Impact of multiple nerves blocks anaesthesia on intraoperative hypotension and mortality in hip fracture surgery intermediate-risk elderly patients: A propensity score-matched comparison with spinal and general anaesthesia

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Short title: **Anaesthesia techniques and hypotension in hip fracture surgery**

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Conflict of interest

Authors declare no competing interests.

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Abstract

Background: A Hip fracture in the intermediate-risk elderly patient is common and associated with a high rate of postoperative morbidity and mortality. There is a lack of consensus on the optimal anaesthetic technique but there is a clear association between intraoperative hypotension and postoperative morbidity and mortality. We aimed to compare the haemodynamic stability of three anaesthesia techniques: general anaesthesia (GA), continuous spinal anaesthesia (CSA), and multiple nerve blocks (MNB).

Methods: The primary outcome was the occurrence of intraoperative hypotension defined by a 30% decrease in mean arterial pressure (MAP) from baseline. Secondary outcomes included incidence of hypotension under 50 mmHg of MAP, time spent below MAP 50 mmHg, use of vasopressors, in-hospital, and 30-day mortality. We performed a propensity score-matched analysis.

Results: After screening and application of the exclusion criteria, 593 patients undergoing hip fracture surgery between the 1st of January 2015 and the 31st of December 2016 were included. The propensity score match analysis selected 43 patients in each group. The incidence of hypotension was significantly higher in the GA group than in the MNB and CSA groups: 39 (90%), 22 (51%), and 23 (53.5%), respectively; $p < 0.0001$. The incidence of MAP < 50 mmHg (59.5%, 23.3%, and 16.3%; $p <$ 0,0001), and the use of vasopressors (93%, 39.5%, and 25.6%; $p <$ 0,0001) were increased significantly in the GA group. With the GA group as a reference, odds ratios were reported in the MNB group at 0.08 [0.022–0.30] ($p = 0.0002$) for hypotension episodes; 0.17 [0.04–0.66] ($p = 0.01$) for hypotension < 50 mmHg for more than 3 min and 0.049 [0.013–0.018] ($p < 0.0001$) for use of vasopressors. The duration of hospital stay, postoperative complications, in-hospital and 30-day mortality rates did not differ significantly between the groups.

Conclusion: CSA and MNB provide better haemodynamic stability than GA. However, whatever the anaesthesia technique used, the mortality rates do not change even if MNB leads to less hypotension.

1. Introduction

The incidence of hip fracture worldwide is expected to be 2.6 million in 2025 (0.03%) [1]. Mortality is about 1.5%–3% at 5 days and 5%–8% 30 days after surgery [2–6]. The overall complication rate is between 6% and 19% according to studies [3–8]. Hypotensive episodes are common during hip fracture surgery in a frail elderly population. In non-cardiac surgery, there is evidence that intraoperative hypotension, namely absolute mean arterial pressure (MAP) < 50 mmHg, is associated with myocardial infarction, acute kidney injury, stroke, and an increased likelihood of mortality [3,9–11]. Absolute thresholds of arterial pressure are easier to use than a percentage decrease from a reliable baseline pressure and can thus more easily be incorporated into anaesthesia team's decisions [11,12]. Recent studies on patients undergoing major surgeries demonstrated reduced postoperative complications by maintaining intraoperative arterial blood pressure close to the preoperative baseline, but only a few data correlated intraoperative hypotension during hip fracture surgery with postoperative morbidity [3,13,14].

Intraoperative hypotension during hip fracture surgery might be associated with increased 30-day mortality regardless of the anaesthetic technique [13,14]. Different anaesthesia techniques, intravenous fluids and/or vasopressors can be used to limit the decrease of intraoperative MAP [15,16]. Studies have shown no benefit of general *versus* spinal anaesthesia on 30-day mortality [17,18]. There is a lack of consensus on the optimal anaesthetic technique for the high/intermediate-risk frail population. Spinal anaesthesia (SA) is often preferred in high-risk patients for its efficacy, minimal effect on mental status and respiratory function

[17,19]. However, because of the high prevalence of comorbidities and a reduction in physiologic compensatory mechanisms in frail patients [20], SA can be associated with severe and prolonged hypotension [3]. Continuous spinal anaesthesia (CSA), using fractionated low doses of local anaesthetic, has proven to maintain haemodynamic stability compared with general anaesthesia (GA) [15,17,21] and single-shot SA [15,22]. Multiple nerve blocks (MNB) might be an interesting alternative to avoid hypotension. Few observational or comparative studies with a small number of patients reported positive results on intraoperative haemodynamic stability of combined nerve block anaesthesia for hip fracture surgery [23–25]. The last clinical research trial [26] including more than 507 000 hip fracture cases reported that the overall comorbidity burden increased among patients undergoing hip fracture repair surgery in the last ten years. Throughout this same period, the incidence of postoperative complications either remained constant and the use of neuraxial anaesthesia decreased over time. Given the proposed benefits of regional anaesthesia, decreased utilisation may be of concern.

There is no study comparing GA, CSA, and MNB in high-risk elderly patients undergoing hip fracture surgery. The primary endpoint of this propensity score-matched analysis was to evaluate if MNB would better maintain intraoperative haemodynamic stability compared with CSA or GA.

2. Materials and methods

2.1. Study design, patients and type of anaesthesia

After ethical committee approval (CERAR IRB 00010254-2016-118) and clinical trial registration (ClinicalTrials.gov NCT03356704), all electronic intraoperative anaesthetic and perioperative records of consecutive patients undergoing hip fracture repair from the 1st of

January 2015 to the 31st of December 2016 were reviewed. The exclusion criteria were: multiple trauma, second hip fracture, single-shot SA, and medical records with missing perioperative data. We used the DxCare software (DxCare, Medasys, France) to access the clinical, laboratory, and outcome data for the pre and postoperative periods. We used eXacto software (eXacto, Mexys, Belgium) to access intraoperative data. Patients were allocated according to GA (total intravenous or inhaled anaesthesia), CSA or MNB. In our institution, three main anaesthesia techniques are used in elderly frail patients scheduled for hip fracture surgery. After a fascia iliaca compartment block, an intravenous propofol target-controlled infusion is started with an initial target plasma concentration set at 1.5 µg/mL, increased by increments of 0.5 ere allocated according to GA (total intravenous or inhaled anaesthesia), CSA or MNB. In our institution, three main anaesthesia techniques are used in elderly frail patients scheduled for hipent block, CSA consisted of an injection, via a 23-gauge multi-perforated catheter, of a loading dose of 2.5 mg of plain 0.5% bupivacaine [15]. Repeated doses of 2.5 mg of plain 0.5% bupivacaine were administered every 5 min until reaching a metameric sensory level at T10. The MNB technique consisted of three different blocks. A lumbar plexus block (Shamrock approach, ultrasound-guided associated with nerve stimulation) was done and 0.25 mL/kg of 0.33% ropivacaine was injected, with a maximum volume at 20 ml. A parasacral and quadratus lumborum 2 (QLB2) blocks were associated each with 0.2 mL/kg of 0.33% ropivacaine and a maximum volume of 15 mL. The rationale was to cover the posterior territory innervated by cluneal nerve endings for hemiarthroplasty and the lateral territory covered by iliohypogastric nerves rami for gamma nails. Superior cluneal posterior branches of the lumbar spinal nerves and L1 root are not anaesthetised by a lumbar plexus block centred on the L4 root [27]. The QLB 2 mainly targets the L1 root that gives iliohypogastric and ilioinguinal nerves and the local anaesthetic solution spreads back to the dorsal branches in cadavers [28]. To limit the risk of haematoma with multiple blocks procedure, we did the nerve blocks in case of normal values of the international normalised ratio and we resumed the use of DOACs for minimally 48 h. If necessary, depending on the plasma concentrations of DOACs, we used prothrombin complex concentrates. Sedation was systematically performed with trivial doses of propofol or ketamine.

2.2. Variables and outcome measurements

Demographic data and baseline characteristics noted from the patient records were age, sex, American Society of Anesthesiologists (ASA) status, anthropometric data, comorbidities, preoperative medications, lifestyle, and autonomy. A simplified frailty index (FI) [29] was calculated for every patient. The index is based on an 11-item evaluation scale in which each item corresponds to a patient's medical condition (**Appendix 1**) The number of items (rated 1) found in the patient divided by the total of 11 items used in the assessment creates the index value. This index is correlated with postoperative patient outcomes [29]. There is a stepwise increase in both morbidity and mortality for each item noted. The type of anaesthesia, the type of surgery, the use of cement, the time to surgery (from patient admission to surgery), the duration of surgery, the baseline values and intraoperative systolic, diastolic and mean arterial pressure, and the use of vasoactive drugs (ephedrine, phenylephrine, and norepinephrine) were noted. In the postoperative period, we collected data from the post-anaesthesia care unit (PACU): postoperative nausea/vomiting and the number of patients requiring morphine. The incidence of the following postoperative complications was noted: myocardial infarction (MI) (the diagnosis of MI was retained only if it was confirmed in the patient file by the cardiologist in charge) and increase in plasma troponin level, pulmonary embolism, pneumonia, and hypoxaemia (defined by the need for oxygen), postoperative cognitive dysfunction and stroke and acute kidney injury (defined as a 1.5-times increase in basal creatinine level according to the AKIN classification). Hospital mortality, 30-day mortality, duration of hospital stay, and admission to the intensive care unit (ICU) were also recorded.

2.3. Endpoints

The primary endpoint for intraoperative hypotension was defined as a decrease in MAP ⩾ 30% from a reliable baseline pressure noted during the pre-anaesthetic visit. Secondary endpoints included hypotension under MAP's threshold of 50 mmHg and the time spent below MAP < 50 mmHg (< 3 min, 3–10 min and > 10 min), the use of vasoactive drugs, hospital stay, hospital mortality, 30-day mortality and postoperative complications.

2.4. Sample size estimation and statistical analysis

According to the study of Biboulet et al. [15], we hypothesiSed that hypotension occurred in more than 80% of patients in the GA group and less than 30% of the CSA and LSPB groups. Assuming an n t hypotension occurred in more than 80% of patients in the GA group and less than 30% of the CSA and LSPB groups. Assuming 5-times increase in basal creatinine level according to than 600 patients were necessary in the initial population to define comparable sub-groups of patients after propensity score matching. Patients in the initial population were divided into 3 groups according to anaesthesia techniques (GA, MNB, CSA). Due to differences in baseline characteristics between patients, we performed a propensity score-matched analysis to adjust for the difference. Similar sub-groups of patients were obtained by matching individual observations with their propensity scores. The primary endpoint was then the number of patients with hypotensive events during surgery defined as a decrease in MAP ⩾ 30% from a reliable baseline pressure. The secondary endpoint was the number of patients with severe hypotensive events defined as (1) MAP < 50 mmHg; (2) duration of hypotensive event > 3 min; (3) need for vasopressors. The data are expressed as means (± SD) or medians (interquartile range) as appropriate for continuous variables and numbers (percentages) for categorical variables. The Shapiro-Wilk test was used to test the normality of continuous variables.

2.4.1. Univariate analysis

Categorical variables were compared using chi-squared or Fisher exact tests. The association between adverse hypotensive events and the anaesthesia technique is expressed by the odds ratio (OR) and its 95% confidence interval. Comparisons of continuous variables were performed by ANOVA or Kruskal-Wallis tests for multiple group comparisons and by t-test or Mann-Whitney test for two-group comparisons.

2.4.2. Propensity score matching method

Logistic regression was conducted with the initial population to evaluate significant covariates that should be included in the propensity score estimation model. This model included the following covariates that were measured before treatment and that are related to the treatment (age, body mass index, Simplified Frailty Score, ASA status 3–4, dependence, chronic obstructive pulmonary disease (COPD), congestive heart failure, hypertension, diabetes mellitus, β-blockers, angiotensin-converting enzyme inhibitors). Then, the propensity score was generated by a multivariable logistic model considering the patient's age, ASA status, frailty index, type of surgery, and cardiac ischemic disease. The selection process was done without replacement; patients were not returned to the sample after being matched. The maximum allowable difference between propensity scores, the calliper, was equal to 0.1. Statistical significance was set at $p < 0.05$. Bonferroni's correction was used for multiple comparisons. Data were analysed with SAS Enterprise version 7.1 (SAS Institute, Cary, NC).

Results

We identified 704 consecutive patients who underwent hip fracture surgery during the study period. Patients excluded from the analysis are reported in the flowchart (**Figure 1**). The analysis included 593 patients who met our inclusion and exclusion criteria: 361 patients in the GA group, 182 patients in the CSA group, and 50 patients in the MNB group. The patient's characteristics, comorbidities, preoperative medications, and surgical data are shown in **Table 1**. There were 3 cases of insufficient intraoperative anaesthesia in the CSA group in the overall population and 1 in the MNB group. After matching with a propensity score analysis, 43 patients were compared in each group (**Table 2**). There was no significant difference in patient demographic data except for congestive heart failure: 3/43 (7%) in GA group, 9/43 (21%) in MNB group and 13/43 (30%) in CSA group (p = 0,05), and use of clopidogrel medication (p = 0.03).

Figure 2 and Table 3 show that there were significantly more hypotensive events in the GA group without significant difference between the MNB and CSA groups. The incidence of hypotension was significantly higher in the GA group than in the MNB and CSA groups: 39 (90%), 22 (51%) and 23 (53.5%), respectively; $p < 0.0001$. The incidence of MAP < 50 mmHg (59.5%, 23.3%, and 16.3%; $p < 0,0001$), the time periods spent with MAP < 50 mmHg (**Figure 3**) and the use of vasopressors (93%, 39.5%, and 25.6%; $p < 0,0001$) were increased significantly in the GA group. For all parameters, there was no difference between the MNB and CSA groups. The ORs for hypotensive events and treatments, with the GA group as a reference, were as follows: group MNB (*vs.* GA) = 0.08 [0.022–0.30] (p = 0.0002), group CSA (*vs.* GA) = 0.08 [0.024–0.33] (p = 0.0003) for hypotension episodes; group MNB (*vs.* GA) = 0.20 [0.08–0.53] (p = 0.001), group CSA (*vs.* GA) = 0.13 [0.048–0.37] ($p < 0.0001$) for MAP < 50 mmHg; group MNB (*vs.* GA) = 0.049 [0.013–0.018] ($p < 0.0001$), group CSA (*vs.* GA) = 0.026 [0.007–0.1] ($p < 0.0001$) for use of vasopressors and group MNB (*vs.* GA) = 0.17 [0.04–0.66] (p = 0.01), group CSA (*vs.* GA) = 0.11 [0.024–0. 53] (p = 0.006) for hypotension < 50 mmHg for more than 3 min.

The incidence of morphine consumption in the PACU was lower in the MNB and CSA groups than in the GA group: 1 (2.3%), 1 (2.3%), and 6 (14%), respectively; p = 0.004. The number of admissions to the ICU was higher in the MNB group; p = 0.04. The duration of hospital stay, complications, in-hospital and 30-day mortality rates did not differ significantly between the three groups (**Table 3**).

Discussion

The results of the present study indicated that MNB and CSA provide better intraoperative arterial pressure control than GA during hip fracture surgery in intermediate-risk elderly patients with no difference between both regional anaesthesia groups. Compared with GA, we found a significantly lower incidence of intraoperative hypotension, hypotensive episodes < 50 mmHg, periods below the threshold of MAP < 50 mmHg and the use of vasopressors in the MNB and CSA groups. However, whatever the anaesthesia technique used, the mortality rates, and postoperative complications did not differ significantly between the groups. Our study is the first to compare the three anaesthesia techniques in a sufficient number of patients using a propensity score analysis.

In our study, the use of both regional anaesthesia techniques significantly limited the incidence of intraoperative hypotension and the percentage of patients with a decrease in the absolute value of intraoperative MAP < 50 mmHg as well as the duration of these events. The ORs rated a significant impact of anaesthetic techniques on hypotensive events and their treatments in favour of the use of regional anaesthesia techniques. The definition of hypotension we used in this study can be debated [30]. A decrease of more than 30% of the MAP detects only clinically relevant hypotension episodes [3,12]. MAP less than absolute thresholds of 50 mmHg for any duration has been reported to increase the risk of MI, kidney injury, and mortality [3,9–14]. Previous studies reported that a MAP < 50 mmHg for only 1 min significantly increased the risk for postoperative complications [9–11]. The associations based on relative thresholds were no stronger than those based on absolute thresholds [11]. What is important in our study is that the age and the ASA score of our patients were higher than all the studies associating the impact of intraoperative hypotension on postoperative morbidity and mortality [9–14]. In a systematic review by Wesselink et al. [14], only two of 42 articles involved patients with a median age > 80 years. The MAP thresholds the authors reported at < 50 mmHg, promoting higher morbidity and 30-day mortality than any other threshold, are reached in 32% of hip fracture patients [3,13].

Despite the difference in intraoperative hypotensive episodes between groups, we are not able to report any difference in-hospital mortality, 30-day mortality, or postoperative complications between the three groups of patients. It might seem paradoxical, as many studies have shown the direct relation between intraoperative hypotension and the risk of poor outcomes, including death (13, 14). In our study, avoiding hypotension does not change the patient's outcome. A recent clinical research trial [26] reported that the comorbidities and risk factors increased among patients undergoing hip fracture repair surgery in the last ten years. However, the incidence of postoperative complications remained constant whatever the anaesthesia technique used. It seems that choosing a different timing of postoperative outcome measurement or report morbidity, as a better metric to measure the outcome, would have end to similar results. This may be partly explained by the fact that patients in all three groups are at intermediate preoperative risk and that the addition of comorbidities could minimise the impact of low intraoperative blood pressure values. Several comorbidities $\geqslant 2$ has been reported as an independent predictor of mortality in patients operated for hip fracture surgery, incorporated or not in the Nottingham Hip Fracture Score [31]. Both comorbidity and old age may significantly predict the probability of death [32], two factors we constantly report in our patients. Finally, more than 20% of patients in the three groups scored ASA 4 after propensity score classification. Rates of death in hospitals have been reported at 1.8% in patients with ASA score 1–2 compared with 16.5% in ASA 4 patients [2]. These results may explain the importance of such a parameter compared with intraoperative hypotensive episodes.

The patients in the GA group received more vasoactive drugs to maintain intraoperative blood pressure thresholds. The use of ephedrine was the first-line vasopressor used in our patients as reported in the literature [16], then phenylephrine when necessary. A recent publication demonstrated that individualised targeted blood pressure, compared with standard management, reduced the risk of postoperative organ dysfunction in high-risk surgical patients [16]. On the other hand, the fact that the patients in the GA group received more bolus of vasoactive drugs might have had some consequences because selective α1-adrenergic agonists such as phenylephrine can promote some negative effects on cardiac output [33].

There is still a debate concerning the impact of anaesthetic technique on the hospital and 30-day mortality and the major complications in that specific group of patients. SA has been compared with GA. On the one hand, neuraxial anaesthesia was associated with a reduction in in-hospital mortality, pulmonary complications, and hospital stay [33,34]. On the other hand, the use of regional anaesthesia compared with GA was not associated with lower mortality risk [35,36]. In our study, we have chosen to not include single-shot SA. This is based on the demonstrated fact that single-shot SA provides less haemodynamic stability than CSA [22]. CSA provides fewer episodes of hypotension compared with a single intrathecal injection of 7.5 mg of bupivacaine [15]. Biboulet et al. [15] previously reported in a prospective randomised study that CSA provided better intraoperative blood pressure control than GA using propofol TCI or sevoflurane in elderly patients with cardiac comorbidities scheduled for hip fracture surgery. In our study, the induction doses of CSA, as well as the cumulating doses, were low (5 mg and 7.5 mg of 0.5% plain bupivacaine, respectively) which is consistent with the literature [15,35]. We did not report that MNB better maintained intraoperative haemodynamic stability compared with CSA. MNB with sedation as the sole anaesthetic technique has been advocated for hip fracture in small numbers of selected patients [23–25]. Our results are consistent with those of de Visme et al. [23] who compared single-shot SA and peripheral nerve blocks (lumbar plexus block, sacral plexus block, and iliac crest block). They did not report any significant difference in haemodynamic stability but they claimed a trend in favour of nerve blocks. Aksoy et al. [25] compared MNB and CSA for hip arthroplasty and reported that the MAP level was significantly higher in the MNB group during the whole intraoperative period. In those studies, the mean age of the patients ranged from 70 to 85 years old. The mean age of our patients in the three groups was 88 years old. Johnston et al. [24] compared MNB (femoral nerve block and lateral cutaneous thigh nerve block) with GA and single-shot SA and did not report any difference in 120-day mortality and hospital length of stay between groups.

The admissions to the ICU increased in the MNB group in our study compared with the GA group. The ICU stay is not related to an increase in complications and mortality in those patients. It can be related, even though not statistically significant, to the higher incidence of COPD and coronary artery disease among the patients, motivating the physicians to follow them more closely. Our results might confirm those of a recent study reporting that GA was associated with a shorter length of stay (1.28, 95% CI, 1.22–1.34) compared with SA in elderly patients scheduled for hip fracture surgery [37].

There are several limitations to our study. Despite the high number of patients and the fact that the same anaesthetists and surgical team managed the patients, it was a monocentric retrospective cohort study. Confounding factors and bias might have been concerned. In MNB, the patient's ASA status might be inaccurate; in some cases, it did not correspond to the real medical condition of the patients who were generally sicker (congestive heart failure) and had more preoperative comorbidities. A high number of patients were taking antiplatelet drugs in both regional anaesthesia groups, particularly clopidogrel in the MNB group. Neuraxial anaesthesia is a classic contraindication in patients taking clopidogrel or anticoagulants. The time between discontinuation of therapy and neuraxial anaesthesia is 5 days for clopidogrel. Early surgery facilitates effective analgesia, allows early mobilisation, and is associated with reduced morbidity and mortality [38]. Although performing deep block procedures after anticoagulants or clopidogrel is controversial, the complications of deep PNBs are less serious than those of neuraxial blockade and resolve without permanent complete neurologic damage. We have to admit that the MNB procedure can be complex and obvious skills should be advocated. The systematic review of Joubert et al. [39] reported that bleeding complications following peripheral nerve blocks were rare in patients receiving antiplatelet and/or anticoagulant medication. The overall estimate of the incidence of bleeding complications was 0.82% (0.64%–1.0%). Bleeding complications were reported mostly with lumbar plexus blocks. In our patients, we did not use deep blocks if severe haemostasis trouble or if curative anticoagulation were noted at the moment of the anaesthetic procedure.

The choice of a simple FI might also be debatable. However, it has been reported that a simple FI predicts disability, complications, and death as well as the more complex index [40,41]. We chose the simplified FI, which seems more suitable for the evaluation of elderly patients. We found a median value of 0.18, which corresponds to a 30-day morbidity rate of about 10%–25% and a 30-day mortality rate of about 1%–5%.

In conclusion, MNB and CSA limit significantly intraoperative hypotension episodes and mainly those with MAP < C50 mmHg compared with GA during hip fracture surgery in frail elderly patients. MNB seems no better than CSA on these points. Although a greater incidence of intraoperative hypotension was observed in intermediate-risk hip fracture patients undergoing GA, the anaesthesia technique per se did not influence the 30-day mortality.

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Table 1: Comparison by anaesthesia type in the initial cohort of 593 patients.

	General anaesthesia (n = 361)	Multiple nerve blocks (n = 50)	Continuous spinal anaesthesia (n = 182)	*p* value
Demographics				
Age (years)	80 [67–87]	86 [81–92]	88 [84–91]	< 0.001
Women n (%)	230 (64)	27 (54)	119 (69)	0.32
Body mass index (kg/m²)	23 [20–26]	23 [21–25]	22 [20–25]	0.29
Comorbidities and scores				
ASA				< 0.001
I	44 (12.2)	0 (0)	2 (1.1)	
II	191 (53)	4 (8)	76 (42)	
III	113 (3.3)	30 (60)	85 (46.7)	
IV	13 (3.6)	16 (32)	19 (10.5)	
Simplified Frailty Index	0.09 [0–0.18]	0.18 [0.09–0.18]	0.18 [0.09–0.18]	0.07
Chronic obstructive pulmonary disease, n *(%)*	20 (5.5)	8 (16)	22 (12)	< 0.001
Hypertension, n (%)	174 (49)	34 (68)	99 (62)	0.005
Congestive heart failure, n (%)	12 (3.3)	12 (24)	24 (13.2)	< 0.001
Diabetes, n (%)	47 (13)	13 (26)	27 (15)	0.05
Coronary Artery Disease, n (%)	33 (9)	18 (36)	29 (16)	< 0.001
Stroke, n (%)	45 (12.5)	10 (20)	26 (14.3)	0.33
Dementia, n (%)	87 (24)	14 (28)	61 (33.5)	0.06
Preoperative medications				
Antiplatelet therapy				
Aspirin n (%)	71 (19.7)	19 (38)	63 (64.6)	< 0.001
Clopidogrel n (%)	36 (10)	10 (20)	2 (1)	< 0.001
Anticoagulation therapy				
Vitamin K antagonist/heparin, n (%)	54 (15)	13(26)	31 (17)	0.14
Direct oral anticoagulants, n (%)	7 (2)	4 (8)	6 (3.3)	0.05
Times				
Time to surgery (h)	24 [16–42]	40.5 [23–55.5]	27 [21–44]	< 0.001
Surgery duration (min)	54 [35–73]	53 [40–63]	53 [38–70]	0.94
Type of surgery				< 0.001
Gamma nail, n (%)	164 (45.4)	27 (54)	94 (51.6)	
Hemiarthroplasty, n (%)	134 (38)	23 (46)	80 (44)	
Dynamic hip screw, n (%)	63 (17.4)	8 (4.4)	0 (0)	
Use of cement, n (%)	111 (30)	21 (42)	72 (39)	0.05

Median, interquartile range [25–75] for quantitative data or n (%) for qualitative data

<u>Table 2</u>: Comparison by anaesthesia type after application of propensity score matched analysis

	General anaesthesia (n = 43)	Multiple nerve blocks (n = 43)	Continuous spinal anaesthesia (n = 43)	*p* value
Demographics				
Age	86 [81–92]	86 [83–92]	88 [84–92]	0.75
Women n (%):	29 (67,4)	24 (55,8)	24 (58,1)	0.45
Body mass index (kg/m^2)	21.7 [20–25]	22.5 [21–25]	21 [19–25]	0.48
Comorbidities				
ASA				0.99
II	5 (11.6)	4 (9.3)	5 (11.6)	
III	29 (64.5)	30 (70)	28 (65.1)	
IV	9 (21)	9 (21)	10 (23.3)	
Simplified Frailty Index	0.18 [0.09–0.27]	0.18 [0.09–0.18]	0.18 [0.09–0.18]	0.80
Chronic obstructive pulmonary disease, n (%)	4(9.3)	6 (14)	3 (7)	0.66
Hypertension, n (%)	28 (65)	28 (65)	34 (79)	0.26
Congestive heart failure, n (%)	4 (9.3)	8 (18.6)	13 (30.2)	0.05
Diabetes, *n* (%)	8 (18.6)	12 (28)	12 (28)	0.51
Coronary artery disease, n (%)	9 (21)	15 (35)	13 (30.2)	0.34
Stroke, n (%)	11 (25.6)	7 (16.3)	7 (16.3)	0.45
Dementia, n (%)	16 (37.2)	12(28)	13 (30.2)	0.62
Preoperative medications				
Antiplatelet therapy				
Aspirin, n (%)	11 (25.6)	15 (35)	20 (46.5)	0.13
Clopidogrel, n (%)	8 (18.6)	9 (21)	1 (2.3)	0.03°
Anticoagulation therapy				
Vitamin K antagonist/heparin, n (%)	12 (28)	12 (28)	10 (23.3)	0.85
Direct oral anticoagulants, n (%)	1(2.3)	3 (7)	1 (2.3)	0.61
Times				
Time to surgery (h)	26 [17–53]	41 [23–55]	31 [22–47]	0.4
Surgery duration (min)	57 [42–65]	53 [40–64]	49 [37–70]	0.56
Type of surgery				0.09
Gamma nail, n (%)	19 (44.2)	24 (56)	19 (44.2)	
Hemiarthroplasty, n (%)	20 (46.5)	19 (44.2)	24 (56)	
Dynamic hip screw, n (%)	4 (9.3)	0 (0)	0 (0)	
Use of cement, n (%)	17 (39.5)	18 (42)	20 (45.6)	0.8

Median, interquartile range [25–75] for quantitative data or n (%) for qualitative data

°: $p = 0.03$: difference between CSA group and both other groups

Table 3: Outcomes by anaesthesia type: perioperative events and postoperative complications

	GA (n = 43)	MNB (n = 43)	CSA (n = 43)	GA *vs.* CSA *vs.* MNB (*p* value)
Haemodynamic				
Intraoperative hypotension, n (%)	39 (90)	22 (51)	23 (53.5)	< 0.0001
MAP < 50 mmHg, n (%)	25 (59.5)	10 (23.3)	7 (16.3)	< 0.0001
Use of vasoactive drugs, n (%)	40 (93)	17 (39.5)	11 (25.6)	< 0.0001
Analgesia				
Morphine in PACU, n (%)	6 (14)	1 (2.3)	1 (2.3)	0.04
Morphine at 24 h, n (%)	10 (23.2)	8 (19)	12 (27.9)	0.21
Surgery				
Time to surgery (h)	26 [17–53]	41 [23–55]	31 [22–47]	0.4
Surgery duration (min)	58 [42–65]	53 [40–64]	51 [37–70]	0.56
Reduction surgery, n (%)	0	1 (2.3)	1 (2.3)	1
Cardiovascular complications				
Myocardial infarction, n (%)	1 (2.3)	2 (4.6)	2 (4.6)	0.812
Troponin plasmatic values (ng/mL)	38 [18–100]	37.5 [21.5–79.8]	83 [33–137]	0.32
Pulmonary complications				
Hypoxaemia (need for O_2), n (%)	6 (14)	12 (28.6)	12 (28)	0.20
Pneumonia, n (%)	2 (4.6)	5 (11.6)	4 (9.3)	0.62
Pulmonary embolism, n (%)	0	1 (2.3)	0	1
Neurologic complications				
Stroke, n (%)	0	1 (2.3)	1 (2.3)	1
POCD, n (%)	18 (42)	18 (42)	13 (30)	0.43
Others complications				
Acute kidney injury AKIN > 1, n (%)	4 (9.3)	2 (4.6)	7 (16.3)	0.197
PONV, n (%)	8 (18.6)	8 (18.6)	7 (16.3)	0.93
Admission in ICU, n (%)	2 (4.6)	11 (25.6)	6 (14)	0.04
Hospital length of stay (days)	7.5 [6–10]	11 [7–22]	9 [7–15]	0.08
Hospital mortality, n (%)	3 (7)	3 (7)	2 (4.6)	1
30-day mortality, n (%)	5 (11.6)	3 (7)	2 (4.6)	0.468

Median, interquartile range [25–75] for quantitative data or n (%) for qualitative data

CSA, continuous spinal anaesthesia; ICU, intensive care unit; MNB, Multiple nerve blocks; PACU, post-anaesthesia care unit; PONV, postoperative nausea and vomiting; POCD, postoperative cognitive dysfunction.

Figure 1: CONSORT flowchart of patient inclusion in the study, and propensity score matching

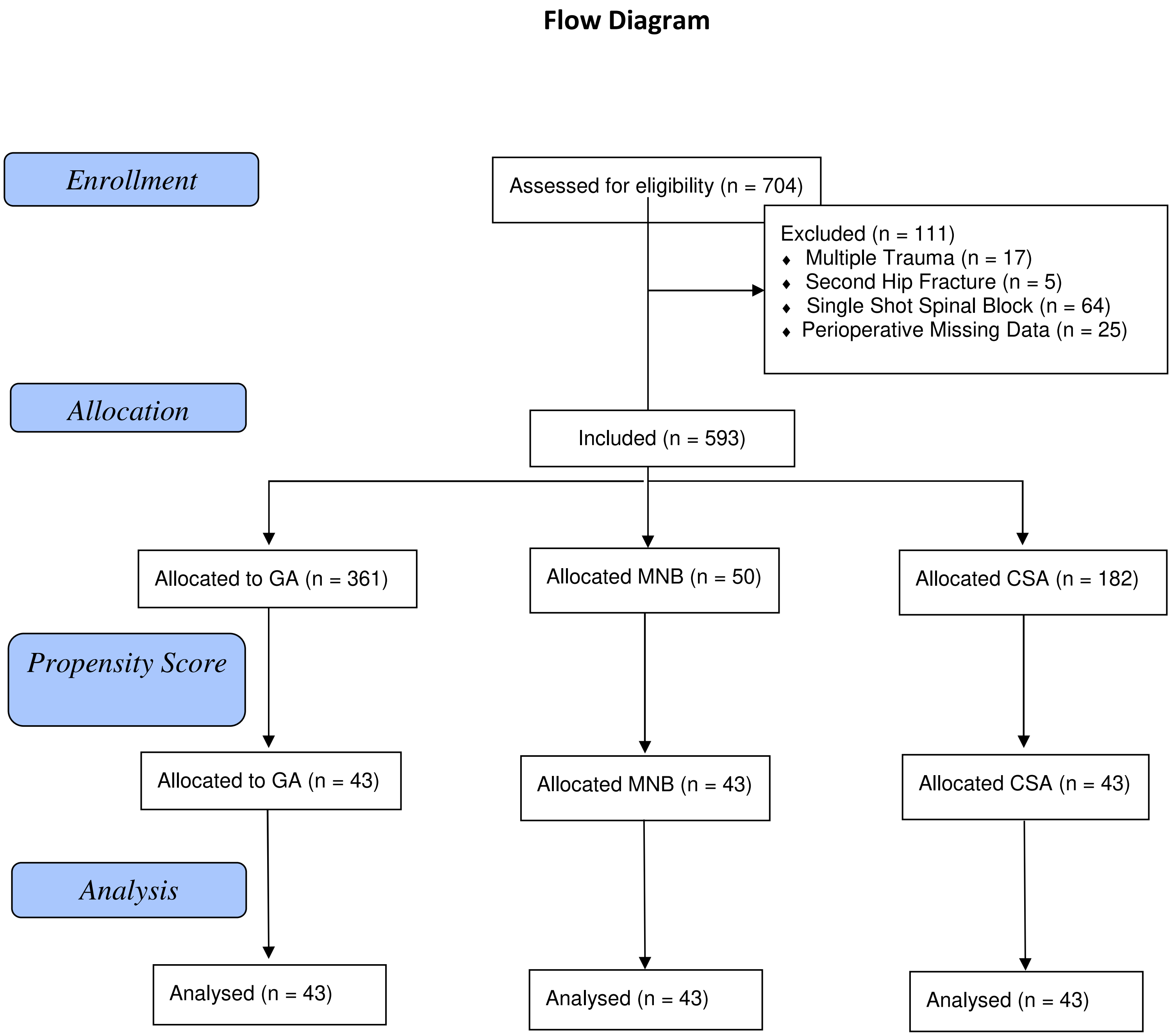
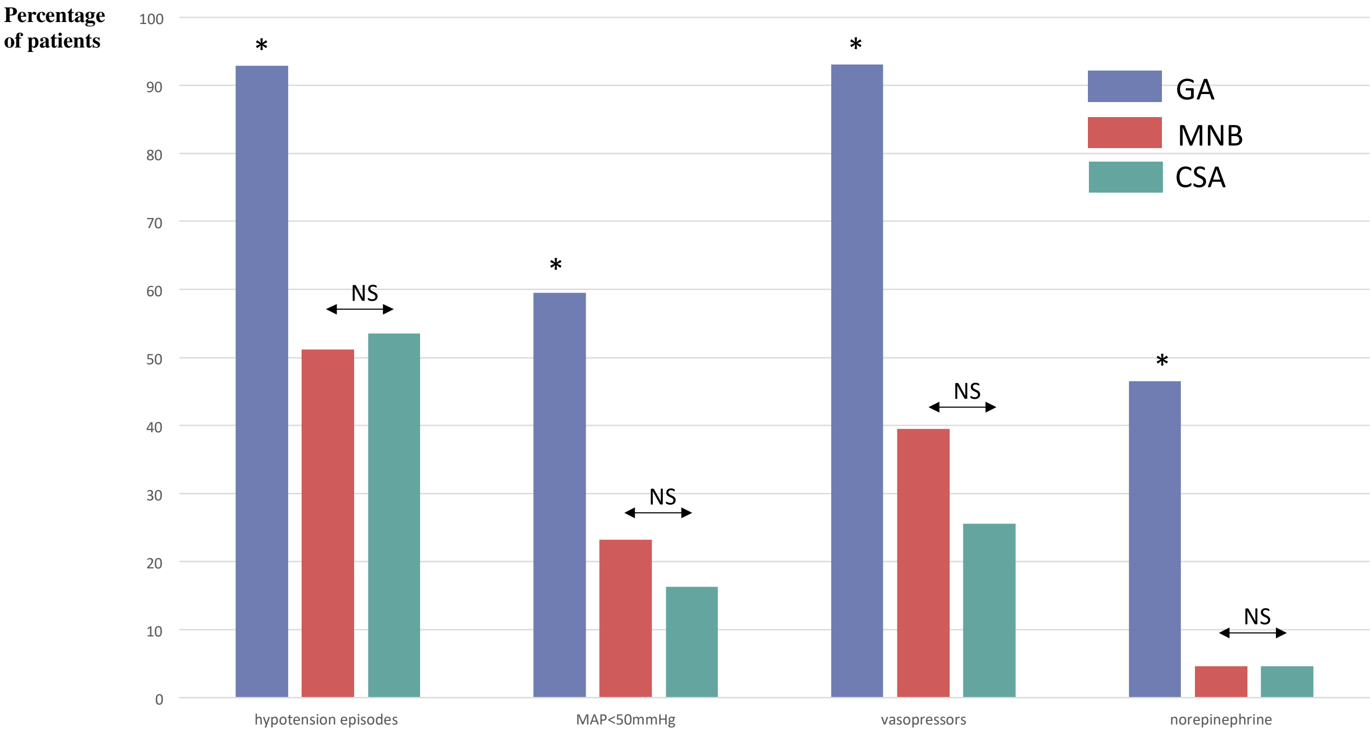
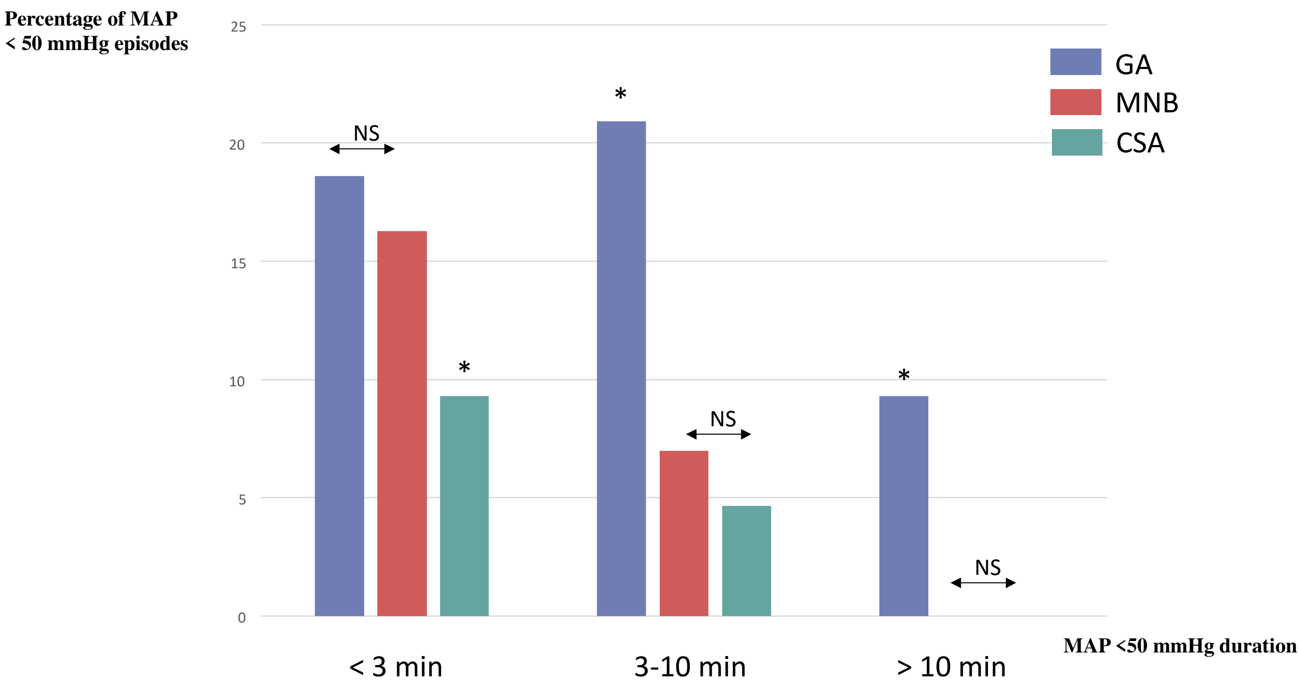


Figure 2: Percentages of patients in the three groups with hypotension episodes, those < 50 mmHg and patients receiving vasopressors



* $p < 0.05$ between GA group and both RA groups

Figure 3: Percentages of hypotension < 50 mmHg during the three determined durations: < 3 min, 3-10 min and > 10 minutes in the three groups



* $p < 0.05$ between groups

Appendix 1: Items used in the simplified Frailty Index

Factors	Points
Functional health status before operation	
Totally dependent	1
Metabolic	
Insulin-dependent diabetes mellitus	1
Respiratory	
History of severe chronic obstructive pulmonary disease or current pneumonia	1
Cardiovascular	
Congestive heart failure within 30 days before surgery	1
Myocardial infarction within 6 months before surgery	1
Previous percutaneous coronary intervention, cardiac surgery or angina within 1 month before surgery	1
Hypertension requiring medication	1
History of revascularisation/amputation for peripheral vascular disease	1
Neurologic	
History of transient ischaemic attack	1
Stroke with deficit	1
Impaired sensibility	1