Cardiac Arrest During Spinal Anesthesia: Common Mechanisms and Strategies for Prevention

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Cardiac arrests during spinal anesthesia are described as "very rare," "unusual," and "unexpected," but are actually relatively common (1–3). The two largest prospective studies designed to evaluate the incidence of complications during spinal anesthesia reported two arrests in 1881 patients (4) and 26 arrests in 40,640 patients (5) for an overall incidence of seven arrests for every 10,000 (0.07%) spinal anesthetics. A review of approximately 4000 regional anesthetics revealed six cases of severe bradycardia (pulse of 20 to 40 bpm) and six others (0.15%) with cardiac arrest after spinal anesthesia (3). These rates are high when compared with an incidence of three arrests from any cause for every 10,000 cases (0.03%) reported for patients undergoing noncardiac surgery (6). The incidence of cardiac arrest with spinal anesthesia is also frequent compared with the rate of one cardiac arrest for every 10,000 cases (0.01%) recently reported for epidural anesthesia (5).

Auroy et al. (5) reported that all but one of the 26 cardiac arrests that occurred during spinal anesthesia were related to the anesthetic. Advanced age and high ASA physical status could contribute to these arrests, but these factors are often conspicuously absent (1,3). The closed claims analysis by Caplan et al. (1) reported 14 cardiac arrests with a mortality rate that exceeded 40% in healthy patients undergoing minor procedures. Comparable outcomes were reported in young patients in a study of 20,000 consecutive spinal anesthetics. One-half of the patients who experienced cardiac arrest in the operating room during spinal anesthesia were <30 years old (7). The fact that many of these arrests occur in healthy young adults during minor surgery raises the possibility that many of them are avoidable.

Keenan and Boyan (8) reviewed all types of anesthesia-related cardiac arrests at a hospital over a 15-yr period and concluded that almost half were related to inadequate ventilation and that two-thirds of the anesthetic cardiac arrests were "avoidable." Does the same pattern apply to the subset of cardiac arrests that occur during spinal anesthesia? Because sedation is used for over 80% of patients who undergo spinal anesthesia (4,9), the potential role of sedation in these arrests must be considered.

The evidence for a respiratory etiology for the arrests that occur during spinal anesthesia is sparse. Spinal anesthesia sensory levels up to T4 do not lead to hypoventilation, but are associated with mild hyperventilation (10,11). Before the widespread use of pulse oximetry, it was argued that oversedation played a key role in the arrests during spinal anesthesia. It is now difficult to invoke hypoxemia as the primary cause of cardiac arrests during spinal anesthesia because they occur in the setting of oxygen saturation readings of 95–100% at the time of the arrests (2,12,13). Studies of the side effects of spinal anesthesia have also failed to corroborate a primary respiratory etiology for these arrests. In fact, none of these prospective studies has found a link between sedation and cardiac arrest during spinal anesthesia (4,5,9).

Because the cardiac arrests that occur after spinal anesthesia are not closely linked with sedation or known effects of spinal anesthesia on respiratory drive, alternative mechanisms should be considered. Evidence for a circulatory etiology for these cardiac arrests comes from physiology studies using healthy volunteers who have experienced bradycardia and cardiac arrest in settings that mimic the effects of spinal anesthesia (14,15). Most of these effects are directly or indirectly related to the blockade of sympathetic efferents during spinal anesthesia. For example, the level of sympathetic blockade during spinal anesthesia is often two to six levels higher than the sensory level, so a patient with a T4 sensory block may have completely blocked cardiac accelerator fibers that originate from T1 to T4 (16). Blockade of these fibers can result in a variety of bradyarrhythmias that are discussed later.

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A more important effect of the inhibition of the sympathetic efferents during spinal or epidural anesthesia is a significant decrease in venous return to the heart. Baron et al. (17) found that cardiac vagal tone is enhanced primarily through reduced venous return. The effect of spinal anesthesia on venous return can be profound. Reductions in the right atrial pressure of 36% after low spinal levels (below T4) and by 53% after higher levels of blockade have been reported (11). With intravascular fluid losses, these effects are even more dramatic. For example, with removal of 10 mL of whole blood per kg of body weight in a study setting, the decrease in central venous pressure during spinal anesthesia averages 66% (10).

These decreases in preload may initiate reflexes that cause severe bradycardia. Three such reflexes have been suggested (13). The first involves the pacemaker stretch. The rate of firing of these cells within the myocardium is proportional to the degree of stretch. Decreased venous return results in decreased stretch and a slower heart rate. The second reflex may be attributable to the firing of low-pressure baroreceptors in the right atrium and vena cava. The third is a paradoxical Bezold-Jarisch reflex, in which mechanoreceptors in the left ventricle are stimulated and cause bradycardia.

Vagal-induced bradycardia has been demonstrated in the study setting. Jacobsen et al. (18) studied the effect of epidural anesthesia on left ventricular diameter with echocardiography in eight unpremedicated young volunteers. Two of them developed bradycardia and hypotension after 25 min with anesthetic levels at T8 and T9. This was associated with a reduction of up to 22% in left ventricular diameter. In both cases, the changes were reversed by head-down position and rapid infusion of IV fluids. Human pancreatic polypeptide was used as a marker of parasympathetic activity and its simultaneous increase with the decreases in heart rate observed is consistent with vagal activation.

Could such reflex responses to decreases in preload cause more than bradycardia? Studies of the hemodynamic effects of graded hypovolemia have demonstrated progressive vagal symptoms including sweating, nausea, and syncope (14). The resulting decreases in central venous pressure were comparable to those observed during spinal anesthesia (10,11). One of the seven healthy subjects progressed from vagal symptoms to abrupt sinus arrest (14). In a separate study, two healthy subjects experienced vagal arrests after they had 10 mL/kg of blood withdrawn to simulate acute blood loss with sensory epidural block levels of T4 to T6 (15).

Taken together, these studies demonstrate that decreases in preload can precipitate not only classic vagal symptoms, but also full cardiac arrest. Although one might assume that maintaining preload during spinal or epidural anesthesia is a uniform practice of anesthetists, the literature demonstrates otherwise. Geffin and Shapiro (3) reported that prophylactic preloading with a bolus of 300 to 750 mL was not practiced during the 5-yr period when they experienced 13 cases of severe bradycardia or cardiac arrest during spinal or epidural anesthesia. Cardiac arrests have also been reported in settings where decreases in afterload are added after epidural anesthesia has been initiated. A report of bradycardia/cardiac arrest during epidural or spinal anesthesia revealed that five of these events were associated with initiating sodium nitroprusside infusions and in two cases pulmonary artery pressures were noted to decrease just before the onset of bradycardia (19).

Because a high degree of cardiac vagal activity can occur during spinal anesthesia (16), patients with strong resting vagal tone should be at increased risk for cardiac arrest during spinal anesthesia. The term "vagotonia" describes the clinical situation of resting bradycardia, atrioventricular block, or complete atrioventricular dissociation that is present in 7% of the population (20). In vagotonic patients asystole can occur when procedures that increase vagal activity are performed (3,12,16,20,21).

There is evidence that other patient-related factors increase the risk of strong vagal effects leading to bradycardia and cardiac arrest during spinal anesthesia. Moderate bradycardia during spinal anesthesia is defined as a heart rate of $<$50 bpm. Spinal anesthesia itself is associated with slowing of the heart and rates below 50 bpm are observed in 9–13% of patients after spinal anesthesia (9,22).

Although vagal effects on heart rate during spinal anesthesia are typically mild, more profound changes may occur. Severe bradyarrhythmias have been reported with T4 levels of sympathetic blockade. In particular, spinal anesthesia has been associated with progression of first-degree heart block to second-degree heart block (23) and with the onset of sick sinus syndrome manifest after spinal anesthesia (24). Complete heart block and cardiac arrest may simply represent the most severe vagal-induced bradyarrhythmia associated with spinal anesthesia (25).

If cardiac arrest after spinal anesthesia is the far end of a spectrum that begins with minor slowing of the heart rate, then factors that have been linked with bradycardia during spinal anesthesia may help predict which patients are at risk for cardiac arrest during spinal anesthesia. Carpenter et al. (9) reported that a baseline pulse of $<$60 bpm was associated with a fivefold increase in the odds of developing moderate bradycardia during spinal anesthesia. Typically, young patients have strong vagal tone, and they reported that ASA physical status I patients have a threefold increased risk for developing moderate bradycardia during spinal anesthesia. Current therapy

with β-blockers or block height above T6 were also important risk factors for bradycardia identified in this study. Others have reported that patients who are <50 years old (22) and patients with first-degree heart block (26) are also at increased risk for moderate bradycardia during spinal anesthesia. These risk factors are summarized in Table 1.

Worsening bradycardia has often been noted before the onset of cardiac arrest during spinal anesthesia (1,5). Although this bradycardia could simply represent an inexorable step in the progression from sinus rhythm to asystole, it is also possible that the bradycardia provides important clues about the etiology and the most appropriate treatment for these arrests. For example, bradycardia can serve as a surrogate marker for extensive sympathetic blockade. This is supported by the observation that 40% of patients with spinal levels above T4 develop moderate bradycardia (4). In addition, bradycardia can help identify patients with excessive vagal tone attributable to other causes such as those with athletic heart syndrome (20) or central volume depletion (14).

Factors known to increase the risk of moderate bradycardia during spinal anesthesia could help identify patients at risk for cardiac arrest during spinal anesthesia. To test if there is any association between the two, the presence or absence of these factors was reviewed by combining the cases of asystole or severe bradycardia after spinal anesthesia reported by Geffin and Shapiro (3), Mackey et al. (13), and Lovstad et al. (27) in Table 2. After excluding patient number 7 (the only patient that received epidural anesthesia) reevaluation of these cases using the risk factors listed in Table 1, suggests that these patients do fit a high-risk profile (see Table 2). At least one risk factor for bradycardia was documented in 17 of the 20 patients who received spinal anesthesia, and in half of the cases (10 of 20 patients) at least two risk factors were mentioned in the case reports. Ten patients were <50 years old, 9 had sensory levels above T6, 5 were ASA physical status I, 3 were taking β-blockers, and 2 had a baseline heart rate of <60. Table 2 may underrepresent the actual number of risk factors for bradycardia, because relevant information such as ASA physical status and baseline electrocardiogram results (heart rate and PR interval) were not consistently reported.

The risk factors listed in Table 1 are also frequently observed in representative case reports (2,12,21,25) available through literature searches using PubMed. In approximately half of these cases, at least two risk factors for bradycardia were identified. This consistent pattern suggests that the risk factors for bradycardia may help identify patients who are more susceptible to vagal predominance leading to circulatory collapse and asystole during spinal anesthesia. The presence of a single risk factor from Table 1 does not make it certain that a patient will experience severe bradycardia or cardiac arrest. However, when two or more of the factors listed in Table 1 are present, the patient may be considered high-risk for bradycardia and cardiac arrest during spinal anesthesia.

Table 1. Risk Factors For Moderate Bradycardia (Pulse <50 bpm) During Spinal Anesthesia

Baseline heart rate <60 bpm
ASA physical status I (versus ASA physical status III or IV)
Use of beta-blocking drugs
Sensory level above T6
Age <50 yr
Prolonged PR interval

Often two or more of these factors are present in patients who receive spinal or epidural anesthesia for labor analgesia or for cesarean delivery. With the similarities between spinal and epidural anesthesia one might expect a comparable rate of cardiac arrest during epidural anesthesia. The decreased incidence of cardiac arrest associated with epidural anesthesia compared with spinal anesthesia is a relatively new finding that has not been explained (5). One possibility is that the incremental dosing and slower onset of epidural anesthesia may allow time for compensatory mechanisms (e.g., upper body vasoconstriction) to compensate for the decrease in preload. Alternatively, the physiologic changes associated with pregnancy may help explain the small rate of cardiac arrest observed in these settings. Pregnancy is associated with changes in autonomic control and at-term heart rates of 90–95 bpm are typical. This may be attributable to decreased parasympathetic tone during pregnancy (28). If vagal predominance plays a key role in the cardiac arrests that occur during spinal or epidural anesthesia, then the weaker vagal tone associated with pregnancy may decrease this risk.

Although multiple factors may lead to cardiac arrest during spinal anesthesia, a common mechanism is vagal predominance. More rigorous patient selection could decrease the risk of cardiac arrest during spinal anesthesia. For example, it may be appropriate to reconsider the use of spinal anesthesia for a patient with "vagotonia." Similarly, it may be prudent to contemplate a different technique when significant blood loss or the use of vasodilators is anticipated. It is difficult to know how much weight to give these factors, but they deserve consideration when selecting the most appropriate anesthetic technique for an individual patient.

When spinal anesthesia has been selected for a patient, maintaining adequate preload is a key to decreasing the risk of bradycardia and cardiac arrest during the case. Observations from physiology studies

Table 2. Risk Factors for Bradycardia Documented in Patients with Severe Bradycardia or Cardiac Arrest During Spinal Anesthesia

Study	Patient	Risk factors for bradycardia (Other factors)
Geffin and Shapiro	1	None
	2	ASA physical status I, age <50 yr
	3	Use of beta-blocking drugs
	4	None
	5	ASA physical status I, age <50 yr, sensory level above T6
	6	ASA physical status I, age <50 yr, baseline heart rate <60 bpm
	7	(Excluded: Patient received epidural anesthesia)
	8	Age <50 yr, sensory level above T6
	9	ASA physical status I, age <50 yr, baseline heart rate <60 bpm
	10	None
	11	ASA physical status I, age <50 yr
	12	Use of beta-blocking drugs
	13	Age <50 yr
Mackey et al.	14	Age <50 yr, sensory level above T6
	15	Use of beta-blocking drugs, sensory level above T6
	16	Sensory level above T6
Lovstad et al.	17	Age <50 yr, sensory level above T6
	18	Sensory level above T6
	19	Sensory level above T6
	20	None
	21	Age <50 yr, sensory level above T6

(14,15) and multiple case reports (3,4) emphasize the importance of volume loading and prompt replacement of fluid losses. Decreases in preload can occur so quickly with altering position, releasing a tourniquet, and other common perioperative events that there may not be time to give sufficient volumes of fluid over several minutes. When an abrupt decrease in preload is suspected, placing the patient in the head-down position and rapidly infusing IV fluids can be helpful (15,18). If this is not possible, or if it does not rapidly reverse vagal symptoms, the administration of atropine or a vasopressor may be appropriate. Anticipating an impending cardiac arrest can be difficult because a large preload deficit and the resulting increase in vagal tone may manifest initially as only bradycardia. Treating mild bradycardia (pulse <60 bpm) during spinal anesthesia may be appropriate especially if the patient has multiple risk factors as listed in Table 1.

Atropine may be recommended to treat bradycardia during spinal anesthesia because glycopyrrolate is ineffective in this setting (4). Treatment of bradycardia with atropine may decrease the morbidity of the arrests that occur during spinal anesthesia. Brown et al. (29) reported three cardiac arrests during a period when 10,080 spinal anesthetics were performed "without an episode of cardiac arrest resulting in neurologic injury." This was attributed to vigilance and their "willingness to utilize IV atropine (0.4–0.6 mg), ephedrine (25–50 mg), and epinephrine (0.2–0.3 mg) in stepwise escalation of therapy when bradycardia develops following spinal anesthesia." Similarly, Geffin and Shapiro (3) reported full recovery in all 12 patients treated for bradycardia or asystole after spinal anesthesia. This treatment included atropine for 11 of the 12 cases. It was typically used in combination with a vasopressor (ephedrine, epinephrine, or phenylephrine) (3). Aggressive vagolytic treatment with atropine and ephedrine were also used in the five successful resuscitations reported by Lovstad et al. (27). Taken together, this represents 20 successful resuscitations in settings where atropine is typically used as the first-line therapy.

Unfortunately, not all of the arrests that occur during spinal anesthesia are successfully treated, and fatal arrests still occur in healthy patients. Recently, a 17-yr-old (ASA I) patient suffered cardiac arrest during a knee arthroscopy using spinal anesthesia and could not be resuscitated despite "adequate resuscitation efforts" (27). When the bradycardia is profound or a full cardiac arrest occurs after spinal anesthesia, the early administration of epinephrine can be critical. The vasodilation caused by spinal anesthesia can make cardiopulmonary resuscitation ineffective. Successful resuscitation requires a coronary perfusion pressure gradient of 15 to 20 mm Hg and during spinal anesthesia this may require epinephrine 0.01 to 0.1 mg/kg (30). Currently, epinephrine is administered during only 25–40% of cardiac arrests after spinal anesthesia and up to 25% of these arrests are fatal (3,5). Earlier and more consistent use of epinephrine has been recommended (1,29,30) and could improve outcomes after cardiac arrest during spinal anesthesia.

Summary

Although many factors can contribute to cardiac arrest during spinal anesthesia, vagal responses to

decreases in preload often play a key role. Patients with risk factors for bradycardia or overt vagal symptoms during spinal anesthesia appear to be at increased risk for cardiac arrest during spinal anesthesia. This information has important implications. For example, the potential for vagal predominance should be considered when recommending spinal anesthesia for a specific patient. When a spinal anesthetic is selected, maintaining preload should be a priority, and prophylactic preloading with a bolus of IV fluid should not be omitted before initiating spinal anesthesia. Standard regimens for volume preloading may not be sufficient to maintain adequate preload, so a low threshold for administering additional fluid boluses, using vasopressors or repositioning the patient to augment venous return, may be appropriate. For patients with bradycardia during spinal anesthesia, the stepwise escalation of treatment of bradycardia with atropine (0.4–0.6 mg), ephedrine (25–50 mg), and, if necessary, epinephrine (0.2–0.3 mg) may be appropriate. For severe bradycardia or cardiac arrest, full resuscitation doses of epinephrine should be promptly administered. With the popularity of spinal anesthesia and the reported frequency of these arrests, the potential impact of these interventions on further improving the safety of spinal anesthesia could be substantial.

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