Laboratory Investigations

Choice of anaesthetic regimen influences haemodynamic response to cemented arthroplasty

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Haemodynamic changes during bilateral cemented arthroplasty (BCA) were compared in dogs anaesthetized with isoflurane/ N_2O (ISOF) or diazepam/fentanyl ($100 \mu\text{g} \cdot \text{kg}^{-1}$)/ N_2O (FENT). Eight animals were anaesthetized with each regimen. After establishing monitoring and recording baseline values, BCA was performed. Haemodynamic measurements included aortic blood pressure (ABP), pulmonary artery pressure (PAP), right and left atrial pressures, and cardiac output. These were recorded at 30, 60, 180 and 300 sec after BCA. Lungs were removed and examined postmortem using quantitative morphometry. Groups demonstrated similar increases in PAP (ISOF 15 ± 2 to 32 ± 7 , FENT 19 ± 4 to 38 ± 13 ; $P > 0.05$ between groups, $P < 0.05$ vs baseline). The proportion

of lung vasculature occluded by fat was not different between groups (ISOF $9.63 \pm 3.38\%$, FENT $8.85 \pm 2.20\%$). Stroke volume decreased similarly in both groups ($P > 0.05$ between groups, $P < 0.05$ vs baseline). However, ABP decreased within one minute of BCA in ISOF (111 ± 17 to 55 ± 27 mmHg, $P < 0.05$) and two of eight dogs died. All FENT dogs survived and hypotension (118 ± 20 to 102 ± 24 mmHg) was transient and less severe ($P < 0.05$ vs ISOF). Increased heart rate (HR) was noted in FENT following BCA (73 ± 8 to 108 ± 25 beats $\cdot \text{min}^{-1}$; $P < 0.05$). Baseline HR was higher in ISOF ($P < 0.05$) and no increase in HR was noted. Systemic vascular resistance decreased in ISOF ($P < 0.05$), but not FENT ($P > 0.05$ vs baseline, $P < 0.05$ vs ISOF). To assess the role of slower baseline HR in FENT (73 ± 8) versus ISOF (131 ± 5), six FENT dogs were paced (130 beats $\cdot \text{min}^{-1}$) with epicardial leads and an AV sequential pulse generator to simulate the ISOF group's baseline HR. Haemodynamic stability was maintained in this group in spite of a more rapid baseline HR. The choice of anaesthetic regimen strongly influenced acute haemodynamic changes in response to BCA.

Key words

ANAESTHESIA, INHALATIONAL: isoflurane;
ANAESTHESIA, INTRAVENOUS: fentanyl;
SURGERY: orthopaedic, cemented arthroplasty;
COMPLICATIONS: hypotension, fat embolism.

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Les changements hémodynamiques survenant pendant une arthroplastie bilatérale cimentée (ABC) sont comparés chez des chiens anesthésiés avec isoflurane/ N_2O (ISOF) et diazepam/fentanyl ($100 \mu\text{g} \cdot \text{kg}^{-1}$)/ N_2O (FENT). Les groupes sont formés de huit animaux chacun. Après avoir établi les valeurs initiales pour le monitoring et l'enregistrement, l'ABC est réalisée. Les mesures hémodynamiques comportent la pression sanguine aortique (PSA), la pression artérielle pulmonaire (PAP), les pressions des oreillettes droite et gauche, et le débit cardiaque. Ces mesures sont enregistrées 30, 60, 180, et 300 sec après l'ABC. Les poumons sont prélevés postmortem et examinés sous morphométrie quantitative. Les groupes ont présentés des augmentations identiques de PAP (ISOF 15 ± 2 à 32 ± 7 , FENT 19 ± 4 à 38 ± 13 , $P > 0,05$ entre les groupes, $P < 0,05$

vs valeur initiale). La proportion de la vasculature pulmonaire obstruée par la graisse n'est pas différente entre les groupes (ISOF $9,63 \pm 3,38\%$, FENT $8,85 \pm 2,20\%$). Le volume systolique diminue uniformément entre les groupes ($P > 0,05$ entre les groupes, $P < 0,05$ vs valeur initiale). Cependant, la PSAA diminue en moins d'une minute après l'ABC dans le groupe ISOF (111 ± 17 à 55 ± 27 mmHg, $P < 0,05$) et deux des huit chiens décèdent. Tous les chiens FENT survivent et l'hypotension (118 ± 20 à 102 ± 24 mmHg) est transitoire et moins importante ($P < 0,05$ vs ISOF). La fréquence cardiaque augmente dans le groupe FENT après l'ABC (73 ± 8 à 108 ± 25 $b \cdot \min^{-1}$; $P < 0,05$). La valeur initiale de la Fc est plus élevée pour ISOF ($P < 0,05$) et on ne constate pas d'augmentation de la Fc. La résistance vasculaire systémique diminue dans le groupe ISOF ($P < 0,05$) mais pas dans le FENT ($P > 0,05$ vs valeur initiale, $P < 0,05$ vs ISOF). Dans le but d'évaluer la contribution de la valeur initiale plus basse de Fc dans le groupe FENT (73 ± 8) vs ISOF (131 ± 5), six chiens FENT ont été électroentraînés (130 $b \cdot \min^{-1}$) avec des électrodes épicaudales et un générateur de pouls AV séquentiel pour simuler la Fc initiale de groupe ISOF. La stabilité hémodynamique de ce groupe est maintenue malgré une Fc initiale plus rapide. Le choix de l'agent anesthésique influence fortement les changements hémodynamiques aigus en réponse à l'ABC.

General anaesthetics alter baseline haemodynamic status and responses to painful stimuli.¹⁻⁵ Understanding the factors which contribute to haemodynamic stability during stressful intraoperative events may promote better outcomes.⁶ The influence of anaesthesia on haemodynamic responses to events associated with systemic hypertension, such as skin incision, tracheal intubation, and aortic manipulation has been reported.¹⁻⁵ We studied the effects of two anaesthetic regimens on haemodynamic changes during cemented arthroplasty associated with pulmonary hypertension and systemic hypotension.

Severe hypotension or cardiac arrest during cemented arthroplasty is rare.⁷ However, transient hypotension is common and occurs in association with reaming of the medullary canal and insertion of a cemented prosthesis.⁸ Prosthesis impaction produces increased intramedullary pressure, which can be >500 mmHg, causing "intravasation" of medullary contents.⁹ Transoesophageal echocardiography has demonstrated frequent episodes of pulmonary embolism of echogenic material during medullary pressurization.

Because cardiovascular instability is unpredictable and hence difficult to study in clinical practice, a dog model¹⁰ of cemented arthroplasty was developed. This model reliably produces severe haemodynamic instability and allows quantitative estimation of pulmonary embolic fat, which is impossible in clinical reports. This facilitates the

study of factors that influence the degree of embolization of medullary contents and the severity of haemodynamic changes. Surgical interventions such as medullary cavity lavage and the use of uncemented arthroplasty^{11,12} reduce the pulmonary fat load and decrease haemodynamic instability in this model. The choice of anaesthetic might influence the haemodynamic response to medullary pressurization during cemented arthroplasty. This study examines haemodynamic responses in dogs anaesthetized with two standardized techniques. We compared a fentanyl-diazepam-nitrous oxide technique with isoflurane-nitrous oxide.

Methods

Approval for this study was obtained through the local animal care committee. All dogs were treated in accordance with the regulations of the Canadian Council on Animal Care.

Anaesthetic techniques/groups

Sixteen healthy adult mongrel dogs were anaesthetized with thiopentone 15 $\text{mg} \cdot \text{kg}^{-1}$ *iv*. The tracheas were intubated and the lungs of all animals were ventilated using a Ventimeter Controller ventilator (Airshields Inc., Hattboro, Pennsylvania) to maintain an arterial partial pressure of carbon dioxide (PaCO_2) between 35 and 40 mmHg. Normal saline was infused intravenously at 5 $\text{ml} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ throughout the experiment.

Dogs were alternately assigned to one of two anaesthetic regimens. Nitrous oxide in oxygen (50:50) was given to all animals as a basal anaesthetic. Eight dogs (fentanyl group) received diazepam 300 $\mu\text{g} \cdot \text{kg}^{-1}$ *iv* immediately after induction and fentanyl citrate 10 $\mu\text{g} \cdot \text{kg}^{-1}$ *iv* while invasive haemodynamic monitors were inserted as described below. Additional doses of fentanyl citrate 10 $\mu\text{g} \cdot \text{kg}^{-1}$ *iv* were given to maintain a mean arterial blood pressure of approximately 120 mmHg. The remainder of fentanyl citrate 100 $\mu\text{g} \cdot \text{kg}^{-1}$ was given ten minutes before drilling and reaming of the femoral medullary cavities.

In the other eight dogs (isoflurane group), inhaled isoflurane (Fortec vaporizer; Cyprane Keighley, England) was titrated to maintain a mean arterial blood pressure of approximately 120 mmHg. Gas from the endotracheal tube was continuously sampled with a Puritan-Bennett Anaesthetic Agent Monitor 222 (Datex Instrumentation Corporation, Finland) to determine the end-expiratory isoflurane concentration. This monitor was calibrated with a reference gas (compressed gas N.O.S., UN1956; Puritan-Bennett monitor calibration mixture) before each study.

All animals received pancuronium bromide 0.15 $\text{mg} \cdot \text{kg}^{-1}$ *iv* after induction of anaesthesia and an ad-

ditional $0.10 \text{ mg} \cdot \text{kg}^{-1}$ while invasive monitoring was established. No adjustments of medication, ventilation, or fluid therapy were made after drilling of the femur began.

A third group of six dogs (pacemaker group) was later studied using the same anaesthetic protocol as in the fentanyl group. In these dogs, atrial and ventricular pacemaker wires were sutured to the epicardium. The heart was paced with a dual chamber pulse generator in DVI mode. A rate of 130 bpm was chosen to simulate (under fentanyl-diazepam-nitrous oxide anaesthesia) the average resting heart rate noted in the isoflurane group. The pulse generator was not adjusted after initial settings were established and capture and sensing were verified. Baseline haemodynamic measurements were recorded prior to pacing and ten minutes after beginning to pace.

Monitoring

An arterial cannula (14 gauge) was inserted into the right femoral artery for blood sampling. A 7F triple-lumen balloon-tipped pulmonary artery catheter was advanced via the left internal jugular vein into the pulmonary artery to measure right atrial pressure (RAP) and pulmonary artery pressure (PAP). An electrical pressure transducing catheter (Millar Instruments, Inc., Houston, Texas) was inserted into the right carotid artery to monitor aortic blood pressure (ABP) continuously. Through a thoracotomy, the aortopulmonary window was dissected and an ultrasonic flow measuring device (Transonic Systems, Inc., Ithaca, N.Y.) was placed around the ascending thoracic aorta for continuous measurement of cardiac output (CO). This device had been previously calibrated using a roller pump with dog blood at the range of flows studied. A 14-gauge catheter was inserted via the left atrial appendage to monitor left atrial pressure (LAP). The thoracotomy incision was left open to atmospheric pressure.

All transducers were calibrated prior to baseline measurements. Heart rate (HR), ABP, RAP, PAP, LAP, and CO were monitored continuously on a Gould ES 1000 recorder (Gould Inc. Instruments Division, Cleveland, Ohio). Using the AT-CODAS software package (Dataq Instruments, Akron, Ohio, USA) and analog-digital conversion, these haemodynamic variables were recorded on computer disk for later analysis. Systemic vascular resistance (SVR) was calculated as $80 (\text{mean ABP} - \text{mean RAP}) / \text{CO}$, and stroke volume (SV) as CO / HR at each time interval.

Surgical technique: bilateral cemented arthroplasty (BCA)

The patellar tendons were exposed and divided, exposing the femoral condyles. The distal medullary cavity was entered by drilling through the patellofemoral groove. Using progressively larger reamers, both femoral medul-

lary cavities were enlarged to a diameter of 9 mm and a depth of 10 cm. Approximately 50 ml of methylmethacrylate cement (Howmedica RO Surgical Simplex P; London, England) was prepared according to the manufacturer's directions and injected under manual pressure into both femoral medullary canals simultaneously. Solid contoured metal prostheses were then simultaneously hammered into both medullary cavities. The time between beginning drilling of the femur and impaction of the prostheses was approximately ten minutes.

Haemodynamic measurements were analyzed before and after reaming, and at 30, 60, 180 and 300 sec following impaction of the femoral prostheses. Measurements before and after reaming were compared to assess whether drilling and reaming of the femoral medullary canal had any haemodynamic effect. Measurements following reaming (prior to cement and prosthesis impaction) were used as baseline values because they were made within three minutes of arthroplasty.

Plasma catecholamine assays

Arterial blood was sampled at each of these measurement times. The arterial plasma concentrations of epinephrine and norepinephrine were determined with high performance liquid chromatography after alumina extraction according to the method of Anton and Sayre.¹³ The sensitivity of these epinephrine and norepinephrine assays is $0.1 \text{ mmol} \cdot \text{L}^{-1}$. The intra-assay coefficients of variation for the epinephrine and norepinephrine measurements were 6 and 5% respectively ($n = 10$). The inter-assay coefficients of variation for the epinephrine and norepinephrine measurements were 9 and 8% respectively ($n = 10$).

Arterial blood gas analysis

Arterial blood samples at each measurement time were analyzed for pH, PaCO_2 , and PaO_2 using a calibrated blood gas machine (Instrumentation Laboratory pH/Blood Gas Analyzer model no. 13040-57; Milan, Italy).

Morphometric assessment

Sixty minutes after BCA, the dogs were killed by injecting potassium chloride into the left atrium. After ligation of the great vessels, the heart and lungs were removed, immersed in formalin, and the lungs were inflated with 10% buffered formalin at a pressure of 25 cm of fixative. After fixation for 72 hr, the lungs were sectioned in the midsagittal plane. Three stratified random blocks of known size were taken from the midsagittal slice of each lung. These samples were postfixed in Flemming's solution for 72 hr, washed in running water for 24 hr, processed for histological examination in the usual manner, and cut at $5 \mu\text{m}$ thicknesses.

TABLE I Baseline haemodynamic data in fentanyl and isoflurane groups (mean $\pm$ SD)

	<i>Pre-ream fentanyl</i>	<i>Post-ream fentanyl</i>	<i>Pre-ream isoflurane</i>	<i>Post-ream isoflurane</i>
ABP (mmHg)	120 $\pm$ 21	118 $\pm$ 20	115 $\pm$ 16	111 $\pm$ 17
RAP (mmHg)	8 $\pm$ 3	8 $\pm$ 3	9 $\pm$ 1	8 $\pm$ 2
PAP (mmHg)	18 $\pm$ 4	19 $\pm$ 4	16 $\pm$ 2	15 $\pm$ 2
LAP (mmHg)	12 $\pm$ 4	13 $\pm$ 4	9 $\pm$ 3	9 $\pm$ 3
HR (beats $\cdot$ min ⁻¹)	84 $\pm$ 17*	73 $\pm$ 8*	138 $\pm$ 27*	134 $\pm$ 28*
SV (ml)	22 $\pm$ 6	22 $\pm$ 6	17 $\pm$ 5	16 $\pm$ 4
CO (L $\cdot$ min ⁻¹)	1.8 $\pm$ 0.4	1.6 $\pm$ 0.3*	2.3 $\pm$ 0.7	2.1 $\pm$ 0.5*
SVR (dyne $\cdot$ sec $\cdot$ cm ⁻⁵)	5449 $\pm$ 1778	6028 $\pm$ 2313	4139 $\pm$ 1438	4091 $\pm$ 1096

*Denotes significant difference between groups ($P < 0.05$) at the same time period.

A coding system was used so that the pathologist who performed the morphometric assessment was unaware of the anaesthetic technique used. Using a morphometric technique previously described,¹⁰⁻¹² he delineated the fat emboli from background and calculated the area and diameter of each embolus.¹⁴ The ratio of area occupied by fat emboli to total area of lung examined is equivalent to the volume proportion of lung tissue occupied by fat (Delesse's principle).¹⁵

The number of fat emboli and volume proportion of lung tissue occupied by fat after cemented arthroplasty in each group were compared. Siegwart *et al.* has shown that the volume of lung occupied by vascular lumen is approximately eight percent.¹⁶ Using these data, the percentage of lung vasculature occluded by fat embolism in our dogs was calculated as (percent lung volume occupied by fat divided by 0.08).

Statistical analysis

Results were analyzed with the SAS (Statistical Analysis Software) statistical computer software package. The SAS general linear model repeated measures analysis of covariance procedure was used to analyze data from sequential measurements. When a significant F ratio was present but no group-time interaction existed, comparisons were made between groups using Tukey's test, and comparisons of haemodynamic values relative to baseline measurements were made with Dunnett's test. If there was significant group-time interaction, comparisons between baseline and other measurements were made within each group using unadjusted pairwise comparisons (LSMEANS procedure with Bonferroni's correction). T tests were used to compare individual data points between groups where differences between groups existed. T tests were used to compare the percent volume of lung vasculature occluded by fat emboli in each group and the weights of the dogs in each group. All values are reported as mean $\pm$ standard deviation. Alpha level for significance was 0.05.

Results

Comparison of fentanyl and isoflurane groups

The mean weight of the 16 dogs was 27.7 $\pm$ 2.7 kg (27.8 $\pm$ 3.2 kg for the fentanyl group and 27.7 $\pm$ 2.3 kg for the isoflurane group; P NS). In the isoflurane group, the mean end-tidal isoflurane concentration at the time of BCA was 0.62 $\pm$ 0.27% (range 0.35–1.00%). No changes in isoflurane concentration were noted for the five minutes following BCA. There was no difference between groups in the proportion of lung vasculature occluded by fat emboli (8.85 $\pm$ 2.20% for the fentanyl group, 9.63 $\pm$ 3.38% in the isoflurane group). There was no atrial septal defect, probe-patent foramen ovale or ventricular septal defect in any dog. All dogs in the fentanyl group survived the study period (60 min). Two of the eight dogs in the isoflurane group died within three minutes of BCA. In these two dogs, ABP decreased within 90 sec of BCA to values less than 50 mmHg and did not recover. Death was declared when both CO and pulse pressure were zero. These dogs were excluded from analysis of haemodynamic data after death. Thus for the isoflurane group, these two dogs were not included in the three-minute or five-minute analyses.

HAEMODYNAMIC MEASUREMENTS

There was no change in any measured haemodynamic variable within groups from before drilling to after reaming of the femoral canal (Table I). There was no difference between groups in RAP, PAP, LAP and SV (Figures 1, 2). Right atrial pressure and PAP increased ($P < 0.05$) from baseline values within one minute of BCA. Pulmonary artery pressure increased ($P < 0.05$) from baseline to one minute after BCA (fentanyl 19 $\pm$ 4 to 38 $\pm$ 13; isoflurane 15 $\pm$ 2 to 32 $\pm$ 7 mmHg). Left atrial pressure and SV both decreased ($P < 0.05$) following BCA (Figures 1, 2).

Mean aortic blood pressure decreased ($P < 0.05$) within one minute of BCA in both groups (fentanyl 118

FIGURE 1 Mean $\pm$ SD of right and left atrial pressures at baseline (post-reaming) and after bilateral cemented arthroplasty (BCA) in each group. * $P < 0.05$ from baseline value to this measurement (post-BCA). No difference between groups was noted.

± 20 to 102 ± 24 ; isoflurane 111 ± 17 to 55 ± 27 mmHg). Decreases from baseline ABP occurred at one minute in the fentanyl group, and at 30 sec, one minute and three minutes in the isoflurane group (Figure 3). Mean aortic blood pressure in the isoflurane group was lower ($P < 0.05$) than ABP in the fentanyl group at 30 sec and one minute after BCA.

Heart rate increased ($P < 0.05$) in the fentanyl group at all time intervals after BCA (73 ± 8 to 108 ± 25 beats $\cdot$ min $^{-1}$ at one minute). The HR was higher ($P < 0.05$) in the isoflurane group than in the fentanyl group at all time intervals except one minute (Figure 3). In the isoflurane group, HR did not change following BCA (Figure 3).

Cardiac output was higher ($P < 0.05$) in the isoflurane group at baseline (Figure 4). However, CO decreased in

FIGURE 2 Mean $\pm$ SD of pulmonary artery pressure and stroke volume at baseline (post-reaming) and after bilateral cemented arthroplasty (BCA) in each group. * $P < 0.05$ from baseline value to this measurement (post-BCA). No difference between groups was noted.

the isoflurane group at 30 sec and one minute after BCA and was unchanged in the fentanyl group.

Calculated SVR decreased ($P < 0.05$) in the isoflurane group, one minute after BCA. SVR was unchanged in the fentanyl group. SVR was lower ($P < 0.05$) in the isoflurane group than in the fentanyl group at 30 seconds and one minute after BCA (Figure 4).

BIOCHEMICAL ANALYSIS

There were no changes in arterial pH, PaCO₂, or PaO₂ in either group from prior to drilling to after reaming of the femoral canals (Table II). Arterial pH and PaO₂ decreased at all time intervals following BCA; PaCO₂ did not change from baseline values in the isoflurane group, but did increase in the fentanyl group from 35

FIGURE 3 Mean $\pm$ SD of aortic blood pressure and heart rate at baseline (post-reaming) and after bilateral cemented arthroplasty (BCA) in each group. * $P < 0.05$ from baseline value to this measurement (post-BCA). † $P < 0.05$ between groups at the same time period.

± 3 mmHg to a maximum of 42 ± 7 mmHg (at five minutes) (Table II). There were no changes in plasma concentrations of epinephrine or norepinephrine in either group from pre-ream to post-ream or from post-ream to any time after BCA (Table II).

Pacemaker group

Because differences in HR (at rest and post-BCA) between the isoflurane and fentanyl groups (Figure 3) could have been an important cause of differences in the haemodynamic response to BCA, a third group of fentanyl-anaesthetized dogs ($n = 6$) was studied. The mean weight of these dogs was 30.5 ± 3.6 kg (no difference vs fentanyl group). There were no differences between this group

FIGURE 4 Mean $\pm$ SD of cardiac output and systemic vascular resistance at baseline (post-reaming) and after bilateral cemented arthroplasty (BCA) in each group. * $P < 0.05$ from baseline value to this measurement (post-BCA). † $P < 0.05$ between groups at the same time period.

prior to pacing and the fentanyl group prior to drilling and reaming (Table III).

To assess whether the slow baseline HR (73 ± 8 bpm) was responsible for haemodynamic stability in the fentanyl group (Figure 3), the response to BCA of the pacemaker group (at a paced baseline of 131 ± 5 bpm) was compared with that of the fentanyl group. After pacing, HR was higher in the pacemaker group than in the fentanyl group and remained higher at all sampling intervals ($P < 0.05$). After pacing, SV and RAP were lower in the pacemaker group than in the fentanyl group at all sampling intervals ($P < 0.05$). There was no difference between the fentanyl and pacemaker groups in the response of any haemodynamic variable following BCA (i.e., no group-time interaction). To reiterate, although HR, SV

TABLE II Biochemical data in fentanyl and isoflurane groups (mean $\pm$ SD)

	Anaesthetic	Pre-ream	Post-ream	30 sec	1 min	3 min	5 min
Epinephrine (nmol $\cdot$ L ⁻¹)	F	2.49 $\pm$ 2.87	2.88 $\pm$ 3.56	2.57 $\pm$ 3.52	2.58 $\pm$ 3.54	2.86 $\pm$ 3.93	2.90 $\pm$ 4.04
	I	2.08 $\pm$ 1.29	2.10 $\pm$ 1.05	1.65 $\pm$ 0.80	1.75 $\pm$ 0.81	1.88 $\pm$ 0.97	1.98 $\pm$ 1.05
Norepinephrine (nmol $\cdot$ L ⁻¹)	F	0.79 $\pm$ 0.45	0.90 $\pm$ 0.49	0.82 $\pm$ 0.70	0.85 $\pm$ 0.71	0.99 $\pm$ 0.84	0.93 $\pm$ 0.82
	I	1.01 $\pm$ 0.43	0.94 $\pm$ 0.46	0.65 $\pm$ 0.47	0.63 $\pm$ 0.36	0.81 $\pm$ 0.32	0.89 $\pm$ 0.59
pH	F	7.30 $\pm$ 0.05	7.32 $\pm$ 0.04		7.26 $\pm$ 0.06*	7.25 $\pm$ 0.05*	7.24 $\pm$ 0.05*
	I	7.34 $\pm$ 0.03	7.33 $\pm$ 0.04		7.31 $\pm$ 0.03*	7.29 $\pm$ 0.04*	7.28 $\pm$ 0.04*
PaCO ₂ (mmHg)	F	37 $\pm$ 3	35 $\pm$ 3		40 $\pm$ 6*†	41 $\pm$ 7*	42 $\pm$ 7*
	I	36 $\pm$ 2	36 $\pm$ 3		34 $\pm$ 3†	37 $\pm$ 4	37 $\pm$ 4
PaCO ₂ (mmHg)	F	191 $\pm$ 46	194 $\pm$ 49		127 $\pm$ 49*	111 $\pm$ 46*	103 $\pm$ 46*
	I	186 $\pm$ 40	185 $\pm$ 39		148 $\pm$ 56*	146 $\pm$ 53*	145 $\pm$ 54*

*Denotes significant difference between post-ream baseline and this value ($P < 0.05$).†Denotes significant difference between groups ($P < 0.05$) at the same time period.TABLE III Pacemaker group: biochemical and haemodynamic response to BCA (mean $\pm$ SD)

Pacemaker	Pre-pace	Post-ream	30 sec	1 min	3 min	5 min
Mean ABP (mmHg)	115 $\pm$ 12	115 $\pm$ 22	106 $\pm$ 34	96 $\pm$ 35*	103 $\pm$ 31	111 $\pm$ 21
Mean RAP (mmHg)	6 $\pm$ 1	5 $\pm$ 3	5 $\pm$ 3†	5 $\pm$ 2*†	6 $\pm$ 3*†	6 $\pm$ 3
Mean PAP (mmHg)	16 $\pm$ 5	16 $\pm$ 3	30 $\pm$ 5*	36 $\pm$ 5*	37 $\pm$ 3*	34 $\pm$ 3*
Mean LAP (mmHg)	10 $\pm$ 4	10 $\pm$ 4	10 $\pm$ 5	10 $\pm$ 4*	10 $\pm$ 4	10 $\pm$ 4
HR (beats $\cdot$ min ⁻¹)	78 $\pm$ 12	131 $\pm$ 5†	138 $\pm$ 13*†	140 $\pm$ 17*†	135 $\pm$ 7*†	132 $\pm$ 4*†
SV (ml)	21 $\pm$ 6	12 $\pm$ 2†	10 $\pm$ 3*†	10 $\pm$ 4*	11 $\pm$ 3*†	11 $\pm$ 3*†
CO (L $\cdot$ min ⁻¹)	1.6 $\pm$ 0.4	1.6 $\pm$ 0.3	1.3 $\pm$ 0.5	1.3 $\pm$ 0.5	1.5 $\pm$ 0.5	1.5 $\pm$ 0.3
SVR (dyne $\cdot$ sec $\cdot$ cm ⁻⁵)	5744 $\pm$ 1703	5702 $\pm$ 1511	6299 $\pm$ 2283	5803 $\pm$ 2138	5796 $\pm$ 2162	5958 $\pm$ 1691
Epinephrine (nmol $\cdot$ L ⁻¹)	2.59 $\pm$ 2.96	2.80 $\pm$ 3.30	2.31 $\pm$ 2.73	3.89 $\pm$ 4.56	4.44 $\pm$ 3.74	3.94 $\pm$ 3.41
Norepinephrine (nmol $\cdot$ L ⁻¹)	0.57 $\pm$ 0.35	0.63 $\pm$ 0.40	0.51 $\pm$ 0.37	0.74 $\pm$ 0.53	0.98 $\pm$ 0.56	0.89 $\pm$ 0.54
pH	7.32 $\pm$ 0.05	7.32 $\pm$ 0.07		7.28 $\pm$ 0.05*	7.26 $\pm$ 0.05*	7.25 $\pm$ 0.05*
PaCO ₂ (mmHg)	38 $\pm$ 2	37 $\pm$ 2		42 $\pm$ 2*	44 $\pm$ 3*	44 $\pm$ 3*
PaO ₂ (mmHg)	208 $\pm$ 37	220 $\pm$ 32		122 $\pm$ 25*	103 $\pm$ 17*	102 $\pm$ 18*

*Denotes significant changes from post-ream baseline at this time in combined data from pacemaker and fentanyl groups ($P < 0.05$).†Denotes significant difference versus the fentanyl group ($P < 0.05$) at this time period.

and RAP were different between the fentanyl and pacemaker groups at baseline, the time course and magnitude of changes in these variables (and all others) were not different between the groups. There were no differences in volume proportion of lung vasculature occluded by fat (at post-mortem), plasma epinephrine or norepinephrine concentrations, or arterial blood gas values between the groups (Table III).

Discussion

This study demonstrates that the choice of anaesthetic agent can influence haemodynamic response to cemented arthroplasty. There was less hypotension and better maintenance of CO in this model with the fentanyl/diazepam/N₂O anaesthetic than with isoflurane/N₂O even though the two groups had equivalent pulmonary vascular occlusion by fat. There was no difference between groups in SV (Figure 2) observed within one minute of BCA. Thus, severe hypotension in the isoflurane group could

be explained by either an inadequate HR response or impaired vasoconstriction under stress (Figure 4).

Epidemiological studies have not shown a difference in severe intraoperative hypotension or perioperative mortality between anaesthetic techniques for cemented arthroplasty,^{17,18} and there is no consensus as to the optimal choice of anaesthetic in patients with pulmonary embolism.¹⁹ Opioids with nitrous oxide^{20,21} or benzodiazepines²² are often chosen for patients in whom haemodynamic stability is important, because of their ability to blunt effectively hypertensive responses to noxious stimuli. However, this property might be deleterious in a situation where a decrease in cardiac output occurs and a sympathoadrenal response could be beneficial. Volatile anaesthetics, such as isoflurane have also been recommended; however, myocardial depression may impair a patient's ability to respond to hypotension.

Analysis of data from the pacemaker group (Table III) suggests that even with a rapid HR, the fentanyl-based

anaesthetic was associated with haemodynamic stability. Differences between the fentanyl and pacemaker groups in HR, SV and RAP were related to pacing. Responses of both fentanyl groups was very similar after BCA. Therefore, the slow HR was not essential for haemodynamic stability. However, with hypotension, the HR did not increase in the isoflurane group (but did increase in the fentanyl and pacemaker groups) and calculated SVR decreased in the isoflurane group (but not the fentanyl or pacemaker groups) (Figure 4). These data suggest that the lack of compensatory HR and SVR responses to the decrease in SV associated with cemented arthroplasty in this model caused more severe haemodynamic instability in the isoflurane group.

Isoflurane has been shown to suppress the baroreflex arc at multiple sites,^{23,24} while fentanyl-based anaesthesia preserves sympathetic responses to hypotension.^{25,26} This may explain differences in haemodynamic response to similar embolic insults in these healthy animals.

There are several potential limitations of this study. First, there may have been differences between groups in depth of anaesthesia. In dogs, fentanyl exerts maximal analgesic and cardiovascular actions in a plasma concentration range of 5–30 ng · ml⁻¹. This requires a total dose of <70 µg · kg⁻¹, and manifests as bradycardia, decreased cardiovascular response to noxious stimuli, and decreased resting cardiac output.²⁷ The addition of 50% nitrous oxide does not alter haemodynamic variables after high-dose fentanyl in dogs.²⁸ An isoflurane dose was chosen by titrating inspiratory concentration for haemodynamic stability during noxious stimuli. Ensuring an identical depth of anaesthesia between groups would be impossible. Drug regimens were chosen to provide adequate anaesthesia in both groups and compare haemodynamic response to cemented arthroplasty under two specific conditions.

Second, there are problems in extrapolating animal data to a clinical situation. Studies using transoesophageal echocardiography²⁹ have demonstrated right ventricular dilatation and echogenic intracardiac material at the time of cement and prosthesis insertion, as in this model.³⁰ However, this experiment involved healthy dogs in a standardized anaesthetic and surgical protocol. This model did not use lavage of the medullary cavities, thereby maximizing embolism of medullary contents and resultant hypotension.^{10–12} We did not reduce (or adjust) the isoflurane concentration at the time of arthroplasty as many clinicians may recommend. Undoubtedly, factors such as interspecies variation, coronary artery disease, preoperative pharmacotherapy, medullary lavage and intraoperative resuscitation and fluid management would alter haemodynamic values.

Third, the role of plasma catecholamine concentrations

in the stress response is unclear. The catecholamine assays in this study suggest that changes in circulating catecholamine levels were not the cause of differences in haemodynamic response. However, the role of serum catecholamines in regulating baroreflex function is incompletely understood, and plasma levels of these molecules do not invariably correlate with haemodynamic changes.^{31,32}

Fourth, the thoracotomy and pericardiotomy in this protocol may have influenced haemodynamic response. The pericardium decreases ventricular compliance and can influence haemodynamic status.^{33,34} Hypotension might have been more severe with both anaesthetics, if the pericardium and thorax were closed after invasive monitoring was established.

These data demonstrate that the choice of anaesthetic can influence the haemodynamic response to medullary pressurization during cemented arthroplasty. The anaesthetic technique can influence the severity and pattern of haemodynamic response to cemented arthroplasty.^{35,36}

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