Feasibility of Targeting Catheter Ablation to the Markedly Low-Voltage Area Surrounding Infarct Scars in Patients With Post-Infarction Ventricular Tachycardia

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Background In routine substrate mapping of the left ventricle, an abnormal area is defined as having an amplitude <1.5 mV. However, that is usually too large for catheter ablation in post-infarction ventricular tachycardia (VT) and the use of strict voltage criteria may produce better outcomes.

Methods and Results Twenty patients with post-infarction VT underwent substrate mapping using an electroanatomic mapping system. Strict voltage criteria were defined as: non-arrhythmogenic area, >0.6 mV; low-voltage area (LVA), >0.1 to ≤0.6 mV; scar, ≤0.1 mV. Radiofrequency applications targeted the LVA only, which was 48±26 cm², 55% smaller than that of the generally targeted area with an amplitude ≤1.5 mV. The prevalence of delayed electrograms (duration ≥150 ms) was significantly higher in the LVAs than in the border areas with an amplitude >0.6 to ≤1.5 mV (33.2% vs 3.7%, p<0.001). With the exception of 2 instances of peri-mitral VT, all VT isthmuses resided within the LVA. During follow-up of 24±13 months, 16 patients (80%) have been free of any VT episodes.

Conclusions Catheter ablation targeting LVAs with an amplitude ≤0.6 mV appears to be useful for efficient and effective treatment of post-infarction VT. (Circ J 2008; 72: 1112–1119)

Key Words: Catheter ablation; Mapping; Myocardial infarction; Ventricular tachycardia

In several studies, radiofrequency (RF) lesions delivered on the basis of voltage maps depicted by an electroanatomic mapping system (CARTO: Biosense Webster, Diamond Bar, CA, USA) have been effective in controlling unmappable ventricular tachycardia (VT). In general, an abnormal area in left ventricular (LV) endocardial mapping has been defined as that having an electrogram amplitude ≤1.5 mV. Although this area certainly contains the VT reentrant circuit, it is usually too large for catheter ablation in patients with structural heart disease.

The endocardial electrical voltage map depicted by the CARTO system may reflect the status of myocardial viability. In a porcine model of chronic infarction, Callans et al found in pathological examination that the infarct size correlated with an area defined by contiguous electrograms with an amplitude ≤1.0 mV and that infarct size on intracardiac echocardiographic imaging correlated with an area defined by contiguous electrograms with an amplitude ≤2.0 mV. However, we hypothesized that an “abnormal” area determined by pathological analysis or echocardiographic imaging differs from an electrically “abnormal” area on the basis of the existence of arrhythmogenicity, and that such an area may be smaller than that defined by pathological or echocardiographic methods. If the isthmus of the VT reentrant circuit commonly resides in this smaller area with a lower electrogram amplitude, and the VT can be cured by RF lesions delivered exclusively within this area, then the current definition of an abnormal area (electrogram amplitude ≤1.5 mV) may define an area too large for VT ablation, resulting in the delivery of unneeded RF applications that may cause unnecessary injury to functioning myocardium.

Therefore, during sinus rhythm we created high-resolution substrate maps that contained a higher number of mapped points than previously reported and adopted new, strict voltage criteria focusing on the markedly low-voltage area (LVA) having an amplitude ≤0.6 mV. The purpose of this study was to evaluate the feasibility of targeting catheter ablation to the markedly LVA around infarct scars detected by high-resolution substrate mapping.

Methods

Patients Twenty consecutive patients (16 men, 4 women; mean age, 64±10 years) with previous myocardial infarction (MI) who presented with recurrent monomorphic VT were included in this study. All patients had suffered a previous anterior (n=9), inferior (n=8), or lateral (n=3) MI. Mean infarct age was 124±114 months; and the mean LV ejection fraction was 32±11% on echocardiographic evaluation. Baseline characteristics of the patients are presented in

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Table 1. The study was approved by the local research ethics committee of Tsukuba University Hospital, and all patients gave written informed consent.

Measurement of Local Electrogram Variables

All patients underwent high-resolution substrate mapping during sinus rhythm with a CARTO system. A 7F catheter with a 4-mm distal tip electrode and 2-mm ring electrodes with 1-mm interelectrode spacing (NaviStar: Biosense Webster) was used. The bipolar signals were filtered between 30 and 400 Hz and displayed at a sweep speed of 100 mm/s on the CARTO system. Fill threshold was set at 10 mm, and the peak-to-peak signal amplitude of the bipolar electrogram was measured automatically and confirmed manually.

In general, a dense scar is defined as having an electrogram amplitude \( \leq 0.5 \text{ mV} \); a border zone, \( >0.5 \text{ mV} \) to \( \leq 1.5 \text{ mV} \); and a normal area, \( >1.5 \text{ mV} \). Soejima et al reported that the electrogram amplitude was \( <0.25 \text{ mV} \) at 84% and \( <0.5 \text{ mV} \) at 98% of electrically unexcitable scar sites.3 Because severely injured tissue around a scar is more likely to exhibit significant slow conduction properties, we defined stricter voltage criteria as follows: non-arrhythmogenic area, amplitude \( >0.6 \text{ mV} \); LVA, amplitude \( >0.1 \) to \( \leq 0.6 \text{ mV} \); and scar area, amplitude \( \leq 0.1 \text{ mV} \) without capture by local bipolar stimulation at maximum output (10 V and 2.0-ms pulse width).

The duration of all local electrograms recorded by the NaviStar catheter was measured manually during the procedure and later reviewed and confirmed. Duration was defined as the time from the earliest electrical activity to the end of the latest component at variable gains in order to achieve the best electrographic definition (Fig 1).13 We ensured the reproducibility of the local electrogram by recording at least 3 consecutive beats. In previous studies, 95% of the recorded electrograms in normal hearts were \( \leq 70 \text{ ms} \) in duration, and the duration of the fractionated electrograms was defined as being \( \geq 133 \text{ ms} \).14,15 Brunckhorst et al described the electrogram duration at sites in the target region to be 157±58 ms.13 In the present study, we defined a delayed electrogram (DE), which was separated by a very low-amplitude signal or isoelectric interval, as having a duration \( \geq 150 \text{ ms} \) (Fig 1).

After the identification of scars by substrate mapping, pace mapping was attempted mainly within the LVA. An excellent pace map was defined as 11 or 12 surface electrogram leads having a QRS morphology identical to that of the clinical VT. The stimulus-QRS (S-QRS) interval was measured as the interval from the stimulus artifact to the earliest QRS onset in all 12 leads of the surface electrogram.

Mapping and Ablation

During sinus rhythm, the substrate map was created by...
carefully identifying all, even tiny, scars. Isthmus could be considered to be located between scar–scar, scar–mitral annulus, and/or scar–non-arrhythmogenic areas. An isthmus of the clinical VT was defined as excellent pace-map sites with various S-QRS intervals. If we found a site where the paced QRS morphology was similar to the clinical VT morphology, detailed pace mapping around the site was undertaken to detect as much of the entire isthmus as possible. To abolish not only the clinical VT isthmus detected by pace mapping but also all possible isthmuses around scars, a linear ablation design was created according to the following 3 guiding principles: (1) lesions must cross through the LVA at sites where an excellent pace map is obtained, (2) lesions must extend between scar and scar within the LVA, and (3) lesions must extend from the scar to the non-arrhythmogenic area (0.6 mV) and/or to the mitral annulus. After the creation of the entire LV map, programmed stimulation with up to 3 extrastimuli was first performed with the NaviStar catheter located near the isthmus, then at the right ventricular (RV) apex, and finally the RV outflow tract, if necessary, to induce VT. If the induced VT was tolerated hemodynamically, entrainment mapping was performed.

As a rule, RF applications were not performed in non-arrhythmogenic areas. The RF energy was delivered via a 7F 4-mm-tip NaviStar catheter in temperature-controlled mode for 60–90s at each ablation site at a maximal target temperature of 55°C and maximum power of 50W. After RF delivery at each site, if pacing at a 5-V output and 2-ms width could capture the ablation site, additional RF energy at the same settings was reapplied to the same site for 30–60s. If the 4-mm-tip NaviStar catheter could not deliver >20W of power because of temperature limiting, a conventional 8-mm-tip ablation catheter (Ablaze, Japan Lifeline, Tokyo, Japan) was used for energy delivery. In such cases, because the 8-mm-tip NaviStar and open-irrigation (ThermoCool: Biosense Webster) catheters were not available in Japan at that time, we had to insert 2 catheters simultaneously into the LV: the 4-mm-tip NaviStar catheter, which was used only for mapping, and the 8-mm-tip conventional catheter, which was inserted from the contralateral femoral artery and used only for ablation. We positioned both catheters at the same site under fluoroscopic guidance and local potentials, and performed RF applications with the 8-mm-tip catheter at the target site navigated to with the 4-mm-tip NaviStar catheter. The endpoint of the procedure was the non-inducibility of clinical VT by programmed stimulation with up to 3 extrastimuli.

Evaluation of Clinical Outcome
Acute outcome was defined as either “success” (absence of inducible VT) or “modification” (absence of inducible clinical VT but with other inducible monomorphic VTs). Monitoring via an implantable cardioverter defibrillator (ICD) was used to evaluate chronic success in 15 patients. Holter ECGs were used in the remaining 5 patients.

Statistical Analysis
Results are expressed as mean±standard deviation (SD). Continuous variables were compared with paired or unpaired t-test as appropriate. Categorical variables were compared by chi-square analysis. When there were significant differences between groups, the Scheffé test was used to compare independent groups. A p-value <0.05 was considered statistically significant. The StatView J-5.0 statistical program (Abacus Concepts, Inc, Berkeley, CA, USA) was used for the analyses.

Results
Mapping and Ablation Data
Combined mapping and ablation time was 154±65 min, and fluoroscopic time was 64±14 min. The number of sites...
mapped was 281±84 points/patient (Table 2). The LVA specified by our voltage criteria contained 67% of these points and had an area of 48±26 cm², which was calculated using a modified CARTO version (Biosense Webster). If the general voltage criterion of ≤1.5 mV was applied, the area of interest was 106±41 cm², indicating that we had targeted a 55% smaller area. Pace mapping was performed at 43±37 points/patient. Clinical VTs were inducible before the ablation procedure in all but 2 patients (nos. 5 and 13). In those 2 patients, the clinically recorded 12-lead electrograms were used to assess the pace map. The number of DEs was 32±18 points/patient. The number of excellent pace map points was 5.9±5.6 points/patient. Only 2 of the induced VTs were tolerated hemodynamically; all others were terminated by burst pacing or direct cardioversion.

All possible isthmuses were linearly ablated during sinus rhythm within the LVA according to the 3 guiding principles (Fig 2A). Although concealed entrainment could be obtained in 2 patients (nos. 5 and 13), RF applications during VT were performed because of mechanical termination of the tachycardia by the catheter and difficulty of re-induction. The number of RF applications was 22±12/patient, duration of RF applications was 27±17 min/patient, and the total length of the linear RF lesions was 63±39 mm/patient. A conventional 8-mm-tip ablation catheter was used in 5 patients. Acute “success” was obtained in 16 patients and “modification” in 4 patients (Table 2). No patient suffered any acute complications during the procedure.

**Relationship Between Electrogram Amplitude and Duration**

We measured both electrogram amplitude and duration at a total of 3,756 points. The relationship between each amplitude category, separated by 0.10-mV intervals, and mean duration is shown in Fig 3A. In the LVA, as the amplitude decreased, the mean duration increased. When the data were divided into 3 groups on the basis of local electrogram amplitude (normal area, >0.6 mV; border area, >0.1 to ≤0.6 mV; LVA, ≤0.1 mV), the mean duration was 74±20 ms, 93±30 ms, and 141±59 ms, respectively (all combinations, p<0.001). The prevalence of DEs was significantly higher in the LVA than in the border area (631/1,898 points; 33.2% vs 36/976 points; 3.7%, p<0.001). In addition, the SD of electrogram duration in each amplitude category, separated by 0.10-mV intervals, was larger in the smaller amplitude categories, especially in those <0.7 mV (Fig 3A). When these SDs were divided into 3 groups (normal area, border area, and LVA), the SDs were 21±4 ms, 28±5 ms (p=0.12 vs normal area), and 54±8 ms (p<0.001 vs normal area or border area), respectively, indicating the possible existence of a more heterogeneous conduction property in the LVA.

**Relationship Between Electrogram Amplitude and S-QRS Interval**

Pace mapping was performed at a total of 857 sites. Most of these (705, 82.3%) were mapped in the LVA, and 168 (23.8%) in the LVA were not captured at maximum output. We constructed an S-QRS interval map to reveal the activation sequence of the isthmus during VT (Fig 2B). The relationship between amplitude category, separated by 0.10-mV intervals, and mean S-QRS interval is shown in Fig 3B. The S-QRS interval was significantly longer in the LVA than in the non-arrhythmogenic area (64±42 ms vs 34±13 ms, p<0.001).
Identification of the Clinical VT Isthmus by Pace Mapping

Before pace mapping, we could presume the location of the clinical VT isthmus from the information obtained from high-resolution substrate mapping in all patients because a clinical VT isthmus commonly exists close to scars. To confirm the isthmus site, we then performed pace mapping around the scars after complete substrate mapping. The isthmus of the targeted clinical VT was detected in 16 patients, and the exit site only in the remaining 4 patients (Table 2). The most important finding was that all but 2 isthmuses resided within the LVA. Those 2 isthmuses (patient nos. 16 and 18), which were located between the scar and mitral annulus and were associated with peri-mitral VT, resided in the non-arrhythmogenic area (Fig 4). Excluding those 2 isthmuses from the analysis, the local amplitude at the isthmus was 0.21±0.09 mV; duration, 179±80 ms; and S-QRS interval, 67±25 ms, and the amplitude at the ablation sites was 0.20±0.12 mV.

Follow-up

The follow-up period was 24±13 months. In the 13 patients who had a very low ejection fraction (≤30%) or who did not undergo an ICD implantation, antiarrhythmic drugs were continued after ablation. Two patients (nos. 7 and 20) suffered recurrences of VT 1 day after the first procedure, so a second procedure was scheduled for each patient 1 week after the first procedure. Detailed data from patient no. 7, who had a broad anterior MI, are shown in Fig 5. The high-resolution substrate map, which displays the ablation line in the first procedure, is shown, as well as the S-QRS interval map, which displays the isthmus of clinical VT1 and clinical VT2. The S-QRS interval map from the second procedure in the same view as that of the first procedure (the entire left ventricle was not mapped) shows the isthmus of clinical VT3. Note that the isthmus of VT3 was located where a tiny scar was missed because of mapping too few sites, which suggests that the occurrence of VT3 after the first procedure was related to inadequate mapping during that procedure.

The reason for the recurrence of clinical VT in patient no. 20 was not related to the ablation design, but rather to inadequate RF power delivery caused by temperature limiting because, in the second procedure, creation of the same ablation line as that used in the first procedure, this time with an 8-mm-tip conventional ablation catheter, resulted in cure of the recurrent VT.

An ICD was implanted in all but 5 patients. Of those, patient no. 8, who suffered incessant VT episodes and who had New York Heart Association class IV heart failure requiring inotropic agent support, died from septic shock 3 days after the ablation procedure. Patient no. 12 died from pump failure related to a second MI suffered 3 months after the ablation procedure. The other 3 patients refused implantation of an ICD.

A VT more rapid than that of their clinical VT was recorded by ICD in 2 patients (nos. 10 and 13). Excluding these patients and the 2 who died, 16 patients (80%) have had no recurrence of any VT, and all patients have been free of clinical VT episodes during the follow-up period.

The LV ejection fraction did not deteriorate post-ablation (pre, 32±11% vs post, 34±10%, NS), and the serum level of B-type natriuretic peptide tended to decrease (pre, 355±351 vs post, 245±163 pg/dl, NS), excluding the 2 dead patients from analysis.
Discussion

Main Findings

The results of the present study reveal the following: (1) the area of the LVA was almost half of that of the generally targeted area, (2) the LVA exhibited slower and more heterogeneous conduction properties indicative of the substrate of a VT reentrant circuit rather than that of a border zone, (3) precise detection of scars by high-resolution substrate mapping is very important for localization of the isthmus and in the design of effective ablation lines, (4) clinical VT isthmuses confirmed by pace mapping do exist within the LVA, and as a result, (5) linear RF applications targeting the markedly LVA surrounding scars results in better long-term outcome for patients with post-infarction VT.

High-Resolution Substrate Maps

In most previous studies, the mean number of mapped
sites has been 70–210.2–7.15 Because our substrate maps of the LVA were of high resolution, this method contributed to precise detection of VT isthmuses related to scars. The data from patient no. 7, who developed a different VT after the first procedure, revealed the importance of detailed substrate mapping to detect all scars existing within the LVA.

Suitability of Strict Voltage Criteria

We evaluated the local electrical characteristics of amplitude, duration, and post-pacing delay in detail. The results of this study support the suitability of these strict voltage criteria for the effective abolition of VT isthmuses for the following reasons.

DEs and Slow Conduction

We noted that the prevalence of DEs was higher in the LVA than in the border area. Brunckhorst et al found that the electrical duration was significantly longer (157±58 ms) at sites within the ablation target area than in those outside the target.13 Bogun et al reported that critical isthmus sites in post-infarction VT are composed of the broadest electrograms mainly displaying isolated potentials, with an electrogram width of >200 ms.29 This suggests that the area with slow conduction, which is needed to form the VT reentrant circuit, may reside within the LVA (≤0.6 mV) rather than within the border zone. Therefore, our RF applications targeting the LVA could effectively and efficiently eliminate the area of slow conduction.

Heterogeneous Conduction Properties

Propagation in the diseased myocardium is not homogeneous, and reentry circuits form in areas with heterogeneous conduction properties.29 Tissue with normal conduction properties (long electrogram duration) and tissue with abnormal conduction properties (long electrogram duration, and slow conduction) coexist within the LVA (Fig 3A). The large SD of electrogram durations noted in the LVA suggests that the LVA has heterogeneous conduction properties and thus could be the substrate of the VT reentrant circuit.

Identification of Clinical VT Isthmus on the Basis of Pace Mapping

VT isthmuses can be identified and part of their course delineated by pace mapping during sinus rhythm. It is likely that pacing sites with long S-QRS intervals are in a potential isthmus, adjacent to regions of conduction block; Stevenson et al reported that an S-QRS interval >40 ms was significantly associated with reentry circuit sites.21 Excellent pace-map sites with various S-QRS intervals, which are the isthmus sites of the clinical VT, were located within the LVA in all but the 2 patients with peri-mitral VT (Figs 2,4,5). Because the reentry circuit of peri-mitral VT is a relatively large macroreentry circuit, it may not always require an isthmus with a strong conduction delay and that also has very low amplitude. We believe this finding to be direct evidence supporting our hypothesis.

Prior Studies

Our findings differ from those of previous studies in various respects. The previous studies reported that the VT isthmus resided not only in dense scar (<0.5 mV), but also in the border zone (>0.5 to <1.5 mV). For example, Marchlinski et al set a linear ablation line in a broad area, from the area showing the lowest amplitude signal (<0.5 mV) to the areas showing a distinctly normal signal (maximum 3.0 mV)! Additionally, Hsia et al indicated that 19% (7/37) of the isthmus sites in their patients resided in the border zone and that the exit sites were more likely located within the border zone (54%, 26/48 sites).4 Moreover, Verma et al reported that the successful ablation site was located in the border zone in 63% of their patients.

The reason for the difference in the isthmus amplitude measurements is unclear. If pace-map findings are focused on determining a design for the ablation line, the exit site would tend to be the target for ablation because it would be easier to match the pace-map QRS morphology to the VT morphology at the exit site than in the central isthmus or entrance site (Fig 5D). If the catheter is positioned closer to the entrance, the stimulated antidromic wave front leaves the protected isthmus at the entrance, propagating to the surrounding myocardium and producing a different QRS morphology.27 Although Verma et al looked for a shorter S-QRS interval relative to VT cycle length2 we tried to identify the entire isthmus by precise detection of scars, as well as by pace mapping. In the present study, this difference in the intention for creating the substrate map may explain why our results differ from those of the previous reports.

Ablation Strategy

We performed linear ablation in all patients as described in a previous report that supports the need for linear RF lesions.16,19 however, later studies have reported that RF ablation of isolated DEs appears effective in controlling unmappable VT.10,12 Bogun et al reported that the older the infarction, the broader the electrogram, and that remodeling over time alters the electrophysiologic properties of peri-infarction tissue.2 Therefore, a relatively narrow electrogram with low amplitude, which is not a DE and thus not the target of ablation, might change over time into a DE and so might become a critical isthmus because of LV remodeling.

We believe this is a limitation of DE-guided ablation, and therefore we performed linear ablation in all patients.

Clinical Implications

The present study revealed the usefulness of a practical ablation strategy for post-infarction VT, which can be summarized as follows.

(1) Set the voltage threshold of the CARTO system to 0.6 mV and the fill threshold to 10 mm or less (ie, disregard any non-arhythogenic area with an amplitude >0.6 mV).

(2) Create a high-resolution substrate map by mapping the LVA very densely and detecting all scars, even tiny ones.

(3) Tag each point where a DE is recorded.

(4) Perform pace mapping around scars and identify the clinical VT isthmus.

(5) Perform simple linear ablation between scar–scar, scar–non-arhythogenic area, and/or scar–mitral annulus, if necessary.

Our strategy is simple because it focuses on the precise detection of scars in a narrow area of markedly low voltage. As a result, our procedure time is shorter than that reported in previous studies1,16,19 although the number of points mapped is much greater. Intensive ablations targeting a narrow area can simplify the procedure and may contribute to a reduction in complications such as heart failure or thromboembolic events.

Study Limitations

Neither the 8-mm-tip NaviStar nor open-irrigation ThermoCool catheters were available in Japan during the study period. Therefore, the only option was to adopt an alternative approach using a 4-mm NaviStar catheter and 8-mm conventional catheter simultaneously. The superiority...
ty of an open-irrigation catheter has been reported previously. The reentrant pathways of post-infarction VT have a complex 3-dimensional nature; Kaltenbrunner et al reported that substrates involving subepicardial and deep septal layers accounted for 32% of post-infarction VTs. It is possible that in some patients the RF energy delivered from the 4-mm tip NaviStar catheter to the endocardium did not penetrate the mid- or subepicardial layers that were part of the VT reentrant circuit, such as in patient no. 20. Therefore, our results cannot be compared directly with the results of studies in which an 8-mm-tip or open-irrigation-tip catheter was used for ablation.

We did not perform complete activation mapping during VT, but a previous study reported that abnormal potentials and/or good-to-perfect pace mapping could be obtained during sinus rhythm at the isthmus sites identified by the VT mapping. Volkmer et al noted that the patient outcome was the same, regardless of whether complete VT mapping or only substrate mapping could be performed. This indicates that either careful mapping of the infarction area during sinus rhythm or pacing is as effective in identifying critical isthmuses as it is during VT mapping. Therefore, we believe that VT mapping is not always necessary for successful VT ablation.

Unipolar pacing is more reliable than bipolar pacing in pace mapping. In this study, pace mapping was attempted using bipolar stimuli from the NaviStar catheter. However, the pacing output was gradually decreased from a maximum output of 10 V to loss of local capture (threshold) at a fixed pulse width of 2.0 ms, and QRS morphology was evaluated just before the loss of capture to avoid anodal capture of the bipolar proximal electrode.

Conclusion

In the present patients with post-infarction VT, catheter ablation targeting the LVA around infarct scars detected by high-resolution substrate mapping resulted in a very high success rate with no deterioration of cardiac function. This strategy appears to be useful for efficient and effective treatment of post-infarction VT.

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References