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Hemodynamic Response to Anesthesia and Pneumoperitoneum in Orthotopic Cardiac Transplant Recipients

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IMMUNOSUPPRESSIVE therapy with cyclosporine has been reported to increase the risk of cholelithiasis in cardiac transplant recipients.[1] This may increase the need for cholecystectomy in these patients.[2] During orthotopic cardiac transplantation, the cardiac plexus is divided, which leads to persistent denervation of the heart, causing abnormal responses to stress.[3,4] Because the posttransplantation cardiac function profile is different from normal innervated cardiac function, hemodynamic changes during laparoscopic cholecystectomy (LC) in these patients may differ from those observed in healthy patients.[5] We evaluated the hemodynamic changes associated with pneumoperitoneum and patient position changes during elective LC in 11 consecutive cardiac transplant recipients.

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Methods

After receiving institutional review board approval, we enrolled in the study 11 consecutive consenting patients who had undergone orthotopic cardiac transplantation and who were scheduled for elective LC. On arrival at the operating room and after being fitted with routine monitoring devices, all patients received 1 to 2 mg intravenous midazolam. Before induction of anesthesia, the radial artery was cannulated using a 20-gauge catheter, and a 7.5 French thermodilution pulmonary artery catheter (model 131-74; Baxter Edwards, Irvine, CA) was introduced through the left internal jugular vein. General anesthesia was induced with administration of etomidate (0.1 to 0.2 mg/kg given intravenously) and alfentanil (75 to 200 μg given intravenously). Vecuronium (0.1 mg/kg given intravenously) was used to facilitate tracheal intubation and maintain muscle relaxation. General anesthesia was maintained with 0.5 to 1.5% isoflurane and intermittent doses of alfentanil (100 to 500 μg given intravenously). Patients' lungs were mechanically ventilated with 50% oxygen in air, and end-tidal carbon dioxide concentrations were maintained between 35 and 40 mmHg. The operation was performed by the same surgeon (M.L.F.) using a standard surgical technique. The intraabdominal pressure was automatically maintained at 15 mmHg with a carbon dioxide insufflator (WISAP insufflator; Semm Systems, München, Germany).

Intraoperative monitoring included continuous electrocardiograms (leads II and V_5), arterial blood pressure, pulse oximetry, capnography, body temperature, peak airway pressures, and neuromuscular function using a nerve stimulator. Hemodynamic variables, including heart rate, mean arterial pressure, pulmonary artery occlusion pressure, central venous pressure, and cardiac output, were recorded at predetermined intervals (T_1 = before induction of anesthesia; T_2 = 5 min after induction of anesthesia but before incision; T_3 = 5 min

after peritoneal carbon dioxide insufflation and reverse Trendelenburg's position and left lateral tilt; T_{4-8} = every 10 min after reverse Trendelenburg's position; T_9 = after deflation of the abdomen and return to supine position; and T_{10} = 10 min after attaining supine position). From these measured variables, cardiac index (CI), systemic vascular resistance (SVR), and pulmonary vascular resistance were calculated. The pressure transducers were located at the level of the right atrium and moved to the same level with changes in patient position. In addition, arterial blood gases were measured before and 20 min after carbon dioxide insufflation.

Data are presented as means ± standard deviations. Data were analyzed using two-way analysis of variance with Tukey-Kramer correction or Kruskal-Wallis test as appropriate. A probability value less than 0.05 was considered statistically significant.

Results

Table 1 shows patients' demographic and clinical characteristics. All patients were classified as American Society of Anesthesiologists physical status 3. The CI decreased significantly after induction of anesthesia, but it returned to preinduction values after carbon dioxide insufflation and reverse Trendelenburg's positioning and did not change significantly thereafter (table 2). The mean arterial pressure decreased significantly after induction of anesthesia, but it returned to preinduction values after insufflation and decreased again 10 min after patients were placed in the reverse Trendelenburg's position and remained significantly lower than baseline until the end of the study (table 2). Compared with postinduction values, the central venous pressure and pulmonary artery occlusion pressure increased after carbon dioxide insufflation and reverse Trendelenburg's positioning and remained significantly high until 20 min and 40 min after reverse Trendelenburg's positioning, respectively. Pulmonary vascular resistance increased after induction of anesthesia and remained significantly high until 20 min after reverse Trendelenburg's positioning. No significant changes in the heart rate and SVR were observed throughout the study (table 2). None of the patients exhibited any adverse effects requiring supportive treatment. The postoperative course was uncomplicated in all cases.

Table 1. Demographic and Clinical Data in Cardiac Transplant Patients Undergoing Laparoscopic Cholecystectomy

Number (n)	11
Sex (M:F)	7:4
Age (yr)	58 ± 7
Weight (kg)	74 ± 14
Height (in)	67 ± 3
Duration of anesthesia (min)	198 ± 44
Duration of surgery (min)	124 ± 26
Duration of CO_2 insufflation (min)	47 ± 13

Values are mean ± SD.

Discussion

We found that the cardiac index does not change significantly during pneumoperitoneum in orthotopic cardiac transplant recipients. This is in contrast to previous reports of a significant decrease in CI during LC in healthy patients[5-7] and in those with significant cardiopulmonary dysfunction.[8,9] The differences in the hemodynamic responses may be due to persistent denervation of the heart and related pathophysiologic changes in the cardiovascular system after orthotopic cardiac transplantation[3,10] or due to differences in anesthetic techniques.

After orthotopic cardiac transplantation, the myocardial contractility and myocardial reserve are normal.[11-13] However, the interruption of the sympathetic and parasympathetic nerve fibers to the donor heart affects the regulation of the cardiovascular system. Adaptation to stress is altered as the heart responds primarily by increasing the stroke volume, which depends on venous return and the Frank-Starling mechanism.[10] In addition, there is a lag period in the hemodynamic response because the cardiac output is increased secondary to humoral reflexes (catecholamine release) rather than to neural reflexes. The absence of vagal tone results in a higher resting heart rate and a loss of normal responses to the Valsalva maneuver. Furthermore, exaggerated responses to catecholamines have been observed in cardiac transplant recipients, which is attributed to an increase in receptor density (up-regulation).[14] Exaggerated responses may also be due to availability of a greater proportion of local catecholamines, which, because of cardiac denervation, are not removed by neuronal uptake.[15]

Hemodynamic changes during LC in patients with an innervated heart include increase in mean arterial pressure, decrease in CI, and increase in SVR. The pos-

Table 2. Measured and Derived Data at Various Time Points during Laparoscopic Cholecystectomy in Cardiac Transplant Recipients

	T_1	T_2	T_3	T_4	T_5	T_6	T_7	T_8	T_9	T_{10}
Heart rate (beats/min)	97 ± 13	89 ± 11	93 ± 13	92 ± 11	91 ± 13	89 ± 13	91 ± 12	91 ± 13	96 ± 15	90 ± 15
MAP (mmHg)	115 ± 18	86 ± 20*	114 ± 21	97 ± 21*	96 ± 15*	97 ± 13*	93 ± 14*	94 ± 17*	99 ± 15*	93 ± 16*
CI (L/min/m^2)	3.2 ± 0.9	2.3 ± 0.5*	2.6 ± 0.6	2.7 ± 0.7	2.7 ± 0.9	2.7 ± 0.8	2.6 ± 0.7	3.0 ± 0.9	3.4 ± 1.2	3.4 ± 1.5
CVP (mmHg)	11 ± 7	10 ± 3	17 ± 5†	16 ± 4†	15 ± 5†	14 ± 6	13 ± 5	13 ± 5	11 ± 3	9 ± 3
PAOP (mmHg)	13 ± 4	11 ± 3	16 ± 4†	17 ± 4†	16 ± 5†	16 ± 5†	15 ± 5†	14 ± 5	14 ± 5	13 ± 4
SVR (dyne/s/cm^5)	1,571 ± 603	1,485 ± 473	1,728 ± 642	1,361 ± 435	1,419 ± 499	1,440 ± 405	1,457 ± 434	1,284 ± 439	1,198 ± 322	1,198 ± 420
PVR (dyne/s/cm^5)	85 ± 60	150 ± 91*	175 ± 65*	148 ± 46*	148 ± 39*	140 ± 31	121 ± 51	135 ± 36	123 ± 39	121 ± 30

T_1 = prior to induction of anesthesia; T_2 = 5 min after induction of anesthesia but prior to incision; T_3 = 5 min after peritoneal CO_2 insufflation and reverse Trendelenburg position and left lateral tilt; T_{4-8} = every 10 min after reverse Trendelenburg position; T_9 = after exsufflation and return to supine position; T_{10} = 10 min after attaining supine position.

Values are mean ± SD.

* $P < 0.05$ *versus* T_1.

† $P < 0.05$ *versus* T_2.

sible causes of the hemodynamic changes observed during LC are complex, and it is difficult to distinguish the effects of increased intraabdominal pressure (from creation of pneumoperitoneum), systemic absorption of insufflated carbon dioxide, and reverse Trendelenburg positioning from those of neurohumoral responses.[16] This may explain the variability in the hemodynamic response observed by various investigators during LC.[5-7,17,18]

Previous studies have reported a biphasic change in CI (*i.e.,* an initial reduction in CI followed by gradual restoration) after creation of pneumoperitoneum.[5,7] After pneumoperitoneum, the CI is reduced by approximately 50% of the baseline.[5] Cunningham and associates[6] reported that in healthy patients, the left ventricular function, as determined by transesophageal echocardiographic estimation of ejection fraction, was preserved after carbon dioxide insufflation and changes in patient position. The reported increase in mean arterial pressure may represent an increase in afterload (SVR), which is attributed to neurohumoral responses during LC.[16] A recent study reported a linear correlation between changes in mean arterial pressure and increases in plasma concentrations of renin and aldosterone.[19] The plasma concentrations of vasopressin increased significantly after pneumoperitoneum and paralleled the time course of increase in SVR.[20]

In contrast to previous reports, we did not observe an increase in mean arterial pressure and SVR or any decrease in CI in our patients with denervated hearts. It is possible, but remains to be demonstrated, that neurohumoral responses during LC in posttransplant patients may be different from those observed in healthy patients.[21-23] The cause-effect relationship between CI and SVR is unclear. The decrease in CI observed by previous authors may have increased the SVR. The initial decrease in CI observed in this study may be due to the myocardial depressive effects of the drugs used to induce anesthesia. The increase in the CI after insufflation may have resulted from an increase in venous return, as suggested by an increase in the central venous pressure and pulmonary artery occlusion pressure. The increase in central venous pressure and pulmonary artery occlusion pressure may be the result of an increase in the intravascular volume due to compression of the abdominal organs (liver and spleen) caused by increased intraabdominal pressure. Furthermore, a 15% increase in blood volume after cardiac transplantation may explain the maintenance of cardiac output.[24] Because the cardiac output in heart transplant recipients depends on the Frank-Starling mechanism, increased intravascular volume should improve cardiac output. On the other hand, measured increases in central venous pressure and pulmonary artery occlusion pressure only reflect transmitted intrathoracic pressures, and the reverse Trendelenburg's position and increased intrathoracic pressure may actually decrease venous return and cardiac filling pressures. Our results, however, seem to support the idea that the Frank-Starling mechanism is activated by increased filling pressures. As observed in this study, retrospective analyses of cardiac transplant patients undergoing noncardiac

surgery found no significant adverse hemodynamic changes.[25]

The increased sensitivity of the transplanted heart to catecholamines,[14] compared with healthy patients, may help preserve cardiac performance by increasing myocardial contractility. In addition, the absence of increased afterload (SVR) also may have maintained the CI.[16] Furthermore, carbon dioxide insufflation in supine patients rather than in those in reverse Trendelenburg's position (as performed in the previous study[5]) may be responsible in part for the maintaining the CI. The lack of a Valsalva response to the pneumoperitoneum may also have played a role in maintaining the CI.

We evaluated the combined effects of carbon dioxide insufflation and reverse Trendelenburg's position because the time period between these two events is usually short. Carbon dioxide insufflation in supine patients and delay between carbon dioxide insufflation and change of position may further modify hemodynamic changes during LC. In addition, use of transesophageal echocardiography may have provided more information, such as left ventricular end systolic and end diastolic areas at every stage of the operation. Furthermore, measurement of the various humoral factors and transmural filling pressures may explain the differences in the hemodynamic changes in these patients.

This preliminary study shows that orthotopic cardiac transplant recipients anesthetized with isoflurane and alfentanil show minimal hemodynamic changes with carbon dioxide insufflation and reverse Trendelenburg's position during LC.

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Remote Cocaine Use as a Likely Cause of Cardiogenic Shock after Penetrating Trauma

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ANESTHESIA in the setting of trauma is often complicated by the effects of acute and chronic substance abuse. Recently, cocaine has become one of the most common drugs used by trauma victims.[1–3] Despite this all-too-common association of cocaine abuse and trauma, little is known of the impact of acute or chronic cocaine use on the physiologic response to trauma. We present a case in which hypotension after penetrating trauma in a patient with a history of chronic cocaine use is mistakenly assumed to be the result of occult blood loss.

Case Report

A 26-y-old man weighing 75 kg drove himself to the emergency room after sustaining a stab wound to the right flank. The patient had no other injuries and no past medical history of cardiac or pulmonary disease. In the emergency room, the patient was alert and cooperative. His systolic blood pressure was 70 to 80 mmHg and his heart rate was 125 bpm. Cardiac and pulmonary examinations revealed no signs of pneumothorax, heart murmur, or penetrating mediastinal or thoracic wounds. The patient's abdomen was mildly tender. His initial hematocrit concentration was 41% and a repeated hematocrit test after he received an uncertain volume of intravenous fluid was 38%. His blood electrolytes were Na^+ = 145 meq/L, K^- = 3.6 meq/L, Cl^- = 106 meq/L, HCO_3^- = 6 meq/L, blood urea nitrogen = 13 mg/dL, and creatinine = 1.9 mg/dL. In light of his hypotension and tachycardia associated with a stab wound, peritoneal lavage was not performed and he was immediately routed to the operating room for an emergency exploratory laparotomy.

On arrival to the operating room he was awake, alert, and relatively cooperative. His initial blood pressure was 80/36 mmHg, his heart rate was 120 bpm, and his temperature was 36°C. During placement of electrocardiograph leads, he complained of chest pain and shortness of breath and was noted to be diaphoretic and clammy. The electrocardiograph monitor showed sinus tachycardia and S-T segment depression. A 12-lead electrocardiograph confirmed a rate of 120 bpm and 4-mm S-T segment depression in leads II, III, AVF, V4, V5, and V6 (fig. 1).

At this time, drug use was considered in the differential diagnosis of this man's evident myocardial ischemia. However, he denied recent use of any drug except alcohol and his denial was confirmed by results of a urine toxicology analysis that were negative for cocaine, marijuana, barbiturates, and benzodiazepines. However, he did admit to using cocaine often, with his most recent ingestion occurring during the previous week.

Given that the patient's hypotension and ischemia were presumed to be the result of intraabdominal blood loss, we felt it necessary to proceed with exploratory laparotomy for definitive treatment. Nonetheless, every effort was made to expeditiously stabilize the patient's condition to permit safe induction of anesthesia and subsequent surgery. An intraarterial catheter was inserted and arterial blood gas analysis revealed pH = 7.05, P_{O_2} = 174 mmHg, Pa_{CO_2} = 25 mmHg, bicarbonate = 7.1 meq/L, and lactate = 9.4 mm/L. A nitroglycerin infusion was begun at 2 $\mu g \times kg^{-1} \times min^{-1}$, producing symptomatic relief of chest pain and dyspnea and reducing S-T segment depression to 1.8 mm without a significant change in blood pressure. A dopamine infusion was begun at 8 $\mu g \times kg^{-1} \times min^{-1}$ and subsequently increased to 10 $\mu g \times kg^{-1} \times min^{-1}$ with an increase in blood pressure to 100/60 mmHg and a decrease in heart rate to 105 bpm.

With the dopamine and nitroglycerin infusions continuing, the patient was hemodynamically stable during induction with 750 μg fentanyl, 10 mg etomidate, and 140 mg succinylcholine. After tracheal intubation, general anesthesia was maintained with 0.5 to 1.2% isoflurane. A pulmo-

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