Cardiothoracic Anesthesia, Respiration and Airway

Decreased heart rate and blood pressure in a recent cardiac transplant patient after spinal anesthesia

[Baisse de la fréquence cardiaque et de la tension artérielle après rachianesthésie chez un patient qui a récemment reçu une greffe cardiaque]

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Purpose: To describe the cardiovascular effects of neuraxial blockade in a heart transplant patient.

Clinical features: A 69-yr-old 70-kg male underwent orthotopic heart transplant (bicaval anastomosis technique) for ischemic cardiomyopathy. Five months after transplantation, the patient underwent a transurethral bladder tumour resection under spinal anesthesia. Two millilitres of bupivacaine 0.75% (15 mg) were injected intrathecally at L_{3-4} and the patient remained seated for approximately 20 sec prior to assuming the lithotomy position. Subsequently, both blood pressure (BP) and heart rate (HR) diminished gradually (BP and HR immediately pre-spinal: 113 mmHg (mean arterial pressure) and 92 beats·min^{-1}, respectively; nadir BP and HR: 94 mmHg (16.8% decrease) 30 min postspinal and 73 beats·min^{-1} (20.7% decrease) 40 min postspinal, respectively). HR and mean BP were highly correlated ($r = 0.9410$, $P < 0.0001$, $R^2 = 0.8854$). The dermatome level of neuraxial anesthesia, determined by sensitivity to pin prick, was T_8 (five minutes) and T_6 (ten minutes) postinjection of spinal anesthetic. Control patients ($n = 10$) undergoing elective urological procedures with identical anesthesia management demonstrated very similar cardiovascular responses.

Conclusions: Although cardiac transplant patients may tolerate neuraxial anesthesia admirably, a fall in HR may ensue which theoretically could have important physiological consequences. It is argued that the change in HR in the transplanted patient was mediated by mechanisms intrinsic to the transplanted heart and/or by reduced catecholamine secretion from the adrenal medulla. It is emphasized that HR changes observed in cardiac transplant patients do not necessarily imply reinnervation of the transplanted organ.

Objectif : *Décrire les effets cardiovasculaires du blocage neuraxial chez un greffé cardiaque.*

Éléments cliniques : *Un homme de 69 ans et 70 kg a subi une transplantation cardiaque orthotopique, selon la technique d'anastomose bicave, pour une cardiomyopathie ischémique. Cinq mois après, il a subi la résection transurétrale d'une tumeur vésicale sous rachianesthésie. L'injection intrathécale de 2 mL de bupivacaïne à 0,75 % (15 mg) a été faite à L_{3-4} et le patient est demeuré assis environ 20 sec avant d'adopter la position de lithotomie. La tension artérielle (TA) et la fréquence cardiaque (FC) ont ensuite diminué graduellement (TA et FC juste avant la rachianesthésie : 113 mmHg (tension artérielle moyenne) et 92 battements·min^{-1} ; TA et FC minimales : 94 mmHg (baisse de 16,8 %) 30 min après la rachianesthésie et 73 battements·min^{-1} (baisse de 20,7 %) 40 min après la rachianesthésie. La FC et la TA moyenne ont été en forte corrélation ($r = 0,9410$, $P < 0,0001$, $R^2 = 0,8854$). Le niveau de l'anesthésie neuraxiale, déterminé par la sensibilité à la piqûre, était de T_8 (cinq minutes) et T_6 (dix minutes) après l'injection de l'anesthésique rachidien. Des patients ($n = 10$) qui ont subi ultérieurement une intervention urologique réglée avec une anesthésie identique ont démontré des réponses cardiovasculaires similaires.*

Conclusion : *Même si les greffés cardiaques peuvent tolérer admirablement l'anesthésie neuraxiale, une chute de la FC peut survenir et entraîner, en théorie, d'importantes conséquences physiologiques. On peut penser que la modification de la FC chez les greffés relevait de mécanismes intrinsèques au cœur transplanté et/ou de la sécrétion réduite de catécholamines provenant de la médullaire surrénale. Il faut souligner que les changements de FC chez les greffés cardiaques ne touche pas nécessairement la réinnervation de l'organe transplanté.*

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HARVESTING of the donor heart for transplant results in complete extrinsic cardiac denervation. In spite of considerable clinical experience with this procedure, reinnervation of the transplanted heart remains controversial.[1] Although there is a substantial body of literature that denies reinnervation,[2–8] there is emerging evidence to suggest that, to some extent, this may occur. Afferent reinnervation is supported by reports of angina accompanied by objective evidence of cardiac ischemia.[9,10] Evidence for sympathetic reinnervation derives from the emergence of a low-frequency heart rate (HR) variability in some transplants,[11–13] and the appearance of appropriate, albeit diminished, reflex changes in HR.[11,14–16] In addition, experiments suggest catecholamine uptake, storage or release from presumed cardiac sympathetic postganglionic neurons in the transplanted heart.[15,17–19] Evidence for parasympathetic reinnervation derives from reports of a high-frequency variability in HR in a small number of transplants,[20,21] and the demonstration of atropine-sensitive reflex changes in HR.[22] In addition, there are a few reports describing vasovagal syncopal-like episodes in cardiac transplant patients.[23–25] The issue of reinnervation may be additionally complicated by the surgical technique. When recipient right and left atrial cuffs are joined to the corresponding donor atria, the remnant recipient right atrium remains innervated and may diminish the potential for reinnervation of the donor heart. With the bicaval anastomosis technique, the recipient's heart is totally excised and there is no innervated recipient atrial tissue to potentially interfere with the process of reinnervation.[26]

While the evidence for limited cardiac reinnervation is intriguing, a careful review of this subject concluded that functional reinnervation of the transplanted heart rarely, if ever, occurs.[1] Accordingly, it is anticipated that changes in HR, normally produced by altered cardiac autonomic tone, are absent in this unique type of patient and a relatively stable HR is expected. In this report we describe the coincidental fall in HR and blood pressure (BP) of a cardiac transplant patient following spinal anesthesia for a urological procedure. These hemodynamic changes are compared with those of patients with a normally innervated heart undergoing similar surgery with the same anesthetic technique. This report is unique in that, as far as we are aware, hemodynamic changes in a cardiac transplant patient following neuraxial anesthesia have heretofore not been described.

Case report

A 69-yr-old 70-kg white man underwent orthotopic heart transplant (bicaval anastomosis technique) for ischemic cardiomyopathy. Co-morbid conditions included diabetes, hypertension, manic depression, diverticulitis, hiatus hernia, and remote history of alcoholism and smoking. Five months following transplantation, the patient underwent a transurethral bladder tumour resection. Laboratory investigation indicated elevated blood urea nitrogen (12.9 $mMol \cdot L^{-1}$) and creatinine 133 ($mMol \cdot L^{-1}$) and anemia (hematocrit 0.25). A 12-lead electrocardiogram (ECG) demonstrated a normal sinus rhythm at 77 $beats \cdot min^{-1}$ and a right bundle branch block. Recent endomyocardial biopsy indicated no evidence for rejection. The patient's medications were tolbutamide 500 mg BID, atorvastatin 30 mg QD, ramipril 2.5 mg QD, fosamax 80 mg QWK, clonazepam 0.5 mg TID, fluoxetine 40 mg QD, omeprazole 20 mg QD, cyclosporine 25 mg BID, prednisone 7.5 mg QD, amlodipine 5 mg QD, sirolimus 1 mg QD, calcium 500 mg BID, and magnesium 100 mg QD.

Following insertion of an *iv* catheter (18 gauge) in an upper extremity (normal saline infused at 100 $mL \cdot hr^{-1}$), midazolam 1.0 mg was administered for sedation. A 27-gauge Whitacre spinal needle was subsequently inserted into the intrathecal space at the L_{3-4} interspace under sterile conditions with the patient in the seated position. Two millilitres of bupivacaine 0.75% (15 mg) were injected, and the patient remained seated for approximately 20 sec prior to assuming the lithotomy position. Monitoring consisted of non-invasive BP recording, ECG (leads II and V), and pulse oximetry. The patient breathed a mixture of room air and oxygen delivered via nasal prongs (2 $L \cdot min^{-1}$). Following injection of spinal anesthetic, both BP and HR gradually diminished (Figure 1; BP and HR immediately pre-spinal: 113 mmHg (mean arterial pressure) and 92 $beats \cdot min^{-1}$, respectively; nadir BP and HR: 94 mmHg (16.8% decrease) 30 min postspinal and 73 $beats \cdot min^{-1}$ (20.7% decrease) 40 min postspinal, respectively). HR and mean BP were highly correlated ($r = 0.9410$, $P < 0.0001$, $R^2 = 0.8854$). The dermatome level of neuraxial anesthesia, determined by sensitivity to pin prick, was T_8 (five minutes) and T_6 (ten minutes) postinjection of spinal anesthetic.

In a subsequent series of ten patients undergoing elective urological procedures [transurethral bladder tumour resection ($n = 6$); transurethral laser prostatectomy ($n = 4$)], HR and BP changes were recorded for comparison. These patients received identical sedation (midazolam 1.0 mg *iv*) spinal neuraxial anesthesia, intraoperative positioning (lithotomy) and fluid management, and

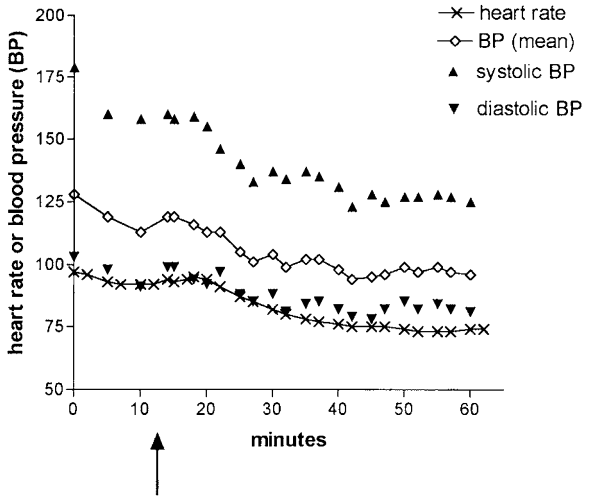

FIGURE 1 Spinal block produces coincident fall in systemic arterial pressure and heart rate in a cardiac transplant patient. Arrow denotes time of intrathecal administration of bupivacaine.

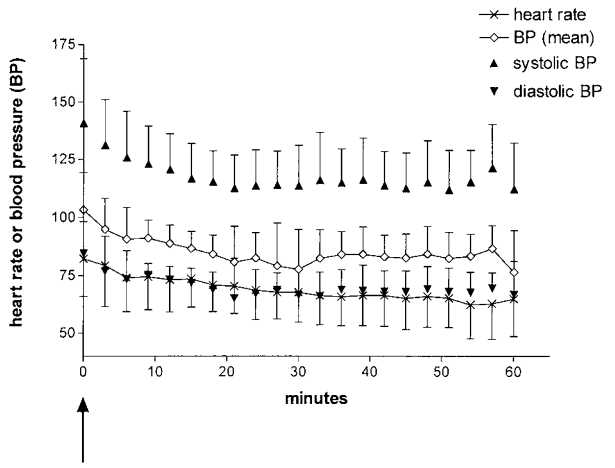

FIGURE 2 Spinal block produces coincident decrease in systemic arterial pressure and heart rate in patients with normally innervated hearts (n = 10; mean ± SD). Cardiovascular response following neuraxial block is essentially similar to that seen in the cardiac transplant patient (Figure 1). Arrow denotes time of intrathecal administration of bupivacaine.

inotropic or vasopressor drugs were not administered. Following injection of spinal anesthetic, BP and HR gradually diminished during the subsequent 60 min period (Figure 2; BP and HR immediately pre-spinal: 103.2 ± 16.0 mmHg (mean arterial pressure; mean ± SD) and 82.4 ± 16.4 beats·min^{-1}, respectively; nadir BP and HR: 77.8 ± 17.1 mmHg (26.1 ± 10.8% decrease) 30 min postspinal and 62.3 ± 14.7 beats·min^{-1} (22.7 ± 9.6% decrease) 54 min postspinal, respectively). HR and mean BP were highly correlated (r = 0.8523, $P < 0.0001$, R^2 = 0.7265). The median dermatome level of neuraxial anesthesia, determined by sensitivity to pin prick, was T_8 (range: T_4–T_{10}, five minutes) and T_6 (range: T_2–T_8, ten minutes) postinjection of spinal anesthetic.

Discussion

We report the coincident fall in HR and BP in a cardiac transplant recipient following spinal anesthesia. These changes were similar to those observed in patients with normally innervated hearts. Such changes in HR are of particular interest when considered in the context of the controversy regarding reinnervation of the transplanted organ.[1] As the patient had undergone transplantation only five months previously, and, as reinnervation of the transplanted heart (when demonstrable) is not evident before one year after transplantation,[14,18,19,26] the response is unlikely to have been mediated by reflex activation of the sinoatrial (SA) node directly *via* the central nervous system. Because the patient underwent transplantation using the bicaval anastomosis technique, changes in donor HR could not have been mediated by altered rate of contraction of remnant innervated atrial tissue.[27–29] Possibly, the hypotension produced by spinal block resulted in cardiac ischemia with decreased perfusion of the SA node of the donor heart. Such a mechanism has been suggested to account for a lethal bradyarrhythmia[30] and for bradycardia following protamine-induced hypotension[31] in transplanted patients. Bradyarrhythmias in the post-transplant period appear to be highly correlated to disruption of the SA node blood supply in the transplanted heart.[32] However, in the present study, as HR and BP both fell gradually without signs of ischemia (ECG unchanged), and the decreases in systemic arterial pressure were modest, such an explanation does not seem plausible. Another possibility is activation of an intrinsic stretch-related mechanism in the transplanted heart. For example, increases in right atrial pressure in the denervated mammalian heart can evoke an increase in HR and, when the pressure is decreased, the pattern is reversed.[33] Such a mechanism may account for the small amplitude, high-frequency variability in HR observed in transplants.[34] HR in the transplanted heart may also be influenced by catecholamines secreted from the adrenal gland, and such

a mechanism appears to mediate, in part, the exercise-induced increase in HR in this type of patient.[35] It is anticipated that a T_6 dermatome-level block, as produced by the neuraxial anesthetic, would significantly diminish sympathetic drive to the adrenal glands[36,37] and thus effect the reduction in HR observed in the transplanted patient. Such a mechanism could also contribute to the decrease in HR observed in the patients with normally innervated hearts, although these decreases may have been somewhat dampened by an intact baroreceptor reflex. Additionally, with these patients, it is conceivable that the fall in HR may have resulted from blockade of sympathetic cardioacceleratory fibres located in mid-thoracic segments.[38]

Regardless of the etiology underlying the cardiac response described in this report, it may be relevant that, preoperatively, the transplanted patient demonstrated a relatively low HR (77 beats·min^{-1}) and right bundle branch block suggesting dysfunction of the sinus node and conducting pathway. Consideration should be given to the possibility that such dysfunction may have contributed to the cardiovascular response described in this report. Of note, a relatively low incidence of sinus node dysfunction is reported with patients who have undergone transplantation using the bicaval anastomosis technique.[39,40] Of course, the effects of perioperative medications on the cardiac responses are unknown.

The cardiac transplant patient poses unique anesthetic challenges resulting from side effects of immunosuppressive agents, graft rejection and denervation. They are particularly sensitive to hypovolemia, as cardiac output is so dependent on preload (Frank-Starling mechanism).[1,3] This report illustrates that although cardiac transplant patients may tolerate neuraxial anesthesia admirably, a fall in HR may ensue which theoretically could have important physiological consequences. It is suggested that the change in HR described in this report was mediated by mechanisms intrinsic to the transplanted heart and/or by reduced catecholamine secretion from the adrenal medulla. As noted previously,[31] changes in HR in cardiac transplant patients should not be interpreted as unequivocal evidence for reinnervation of the transplanted organ.

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