for harvest (40 ± 5 minutes after start of anoxia) and using retrograde coronary sinus reperfusion, and have again easily separated all animals from bypass after transplantation [2]. Therefore, we believe that the mode and methods of reperfusion, rather than the mechanisms of death, are the most important factors predicting resuscitation success.

Despite these encouraging findings, it is essential that investigators focus further efforts into defining the ultimate period of warm ischemia that hearts of different ages from various species can sustain and still be successfully reanimated, and whether such hearts will function long-term.

Steven R. Gundry, MD
Division of Cardiothoracic Surgery
Department of Surgery, RM 2562B
Loma Linda University Medical Center
11234 Anderson St
PO Box 2000
Loma Linda, CA 92354-0200

References

Beneficial Effect of Nicardipine on Perioperative Myocardial Ischemia

To the Editor:

In spite of a dramatic improvement in myocardial preservation techniques, cell damage may still occur during cardiopulmonary bypass (CPB). This can be expressed as postoperative increase in creatinine kinase or as early perioperative electrocardiographically identifiable ischemia. This may be observed in any kind of operation using CPB, although the additional contribution of coronary artery disease and coronary artery bypass grafting renders it more problematic. Duration of CPB, graft occlusion, inadequate flow through an internal mammary artery graft, and ventricular hypertrophy have been shown to enhance the risk of perioperative myocardial ischemia. Whatever the cause, perioperative myocardial ischemia can lead to permanent ventricular dysfunction if not promptly resolved. In the absence of anatomical or technical abnormalities that could be perioperatively corrected, coronary artery spasm and low-reflow phenomenon would be the most probable causes of perioperative myocardial ischemia.

Specific pharmacological treatment could play a crucial role. Nicardipine, a calcium-channel blocker, would appear to be the drug of choice in such a circumstance because of its specific coronary dilating property, its minimal negative inotropic effect (when compared with nifedipine), its potent systemic vasodilatory action, and its inhibitory effect on endothelin secretion. One of us has previously reported the beneficial effect of intracoronary infusion of a large dose of nifedipine in patients suspected of having coronary spasm in the postoperative course of coronary artery bypass grafting [1, 2]. However, the above-mentioned properties of nicardipine and their possible synergistic effect prompted us to use this drug in similar circumstances of perioperative myocardial ischemia when other means were shown to be unsuccessful.

Between February and December 1991, 12 patients with perioperative myocardial ischemia have been successfully treated by intracoronary infusion of nicardipine in our institution. In all cases myocardial preservation has been achieved by the combination of antegrade and retrograde crystalloid cardioplegia (St. Thomas No. 1), topical cooling, and moderate systemic hypothermia (30°C). Patients' characteristics, the onset and degree of ischemia, dose and route of administration of nicardipine, and electrocardiographical evolution are reported in Table 1. The 11 patients who underwent coronary artery bypass grafting showed ST segment elevation in at least one revascularized area. In the patient who received a heart transplant the anterior part of the heart was involved. Six patients displayed severe hemodynamic alteration. The onset of perioperative myocardial ischemia ranged from 1 to 13 minutes after weaning off CPB. The grafts were explored and shown to be patent and nontwisted. Although all the patients were put back on CPB at least once and received nitrates and inotropes, no electrocardiographical improvement was observed. However, ST segment was normalized within a period ranging from 1 to 7 minutes after administration of a 5-mg bolus of nicardipine. Nicardipine administration was usually

Table 1. Nicardipine in Perioperative Myocardial Ischemia

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Procedure</th>
<th>Time of CPB (min)</th>
<th>Onset (min after CPB)</th>
<th>ST segment elevation (mm)</th>
<th>Route</th>
<th>Dose (mg)</th>
<th>Onset of ST normalization (min after NIC infusion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>F</td>
<td>Heart Tx</td>
<td>130</td>
<td>5</td>
<td>3.0 anterior</td>
<td>AR</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>64</td>
<td>M</td>
<td>CABG 2 IMA</td>
<td>40</td>
<td>3</td>
<td>2.7 anterior</td>
<td>AR</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>68</td>
<td>F</td>
<td>CABG 2 SG</td>
<td>45</td>
<td>7</td>
<td>2.0 anterior</td>
<td>SG</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>76</td>
<td>F</td>
<td>CABG 3 SG</td>
<td>66</td>
<td>4</td>
<td>3.0 anterior</td>
<td>AR</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>M</td>
<td>CABG IMA</td>
<td>35</td>
<td>5</td>
<td>2.9 anterior</td>
<td>AR</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>76</td>
<td>M</td>
<td>CABG 4 SG</td>
<td>75</td>
<td>3</td>
<td>2.5 inferior</td>
<td>SG</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>75</td>
<td>M</td>
<td>CABG IMA, 2 SG</td>
<td>69</td>
<td>6</td>
<td>2.0 anterior</td>
<td>AR</td>
<td>5</td>
<td>3</td>
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<tr>
<td>8</td>
<td>71</td>
<td>M</td>
<td>CABG IMA, 1 SG</td>
<td>55</td>
<td>1</td>
<td>1.5 anterior</td>
<td>AR</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>56</td>
<td>M</td>
<td>CABG 2 IMA</td>
<td>56</td>
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<td>2.8 anterior</td>
<td>AR</td>
<td>5</td>
<td>7</td>
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<tr>
<td>10</td>
<td>66</td>
<td>M</td>
<td>CABG IMA, GEA</td>
<td>78</td>
<td>4</td>
<td>1.9 inferior</td>
<td>AR</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>11</td>
<td>66</td>
<td>M</td>
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<td>75</td>
<td>10</td>
<td>2.5 anterior</td>
<td>AR</td>
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<td>6</td>
</tr>
<tr>
<td>12</td>
<td>61</td>
<td>M</td>
<td>CABG IMA, GEA</td>
<td>67</td>
<td>7</td>
<td>3.0 anterior</td>
<td>AR</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

AR = aortic root; CABG = coronary artery bypass grafting; GEA = gastroepiploic artery; IMA = internal mammary artery; NIC = nicardipine; SG = saphenous vein graft; Tx = transplantation.
followed by a short period of deep systemic hypotension and electromechanical cardiac arrest. It is therefore mandatory to administer such a dose of nicardipine during full-flow CPB. When electrocardiographic changes were only observed in a territory revascularized by a vein graft, this was used as a unique route of injection (patients 3 and 6). All patients were subsequently weaned off CPB and had an uneventful postoperative course. No evidence of myocardial infarction has been shown in any of them.

Experimental and clinical data have clearly shown the protective effect of parenteral administration of nicardipine on various forms of myocardial ischemia [3, 4], eg, limitation of myocardial infarction size after coronary artery ligation, prevention and delay of the transient ischemia occurring during percutaneous transluminal coronary angioplasty, and improvement of perfusion in areas chronically ischemic. Our preliminary data strongly suggest that intracoronary bolus infusion of nicardipine could dramatically modify the outcome of perioperative myocardial ischemia after CPB.

This beneficial effect of nicardipine could be explained on several grounds. The inhibition of myocardial adenine triphosphate breakdown might be crucial immediately after cardiopulmonary arrest, as the myocardium is restoring energy. The coronary dilating selectivity [4] leads to the enhancement of collateral blood flow, and this could have a beneficial effect on coronary artery spasm. In that respect, although the mechanism of coronary spasm is not known, calcium ions are thought to play a key role in the genesis of spasm [5]. As a calcium-channel blocker with an inhibitory effect on endothelin, nicardipine might counteract the spasm via those two pathways. The low-reflow phenomenon, an impairment of postischemic coronary flow, is an important issue to be addressed. Indeed, one of us has recently provided experimental data indicating clearly that low reflow can be enhanced by coronary dilating drugs with a subsequent improvement of postischemic recovery of cardiac mechanical function after prolonged cardiopulmonary arrest [6].

In conclusion, we believe that in the presence of perioperative myocardial ischemia without any anatomical cause, nicardipine can be used as the drug of choice as a last resort. We believe that the pharmacological properties of nicardipine could explain an improvement of low reflow and coronary spasm, the most probable causes of perioperative myocardial ischemia when anatomical etiology has been ruled out.

Mohamed Amrani, MD
Amin Matta, MD
Robert A. Dion, MD

Departments of Cardiovascular Surgery and Anesthesiology
Université Catholique de Louvain
Cliniques Universitaires Saint-Luc
Ave Hippocrate, 10
1200 Brussels, Belgium

References

Open Lung Biopsy
To the Editor:

I would like to congratulate Drs Chechani, Landreneau, and Shaikh [1] for finally refuting the last conclusion of Gaensler and Carrington's previously considered landmark article on open lung biopsy. Despite multiple inaccuracies, unfortunately, that study has been considered the "gold standard" for managing patients with diffuse pulmonary disease refractory to medical management [2]. This, misinformation, however, has hampered chest physicians for approximately 30 years.

Doctors Gaensler and Carrington declared that biopsy of the roentgenographically most involved region (usually the lower lobes) in patients with chronic diffuse infiltrative lung disease is likely to show meaningless histological findings and that biopsy of lingular and middle lobes should be avoided [2, 3]. These inappropriate conclusions were initially refuted when I reported the results of my study demonstrating the significant sensitivity and specificity of lingular biopsies in patients with similar pathology [4, 5].

Doctor Miller and associates [6] subsequently confirmed our results and then refuted Drs Gaensler and Carrington's conclusions concerning right middle lobe biopsies. Dr Chechani and associates [1] have proven that biopsies of the roentgenographically most involved region are similarly most significant histologically, finally disproving Gaensler and Carrington's last conclusion.

It is imperative that the misinformation espoused by Drs Gaensler and Carrington finally be laid to rest to aid in the resolution of the management of a vexing and extremely important clinical problem. This entity is of added importance to thoracic surgeons, as many patients with diffuse infiltrative lung disease are hemodynamically compromised and extremely ill. A surgical approach that is simpler and expeditious while offering a definitive diagnosis is thusly extremely advantageous [4, 5]. With the increasing use of thoracoscopy, biopsy of the lingula or right middle lobe may be somewhat less important but still should be remembered as an approach that satisfies the above criteria for bilateral diffuse pulmonary disease, and is another alternative in the armamentarium of the thoracic surgeon.

Lewis Wetstein, MD
143 South St
Freehold, NJ 07728

References