Regional myocardial function during contiguous ischaemia in an anaesthetized canine model: comparison of six methods of measurement†

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Summary
During acute myocardial ischaemia, the function of the unaffected muscle is the primary determinant of residual cardiac performance. We compared six methods of measuring regional function in the remaining non-ischaemic segment after acute ligation of the left anterior descending (LAD) coronary artery in 16 dogs. Preparation included left ventricular micromanometers, regional sonomicrometer transducers to measure segment length and wall thickness, caval occluders and left atrial catheters for injection of radioactive microspheres to measure regional blood flow. Pulmonary artery, central venous and systemic arterial pressures were measured and regional coronary venous blood was collected for direct myocardial oxygen consumption (VO₂) calculations. Under basal high-dose fentanyl–neuromuscular blocker anaesthesia, the LAD was occluded after addition of halothane or isoflurane at 0.5 or 1.5 MAC concentrations. Regional myocardial function of the non-ischaemic segment was assessed by the following computer-derived indices: percent systolic wall thickening (% WT), velocity of shortening (vₖ), percent systolic shortening (% SS), regional stroke work (RSW), regional preload recruitable stroke work (RPRSW) and regional end-systolic elastance (Ees). No index demonstrated enhanced function in the non-ischaemic segment after LAD ligation and all monitors, except Ees, were sensitive to depression of function represented by a decrease in values after administration of halothane and isoflurane (P < 0.05). Ees values increased with the addition of isoflurane and remained constant with halothane. Circulating concentrations of catecholamines were unchanged after ischaemia, while inhalation agents caused a decrease in the concentrations of adrenaline and dopamine (P < 0.05), but not noradrenaline. Overall, % WT, obtained without complex derivations, monitored regional function well, correlated most closely with load-independent RPRSW and portrayed the lack of augmented function in the normal segment. Ees appeared inconsistent, and consequently unreliable, as an index of regional function. (Br. J. Anaesth. 1994; 73: 371–379)

Key words

After acute myocardial ischaemia, the remaining non-ischaemic myocardium must assume added pumping activity to avoid a decrease in function. Several studies have examined the effect of regional ischaemia on the remaining normally perfused muscle with conflicting results. Preparations with strain gauge measurements demonstrated either augmented function [1] or mild depression [2]; wall thickness indicators of myocardial function varied also when adjacent muscle was made ischaemic [3–5]. Ultrasonic transit-time investigations have shown that, when augmentation of function occurred, it was primarily in the isovolumic phase of contraction and was load dependent [6, 7]. However, ejection phase monitors revealed some increased function [8], particularly in the area adjacent to the ischaemia [9].

Proposed mechanisms for compensation of function in the normal myocardium include the Frank–Starling mechanism and regional intraventricular unloading of the non-ischaemic zone into the area of ischaemia [10]. The amount of compensation appears to be most evident in the region adjacent to the ischaemic zone [11], while distant normal regions have less pronounced changes [9]. Although the primary compensatory mechanisms explaining this increase in normal regional function involve activation of mechanical (unloading) or intrinsic (Frank–Starling) factors, the role of hormonal factors such as circulating catecholamines is unknown.

The predominant methods of measuring regional muscle function in previous studies have included observing changes in myocardial segment length of wall thickness using miniature piezoelectric crystals, the output of epicardial strain gauges and echocardiographic studies. The piezoelectric crystal technique with continuous measurement of changes in segment length seems to provide the most quantitative data and has been used in more recent studies [11].

With most investigations, the anaesthetic agents used have been pentobarbitone or chloralose–urethane, which may have profound effects on...
myocardial function [12, 13] and confuse conclusions on the contractile performance of the normal myocardium during ischaemia.

The purpose of this study was to answer, in a dog model of ischaemia, the following questions. (1) With an opioid anaesthetic (similar to that used in patients with coronary disease), does the remaining normal myocardium compensate during acute regional ischaemia? (2) Is there a difference in the response of the compensating normal myocardium between halothane and isoflurane anaesthesia? (3) What measurement in the normal myocardium is the best assessment of changes in regional performance? (4) Does a change in circulating catecholamines explain any difference in regional myocardial function after adjacent ischaemia?

Materials and methods

Our study was approved by the Institutional Committee for Animal Use and Care at the University of California, Davis, and all experiments were carried out according to the NIH guidelines for use of laboratory animals.

We studied 16 mongrel dogs of both sexes, weighing mean 22.9 (SEM 0.7) kg. The animals were anaesthetized with i.v. fentanyl 100 μg kg⁻¹ priming dose and an infusion of 1–2 μg kg⁻¹ min⁻¹, nitrous oxide in oxygen and the neuromuscular blocker dimethylurea 0.4 mg kg⁻¹, repeated when necessary. Respiration was controlled by a Harvard animal respirator and minute ventilation and oxygen concentration were adjusted to maintain normal carbon dioxide and oxygen partial pressures in arterial blood-gas samples. A lactated Ringer's solution was infused at 5 mg kg⁻¹ h⁻¹ as a baseline infusion throughout the experiment, with bolus increases when decreases in left atrial pressure occurred.

Semi-rigid catheters were placed into the thoracic aorta via the femoral artery for microsphere reference sampling and via the left carotid artery for measurement of supravalvular aortic pressure. A pulmonary artery flow-directed catheter was inserted via the external jugular vein for measurement of cardiac output by the thermodilution technique, using cold saline and an Edwards computer (Model 9520A, Santa Ana, CA, USA); all cardiac output values were the mean of triplicate measurements.

Under aseptic surgical conditions, a left thoracotomy was performed at the fifth intercostal space. A soft silastic tube catheter was positioned in the left atrium for injection of radioactive microspheres and for measurement of left atrial pressure. Inflatable hydraulic occluders were placed around both venae cavae. Through a stab wound in the apex of the left ventricle a micromanometer (Konigsberg Model P7, Pasadena, CA, USA) was inserted for measurement of left ventricular pressure and secured with a purse-string suture. The left ventricular micromanometer was calibrated in vitro before insertion into the heart and during the experiment was periodically re-calibrated using left atrial pressure as a correlate of left ventricular end-diastolic pressure (LVEDP) and aortic systolic pressure for left ventricular systolic pressure. A pulsed Doppler flow transducer was placed around the left anterior descending coronary artery (LAD) just distal to the first diagonal branch and a ligature snare was placed loosely around the same artery just proximal to the second diagonal branch. Regional segmental length and wall thickness were measured with a Triton sonomicrometer (Model 120, San Diego, CA, USA). Ultrasonic crystals were implanted in pairs into the endocardium approximately 12–17 mm apart in the area supplied by the anterior circumflex artery at least 3 cm from the area supplied by the left circumflex artery at least 3 cm from the area supplied by the left ventricle (L.V) supplied by the LAD. The crystals were placed just distal to the first marginal branch of anterior circumflex artery and just below the artery itself. Crystals were positioned topographically for maximum shortening during systole. Wall thickness transducers were placed in the subendocardium and epicardium near the segmental length crystals. Proper alignment was confirmed with a Tektronix oscilloscope (Model RM647, Beaverton, OR, USA). After anticoagulation with heparin 5000 UI, a small concomitant epicardial vein on the LV surface in the region of a small tributary of the circumflex artery was cannulated to allow coronary venous blood measurements. Free drainage of the catheter was allowed against a back pressure of 3 cm H₂O to mimic normal distal venous pressure and blood was collected anaerobically before analysis. Figure 1 illustrates the preparation.

Core body temperature was maintained at 37–38.5 °C with a heating pad and radiant energy. All haemodynamic data were recorded on a direct writing polygraph (Gould, Model 2800S, Cleveland, OH, USA) and an analogue frequency-modulation tape recorder (Kyowa Electronic Instruments, Tokyo, Japan) for subsequent analysis. A mass spectrometer (Allegheny International Medical Technology, St Louis, MO, USA) was used to...
examine end-tidal blood-gas concentrations throughout the experiment.

**PHYSIOLOGICAL VARIABLES**

Mean arterial pressure, stroke volume, pulmonary vascular resistance and systemic vascular resistance (SVR) were calculated using standard formulae. Regional blood flow in the heart was measured with radioactive microspheres as described previously [14]. Briefly, approximately 2–3 × 10^6 microspheres (15 μm) labelled with either 99Nb, 85Ce, 141Ce or 89Sr were injected into the left atrium over 20 s. A reference blood sample was obtained from the aortic catheter beginning 15 s before injection of microspheres and continuing for 2 min at a constant rate of 7.75 ml min⁻¹. The order of isotopes was randomized and, after the experiment was completed, the animal was killed. The sampled heart was removed, sectioned, weighed and counted for radioactivity. Regional blood flow was calculated from the ratio of the radioactive count of the measured sample over that of the reference blood sample. The ischaemic region of the left ventricle produced during the experiment by ligation of the LAD was identified at the time of death by intracoronary injection of methylene blue through an arteriotomy distal to the site of ligation. Two samples were obtained from the unstained LV myocardium at least 3 cm from the stained area and the blood flow values obtained for each sample were averaged for normal LV flow values. Placement of the segment length and wall thickness crystals was verified at death, particularly their distance from the ischaemic zone and position in the endocardium.

Coronary venous and arterial blood samples were used to estimate the blood oxygen content (IL CoOximeter 282, Lexington, MA, USA) which was used in the calculation of regional myocardial oxygen consumption. Regional myocardial oxygen consumption was determined by the arterial–venous oxygen content difference multiplied by regional myocardial blood flow. In six of eight dogs in each group complete data were obtained for venous oxygen content values. In two animals in each group coronary catheter occlusion or inadequate sampling precluded further analysis.

Circulating noradrenaline, adrenaline and dopamine concentrations were derived from central venous blood using standard HPLC technology with the aid of an electrochemical detector [15].

After instrumentation, nitrous oxide was replaced by an oxygen–air mix to maintain arterial oxygen saturation greater than 100 mm Hg. The lungs were hyperinflated to reduce atelectasis and the thoracotomy closed loosely. Fentanyl was continued at a rate of 1–2 mg kg⁻¹ min⁻¹ and 1 h elapsed before baseline measurements were made.

Baseline measurements included phasic arterial and venous pressures, left ventricular pressure including dP/dtLV, triplicate cardiac output measurements by thermal dilution and left atrial and phasic pulmonary artery pressures, recorded during apnoea. Wall thickness and segmental length variables were recorded continuously throughout the measurement period. Immediately thereafter, both venae cavae were occluded to reduce inflow for measuring LV regional end-systolic elastance and preload recruitable stroke work.

After baseline measurements were obtained, the LAD occlusive snare was closed to the point of ablation of flow in the LAD transducer and, after 30 min of stabilization, post-occlusion haemodynamic blood flow and metabolic indices were obtained. At this point, the initial left atrial injection of microspheres was made. All measurements were performed during stable conditions with the animal in sinus rhythm.

After the post-ischaemic stabilization period, the dogs were allocated randomly to receive either halothane or isoflurane anaesthesia at either low to high or low to high sequential concentrations. Thirty minutes was allowed for equilibration at each anaesthetic concentration. Both the low (0.4% halothane and 0.6% isoflurane, approximately 0.5 MAC) and high (1.2% halothane, 1.8% isoflurane, approximately 1.5 MAC) alveolar concentrations were equipotent. The sequence of low or high anaesthetic concentration was randomized to allow for the effects of time on the preparation. Eight dogs were included in each anaesthetic group.

At each measurement time, data were obtained for the following calculations: (1) regional myocardial end-systolic elastance (Ees) using the normal region segmental length and ventricular pressure [16], (2) maximum velocity of systolic shortening (vₛ) of the normal segment [17], (3) percent systolic shortening (% SS) of the segment where the end of systole was considered 20 ms before maximum negative dP/dtLV [2, 18], (4) regional stroke work (RSW) measured from the pressure–length loop (i.e. total area described by the pressure–length relationship) [16], (5) regional preload recruitable stroke work (RPRSW) calculated from the relationship between end-diastolic segment length and stroke work [19], and (6) percent systolic thickening (% WT) from the wall thickness transducer in the normal myocardium using the same systolic end-point as % SS [20]. All calculations were made using the Asyst language on a 386-based computer. For measurement of Ees and RPRSW, the calculations were derived from the first five or six beats observed during the decrease in LVP after inflow occlusion, in order to precede any effect of reflex augmentation of cardiac function. Both RPRSW and RSW pressure–length loops were analysed for calculation of the percent isovolumic shortening, systolic lengthening and post-systolic shortening components of the loops during each event [21].

Data were transferred from FM tape to disk storage at 200 Hz via a multichannel analogue to digital converter for future analysis. An example of the RPRSW derivation is shown in figure 2 and the Ees calculation in figure 3. For the purpose of comparison, RPRSW was considered the "gold standard" of regional performance indices. The other regional variables were compared with RPRSW over the same heart beats by correlation coefficients.

Central venous blood samples were obtained for
Figure 2 An example of the derivation of regional preload recruitable stroke work (RPRSW) during low-dose halothane inhalation. The area defined by the integral of LVP times segmental length (segmental stroke work (SW)) is plotted beat-to-beat vs end-diastolic segmental length during inflow occlusion. The slope of the comparison (49.8) describes RPRSW for that contractile state. Increased slope denotes an enhanced contractile state while a decreased slope identifies a depressed myocardium. The mean r value for all individual RPRSW slope measurements was 0.93 (0.01).

Figure 3 An example of the derivation of regional end-systolic elastance (Ees) during control conditions. Beat-to-beat end-systolic segmental length is plotted vs concurrent left ventricular pressure (LVP) during inflow occlusion. The slope of the resultants line (59.3) defines regional Ees for that contractile state. Changes in slope reflect changes in contractility similar to RPRSW. The mean r value for all individual Ees measurements was 0.89 (0.08).

indices of regional myocardial performance. All values are expressed as mean (SEM).

Results

There were no differences in haemodynamic data between the halothane and isoflurane groups at control or during ischaemia, except in ventricular transmural blood flow (table 1). At low concentrations of isoflurane there was a statistically significant increase in flow while high-dose halothane significantly reduced flow. At high concentrations of both agents there was a significant decrease in oxygen consumption in the normal myocardial region (P < 0.05). Heart rate increased with both agents while

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Mean (SEM) haemodynamic data in dogs anaesthetized with high-dose fentanyl and subjected to regional myocardial ischaemia and subsequent graded doses (low and high) of halothane or isoflurane. Significant differences (P &lt; 0.05): *compared with control; †compared with no agent; ‡halothane vs isoflurane</th>
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<tr>
<td>Ischaemia</td>
<td>Control</td>
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<tr>
<td>Cardiac output (litre min⁻¹)</td>
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<td>Halothane</td>
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<tr>
<td>Isoflurane</td>
<td>2.57 (0.15)</td>
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<td>MAP (mm Hg)</td>
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<tr>
<td>Halothane</td>
<td>95.4 (4.0)</td>
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<tr>
<td>Isoflurane</td>
<td>95.2 (3.4)</td>
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<tr>
<td>Heart rate (beat min⁻¹)</td>
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<tr>
<td>Halothane</td>
<td>69 (4)</td>
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<tr>
<td>Isoflurane</td>
<td>77 (8)</td>
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<td>LVEDP (mm Hg)</td>
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<td>7.9 (0.4)</td>
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<tr>
<td>Isoflurane</td>
<td>5.6 (1.2)</td>
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<td>SVR (dyn s cm⁻⁵)</td>
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<tr>
<td>Halothane</td>
<td>3009 (207)</td>
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<tr>
<td>Isoflurane</td>
<td>2906 (168)</td>
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<td>Myocardial LV transmural blood flow (ml min⁻¹/100 g)</td>
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<tr>
<td>Halothane</td>
<td>93.3 (7.5)</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>97.1 (5.0)</td>
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<td>Myocardial LV PO₂ (ml min⁻¹/100 g)</td>
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<tr>
<td>Halothane</td>
<td>9.65 (0.51)</td>
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<tr>
<td>Isoflurane</td>
<td>10.01 (0.95)</td>
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</tbody>
</table>

measurement of catecholamine concentrations at each stage.

STATISTICAL ANALYSIS

Data were analysed by comparison within each group at each stage and between each group using a three-factor analysis of variance with repeated measures [22]. The Newman–Keul test was used to determine significant differences between pairs of mean values within a group and between agents, with a significance level at 0.05. Linear regression analysis was used to determine the correlation coefficients between RPRSW and the other five indices of regional myocardial performance. All values are expressed as mean (SEM).
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Table 2: Pre-ischaemic control values (mean (SEM)) of regional contractility in the normal regional myocardium. % WT = Percent systolic thickening of the ventricular wall; \( v_s \) = velocity of systolic shortening; % SS = percent systolic shortening; SW = stroke work; RPRSW = regional preload recruitable stroke work; \( E_{es} \) = end-systolic elastance

<table>
<thead>
<tr>
<th></th>
<th>Halothane</th>
<th>Isoflurane</th>
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<tbody>
<tr>
<td>% WT</td>
<td>13.8 (2.2)</td>
<td>15.6 (2.4)</td>
</tr>
<tr>
<td>( v_s ) (mm s(^{-1}))</td>
<td>13.0 (1.5)</td>
<td>14.3 (2.1)</td>
</tr>
<tr>
<td>% SS</td>
<td>12.2 (1.0)</td>
<td>10.9 (1.2)</td>
</tr>
<tr>
<td>SW (mm Hg mm(^{-1}))</td>
<td>157 (20)</td>
<td>162 (39)</td>
</tr>
<tr>
<td>RPRSW (erg cm(^{-2}) x 10(^{2}) mm(^{-1}))</td>
<td>89 (7)</td>
<td>92 (8)</td>
</tr>
<tr>
<td>( E_{es} ) (mm Hg mm(^{-1}))</td>
<td>38.6 (9.1)</td>
<td>45.2 (5.8)</td>
</tr>
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Figure 4: Percent systolic wall thickening (%WT), velocity of shortening (\( v_s \)) and percent systolic shortening (%SS) as percentage of pre-ischaemic control values. Data are mean (SEM) of each monitor for the original control calculation obtained during high-dose fentanyl anaesthesia and before ligation of the LAD coronary artery. No agent indicates high-dose fentanyl anaesthesia after ligation of the LAD artery, but before administration of halothane (\( \square \)) or isoflurane (\( \bullet \)). Low agent and high agent represent 0.5 MAC and 1.5 MAC of the anaesthetics, respectively. *P < 0.05 compared with control value.

Figure 5: Regional stroke work (RSW), regional preload recruitable stroke work (RPRSW) and end-systolic elastance (\( E_{es} \)) as percentage of pre-ischaemic control values. Conditions as in figure 4.

arterial pressure decreased. Similarly, LVEDP decreased significantly with both anaesthetics and SVR was reduced by high-dose isoflurane. Throughout the study core body temperature remained within 0.5 °C of control for all dogs and there were no significant changes in \( P_{aco_2} \) (approximately 5.3 kPa) or \( P_{ao_2} \) (approximately 16 kPa) throughout the study. Part of these data have been presented elsewhere in another context [23].

The baseline control values for the six regional performance variables calculated before LAD ischaemia are presented in Table 2. After the onset of ischaemia, the addition of the anaesthetic agents caused a reduction in % WT, \( v_s \), and % SS which were significant with the high doses in all dogs (fig. 4). Similarly, RSW and RPRSW declined with increasing concentration of anaesthetic agents although significance was reached for RSW at the low in addition to the high concentration (fig. 5). In contrast, regional \( E_{es} \) increased significantly with low-dose isoflurane and remained statistically unchanged during the other interventions. The mean correlation coefficients for the slopes of all calculated regional \( E_{es} \) and RPRSW values were 0.89 (0.08) and 0.93 (0.01), respectively.

There were two distinct variations in the early systolic portion of the pressure–dimension area curves. In 36% of the total events for all dogs, there was a predominance of early systolic lengthening and in 54% of the events, isovolumic shortening predominated. The overall percentage of the isovolumic portion of systolic shortening increased minimally from 8.5 (4.2)% at control to 9.3 (5.3)% during ischaemia for all dogs. With the addition of halothane and isoflurane, the percentage increased to 18.3 (4.7)% . There was no difference between the two groups. The percentages of the total pressure–dimension area that represented early systolic lengthening were 3.3 (2.0)% , 8.1 (3.7)% and 16.4 (4.6)% for control, ischaemia and anaesthetic agents, respectively. Similarly, the percentage of area derived during post-systolic shortening increased from...
control, ischaemia and anaesthetic administration.

2.7 (1.9)% to 13.5 (5.3)% to 18.7 (5.4)% during adjacent ischaemic insult, we found no evidence of agressive decrease in adrenaline and dopamine concentrations with the addition of graded doses (low and high) of halothane or isoflurane. *P < 0.05 compared with control value

In all dogs there was no difference between halothane and isoflurane, but statistical significance was attained when comparing the anaesthetic agents with control values in the pre-ejection systolic area and post-systolic shortening calculations.

Discussion

With all methods of measuring the response of the normal left ventricular myocardium to a sudden adjacent ischaemic insult, we found no evidence of a compensatory increase in function in that remaining normal myocardium. These data are in conflict with the results of Gallagher and colleagues [24] and Noma and colleagues [6], but are supported by the work of others [17, 25-27] in which remote normal area function was not augmented during regional ischaemia. The same lack of augmentation has been noted in the right ventricle [28]. This may be explained partly by "free radicals" released by ischaemia contributing to myocardial damage in the seemingly normal region [29], but another explanation is in the selection of, and amount of, the coronary artery bed made ischaemic.

It is now well known that the portion of the left ventricle perfused by the LAD is considerably more muscular than that perfused by the anterior circumflex artery [18] and wall motion studies have shown an attenuated response to pharmacological intervention in the basal segments compared with the apex [30]. Consequently, occlusion of the LAD produces less compensatory augmented function in the intact anterior circumflex artery bed compared with the increased thickening observed in the LAD bed during occlusion of the anterior circumflex artery [31]. The mechanism by which compensatory augmented function occurs is controversial and may involve regional adaptation of the Frank-Starling mechanism [10] or a combination of regional architectural differences and wall geometry [31]. Our animals were made ischaemic only in the distal LAD bed, so it is not surprising that there was no evidence of compensatory augmented performance in the non-ischaemic zones.

In a series of canine experiments, Noma and colleagues demonstrated progressive lessening of augmented function in the non-ischaemic zone of myocardium as the ischaemic area was reduced in size [6]. Similar findings have been observed by others with the proposition that a greater ischaemic segment size causes larger LV dysfunction to the point that the resultant increase in LVEDP increases non-ischaemic segment function by the Frank-Starling mechanism [7]. This argument may help to explain the lack of augmentation of function in the normal myocardium of our dogs as the LAD ligation was quite distal (at the second diagonal branch) and may have disrupted global ventricular function less than in studies where compensatory augmented function was evident. Indeed, LVEDP in our dogs was unchanged by coronary ligation.

This view is supported by the work of Kim and colleagues in which the LAD artery was ligated high above the marginal branches, rendering the majority of the anterior LV wall ischaemic [32]. There was augmented regional function in the remaining non-ischaemic muscle, particularly with fentanyl anaesthesia, but with a concomitant increase in LVEDP of 73%.

All our measurements of regional performance in the normal myocardium were made at least 2 cm from the lateral border of the ischaemic zone. Gallagher and co-workers [5] demonstrated a progressive reversal of functional impairment across the lateral border of the ischaemic zone. They proposed that measurements greater than 1 cm from the ischaemic border did not suffer depression of
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Regional performance. Our transducers were definitely beyond this threshold distance. The percentage isovolumic shortening observed in our dogs during control states was somewhat lower than those reported in the anterior circumflex artery distribution by Ohtsuka and colleagues (33%) [8] and Noma and colleagues (22%) [6], but was certainly greater than the 1.5% described in the LAD distribution [7]. The reported effect of distant ischaemia on percentage isovolumic shortening in the non-ischaemic myocardium is variable [6-8]. The increase in isovolumic percentage systolic shortening in our animals caused by the addition of volatile agents was consistent, but not significant, and contributed to no more than 20% of the total shortening. In addition, we observed no significant increase in systolic lengthening or post-systolic shortening in the normally perfused myocardium of our animals during the transition from control to ischaemia. The control and ischaemic values in our study were somewhat greater than those reported by Safwat and co-workers [33], but their animals were studied in the LAD bed which is known to differ from the circumflex artery bed in control measurements [18] and with chemical intervention [30]. Overall, placement of the sonomicrometer transducers in the normal myocardium was not a major factor in the failure to delineate augmented function in our animals.

Additionally, measurements that most clearly demonstrate augmented function in the normal myocardium are indices of isovolumic rather than ejection phase variables [8], particularly during induced anterior circumflex artery ischaemia [34]. All of our six regional function variables depended, to a great extent, on ejection phase calculations, particularly % SS. Certainly, this aspect may have attenuated the sensitivity of our preparation to changes in regional function in the remaining normal myocardium.

The basal anaesthetic used for an experiment may influence the regional ventricular response to myocardial segment ischaemia. Studies in which pento-barbitone was the basal anaesthetic reported a uniform increase in “normal” segment function of the ventricle during contiguous ischaemia [6-10]. Similarly, animals anaesthetized with halothane exhibited augmented function in the non-ischaemic myocardium with a concurrent adjacent ischaemic segment [5, 24, 34]. When chloralose or urethane, or both, were administered under the same circumstances, augmented function was evident in some investigations [31, 35] but not in others [2, 25]. It is apparent that the type of anaesthesia used may have an effect on the results. In fact, when chronically instrumented conscious animals were studied, there was little support for acute augmented function in the non-ischaemic segment of the myocardium [26, 34]. High-dose fentanyl anaesthesia causes little cardiovascular disturbance [36, 37] and is an effective anaesthetic in the dog [38]. Possibly our opioid anaesthetic technique allowed a closer physiological approximation to the awake state.

We attempted to assess which of our six methods were specific in assessing myocardial depression and sensitive to the dose-effect response caused by the two concentrations of inhalation anaesthetics. % WT, % SS, RSW and RPRSW demonstrated both of these attributes. By these criteria, regional Ees was a poor assessment of regional myocardial function during adjacent muscle ischaemia. It lacked specificity to changes in regional myocardial depression and remained insensitive to deepening or lightening of the volatile agent. Through the progression of our study from “no agent” to “high agent”, there were decreases in myocardial VO₂ (table 1) and catecholamine concentrations (table 4) which clearly do not support improved function in the normal segment displayed by regional Ees during exposure to anaesthetic. Certainly global Ees is currently accepted for measurement of overall left ventricular contractility under normal conditions [39], but has been shown to lack linearity at loading extremes [40]. When examined previously as a monitor of regional function, it was inconsistent in identifying marked depression of the regional contractile state [41, 42], a situation similar to the lack of sensitivity of regional Ees in our study.

Conversely, RSW appeared markedly sensitive during myocardial depression (a nearly 80% reduction in stroke work during 1.5 MAC of halothane). With preload compensation, RPRSW attenuated this exaggerated response and demonstrated 60% depression of myocardial performance in the normal myocardium during high-dose halothane. RSW is highly preload dependent; yet by normalizing preload with RPRSW [19] the exaggerated response to the inhalation agents was reduced. Indeed, the degree of depression of RPRSW produced by halothane and isoflurane in our dogs was similar to that reported previously by Pagel and colleagues [43].

Among the measurements investigated, % WT, % SS and RPRSW appeared grossly similar for accuracy and sensitivity, as observed in figures 4 and 5. However, when compared with RPRSW as a standard index, % WT was a closer correlate than the other variables and would seem to be superior in accuracy when assessing regional performance (table 3). A measurement as simple to obtain as % WT makes it singularly attractive as a monitor of regional myocardial function. Indeed, it has been used as an index of regional contractility in invasive animal preparations in many investigations [34, 44-47] and has recently been measured accurately from a single epicardial transducer [48]. Using echocardiography [49, 50], MRI [51] and gated perfusion scanning [52], % WT has been established also as a non-invasive monitor of regional ventricular function in humans.

The baseline serum concentrations of adrenaline, noradrenaline and dopamine in our animals were comparable with those reported in human studies [53, 54] and in reference analysis [Waters Application Brief M3500.12]. Both dopamine and adrenaline concentrations decreased stepwise and significantly with increasing anaesthetic concentration; however, there was no difference in the catecholamine response between the two anaesthetics with increasing concentrations. This observation is
in conflict with human studies by Bernard and colleagues who reported increasing adrenaline and noradrenaline concentrations in patients receiving isoflurane, but not in those receiving enflurane [53]. On the other hand, Crozier and colleagues demonstrated a progressive decrease in plasma adrenaline concentration in patients anaesthetized with either isoflurane or halothane, although the response was exaggerated with halothane [54]. Interestingly, they observed only a small decrease in noradrenaline with increases in both anaesthetic concentrations. This small decrease failed to reach statistical significance in their study; a similar stability of circulating noradrenaline was present in our investigation. The increase observed by Bernard and colleagues may have been induced by surgical stimulation.

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