Regional Anesthesia and Pain

Similar incidence of hypotension with combined spinal-epidural or epidural alone for knee arthroplasty

[L'anesthésie rachidienne et péridurale combinée, et péridurale seule, ont une incidence similaire d'hypotension lors de l'arthroplastie du genou]

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Background: We hypothesized that the incidence of hypotension during total knee replacement (TKR) surgery is lower in patients given combined spinal-epidural (CSE) anesthesia vs those receiving epidural anesthesia alone.

Methods: In a prospective study, 80 American Society of Anesthesiologists I-II patients (aged 40–80 yr), undergoing elective TKR surgery were randomly assigned to either CSE anesthesia (CSE, $n = 40$) or epidural anesthesia alone (Epidural, $n = 40$). Hemodynamic measurements included oscillometric mean arterial blood pressure (MAP), heart rate (HR), and cardiac index (CI) as determined by thoracic bioimpedance; systemic vascular resistance (SVR) was calculated. Our primary endpoint (outcome) was the number of hypotension episodes (defined as MAP < 70 mmHg).

Results: Using univariate analysis, we found no differences between the groups in regards to MAP, HR, CI, or SVR during the perioperative period. The incidence of hypotension was similar in both groups (two patients in each group), as was the incidence of bradycardia (12 patients in CSE, 7 in Epidural; $P = 0.2$). There were no differences between groups in other hemodynamic measurements including CI and calculated SVR. Analgesia supplementation with fentanyl was more frequently required in the Epidural group (20 *vs* 6 patients – $P = 0.03$).

Conclusion: Combined spinal-epidural anesthesia and epidural anesthesia alone during TKR surgery are associated with the same incidence of hypotension with statistically and clinically similar hemodynamic responses.

***Objectif** : Nous avons émis l'hypothèse que l'incidence d'hypotension pendant l'arthroplastie totale du genou (ATG) serait plus faible avec l'anesthésie rachidienne et péridurale combinée (RPC) qu'avec l'anesthésie péridurale seule.*

***Méthode** : Lors d'une étude prospective, 80 patients d'état physique ASA I-II, de 40 à 80 ans, subissant une ATG réglée, ont été répartis aléatoirement pour recevoir une anesthésie RPC (groupe RPC, n = 40) ou péridurale seule (groupe péridural, n = 40). Les mesures hémodynamiques comprenaient la tension artérielle moyenne (TAM) oscillométrique, la fréquence cardiaque (FC) et l'index cardiaque (IC) déterminé par la bio-impédance thoracique; la résistance vasculaire générale (RVG) a été calculée. Notre principal paramètre était le nombre d'épisodes d'hypotension définie par une TAM < 70 mmHg).*

***Résultats** : Selon une analyse univariée, il n'y avait aucune différence intergroupe quant à la TAM, la FC, l'IC ou la RVG périopératoires. L'incidence d'hypotension était similaire dans les deux groupes (deux dans chaque groupe), aussi l'incidence de bradycardie (12 avec l'anesthésie RPC et 7 avec la péridurale ; P = 0,2). Les autres mesures hémodynamiques ne présentaient pas de différence intergroupe, y compris l'IC et la RVG calculée. Un supplément d'analgésie avec du fentanyl a été plus souvent requis dans le groupe péridural (20 vs 6 patients – P = 0,03).*

***Conclusion** : L'anesthésie rachidienne et péridurale combinée et l'anesthésie péridurale seule, utilisées pendant l'ATG, sont associées à la même incidence d'hypotension et à des réactions hémodynamiques similaires au plan statistique et clinique.*

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NEURAXIAL anesthesia techniques for major lower extremity surgery include epidural anesthesia alone, spinal anesthesia alone, or the combination of spinal and epidural anesthesia. Analgesia and surgical conditions provided by spinal anesthesia alone or combined spinal-epidural (CSE) anesthesia are superior to those provided by epidural anesthesia alone.[1,2] Combined spinal-epidural anesthesia compared to epidural or spinal anesthesia alone produces superior muscle relaxation, improved sensory block[3,4] and also, fewer hypotensive episodes have been claimed for CSE.[5]

Patients undergoing total knee replacement (TKR) are usually elderly and they often have concomitant diseases which compromise cardiovascular stability. Regional anesthetic techniques are most commonly used for TKR. The cardiovascular effects of epidural anesthesia are complex and predominantly related to the level of analgesia and dose of local anesthetic. The pharmacological effect of systemically absorbed local anesthetic drugs, inclusion of epinephrine in the local anesthetic solution, extent of sympathetic denervation, autonomic system impairment, baseline blood volume, and preanesthetic cardiovascular function of the patient are also important factors.[6,7] About 18% of patients develop hypotension during epidural anesthesia[8] and 30% during spinal anesthesia.[9]

Previous studies reported that women undergoing Cesarean delivery under CSE anesthesia (targeting a T_4 sensory level) suffered less hypotension than those receiving epidural or spinal anesthesia alone.[3,5] We therefore tested the hypothesis that during TKR surgery the incidence of hypotension is lower in patients given CSE anesthesia than those receiving epidural anesthesia alone.

Methods

With approval of our Institutional Review Board and written informed consent, we recruited 80 American Society of Anesthesiologists Physical Status I–II patients, aged 40–80 yr, scheduled for primary elective TKR. We excluded patients in whom regional anesthesia was contraindicated (coagulopathy, infection at the puncture site) and patients with a history of congestive heart failure and/or an ejection fraction < 50% (per echocardiography, if available). Medications that could have altered coagulation and/or hemostasis were stopped.

Protocol

No preoperative anxiolytic medication was administered, but patients continued their routine medications. Participating patients were randomly allocated to receive either CSE anesthesia (CSE group) or epidural (Epidural group). Randomization was based on computer-generated codes that were maintained in sequentially numbered opaque envelopes. Before starting anesthesia, all patients received lactated Ringer's solution (500 mL over 20 min) heated to 37°C. Regional anesthesia was performed with patients in the sitting position at the L_3–L_4 or L_2–L_3 interspace. As per protocol, the first interspace chosen was L_3–L_4. If the attempt at this level failed, the L_2–L_3 level was the next choice.

The lumbar space was assessed by visual inspection. Epidural anesthesia was performed with an 18-G Tuohy needle and 20-G catheter (Braun, Melsungen AG, Germany). The CSE was performed with an 18-G epidural needle, 20-G multiport catheter, and a 27-G pencil point spinal needle (Braun, Melsungen AG, Germany). The needles were inserted with the aperture oriented cephalad. Epidural anesthesia was induced with 0.5% bupivacaine as a 5-mL bolus followed by 5 mL every five minutes for a total of 20 mL. Combined spinal-epidural anesthesia was induced with 2 mL isobaric spinal bupivacaine 0.5%, followed by an epidural supplemental dose of 5 mL of bupivacaine 0.5%, 15 min after the spinal injection. The doses of local anesthetics were chosen from previously published studies for both epidural[10] and CSE.[11] However in our study, the recommended spinal dose was reduced by a third (from 15 to 10 mg), as a lower block height was required.

In both groups, hypotension [mean arterial blood pressure (MAP) < 70 mmHg] was treated with a bolus of 200 mL of Lactated Ringer's solution. If the hypotension persisted for > five minutes, 5 mg ephedrine was given intravenously. Bradycardia [heart rate (HR) < 50 beat·min^{-1}] was treated with 0.5 mg *iv* atropine. Throughout surgery, fluids were given at a rate of 10 mL·kg^{-1}·hr^{-1}. Just before releasing the tourniquet, a 200-mL bolus of lactated Ringer's solution was infused rapidly. Patients were warmed with forced-air and fluids were infused at 37°C. The urinary bladder was catheterized in every patient. Tourniquets [with inflation pressures individualized to systolic blood pressure (SBP) plus 100 mmHg] were used in all cases, and all prostheses were cemented.

The sensory level, measured with a pinprick, was assessed every five minutes during the first 30 min of anesthesia, and subsequently every 15 min. The highest sensory level was also recorded. With a two-segment sensory block regression, 5 mL of 0.5% bupivacaine was administered epidurally to patients in both groups. Patients who expressed discomfort because of the tourniquet, were given 50 µg *iv* fentanyl and 1 mg

TABLE I Morphometric and demographic characteristics and anesthetic management

	CSE (n = 40)	*Epidural (n = 40)*	*P*
Age (yr)	76 ± 4	75 ± 5	0.100
Sex M/F (%)	60/40	50/50	0.500
Duration of surgery (min)	172 ± 40	170 ± 30	0.700
Time to readiness for surgery (min)	15 ± 5	25 ± 3	0.030
Mean sensory level 30 min after the block	T8 ± 3	T7 ± 4	0.400
Highest sensory level 30 min after the block	T5	T6	—
Modified Bromage score			
At 15 min after induction	3 (2-3)	1 (0-2)	0.002
At the end of surgery	2 (1-3)	1 (0-2)	0.003
After one hour in recovery room	2 (1-2)	1 (0-1)	0.001
Number of patients requiring top-ups	3	4	0.300
Total number of top-ups administered	3	4	0.300
Sensory levels 15 min after top-ups	T9 ± 2	T9 ± 3	0.700
Total fluid input (mL)	2,500 ± 300	2,350 ± 200	0.100
Urine output ($mL \cdot hr^{-1}$)	85 ± 20	80 ± 10	0.300

CSE = combined spinal-epidural anesthesia. Results are presented as means ± standard deviations or median (range).

iv midazolam. Postoperative analgesia was provided by a continuous epidural infusion of 6 to 10 $mL \cdot hr^{-1}$ of 0.2% ropivacaine. The infusion of epidural ropivacaine for postoperative analgesia was started after the patient regained full motor strength as determined by a modified Bromage scale score of 0. Motor block was assessed using a modified Bromage scale (0 = no motor block, 1 = inability to raise extended legs, 2 = inability to flex knees, and 3 = inability to flex ankle joints).[12]

Measurements

Morphometric and demographic characteristics of the patients were recorded. Motor block level was recorded every five minutes after induction of anesthesia for the first 30 min, and then every 15 min during and after surgery until full motor strength was regained. The sensory level was assessed bilaterally, in the midclavicular line. We recorded the time to readiness for surgery (sensory level at T_{10} or higher), time to two-segment sensory regression, the duration of surgery, the duration of tourniquet inflation, and time from the end of surgery until the postoperative analgesic epidural infusion was begun. The number of patients who required top-ups, the total number of top-ups and the sensory level 15 min after top-up administration was also recorded.

Our primary endpoint (outcome) was episodes of hypotension, which we defined as MAP < 70 mmHg. A secondary endpoint was the number of bradycardic episodes, defined as HR < 50 $beat \cdot min^{-1}$. The rational for choosing our primary endpoint was the following: an MAP of < 70 mmHg was chosen as a primary endpoint since this pressure is the lower limit for brain autoregulation (this lower limit has nevertheless, a considerable interindividual variation).[13] A HR < 50 $beat \cdot min^{-1}$ was taken as another endpoint, as this HR is considered a risk factor for the development of cardiac arrest during regional anesthesia.[14]

Mean arterial pressure, SBP, diastolic blood pressure and HR were measured oscillometrically (AS/5™, Datex- Ohmeda Division, Anaesthesia Monitor, Instrumentarium Corp., Datex-Ohmeda, Helsinki, Finland). Cardiac index was determined using thoracic bioimpedance readings (BoMed® Medical MFG. Ltd, Model NCCOM3, Irvine, CA, USA). Blood pressure and HR were recorded before starting anesthesia (baseline) and at five-minute intervals throughout surgery. Cardiac index was measured before starting anesthesia (baseline), every five minutes after initiation of the block for the first 30 min, and every 30 min afterwards. In addition, hemodynamic values were recorded after the skin was being closed, before tourniquet release, ten minutes after tourniquet release, and one hour after arriving in the recovery room. Systemic vascular resistance (SVR) was calculated using the standard formula.[15]

The total amount of local anesthetic was recorded, as was the number of patients who required epidural top-up, atropine, or ephedrine. The amount of fluid and blood infused, urinary output, and the estimated blood loss were also recorded. Arrhythmias (defined as runs of ventricular tachycardia, ventricular fibrillation, paroxysmal supraventricular tachycardia, atrial

fibrillation, or cardiac arrest) were recorded, as were cardiovascular complications (intraoperative ischemia and myocardial infarction). Intraoperative myocardial ischemia was defined as a new 2-mm segment (ST) depression or new 1-mm ST elevation on an automatic ST analyzer (AS/5™, Datex- Ohmeda Division, Anaesthesia Monitor, Instrumentarium Corp., Datex-Ohmeda, Helsinki, Finland). The total number of patients who received fentanyl and midazolam and the total dose of fentanyl were also recorded. Investigators blinded to the anesthetic technique recorded all measurements.

Data analysis

Our hypothesis was that during TKR surgery the incidence of hypotension is lower in patients given CSE anesthesia than those receiving epidural anesthesia alone. Our primary endpoint for sample size calculation was the incidence of hypotension episodes (MAP < 70 mmHg). In a pilot study of 20 patients (ten per group) we found an incidence of hypotension (MAP < 70 mmHg) of 10% in the CSE group and 40% in the Epidural group (a difference of 30%). Therefore, we considered clinically significant any difference between the groups ≥ 30%. Based on this assumption we calculated that the sample size needed to achieve a power of 80% with a two-sided α of 0.05, using the binomial approximation to normal distribution, was 40 patients per group.

Data were evaluated for normal distribution using the Kolmogorov-Smirnov test. Continuous variables with normal distribution were compared with the Student's t test and those with distribution significantly differing from normal were compared using the Mann-Whitney U or median tests. Categorical data were described using frequency counts and percentages and compared using Chi-square (with Yates correction) or Fisher's exact tests, as appropriate. The two groups were compared with univariate analysis.

Data analysis was performed using the SPSS for Windows (SPSS Inc, Chicago, IL, USA). Results are presented as means ± standard deviations; $P < 0.05$ was considered statistically significant.

Results

No patient required general anesthesia due to failure of neuraxial block and no patient was excluded at any stage of the study. Morphometric and demographic characteristics of the patients were similar in both groups (Table I). There were also no differences in the surgical management of the groups. Injection site was L_3–L_4 in 80% of the CSE group and in 75% of the Epidural group. Tourniquet time was 130 ± 20 min in the CSE group and 136 ± 15 min in the Epidural group. The time to two-segment regression was 120 ± 20 min and 132 ± 22 min in the CSE and Epidural groups, respectively. The time to start of the postoperative epidural infusion of local anesthetic (measured from the end of surgery) was 95 ± 10 min in the CSE and 70 ± 7 min in the Epidural group ($P = 0.10$). Blood loss (from the tourniquet release to the end of surgery) was 130 ± 30 mL and 150 ± 50 mL, in the CSE and Epidural groups, respectively. No patient required a blood transfusion during the study period.

The modified Bromage scores were significantly greater in patients receiving CSE 15 min after induction, at the end of surgery, and one hour after surgery. Patients given CSE were ready for surgery faster than those given epidural anesthesia alone (Table I). The number of patients requiring top-ups, total number of top-ups and sensory levels following top-ups (in patients who received them) were similar.

There were no statistically significant or clinically important differences between the groups with regard to MAP, HR, cardiac index, or SVR (Table II). More patients in the Epidural group required fentanyl boluses ($P = 0.03$, Table III), while the total mean dose of fentanyl was 300 ± 50 μg in the CSE group and 1000 ± 100 μg in the Epidural group. The number of patients who developed bradycardia (e.g., HR < 50 beat·min^{-1}) did not differ significantly between the groups (Table III). Five patients in the CSE group and six in the Epidural group received ß-blockers preoperatively. The number of patients requiring atropine was similar for both groups. Only two patients in each group had an episode of hypotension (MAP < 70 mmHg), (Table III). Tourniquet inflation and deflation had no statistically significant impact on any of the hemodynamic variables. There were no intraoperative or postoperative complications in either group.

Discussion

Contrary to our primary hypothesis, our results showed that CSE anesthesia and epidural only anesthesia during TKR surgery are associated with a comparable incidence of hypotension.

Our findings contrast with previous studies in women undergoing Cesarean delivery under CSE anesthesia who experienced less hypotension than those given epidural or spinal anesthesia alone.[3–5] The results may have differed due to the absence of pregnancy-specific changes including aortocaval compression, and also due to the fact that the mean highest sensory block achieved in our patients was different from that required to achieve analgesia for Cesarean section (T_4).

TABLE II Hemodynamic measurements

	CSE (n = 40)	*Epidural (n = 40)*	*P*
Mean arterial pressure (mmHg)			
Baseline (before anesthesia)	100 ± 20	102 ± 15	0.90
Mean intraoperative value	95 ± 10	90 ± 20	0.48
MAP lowest value	68	65	
MAP highest value	120	117	
10 min before tourniquet release	93 ± 10	91 ± 20	0.80
10 min after tourniquet release	88 ± 15	89 ± 10	0.77
End of surgery	100 ± 20	103 ± 25	0.72
One hour in PACU	88 ± 10	91 ± 16	0.19
Heart rate (beat·min^{-1})			
Baseline (before anesthesia)	85 ± 12	83 ± 8	0.50
Mean intraoperative value	70 ± 10	74 ± 12	0.60
HR lowest value	45	47	
HR highest value	98	92	
10 min before tourniquet release	72 ± 15	74 ± 22	0.50
10 min after tourniquet release	79 ± 15	80 ± 20	0.80
End of surgery	82 ± 24	80 ± 18	0.72
One hour in PACU	84 ± 12	84 ± 13	1
Cardiac index (L·min^{-1}·m^{-2})			
Baseline (before anesthesia)	3.6 ± 0.8	3.5 ± 1	0.80
Mean intraoperative value	3.5 ± 1	3.4 ± 1	0.90
Cardiac index lowest value	2.7	2.5	
Cardiac index highest value	4.5	4.5	
10 min before tourniquet release	3.4 ± 1	3.3 ± 0.7	0.90
10 min after tourniquet release	3.3 ± 0.7	3.2 ± 0.7	0.65
End of surgery	3.4 ± 0.8	3.3 ± 0.7	0.30
One hour in PACU	3.4 ± 0.8	3.4 ± 0.9	0.95
Systemic vascular resistance (dynes·sec^{-1}·cm^{-5})			
Baseline (before anesthesia)	1180 ± 170	1120 ± 270	0.52
Mean intraoperative value	950 ± 150	980 ± 170	0.54
SVR lowest value	800	810	
SVR highest value	1,400	1,390	
10 min before tourniquet release	1100 ± 140	1163 ± 110	0.66
10 min after tourniquet release	930 ± 190	970 ± 110	0.75
End of surgery	990 ± 190	978 ± 160	0.8
One hour in PACU	1220 ± 190	1210 ± 110	0.9

CSE = combined spinal-epidural anesthesia; MAP = mean arterial blood pressure; PACU = postanesthesia care unit; HR = heart rate; SVR = systemic vascular resistance. Data are expressed as means ± SDs.

TABLE III Principal result

	CSE (n = 40)	*Epidural (n = 40)*	*P*
Ephedrine	10	13	0.1
Atropine	12	11	0.80
Fentanyl	6	20	0.03
MAP < 70 mmHg	2	2	1.00
Heart rate < 50 beat·min^{-1}	12	7	0.2

CSE = combined spinal-epidural anesthesia; MAP = mean arterial pressure. Results are presented as numbers of patients.

The absence of hemodynamic changes in both groups may be explained by the relatively low dose of plain bupivacaine used in the spinal phase of CSE, and by the gradual administration of local anesthetics in the Epidural group. The small amount of local anesthetic injected into the subarachnoid space of patients in the CSE group may have ameliorated the hemodynamic changes that are common with spinal anesthesia, secondary to rapid and extensive sympathetic block. Indeed, there were no statistically significant or clinically important differences in MAP between groups or within each group at different time points.

Major factors related to the level of spinal anesthetic block include baricity of the anesthetic solution, patient position, and the dose of local anesthetic.[16] Considering that the extent of sympathetic blockade with the resultant hemodynamic changes is correlated with the sensory level of the block, and that with hyperbaric solutions this latter factor is not influenced by the dose of the local anesthetic,[17] it would not be expected that changes in the dose of spinal hyperbaric anesthetic will affect the hemodynamic responses.[3–5] However, this may not be true for isobaric local anesthetics, the type of solutions used in our study. Furthermore, Carpenter *et al.*[18] demonstrated that a major determinant of spinal block is the volume of cerebrospinal fluid (CSF). With a given volume of CSF, the dose of local anesthetic injected within this CSF volume will influence the spinal block characteristics. Moreover, a change in the dose of epidurally administered local anesthetic would affect the sensory level, and therefore the extent of hemodynamic changes recorded. Further studies are warranted to investigate the hemodynamic effects with different doses of local anesthetics.

We used bioimpedance cardiography to investigate non-invasively the mechanisms of changes in MAP and HR with the two anesthetic techniques. Thoracic bioimpedance (impedance cardiography) is a non-invasive technique that measures changes in the transthoracic electrical impedance induced by ejection of blood into the thoracic ascending aorta.[19] Bioimpedance is a useful technique for non-invasive hemodynamic monitoring in regional anesthesia.[20,21] The bioimpedance method has been validated with the dye dilution technique during epidural or general anesthesia for Cesarean section. Milsom *et al.*[22] showed that there was no significant difference between the mean changes in stroke volume determined by the two techniques during serial measurements. Impedance cardiography was found to be a safe, reliable, non-invasive

technique for the measurement of changes in stroke volume during Cesarean section.

The number of episodes of bradycardia was similar in the two groups (Table III). The CSE group did not require more atropine than did the Epidural group. However, patients having spinal anesthesia tend to develop bradycardia and in rare cases - an incidence of 2.7 to 2.9 per 10,000[23,24] - cardiac arrest, for several reasons. One of the possible mechanisms may be a reflex bradycardia, possibly associated with low right-sided cardiac filling pressures.[25] Although this phenomenon may occur during both types of neuraxial anesthesia, it is possibly more common during spinal anesthesia.[24,26–28] Predisposing conditions that increase the risk of bradycardia with regional anesthesia include low baseline HR and vagal predominance.[29] Prompt augmentation of central venous filling with *iv* fluids, and potent α-agonists and positional change may improve organ perfusion[28,29] and eventually prevent progression to cardiac arrest. We speculate that the reason for the lack of difference in the incidence of bradycardia in the CSE patients may have been the use of relatively low doses of local anesthetics.

Tourniquet release may lead to serious hemodynamic fluctuations. In one study, the blood pressure measured up to 30 min after release of a pneumatic thigh tourniquet was decreased.[30] We found no significant changes in any hemodynamic variable upon the tourniquet release in either group. As we measured blood pressure non-invasively, it is possible that transient episodes of hypotension after tourniquet release were not documented. However, it is unlikely that such short episodes would be of any clinical concern.

Tourniquet pain occurs less frequently with intense regional anesthesia (i.e., spinal block), but the incidence may be up to 30% during epidural anesthesia with bupivacaine 0.5% with epinephrine.[31] A greater number of Epidural patients experienced some pain or discomfort related to the tourniquet, and required more fentanyl administration ($P = 0.03$ when compared to CSE). Although half of the Epidural patients received *iv* fentanyl supplementation (a total dose of 1,000 μg) this probably did not contribute to the development of bradycardia in this group of patients, considering that CSE patients received less than a third of this fentanyl dose (300 μg).

We conclude that CSE anesthesia and epidural anesthesia alone are associated with a comparable incidence of hypotension during TKR, with statistically and clinically similar hemodynamic responses.

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