P=0.001) and FTI (209 g*s [Q25-Q75: 163-260 g*s] vs. 627 g*s [Q25-Q75: 273-838 g*s, P=0.005]) than sites where CTI block persisted after the 30 minute waiting period. Each 1g increase in CF was associated with a 16% reduction in risk of recovered CTI conduction (95% confidence interval: 4-27%, P=.01).

**Discussion**

This prospective study demonstrated that when experienced operators use surrogate markers of tissue contact during CTI ablation, and were blinded to real-time CF readings, there were a very high prevalence of low contact lesions (40% overall). Contact force varied according to anatomic location within the CTI with the tricuspid annular region having the highest percentage of low contact applications (54%) and the caval aspect of the isthmus the lowest percentage (27%). Low contact correlated both with time to achieve isthmus block and also the incidence of acute recovery of conduction. Importantly, each 1g increase in CF reduced the risk of subsequent reconnection by 16%. The study also emphasizes the wide variability in
CF parameters within each CTI segment when surrogate markers of contact were used.

Prior studies

CTI ablation for “typical” atrial flutter remains one of the most common ablation procedures performed either stand-alone or as part of an atrial fibrillation ablation procedure. The CTI is readily accessible and with contemporary technology (long sheaths and irrigated catheters) CTI block can be achieved in almost 100% of patients. Yet despite the apparent ease of this procedure, the rate of recurrent CTI conduction remains surprisingly high. A recent study of 52 patients who underwent CTI ablation with demonstrable bidirectional conduction block during the index procedure observed a 23% recurrent conduction rate at late re-study. This accords with observations regarding rates of recurrent clinical flutter in a meta-analysis of all published studies on catheter ablation of AFl, where single procedure success rates was 92%. Factors previously implicated in difficulties achieving persistent CTI block have focused on variants in anatomic topography (such as prominent sub-Eustachian pouches, prominent pectinates, or a prominent Eustachian ridge), and thick myocardium. The current study demonstrates that poor tissue contact is frequently observed during CTI ablation and potentially results in failure to create transmural lesions.

Since the introduction of CF-sensing catheters, the importance of CF on transmural RF lesion formation has been prospectively investigated in numerous experimental studies, with CF parameters shown to be strongly and linearly correlated to RF ablation lesion size, volume and depth. In human studies, low
CF has been implicated in longer duration of ablation to achieve acute pulmonary vein isolation\textsuperscript{1,8,14}, higher likelihood of acute pulmonary vein reconnection\textsuperscript{1,2,8} and late recurrence of AF\textsuperscript{3,15}. In a recent experimental study specific to the CTI, Frances et al examined the relationship between CF imparted and lesion transmurality at histopathology in swine. Lesions were never transmural with CF <10g and a strongly positive correlation was found between average CF and lesion depth ($r=0.85$, $P<0.001$).\textsuperscript{16}

The influence of anatomic region on CF parameters as appreciated in this study has important implications for enhancing procedural success. For example, Morton et al demonstrated that the CTI was significantly thicker adjacent to the TA and became progressively thinner toward the caval CTI adjacent to the Eustachian ridge.\textsuperscript{17} In the current study the annular region had the lowest CF; this combined with thicker atrial myocardium in this region may explains the increased risk of reconnection at the annular CTI noted in prior studies.\textsuperscript{12,18} A potential explanation for the higher CF at the caval end may be due to the close proximity of the ablation catheter tip to the rigid fulcrum provided by a non-steerable sheath, and, when combined with maximum catheter flexion and inferior traction on the sheath allows a higher CF to be delivered than other regions in the CTI. Similarly the longer distance from the sheath fulcrum or insufficient “reach” may explain the lower CF at the annular CTI. Such knowledge of region-dependent influence of CF and real-time CF sensing ability may result in operators changing their catheter-sheath orientation or prompt the use of steerable sheaths.

Our findings also provide further confirmation that surrogate markers do not serve as a reliable predictors of actual contact\textsuperscript{1,4,5,14,19–21}. We have previously shown
that when experienced operators blinded to CF performed PVI using surrogate markers, there was marked variability in CF within and between different anatomic segments at the PV antra.\textsuperscript{8} Recently, a poor relationship between CF and unipolar amplitude, bipolar amplitude, or baseline impedance during left atrial mapping has been demonstrated, predominantly due to a large degree of overlap between these measures and actual CF.\textsuperscript{4,14,15,19,20} Impedance fall with ablation, although correlated with CF, also exhibits significant overlap thus only being a modest predictors of actual CF.\textsuperscript{14,22}

**Limitations**

The relationship of CF parameters and long term recurrence of CTI conduction was not examined, but is worthy of further investigation. Nevertheless we demonstrated a remarkably high incidence of low contact applications, a finding not previously appreciated for this region.

**Conclusions**

Using surrogate markers of “good contact” during ablation performed by experienced operators in the absence of real-time CF sensing resulted in nearly half of all lesions being delivered with low CF and marked region-specific variability in CF. Low CF was implicated in longer time to achieve conduction block and increased risk of acute reconnection. These findings underscore the importance of real-time CF measurements for optimizing ablation of typical atrial flutter.
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Disclosures

None.
References


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**Figure Legends**

**Figure 1**
Average CF at different anatomic segments of the CTI (A) and incidence of lesions with a low average CF (<10g).

**Figure 2**
FTI at different anatomic segments of the CTI (A) and incidence of lesions with a low FTI (<400 g*s).

**Figure 3**
Correlation between number of lesions with low average CF (<10g, A) and low FTI (400 g*s) and total ablation time to achieve acute bidirectional CTI block.
Figures

Figure 1

(A) Average CF (g)

- Median (Q25-Q75): Annular 9 (5-15), Mid 12 (5-19), Caval 18 (9-26)

(B) % of lesions with low CF (<10g)

- Annular 54, Mid 44, Caval 27

P<0.001 between all groups

Figure 2

(A) Force-time integral (g*s)

- Median (Q25-Q75): Annular 208 (128-376), Mid 279 (132-513), Caval 444 (223-766)

(B) % of lesions with low FTI (<400g*s)

- Annular 77, Mid 65, Caval 47

P<0.001 between all groups
Figure 3

(A)

RF time to induce bidirectional CTI block (s) vs. No of lesions with average CF <10g

$r^2 = 0.6, P < 0.001$

(B)

RF time to induce bidirectional CTI block (s) vs. No of lesions with average FTI <400 g*s

$r^2 = 0.8, P < 0.001$
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