Experimental Evidence of Regional Myocardial Ischemia during Beating Heart Coronary Bypass: Prevention with Temporary Intraluminal Shunts

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Sylvio M. A. Gandra, MD, Luiz A. Rivetti, MD

Department of Cardiovascular Surgery, Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, Brazil

ABSTRACT

Background: Our center has been performing beating heart coronary artery bypass grafting with a temporary intraluminal shunt since 1983. Based on our clinical observations of more than 846 surgical cases, we believe that a temporary intraluminal shunt (TIS) greatly reduces the risk of the patient developing regional myocardial ischemia during clamping of the coronary artery. To seek evidence in support of our clinical observations, we evaluated the effects of coronary clamping with and without TIS in a porcine experimental model.

Methods: We compared 2 groups of healthy Landrace pigs that underwent the same period of coronary occlusion but differed only in whether a TIS was used. The shunt device was a straight flow-through silicone tube that has been described in detail in previous publications. Ischemic changes during the test period were detected via analysis of monophasic action potential (MAP) recordings. MAPs were recorded with the contact electrode technique, which has been shown to be specific for ischemia. In group I (no shunt) animals (n = 25), MAPs were monitored during a single 15-minute occlusion of the left anterior descending (LAD) coronary artery without any form of distal perfusion. In group II (shunted) animals (n = 15), MAPs were sampled over the same intervals after the LAD was snared and opened and the TIS was introduced within the first 2 minutes. Infarct analysis using biochemical end points (serum lactate dehydrogenase [LDH] and creatine phosphokinase–myocardial band [CPK-MB]) was performed with standard serologic assays.

Results: Confirming the presence of regional ischemia in group I (no shunt) were significant changes from baseline in measurements of mean action potential duration, upstroke velocity (dV/dt), and total MAP area (millivolts·milliseconds). The presence of ischemia in group I was also confirmed by significant elevations in serum LDH and CPK-MB levels. Furthermore, the use of lidocaine was greater in group I (no shunt) animals than in group II (shunted) animals because of the greater frequency of ventricular arrhythmias in group I (P = .001). Six animals (24%) in group I and no animals in group II developed ventricular fibrillation during the 15 minutes of occlusion (P = .046). Ischemic changes in the MAP were found only prior to shunt insertion in Group II animals, and the MAP then promptly returned to normal a few minutes after TIS flow was established. Statistical analysis revealed significant differences between group I and group II in MAP duration, dV/dt, total area, lidocaine requirements, incidence of ventricular fibrillation, and serum LDH levels.

Conclusions: There has been controversy about the relative effectiveness of temporary intraluminal shunting for reducing the risk of regional myocardial ischemia during beating heart coronary artery bypass grafting. At least in this porcine model, we could demonstrate a positive effect of shunting, which parallels our clinical experience using TIS in hundreds of patients for the past 2 decades. In the animal model, we demonstrated preservation of the MAP, as well as a reduction in both the incidence of ventricular arrhythmias and the serum levels of ischemic by-products, when temporary intraluminal shunting was used. It is our conclusion that intraluminal shunts do protect the vulnerable myocardium from regional ischemia during the period of temporary coronary occlusion necessary for construction of a bypass graft on the beating heart. Temporary intraluminal shunting is a cost-effective adjunct that can increase safety and reliability in off-pump coronary artery bypass grafting.

INTRODUCTION

The recent introduction of minimally invasive direct coronary artery bypass (MIDCAB) and other limited access procedures has stimulated a dramatic resurgence in the techniques of beating heart surgery. However, the concepts of beating heart coronary grafting are not new. In fact, the original cases of coronary artery revascularization reported in the late 1950s and early 1960s were performed without cardiopulmonary bypass (CPB) [Murray 1954, Kolessov 1967, Sabiston 1974, Connolly 1978].

Despite the worldwide popularity of CPB and cardioplegia for coronary bypass surgery, a small subset of surgeons
continued to explore and develop beating heart grafting techniques and eventually gained powerful insights from the large volumes of clinical cases [Fanning 1978, Benetti 1980, Buffalo 1985, Corso 1991]. In the past 2 years, there has been widespread adoption of beating heart grafting techniques worldwide. Off-pump coronary artery bypass (OPCAB) surgery has been further enhanced by the introduction of new specialized equipment aimed at improving mechanical stabilization and visualization of the coronary target.

One of the great challenges of OPCAB is limiting ischemia during the brief period of coronary artery occlusion required for graft construction. Our experience with off-pump coronary grafting [Rivetti 1991, Rivetti 1997, Rivetti 1998] and the recent experiences with MIDCAB have shown that not all patients manifest classic electrocardiographic evidence of ischemia when the target vessel is occluded. Trans-esophageal echocardiography during MIDCAB can reveal wall motion abnormalities during graft construction despite relatively normal surface electrocardiograms. Contractility changes, hypotension, ventricular dilatation, or ventricular fibrillation can occur in an unpredictable fashion. Pfister and colleagues estimated that intraoperative ischemic events during temporary coronary occlusion occur in 4.5% of cases [Pfister 1992]. The right coronary artery appears to be the most vulnerable territory, with bradycardia, heart block, and hypotension occurring even after short periods of occlusion.

Most intraoperative ischemic episodes can be successfully managed with anesthesia and/or pharmacologic agents for the short periods of time necessary to construct a single bypass. However, now that multiple bypasses are being performed without CPB, concern has arisen that the consequences of ischemia can escalate or become cumulative with each additional vessel that is clamped.

Our concern about regional ischemia during beating heart coronary surgery began with observations of hypocontractility and regional myocardial cyanosis during our initial off-pump experience (circa 1983). These observations prompted us to develop an alternative strategy using a temporary intraluminal shunt (TIS) and designed to limit ischemia during the period of anastomotic construction. The device and our initial case experience have been reported previously [Rivetti 1997, Rivetti 1998]. After our experience with a large number of patients, it is clear that the shunt is beneficial and effective [Rivetti 1998]. Our group has previously reported that surgical mortality and morbidity are very low when a TIS is used in beating heart coronary bypass grafting (CABG) [Rivetti 1998].

To establish in a more quantitative manner the benefits of using a TIS, we decided to develop an experimental model to evaluate the extent of myocardial protection provided by shunting. Furthermore, we wanted to evaluate the effect of the use of a shunt on the extent of the regional ischemia that occurs after total occlusion of the target coronary artery.

MATERIALS AND METHODS

An experimental model was developed to evaluate regional myocardial ischemia during beating heart coronary bypass with and without temporary intraluminal shunting. A special electrophysiological method was used that enabled the detection of myocardial ischemia through monophasic action potential (MAP) recording [Franz 1984]. We also monitored traditional biochemical markers of cell damage, ie, serum levels of lactate dehydrogenase (LDH) and creatine phosphokinase–myocardial band (CPK-MB).

Forty male and female Landrace pigs aged 3 to 4 months and weighing 16 to 32 kg were chosen and were divided in 2 groups. In group I (no shunt), 25 animals underwent 15 minutes of snare occlusion of the left anterior descending (LAD) coronary artery proximal to the first or second diagonal branch without any form of distal perfusion (Figure 1A). In group II (shunted), 15 animals underwent intraluminal shunt placement during a brief period of snare occlusion (Figure 1B). During shunt insertion, the proximal snare was loosened and...
not reapplied afterwards. The TIS device was a single-lumen, straight-through silicone perfusion shunt originally described by Rivetti and Gandra [Rivetti 1991, Rivetti 1997].

Preinduction sedation was obtained with 0.02 mg/kg acepromazine, 0.75 mg/kg midazolam, and 0.875 mg/kg atropine administered intramuscularly. Anesthesia induction was performed with 15 mg/kg sodium pentobarbital administered intravenously. In all animals the heart was exposed through a longitudinal sternectomy while respiration was maintained with room air and a Harvard respirator through a cuffed endotracheal tube. The femoral artery was cannulated with a Statham P23 transducer (Gould Inc, Dayton, OH, USA) connected to a Beckman R8-6H polygraph (Beckman Coulter, Fullerton, CA, USA). Throughout the experiments surface electrocardiograms and blood pressure tracings were recorded (Figure 2). Before coronary occlusion, all animals intravenously received 0.07 mg/kg verapamil and 3 mg/kg of heparin. Verapamil was used to increase regional myocardial protection before the onset of ischemia [Luz 1980, Nayler 1981, Buffolo 1983].

Monophasic Action Potential Recordings

MAP recordings were obtained with a handheld contact epicardial probe placed over the distal LAD territory as described previously [Franz 1984]. Baseline action potentials were recorded before any manipulations. For group I (no shunt) animals, MAPs were recorded at 5, 10, and 15 minutes following proximal snare occlusion. For group II (shunted) animals, the probe was placed in the same territory at the same time intervals, beginning with the snare occlusion used to open the coronary and to place the shunt.

The amplitude of the MAP in millivolts was measured as the distance from the baseline to the highest point of the plateau (Figure 3). The duration of the MAP was measured at a level of 30% repolarization (ie, T30), as defined by the percentage of plateau amplitude (Figure 3). The maximum rate of voltage rise of the MAP (dV/dt max) was obtained by online electronic differentiation and was recorded in another polygraph channel (Figure 2). The area under the MAP curve, as defined by the action potential contour and the horizontal baseline, was also measured.

Biochemical Markers of Ischemia

At 5 minutes before and 15 minutes after the beginning of the experiments in both groups, blood samples were obtained for biochemical assays of the serum concentrations LDH and CPK-MB. LDH levels were assayed by the technique of Noll and Bergmeyer [Noll 1974]. CPK-MB levels were measured by the technique of Würzburg [Würzburg 1981].

Statistical Analysis

To ensure comparisons between values of MAP duration, we standardized the heart rates by the Bazett formula to a frequency of 60 beats per minute [Bazett 1920]. The significance of comparisons of maximum changes versus baseline measurements was assessed for both groups by means of the paired t test. The significance of maximum changes between the 2 groups was assessed by means of the t test. The significance of differences in the occurrence of ventricular fibrillation events between the 2 groups was assessed by means of the Fisher exact test. A difference was deemed significant at P = .05.

RESULTS

By means of the paired t test, the Table compares the characteristics of the MAP duration (T30), the MAP amplitude (Amax), the area under MAP waveforms (mv.ms), and the upstroke velocity (dV/dt) in each one of the two groups.

Group I (No Shunt) Animals

The typical response of the MAP within 5 minutes of unshunted coronary occlusion included reduced MAP duration and amplitude (Figure 4) compared with baseline values. The area under the MAP curve declined by more than 55% within 15 minutes (Figure 4), indicating reductions in both

![Figure 2. Electrophysiological recordings. BP indicates blood pressure; MAP, monophasic action potential; dV/dt, first time derivative of the MAP (MAP upstroke velocity); ECG, electrocardiogram.](image1)

![Figure 3. Monophasic action potential (MAP) record. T30 indicates duration at 30% repolarization.](image2)
action potential duration and amplitude (approximately 35.5% and 6.8%, respectively). Although the reduction in amplitude by itself was not statistically significant, we noticed important changes in the MAP area (−55%) and dV/dt (−24.5%) during the ischemia time (Figure 4). MAP waveform morphology changed from an almost rectangular to a triangular shape (Figure 5).

**Group II (Shunted) Animals**

In comparison with nonshunted animals, group II (shunted) animals showed improved preservation of action potential duration, amplitude, total MAP area, and waveform morphology following insertion of the TIS (Figure 4). MAP area actually increased by a mean of 3.1% over the 15 minutes of experimental observation (Figure 4) while the waveform maintained its normal rectangular shape (Figure 5). Although the MAP duration decreased by 33.5% in group I (no shunt) animals, it actually increased by a mean of 10.5% following the insertion of the TIS (Figure 4). The decrease in dV/dt in group I (no shunt) animals was a mean of −24.5% at 15 minutes, whereas the decrease was only −5.2% when a shunt was used (Figure 4). Similarly, the decrease in the area

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**Comparison of the Characteristics of Monophasic Action Potential Characteristics for the 2 Groups***

<table>
<thead>
<tr>
<th></th>
<th>Group I (No Shunt) (n = 25)</th>
<th></th>
<th>Group II (Shunt) (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>Mean</td>
<td>P</td>
<td>Range</td>
</tr>
<tr>
<td>T30, ms</td>
<td>97-400</td>
<td>227.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Amax, mV</td>
<td>14.6-74.1</td>
<td>34.23</td>
<td>.018</td>
</tr>
<tr>
<td>Area, mV·ms</td>
<td>2543-14,350</td>
<td>6330.59</td>
<td>.0359</td>
</tr>
<tr>
<td>dV/dt, V/s</td>
<td>1.19-5.98</td>
<td>2.79</td>
<td>.006</td>
</tr>
</tbody>
</table>

*T30 indicates monophasic action potential (MAP) duration; Amax, MAP amplitude; Area, area subtended by the MAP curve; dV/dt, MAP upstroke velocity. Statistical comparisons were made in each group by means of the paired t test.

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Figure 4. Comparison of the monophasic action potential (MAP) duration (T30), MAP amplitude (Amax), MAP area (millivolts·milliseconds), and MAP upstroke velocity (dV/dt) between shunted and nonshunted animals.

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under the MAP curves averaged –55.8% at 15 minutes in group I (no shunt), whereas it was only –4.9% in group II (shunted) animals (Figure 4).

The sensitivity of this model to ischemia is illustrated by the transient decrease in MAP area (–10%) seen within the first 5 minutes of the experiment in group II animals and with a recovery to baseline at 10 minutes (Figure 4). This result indicates that ischemia already is developing during the time it takes to open the coronary and insert a shunt (an average of 2 minutes, 14 seconds). This ischemia is followed by a recovery in MAP area once shunt flow is established. This is another observation that confirms the ability of the shunt to provide nutrient flow to the distal bed and to alleviate the ischemia caused by arterial clamping.

**Comparison of Groups I and II**

Statistical analysis did not show any significant differences between group I (no shunt) and group II (shunted) with regard to Amax or dV/dt (Figure 4). However, there were significant differences between the groups with respect to MAP duration and MAP area (Figure 4). These results indicate that area and duration are more sensitive indicators of ischemia than is either dV/dt or Amax.

**Arrhythmias**

Within a period of 3 to 15 minutes after occlusion of the LAD coronary artery, frequent premature ventricular contractions occurred in most of the animals. These observations had previously been reported in the literature [Blumgart 1941, Thal 1956, Yabuki 1959, Blair 1969, Downar 1977, Russel 1979, Janse 1981, Janse 1986, Dilly 1988, Abe 1989]. In group I (no shunt), a mean of 8.745 mg/kg of intravenous lidocaine was used compared with a mean of only 2.6 mg/kg administered in group II (shunted) (P = .001 by the t test).

The reported incidence of ventricular fibrillation during acute coronary occlusion is between 10% and 78% [Yabuki 1959, Janse 1981]. In our experiments, ventricular fibrillation occurred in 6 unshunted animals from group I at 4, 6, 7, 9, 10, 11, and 14 minutes postclamp. However, there were no episodes of ventricular fibrillation in group II (shunted) animals. The Fisher exact test demonstrated that the incidence of ventricular fibrillation was significantly different between the 2 groups (P = .046).

**Biochemical Data**

In group I (no shunt) animals, a 14-fold rise in serum LDH levels was accompanied by a 3.3% rise in CPK-MB levels during the 15 minutes of coronary occlusion (Figure 6). There was no corresponding rise in either marker for the shunted group (Figure 6). The difference in final LDH levels between the 2 groups was statistically significant by the paired t test (P = .018).

**Discussion**

OPCAB grafting is gaining momentum throughout the world as an alternative strategy to reduce morbidity, cost, and operative risk during surgical revascularization of the heart. Compared with CPB and cardioplegic arrest, the beating heart presents several unique challenges for the surgeon and anesthesiologist during graft construction. For the surgeon, motion and anastomotic bleeding create technical challenges; for the anesthesiologist, cardiac ischemia during coronary clamping in the unsupported (non-CPB) setting risks
hypotension, arrhythmias, and infarction. This physiology is further aggravated by the hypotension caused by cardiac displacement and positioning.

OPCAB appears to work primarily because the time period of ischemia is limited, and often preestablished collaterals beyond a significant proximal obstruction are feeding the region. However, the surgeon cannot gauge in any quantifiable way before the procedure the extent of the collaterals or the risk for intraoperative ischemia. This reality explains why there continue to be unpredictable episodes of ischemia during some of these cases. There is no question that the beating heart grafting procedure is an ischemic model despite the favorable conditions of deep general anesthesia and a controlled heart rate. With increasing clinical experience, more and more surgeons are facing during OPCAB the occasional episode of profound ST-segment change, ventricular dilatation, ventricular arrhythmias, bradycardia, asystole, or even intraoperative infarction.

In our initial off-pump experience, regional myocardial dysfunction and cyanosis could be observed grossly. To improve the safety and ease of beating heart cases, we developed an intraluminal shunt that has been shown to provide several advantages [Rivetti 1992, Rivetti 1997]. First, the shunt inhibits back-bleeding from the open coronary artery; this feature improves visualization and thus facilitates suturing. It reduces the need for irrigation or blower devices and thus frees up operating personnel for other tasks. Second, the shunt protects against accidental mis-suturing of the back wall or a purse-stringing of the anastomosis. Finally, removal of the shunt without resistance verifies that the anastomosis is patent without further need for investigation or confirmation.

One of the remaining controversies centers on the question of whether shunts actually do prevent ischemia. The internal diameter of these shunts is small, and thus the flow rates are in the range of only 10 to 20 mL/min.

This fact raises the parallel question of how much flow is necessary to protect the distal bed during the 15 minutes needed for unhurried, safe graft construction. At this time we have no quantitative answer but suspect that the flow rates do not need to be very high to obtain a beneficial effect. In clinical cases, we frequently observe brisk pulsatile bleeding from the open end of the shunt during insertion despite high-grade proximal coronary disease. Frequently, this ejection jet is quite impressive. TIS insertion is also followed by improved color and contractility in the myocardium, another confirmation of flow that was not present prior to shunt insertion. Acute bradycardia and hypotension during right coronary artery snaring will usually reverse with the insertion of a shunt. These clinical observations imply that the internal diameter of the TIS is sufficient to deliver flow despite proximal coronary obstruction. What has been lacking is experimental proof of the ability of the shunt to prevent ischemia.

We chose to evaluate our shunt in Landrace pigs, which have hearts similar to humans, normal coronary arteries, and few collaterals [Smith 1918, Lumb 1963, Fedor 1978, Dilly 1987]. Ischemia was investigated at the cellular level with MAPs, as described in several earlier studies [Franz 1983, Franz 1984, Franz 1986, Franz 1991, Mohabir 1991]. MAP parameters should be measured during experiments in which the heart rate remains constant within 5% variation before and during interventions [Hoffman 1954, Boyett 1978, Franz 1980, Leiner 1992]. Therefore, it was necessary to convert all measurements acquired in our experiments to a cardiac frequency of 60 beats per minute with the Bazett formula [Bazett 1920].

During myocardial ischemia there is always a decrease in the duration of the MAP [Carmeliet 1978, Lab 1978, Franz 1984, Platou 1984, Fozzard 1985, Taggart 1986, Dilly 1987, Taggart 1988a, Sutton 1989]. This decrease in MAP duration in proportion to increasing ischemic time was observed at 30%, 50%, 60%, 70%, and 90% of the repolarization level [Mohabir 1991]. We found similar results in our control animals (group I) in which a significant decrease in MAP duration occurred with longer periods of clamping (Figure 4). Franz and colleagues reported that progressive reduction of the MAP total area was a reliable index of ischemia [Franz 1986]. We also found in our control animals a significant reduction (~55%) in MAP area following 15 minutes of unprotected coronary occlusion (Figure 4). In group II, the same coronary was occluded for a short period of time (averaging 2 minutes, 14 seconds) to allow for the introduction of the TIS, after which the snare was not reapplied. We noticed transient decreases in Amax, dV/dt, and MAP area during this time, which we believe were due to ischemia that occurred during the brief cessation of blood flow necessary to open the coronary
and place the shunt. The MAP parameters normalized quickly after shunt flow was established, again confirming the effectiveness of shunting (Figure 4) [Trautwein 1956, Levites 1975, Lab 1980, Taggart 1988b]. At the completion of 15 minutes with the shunt in place, all MAP characteristics were restored, including duration and morphology. In fact, MAP duration actually increased during the shunted period (Figure 4). This observation has also been reported previously in the literature [Trautwein 1956, Levites 1975, Taggart 1988b].

Multiple investigators have reported that off-pump CABG is beneficial to patients and results in reduced perioperative morbidity and mortality compared with traditional methods that use CPB [Benetti 1984, Buffolo 1986]. According to some authors, unprotected occlusion of the coronary artery during anastomotic construction does not increase morbidity [Buffolo 1990, Benetti 1991]. These workers did not report significant elevations in myocardial enzyme levels during occlusion of the coronary artery or in the postoperative period [Benetti 1985, Buffolo 1985]. However, our group has observed changes in regional wall motion, color, and arrhythmias with unprotected coronary artery clamping.

Our laboratory model has shown that despite the small diameter of the TIS there is a measurable protective effect that reduces or eliminates regional myocardial ischemia during OPCAB. In the normothermic beating heart, action potential alterations typical of ischemia develop very quickly after coronary occlusion and reverse to normal after shunt insertion. The presence of ventricular irritability and fibrillation is eliminated by the use of a shunt in this animal model. The requirement for lidocaine was cut by two thirds in the shunted animals, and ventricular fibrillation occurred only in the nonshunted group. Finally, enzyme markers of myocardial injury were elevated only in the nonshunted group.

Some surgeons propose that shunts reduce ischemia simply by preventing the back-bleeding that would otherwise create a form of “steal” syndrome from the open coronary via the draining away of the collateral supply. However, the results with our model disagree with this explanation. In group I, the coronary was never opened, so the ischemic effects we observed in the MAP could not have been due to uncontrolled back-bleeding.

**Study Limitations**

One of the drawbacks of this animal model is the relatively normal (unobstructed) coronary arteries typical of the porcine heart. We accept that this model is not an exact replica of the clinical situation in which the distal bed is often protected by collaterals that permeate into areas of chronic ischemia. However, because there are not likely to be any collaterals in the normal porcine model, we believe that this model in some ways provides a better means of defining whether ischemia can be prevented solely by passive flow through the shunt. What we cannot comment on, either in this model or in clinical cases, is how the presence of a proximal coronary artery stenosis affects the efficiency of the TIS in clinical cases. However, it is our observation that there is often quite an impressive flow from the open end of the shunt, implying that the TIS does deliver sufficient pressure and flow distally.

**CONCLUSIONS**

These experimental results validate our clinical observations and reinforce our conviction that using an intraluminal shunt results in less myocardial ischemia than the unprotected beating heart technique. We believe that these beneficial effects on ischemia, along with the technical enhancements offered by the TIS (bloodless field, anastomotic confirmation, and so forth), indicate that shunting is a low cost and powerful adjunct to the performance of OPCAB grafting that can further reduce the morbidity of this procedure. If ischemia during OPCAB could be avoided altogether, an unhurried, high-quality, and reliable anastomosis can be performed with the same security and low risk provided by CPB and cardioplegia.

**REFERENCES**


