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# The Risk Factors for Spinal Anesthesia-induced Hypotension in Patients Undergoing Hip Fracture Surgery among the Elderly: A Retrospective Cohort Study

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**Introduction:** Hip fractures are increasing as the population ages, this is becoming a major public health problem, increasing the burden of all countries. Hip fracture surgery can be undertaken with spinal anesthesia; however, hypotension is the most common side effect of this technique. Spinal anesthesia-induced hypotension, even when treated, can lead to deterioration of the organs and systemic diseases.

**Objective:** We aimed to examine the modifiable risk factors of pre-operative hypotension among elderly patients, who underwent hip fracture surgery utilizing spinal anesthesia.

**Materials and Methods:** A retrospective cohort study was conducted in a university hospital, Thailand. Hip fracture patients who underwent hip fracture surgery under spinal anesthesia between; January 2014 and June 2019, were enrolled in this study. We collected patient characteristic, premedication, anesthetic factors and surgical factors from anesthetic and medical records of the hospital information system, and statistical analysis was performed using R program.

**Results:** From the 186 patients, the incidence of spinal anesthesia-induced hypotension was 46.8%. The dependent risk factors with increased risk of hypotension after spinal anesthesia were; increasing age, decreasing of baseline systolic blood pressure, American Society of Anesthesiologists (ASA) classification 3, sensory analgesia; equal to or higher than T5 (adjusted odd ratio; adj. OR=7.16), and those who received antihypertensive drugs more than 1 type as premedication (adj. OR= 6.91).

**Conclusion:** The number of antihypertensive drugs for premedication, and sensory analgesia were modifiable risk factors of hypotension after spinal anesthesia in hip fracture surgery.

**Keywords:** hip fracture, hypotension, premedication drug, spinal anesthesia

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Hip fractures are a major public health problem, placing a burden on all countries, additionally the prevalence of this disease is increasing as the population's age. The majority of hip fractures occur in the elderly population, with many co-morbidities and generally require surgical treatment.[1-3] This surgery carries with it a high amount of risk, with a high 30-day mortality rate (4-11.7%)[2,4-6] coupled with high, major adverse cardiac events (24.8%).[7]

Hip fracture surgery can be done under spinal anesthesia, with the benefits of postoperative pain control and decreasing postoperative pulmonary complications; however, the most common side effect is hypotension, which occurred in 33-40% of cases.[8] Spinal anesthesia-induced hypotension, even if it is treated, can lead to critical organ hypoperfusion and deteriorate systemic diseases[9-11] Especially in elderly patients, who have an increased risk of spinal anesthesia-induced hypotension, because of the

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physiologic changes such as autonomic dysfunction and decreasing in cardiac reserve, arterial compliance, vascular elasticity, baroreceptor sensitivity and left ventricular compliance.

Interestingly, the increasing risk of death from hip fracture surgery was associated with falling blood pressure detected during the perioperative period.[12] Most previous studies focused on prevention and treatment of hypotension after spinal anesthesia, and at present, only few studies have been identified risk factors, and no study, in hip fracture surgery yet.

This study aimed to find modifiable risk factors of hypotension after spinal anesthesia in patients undergoing hip fracture surgery. One of the modifiable risk factors is premedication with antihypertensive drugs, which is still an individual decision of the anesthesiologist; due to concerns over intraoperative hypotension[13], and this factor may have an effect on blood pressure after spinal anesthesia. Until now, no studies are determining the risk factors of hypotension after spinal anesthesia in hip fracture patients among the elderly. Hence, finding the modifiable risk factors of spinal anesthesia-induced hypotension in hip fracture surgery patients will help with the perioperative management for the anesthesiologist, and may be beneficial for intraoperative and postoperative outcomes.

## Materials and Methods

A retrospective cohort study was conducted in a university hospital, which is tertiary care and referral center in Southern Thailand. After the approval from the Ethics Committee of Faculty of Medicine, Prince of Songkla University was obtained eligible patients were identified from the hospital information system database, using a search term through a specific ICD10 including; 1) S720 (fracture of neck of femur), 2) S721 (pertrochanteric fracture), and 3) S722 (subtrochanteric fracture) who underwent one of the following procedures; which were coded by ICD9cm; 1) 79.15 (Closed reduction of fracture with internal fixation of femur), 2) 79.25 (Open reduction of fracture without internal fixation of femur), 3) 79.35 (Open reduction of fracture with internal fixation of femur), 4) 81.51 (Total hip replacement), 5) 81.52 (Partial hip replacement), and 6) 81.53 (Revision of hip replacement, not otherwise specified); during January 2014 until June 2019. Patients undergoing hip fracture surgery, who were anesthetized by spinal anesthesia, with an age of more than 60 years were included. Those who had hypotensive episodes before spinal anesthesia, multiple fractures or were converted to general anesthesia within 1 hour after spinal anesthesia were excluded from our study.

The outcome was to examine the risk factors of hypotension in elderly patients with hip fracture surgery, having undergone spinal anesthesia. Hypotension after spinal anesthesia was defied as: at least one episode and at least one minute of mean arterial pressure less than 65 mmHg or mean arterial pressure less than 20% of baseline[14] in patients having hypertension as an underlying disease, within 1 hour after spinal anesthesia.

Baseline patient characteristics, underlying diseases, premedication, anesthetic and surgical factors were reviewed and obtained from the anesthetic and medical records of the hospital information system as independent variables. Patient's characteristic information included: age, gender, body weight, height, body mass index, baseline blood pressure (at ward just before patient was sent to the operating room) and ASA classification. Underlying diseases, including diabetes, hypertension, previous congestive heart failure, previous coronary artery disease, previous stroke, dyslipidemia and chronic kidney disease were also acquired and recorded. Premedication drugs, which were Angiotensin-Converting Enzyme inhibitors (ACEI) or Angiotensin II receptor blocker (ARB), Alpha-adrenergic blockers, Beta-adrenergic blockers, Calcium channel blockers, Diuretics and Diazepam were recorded. The anesthetic factors, including type and dose of local anesthetic, intrathecal opioids added, intravenous sedation during spinal block, preload/coload and sensory analgesic level before the operation started were also acquired and recorded. Additionally, the surgical factors and type of fracture were recorded.

The sample size was calculated based on the formula of two-proportion difference of prevalence of hypotension after spinal anesthesia in low dose local anesthetic, 30%, and in high dose local anesthetic, 50%.[15] A total of 186 patients were required. Statistical analysis was performed using the R program (language and environment for statistical computing; version 3.4.5; R Core team, Vienna, Austria). Continuous variables, such as age, height, body weight and baseline systolic blood pressure were demonstrated as mean ± SD or median (IQR); depending on which one was appropriate for distribution of data. Discrete variables were demonstrated as frequency and percentage. Either, Chi-square ($\chi^2$) test or Fisher's Exact test were used to find the association of the risk factors and hypotension after spinal anesthesia. Multivariable analysis with multiple logistic regressions was used to determine the effect of each independent variable; after adjusting for the other independent variables.

## Results

From table 1, 186 patients aged over 60 years were eligible for this present study. Most of the population were female (68.3%). Their body weight, height, and body mass index were within the normal range. Around 50% of the patients were classified in ASA classification 3. For underling disease, the proportion of patients who had hypertension, dyslipidemia, and diabetes mellitus was 72.6%, 38.7%, and 23.7%, respectively, while patients who had previous coronary artery disease, previous stroke, and chronic kidney disease was less than 10% in this study (9.7%, 8.6%, and 6.5%, respectively).

Table 2 shows the proportion of patients who received premedication drugs before surgery. For premedication drugs, the proportion of patients who received antihypertensive drug as premedication; Calcium blocker, Beta blocker, ACEI or ARB, Alpha blocker and Diuretic were 32.3%, 20.4%, 4.8%, 1.1% and 1.1% respectively. However, there were 8.6% of patients who received antihypertensive drugs more than 1 type as premedication. Moreover, there were 6.5% who were sedated by diazepam before the surgery. For spinal anesthesia, 0.5% hyperbaric bupivacaine was used as a local anesthetic in 63.4% in the study. Mean of dose hyperbaric bupivacaine was 2.2 milliliters (ml.) and isobaric bupivacaine was 3.0 ml. The intrathecal opioid was 33.3%. They were sedated with fentanyl and/or midazolam intravenous drug before spinal anesthesia for 48.4%. and mean of preload/coload was 458.8 ml. Moreover, the highest and lowest level of analgesia was T2 and T12 respectively. Furthermore, the sensory level before the operation started which equal or more than T5 level was 20.4%.

All parameters were analyzed by the Chi-square and Fisher exact test (Table 3). The incidence of spinal anesthesia-induced hypotension was 46.8% which were female for 67.8% and male for 32.2 %. The factors associated with hypotension after spinal anesthesia were age, systolic blood pressure, ASA classification, premedication with antihypertensive drugs (beta-blockers), combined antihypertensive drugs as premedication and a sensory analgesia level equal to or higher than T5 ($p<0.05$). Moreover, dose of hyperbaric bupivacaine and isobaric bupivacaine were recorded and analyzed in this study, which were not statistically significant, p-value = 0.472 and p-value = 0.208 respectively.

After multivariate logistic regression (Table 4), the dependent factors that increased the risk of hypotension after spinal anesthesia in the elderly with hip fracture were increasing of age, decreasing of baseline systolic blood pressure, ASA classification III and sensory analgesia equal to or higher than T5, with adj. OR of 7.16. In addition, the patient who received antihypertensive drug more than 1 type as premedication had approximately seven times of the increased risk of hypotension, adj. OR was 6.91. Moreover, the high risk of premedication for hypotension after spinal anesthesia is Beta adrenergic blocker (p-value = 0.014).

In addition, the mortality rate during admission was 0% in both the hypotension and non-hypotension group.

**Table 1** Demographics data, underlying diseases, medications, and type of fracture of hip fractured patients

| Parameter | Number (%) Total = 186 | Mean ± S.D. |
|---|---|---|
| Age (years) | | 80.79 ± 8.38 |
| Sex | | |
| Female | 127 (68.3) | |
| Male | 59 (31.7) | |
| Systolic blood pressure | | 136.33 ± 18.81 |
| Body weight (kg.) | | 54.75 ± 11.32 |
| Height (cm.) | | 156.44 ± 8.72 |
| Body mass index (kg/m$^2$) | | 22.30 ± 3.80 |
| ASA classification (%) | | |
| ASA class 1 and 2 | 90 (48.3) | |
| ASA class 3 | 96 (51.6) | |
| Underlying disease (%) | | |
| Hypertension | 135(72.6) | |
| Dyslipidemia | 72(38.7) | |
| Diabetes mellitus | 44 (23.7) | |
| Previous Coronary artery disease | 18 (9.7) | |
| Previous Cerebrovascular disease | 16 (8.6) | |
| Chronic kidney disease | 12 (6.5) | |
| Type of fracture | | |
| Neck of femur fracture | 86(46.3) | |
| Trochanteric fracture | 94 (50.5) | |
| Subtrochanteric fracture | 6 (3.2) | |

ASA: American Society of Anesthesiologists, S.D.: Standard Deviation, kg.: Kilogram, cm.: Centimeter, m$^2$: Square meter

**Table 2** Premedication and spinal anesthesia

| Parameter | Number (%) | Mean ± S.D. |
|---|---|---|
| Premedication drugs | | |
| Calcium blocker | 60 (32.3) | |
| Beta blocker | 38 (20.4) | |
| ACEI or ARB | 9 (4.8) | |
| Alpha blocker | 1(0.5) | |
| Diuretic | 2(1.1) | |
| Diazepam | 12 (6.5) | |
| Premedication with antihypertensive drugs | | |
| 1 type | 77(41.4) | |
| > 1 type | 16(8.6) | |
| Spinal bupivacaine | | |
| Hyperbaric | 118 (63.4) | |
| dose (ml.) | | 2.2 (0.3) |
| Isobaric | 68 (36.6) | |
| dose (ml.) | | 3.0 (0.4) |
| Intrathecal opioid | 62 (33.3) | |
| Intravenous sedation before spinal block | 90 (48.4) | |
| Preload/coload(ml.) | | 458.8 (227.8) |
| Sensory analgesia level | | |
| ≥ T5 | 38 (20.4) | |
| < T5 | 148 (79.6) | |

*ACEI: Angiotensin-converting-enzyme inhibitor, ARB: Angiotensin II receptor blocker, ml.: milliliters*

**Table 3** Independence factors of hypotension after spinal anesthesia in elder patients, who underwent hip fracture surgery

| | Hypotension (%) | Non-hypotension (%) | P value |
|---|---|---|---|
| Number | 87 (46.8) | 99 (53.2) | |
| Age (years) | | | 0.002* |
| median (IQR) | 83 (80.0,87.5) | 81 (74.0,85.0) | |
| Sex | | | 1 |
| Female | 59 (67.8) | 68 (68.7) | |
| Male | 28 (32.2) | 31 (31.3) | |
| Systolic blood pressure | | | 0.019* |
| median (IQR) | 130 (120.0,140.0) | 140 (129.50151.5) | |
| Body mass index (kg./$m^2$) | | | 0.650 |
| < 25 | 67 (77.0) | 80 (80.8) | |
| 25-35 | 20 (23.0) | 19 (19.2) | |
| ASA classification* | | | 0.025* |
| 1 and 2 | 34 (39.1) | 56 (56.6) | |
| 3 | 53 (60.9) | 43 (43.4) | |
| Underlying disease | | | |
| Hypertension | 68 (78.2) | 67 (67.7) | 0.241 |
| Dyslipidemia | 37 (42.5) | 35 (35.4) | 0.394 |
| Diabetes mellitus | 25 (28.7) | 19 (19.2) | 0.278 |
| Previous Coronary artery disease | 10 (11.5) | 8 (8.1) | 0.591 |
| Previous Cerebrovascular disease | 7 (8.0) | 9 (9.1) | 1 |
| Chronic kidney disease | 5 (5.7) | 7 (7.1) | 0.946 |
| Premedication | | | |
| Calcium blocker | 32 (36.8) | 28 (28.3) | 0.280 |
| ACEI or ARB | 4 (4.6) | 5 (5.1) | 1 |
| Beta blocker | 25 (28.7) | 13 (13.1) | 0.014* |
| Diuretic | 1 (1.1) | 1 (1.1) | 1 |
| Alpha blocker | 1 (1.1) | 0(0.0) | 0.468 |
| Diazepam | 2 (2.3) | 10 (10.1) | 0.063 |
| Premedication with antihypertensive drugs | | | 0.028* |
| 1 type | 38 (43.7) | 39 (39.4) | |
| >1 type | 12 (13.8) | 4 (4.0) | |
| Spinal bupivacaine | | | 0.482 |
| Hyperbaric | 58 (66.7) | 60 (60.6) | |
| Isobaric | 29 (33.3) | 39 (39.4) | |
| Hyperbaric bupivacaine | | | 0.472 |
| median(IQR) | 2.2 (2,2.4) | 2.2 (2,2.3) | |
| Isobaric bupivacaine | | | 0.208 |
| median(IQR) | 3.2 (3,3.2) | 3.0 (2.8,3.2) | |
| Intrathecal opioid | 25 (28.7) | 39 (39.4) | 0.170 |
| Intravenous sedation before spinal anesthesia | 38 (43.7) | 52 (52.5) | 0.290 |
| Sensory analgesia level | | | < 0.001* |
| ≥ T5 | 28 (32.2) | 10 (10.1) | |
| < T5 | 59 (67.8) | 89 (89.9) | |

*ASA: American Society of Anesthesiologists, ACEI: Angiotensin-converting-enzyme inhibitor, ARB: Angiotensin II receptor blocker, IQR: Interquartile range, kg: Kilogram, $m^2$: Square meter, ml.: milliliters*

**Table 4** Multivariate Logistic Regression and parameters associated with hypotension

| Parameter | Crude OR (95%CI) | Adj. OR (95%CI) | P value (LR-test) |
|---|---|---|---|
| Age | 1.07 (1.03,1.11) | 1.07 (1.03,1.13) | 0.001* |
| Systolic blood pressure | 0.98 (0.97,1) | 0.98 (0.96,0.99) | 0.009* |
| ASA classification: 3 vs. 1 and 2 | 2.03 (1.13,3.65) | 2.1 (1.02,4.31) | 0.042* |
| Sensory analgesia higher than T5 | 4.22 (1.91,9.34) | 7.16 (2.8,18.3) | <0.001* |
| Premedication with antihypertensive drug | | | 0.004* |
| 1 type | 1.47 (0.8,2.71) | 2.32 (1.09,4.91) | |
| > 1 type | 4.54 (1.36,15.16) | 6.91 (1.79,26.58) | |
| Spinal bupivacaine: hyperbaric vs. isobaric | 1.3 (0.71,2.37) | 1.75 (0.85,3.62) | 0.126 |
| Intrathecal opioid: added vs. none | 0.62(0.34,1.15) | 0.75(0.36,1.56) | 0.439 |

*ASA: American Society of Anesthesiologists, OR: odd ratio, adj. OR: Adjust odd ratio, 95% CI: 95%* Confidence Interval, *LR-test: Likelihood Ratio Test*

## Discussion

This study found five factors that increased risk of hypotension after spinal anesthesia in the multivariate logistic model, these included; age, baseline systolic blood pressure (SBP), ASA classification and 2 modifiable risk factors; sensory analgesia and number of antihypertensive drugs for premedication.

Incidence of hypotension after spinal anesthesia from this study was 46.8%; compared with the study of Thitima et al. (40.8%)[15], Carpenter et al. (33%)[16], and Hartmann et al. (8.2%).[17] The incidence varies due to the criteria of hypotension. While our study was mean arterial pressure (MAP)<65 mmHg or decrease in MAP>20% of base line, due to the cerebral autoregulation[18]; Carpenter and Thitima defined hypotension as systolic blood pressure<90 mmHg, and Hartmann defined it as a decrease in MAP of>30%. However, incidence from this study was high, because we studied elderly patients, and hip fracture surgery for this population base is considered to be a high risk operation.[1,4]

We mainly studied the elderly to super elderly patients, and our results were similar to Pereira et al. and Trakkila and Isola.[19,20] The increasing age at 1 year, from 60 year-old, may increase the risk of hypotension after spinal anesthesia, by a factor of 1 time (OR=1.07, p = 0.001) due to physiologic changes in the elderly, such as autonomic dysfunction and decrease in the cardiac reserve and baroreceptor sensitivity.

Similar to earlier studies[15,20,21], the results of this present research, revealed that the decrease of baseline SBP is associated with an increased risk of developing hypotension. Low baseline SBP may have narrow safety margins of hypotension in any criteria.

ASA classification 3 was one of the significant factors which were accordant with the previous findings of Hartmann et al. and Pereira et al.[17,19] The American Society of Anesthesiologists defined ASA classification 3 as a patient with severe systemic disease that could be the reason for associated, increased risk of hypotension after spinal anesthesia.

For sensory analgesia, our findings support those of the previous reports[15,16,21], and type of operation. Level of blockage higher than T5 was the only one modifiable factor that could be confirmed the basic knowledge that sensory analgesia equal to or higher than T5 was a risk factor of hypotension after spinal anesthesia. From multivariate logistic regression, this factor significantly increased the risk of hypotension, by approximately 7 times (adj. OR=7.16, p-value<0.001). Although, hip fracture surgery does not require a sensory level higher than T5, there were about 20% of patients from this study who had a high sensory analgesia level (>T5). From these results, we suggest that all anesthesiologists should be aware and consider control the sensory analgesia level not higher than T5.

In general, for the prevention of intraoperative hypertensive crisis, the anesthesiologist will administer the patient's current antihypertensive drugs for premedication in the morning before surgery. Type and the combination of antihypertensive drugs is based on the opinion of the anesthesiologist. The multivariate logistic regression showed that patients who received more than 1 type of antihypertensive drug as premedication had a significantly, associated increased risk of hypotension, as much as by approximately 7 times (OR = 6.91). From this study, premedication with beta blockers was the only factor among antihypertensive drugs to be associated with hypotension after spinal anesthesia. The findings from our study could help the anesthesiologist to decide upon the optimal amount of premedication of antihypertensive drugs to be administered, for balancing risks and benefits of hypotension after spinal anesthesia and intraoperative hypertensive crisis. In the patient who currently had antihypertensive drug more than 1 type, the authors would recommend that holding or limiting them to only 1 type on the morning of surgery could decrease the incidence of spinal anesthesia-induced hypotension.

The strength of our study was that this is the first study that aimed to examine the association between antihypertensive as premedication, and hypotension after spinal anesthesia. In addition, we mainly studied elderly to super elderly patients, and in only one high risk operation (hip fracture surgery). Because of these reasons, our findings were suitable to apply for these groups of patients. However, there are some limitations in retrospective study. Different type of spinal bupivacaine used were included, despite this could be a confounding factor. Nonetheless, from this study, type and dose of spinal bupivacaine were not associated with hypotension after spinal anesthesia. The secondary data analysis from the hospital database that could not recruit some parameters was our limitation. Nevertheless, our database, which has been developing for over 15 years, was reliable and all important parameters associated with this study were included.

For further studies, a large multicenter retrospective cohort study, or a randomized control trial is required to find more modifiable risk factors, such as other premedication drugs for prevention of hypotension after spinal anesthesia.

## Conclusion

Hip fractures are increasing as the population ages. Hypotension after spinal anesthesia is a common side effect, and even if treated it can lead to deterioration of systemic diseases. Finding risk factors of hypotension after spinal anesthesia will help the perioperative management, and may provide benefits for intraoperative and postoperative outcomes. Tailoring the dosage of bupivacaine for geriatric patients, especially in those who had premedication with multiple types of anti-hypertensive drug to aim for the sensory analgesia at T10 level or prevent the higher block than T5 level should decrease the incidence of spinal anesthesia-induced hypotension. However, balancing risks and benefits of hypotension after spinal anesthesia and intraoperative hypertensive crisis should be considered for providing antihypertensive drugs as premedication.

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