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Severe Bradycardia during Spinal and Epidural Anesthesia Recorded by an Anesthesia Information Management System

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Background: **Bradycardia and asystole can occur unexpectedly during neuraxial anesthesia. Risk factors may include low baseline heart rate, first-degree heart block, American Society of Anesthesiologists physical status 1, β-blockers, male gender, and high sensory level. Anesthesia information management systems automatically record large numbers of physiologic variables that are combined with data input from the anesthesiologist to form the anesthesia record. Such large databases can be scanned for episodes of bradycardia.**

Methods: **To select spinal and epidural anesthetics that did not also involve general anesthesia, 57,240 automated anesthesia records were scanned. Obstetrical patients and patients younger than age 12 yr were excluded. The electronic records selected were then scanned for episodes of moderate (heart rate < 50 and ≥ 40 beats/min) or severe (heart rate < 40 beats/min) bradycardia.**

Results: **A total of 6,663 cases (11.6%) met the inclusion criteria. Among the 677 cases of bradycardia (10.2%) were 46 cases of severe bradycardia (0.7%). In the final multivariate logistic regression analysis, baseline heart rate less than 60 beats/min ($P \leq 0.0001$) and male gender ($P \leq 0.05$) contributed significantly to risk for a severe bradycardia episode (odds ratio [OR]), 14.1 and 95% confidence interval [CI], 6.9–28.0, and OR, 2.1 and 95% CI, 1–4.3, respectively). For the 631 episodes of moderate bradycardia (9.5%), the final multivariate model included baseline heart rate less than 60 beats/min (OR, 16.2; 95% CI, 12.4–22.0), age younger than 37 yr (OR, 1.4; 95% CI, 1.1–1.7), male gender (OR, 1.4; 95% CI, 1.2–1.8), nonemergency status (OR, 1.7; 95% CI, 1.2–2.4), β-blockers (OR, 1.6; 95% CI, 1.1–2.3), and case duration (OR, 2.0; 95% CI, 1.6–2.4) as significant risk factors. Time of occurrence of a bradycardia event was distributed widely across the entire duration of a case.**

Conclusions: **Moderate or severe bradycardia may occur at any time during neuraxial anesthesia, regardless of the duration of anesthesia. Low baseline heart rate increases the risk for bradycardia.**

BRADYCARDIA and asystole, with serious consequences, can occur unexpectedly in healthy patients receiving neuraxial anesthesia.[1–3] These arrhythmias after the induction of neuraxial anesthesia are well documented in case reports[4–9] and studies.[1,10–13]

Specific clinical risk factors that contribute to the development of bradycardia have been evaluated. Carpenter *et al.* studied 952 patients receiving spinal anesthesia and found a 13% incidence of bradycardia that was associated with low baseline heart rate (BHR), American Society of Anesthesiologists (ASA) physical status 1, preoperative use of β-adrenergic blocking agents (β-blockers), and high-peak sensory level.[11] Patients designated ASA physical status 1 had 3.5-fold increased odds for bradycardia as compared with patients designated ASA physical statuses 3 and 4. Curatolo *et al.* found that the use of a tourniquet and female gender were associated with a reduced incidence of bradycardia during epidural anesthesia.[10] Liu *et al.* associated prolonged PR interval in the electrocardiogram with increased incidence of bradycardia during spinal anesthesia.[14] The pathophysiology of bradycardia and circulatory collapse during neuraxial anesthesia is unknown, but a number of theories have been offered.[12,15–23] These theories focus primarily on the similarity to vasovagal syncope, wherein a decrease in venous return in combination with increased inotropic state of the left ventricle can trigger bradycardia and hypotension, which may result in dizziness or loss of consciousness. There is considerable speculation that a paradoxical form of the Bezold–Jarisch reflex is somehow involved.

Anesthesia information management systems (AIMS) automatically record a large number of physiologic variables that are combined with data input from the anesthesiologist to form the anesthesia record. The AIMS database permits a high degree of precision in the recording of physiologic variables. All data are stored electronically. In our department, an AIMS has been used successfully to detect intraoperative incidents for quality improvement.[24] In addition, such large databases can be scanned and searched for factors associated with adverse events, such as bradycardia, that might otherwise go unnoticed.

The goal of the present study was to evaluate the contributions of patient characteristics and intraoperative factors to the occurrence, severity, and clinical course of bradycardia during neuraxial anesthesia. We wished to use multivariate models of these characteristics and factors to develop profiles of patients more at risk for bradycardia. We specifically tested the hypotheses that younger age, male gender, β-blockers, ASA 1 and 2 physical status, and low preinduction BHR increased the risk for bradycardia during neuraxial anesthesia.

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Materials and Methods

Data Collection and Verification

By 1994, a computerized anesthesia record-keeping system (Compurecord; ARI-Agilent Technologies, Pittsburgh, PA) was installed in both of this institution's clinical sites (St. Luke's and Roosevelt divisions). In addition to full demographic data and intraoperative medications, this system records the most recently measured values for blood pressure, heart rate, and hemoglobin oxygen saturation (measured by finger pulse oximetry) every 15 s. The automated anesthesia records of all surgical cases performed in the operating rooms of St. Luke's-Roosevelt Hospital Center for a 2-yr period were scanned to select spinal and epidural anesthetics that did not also involve general anesthesia. Scanning of automated records was performed using a proprietary software component provided with our AIMS (Processed Quality Assurance, Compurecord; ARI-Agilent Technologies), which enables the selection of cases based on specific inclusion criteria and definitions of bradycardia. Obstetrical patients and patients younger than 12 yr were excluded from the study. The presence of bradycardia was defined as a heart rate less than 50 beats per minute (bpm) for at least four 15-s consecutive recording epochs.[11] For the purpose of analysis, levels of bradycardia were defined as severe for heart rates less than 40 bpm and moderate for heart rates less than 50 and 40 bpm or more.

To eliminate artifacts that may have been recorded, each automated anesthesia record involving bradycardia was reviewed by an anesthesiologist (J.B.L. or K.V.S.) who: (1) established that the case matched the criteria for inclusion in the study; (2) verified anesthesia starting and ending times, anesthesia induction, and surgical start times; (3) identified BHR when monitoring began; (4) checked the duration of the bradycardia episode and the nadir heart rate; (5) reviewed for missing data, *e.g.*, height, weight, and obtained these data (as possible) from patients' hospital medical records; (6) recorded medical conditions based on the free form narrative history and physical included in the electronic database (*e.g.*, hypertensive nephropathy, hypertension, or high blood pressure are equivalent); and (7) recorded preoperative medications. In addition, patients' hospital medical records were reviewed for mortality occurring within 48 h of surgery.

Blood pressure was measured and electronically recorded at baseline and at least every 5 min throughout the procedure. Heart rate and hemoglobin oxygen saturation were measured continuously and electronically recorded at 15-s intervals. After examining the methods used in this study, the Institutional Review Board of St. Luke's-Roosevelt Hospital Center determined that these methods belonged to a category that did not require its review or approval.

Statistical Methods

Demographic data are presented as mean ± standard deviation for continuous variables (*e.g.*, age) and as frequencies and percentages for discrete variables (*e.g.*, gender). In the urban population studied, the 25th percentile for age is established at 37 yr; hence, this was used to dichotomize the younger (≤37 yr) from the older patients (≥37 yr) for the statistical analyses. ASA physical status 1 and 2 patients (76%) were presumed to have similar clinical risks and, hence, were combined for data analyses. ASA physical status 3 patients were presumed to have different clinical risks from ASA physical status 4 patients but were combined to retain sufficient statistical power for analyses.

For continuous variables, patients who had bradycardia were compared with those who did not by Student *t* test. Similarly, one-way ANOVA was used to test associations among levels of bradycardia (severe, moderate, none) for continuous variables. Associations between the occurrence of bradycardia and discrete variables were tested by chi-square or by Fisher exact test, as appropriate. *A priori* assumptions regarding the contributions of age, gender, ASA physical status, specific medical conditions (including diabetes, atherosclerotic heart disease, and body mass index), chronic medications, and length of surgery (case duration) to the incidence of bradycardia guided the analysis. Variables that achieved a $P \leq 0.10$ level of significance on univariate analysis were retained for multivariate analysis. To not exclude a variable prematurely, no adjustments were made for multiple comparisons during the univariate analysis.

For the multivariate logistic regression models, variables pertaining to patient characteristics were entered first. Preexisting medical conditions and medications noted from the medical history were subsequently added to describe more fully the risk profile for bradycardia. Thus, odds ratios (OR) and 95% confidence intervals (CI) derived from the patient characteristics and full models were obtained in a stepwise fashion. Variables reported as significant contributors to bradycardia in the multivariate analysis achieved the $P < 0.05$ critical level of significance. Statistical analyses were performed using the Statistical Package for the Social Sciences version 5.0.2 (SPSS for Windows, Chicago, IL).

Results

The Department of Anesthesiology administered 57,240 anesthetics during the study period. Only the first operation was chosen for patients who received neuraxial anesthesia on more than one occasion during the study period. Of these, 6,663 cases (11.6%) involved spinal or epidural anesthesia and met the inclusion criteria. There were 677 cases of bradycardia for an inci-

Table 1. Patient Characteristics Evaluated With Respect to Bradycardia in Patients Undergoing Spinal or Epidural Anesthesia: Univariate Analysis

Variable	Totals		No Bradycardia		Moderate 40–50 bPM		Severe <40 bPM		
	No.	%	No.	%	No.	%	No.	%	*P*-value
Type of anesthesia									
Spinal	4,665	70	4,170	69.7	467	74.0	28	60.9	0.03§
Epidural	1,998	30	1,816	30.3	164	26.0	18	39.1	
Age (yr)*	—	—	55.2	±20.4	52.8	±21.3	55.9	±21.9	0.02§
ASA physical status									
1 and 2	5,078	76	4,536	75.8	507	80.3	35	76.1	0.04§
3 and 4	1,585	24	1,450	24.2	124	19.7	11	23.9	
Emergency									
Yes	1,101	17	1,040	17.4	56	8.9	5	10.9	0.00001§
No	5,562	83	4,946	82.6	575	91.1	41	89.1	
Body mass index									
< 30	5,453	84	4,862	83.6	550	88.7	41	89.1	0.003§
≥30	1,026	16	951	16.4	70	11.3	5	10.9	
Baseline heart rate	—	—	83.8	±14.6	65.5	±10.3	65.5	±13.2	0.00001†§
Gender									
Male	3,669	55	3,210	53.6	425	67.4	34	73.9	0.00001†§
Female	2,994	45	2,776	46.4	206	32.6	12	26.1	
Hypertension									
Yes	1,723	26	1,559	26.0	153	24.2	11	23.9	NS
No	4,940	74	4,427	74.0	478	75.0	35	76.1	
History of diabetes									
Yes	764	11	716	12.0	43	6.8	5	10.9	0.0006§
No	5,899	89	5,270	88.0	588	93.2	41	89.1	
β-blockers									
Yes	416	6	347	5.8	65	10.3	4	8.7	0.00004§
No	6,247	94	5,639	94.2	566	89.7	42	91.3	
Calcium channel blockers									
Yes	654	10	581	9.7	69	10.9	4	8.7	NS
No	6,009	90	5,405	90.3	562	89.1	42	91.3	
Angiotensin-converting enzyme inhibitors									
Yes	568	8	509	8.5	56	8.9	3	6.5	NS
No	6,095	92	5,477	91.5	575	91.1	43	93.5	
β-agonists									
Yes	321	5	298	5.0	21	3.3	2	4.3	NS
No	6,342	95	5,688	95.0	610	96.7	44	95.7	
Diuretics									
Yes	466	7	416	6.9	47	7.4	3	6.5	NS
No	6,197	93	5,570	93.1	584	92.6	43	93.5	
α_1-blockers									
Yes	90	1	74	1.2	16	2.5	0	0.0	0.02§
No	6,573	99	5,912	98.8	615	97.5	46	100	
α_2-agonists									
Yes	32	1	28	0.5	4	.6	0	0.0	NS
No	6,631	99	5,958	99.5	627	99.4	46	100	
Digoxin									
Yes	227	3	203	3.4	23	3.6	1	2.2	NS
No	6,436	97	5,783	96.6	608	96.4	45	97.8	

* Values are presented as mean ± SD. † Severe bradycardia compared to no bradycardia. § Moderate bradycardia compared to no bradycardia.
ASA = American Society of Anesthesiologists; bpm = beats per minute; NS = not significant.

dence of 10.2%, and there were no deaths. There were 48 patients with a BHR between 40 and 50 bpm on initiation of monitoring in the operating room. For 43 of these patients, heart rates continued above 40 bpm for the duration of the surgical procedure. These patients were not considered to have had episodes of bradycardia, so for the statistical analyses, they were included in the nonbradycardia group. There was nothing unusual in the demographic composition of this group, including the use of β-blockers, which was 14%. The remaining five patients were maintained in the bradycardia group because their heart rates were below 40 bpm during the surgical procedure.

Approximately twice as many spinal than epidural anesthetics were administered during the period of study. Spinal anesthesia was associated with an increased frequency of bradycardia episodes (10.6%), compared with epidural anesthesia (9.1%) (table 1). Among the 677 cases of bradycardia, 46 were severe, comprising nearly 1% of the patients included in this study.

Table 2. Risk of Severe Bradycardia (< 40 bpm) in Patients Undergoing Neuraxial Anesthesia: Steps in Multivariate Analysis

	Patient Characteristics		Patient Characteristics + Medical History		Patient Characteristics + Medical History + Chronic Medications		Patient Characteristics + Medical History + Chronic Medications + Case Duration	
	OR (risk)	95% CI	OR (risk)	95% CI	OR (risk)	95% CI	OR (risk)	95% CI
Baseline heart rate < 60 bpm	14.2	7.0—28.9	14.2	7.0—29.0	14.0	6.8—28.8	14.1	6.9—28.0
Age < 37 yr	NS		NS		NS		NS	
Male gender	2.0*	1.0—4.0	2.0*	1.0—4.0	2.0	1.0—4.1	2.1	1.0—4.3
Nonemergency	NS		NS		NS		NS	
ASA physical status 1–2	NS		NS		NS		NS	
Body mass index < 30	NS		NS		NS		NS	
Hypertension			NS		NS		NS	
Absence of diabetes			NS		NS		NS	
β-blockers					NS		NS	
α_1-blockers					NS		NS	
Case duration (min)							NS	

Values are appressed as odds ratios (OR) with $P < 0.05$ with their 95% confidence intervals (CI).

* $P < 0.06$.

ASA = american Society of Anesthesidogists; NS = not significant, $P > 0.05$.

Patient Characteristics, Medical History, Chronic Medications, and Case Duration: Univariate Analyses

On univariate analysis, patient characteristics that were risk factors for having a bradycardia episode included younger age, healthy patients (ASA physical status 1 or 2), nonemergency status, body mass index less than 30, low BHR, history of diabetes, use of β-blockers, use of alpha$_1$ blockers (α_1-blocker), and male gender (Table 1).

Severe Bradycardia. BHR less than 60 bpm increased risk for a severe bradycardia episode 16-fold (OR, 16.0; 95% CI, 8.0, 32.0). Risk for severe bradycardia for male patients was elevated more than 2-fold (OR, 2.5; 95% CI, 1.3, 4.7). None of the other factors studied, including age, diabetes, body mass index, or chronic medications, contributed to the risk for severe bradycardia.

Moderate Bradycardia. BHR less than 60 bpm increased risk for a moderate bradycardia episode 18-fold (OR, 18.3; 95% CI, 14.3, 23.6). Risk for moderate bradycardia for male patients was elevated nearly 2-fold (OR, 1.8; 95% CI, 1.5, 2.1) and was 50% higher for age younger than 37 yr (OR, 1.5; 95% CI, 1.2, 1.7). Chronic medications that contributed significantly to risk for moderate bradycardia were β-blockers and α_1-blockers, each doubling the risk (OR, 1.9 and 95% CI, 1.4, 2.5 and OR, 2.1 and 95% CI, 1.2, 3.6, respectively). Digoxin did not contribute to the risk for moderate bradycardia.

Patient Characteristics, Medical History, Chronic Medications, and Case Duration: Multivariate Analyses

Severe Bradycardia. In the final multivariate logistic regression model, BHR less than 60 bpm ($P \leq 0.0001$) and male gender ($P \leq 0.05$) continued to be the patient

Table 3. Risk of Moderate Bradycardia (< 50 and ≥ 40 bpm) in Patients Undergoing Neuraxial Anesthesia: Steps in Multivariate Analysis

	Patient Characteristics		Patient Characteristics + Medical History		Patient Characteristics + Medical History + Chronic Medications		Patient Characteristics + Medical History + Chronic Medications + Case Duration	
	OR (risk)	95% CI	OR (risk)	95% CI	OR (risk)	95% CI	OR (risk)	95% CI
Baseline heart rate < 60 bpm	16.0	12.4–20.7	15.9	12.3–20.5	15.4	11.9–19.9	16.2	12.4–22.0
Age < 37 yr	1.3	1.1–1.7	1.4	1.1–1.7	1.4	1.1–1.8	1.4	1.1–1.7
Male gender	1.3	1.1–1.6	1.4	1.1–1.7	1.3	1.1–1.6	1.4	1.2–1.8
Nonemergency	1.7	1.2–2.3	1.7	1.2–2.3	1.7	1.2–2.3	1.7	1.2–2.4
ASA physical status 1–2	NS		NS		NS		NS	
Body mass index < 30	NS		NS		NS		NS	
Hypertension			NS		NS		NS	
Absence of diabetes			1.5*	1.0–2.1	1.4*	1.0–2.1	1.5*	1.1–2.1
β-blockers					1.6	1.1–2.3	1.6	1.1–2.3
α_1-blockers					NS		NS	
Case duration (min)							2.0	1.6–2.4

Values are expressed as odds ratios (OR) with $P < 0.05$ with their 95% confidence intervals (CI).

* $P < 0.06$.

ASA = American Society of Anesthesiologists; NS = not significant, $P > 0.05$.

Table 4. Temporal Characteristics of Bradycardia in 677 Patients Undergoing Neuraxial Anesthesia

	Moderate Bradycardia 40 ≤ bpm < 50 (n = 631) 131.5 ± 3.6		Severe-Bradycardia <40 bpm (n = 46) 129.5 ± 10.3	
	Mean ± SEM	Median (quartile 1st, 3rd)	Mean ± SEM	Median (quartile 1st, 3rd)
Time from induction to heart rate < 50	50.7 ± 1.8	39 (17, 71)	37.8 ± 6.6	23 (8, 46)
Time from induction to heart rate < 45	*64.0 ± 4.8*	53 (22, 86)	51.0 ± 7.3	36 (17, 63)
Time from induction to heart rate < 40			*63.0 ± 8.1*	44 (28, 93)
Time from induction to heart rate < 35			*64.0 ± 12.9*	51 (33, 85)

Data are means ± SEM and medians with quartiles (1st, 2nd) of the time from induction of neuraxial anesthesia to the occurrence of a bradycardia event.

characteristics that contributed significantly to risk for a severe bradycardia episode (table 2).

Moderate Bradycardia. In the final multivariate model, patient characteristics that contributed significantly to risk for a moderate bradycardia episode were BHR less than 60 bpm (OR, 16.2; 95% CI, 12.4–22.0), age younger than 37 yr (OR, 14; 95% CI, 1.1–1.7), male gender (OR, 1.4; 95% CI, 1.2–1.8), and nonemergency status (OR, 1.7; 95% CI, 1.2–2.4) (table 3). Absence of diabetes fell short of statistical significance ($P = 0.06$) in the multivariate model. Of the chronic medications, only β-blockers increased risk in the multivariate model (OR, 1.6; 95% CI, 1.1–2.3). Case duration was a significant risk for moderate bradycardia in the multivariate model (OR,

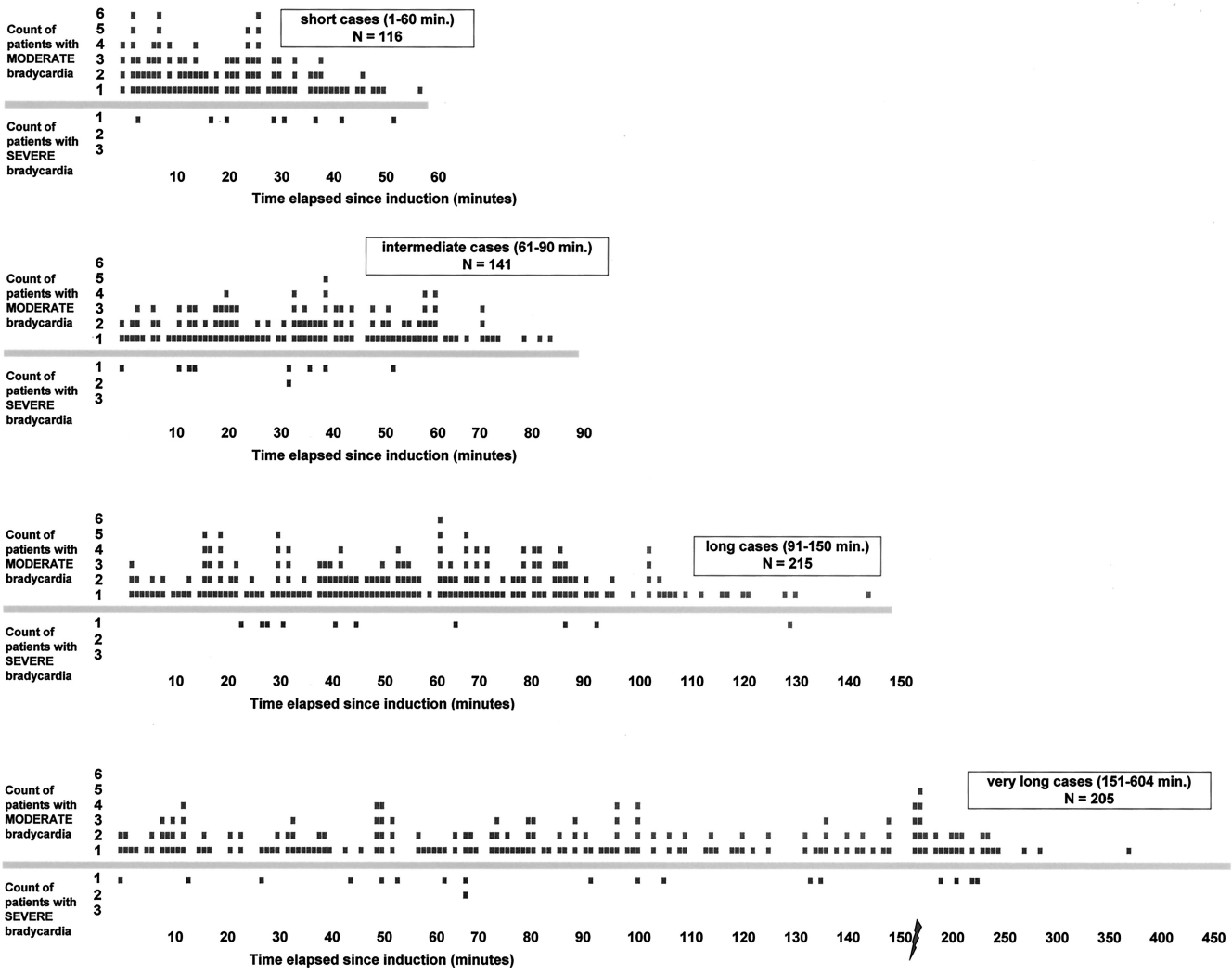

Fig. 1. Relationship between case duration and timing of episode of bradycardia. Each point corresponds to an episode of bradycardia. The points are plotted at the time elapsed since induction of neuraxial anesthesia when the episode of bradycardia occurred. The purpose of separating short, intermediate, long, and very long cases is to illustrate that episodes of bradycardia occur throughout the period of the anesthetic, regardless of case duration.

2.0; 95% CI, 1.6–2.4). Thus, in the final multivariate model, BHR less than 60, age younger than 37 yr, male gender, nonemergency status, β-blockers, and case duration were significant risk factors for moderate bradycardia.

Temporal Characteristics of Bradycardia. Duration of surgery was longer for patients who had any bradycardia event (130 ± 3 min) than those who did not (107 ± 1 min) ($P < 0.0001$). There was no significant difference in the mean duration of surgery between the moderate (131.5 ± 3.6 min) and severe bradycardia (129.5 ± 10.3) groups (table 4). For patients who had a bradycardia event, the lowest heart rate occurred, on average, in the 10-min interval between 55 and 65 min after induction (table 4, *italicized data*). However, the occurrence of the bradycardia event for both moderate and severe bradycardia was distributed widely across the entire duration of the case, regardless of case duration (fig. 1). For patients whose heart rates decreased to 35 or less, progression from a heart rate of 45 to 35 or less was rapid (table 4).

Discussion

Low-baseline Heart Rate Is a Strong, Independent Risk Factor for Severe and Moderate Bradycardia

The overall incidence of bradycardia less than 50 bpm during spinal and epidural anesthesia found in this study (10.2%) is similar to that found by found by Carpenter *et al.* (13%).[11] However, the risk contributed by BHR was found to be three times higher than that found by Carpenter *et al.* Male gender was also an independent risk for severe and moderate bradycardia, with a 2.1-fold and 1.4-fold increase in risk, respectively (tables 2 and 3). Thus, gender was clearly less influential as a risk factor than BHR.

Although none of the other factors we evaluated, including β-blockers and age, remained in the multivariate model for severe bradycardia, a number of significant risk factors for moderate bradycardia remained in the final multivariate model. For instance, age in the first quartile of the study population (younger than 37 y), nonemergency, absence of diabetes, β-blockers, and longer case duration increased the odds for moderate bradycardia between 1.4-fold and 2.0-fold in the multivariate model (tables 2 and 3). Contrary to the findings of Carpenter *et al.*,[11] our multivariate model found no difference in the incidence of bradycardia between ASA physical status 1 or 2 patients when compared with ASA physical status 3 or 4 patients (tables 2 and 3).

Nature of the Difference between Severe and Moderate Bradycardia

Surprisingly, most of the variables that were preconceived as risk factors for bradycardia failed to correlate with severe bradycardia in the multivariate model. This is especially interesting in light of the finding of multiple independent risk factors for the moderate bradycardia group. The moderate bradycardia group has a higher incidence of recognizable risk factors when compared with the severe bradycardia group. Which mechanisms leading to bradycardia might be called on to explain this paradox? Mackey *et al.* suggest that in the cases of severe bradycardia or asystole, the Bezold–Jarisch reflex would be one likely candidate.[7] The paradoxical effect of increasing cardiac inhibitory neural activity from an underfilled hypercontractile left ventricle is frequently referred to as the Bezold–Jarisch reflex. However, the Bezold–Jarisch reflex, as originally identified by Bezold in 1867, and confirmed by Jarisch in 1939, actually refers to the induction of profound bradycardia and hypotension in response to the intravenous injection of certain chemical cardiac irritants.[23]

The Bezold–Jarisch reflex has been invoked to explain the occurrence of head-up tilt table-induced syncope, because changes in sympathetic activity may be responsible for the syncope induced during this procedure.[25] Studies using tilt table testing in patients with inducible vasovagal reactions termed "vasodepressor dysfunction" or "neurally mediated syncope" have demonstrated increased heart rate and blood pressure just before syncope,[26,27] with transiently increased ventricular contractions.[20] In addition, catecholamine levels are elevated immediately before tilt table-induced syncope, and both syncope and excess catecholamine elaboration can be obliterated by oral administration of β-blockers or enalapril for days or weeks before the tilt table test.[25,28–30] Nevertheless, the effectiveness of β-adrenergic blockade on ventricular mechanoreceptors remains controversial.[16,17]

In the subset of patients with a BHR less than 60, we found chronic use of oral β-blockers to be neither risk-inducing nor protective. The fact that chronic use of oral β-blockers is an independent risk factor in the moderate bradycardia group suggests a direct drug effect; however, the reason for the lack of effect in the severe bradycardia group is not clear. Whereas previous oral administration of β-blockers prevented tilt table syncope attributed to the Bezold–Jarisch reflex, the chronic use of oral β-blockers did not prevent bradycardia associated with neuraxial anesthesia in this study. So, because oral β-blockers do prevent bradycardia and syncope induced by head-up tilt testing but failed to prevent bradycardia associated with neuraxial anesthesia in this study, it may be possible to cast doubt on the assumption that the Bezold–Jarisch reflex is the causative mechanism of bradycardia associated with neuraxial anesthesia.

Patients who present with a low BHR presumably have an increase in resting vagal tone and perhaps a more responsive vagal reflex; yet, there is no evidence that patients with a low BHR have intrinsic electrical disturbances such as sick sinus syndrome or atrioventricular block. Epidural and spinal anesthesia cause inhibition of

the preganglionic sympathetic efferent limb of the autonomic nervous system. It has been suggested that the resulting decreased venous return to the heart during spinal and epidural anesthesia may initiate a number of reflexes that precipitate bradycardia by a spared parasympathetic nervous system.[31] These reflexes can occur by blockade of cardiac accelerator fibers when the level of sympathetic blockade extends above T_4.[32] Although Carpenter *et al.*[11] reported that the patients with heart rates less than 30 bpm had peak sensory block levels of T_4–T_8, it is possible that the level of sympathetic blockade extended as many as six levels higher.[33,34] Another theory suggested to explain these reflexes involves collapse–firing of veno-atrial stretch receptors, located in the right atrium and vena cava, caused by invagination of the walls of the underfilled atria and great veins.[35,36] Finally, ventricular mechanoreceptors located primarily in the inferoposterior ventricular wall (nonmyelinated C-fibers) may play a role in initiating the bradycardia reflex. Our finding that patient history of diabetes and its association with the absence of bradycardia could be related to cardiac denervation syndrome.[37]

Timing of Bradycardia

Carpenter *et al.* reported a mean time of onset of bradycardia ($<$ 50 bpm) of 47 $\pm$ 38 min after induction of spinal anesthesia with a range of 1 to 204 min.[11] They state that "these mean times should not mislead one, however. Side effects occurred at all times during spinal anesthesia in patients who had been stable for 1h or longer. . .." In the present study, we found a similar mean time to bradycardia ($<$ 50 bpm) of 58 min and a wide range of time to bradycardia (1–495 min).

Figure 1 illustrates the broad scatter of the timing of episodes of bradycardia found in our study. This broad scatter indicates that the anesthesiologist must be prepared to treat moderate and severe bradycardia at any time after the induction of anesthesia. This finding may conflict with often-held clinical notions that the hemodynamic instability that may result from neuraxial anesthesia is a phenomenon that occurs within the first 30 min. Indeed, a patient who has been hemodynamically stable for 1 h or more is still at risk for moderate or severe bradycardia, which, if left untreated, may lead to asystole.

Differences between Our Study and Carpenter et al.*'s*

Our study was inspired by the findings of Carpenter *et al.*[11] It occurred to us that the power of the AIMS to collect heart rate data from a large number of cases at a high frequency and with a high degree of precision over long periods of time would give us the opportunity to clarify some of the compelling questions left unanswered by that study. In an effort to remove the confounding effects of general anesthesia, we excluded patients who had combined neuraxial and general anesthesia, whereas 12% of patients in the previous study also had general anesthesia. In addition, we included epidural and spinal anesthetics, because there exists a risk for bradycardia in both.[10,14]

Limitations of this Study

Items of information such as dermatomal level of sensory block, the nature and timing of treatments of bradycardia, fluid and blood loss data, and comments describing symptoms related to bradycardia (nausea or dizziness), were entered into the AIMS in a free-form manner, with varying degrees of precision, by clinicians who were not aware that the information would be analyzed in a study. Therefore, the reliability of that information was judged to be too low to justify any analysis in this retrospective study to prevent misleading conclusions. The strength of the study derives from its access to a large number of cases with precisely and frequently recorded vital signs.

In summary, this study demonstrated that during the administration of neuraxial anesthesia, the anesthesiologist must maintain vigilance for bradycardia throughout the entire case, regardless of the duration of anesthesia. Furthermore, patients with a BHR less than 60 have a significantly increased risk for moderate or severe bradycardia. The underlying mechanisms resulting in moderate and severe bradycardia during neuraxial anesthesia may be different, but in any event, remain poorly understood.

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