Intramural Ventricular Recording and Pacing in Patients With Refractory Ventricular Tachycardia

Initial Findings and Feasibility With a Retractable Needle Catheter

Amir AbdelWahab, MBCh, MSc, MD; William Stevenson, MD; Kara Thompson, MSc, BSc; Ratika Parkash, MD; Christopher Gray, MD; Martin Gardner, MD; John Sapp, MD

Catheter ablation is an important therapeutic option for ventricular tachycardia (VT), yet it remains ineffective in some patients despite technical advances, including 3-dimensional mapping, irrigated radiofrequency ablation, the availability of epicardial mapping and ablation, and intracoronary ethanol ablation. A common limitation is the existence of reentry substrate that is beyond the reach of ablation with the use of standard techniques. Preclinical work has demonstrated that a catheter with an extendable/retractable electrically active needle can record intramural cardiac electrograms, pace, and create deep myocardial lesions. The addition of intramyocardial saline infusion, likely creating an interstitial virtual ablation electrode, permits the creation of large, deep myocardial lesions. Initial human experience suggested that some treatment-refractory VTs could be brought under control using this technique.

Intramural electrograms have been previously recorded in transplanted hearts and animal models of scar-related VT.

This needle electrode is a single tube of the nickel titanium alloy, nitinol. Unipolar electrograms can be recorded from the needle, and bipolar electrograms can be recorded between the needle and the ring electrode 4.5 mm proximal to the tip of the catheter, which is intracavitary if orientation is perpendicular, producing a semibipolar recording. The needle also allows unipolar pacing and delivery of radiofrequency (RF) current. We have previously reported the clinical procedural data of this needle catheter in 8 initial patients. We sought to extend our report by comparing characteristics of human intramural electrograms with corresponding endocardial electrograms in these patients.

Methods

Study Population

Patients with recurrent VT, despite antiarrhythmic drug therapy and at least 1 attempt at catheter ablation, were offered catheter ablation with the use of an infusion needle catheter as previously reported.

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From the Heart Rhythm Service, Department of Medicine, Division of Cardiology, QEII Health Sciences Centre, Halifax, Nova Scotia, Canada (A.A., R.P., C.G., M.G., J.S.); Electrophysiology and Pacing Service, Department of Cardiovascular Medicine, Cairo University, Cairo, Egypt (A.A.); Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA (W.S.); and Research Methods Unit, Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada (K.T.).

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Correspondence to Amir AbdelWahab, MBCh, MSc, MD, Heart Rhythm Service, QEII Health Sciences Centre, Dalhousie University, Room 2501 E Halifax Infirmary, 1790 Summer St, Halifax, Nova Scotia B3H 3A7, Canada. E-mail amir.abdelwahab@cdha.nshealth.ca

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WHAT IS KNOWN
• The feasibility of using a needle-tipped catheter to ablate intramural arrhythmogenic substrate which is too deep for usual techniques has been previously shown.
• Electrogams and pacing from the endocardium and epicardium have been well characterized in relation to ventricular arrhythmias and arrhythmogenic substrate.

WHAT THE STUDY ADDS
• Intramural electrogram characteristics are shown to have similar characteristics to those recorded from the cardiac surface during sinus rhythm, and relate to presence of scar.
• The needle catheter was capable of intramural pacing and recording, permitting traditional electrophysiologic mapping techniques; ablation was tended to be more likely to terminate ventricular arrhythmias when intramural activation was relatively early.
• These findings may be useful for selecting ablation targets during VT and for substrate mapping.

All patients provided informed consent for use of this therapy, which was approved through the Special Access Program of Health Canada."There the institutional research ethics board approved the review and reporting of cases.

Electroanatomical Mapping and Infusion Needle Ablation
Patients were brought to the electrophysiology laboratory in the fasting state. Multipolar electrode catheters and an intracardiac echocardiography catheter were placed from the femoral veins. Left ventricular access was gained via transeptal puncture and a deflectable sheath (Aglis large curl, St. Jude Medical, St. Paul, MN) or via a retrograde aortic approach. Left ventricular substrate mapping was initially performed with a standard 3.5-mm irrigated tip mapping catheter and an electroanatomic mapping system (Carto; Biosense Webster, Diamond Bar, CA). VT was induced with programmed ventricular stimulation. After a voltage map was created, the standard mapping catheter was replaced with a needle-tipped ablation catheter (Figure 1). The deflectable catheter has a distal bipole with an extendable/retractable 27-gauge nitinol needle. The needle has an embedded thermocouple and has a central lumen through which saline can be infused. A position sensor within the tip is compatible with an electroanatomic mapping system (Carto; Biosense Webster). The needle depth can be adjusted and locked in the extended or retracted position. In its fully retracted position, it is entirely within the needle, whereas, when fully deployed, it can extend 12 mm beyond the tip. An adjustable plunge activator on the handle permits the depth of extension to be preset and locks the needle in position when deployed. The needle has a lumen that opens at its tip and allows for continuous infusion throughout the procedure. A pump (Thermoool; Biosense Webster) and 3-way manifold permit injection before and throughout RF application. Infusion flow rate was set at 1 mL/min and was increased to 2 mL/min for 30 s before and during RF delivery.

During catheter manipulation, the needle was kept retracted and irrigated with 0.9% saline mixed with 2 U/mL heparin at ambient temperature. Target sites were sought within areas of reduced bipolar or unipolar signal amplitude, which were thought to be components of VT circuits based on endocardial activation/entrainment mapping, when possible, or substrate/pacemapping. The catheter tip was placed at sites of interest with attempted orientation perpendicular to the endocardial surface. The needle was extended 7 to 9 mm into the myocardium. Intramural electrograms were recorded from the needle, and pacing was performed (10 mA, 2-ms pulse width).

Electrogram Acquisition and Filtering
Recording and pacing were possible from both the external electrodes and from the needle. The recording system was configured to permit bipolar recordings between the needle and ring electrode (filtered at 30–500 Hz) and between the needle and an inferior vena cava electrode (referred to as unipolar recordings; filtered at 30–500 Hz, and separately displayed and filtered at 0.5–500 Hz; Cardiolab, GE Healthcare). Bipolar and unipolar electrograms from the catheter tip were also recorded on the electroanatomic mapping system (Carto; filtered at 16–500 Hz and at 1–240 Hz, respectively).

Electrogram Selection for Analysis
The needle was extended within the myocardium at sites where endocardial mapping raised clinical suspicion of deeper culprit substrate because activation time, pace-mapping, or entrainment suggested that it was close to the VA origin. Electrograms were recorded from sites where the needle was deployed within the myocardium and were included for analysis. For sites where RF energy was delivered more than once, the electrogram was analyzed before the first RF application. Fractionation was defined as the number of positive and negative peaks of the recorded bipolar electrogram. Late potentials were defined as electrograms on bipolar recordings that occurred after the end of the surface QRS complex during sinus or paced rhythm. Intramural to endocardial conduction time was defined as the difference between needle electrode to QRS and endocardial electrogram to QRS at the same site.

Unipolar pacing from the needle was performed between the needle and the inferior vena cava electrode at 10 mA with a pulse width of 2 ms.

Statistical Analysis
Continuous variables were expressed as mean±SD and were tested for distributional properties (such as normal and lognormal) using Kolmogrov–Smirnov test, histograms, and probability plots (QQ plots). Correlations between continuous variables were assessed using maximum likelihood estimation to account for multiple measurements on the same subject. Generalized linear mixed models were used to compare intramural and endocardial electrogram outcomes. Unstructured covariance structure was used to account for correlation between needle site and clustering of observations on same subject. Generalized linear mixed models were used to compare outcomes at termination sites and different scar zones. Unstructured covariance structure was used to account for correlation between needle site and clustering of observations on same subject.

Generalized linear mixed models were used to compare outcomes at termination sites and different scar zones. Unstructured covariance structure was used to account for correlation between needle site and clustering of observations on same subject.

Results
Study Population
Electrograms were analyzed in 8 patients with recurrent VT (6 men), age 54 (limits, 13–70). Ventricular function was reduced in all patients (ejection fraction 29±11%) associated with nonischemic cardiomyopathy in 6 patients and ischemic heart disease in 2 patients. All patients had recurrent VT despite
antiarrhythmic drug combinations, including amiodarone. All patients had undergone previous endocardial catheter ablation attempts (mean, 2; limits, 1–4), and 4 patients had undergone an ineffective epicardial procedure.

**Procedures**

Patients had 1 to 7 inducible or spontaneous monomorphic ventricular arrhythmias (median, 2). In 7 patients, some intramural mapping with the needle electrode was possible for at least 1 VT (VT was not reproducibly inducible in 1 patient). In each of these, a VT was identified with earlier intramural signal than the adjacent endocardial activation time, but mapping during VT was limited because of hemodynamic intolerance and the inducibility of multiple VT morphologies or lack of reproducible inducibility. In 6 patients, at least 1 VT was terminated with intramural needle infusion and ablation. Details of acute and long-term procedure outcomes, as well as associated complications, have been previously reported.13

Endocardial electrograms were collected from 2309 sites; the needle was deployed at a total of 75 sites with suspected intramural substrate (median, 10 deployment sites/patient; range, 4–14; first to third quartiles, 6.75–11.5). The rhythm during deployment at these sites was VT in 35, premature ventricular complexes in 12, sinus in 25, and biventricular-paced rhythm in the remaining 3 sites. The rhythm during deployment at these sites was VT in 35, premature ventricular complexes in 12, sinus in 25, and biventricular-paced rhythm in the remaining 3 sites.

Figure 1. Picture of the needle ablation catheter with its needle retracted (top right) and extended (bottom right). Left. Fluoroscopy image shows the needle catheter advanced to the left ventricle through a trans-septal sheath and its needle deployed in the inferior septum. Contrast injected through the needle confirms intramyocardial location (*) before irrigated radiofrequency delivery.

Pacing From the Needle Catheter

Unipolar pacing from the needle catheter was successfully performed at 19 sites, 18 of which matched or nearly matched the targeted VA. The mean stim-QRS (stimulus to QRS) duration was 60±51 ms (limits, 0–192 ms; Figure 4). Entrainment from the needle catheter during VT was successfully performed at 5 sites (Figure 5).

**Termination Sites**

Needle ablation was attempted during VT at 28 sites and terminated the arrhythmia at 12 sites (43%). Sites with VA termination during needle RF ablation did not show any significant differences when compared with nontermination sites in terms of endocardial electrogram characteristics (Table 2). However, there was a trend for earlier intramural bipolar electrograms with longer intramural to endocardial conduction time at termination sites. (Table 2) No significant differences were observed in bipolar and unipolar needle electrogram amplitudes, electrogram duration, or degree of electrogram fractionation. There was lower average temperatures (55±3.8°C versus 57±1.5°C; P=0.15) and higher delivered power (17.5±5.1 versus 13±6.9 W; P=0.08) at termination sites (Table 2), although not statistically significant. The average time to termination was 11±7 s.
Scar Definition Based on Electrogram Voltage

Needle deployment sites were defined as normal myocardium (n=5) if they had normal endocardial unipolar and bipolar electrogram amplitudes (>8.3 and >1.5 mV, respectively; on the electroanatomic mapping system); transmural scar (n=41) if they had reduced unipolar and bipolar electrogram amplitudes (≤8.3 and ≤1.5 mV, respectively); and epicardial/intramural scar (n=12) if they had reduced unipolar electrogram and preserved bipolar electrogram amplitudes (≤8.3 and >1.5 mV, respectively; Table 3).19 Needle unipolar and semibipolar electrograms had lower amplitude at sites of transmural scar compared with normal myocardium or epicardial/intramural scar compared with normal myocardium or epicardial/intramural scar.

**Table 1. Characteristics of Intramural Electrograms in Comparison With Corresponding Endocardial Electrograms at Needle Deployment Sites**

<table>
<thead>
<tr>
<th></th>
<th>Endocardial (n=75)</th>
<th>Intramural (n=75)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bipolar amplitude, mV</td>
<td>0.6±0.5</td>
<td>1.5±1.4</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>0.5 (0.3, 0.9)†</td>
<td>1.0 (0.7, 2.1)†</td>
<td></td>
</tr>
<tr>
<td>Unipolar amplitude, mV</td>
<td>1.8±1.3</td>
<td>1.7±1.2</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>1.4 (1.0, 2.3)†</td>
<td>1.3 (0.7, 2.2)†</td>
<td></td>
</tr>
<tr>
<td>Bipolar EGM duration, ms</td>
<td>112±51</td>
<td>131±66</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>96 (79, 142)†</td>
<td>103 (84, 173)†</td>
<td></td>
</tr>
<tr>
<td>EGM to QRS during VA, ms‡</td>
<td>−15±21</td>
<td>−29±34</td>
<td>0.001</td>
</tr>
<tr>
<td>EGM fractionation (no. of peaks)</td>
<td>7.3±3.6</td>
<td>7.5±3.1</td>
<td>0.53</td>
</tr>
<tr>
<td>Late potentials§</td>
<td>10 (35.7%)</td>
<td>15 (53.6%)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Bipolar electrograms were filtered at 30–500 Hz and unipolar electrograms at 0.5–500 Hz. EGM indicates electrogram; and VA, ventricular arrhythmias including ventricular tachycardia and premature ventricular complexes.

*Generalized linear mixed models (lognormal for the first 3 variables; normal, Poisson, and binomial for the last 3 variables, respectively).
†Median (Quartile 1, Quartile 3) is reported for continuous variables not meeting normality assumption.
‡Among 47 sites recorded during ventricular arrhythmias.
§Among 28 sites mapped during sinus rhythm or ventricular pacing.

**Figure 2. Top right,** An anteroposterior view of an endocardial bipolar voltage map of the left ventricle. White tags are needle deployment sites. Brown tags are needle ablation sites. Recordings from 2 needle deployment sites at the superior border of a septal scar are shown in the bottom panels with the endocardial (Endo Bi) and needle semibipolar (Ndl Bi) ventricular electrograms (EGMs) during ventricular tachycardia (VT). **Bottom right,** The needle EGM onset starts before the endocardial EGM and QRS onset by 21 ms. **Bottom left,** The needle EGM precedes the endocardial EGM and QRS onset by 60 ms. Needle ablation at this site resulted in immediate termination of the VT (top left). Abl indicates ablation.
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scar sites (Table 3). During ventricular arrhythmias, sites of transmural scar tended to have earlier endocardial and needle electrograms compared with the other 2 types of sites.

Discussion
This is the first detailed analysis of electrograms recorded from an intramural needle during catheter mapping and ablation in humans. We found that recordings from the needle were feasible, often had features that can be used to determine if the site may be desirable for ablation and to define scar. Pacing from the needle is also possible and can be used for pacemapping and entrainment mapping.

There are several important considerations in interpreting this data. Importantly, the needle is a single solid piece of nitinol capable of extending ≤11 mm into the myocardium. It does not contain additional isolated microelectrodes on its surface. Hence, the recordings are expected to be different from those of plunge microelectrodes that have been used intraoperatively and in animal models.14–16 We analyzed both unipolar recordings and semibipolar recordings (between the needle and the ring electrode of the catheter). Semibipolar recordings have the potential for better rejection of far-field recordings than unipolar recordings and would be expected to be less affected by wavefront direction compared with bipolar recordings.20 In some cases, however, the ring electrode may be in contact with myocardium if the catheter is not perpendicular to the myocardium. Although we focus attention on the intramural nature of the needle recordings, the most proximal portion of the needle is at the endocardial surface. It should also be recognized that the depth of the needle beneath the endocardial surface varies not only with the length of the needle, but with the angle of the needle with respect to the endocardial surface. It is also possible that in some cases the needle could be deployed with a gap between the dome electrode and the endocardium such that a portion of the needle is in the blood pool.

Intramural Scar Electrograms
Identification of regions of scar, consisting of fibrosis with some surviving myocardial cells, is an important component of identifying the substrate for scar-related reentrant arrhythmias and is generally sought based on analysis of electrogram amplitude. A bipolar electrogram amplitude

![Figure 3. Needle semibipolar (Ndl Bi) and unipolar (Ndl Uni) and endocardial bipolar (Endo Bi) and unipolar (Endo Uni) recordings during sinus rhythm from sites at a low voltage scar margin are shown. A distinct sharp late potential (*) was seen only on the needle electrograms with a corresponding rounded far-field signal on the endocardial recordings.](http://circep.ahajournals.org/)

![Figure 4. Middle. A right anterior oblique view of a bipolar endocardial voltage map of the left ventricle showing a basal septal scar. White markers are needle deployment sites; brown markers are needle ablation sites. Two sites where pacemapping from the needle (Needle PM) matched a ventricular tachycardia (VT) QRS morphology suggesting the exit location are indicated and the pacemapping shown in the right and left panels along with the VT. Left, A long stimulus to QRS (stim-QRS) delay of 105 ms with 12/12 pacematch to VT#4. Right, Close pacematch to VT# 3 with stim-QRS delay of 68 ms.](http://circep.ahajournals.org/)
<1.5 mV is a robust indicator of scar. Magnetic resonance imaging studies in patients with nonischemic cardiomyopathy and VT suggest that midmyocardial scars account for 27% to 100% of total scars, mostly in the septum, inferior and lateral walls. At some of these sites, only 2 mm of viable endocardium was sufficient to generate signal amplitude.

Table 2. Characteristics of Local Electrogram at VA Termination Sites During Irrigated Needle RF Application

<table>
<thead>
<tr>
<th></th>
<th>Termination Site (n=12)</th>
<th>Nontermination Site (n=16)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocardial EGM to QRS, ms</td>
<td>−24±16</td>
<td>−22±24</td>
<td>0.51</td>
</tr>
<tr>
<td>Endocardial bipolar amplitude, mV</td>
<td>0.7±0.9</td>
<td>0.7±0.3</td>
<td>0.31‡</td>
</tr>
<tr>
<td></td>
<td>0.4 (0.2, 0.8)†</td>
<td>0.6 (0.4, 0.9)†</td>
<td></td>
</tr>
<tr>
<td>Endocardial unipolar amplitude, mV</td>
<td>1.9±1.2</td>
<td>1.5±0.9</td>
<td>0.84‡</td>
</tr>
<tr>
<td></td>
<td>1.2 (1.0, 2.0)†</td>
<td>1.3 (0.9, 2.0)†</td>
<td></td>
</tr>
<tr>
<td>Endocardial EGM duration, ms</td>
<td>118±65</td>
<td>121±50</td>
<td>0.96‡</td>
</tr>
<tr>
<td></td>
<td>96.5 (81.5, 130.5)†</td>
<td>116.5 (79.5, 165.0)†</td>
<td></td>
</tr>
<tr>
<td>Endocardial EGM fractionation (no. of peaks)</td>
<td>6.4±2.6</td>
<td>7.5±2.7</td>
<td>0.41§</td>
</tr>
<tr>
<td>Needle EGM to QRS, ms</td>
<td>−54±37</td>
<td>−36±33</td>
<td>0.15</td>
</tr>
<tr>
<td>Intramural to endocardial conduction time, ms</td>
<td>−30±30</td>
<td>−15±28</td>
<td>0.17</td>
</tr>
<tr>
<td>Needle semibipolar amplitude, mV</td>
<td>1.6±1.3</td>
<td>1.4±1.0</td>
<td>0.63‡</td>
</tr>
<tr>
<td></td>
<td>1.0 (0.6, 2.3)†</td>
<td>0.9 (0.7, 1.6)†</td>
<td></td>
</tr>
<tr>
<td>Needle unipolar amplitude, mV</td>
<td>1.9±1.3</td>
<td>1.4±0.9</td>
<td>0.81‡</td>
</tr>
<tr>
<td></td>
<td>1.5 (1.1, 3.3)†</td>
<td>1.3 (0.7, 2.0)†</td>
<td></td>
</tr>
<tr>
<td>Needle EGM duration, ms</td>
<td>180±105</td>
<td>136±66</td>
<td>0.19‡</td>
</tr>
<tr>
<td></td>
<td>142.5 (88.5, 299.5)†</td>
<td>120.5 (78.5, 191.0)†</td>
<td></td>
</tr>
<tr>
<td>EGM fractionation, no. of peaks</td>
<td>7.6±3.2</td>
<td>8.3±3.0</td>
<td>0.93§</td>
</tr>
<tr>
<td>RF parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RF time, s)</td>
<td>52±28</td>
<td>53±26</td>
<td>0.74</td>
</tr>
<tr>
<td>RF maximum temperature, °C</td>
<td>62±2.5</td>
<td>62±1.7</td>
<td>0.79</td>
</tr>
<tr>
<td>RF maximum power, W</td>
<td>25±6.5</td>
<td>22±8.6</td>
<td>0.31</td>
</tr>
<tr>
<td>RF average temperature, °C</td>
<td>55±3.8</td>
<td>57±1.5</td>
<td>0.15</td>
</tr>
<tr>
<td>RF average power, W</td>
<td>17.5±5.1</td>
<td>13±6.9</td>
<td>0.077</td>
</tr>
</tbody>
</table>

EGM indicates electrogram; RF, radiofrequency; and VA, ventricular arrhythmias including ventricular tachycardia and premature ventricular complexes.

*Generalized linear mixed models.
†Median (Quartile 1, Quartile 3) is reported for continuous variables not meeting normality assumption.
‡Lognormal.
§Negative binomial, and normal for the rest.
In this clinical series, needle deployment with or without intramural RF delivery was performed at sites which were suspected to be important arrhythmogenic substrate. When intramural RF delivery was performed at sites which were suspected to be important arrhythmogenic substrate, facilitation of intramural components of the arrhythmia substrate.

Limitations
This is the initial data from our feasibility study in a small number of patients. A number of factors can potentially affect the electrogams recorded as discussed above. We did not investigate pacing threshold, which may also be a useful indicator of the nature of fibrosis and surviving myocardium. Only 1 patient did not have an implantable cardioverter defibrillator and had a preprocedure magnetic resonance imaging. We did not have the original images available to analyze. In the other patients, confirmation of scar distribution in the midmyocardium or epicardium by delayed enhancement magnetic resonance imaging was not performed because of the presence of an implantable cardioverter defibrillator.

Criteria for identifying the optimal sites for needle deployment are not yet well defined. We attempted to identify the endocardial region that seemed closest to the arrhythmia origin based on endocardial mapping findings, including substrate mapping, entrainment, and electrogram timing and characteristics, and deployed the needle in that region. In addition, we could not identify any specific characteristics of endocardial electrogams that can predict intramural electrogams characteristics. Further studies in larger numbers of patients may allow us to better predict sites where needle deployment is likely to identify a suitable ablation target.

Conclusions
Electrogams obtained from this intramural needle show similar features to endocardial signals in regions of potential arrhythmia substrate. Sites with suspected intramural substrate had early activation relative to the endocardium; sites with earlier intramural activation times and greater RF power delivery tended to be more likely to terminate ventricular arrhythmias. The needle can be repeatedly deployed. These findings indicate that intramural recording can potentially be
used to guide ablation. Electrogram amplitude is greater than that seen in bipolar recordings from the overlying endocardium, indicating that parameters to define scar will need to be defined specifically for this electrode and recording method. The combination of needle and endocardial recordings at a site may help refine identification of intramural substrate.

Acknowledgments

Catheters were provided free of charge by Biosense Webster.

Disclosures

Dr AbdelWahab has received fellowship support from Biosense Webster from 2006 to 2008 and has a current trainer agreement with Biosense Webster, both are unrelated to this study. Dr Stevenson is a coholder of a patent for the needle catheter that is consigned to Brigham and Women’s Hospital. Dr Sapp is a coholder of a patent for the needle catheter, rights assigned to Brigham and Women’s Hospital. Dr Stevenson is a coholder of a patent from 2006 to 2008 and has a current trainer agreement with Biosense Webster. Drs Stevenson and Sapp report no conflicts.

References


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