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Please cite this article as https://doi.org/10.4097/kja.19493

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Title: Risk factors associated with hypotensive bradycardic events during open shoulder surgery in the beach chair position

Short running head: Risk factors for hypotensive bradycardic events

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[The authors have no conflict of interest, *i.e.* personal, professional, or business affiliation relevant to the paper.]

IRB number: SMC 2019-01-061

Clinical Trial Registration: Clinical Research Information Service (CRIS: https://cris.nih.go.kr/cris/en/; ref: KCT0003642)

Word Count in manuscript: 2,676

The number of tables: 3

The number of figures: 1

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Risk factors associated with hypotensive bradycardic events during open shoulder surgery in the beach chair position

Running title: Risk factors for hypotensive bradycardic events

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Abstract

Background: Shoulder surgery in the beach chair position frequently causes hypotensive bradycardic events (HBEs), which are potentially associated with an increased risk of cerebral hypoperfusion. Here, we aimed to investigate the incidence and characteristics of symptomatic HBEs that require pharmacological interventions, and to identify specific risk factors associated with symptomatic HBEs.

Methods: We retrospectively examined the records of all patients aged ≥ 18 years who underwent shoulder arthrotomy in the beach chair position between January 2011 and December 2018 at a tertiary hospital. For patients who experienced HBEs while in the beach chair position, the minimum heart rate and systolic blood pressure were noted, as was the total dose of ephedrine or atropine.

Results: Symptomatic HBEs occurred in 61.0% of all cases (256/420). Two patients with symptomatic HBEs experienced postoperative neurological complications. Multivariable logistic regression analysis showed that preoperative interscalene brachial plexus block (ISB) and advanced age were risk factors associated with symptomatic HBEs (odds ratio [OR] = 3.240, 95% confidence interval [CI] = 2.003–5.242, *P* < 0.001; OR = 1.060 for each 1-year increase, 95% CI = 1.044–1.076, *P* < 0.001, respectively). Receiver operating curve analysis revealed that a threshold of 62 years of age had a moderate degree of accuracy for predicting symptomatic HBEs (area under curve

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= 0.764; 95% CI = 0.720–0.804; $P < 0.001$).

Conclusions: Considering the increasing risk of neurocognitive complications with aging, proactive hemodynamic management is needed, especially for elderly patients undergoing shoulder surgery in the beach chair position using ISB.

Keywords: Aged; Bradycardia; Hypotension; Interscalene block; Reflex; Shoulder surgery; Sitting position.

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Introduction

Shoulder surgery has become an increasingly common orthopedic procedure and is frequently performed in the beach chair position. Major advantages of this position include enhanced shoulder joint access, reduced bleeding, and broader anatomic perspective, facilitating tension-free examination of capsular anatomy [1].

However, this position is associated with considerable hemodynamic instability, which causes an increased risk of cerebral hypoperfusion [2–4]. Cerebral perfusion pressure decreases by approximately 15% in the sitting position in non-anesthetized patients and further decreases under anesthesia because of vasodilation and impaired venous return. Hypotensive bradycardic events (HBEs), a form of vasovagal reflex unique to the beach chair position, can potentially increase the risk of neurocognitive complications [5]. In South Korea, neurological injuries related to the beach-chair position for shoulder surgery were identified as typical injury profiles in the recent Korean Society of Anesthesiologists Legislation Committee report [4].

Although disastrous consequences of cerebral hypoperfusion have been limited to only a few reported cases, HBEs are not infrequent; thus, prediction of HBEs comprises a basic measure for proactive hemodynamic management. Therefore, we performed a retrospective chart review of adult patients who underwent open shoulder surgery in the beach chair position between January 2011 and December 2018 at our institution, to investigate the incidence and characteristics of HBEs

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and identify specific risk factors for clinically relevant HBEs.

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Materials and Methods

The present study was registered with the Clinical Research Information Service (CRIS: https://cris.nih.go.kr/cris/en/; ref: KCT0003642). The Institutional Review Board of our hospital (approval date: January 22, 2019) approved the study and waived the requirement for informed consent.

We retrospectively examined the records of all patients aged ≥ 18 years who underwent shoulder arthrotomy in the beach chair position during an 8-year period (January 1, 2011–December 31, 2018). Because most shoulder arthroscopic surgeries were performed in the lateral decubitus position at our hospital, we excluded patients who underwent shoulder arthroscopic surgery from this comparative analysis of HBEs. In addition, patients who underwent concurrent surgeries other than shoulder arthrotomy, and those who had an artificial pacemaker, were excluded from the study.

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All operations were performed by the same senior surgeon, who accrued extensive experience prior to 2011. Patients who underwent shoulder arthrotomy were routinely positioned with the back portion of the table at an approximately 60-degree angle, and with the hip and knee flexed; they remained in that position throughout the operation. In the beach chair position, the blood pressure cuff or arterial catheter was placed on the arm of the non-operative side, and intravenous access was attained.

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Anesthesia was maintained primarily with inhalational anesthetics (sevoflurane or desflurane), which were titrated based on the hemodynamic response of the patient and the judgment of the anesthesia team. In rare cases, anesthesia was maintained with total intravenous anesthesia (TIVA) using propofol and remifentanil.

When interscalene brachial plexus block (ISB) was performed for postoperative pain control and supplemental intraoperative analgesia, 15–20 mL of 0.75% ropivacaine with 1:200,000 epinephrine was typically injected via ultrasound-guidance. Immediately before their arrival in the operating room, patients received the block in a separate regional block room.

HBEs were defined as a reduction in heart rate of more than 30 beats per minute (bpm) within a 5-minute interval, any reduction below 50 bpm, and/or a reduction in systolic blood pressure of more than 30 mmHg within a 5-minute interval, or any systolic pressure below 90 mmHg while in the beach chair position [6–8]. These events were treated with intravenous atropine (0.5 mg) or ephedrine (5 mg) (or both), in accordance with our hospital’s protocol. Symptomatic HBEs, the primary outcome of the study, were defined as those HBEs requiring the aforementioned pharmacological interventions.

The minimum heart rate and systolic blood pressure were recorded during each HBE and used in the statistical analysis. The time between reaching the beach chair position and the first occurrence of an HBE was defined as the HBE onset time.

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The following were also noted for each case: demographic data, American Society of Anesthesiologists (ASA) physical status, current smoking status (current smokers were those who smoked within 1 week of surgery and had smoked at least 10 cigarettes per day for more than 1 year), alcohol abuse (*i.e.*, an average of 3–4 drinks per day, four or more times per week), history of bradycardia, atrial fibrillation, hypertension, diabetes mellitus (DM), stroke, preoperative medication with β-adrenergic blockers, type of surgery and anesthesia, duration of surgery, estimated blood loss (EBL), preoperative application of ISB, and total dose of atropine or ephedrine as treatment for HBEs. In addition, neurological complications during hospitalization were examined in each case. At our hospital, antihypertensive drugs except diuretics were administered with a sip of water on the day of surgery.

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Statistical analysis

Statistical analyses were performed using MedCalc for Windows software (ver. 18.11.; MedCalc Software, Ostend, Belgium). In all analyses, $P < 0.05$ indicated statistical significance. Univariable analyses were first performed to explore associations between variables of interest and the occurrence of symptomatic HBEs. Continuous variables were tested for normality using the Kolmogorov–Smirnov test. Non-normally and normally distributed continuous variables were analyzed with the Mann–Whitney U test and unpaired *t*-test, respectively. Categorical variables

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were analyzed with the χ^2 test or Fisher's exact test, as appropriate.

Second, a forward stepwise multivariable logistic regression analysis was conducted to identify independent risk factors for symptomatic HBEs. Any variables that were significant at $P \leq 0.2$ in the univariable analysis were candidates for inclusion in the multivariable analysis. Model goodness-of-fit was evaluated using the Hosmer–Lemeshow test. Independent risk factors are expressed as odds ratios (ORs) with 95% confidence intervals (CIs).

Receiver operating characteristic (ROC) curves were constructed to explore the sensitivity and specificity of each continuous variable identified as an independent predictor. Then, the optimal cutoff points for each predictor were determined at the maximum area under the curve (AUC) for the corresponding ROC curve.

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Results

Of the eligible subjects, 11 were excluded from the final analyses because of concurrent surgeries other than shoulder arthrotomy (n = 9) or artificial pacemaker insertion state (n = 2). In total, 420 patients were analyzed (Fig. 1).

HBEs occurred in 311 patients (74.0%), of whom 256 (61.0% of all subjects) experienced symptomatic HBEs that required pharmacological interventions. The most common form of symptomatic HBE was hypotension alone (195/256, 76.2%). Notably, 53 of the patients who had symptomatic HBEs experienced both hypotension and bradycardia, whereas eight patients experienced bradycardia alone.

Two patients with symptomatic HBEs exhibited postoperative neurological complications (contralateral isolated hypoglossal nerve palsy in a 74-year-old man and acute brain infarct in the basal ganglia in a 77-year-old woman). In both of these patients, symptoms were resolved by conservative treatment during hospitalization.

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Univariable and multivariable analyses of patients with and without symptomatic HBEs

In univariable analyses, significant differences were observed between patients with and without symptomatic HBEs in terms of gender, age, current smoking status, ASA physical status, EBL, duration of surgery, history of hypertension, DM, bradycardia, preoperative use of β-blocker,

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preoperative ISB, and type of anesthesia ($P < 0.05$, Table 1).

In addition to these 12 variables, one variable associated with symptomatic HBEs (at $P \leq 0.2$) in the univariable analysis (operation site) was included in the multivariable logistic regression analysis. Finally, preoperative ISB and advanced age were identified as independent risk factors associated with symptomatic HBEs (Table 2).

Preoperative ISB increased the risk of HBEs by nearly three-fold (OR = 3.240, 95% CI = 2.003–5.242, $P < 0.001$). When age was included as a continuous variable, advanced age was a strong risk factor for HBEs (OR = 1.060 for each 1-year increase, 95% CI = 1.044–1.076, $P < 0.001$). ROC analysis indicated that the optimal age threshold to predict symptomatic HBEs was > 62 years (sensitivity: 84.8%; specificity: 62.2%); a threshold of 62 years had moderate accuracy (AUC = 0.764; 95% CI = 0.720–0.804; $P < 0.001$) (Fig. 2).

When restricted to patients who received ISB, the site of blockade did not influence the risk of symptomatic HBEs (76.1% [137/180] on the right side *vs*. 69.6% [64/92] on the left side, P = 0.245)

Characteristics of symptomatic HBEs

The majority of symptomatic HBEs (207/256, 80.9%) occurred within 30 minutes after the beach chair position was achieved; the median (interquartile range) symptomatic HBE onset time was

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15.0 min (range: 5.0–30.0 min). While atropine was administered once in each case where it was needed, ephedrine was administered more than twice in 64.6% of patients who needed such treatment. In 20 patients, ≥ 30 mg of ephedrine was administered during surgery (Table 3).

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Discussion

The present study showed that clinically relevant HBEs requiring pharmacological intervention were a common phenomenon, occurring in 61.0% of adult patients who underwent open shoulder surgery in the beach chair position. To the best of our knowledge, the present study is the first to evaluate HBEs that occurred solely during open shoulder surgery. Although the definitions of HBEs are not identical among studies, the incidence observed in our current study is well within the published range (20.6–76.0%) for HBEs in arthroscopic shoulder surgery [7,9,10]. Although there is a high incidence of HBEs, their clinical significance during shoulder surgery is typically ignored by practitioners. This is primarily because HBEs are brief, and most respond rapidly to administration of anticholinergics or ephedrine. However, such events can lead to devastating complications associated with cerebral hypoperfusion, due to overestimation of cerebral perfusion pressure (frequently lower than blood pressure measured at the arm) and vascular compromise related to malpositioning of the head and neck [2].

In the present study, the majority of symptomatic HBEs (80.9%) occurred within 30 min after achieving the beach chair position, which is consistent with the time described in prior reports [3,8]. HBEs and orthostatic hypotension may have a similar triggering mechanism and involve the same efferent reflex limb [10]. The classical definition of orthostatic hypotension is a reduction in blood pressure within 3 min of standing. However, Roy et al. [12] reported that a considerable number

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of patients experienced a reduction in blood pressure within 10–45 min of beginning tilt-table testing.

HBEs are generally accepted as a form of vasovagal syncope mediated by the Bezold-Jarisch reflex, which occurs when venous pooling and increased sympathetic tone induce a low-volume hypercontractile ventricle [2,3,9,13]. By this mechanism, surgical positioning with the patient in the beach chair position induces an abrupt withdrawal of sympathetic outflow and an increase in vagal tone, which results in bradycardia and/or hypotension.

In this regard, a preoperative state of increased sympathetic tone might predispose patients to subsequent HBEs. Consistent with this hypothesis, epinephrine administered with a local anesthetic mixture for ISB [7], or added to irrigation fluid during shoulder arthroscopy [8], increased the incidence of HBEs. However, studies regarding the preventive effect of preoperative administration of β-adrenergic blockers have shown conflicting results [6,13]. In the present study, preoperative use of β-adrenergic blockers did not constitute an independent risk factor associated with the onset of HBEs. These mixed results may be attributed to the difference between acute intraoperative medication and chronic antihypertensive medication. Moreover, such results may be influenced by the different effects on β1- and β2-adrenergic receptors of β-adrenergic blockers according to the type and dose, both in prior studies and in our study.

In the present study, preoperative ISB was an independent risk factor associated with the onset of

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HBEs. Its association with HBEs has been proposed by many investigators [3,6,7,9], they suggested that the ISB procedure, or the use of epinephrine as an additive to the local anesthetic solution, might contribute to the development of HBEs in the beach chair position. Notably, ipsilateral stellate ganglion block is frequently accompanied by ISB (in up to 75% of cases); subsequent stellate ganglion block induces a reduced sympathetic and/or increased parasympathetic influence, thereby increasing the risk of HBEs [14,15]. However, one prospective randomized study revealed a similar incidence of HBEs between patients who underwent general anesthesia alone and those who underwent general anesthesia combined with ISB [10]. The most likely source of the difference between that study and ours is the age of the study cohorts (52.0 ± 9.5 *vs.* 63.3 ± 17.9 years) and different HBE evaluation periods (*i.e.*, throughout surgery beginning immediately after the start of TIVA *vs.* restricted to the time in which the patient was in the beach chair position).

Depending on the ISB side, differences in hypotension and/or bradycardia develop due to hemispheric lateralization of autonomic cardiovascular control (*i.e.*, sympathetic predominance in the right hemisphere and parasympathetic predominance in the left hemisphere) [15]. Based on this theory, one retrospective study proposed right-side ISB as a possible contributing factor to the occurrence of HBEs [9]. In that study, the incidence of HBEs in patients with right-sided blocks was 27.3% (12/44), whereas it was 5.3% (1/19) in patients with left-sided blocks. However, there

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was no predominance of right-sided blocks among patients with symptomatic HBEs in the present study (76.1% in right-sided blocks *vs.* 69.6% in left-sided blocks, $P = 0.245$). Another study also failed to find a predominance of right-sided blocks associated with symptomatic HBEs [6].

In the present study, advanced age was identified as a strong risk factor associated with the onset of symptomatic HBEs. An age of > 62 years, which was the optimal threshold in ROC analysis, predicted symptomatic HBEs with a moderate degree of accuracy. Aging is associated with a reduction of sympathetic-parasympathetic control of cardiac rhythm, which manifests as an increased prevalence of orthostatic hypotension. Although different afferent pathways are involved, advanced age has also been identified as an independent risk factor of vagally mediated bradycardia after peritoneal stretching or manipulation of abdominal visceral organs [16]. It is uncertain whether age-related autonomic changes directly promote the Bezold-Jarisch reflex. Presumably, age-related autonomic and baroreflex dysfunction might increase the risk of HBEs in the elderly [17].

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In particular, an increased risk of HBEs in the elderly is clinically important in that appropriate regulation of cerebral blood flow declines in an age-related manner [18]. In addition, minimum cerebral perfusion pressure increases to the hypertensive range in an age-related manner [18]. Thus, a brief HBE can increase the risk of cerebral ischemia and contribute to neurocognitive complications in the elderly. Indeed, in the present study, postoperative neurological

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complications occurred solely in elderly patients with symptomatic HBEs (hypoglossal nerve palsy in a 74-year-old man and acute brain infarct in a 77-year-old woman). Because no intracranial vascular lesion or mass was identified postoperatively in either of these two cases, intraoperative cerebral hypoperfusion could not be ruled out as a causative mechanism [19].

This study had several potential limitations. First, the involvement of multiple practitioners for management of HBEs might have resulted in inconsistency regarding assessment of symptomatic HBEs. When HBEs occurred, 0.5 mg atropine or 5 mg ephedrine was administered intravenously, in accordance with our institutional treatment protocol (typically based on severity and duration). Thus, we do not believe that the characteristics of symptomatic HBEs were influenced by the presence of multiple practitioners. Second, a variety of beach chair position angles were used (*i.e.*, between 45 and 80 degrees, according to surgeon preference); thus, our results did not match those obtained in studies where the beach chair position angle differed from ours [20]. Lastly, we did not precisely assess the severity of symptomatic HBEs, due to the inherent limitations of the retrospective study design. However, the minimum heart rate and systolic blood pressure, as well as the total dose of atropine or ephedrine administered as treatment for HBEs, may serve as indicators of HBE severity.

In conclusion, the present study revealed a high incidence (61.0%) of clinical relevant HBEs requiring pharmacological interventions in adult patients who underwent open shoulder surgery in

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the beach chair position. In addition, ISB prior to general anesthesia and advanced age were identified as risk factors associated with clinically relevant HBEs. Thus, in the context of the age-related increase in risk of neurocognitive complications, careful hemodynamic monitoring and vigilant maintenance of adequate cerebral perfusion pressure are needed, especially for elderly patients undergoing shoulder surgery in the beach chair position using ISB.

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Table 1. Comparison of clinical characteristics between patients with and without symptomatic hypotensive bradycardic events (HBEs)

	With symptomatic HBEs (n = 256)	Without symptomatic HBEs (n = 164)	P-value
Gender: female/male	179 (69.9%)/77 (30.1%)	73 (44.5%)/91 (55.5%)	< 0.001*
Age (years)	70.3 ± 12.1	52.3 ± 20.0	< 0.001*
Current smoking: yes/no	12 (4.7%)/244 (95.3%)	23 (14.0%)/141 (86.0%)	0.001*
Alcohol abuse: yes/no	34 (13.3%)/222 (86.7%)	17 (10.4%)/147 (89.6%)	0.372
BMI (kg/m^2)	25.2 ± 3.6	25.3 ± 3.6	0.723
ASA physical status: I/I/III	29 (11.3%)/176 (68.8%)/51 (19.9%)	70 (42.7%)/76 (46.3%)/18 (11.0%)	< 0.001*
EBL (mL)	258.5 ± 217.9	189.1 ± 197.5	0.001*
Duration of surgery (min)	119.1 ± 30.4	107.7 ± 38.7	0.002*
Operation site: right/left	166 (64.8%)/90 (35.2%)	96 (58.5%)/68 (41.5%)	0.193
History of hypertension: yes/no	162 (63.3%)/94 (36.7%)	51 (31.1%)/113 (68.9%)	< 0.001*
History of DM: yes/no	53 (20.7%)/203 (79.3%)	20 (12.2%)/144 (87.8%)	0.025*
History of atrial fibrillation: yes/no	13 (5.1%)/243 (94.9%)	6 (3.7%)/158 (96.3%)	0.495
History of bradycardia: yes/no	26 (10.2%)/230 (89.8%)	5 (3.0%)/159 (97.0%)	0.007*
Preoperative use of β-blocker: yes/no	31 (12.1%)/225 (87.9%)	10 (6.1%)/154 (93.9%)	0.043*
Preoperative ISB: yes/no	201 (78.5%)/55 (21.5%)	71 (43.3%)/93 (56.7%)	< 0.001*
Type of anesthesia: ISB only/inhalational/inhalational + remifentanil/TIVA	5 (2.0%)/183 (71.5%)/67 (26.2%)/1 (0.3%)	2 (1.2%)/89 (54.3%)/71 (43.3%)/2 (1.2%)	0.002*

Data are presented as means ± standard deviations or numbers (proportions).

BMI: body mass index, ASA: American Society of Anesthesiologists; EBL: estimated blood loss; DM: diabetes mellitus; ISB: interscalene brachial plexus block; TIVA: total intravenous

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anesthesia.

*Statistically significant difference ($P < 0.05$).

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Table 2. Multivariable logistic regression analysis: independent risk factors associated with symptomatic hypotensive bradycardic events

Variable	OR	95% CI	*P*-value
Preoperative ISB	3.240	2.003–5.242	< 0.001
Age	1.060	1.044–1.076	< 0.001

ISB: interscalene brachial plexus block; OR: odds ratio; CI: confidence interval.

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Table 3. Clinical characteristics of symptomatic hypotensive bradycardic events (HBEs)

Variable	Patients with symptomatic HBEs (n = 256)
HBEs onset time (min)	15.0 (5.0–30.0)
Minimum HR (bpm) in patients with bradycardia (n = 61)	47.0 (44.0–49.0)
Minimum SBP (mmHg) in patient with hypotension (n = 248)	78.0 (73.0–82.0)
Patients who required ephedrine administration	246 (96.1%)
1 dose	87
2 doses	50
≥ 3 doses	109
Patients who required atropine administration	46 (18.0%)

Values are medians (interquartile ranges) or numbers (proportions).

HR: heart rate; BPM: beats per minute; SBP: systolic blood pressure.

HBEs onset time was defined as the time between reaching the beach chair position and the first occurrence of an HBE.

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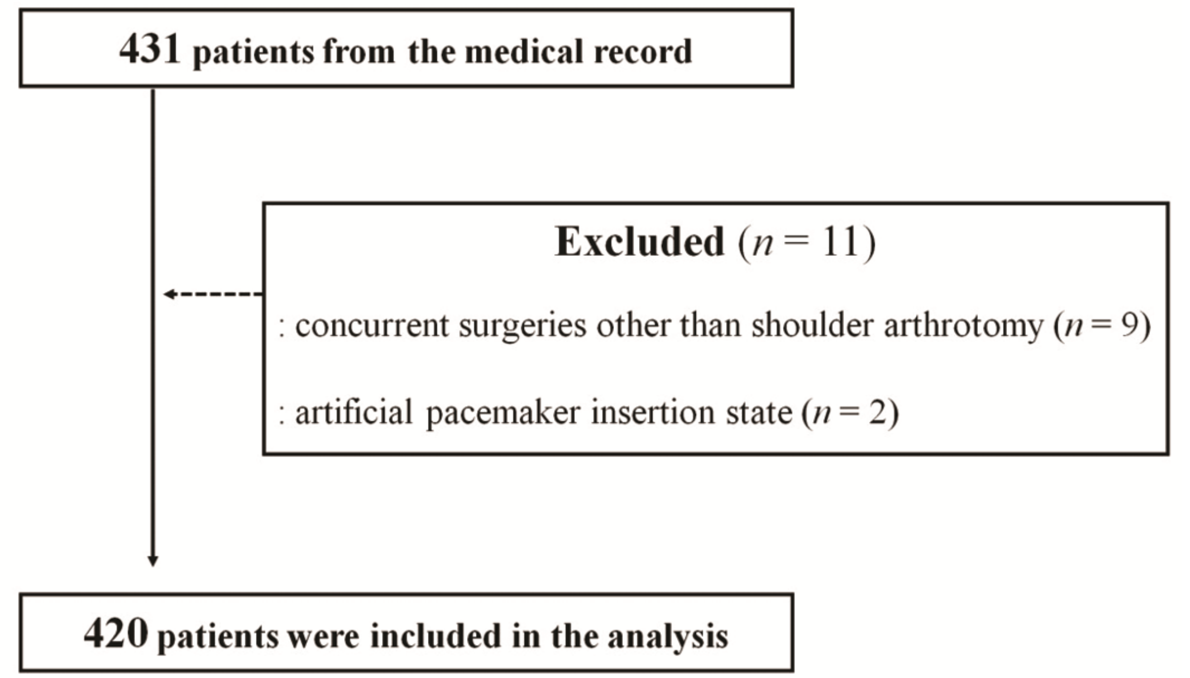

Figure 1. Flow diagram of the study.

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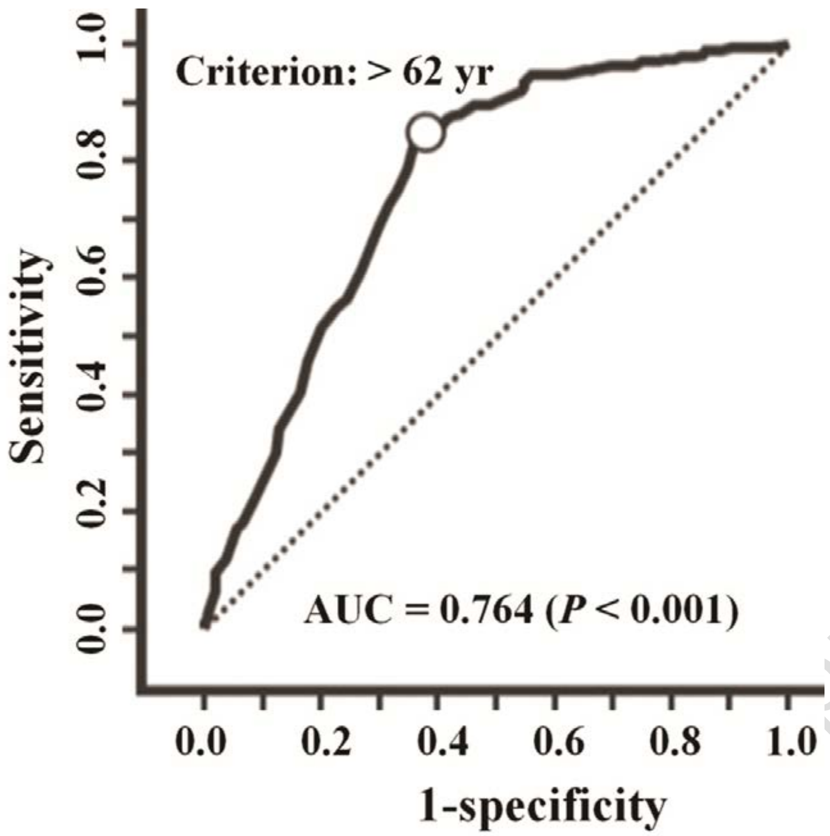

Figure 2. Receiver operating characteristic curves for patient age. Circle (○) indicates the optimal cutoff point for prediction of symptomatic hypotensive bradycardic events. AUC: area under curve.

Epub ahead of print

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