Selective Activation of the $K^{+}_{\text{ATP}}$ Channel Is a Mechanism by Which Sudden Death Is Produced by Low-Energy Chest-Wall Impact (Commotio Cordis)

Mark S. Link, MD; Paul J. Wang, MD; Brian A. VanderBrink, BA; Erick Avelar, MD; Natesa G. Pandian, MD; Barry J. Maron, MD; N.A. Mark Estes III, MD

Background—Sudden death due to relatively innocent chest-wall impact has been described in young individuals (commotio cordis). In our previously reported swine model of commotio cordis, ventricular fibrillation (with T-wave strikes) and ST-segment elevation (with QRS strikes) were produced by 30-mph baseball impacts to the precordium. Because activation of the $K^{+}_{\text{ATP}}$ channel has been implicated in the pathogenesis of ST elevation and ventricular fibrillation in myocardial ischemia, we hypothesized that this channel could be responsible for the electrophysiologic findings in our experimental model and in victims of commotio cordis.

Methods and Results—In the initial experiment, 6 juvenile swine were given 0.5 mg/kg IV glibenclamide, a selective inhibitor of the $K^{+}_{\text{ATP}}$ channel, and chest impact was given on the QRS. The results of these strikes were compared with animals in which no glibenclamide was given. In the second phase, 20 swine were randomized to receive glibenclamide or a control vehicle (in a double-blind fashion), with chest impact delivered just before the T-wave peak. With QRS impacts, the maximal ST elevation was significantly less in those animals given glibenclamide ($0.16\pm0.10$ mV) than in controls ($0.35\pm0.20$ mV; $P=0.004$). With T-wave impacts, the animals that received glibenclamide had significantly fewer occurrences of ventricular fibrillation (1 episode in 27 impacts; 4%) than controls (6 episodes in 18 impacts; 33%; $P=0.01$).

Conclusions—In this experimental model of commotio cordis, blockade of the $K^{+}_{\text{ATP}}$ channel reduced the incidence of ventricular fibrillation and the magnitude of ST-segment elevation. Therefore, selective $K^{+}_{\text{ATP}}$ channel activation may be a pivotal mechanism in sudden death resulting from low-energy chest-wall trauma in young people during sporting activities. (Circulation. 1999;100:413-418.)

Key Words: ventricular fibrillation ■ death, sudden ■ chest trauma ■ sports

Sudden death may occur in young sports participants when a baseball or other projectile strikes the victim over the precordium, even in the absence of structural damage to the chest wall and heart. This phenomenon is termed commotio cordis, and it predominantly affects individuals aged 5 to 18 years without preexisting heart disease. A 1996 United States Consumer Product Safety Commission report found 38 deaths from baseball blows to the chest between 1973 and 1995. In addition, commotio cordis has been reported in ice hockey, lacrosse, and softball and as the consequence of fistfights; indeed, it may be more common than initially believed. Currently, the Commotio Cordis Registry (Minneapolis, Minn) has recorded 70 victims of commotio cordis. In our previously described model of commotio cordis, we observed ventricular fibrillation with 30-mph impacts occurring 15 to 30 ms before the peak of the T-wave. In addition, ST-segment elevation was produced by impacts on the QRS and ST segments. However, the cellular mechanisms responsible for these striking electrophysiologic consequences of blunt chest impact are unknown. Because many of the profound electrophysiologic consequences observed in our experimental model of commotio cordis are similar to those of myocardial ischemia, we hypothesized that the cellular mechanisms for ST-segment elevation and ventricular fibrillation in these 2 circumstances may also be comparable.

The cardiac $K^{+}_{\text{ATP}}$ channel is normally inactive, as it is inhibited by physiological concentrations of ATP. The opening of the channel is associated with a reduction in the cellular ATP/ADP ratio, such as occurs in myocardial ischemia. It is thought that activation of this channel is responsible for the ST-segment elevation observed in myocardial ischemia. Furthermore, activation of this channel increases the likelihood of ventricular fibrillation occurring during myocardial ischemia. Glibenclamide is a sulfonylurea that primar-
administered to animals subsequently subjected to low-energy chest-wall impact. In which 10 impacts were delivered to the QRS in 9 animals. The results of these experiments were compared with those previously studied animals that were not given glibenclamide and received 10 QRS impacts, ST segment elevation was 0.35±0.20 mV, more than 2-fold greater than the animals who were given glibenclamide (P=0.004). In both groups of animals, the maximum ST-segment elevation was present on the first beat after impact and decreased to baseline over the following 30 to 60 s, without development of Q-waves or T-wave abnormalities (Figure 2). In animals subjected to QRS impact, there were no differences between glibenclamide-treated and control animals with regard to the occurrence of transient heart block (3 of 14 [21%] versus 4 of 10 [40%]) or left bundle branch pattern (14 of 14 versus 9 of 10). Ventricular fibrillation did not occur with QRS impacts (Table 1).

Methods
Juvenile domesticated swine, 4 to 8 weeks old and weighing 8 to 12 kg, were used in this study. The research protocol was approved by the Animal Research Committee of the New England Medical Center in conformity with the regulations of the Association for Assessment and Accreditation of Laboratory Animal Care. Animals were anesthetized with ketamine and isoflurane and intubated; intravenous catheters were placed; and an infusion of 5% dextrose was begun. Electrophysiologic stimulator triggered from surface electrocardiographic input. Velocity of impact object was measured by chronograph (Oehler Research) modified for low velocity.

To test the hypothesis that abrupt mechanical activation of the K$_{ATP}$ channel may be a mechanism by which virtually instantaneous sudden death results from chest-wall impact, glibenclamide (a selective blocker of the K$_{ATP}$ channel) was administered to animals subsequently subjected to low-energy chest-wall impact.

Discussion
Our swine model of chest impact–related sudden death shares many similarities with the human phenomenon of commotio heartis.
cordis, including the importance of impact location and velocity, difficulty with resuscitation, and absence of significant thoracic or cardiac injury. In the present and previous studies, we showed that the initiation of ventricular fibrillation (and, thus, sudden death) with low-energy chest-wall blows is critically dependent on the timing of the blow to a vulnerable portion of the cardiac cycle. Ventricular fibrillation occurred instantaneously with 30-mph impacts just before the T-wave peak, and it was not preceded by intervening ventricular tachycardia, conduction abnormalities, or ischemic ST changes. Our obser-

table 1. Electrophysiological Consequences of Low-Energy Chest Impact During the QRS Segment, With and Without the Prior Administration of Glibenclamide

<table>
<thead>
<tr>
<th>Electrophysiological Result</th>
<th>Control* Group</th>
<th>Glibenclamide Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular fibrillation or polymorphic ventricular tachycardia</td>
<td>0 (9 animals; 10 impacts)</td>
<td>0 (6 animals; 14 impacts)</td>
<td>1.0</td>
</tr>
<tr>
<td>ST-segment elevation, mV</td>
<td>0.35±0.20</td>
<td>0.16±0.10</td>
<td>0.004</td>
</tr>
<tr>
<td>Left bundle branch block</td>
<td>9 (80%)</td>
<td>14 (100%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Complete heart block</td>
<td>4 (40%)</td>
<td>3 (21%)</td>
<td>0.39</td>
</tr>
</tbody>
</table>

*Control animals were from a prior and previously reported experiment.
vations imply that the ventricular fibrillation produced by low-energy chest blows is not secondary to coronary spasm, myocardial ischemia, hemorrhage, heart block, or ventricular tachycardia, but rather is a primarily electrical phenomenon.

Nevertheless, the cellular mechanisms responsible for this electrical event are unknown.

In experimental models of myocardial ischemia, ST-segment elevation and ventricular arrhythmias are due, in

<table>
<thead>
<tr>
<th>Electrophysiological Result</th>
<th>Control Group (10 animals; 18 impacts)</th>
<th>Glibenclamide Group (10 animals; 27 impacts)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular fibrillation</td>
<td>6 (33%)</td>
<td>1 (4%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Polymorphic ventricular tachycardia</td>
<td>2 (11%)</td>
<td>0</td>
<td>0.30</td>
</tr>
<tr>
<td>ST-segment elevation, mV</td>
<td>0.07 ± 0.04*</td>
<td>0.11 ± 0.07†</td>
<td>0.09</td>
</tr>
<tr>
<td>Bundle branch blocks</td>
<td>3 (25%)*</td>
<td>4 (15%)†</td>
<td>0.66</td>
</tr>
<tr>
<td>Complete heart block</td>
<td>2 (17%)*</td>
<td>3 (12%)†</td>
<td>0.64</td>
</tr>
</tbody>
</table>

*Data based on 12 chest impacts.
†Data based on 26 chest impacts.

Figure 3. Six-lead ECG showing consequences of chest impact timed to upstroke of T-wave peak with 150-g spherical object (size and weight of regulation baseball) delivered at 30 mph. Top, Control animal demonstrating ventricular fibrillation initiated instantaneously with impact. Bottom, Animal given 0.5 mg/kg glibenclamide demonstrates only initiation of premature ventricular contraction, but no ventricular fibrillation.
part, to selective activation of the \( K^+_{\text{ATP}} \) channel.\textsuperscript{11–19} Blocking this channel with glibenclamide reduces these electrophysiologic effects of ischemia.\textsuperscript{11–19,24,25} Because the ST-segment elevation and ventricular fibrillation seen in our experimental model of commotio cordis are similar to those reported in myocardial ischemia, we hypothesized that these entities may share the same or similar cellular mechanisms. Therefore, to test the hypothesis that activation of the \( K^+_{\text{ATP}} \) channel was involved in the profound electrophysiologic consequences of modest chest-wall blows (including sudden cardiac death), we designed a double-blind study in which a selective blocker of the \( K^+_{\text{ATP}} \) channel (glibenclamide) or a placebo was administered to swine before delivering a chest blow. Glibenclamide was chosen because its ability to block the \( K^+_{\text{ATP}} \) channel has been well established.\textsuperscript{20,21} Indeed, in our present experiment with low-energy chest-wall blows, the incidence of ventricular fibrillation was significantly reduced from 33% of impacts (60% of animals) in controls to only 4% of impacts (10% of animals) in glibenclamide-treated animals. These results suggest that it is the immediate mechanical activation of the \( K^+_{\text{ATP}} \) channel by low-energy chest-wall impact that is, in part, responsible for the ventricular fibrillation seen in our experimental model and, by inference, in sudden death on the playing field in young athletes.

Prominent ST-segment elevation was also produced in our model of commotio cordis,\textsuperscript{9} and it has also been reported in a few survivors of commotio cordis.\textsuperscript{5,26,27} We found that ST-segment elevation was most pronounced with QRS impacts, but it was observed with chest impacts throughout the cardiac cycle.\textsuperscript{9} ST-segment elevations were most marked on the beat following the impact; then, they decayed and normalized over the next 30 to 60 s. In the present study, glibenclamide attenuated the ST-segment elevation observed with QRS impacts, substantiating our hypothesis that the \( K^+_{\text{ATP}} \) Channel is activated by mechanical trauma to the chest wall in commotio cordis. It is presently unresolved as to why ST-segment elevation was more pronounced with QRS strikes compared with T-wave strikes.\textsuperscript{9}

The present experiment provides convincing evidence that chest-wall impacts occurring on both T-wave and QRS segments result in activation of the \( K^+_{\text{ATP}} \) channel (Figure 4). Whether this activation leads to ventricular fibrillation or to ST-segment elevation depends on the timing of the impact. As seen in our previous experiment,\textsuperscript{9} only impacts that occurred during the vulnerable time period of repolarization caused ventricular fibrillation. That a vulnerable period for the initiation of ventricular fibrillation exists suggests that a second trigger or condition is necessary (in addition to \( K^+_{\text{ATP}} \) channel activation) for ventricular fibrillation to result from a mechanical force such as a low-energy chest-wall blow. At the current time, this additional trigger or condition is unknown, but it is likely related to the dispersion of repolarization that is present during the vulnerable period of the cardiac cycle.

We previously observed marked hemorrhage in the AV bundle and bundle branches in 1 of 2 animals with transient heart block induced by chest-wall impact, suggesting that direct trauma to the conduction system caused the manifestations of heart block.\textsuperscript{9} In support of this theory, in the present study, we found no difference in the incidence of heart block or left bundle branch block in the glibenclamide-treated or control animals. Thus, these observations, taken together, suggest that the left bundle branch block and transient heart block that was observed in our experiments is primarily a consequence of direct mechanical trauma rather than activation of the \( K^+_{\text{ATP}} \) channel.

In conclusion, in this experimental model of commotio cordis, glibenclamide significantly decreased the incidence of ventricular fibrillation and the magnitude of ST segment elevation. Therefore, direct mechanical activation of the \( K^+_{\text{ATP}} \) channel seems to be an important cellular mechanism by which ventricular fibrillation occurs in commotio cordis.

Acknowledgments

Supported by a grant from The National Operating Committee on Standards for Athletic Equipment, Overland Park, Kansas. The opinions expressed herein are those of the authors and do not necessarily reflect the opinions of the committee. We are indebted to Darisse A. Paquette, CMI, for her assistance with the figures.

References


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Circulation. 1999;100:413-418
doi: 10.1161/01.CIR.100.4.413

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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