A multifilamented electrode in the middle cardiac vein reduces energy requirements for defibrillation in the pig

P R Roberts, S Allen, T Betts, J F Urban, D E Euler, S Crick, R H Anderson, M J Kallok, J M Morgan

Abstract
Objective—To compare the defibrillation efficacy of a novel lead system placed in the middle cardiac vein with a conventional non-thoracotomy lead system.

Methods—In eight pigs (weighing 35–71 kg), an electrode was advanced transvenously to the right ventricular apex (RV), with the proximal electrode in the superior caval vein (SCV). Middle cardiac vein (MCV) angiography was used to delineate the anatomy before a three electrode system (length 2 × 25 mm + 1 × 50 mm) was positioned in the vein. An active housing (AH) electrode was implanted in the left pectoral region. Ventricular fibrillation was induced and biphasic shocks were delivered by an external defibrillator. The defibrillation threshold was measured and the electrode configurations randomised to: RV→AH, RV+MCV→AH, MCV→AH, and RV→SCV+AH.

Results—For these configurations, mean (SD) defibrillation thresholds were 27.3 (9.6) J, 11.9 (2.9) J, 15.2 (4.3) J, and 21.8 (9.3) J, respectively. Both electrode configurations incorporating the MCV had defibrillation thresholds that were significantly less than those observed with the RV→AH (p < 0.001) and RV→SCV+AH (p < 0.05) configurations. Necropsy dissection showed that the MCV drained into the coronary sinus at a location close to its orifice (mean distance = 2.7 (2.2) mm). The MCV bifurcated into two main branches that drained the right and left ventricles, the left branch being the dominant vessel in the majority (6/7) of cases.

Conclusions—Placement of specialised defibrillation electrodes within the middle cardiac vein provides more effective defibrillation than a conventional tight ventricular lead. (Heart 2000;84:425–430)

Keywords: ventricular defibrillation; defibrillation threshold; implantable cardioverter defibrillator; middle cardiac vein

The coronary venous system is an attractive site for ventricular defibrillation as it is located on the epicardial surface of the heart. Arruda and colleagues first showed the feasibility of ventricular defibrillation in the middle cardiac vein (MCV).1 In a canine model they produced a 37% reduction in the defibrillation threshold compared with a right ventricle to superior caval vein (SCV) configuration when a single 2 French lead was placed in the middle cardiac vein and the shock was delivered to the superior caval vein. Early cardioverter defibrillators used epicardial patches placed at thoracotomy on opposite sides of the heart. Transvenous devices avoid the need for thoracotomy, but generally have higher defibrillation thresholds than epicardial systems.2 The exact mechanism underlying the lowered defibrillation energy requirements with epicardial patches is unknown. They may encompass more of the ventricular myocardium within the shock field or increase the voltage gradient in specific areas, such as the interventricular septum.

The middle cardiac vein is a structure originating on the posterior surface of the apex of the left ventricle and draining into the coronary sinus distal to the small cardiac vein or the orifice of the coronary sinus. To our knowledge, there has been no previous systematic evaluation of defibrillation using multiple electrodes placed in this vein.

Methods
Animal experimentation was carried out with UK Home Office approval under an approved project license. This is in accordance with guidelines of the American Heart Association/National Institutes of Health (AHA/NIH) for the humane care and use of laboratory animals.

ANIMAL PREPARATION AND MONITORING
Eight female pigs of crossbred variety (Landrace and Large White) weighing 35–71 kg (mean (SD), 54 (13) kg) were anaesthetised with a continuous intravenous infusion of alphaxalone (9 mg/kg/h) and alphadolone acetate (3 mg/kg/h) (Saffan, Mallinckrodt Veterinary, Uxbridge, Middlesex, UK). The animals were intubated with a cuffed endotracheal tube and ventilated using room air supplemented with oxygen. The tidal volumes and respiratory rates were adjusted depending on arterial blood gas concentrations. The femoral artery was cannulated for continuous arterial blood pressure monitoring and sampling. Arterial blood samples were analysed hourly for pH, PaCO₂, PaO₂, HCO₃⁻, and K⁺. All these variables were maintained within normal limits for the duration of each study. Arterial pressure, ECG, and rectal temperature were monitored continuously throughout the study.
The defibrillation threshold was established for each randomised electrode configuration (table 1) using a modified four reversal binary search method. The starting energy was 16 J, with subsequent shock levels changed (increased/decreased) depending on the animals’ response (failure/success). The energy of subsequent shocks was increased or decreased in steps of 8, 4, 2, and 1 J, with all subsequent intervals at 1 J. When at the 1 J step size, the shock energy was increased/decreased until three successful shocks were obtained that were either preceded or followed by a failed shock. The defibrillation threshold was calculated as the mean of the three successful shocks. If any test shock failed, the animal was immediately rescued using a 40 J biphasic shock. The animal was allowed to recover haemodynamic function (return of heart rate and blood pressure to baseline level) between each fibrillation/defibrillation cycle, for a minimum of three minutes.

### Table 1 Summary of defibrillation thresholds (DFT), shock impedances, leading edge voltages (LEV), and leading edge currents (LEC) for all electrode configurations assessed (anode → cathode)

<table>
<thead>
<tr>
<th></th>
<th>RV→AH</th>
<th>MCV+RV→AH</th>
<th>MCV→AH</th>
<th>RV→SCV+AH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DFT (J) (mean (SD))</strong></td>
<td>27.3 (9.6)</td>
<td>11.9 (2.9)</td>
<td>15.2 (4.3)</td>
<td>21.8 (9.3)</td>
</tr>
<tr>
<td>p Value (&lt;RV→AH)</td>
<td>&lt; 0.05</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>p Value (&lt;RV→SCV+AH)</td>
<td>&lt; 0.05</td>
<td>&lt; 0.01</td>
<td>&lt; 0.05</td>
<td></td>
</tr>
<tr>
<td><strong>Impedance (Ω) (mean (SD))</strong></td>
<td>52.0 (2.6)</td>
<td>42.1 (3.7)</td>
<td>49.9 (2.6)</td>
<td>43.8 (2.6)</td>
</tr>
<tr>
<td>p Value (&lt;RV→AH)</td>
<td>&lt; 0.001</td>
<td>&gt; 0.05</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>p Value (&lt;RV→SCV+AH)</td>
<td>&lt; 0.001</td>
<td>&gt; 0.05</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td><strong>LEV (V) (mean (SD))</strong></td>
<td>510 (98)</td>
<td>305 (41)</td>
<td>375 (57)</td>
<td>417 (83)</td>
</tr>
<tr>
<td>p Value (&lt;RV→AH)</td>
<td>&lt; 0.05</td>
<td>&lt; 0.01</td>
<td>&lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>p Value (&lt;RV→SCV+AH)</td>
<td>&lt; 0.001</td>
<td>&gt; 0.05</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td><strong>LEC (A) (mean (SD))</strong></td>
<td>9.8 (1.7)</td>
<td>7.3 (1.0)</td>
<td>7.5 (1.0)</td>
<td>9.6 (1.8)</td>
</tr>
<tr>
<td>p Value (&lt;RV→AH)</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
<td>&gt; 0.05</td>
<td></td>
</tr>
<tr>
<td>p Value (&lt;RV→SCV+AH)</td>
<td>&gt; 0.05</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
<td></td>
</tr>
</tbody>
</table>

AH, active housing; MCV, middle cardiac vein; RV, right ventricular apex; SCV, superior caval vein.

### INSTRUMENTATION
The right external jugular vein was cannulated and an Angelflex defibrillation electrode (Angieon Corporation, Minneapolis, Minneapolis, USA) was advanced to the right ventricular apex (RV) under fluoroscopic guidance with the proximal defibrillation electrode located in the superior caval vein. Its stability in this position was ensured with repeated fluoroscopy. The middle cardiac vein was identified using standard angiographic techniques. Through three individual shortened 8 French percutaneous transvenous coronary angioplasty guiding catheters, individual electrodes were positioned in its main (50 × 1.8 mm) and two proximal tributaries (25 × 1.8 mm). Each electrode was mounted in a polyvinyl chloride sheath with a stylet running through it and into the centre of the defibrillation coil. Having satisfactorily positioned the coil in the venous system the sheath and catheter could be retracted and the stylet removed, leaving the defibrillation coil in situ attached to a fine (0.5 mm) insulated drawn braised strand (DBS) cable. Once all three electrodes were positioned, their distal terminals were connected in parallel. An active housing (AH) can electrode (43 ml) was implanted into a pocket fashioned in the subcutaneous tissue of the left pectoral region of the chest wall.

### SHOCK WAVEFORM
The pigs were defibrillated with a biphasic rectangular waveform with a phase 1 duration of 4.8 ms and a phase 2 duration of 2.4 ms, with 0.2 ms between phases. The leading edge voltage of phase 2 was 50% of the amplitude of phase 1. The waveform was delivered by an external research defibrillator (ARD9000, Angieon Corporation) that operates as a high voltage, linear amplifier. A rectangular waveform was selected so as to maintain a constant waveform duration, constant voltage, and constant tilt during each phase. Ventricular fibrillation was induced using 60 Hz alternating current of 10 V for one second delivered through the defibrillation electrodes. Each test shock was delivered after 10 seconds of ventricular fibrillation.

### DEFIBRILLATION PROTOCOL
The defibrillation threshold was established for each randomised electrode configuration (table 1) using a modified four reversal binary search method. The starting energy was 16 J, with subsequent shock levels changed (increased/decreased) depending on the animals’ response (failure/success). The energy of subsequent shocks was increased or decreased in steps of 8, 4, 2, and 1 J, with all subsequent intervals at 1 J. When at the 1 J step size, the shock energy was increased/decreased until three successful shocks were obtained that were either preceded or followed by a failed shock. The defibrillation threshold was calculated as the mean of the three successful shocks. If any test shock failed, the animal was immediately rescued using a 40 J biphasic shock. The animal was allowed to recover haemodynamic function (return of heart rate and blood pressure to baseline level) between each fibrillation/defibrillation cycle, for a minimum of three minutes.

### DATA ACQUISITION AND STATISTICAL ANALYSIS
All data were recorded on the ARD9000 including calculations of the individual shock impedance and energy along with leading edge voltage and current. The mean defibrillation threshold and standard deviation were calculated for each electrode configuration. All the configurations were then compared using a repeated measures analysis of variance (ANOVA). If the ANOVA yielded a significant F value (p < 0.05) then the individual group means were compared using a Student-Newman-Keuls test. All differences were considered to be significant at a probability value of p < 0.05. Values are given as mean (SD). The number of animals required to establish a statistical difference between electrode configurations was calculated before the start of the study using power calculations. All statistics were calculated using GraphPad Instat, version 2.01.

### ANATOMICAL EVALUATION
At necropsy the hearts (n = 7) were removed from the thoracic cavity. Angiography of the middle cardiac vein using a diluted barium solution was performed and single frame radiographs taken in anteroposterior and lateral views. The hearts were fixed by immersion in 10% formal saline. Silicon rubber was pumped manually through the orifice of the coronary sinus and massaged throughout the entire coronary venous system, paying particu-
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Figure 1  Diagrammatic representation of the posterior (caudal) surface of the pig heart illustrating the coronary venous system. The extent of the coronary sinus is shown, together with the relation of the orifice of the middle cardiac vein to the orifice of the coronary sinus. The main trunk of the middle cardiac vein bifurcates into the left and right branches, although occasionally it may trifurcate, with the addition of a middle branch. The azygous vein is a dominant vessel in the pig heart, which drains into the (right) superior caval vein although occasionally it may trifurcate, with the addition of a middle branch. The azygous vein is a dominant vessel in the pig heart, which drains into the (right) superior caval vein.

Results

In all eight animals the three electrode configuration was successfully deployed in the middle cardiac vein with no complications (fig 2). Easiest deployment was in the larger animals (63–70 kg, 15 minutes total procedure time). In the smaller animals (<36 kg) there was some difficulty positioning the last electrode in a proximal branch of the vein, resulting in longer procedure times (maximum 60 minutes). In all eight animals the final anatomical arrangement of the lead system was comparable with the long electrode in the dominant middle cardiac vein and its branches to the surrounding musculature.

Defibrillation Protocol

There was a significant reduction in the defibrillation thresholds of those electrode combinations involving the middle cardiac vein compared with conventional configurations (fig 3). The defibrillation threshold of MCV+RV→AH (11.9 (2.9) J) showed a 56% reduction (p < 0.001) compared with RV→AH (27.3 (9.6) J). The MCV→AH (15.2 (4.3) J) configuration was similarly less than RV→AH (p < 0.001). There was no significant difference between the energy levels of the two configurations incorporating the middle cardiac vein (p > 0.05). Both MCV→AH (p < 0.05) and MCV+RV→AH (p < 0.01) were more effective than the conventional three electrode configuration of RV→SCV+AH (21.8 (9.3) J). While the weight of the animals covered a large range (35–71 kg) there was no correlation observed between weight and the proportional reduction in defibrillation threshold seen with each configuration. Leading edge voltages and currents are displayed in table 1. The leading edge currents of MCV+RV→AH and MCV→AH were 25% (p < 0.01) and 23% (p < 0.01) less than that of the RV→AH configuration. They were also significantly less than RV→SCV+AH. There was no difference in the leading edge currents of the two configurations not incorporating the MCV.

The shock impedance of the MCV→AH pathway was 49.9 (2.6) ohms and not significantly different from the impedance of the RV→AH pathway (52.0 (2.6) ohms). Adding an SCV electrode to the RV→AH pathway significantly decreased the impedance to 43.6 (2.6) ohms (p < 0.001) compared with either of the two electrode pathways. Combining the MCV lead with the RV lead (MCV+RV→AH) led to a shock impedance (42.1 (3.7) ohms) that was significantly less than the shock impedance of both of the two electrode pathways (RV→AH or MCV→AH), but not different from the other three electrode pathway (RV→SCV+AH).

ANATOMICAL EVALUATION

The orifice of the middle cardiac vein was generally located close to or at the orifice of the coronary sinus (mean distance 2.7 mm (2.2) mm; n = 7). The small cardiac vein was not particularly well developed and was noted to drain into the coronary sinus at a similar location to the orifice of the middle cardiac vein.

Figure 2  Lateral radiograph of thorax showing the multifilamented middle cardiac vein electrodes in place along with the conventional right ventricular and superior vena caval electrodes.
In general, the middle cardiac vein bifurcated into two main branches, left and right. In two of the seven hearts examined, a third mid-branch was noted. Variation was observed in the location at which this bifurcation occurred (mean 23.5 (10.9) mm from orifice of middle cardiac vein). Proximal branching (< 25 mm from the orifice), occurred in pigs 1, 2, and 6. Distal branching occurred in pigs 3 and 5. In pig 4 the middle cardiac vein was much shorter and did not reach the apical musculature. Consequently, in this heart the terminal region of the main branch of the middle cardiac vein reached the musculature of the interventricular septum at a much higher position (fig 4). In the majority of the hearts examined (pigs 1–3, 5, and 6) it was the right branch of the bifurcating middle cardiac vein that had the closest relation with the musculature of the interventricular septum (fig 5). The left branch of the middle cardiac vein was more closely related to the musculature of the posterior left ventricular free wall, and in two of the hearts examined (pigs 3 and 6) it was observed to anastomose with the marginal vein. The exception was pig 4, which possessed a short extension of the middle cardiac vein, with only a single main branch. This was reflected in its more proximal relation to the interventricular septum mentioned previously (fig 4). While there were differences in anatomy between animals, there was no clear correlation with defibrillation threshold. Specifically, there was no apparent effect on defibrillation threshold observed in those animals with shorter middle cardiac veins.

There was no evidence of any damage to the middle cardiac vein or its tributaries in any of the animals. In particular no rupture was seen that would suggest erosion of the electrodes after multiple defibrillation shocks. Examination of each heart at necropsy showed that there was no evidence of acute myocardial infarction.

**Discussion**

We have shown a 56% (p < 0.001) reduction in the defibrillation threshold using a lead system.
placed in the middle cardiac vein in conjunction with a conventional right ventricular apical lead. The configuration (MCV→AH) that did not use a right ventricular shocking electrode produced a defibrillation threshold that was 44% (p < 0.001) lower than the conventional RV→AH configuration most commonly used in clinical implantable cardioverter defibrillator devices. This observation raises the possibility that a middle cardiac vein shocking electrode may replace the right ventricular shocking coil that is currently employed in all transvenous lead systems. Furthermore, a middle cardiac vein electrode may also be placed in parallel with a right ventricular shocking lead to improve defibrillation efficacy. In clinical practice if the defibrillation threshold with the RV→AH configuration is unacceptably high, an electrode in the superior caval vein is usually incorporated into the configuration. In this study, the addition of a superior caval vein electrode as a third electrode (RV→SCV + AH) lowered the defibrillation threshold by 20% (p < 0.05) compared with the RV→AH pathway. However, the addition of a middle cardiac vein electrode as a third electrode (MCV + RV→AH) lowered the defibrillation threshold by 45% (p < 0.001) compared with the three electrode pathway that included the superior caval vein.

It is possible that the epicardial location of the middle cardiac vein results in more of the myocardium being incorporated into the shock field, so that a greater mass is defibrillated. A conventional shock from RV→AH results in areas of low potential gradient in the apical region of the right and left ventricles. Placement of a lead in a location closer to the left ventricle may result in higher voltage gradients in the left ventricle, thus increasing the mass of ventricle in which activation fronts are halted. The interventricular septum has been identified as a structure important in ventricular defibrillation. Singer and colleagues showed that trans-septal defibrillation was more effective than conventional defibrillation. The interventricular septum constitutes a significant mass of myocardium. Ensuring a favourable potential gradient over this structure may result in a greater mass of myocardium being successfully defibrillated. The close proximity of a shocking electrode in the middle cardiac vein to the septum may account for the significant reduction in the defibrillation threshold. The nature of the design of the lead system deployed in the middle cardiac vein may have had a significant impact on reduction in defibrillation energy requirements. We have previously documented that defibrillation using a superior caval vein electrode (4080, Angeon Corporation) placed in the middle cardiac vein in combination with the RV→AH configuration can reduce the defibrillation threshold by 30%. Having several filaments will result in increasing the electrode surface area, leading to a decrease in the shock impedance and creating a more even current density through the ventricles. It is not clear from this study whether the position of individual filaments relative to one another has an effect on defibrillation efficacy.

While the addition of an electrode system in the middle cardiac vein has significantly reduced the defibrillation threshold, the number of patients that have unacceptable thresholds with current lead systems is very few. However, the clinical impact of such a system might be on device longevity and size. Increasing attention is being placed on left ventricular pacing through the coronary venous system for patients with heart failure. It might therefore be possible to incorporate a defibrillation electrode system into the pacing system, thereby allowing left ventricular pacing and defibrillation with reduced thresholds.

The anatomical evaluation of the middle cardiac vein in the pig led to a number of important new observations. The orifice of the middle cardiac vein was located at or near to the orifice of the coronary sinus. The middle cardiac vein clearly had two main branches, right and left, with the latter being dominant in six of the seven hearts studied. The bifurcation into the two branches could be seen either proximally (in three) or distally (in four). Of significance is the relation to the interventricular septum, which was noted to be very close to the right branch of the middle cardiac vein.

While the results of this study suggest that the middle cardiac vein offers promise as a site for a defibrillation electrode, it needs further evaluation. The porcine model may mimic the scenarios in defibrillation of the human heart, but inevitably there are several distinct differences. The relation of the porcine heart within the thorax and mediastinum is of a different orientation to that of man and so direct comparisons may not be valid, especially if we are trying to explain the mechanism in terms of shock vectors and fields. The precise anatomy of the middle cardiac vein in man has not been systematically evaluated. Nevertheless it has been reported that the middle cardiac vein drains into the coronary sinus distal to its orifice and certainly more distal to the small cardiac vein. The porcine coronary circulation is generally thought to be closely similar to the anatomy of the human coronary circulation. The experimental results presented here suggest that the middle cardiac vein should be explored as a potential site for the deployment of defibrillation electrodes in patients receiving implantable cardioverter defibrillator devices. This study has been an acute evaluation. The chronic effects of electrode placement within the coronary venous system have not been addressed. In particular the impact of possible coronary venous thrombosis and the ease with which the leads might be extracted in the event of an infection need to be carefully evaluated. In this study the middle cardiac vein was cannulated from the right jugular vein. In previous studies we have cannulated this vein using a left sided approach. In clinical practice most implantable cardioverter defibrillators are implanted using a left sided approach. We have not noticed any difference in the ease of cannulation of the middle cardiac vein using a right or left sided approach. In our
experience in humans, during placement of coronary venous electrodes for heart failure pacing we have found that the middle cardiac vein is easily cannulated using a left subclavian/cephalic approach. For this technique to become clinically acceptable it needs to be safe and easily performed. One of the key factors would be the method of deployment of the electrodes. We would anticipate a catheter system similar to those currently being used to deploy heart failure pacing electrodes.

There was no evidence in this study of significant myocardial injury, and in particular no evidence of rupture or perforation of the middle cardiac vein. This would support the safety aspect of this technique, especially as each animal received many more shocks than would be expected in clinical practice. The safety aspect of chronic implantation of such electrodes needs further evaluation. In particular the extraction of such leads may require careful assessment. There has been little evaluation of the ease of extraction of electrodes placed in the coronary venous system for heart failure pacing. With the substantial number of these leads currently being implanted worldwide, the ease and safety of extraction should become apparent with the course of time.

**CONCLUSIONS**

We have shown that the use of a multifila-
mented lead system deployed in the middle cardiac vein and its branches resulted in a 56% reduction in the energy requirements for defibrillation compared with the conventional RV→AH configuration commonly employed in clinical practice.

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**Electronic pages**

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The following electronic only articles are published in conjunction with this issue of *Heart.*

**Successful treatment of aconitine induced life threatening ventricular tachyarrhythmia with amiodarone**

*D-F Yeih, F-T Chiang, S K S Huang*

With the increasing trend of cross mixing of populations, aconitine induced poisoning and its related arrhythmias may be more frequently encountered worldwide. However, the clinical experience is often too limited to draw any conclusion on the optimal treatment for tachycardia induced by aconitine intoxication. The clinical presentation, serial ECG changes, and responses to antiarrhythmic agents are reported in a 61 year old man with aconitine induced life threatening ventricular tachyarrhythmia. Amiodarone was effective in suppressing polymorphic ventricular tachycardia, which might provide an example of successful pharmacological intervention in aconitine induced ventricular tachyarrhythmia. *(Heart 2000;84:e8) www.heartjnl.com/cgi/content/full/84/4/e8*

**Pentacuspid aortic valve diagnosed by transoesophageal echocardiography**

*M Gemri, A Cengel, T Timurkaynak*

Congenital aortic valve anomalies are quite a rare finding in echocardiographic examinations. A case of a 19 year old man with a pentacuspid aortic valve without aortic stenosis and regurgitation, detected by transoesophageal echocardiography, is presented. *(Heart 2000;84:e9) www.heartjnl.com/cgi/content/full/84/4/e9*