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CASE SERIES

Neuroselective Sensory-Over-Motor Dissociation, Rapid Blockade Onset, and Hemodynamic Autoregulation With 10 µg Intrathecal Dexmedetomidine in High-Risk Orthopedic and Gynecological Surgery: An Observational Analytic Case Series

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ABSTRACT

Background: Subarachnoid block gives dense blockade for orthopedic and gynecological surgery, but plain local anesthetics give brief analgesia. Intrathecal dexmedetomidine (DXM), a selective α_2-adrenergic agonist, prolongs block in low-risk patients. Data in high-risk patients are scarce.

Objective: To describe block onset, regression, pain scores, and hemodynamic course after 10 µg of intrathecal DXM added to hyperbaric bupivacaine in four high-risk patients.

Methods: Four consecutive women (29–73 years) were operated on at Dr. Saiful Anwar Regional General Hospital, Malang, Indonesia (Protocol: CMHC/EC/IRB/2026/0814). Each received 0.5% hyperbaric bupivacaine (15–20 mg) plus 10 µg DXM, by L4–L5 subarachnoid block (Cases 1–3) or combined spinal-epidural anesthesia (Case 4). Onset, hemodynamics, and Numerical Rating Scale (NRS) pain scores were recorded from T_0 to T_4.

Results: All patients reached the target block (T6–T10). Sensory onset was ≤ 1 min and Modified Bromage 2 motor block appeared at 3 min; the published mean to Bromage 3 with 5 µg is 11.6 min. Motor inhibition lasted 300 min and analgesia 300–360 min (mean 330 ± 24.5 min), with NRS 0–2 in the first 4 h and 3–4 at 5–6 h. MAP was 70 mmHg in a post-stroke patient. A fall to 50/30 mmHg during bone curettage resolved with 1,000 mL crystalloid and ephedrine. Multimodal and neuraxial analgesia were also given.

Conclusion: In four patients, 10 µg of intrathecal DXM was followed by rapid block onset and 5–6 h of analgesia, with no recorded respiratory depression. The series cannot establish effect or mechanism, so controlled studies are needed.

1. Introduction

Neuraxial regional anesthesia includes single-shot subarachnoid block (RA-SAB) and combined spinal-epidural (CSE) techniques. It is a mainstay of perioperative care for lower abdominal, inguinal, obstetric, gynecological, urogenital, and lower-extremity orthopedic surgery.[1] A local anesthetic placed directly in the cerebrospinal fluid (CSF) of the subarachnoid space reversibly inhibits voltage-gated sodium channels (Nav1.7, Nav1.8, and Nav1.9) along the spinal nerve roots and dorsal horn. This produces somatic, visceral, autonomic, and neuroendocrine stress-response blockade.[2] Compared with general anesthesia, neuraxial blockade avoids endotracheal intubation and mechanical ventilation. It attenuates the surgical surge of catecholamines and cortisol. It reduces perioperative thromboembolic and pulmonary complications, preserves airway reflexes, and speeds early recovery in the postanesthesia care unit (PACU).[3] One limitation persists. Plain or hyperbaric amide local anesthetics, such as 0.5% hyperbaric bupivacaine or ropivacaine, act as analgesics for a short time, typically 150 to 210 minutes.[4] When subarachnoid local anesthetic concentrations fall below the minimum blocking threshold, patients often feel abrupt rebound pain early after surgery. They then need high-dose systemic rescue analgesics, which impair mobilization and hemodynamic stability.

Many intrathecal adjuvants have been tried to extend the short duration of a single-shot subarachnoid block. They include hydrophilic and lipophilic opioids (morphine, fentanyl, sufentanil, and buprenorphine), N-methyl-D-aspartate (NMDA) receptor antagonists (ketamine and esketamine), γ-aminobutyric acid (GABA) modulators (midazolam), cholinesterase inhibitors (neostigmine), corticosteroids (dexamethasone), divalent cations (magnesium sulfate), and α_2-adrenergic receptor agonists (clonidine and dexmedetomidine). Intrathecal dexmedetomidine has been compared directly with intrathecal fentanyl as an opioid alternative.[5] Intrathecal opioids remain the most common neuraxial additives, but µ-opioid receptor-mediated adverse events limit their use. These include dose-dependent pruritus (reported in 30% to 70% of patients)[6], postoperative nausea and vomiting (PONV), urinary retention that requires prolonged bladder catheterization, and delayed gastrointestinal motility. Delayed rostral respiratory depression can be life-threatening, especially in frail geriatric patients with little ventilatory reserve. For this reason, contemporary Enhanced Recovery After Surgery (ERAS) pathways increasingly favor non-opioid strategies, including α_2-agonist adjuvants, that prolong analgesia and avoid µ-opioid receptor toxicity.[7,8]

Dexmedetomidine (DXM) is the pharmacologically active dextro-enantiomer of medetomidine (4-[(1S)-1-(2,3-dimethylphenyl)ethyl]-1H-imidazole). It is a highly selective, second-generation α_2-adrenergic receptor agonist. Its α_2:α_1 adrenoceptor binding selectivity ratio is 1,620:1, nearly eightfold higher than that of the prototype α_2-agonist

clonidine (220:1).[9] Given perineurally or intrathecally in low microgram doses (typically 3 to 15 µg), DXM acts on the spinal cord dorsal horn and primary afferent nerve fibers by two synergistic antinociceptive mechanisms. Presynaptically, DXM binds Gi/o-protein-coupled α2A and α2C adrenoceptors on unmyelinated C-fiber and lightly myelinated Aδ-fiber nociceptive terminals in the substantia gelatinosa (lamina II of Rexed). It inhibits adenylate cyclase, lowers intracellular cyclic adenosine monophosphate (cAMP), and blocks N-type and P/Q-type voltage-gated calcium (Ca^{2+}) channels. Less substance P, calcitonin gene-related peptide (CGRP), and glutamate is then released by exocytosis. Postsynaptically, DXM activates dorsal horn α_2-adrenoceptors coupled to G-protein-coupled inwardly rectifying potassium (GIRK) channels. Potassium (K^+) efflux shifts the resting membrane potential toward hyperpolarization (from approximately −70 mV to −85 mV). Projection neurons become refractory to depolarizing nociceptive volleys.[10] Electrophysiological studies add one more point. In rat dorsal root ganglion neurons, DXM inhibits hyperpolarization-activated cyclic nucleotide-gated (Ih) cation currents.[11] A weaker effect on large, heavily myelinated Aα motor axons has been proposed but not shown directly. If present, this difference in ion-channel selectivity could give a 'sensory-over-motor dissociation' window, in which postoperative analgesia continues after lower-extremity motor conduction has recovered.[12]

Controlled studies in homogeneous American Society of Anesthesiologists (ASA) physical status I–II cohorts have shown that intrathecal DXM prolongs sensory and motor blockade and analgesia.[13–15] A gap remains. The longitudinal block kinetics, the sensory-motor recovery pattern, and the hemodynamic course of a standardized 10 µg intrathecal DXM regimen are poorly described in heterogeneous, high-risk surgical patients with complex neurovascular, oncological, metabolic, and neurodegenerative comorbidities.[16] Four clinical situations illustrate the problem. Geriatric survivors of ischemic stroke who undergo subtrochanteric femur fracture fixation need a Mean Arterial Pressure (MAP) at or above 70 mmHg to protect cerebral perfusion pressure (CPP) despite preganglionic sympathetic blockade. Patients who undergo intramedullary nailing and polymethylmethacrylate (PMMA) bone cement augmentation for pathological femur fractures face acute intraoperative vasovagal and bone cement implantation hemodynamic instability. Patients with Type 2 Diabetes Mellitus (T2DM) or Parkinson's disease who have major gynecological laparotomy need neuroendocrine and extrapyramidal stability, without dopamine-antagonist or opioid-induced complications.[17] This case series describes four findings in four distinct high-risk orthopedic and gynecological patients who received 10 µg of intrathecal DXM: block onset (≤ 1 min sensory onset to T10 and 3 min to Modified Bromage 2), the time course of motor and analgesic regression (5 hours of motor inhibition and 5–6 hours of analgesia), the hemodynamic course in a post-stroke patient, and the course of one hypotensive episode with its rescue. The objective was to describe block kinetics, postoperative Numerical Rating Scale (NRS) pain trajectories, hemodynamics, and the Naranjo assessment of the one adverse event after 10 µg of intrathecal DXM added to hyperbaric bupivacaine for spinal and combined spinal-epidural anesthesia.

2. Methods

2.1. Study Design and Setting

This was a single-center descriptive case series with prospective perioperative observation. It described the neuropharmacological kinetics, sensory-motor block regression, and hemodynamic profile of 10 µg intrathecal dexmedetomidine given with 0.5% hyperbaric bupivacaine. Four consecutive female patients underwent major lower-extremity orthopedic or pelvic gynecological surgery at the Department of Anesthesiology and Intensive Therapy, Dr. Saiful Anwar Regional General Hospital / Faculty of Medicine, Universitas Brawijaya, Malang, East Java, Indonesia, during August 2025. Reporting followed the PROCESS 2020 guideline for surgical case series.[18]

2.2. Participants and Eligibility

Eligible patients were adult and geriatric women who presented to the Emergency Department or the elective surgical wards of Dr. Saiful Anwar Regional General Hospital. They needed definitive lower-extremity orthopedic osteosynthesis or infraumbilical/pelvic gynecological laparotomy that was suitable for regional subarachnoid block (RA-SAB) or combined spinal-epidural (CSE) anesthesia. Three inclusion criteria applied: (1) documented American Society of Regional Anesthesia and Pain Medicine (ASRA) hemostatic safety for neuraxial puncture, defined as a platelet count ≥ 142.00 × 10^3/µL, prothrombin time (PT) ratio ≤ 1.20, and activated partial thromboplastin time (aPTT) within safe institutional parameters; (2) no absolute contraindication to neuraxial blockade, such as patient refusal, localized lumbar skin infection at L3–L5, uncorrected hypovolemic shock, or severe fixed cardiac outflow tract obstruction; and (3) complete longitudinal documentation of baseline primary survey vital signs, preoperative hematological and biochemical profiles, intraoperative multiparameter hemodynamics, sensory/motor onset and regression times, and postoperative Numerical Rating Scale (NRS) pain scores over an observation period of at least 6 hours. The cohort comprised four clinically distinct phenotypes. Case 1 was a 73-year-old female with prior ischemic stroke and a closed left subtrochanteric femur fracture, Seinsheimer Type IIB. Case 2 was a 48-year-old female with multiple osteolytic lesions and a pathological left lesser trochanter fracture secondary to Non-Hodgkin's Lymphoma with bone involvement. Case 3 was a 29-year-old female with secondary amenorrhea due to Asherman's syndrome and Type 2 Diabetes Mellitus on oral antidiabetic therapy. Case 4 was a 63-year-old female with a 14 cm giant ovarian cystoma and Parkinson's disease with resting tremor.

2.3. Anesthetic Technique and Observation Protocol

All patients followed a standardized five-phase longitudinal perioperative observation protocol. T_0 was the baseline pre-induction primary and secondary survey. T_1 was the early post-intrathecal injection onset window at 1 to 3 minutes. T_2 covered intraoperative surgical maintenance and surveillance for the hemodynamic nadir at 15 to 60 minutes. T_3 was the motor block recovery threshold at 5 hours [300 minutes] after injection, defined as the first voluntary lower-extremity movement. T_4 was complete spinal block resolution and the postoperative analgesic transition at 5 to 6 hours [300 to 360 minutes]. In Cases 1, 2, and 3, single-shot RA-SAB was performed under strict aseptic technique at the L4–L5 intervertebral space. The dose was 20 mg (4 mL) of 0.5% hyperbaric bupivacaine with 10 µg of preservative-free dexmedetomidine (mass ratio 0.5 µg DXM per mg bupivacaine). The target cephalad sensory dermatomes were

T10 (Cases 1 and 2) and T8 (Case 3). In Case 4, CSE anesthesia used an intrathecal injection at L4–L5 of 15 mg (3 mL) of 0.5% hyperbaric bupivacaine plus 10 µg DXM (mass ratio 0.67 µg/mg, targeting T6). An epidural catheter was inserted at L3–L4 (catheter tip at T9–T10) and delivered intraoperative 0.75% ropivacaine (10 mL total volume) across T6–L1. Cephalad sensory blockade was assessed every 30 seconds by bilateral pinprick loss. Motor blockade was graded with the Modified Bromage Scale (0 = no motor block, full hip/knee/ankle flexion; 1 = inability to raise extended leg, able to flex knee; 2 = inability to flex knee, able to flex ankle; 3 = complete lower-limb motor paralysis). A GE B40i multiparameter monitor provided continuous intraoperative surveillance. It recorded systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP = SBP − DBP), Mean Arterial Pressure (MAP = DBP + [SBP − DBP]/3), heart rate (HR), Lead II electrocardiography (ECG), respiratory rate (RR), and peripheral capillary oxygen saturation (SpO_2).

2.4. Comparison With Published Values

To place the clinical and pharmacodynamic performance of the 10 µg intrathecal DXM regimen in context, individual patient trajectories and cohort means were compared with three objective benchmarks. The first was the institutional laboratory reference intervals at Dr. Saiful Anwar Regional General Hospital (Hemoglobin 13.40–17.70 g/dL, Hematocrit 39.90–51.00%, Erythrocytes 4.00–5.50 × 10^6/µL, Leukocytes 4.30–10.30 × 10^3/µL, Platelets 142.00–424.00 × 10^3/µL, Sodium 136.0–145.0 mmol/L, Potassium 3.50–5.10 mmol/L, Chloride 98.0–107.0 mmol/L, Random Blood Glucose < 200 mg/dL, Albumin 3.50–5.20 g/dL, Urea 16.6–48.5 mg/dL, Creatinine 0.67–1.17 mg/dL, and AST/ALT 10–50 U/L). The second was published pharmacodynamic values for low-dose (3–5 µg) intrathecal DXM (mean motor onset latency of 11.6 minutes to Bromage 3) and for spinal anesthesia with local anesthetic alone (median analgesia duration 204 minutes [range 68.9–406 minutes]) versus intrathecal DXM (363.6 minutes [range 252.3–824 minutes]). A meta-analysis reported a pooled mean prolongation of analgesia of 191.3 minutes.[19–22] The published onset value refers to Bromage 3 and this series recorded Bromage 2, so these comparisons are descriptive only. The third was a hemodynamic threshold set for Case 1: intraoperative MAP ≥ 70 mmHg in a post-stroke geriatric patient, to protect cerebral perfusion pressure (CPP = MAP − ICP).

2.5. Statistical Analysis

A four-patient case series (n = 4) spanning distinct orthopedic and gynecological procedures calls for simple descriptive statistics. Continuous variables are given as individual values and, where useful, as Mean ± sample Standard Deviation (SD) with Median and Range (Minimum–Maximum). Relative deviations of biomarkers from the institutional lower or upper limits of normal (LLN/ULN), and serial hemodynamic changes across timepoints T_0 to T_4, were calculated as $\Delta\% = [(Tn - T_0) / T_0] \times 100\%$. Blood urea nitrogen (BUN) was derived from serum urea as BUN = Urea / 2.1428, and the De Ritis ratio was computed as AST / ALT. No causal framework was applied, because the series has no comparator. The one perioperative adverse hemodynamic event was classified with the Naranjo Adverse Drug Reaction (ADR) Probability Scale (score ≤ 0 = Doubtful; 1–4 = Possible; 5–8 = Probable; ≥ 9 = Definite) together with the World Health Organization–Uppsala Monitoring Centre (WHO-UMC) causality categories.

2.6. Ethical Approval

Ethical clearance for this case series was granted by the CMHC Research Center Ethics Committee, Indonesia (Protocol Approval Number: 2025/0814), in line with institutional clinical governance at Dr. Saiful Anwar Regional General Hospital, Malang. All clinical procedures, neuraxial anesthetic interventions, and perioperative monitoring protocols complied with the ethical principles of the World Medical Association Declaration of Helsinki (2013 revision) and the International Committee of Medical Journal Editors (ICMJE) standards for privacy and confidentiality. Before inclusion, all four patients and their legally authorized family representatives gave written informed consent for neuraxial anesthesia, surgical intervention, clinical and radiological documentation, and scientific publication. All diagnostic radiographs, multiparameter physiological monitoring records, and clinical images were de-identified before analysis to protect patient confidentiality.

3. Results

3.1. Patients and Baseline Findings (T_0)

The four-patient cohort (n = 4; 100% female) had ages from 29 to 73 years, a mean age of 53.25 ± 19.15 years, and a median of 55.50 years. Two patients had major proximal femur orthopedic surgery (Cases 1 and 2; 50%) and two had major pelvic gynecological laparotomy (Cases 3 and 4; 50%). Every patient had significant systemic comorbidities that called for tailored perioperative risk stratification. Case 1 was a 73-year-old female admitted through the Emergency Department of Dr. Saiful Anwar Regional General Hospital. She had had severe left hip pain, thigh swelling, and inability to bear weight for 5 days, after slipping from her bed at home and falling onto her left side. In 2024 she had an ischemic stroke with residual left lower-extremity motor paresis and mild facial lip asymmetry, and she took routine oral citicoline neuroprotective therapy. She had no prior seizures, syncope, vomiting, or sphincter dysfunction. At the baseline primary survey (T_0) her airway was patent, without stridor or gargling. Breathing was spontaneous and symmetrical at a respiratory rate (RR) of 20 breaths/min, with peripheral oxygen saturation (SpO_2) of 99% on room air. Blood pressure (BP) was 153/70 mmHg. This gives a widened pulse pressure (PP) of 83 mmHg (+107.50% above the physiological 40 mmHg reference, reflecting geriatric arterial stiffness) and a baseline Mean Arterial Pressure (MAP) of 97.67 mmHg. Heart rate (HR) was 100 beats/min, the extremities were warm, and capillary refill time (CRT) was < 2 seconds. She was alert with a Glasgow Coma Scale (GCS) score of 15 ($E_4V_5M_6$), isocoric 3 mm/3 mm light-reactive pupils, and a core temperature of 36.5°C.

Case 2 was a 48-year-old female who came to the Emergency Department with acute left groin and proximal thigh pain after a low-energy domestic slip-and-fall. In 2024 a right cervical lymph node excisional biopsy had confirmed Non-Hodgkin's Lymphoma (NHL). It was complicated by osteolytic bone involvement with a pathological fracture of the left lesser trochanter. At admission (T_0) she had a patent airway and spontaneous breathing at RR 18 breaths/min with SpO_2 98% on room air. Her baseline systemic arterial pressure was borderline low at 100/66 mmHg (PP 34 mmHg; MAP 77.33 mmHg). HR was 89 beats/min, CRT < 2 seconds, GCS 15 ($E_4V_5M_6$), pupils isocoric at 3 mm/3 mm, and core temperature 36.5°C. Her left lower limb was immobilized on a Böhler-Braun skin traction frame. Case 3 was a 29-year-old female who presented for elective hysterectomy. She had a 6-month history of secondary amenorrhea caused by severe

Asherman's syndrome (confirmed histopathologically as chronic endometritis) after two uterine curettage procedures under general anesthesia with total intravenous anesthesia (GA-TIVA) in 2019 and February 2025. She also had a 2-year history of Type 2 Diabetes Mellitus (T2DM) on regular oral antidiabetic drugs (OAD). Her T_0 primary survey showed RR 18 breaths/min, SpO_2 97% on room air, BP 126/92 mmHg (PP 34 mmHg; MAP 103.33 mmHg), HR 86 beats/min, GCS 15 ($E_4V_5M_6$), and core temperature 36.5°C. Case 4 was a 63-year-old female with a 4-month history of progressive abdominal distension, mechanical dyschezia, and dysuria caused by a giant ovarian cystoma 14 cm in diameter. She had been diagnosed with Parkinson's disease in June 2025. It showed as a classic right-hand resting tremor without cranial nerve palsies, and she was on routine outpatient neurological therapy. She had had an open appendectomy in 1977. At T_0 she had RR 18 breaths/min, SpO_2 97% on room air, BP 112/84 mmHg (PP 28 mmHg; MAP 93.33 mmHg), HR 88 beats/min, GCS 15 ($E_4V_5M_6$), and temperature 36.5°C. At the cohort level, baseline T_0 vital signs were: mean SBP 122.75 ± 22.82 mmHg, mean DBP 78.00 ± 12.11 mmHg, mean PP 44.75 ± 25.63 mmHg, mean MAP 92.92 ± 11.18 mmHg (median 95.50 mmHg), mean HR 90.75 ± 6.29 beats/min, mean RR 18.50 ± 1.00 breaths/min, and mean SpO_2 97.75 ± 0.96%, as detailed in Table 1.

Table 1. Baseline Characteristics, Comorbidities, Surgical Pathologies, and Admission Vital Signs (T_0) of the Four Patients (n = 4).

Clinical Domain / Parameter	Case 1 (Geriatric Cerebrovascular-Orthopedic)	Case 2 (Lymphoma With Bone Involvement)	Case 3 (Endocrine-Gynecological Pathology)	Case 4 (Neurodegenerative-Gynecological Oncology)	Cohort Summary (Mean ± SD / Median [Range])
Age (years) & Sex	73 years, Female	48 years, Female	29 years, Female	63 years, Female	53.25 ± 19.15 years (Median: 55.50; Range: 29–73); 100% Female (4/4)
Primary Surgical Diagnosis	Closed fracture of left subtrochanteric femur (Seinsheimer Type IIB) after mechanical slip-and-fall onto left side (5 days prior)	Multiple lytic lesions with pathological fracture of left lesser trochanter due to bone involvement by Non-Hodgkin's Lymphoma (NHL)	Secondary amenorrhea (6 months) due to Asherman's syndrome (histopathology: chronic endometritis)	Giant ovarian cystoma (14 cm diameter) with 4-month pelvi-abdominal distension, dyschezia, and dysuria	2 Proximal femur fractures (50%); 2 Uterine/ovarian pathologies (50%)
Systemic Comorbidities & Medical History	Ischemic stroke (2024) with residual left leg paresis & facial lip deviation; thoracic dextroscoliosis & aortosclerosis; oral citicoline	Right cervical lymph node excision for Non-Hodgkin's Lymphoma (2024); osteolytic femoral lesion	Type 2 Diabetes Mellitus (2 years, on routine OAD); two prior uterine curettages under GA-TIVA (2019 & Feb 2025)	Parkinson's disease (since June 2025, right-hand resting tremor, on dopaminergic therapy); prior appendectomy (1977)	Neurological/vascular (50%), Lymphoma with bone involvement (25%), Endocrine T2DM (25%)
Definitive Surgical Procedure	Open reduction and internal fixation (ORIF) of left subtrochanteric femur	Curettage of lytic lesion + intramedullary (IM) femur nailing + PMMA bone cement augmentation	Total abdominal hysterectomy	Comprehensive surgical staging: Total abdominal hysterectomy & bilateral salpingo-oophorectomy (TAH-BSO)	100% Major lower-limb orthopedic or pelvic laparotomy procedures
Airway & Respiratory Status (T_0)	Patent; spontaneous symmetrical breathing; RR 20 breaths/min; SpO_2 99% (room air)	Patent; spontaneous symmetrical breathing; RR 18 breaths/min; SpO_2 98% (room air)	Patent; spontaneous symmetrical breathing; RR 18 breaths/min; SpO_2 97% (room air)	Patent; spontaneous symmetrical breathing; RR 18 breaths/min; SpO_2 97% (room air)	RR: 18.50 ± 1.00 breaths/min (18–20); SpO_2: 97.75 ± 0.96% (97–99%)
Baseline Blood Pressure & Pulse Pressure (T_0)	153/70 mmHg (PP: 83 mmHg; widened arterial stiffness phenotype)	100/66 mmHg (PP: 34 mmHg; borderline-low baseline reserve)	126/92 mmHg (PP: 34 mmHg; normotensive)	112/84 mmHg (PP: 28 mmHg; normotensive)	SBP: 122.75 ± 22.82 mmHg; DBP: 78.00 ± 12.11 mmHg; PP: 44.75 ± 25.63 mmHg
Baseline Mean Arterial Pressure (MAP, T_0)	97.67 mmHg (CPP target: MAP ≥ 70 mmHg)	77.33 mmHg	103.33 mmHg	93.33 mmHg	92.92 ± 11.18 mmHg (Median: 95.50; Range: 77.33–103.33 mmHg)
Baseline Heart Rate & Perfusion (T_0)	100 beats/min; warm extremities; CRT < 2 s	89 beats/min; warm extremities; CRT < 2 s	86 beats/min; warm extremities; CRT < 2 s	88 beats/min; warm extremities; CRT < 2 s	HR: 90.75 ± 6.29 beats/min (Median: 88.50; Range: 86–100); CRT < 2 s (100%)
Neurological Examination & Core Temp (T_0)	Alert, GCS 15 ($E_4V_5M_6$); pupils 3/3 mm reactive; left thigh swelling on Böhler-Braun skin traction; 36.5°C	Alert, GCS 15 ($E_4V_5M_6$); pupils 3/3 mm reactive; left leg on Böhler-Braun skin traction; 36.5°C	Alert, GCS 15 ($E_4V_5M_6$); pupils 3/3 mm reactive; no lateralization; 36.5°C	Alert, GCS 15 ($E_4V_5M_6$); pupils 3/3 mm reactive; right resting tremor; no CN palsy; 14 cm abdominal mass; 36.5°C	GCS 15 in 4/4 (100%); Core Temp: 36.5°C in 4/4

Note: Abbreviations: CPP, cerebral perfusion pressure; CN, cranial nerve; CRT, capillary refill time; DBP, diastolic blood pressure; GA-TIVA, general anesthesia with total intravenous anesthesia; GCS, Glasgow Coma Scale; HR, heart rate; IM, intramedullary; MAP, mean arterial pressure (calculated as DBP + [SBP − DBP]/3); NHL, Non-Hodgkin's Lymphoma; OAD, oral antidiabetic drugs; ORIF, open reduction and internal fixation; PMMA, polymethylmethacrylate; PP, pulse pressure (SBP − DBP); RR, respiratory rate; SBP, systolic blood pressure; SD, standard deviation; SpO_2, peripheral capillary oxygen saturation; T2DM, type 2 diabetes mellitus; TAH-BSO, total abdominal hysterectomy and bilateral salpingo-oophorectomy; T_0, baseline preoperative admission evaluation.

3.2. Preoperative Imaging and Laboratory Findings

Preoperative physical and radiological evaluation of Case 1 confirmed significant cardiopulmonary and orthopedic pathology that required careful neurovascular anesthetic planning. Inspection of the left lower extremity showed marked proximal thigh soft-tissue swelling, shortening, and external rotational deformity. In the Emergency Department the limb was first stabilized with adhesive skin traction over a padded green Böhler-Braun splint frame. A preoperative anteroposterior (AP) chest radiograph showed thoracic dextroscoliosis and prominent aortic arch calcification,

consistent with geriatric aortosclerosis. This matched her widened baseline pulse pressure of 83 mmHg (153/70 mmHg). AP pelvic, lateral left femur, and AP left femur radiographs (obtained on 9 August 2025) showed a complete, displaced, comminuted left intertrochanteric-to-subtrochanteric femur fracture, classified as Seinsheimer Type IIB. There was proximal femoral shaft overriding, varus angulation, and extensive peri-articular soft-tissue swelling, as shown in Figure 1.

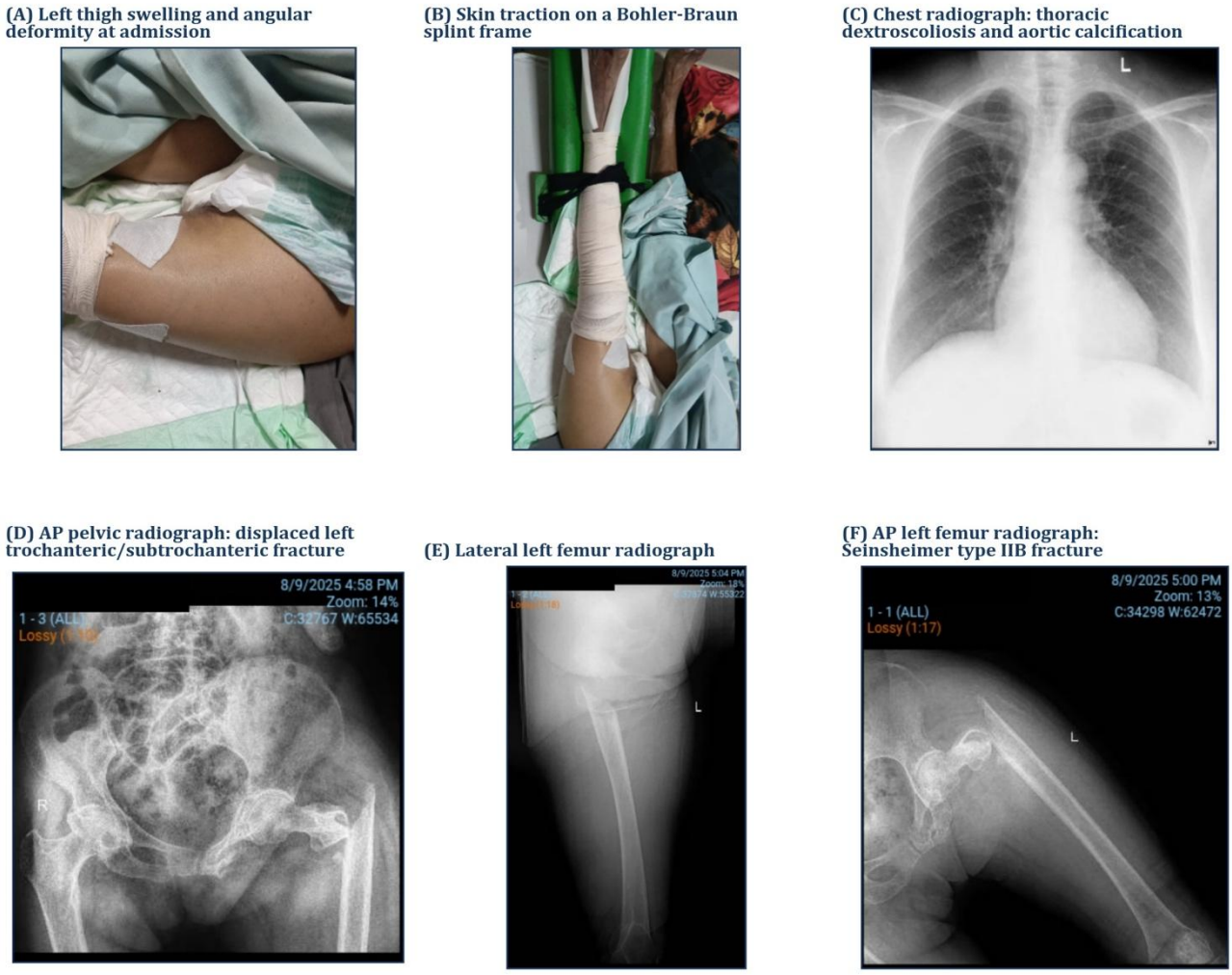


Figure 1. Case 1: Preoperative Findings (T_0). (A) Left thigh swelling and angular deformity at admission. (B) Skin traction on a Böhler-Braun splint frame. (C) Chest radiograph with thoracic dextroscoliosis and aortic arch calcification. (D–F) Anteroposterior pelvic, lateral left femur, and anteroposterior left femur radiographs of a displaced comminuted Seinsheimer Type IIB left subtrochanteric femur fracture. Overlay text on panels D–F comes from the radiograph viewer.

Preoperative hematological, coagulation, electrolyte, and hepatorenal profiles of the four patients showed distinct baseline metabolic phenotypes. All patients were eligible for neuraxial blockade on hemostatic grounds. In Case 1 (analyzed on 10 August 2025), the complete blood count showed moderate anemia attributed to the subtrochanteric fracture hematoma. Hemoglobin (Hb) was 8.70 g/dL (−35.07% below the institutional lower limit of normal [LLN] of 13.40 g/dL) and hematocrit (Hct) was 25.60% (−35.84% below the LLN of 39.90%). Red blood cell [RBC] count was 5.76 × 10^6/µL, interpreted as microcytic erythrocytosis (+4.73% above the upper limit of normal [ULN] of 5.50 × 10^6/µL). Leukocytes were normal (WBC 7.49 × 10^3/µL; reference 4.30–10.30 × 10^3/µL), and platelet reserve was good (PLT 271.00 × 10^3/µL; reference 142.00–424.00 × 10^3/µL). Serum electrolytes in Case 1 showed normonatremia (Na^+ 138.0 mmol/L) and normochloremia (Cl^- 99.0 mmol/L). Mild preoperative hypokalemia was present, with serum potassium (K^+) at 3.06 mmol/L (−12.57% below the LLN of 3.50 mmol/L). Albumin was mildly low (3.37 g/dL; −3.71% below the LLN of 3.50 g/dL). Other values were normal: random blood glucose [GDS] 138 mg/dL, serum urea 24.8 mg/dL (derived BUN 11.59 mg/dL), AST 16 U/L, and ALT 13 U/L (De Ritis ratio 1.23). Creatinine was low-normal and sarcopenic at 0.41 mg/dL (−38.81% below the LLN of 0.67 mg/dL; urea-to-creatinine ratio 60.49). Coagulation was intact (PT 9.6 s [control 11.1 s, ratio 0.86]; aPTT 20.6 s [control 26.6 s, ratio 0.77]). Case 2 had mild oncological anemia, with Hb 10.90 g/dL (−18.66% vs LLN) and Hct 32.30% (−19.05% vs LLN). Her RBC count was 5.76 × 10^6/µL, WBC 6.69 × 10^3/µL, and platelets 308.00 × 10^3/µL, all normal except the anemia. In Case 3 (analyzed on 11 August 2025) laboratory values were within or marginally below institutional limits: Hb 13.50 g/dL, Hct 39.40%, WBC 8.65 × 10^3/µL, PLT 288.00 × 10^3/µL, PT 10.3 s (control 11.3 s), aPTT 29.2 s (control 25.6 s), Na^+ 138.0 mmol/L, K^+ 3.95 mmol/L, and Cl^- 105.0 mmol/L. Glycemic status on OAD was well controlled (GDS 87 mg/dL). Albumin was 4.45 g/dL, urea 17 mg/dL (BUN 7.94 mg/dL), creatinine 0.67 mg/dL (urea/creatinine ratio 25.37), AST 22 U/L, and ALT 10 U/L

(De Ritis ratio 2.20). Case 4 also had normal hemostatic and electrolyte homeostasis, with Hb 12.50 g/dL (−6.72% vs LLN), Hct 38.60% (−3.26% vs LLN), WBC 6.66 × 10^3/µL (6,660/µL), PLT 262.00 × 10^3/µL, Na^+ 138.0 mmol/L, K^+ 4.07 mmol/L, and Cl^- 105.0 mmol/L. Across the four patients the cohort mean Hb was 11.40 ± 2.09 g/dL, mean Hct 33.98 ± 6.42%, mean WBC 7.37 ± 0.94 × 10^3/µL, mean PLT 282.25 ± 20.21 × 10^3/µL, Na^+ 138.0 mmol/L in all four patients, mean K^+ 3.73 ± 0.46 mmol/L, and mean Cl^- 103.00 ± 2.83 mmol/L, as summarized in Table 2.

Table 2. Preoperative Hematological, Coagulation, Electrolyte, and Hepatorenal Values (T_0) Relative to Institutional Reference Intervals.

Laboratory Parameter (Units)	Institutional Reference Interval	Case 1 (10 August 2025; Δ% vs Ref)	Case 2 (Pre-Op; Δ% vs Ref)	Case 3 (11 August 2025; Δ% vs Ref)	Case 4 (Pre-Op; Δ% vs Ref)	Cohort Mean ± SD (Range)
Hemoglobin, Hb (g/dL)	13.40–17.70	8.70 (−35.07% vs LLN; Moderate anemia)	10.90 (−18.66% vs LLN; Mild anemia)	13.50 (Within normal limits)	12.50 (−6.72% vs LLN; Borderline)	11.40 ± 2.09 (8.70–13.50)
Hematocrit, Hct (%)	39.90–51.00	25.60 (−35.84% vs LLN)	32.30 (−19.05% vs LLN)	39.40 (−1.25% vs LLN)	38.60 (−3.26% vs LLN)	33.98 ± 6.42 (25.60–39.40)
Erythrocytes, RBC (× 10^6/µL)	4.00–5.50	5.76 (+4.73% vs ULN; Microcytic erythrocytosis)	5.76 (+4.73% vs ULN)	4.68 (Normal normocytic profile)	4.42 (Normal normocytic profile)	5.16 ± 0.71 (4.42–5.76)
Leukocytes, WBC (× 10^3/µL)	4.30–10.30	7.49 (Normal; 72.72% of ULN)	6.69 (Normal; 64.95% of ULN)	8.65 (Normal; 83.98% of ULN)	6.66 (Normal; 64.66% of ULN)	7.37 ± 0.94 (6.66–8.65)
Platelets, PLT (× 10^3/µL)	142.00–424.00	271.00 (Normal hemostatic reserve)	308.00 (Normal hemostatic reserve)	288.00 (Normal hemostatic reserve)	262.00 (Normal hemostatic reserve)	282.25 ± 20.21 (262.00–308.00)
Prothrombin Time, PT (s)	Control: 11.1–11.3	9.6 (Control 11.1; Ratio 0.86 — Normal)	10.1 (Control 11.2; Ratio 0.90 — Normal)	10.3 (Control 11.3; Ratio 0.91 — Normal)	10.3 (Control 11.3; Ratio 0.91 — Normal)	10.08 ± 0.33 (9.6–10.3)
Activated Partial Thromboplastin Time, aPTT (s)	Control: 25.6–26.6	20.6 (Control 26.6; Ratio 0.77 — Normal)	25.4 (Control 26.0; Ratio 0.98 — Normal)	29.2 (Control 25.6; Ratio 1.14 — Safe for SAB)	29.2 (Control 25.6; Ratio 1.14 — Safe for CSE)	26.10 ± 4.07 (20.6–29.2)
Serum Sodium, Na^+ (mmol/L)	136.0–145.0	138.0 (Normonatremia)	138.0 (Normonatremia)	138.0 (Normonatremia)	138.0 (Normonatremia)	138.0 in 4/4
Serum Potassium, K^+ (mmol/L)	3.50–5.10	3.06 (−12.57% vs LLN; Mild hypokalemia)	3.84 (Normokalemia)	3.95 (Normokalemia)	4.07 (Normokalemia)	3.73 ± 0.46 (3.06–4.07)
Serum Chloride, Cl^- (mmol/L)	98.0–107.0	99.0 (Normochloremia)	103.0 (Normochloremia)	105.0 (Normochloremia)	105.0 (Normochloremia)	103.00 ± 2.83 (99.0–105.0)
Random Blood Glucose, GDS (mg/dL)	< 200.0	138.0 (Normoglycemia)	112.0 (Normoglycemia)	87.0 (Controlled T2DM on OAD)	94.0 (Normoglycemia)	107.75 ± 22.74 (87.0–138.0)
Serum Albumin (g/dL)	3.50–5.20	3.37 (−3.71% vs LLN; Mild hypoalbuminemia)	3.82 (Normal oncotic reserve)	4.45 (Normal oncotic reserve)	4.45 (Normal oncotic reserve)	4.02 ± 0.53 (3.37–4.45)
Serum Urea / BUN (mg/dL)	16.6–48.5 (BUN: 7.8–22.7)	24.8 / BUN 11.59 (Normal renal clearance)	21.4 / BUN 10.00 (Normal renal clearance)	17.0 / BUN 7.94 (Normal renal clearance)	17.0 / BUN 7.94 (Normal renal clearance)	Urea: 20.05 ± 3.78; BUN: 9.37 ± 1.77
Serum Creatinine (mg/dL) & Urea/Cr Ratio	0.67–1.17	0.41 (−38.81% vs LLN; Sarcopenic; Ratio 60.49)	0.68 (Normal; Ratio 31.47)	0.67 (Normal; Ratio 25.37)	0.67 (Normal; Ratio 25.37)	SCr: 0.61 ± 0.13 (0.41–0.68)
AST (SGOT) / ALT (SGPT) (U/L) & De Ritis	AST: 10–50 / ALT: 10–50	16 / 13 (De Ritis ratio: 1.23 — Normal)	19 / 14 (De Ritis ratio: 1.36 — Normal)	22 / 10 (De Ritis ratio: 2.20 — Normal)	22 / 10 (De Ritis ratio: 2.20 — Normal)	AST: 19.75 ± 2.87; ALT: 11.75 ± 2.06

Note: Abbreviations: ALT (SGPT), alanine aminotransferase; aPTT, activated partial thromboplastin time; AST (SGOT), aspartate aminotransferase; BUN, blood urea nitrogen (calculated as Urea / 2.1428); GDS, random blood glucose (gula darah sewaktu); Hct, hematocrit; Hb, hemoglobin; LLN, lower limit of normal; OAD, oral antidiabetic drugs; PLT, platelets; PT, prothrombin time; RBC, red blood cells; SCr, serum creatinine; SD, standard deviation; T2DM, type 2 diabetes mellitus; ULN, upper limit of normal; WBC, white blood cells; Δ%, percentage deviation from reference boundary [[(Observed − Limit)/Limit] × 100%). All coagulation parameters (PLT ≥ 262.00 × 10^3/µL, PT 9.6–10.3 s, aPTT 20.6–29.2 s) satisfied ASRA neuraxial safety criteria prior to L4–L5/L3–L4 puncture.

3.3. Block Onset and Regression (T_1 to T_4)

Intraoperative multiparameter monitoring in Case 1 confirmed that 10 µg of intrathecal DXM with 20 mg of 0.5% hyperbaric bupivacaine at the L4–L5 interspace (T10 dermatome target) gave smooth, controlled sympathetic modulation. MAP stayed at the 70 mmHg threshold set for this post-stroke patient. Because of the 2024 ischemic stroke and the widened baseline pulse pressure (153/70 mmHg; MAP 97.67 mmHg), the anesthetic protocol required continuous hemodynamic surveillance during the first 30 to 60 minutes after injection. The aim was to keep MAP ≥ 70 mmHg and protect cerebral perfusion pressure, with intravenous atropine and vasopressors ready at the bedside. The GE B40i multiparameter monitor in the operating room captured the T_2 maintenance equilibrium directly. Blood pressure was 90/63 mmHg, with a monitor MAP readout of exactly 70 mmHg (calculated formula MAP 72.00 mmHg; ΔMAP = −26.28% from baseline 97.67 mmHg with the formula MAP, or −28.33% with the monitor reading). Pulse pressure was 27 mmHg (ΔPP = −67.47%). Sinus heart rate on ECG was 78 beats/min (plethysmographic pulse rate 79 beats/min; ΔHR = −22.00% from baseline 100 beats/min). Lead II ST-segment level was +0.4 mV without ischemic depression, and SpO_2 was 98%. These findings are shown in Figure 2, together with Case

2's preoperative Böhler-Braun skin traction presentation and the biomarker deviation profiles of the cohort.

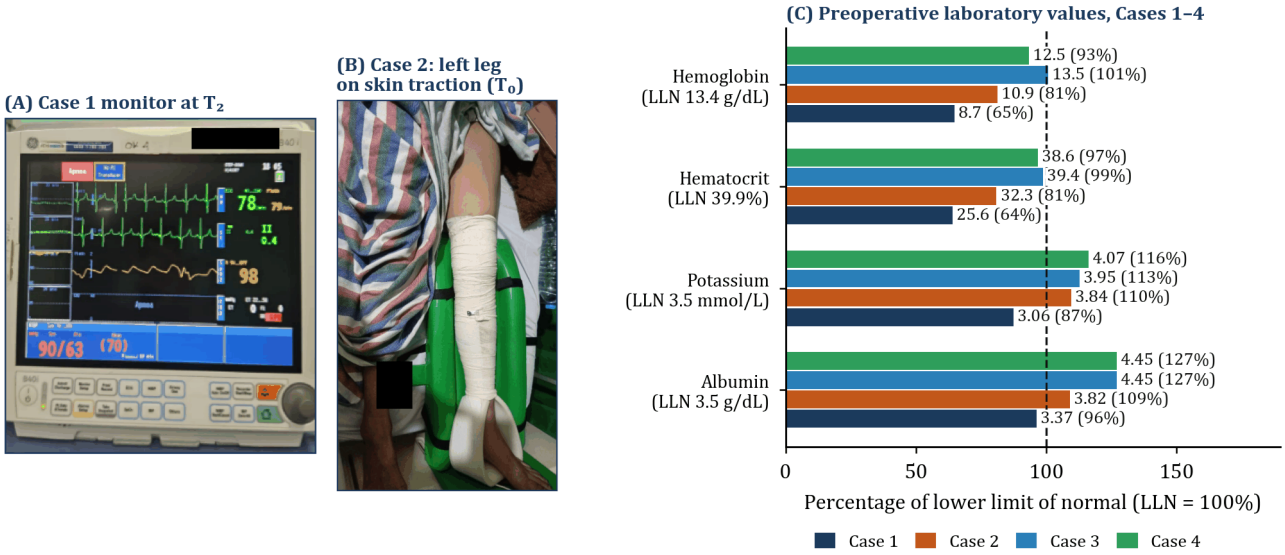


Figure 2. Intraoperative Monitor in Case 1, Skin Traction in Case 2, and Preoperative Laboratory Values. (A) GE B40i monitor capture at T_2 in Case 1: BP 90/63 mmHg, MAP 70 mmHg, HR 78 beats/min, Lead II ST +0.4 mV, SpO_2 98%. (B) Case 2 (48-year-old female with a pathological left lesser trochanter fracture) on skin traction at T_0. (C) Hemoglobin, hematocrit, potassium, and albumin of Cases 1–4 as a percentage of the institutional lower limit of normal.

Longitudinal evaluation of neuraxial blockade kinetics showed rapid onset in all four patients (n = 4) after 10 µg of intrathecal DXM, and analgesia that outlasted motor block in three of them. In Cases 1, 2, and 3, single-shot RA-SAB at L4–L5 used 20 mg (4 mL) of 0.5% hyperbaric bupivacaine plus 10 µg of intrathecal DXM (0.5 µg DXM per mg bupivacaine). The target cephalad sensory block was reached at T10 in Case 1 (subtrochanteric femur open reduction and internal fixation [ORIF]), T10 in Case 2 (curettage of the lesser trochanter lesion, intramedullary nailing, and PMMA bone cement augmentation), and T8 in Case 3 (total abdominal hysterectomy). Case 4 needed comprehensive surgical staging (total abdominal hysterectomy and bilateral salpingo-oophorectomy [TAH-BSO]) for her 14 cm giant ovarian cystoma, and the aim was to limit hemodynamic and neurological stress in the setting of Parkinson's disease. A CSE technique was therefore used. Intrathecal hyperbaric bupivacaine was reduced by 25% to 15 mg (3 mL) and given with 10 µg of intrathecal DXM (0.67 µg/mg) at L4–L5 to reach a T6 sensory block. Intraoperatively the block was supplemented through an L3–L4 epidural catheter (tip at T9–T10) with 10 mL of 0.75% ropivacaine covering T6–L1. In 100% of the cohort (4/4 patients), sensory blockade to the T10 dermatome was reached within ≤ 1.0 minute (60 seconds) of injection. Modified Bromage score 2 motor blockade was reached at 3 minutes (180 seconds), compared with a published mean of 11.6 minutes to Bromage 3 for lower-dose (5 µg) intrathecal DXM regimens (a different end point; descriptive comparison only). Motor inhibition lasted 5 hours (300 minutes) before the first voluntary lower-extremity movement (T_3). Complete spinal motor resolution came at 6 hours (360 minutes; T_4). Effective postoperative analgesia lasted 5 to 6 hours (300 to 360 minutes; cohort mean 330.0 ± 24.5 minutes, against a published median of 204 minutes for local anesthetic alone). The interval between the first leg movement and the end of analgesia was 30, 30, 0, and 60 minutes in Cases 1 to 4. Postoperative Numerical Rating Scale (NRS) pain scores stayed at 0–2 throughout the first 4 hours. They rose only gradually to 3–4 at 5–6 hours despite full motor recovery, as shown in Figure 3.

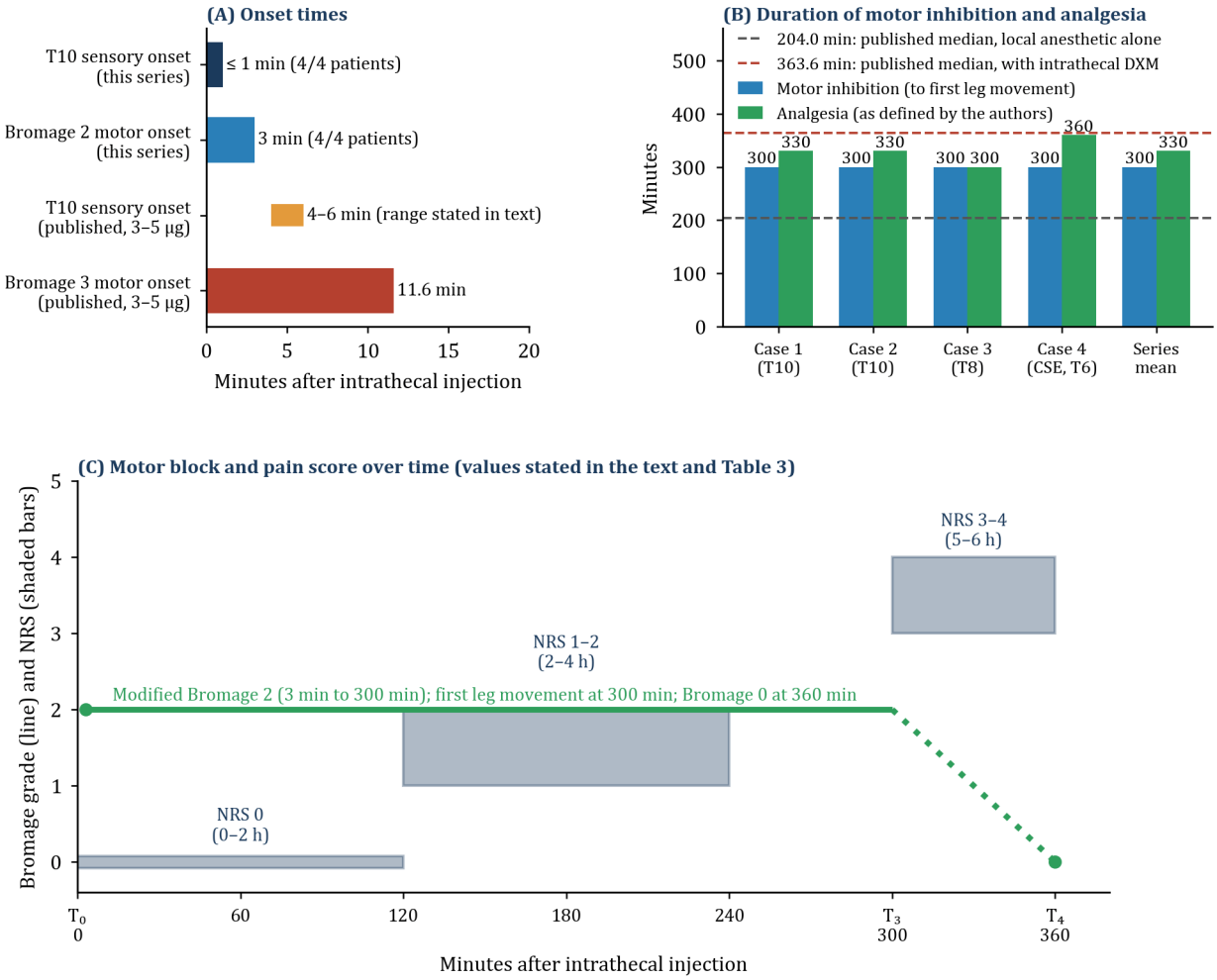


Figure 3. Block Onset and Duration After 10 µg of Intrathecal Dexmedetomidine (Cases 1–4). (A) T10 sensory onset (≤ 1 min) and Modified Bromage 2 motor onset (3 min) against published values for 3–5 µg doses (Bromage 3 end point). (B) Duration of motor inhibition and analgesia in each case against published medians for local anesthetic alone (204.0 min) and with intrathecal DXM (363.6 min). (C) Modified Bromage grade and NRS ranges stated in the text and Table 3. [Author query: sources of the published values, and Bromage and NRS values at each time point]

3.4. Postoperative Analgesia

Blockade regressed between 5 and 6 hours after injection (T_3–T_4), and rebound pain had to be prevented. Each patient therefore received a structured, procedure-specific multimodal analgesic regimen that was started before neuraxial induction. In Case 1 (73-year-old post-stroke subtrochanteric femur ORIF), preemptive analgesia was intravenous ketorolac 30 mg preoperatively, with spinal analgesia intraoperatively and scheduled intravenous ketorolac 3 × 30 mg/24 h (90 mg/day) postoperatively. Her NRS pain score stayed at 0–2 early and ≤ 3 at 6 hours, and she needed no systemic opioids that could precipitate post-stroke delirium or respiratory depression. Case 2 (48-year-old with an NHL pathological lesser trochanter fracture, curettage, IM nailing, and PMMA bone cement augmentation) received preemptive intravenous ketorolac 30 mg and intraoperative spinal anesthesia. Postoperatively she had a targeted neuraxial/perineural infusion of 0.25% ropivacaine plus 1 mg morphine in 10 mL total volume every 12 hours. This controlled the intense periosteal and oncological bone pain (NRS 0–2 initially, rising gradually to 3–4 at 5–6 hours). In Case 3 (29-year-old with Asherman's syndrome, hysterectomy, and T2DM), preoperative intravenous metamizole 1.0 g and intraoperative T8 spinal blockade were followed postoperatively by intravenous metamizole 3 × 1.0 g/24 h and oral paracetamol 4 × 750 mg/24 h (3.0 g/day). This avoided NSAID-induced renal prostaglandin inhibition in diabetes, and NRS stayed ≤ 3. In Case 4 (63-year-old with a giant ovarian cystoma, TAH-BSO, and Parkinson's disease), preoperative intravenous metamizole 1.0 g and intraoperative CSE blockade were followed postoperatively by epidural 0.25% ropivacaine plus 20 µg fentanyl in 10 mL total volume every 8 hours, with intravenous metamizole 3 × 1.0 g/24 h. Visceral and somatic pain control was smooth (NRS 0–2 early → 3 at 6 hours), without systemic opioid or butyrophenone/metoclopramide exposure, as detailed in Table 3. Cases 2 and 4 received neuraxial opioids (morphine and fentanyl), and all patients received scheduled non-opioid analgesics, so analgesic duration cannot be attributed to the intrathecal adjuvant alone.

Table 3. Anesthetic Technique, Intrathecal Dexmedetomidine (10 µg) Dosing, Block Onset and Regression, and Multimodal Analgesia.

Anesthetic & Kinetic Parameter	Case 1 (Subtrochanteric Femur ORIF)	Case 2 (Bone Involvement Femur Curettage + IM Nail + Cement)	Case 3 (Asherman's Syndrome Hysterectomy)	Case 4 (14 cm Ovarian Cystoma Staging TAH-BSO)	Cohort Kinetic Summary & Benchmark Comparison
Neuraxial Technique & Interspace	RA-SAB (Single-shot spinal) at L4–L5 interspace	RA-SAB (Single-shot spinal) at L4–L5 interspace	RA-SAB (Single-shot spinal) at L4–L5 interspace	Combined Spinal-Epidural (CSE): SAB at L4–L5; Epidural at L3–L4 (tip at T9–T10)	75% RA-SAB (3/4); 25% CSE (1/4); 100% L4–L5 intrathecal puncture
Intrathecal Hyperbaric Bupivacaine 0.5% Dose	20 mg (4 mL of 0.5% heavy bupivacaine)	20 mg (4 mL of 0.5% heavy bupivacaine)	20 mg (4 mL of 0.5% heavy bupivacaine)	15 mg (3 mL of 0.5% heavy bupivacaine; −25% dose reduction for CSE)	18.75 ± 2.50 mg (Median: 20 mg; Range: 15–20 mg)
Intrathecal Dexmedetomidine (DXM) Adjuvant Dose	10 µg intrathecal (DXM:Bupivacaine ratio = 0.50 µg/mg)	10 µg intrathecal (DXM:Bupivacaine ratio = 0.50 µg/mg)	10 µg intrathecal (DXM:Bupivacaine ratio = 0.50 µg/mg)	10 µg intrathecal (DXM:Bupivacaine ratio = 0.67 µg/mg)	10 µg in all patients (ratio 0.50–0.67 µg/mg)
Target Cephalad Sensory Dermatomal Level	T10 (somatic/periosteal femoral & hip capsule coverage)	T10 (somatic/periosteal femoral & lesser trochanter coverage)	T8 (pelvic visceral & uterine peritoneal coverage)	T6 (upper abdominal/pelvic staging; epidural ropivacaine 0.75% 10 mL T6–L1)	Range: T6–T10 (2 at T10 [50%], 1 at T8 [25%], 1 at T6 [25%])
Sensory Block Onset to T10 (T_1)	≤ 1 min (60 s)	≤ 1 min (60 s)	≤ 1 min (60 s)	≤ 1 min (60 s)	≤ 1 min in 4/4
Motor Block Onset to Modified Bromage 2 (T_1)	3 min (180 s)	3 min (180 s)	3 min (180 s)	3 min (180 s)	3 min in 4/4 (published mean to Bromage 3 with 5 µg DXM: 11.6 min)
Duration of Motor Inhibition (T_3, Initial Leg Movement)	300 min (first leg movement)	300 min (first leg movement)	300 min (first leg movement)	300 min (first leg movement)	300 min in 4/4; complete recovery at 360 min
Duration of Effective Postoperative Analgesia (T_4)	330 min	330 min	300 min	360 min	330 ± 24.5 min (range 300–360); published median with local anesthetic alone: 204 min
Postoperative NRS Pain Trajectory (0–10 Scale)	0–2h: NRS 0; 2–4h: NRS 1–2; 5–6h: NRS 3 (mild)	0–2h: NRS 0; 2–4h: NRS 1–2; 5–6h: NRS 3–4 (mild-mod)	0–2h: NRS 0; 2–4h: NRS 1; 5–6h: NRS 3 (mild)	0–2h: NRS 0; 2–4h: NRS 1; 5–6h: NRS 3 (mild)	Early (0–4 h): NRS 0–2 (100%); Late (5–6 h): NRS 3–4 after motor recovery
Preoperative & Intraoperative Analgesia	Pre-op: IV Ketorolac 30 mg; Intra-op: Spinal regimen	Pre-op: IV Ketorolac 30 mg; Intra-op: Spinal regimen	Pre-op: IV Metamizole 1 g; Intra-op: Spinal regimen	Pre-op: IV Metamizole 1 g; Intra-op: CSE + Epidural Ropivacaine 0.75% 10 mL	Preemptive non-opioid analgesia in 4/4
Postoperative Multimodal Maintenance Analgesia	IV Ketorolac 3 × 30 mg/24 h (90 mg/day; no systemic opioid required)	Epidural/perineural Ropivacaine 0.25% + Morphine 1 mg in 10 mL q12h	IV Metamizole 3 × 1 g/24 h + Oral Paracetamol 4 × 750 mg/24 h (3 g/day)	Epidural Ropivacaine 0.25% + Fentanyl 20 µg in 10 mL q8h + IV Metamizole 3 × 1 g	Procedure-specific multimodal analgesia; neuraxial opioid in Cases 2 and 4; no IV bolus opioid recorded

Note: Abbreviations: COX, cyclooxygenase; CSE, combined spinal-epidural; DXM, dexmedetomidine; IM, intramedullary; IV, intravenous; NRS, Numerical Rating Scale (0 = no pain, 10 = worst imaginable pain); ORIF, open reduction and internal fixation; PMMA, polymethylmethacrylate; q8h/q12h, every 8 or 12 hours; RA-SAB, regional anesthesia subarachnoid block; TAH-BSO, total abdominal hysterectomy and bilateral salpingo-oophorectomy; T_1, block onset window (1–3 min); T_3, motor recovery threshold (5 h / 300 min); T_4, complete spinal resolution and analgesic transition window (5–6 h / 300–360 min).

3.5. Hemodynamic Course and the Hypotensive Event

Longitudinal hemodynamic trajectories from T_0 to T_4 showed stable cardiovascular and respiratory homeostasis in Cases 1, 3, and 4. They also showed the course of an acute intraoperative hypotensive event in Case 2. Case 3 had baseline BP 126/92 mmHg, MAP 103.33 mmHg, and HR 86 beats/min. Case 4 had baseline BP 112/84 mmHg, MAP 93.33 mmHg, and HR 88 beats/min. At T_2 (intraoperative maintenance) both showed only mild, physiological sympathetic attenuation (Case 3: BP 112/78 mmHg, MAP 89.33 mmHg [ΔMAP = −13.55%], HR 74 beats/min [ΔHR = −13.95%]; Case 4: BP 102/74 mmHg, MAP 83.33 mmHg [ΔMAP = −10.71%], HR 76 beats/min [ΔHR = −13.64%]). Neither needed a vasopressor or anticholinergic. Case 2, by contrast, entered the operating room with a borderline-low baseline arterial pressure of 100/66 mmHg (MAP 77.33 mmHg, PP 34 mmHg, HR 89 beats/min) and mild oncological anemia (Hb 10.90 g/dL). After the T10 spinal block began (T_1 BP 94/62 mmHg, MAP 72.67 mmHg), she stayed hemodynamically stable until surgical evacuation and intramedullary curettage of the osteolytic lesser trochanter lesion (T_2). The authors interpret the event as a possible acute visceral/periosteal vasovagal reflex (a Bezold-Jarisch-like cardioinhibitory and vasodepressor response) added to the T10 preganglionic sympathetic blockade; the reflex was not tested. Arterial pressure fell acutely to a nadir of 50/30 mmHg (PP 20 mmHg [ΔPP = −41.18%]; MAP 36.67 mmHg [ΔMAP = −52.58% from baseline]; HR 62 beats/min). The rescue protocol was executed at once: rapid 1,000 mL crystalloid fluid loading and a direct intravenous ephedrine bolus. Within minutes it restored normotensive circulation (BP 102/68 mmHg, MAP 79.33 mmHg, HR 80 beats/min). No perioperative hypoxia (SpO_2 97–98%), myocardial ischemia, or postoperative neurological sequela was recorded. In all four patients, respiratory rate (18–20 breaths/min) and peripheral oxygen saturation (SpO_2 97–99%) stayed within these ranges throughout surgery and recovery, as shown in Figure 4.

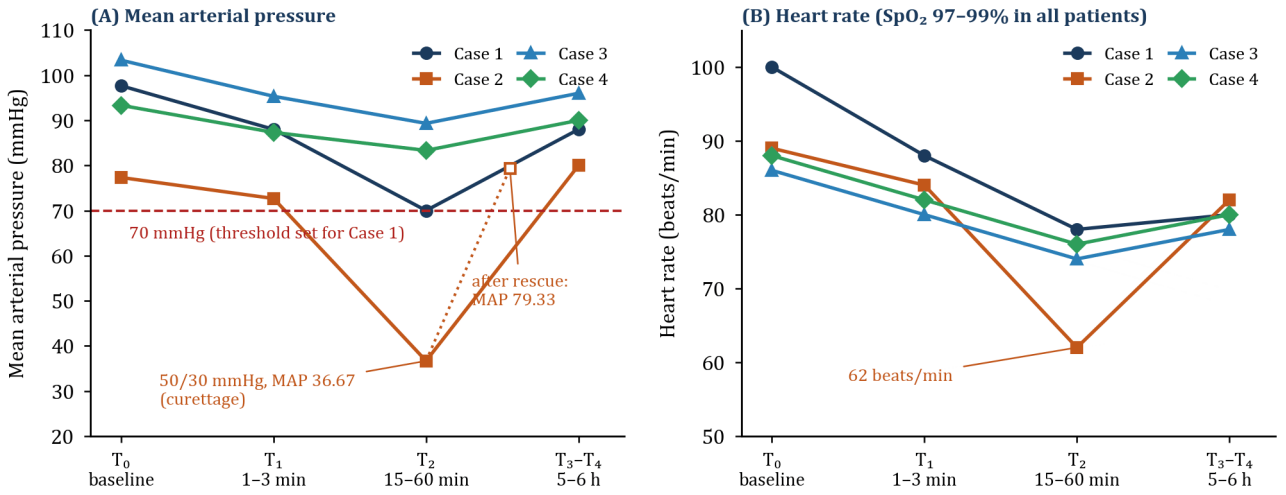


Figure 4. Hemodynamic Course of Cases 1–4 (T_0–T_4). (A) Mean arterial pressure (formula MAP; monitor reading 70 mmHg at T_2 in Case 1). The dotted line shows the rescue in Case 2 (50/30 mmHg to MAP 79.33 mmHg). (B) Heart rate; SpO_2 stayed at 97–99% in all patients.

3.6. Adverse Event Assessment and Comparison With Published Studies

No adverse drug event was recorded in Cases 1, 3, and 4. None had drug-attributable hypotension, bradycardia that needed atropine, shivering, or PONV, and the post-stroke (Case 1) and Parkinsonian (Case 4) neurological baselines were unchanged on clinical examination. In Case 2 the Naranjo ADR score was +3 ('Possible' ADR; WHO-UMC 'Conditional/Possible'). T10 spinal sympathectomy lowered baseline vascular tone, but the acute drop to 50/30 mmHg occurred during surgical curettage of the femoral lesion, on a background of borderline baseline blood pressure (100/66 mmHg), and it responded at once to fluid loading and ephedrine, as summarized in Table 4. The timing of the response after injection (onset within 3 minutes, regression after 5 to 6 hours) is given in Table 3.

Table 4. Hemodynamic Course (T_0 to T_4), Intraoperative Event, and Naranjo/WHO-UMC Assessment

Hemodynamic / Causality Domain	Case 1 (73 y, Post-Stroke CPP Target MAP ≥ 70 mmHg)	Case 2 (48 y, NHL Bone Involvement Curettage + Cement Augmentation)	Case 3 (29 y, Asherman's Syndrome + Controlled T2DM)	Case 4 (63 y, 14 cm Ovarian Cystoma + Parkinson's Disease)	Longitudinal Delta (Δ%) & Pharmacovigilance Verdict
T_0 Baseline Pre-Induction Hemodynamics	BP 153/70 mmHg (MAP 97.67, PP 83.0); HR 100 bpm; RR 20/min; SpO_2 99%	BP 100/66 mmHg (MAP 77.33, PP 34.0); HR 89 bpm; RR 18/min; SpO_2 98%	BP 126/92 mmHg (MAP 103.33, PP 34.0); HR 86 bpm; RR 18/min; SpO_2 97%	BP 112/84 mmHg (MAP 93.33, PP 28.0); HR 88 bpm; RR 18/min; SpO_2 97%	Cohort T_0 MAP: 92.92 ± 11.18 mmHg; HR: 90.75 ± 6.29 bpm
T_1 Post-Intrathecal Onset (1–3 min: Sensory T10 ≤ 1 min, Bromage 2 at 3 min)	BP 132/66 mmHg (MAP 88.00; ΔMAP −9.90%); HR 88 bpm; SpO_2 99%	BP 94/62 mmHg (MAP 72.67; ΔMAP −6.03%); HR 84 bpm; SpO_2 98%	BP 118/84 mmHg (MAP 95.33; ΔMAP −7.74%); HR 80 bpm; SpO_2 98%	BP 106/78 mmHg (MAP 87.33; ΔMAP −6.43%); HR 82 bpm; SpO_2 98%	Cohort T_1 MAP: 85.83 ± 9.52 mmHg (Mean ΔMAP: −7.53%)
T_2 Intraoperative Maintenance / Nadir (15–60 min Post-Injection)	GE B40i Monitor: BP 90/63 mmHg (MAP 70.00 [formula 72.00], PP 27.0; ΔMAP −26.28% formula; −28.33% monitor); HR 78 bpm (Pleth 79, ΔHR −22.00%); ST II +0.4 mV; SpO_2 98%	Transient nadir during curettage of the femoral lesion: BP 50/30 mmHg (MAP 36.67, PP 20.0; ΔMAP −52.59%); HR 62 bpm; SpO_2 97% → Rapidly reversed to BP 102/68 mmHg (MAP 79.33)	Stable intraoperative course: BP 112/78 mmHg (MAP 89.33; ΔMAP −13.55%); HR 74 bpm (ΔHR −13.95%); RR 18/min; SpO_2 98%	Stable CSE + epidural course: BP 102/74 mmHg (MAP 83.33; ΔMAP −10.71%); HR 76 bpm (ΔHR −13.64%); RR 18/min; SpO_2 98%	Case 1 MAP at the 70 mmHg threshold; Case 2 transient nadir reversed in < 5 min
Intraoperative Rescue and Surveillance	Strict 30–60 min surveillance; atropine & vasopressor on standby; MAP at 70 mmHg without bolus rescue	Immediate 1,000 mL crystalloid fluid loading + direct IV ephedrine bolus → complete normotensive restoration	Standard maintenance crystalloid co-loading; no vasopressor or anticholinergic required	Gradual CSE block titration (15 mg spinal bupivacaine + epidural ropivacaine); no vasopressor required	1/4 (25%) required transient vasopressor/fluid rescue during surgical bone curettage
T_3–T_4 Postoperative Recovery (5–6 h: Motor Recovery & Analgesic Window)	BP 128/68 mmHg (MAP 88.00); HR 80 bpm; SpO_2 99%; NRS 0–2 → 3; intact post-stroke neurology	BP 104/68 mmHg (MAP 80.00); HR 82 bpm; SpO_2 98%; NRS 0–2 → 3–4; full motor recovery	BP 120/84 mmHg (MAP 96.00); HR 78 bpm; SpO_2 98%; NRS 0–2 → 3; normoglycemic recovery	BP 110/80 mmHg (MAP 90.00); HR 80 bpm; SpO_2 98%; NRS 0–2 → 3; no worsening of Parkinsonian tremor	SpO_2 97–99% and RR 18–20/min in all four; no PONV, pruritus, or shivering recorded
Naranjo ADR Probability Score and WHO-UMC Classification	No adverse drug event recorded; Naranjo not applicable	Naranjo +3 (Possible ADR; WHO-UMC Conditional/Possible): hypotension during curettage, baseline BP 100/66 mmHg, T10 sympathectomy	No adverse drug event recorded; Naranjo not applicable	No adverse drug event recorded; Naranjo not applicable	Naranjo assessed only for the hypotensive episode in Case 2; no other adverse event recorded

Note: Abbreviations: ADR, adverse drug reaction; BP, blood pressure; bpm, beats per minute; CPP, cerebral perfusion pressure; CSE, combined spinal-epidural; DXM, dexmedetomidine; HR, heart rate; IV, intravenous; MAP, mean arterial pressure; NHL, Non-Hodgkin's Lymphoma; NRS, Numerical Rating Scale; Pleth, plethysmographic pulse rate; PONV, postoperative nausea and vomiting; PP, pulse pressure; RR, respiratory rate; SpO_2, peripheral oxygen saturation; ST II, electrocardiogram Lead II ST-segment deviation; T2DM, type 2 diabetes mellitus; WHO-UMC, World Health Organization–Uppsala Monitoring Centre.

For external validity, the clinical and pharmacodynamic outcomes of our four-patient cohort were set against contemporary peer-reviewed randomized controlled trials and systematic meta-analyses published between 2021 and 2026. These evaluated intrathecal and perineural dexmedetomidine in orthopedic, obstetric, gynecological, and geriatric surgical populations.[23] The comparative matrix shows that our sensory onset latency (≤ 1 min to T10), motor onset latency (3 min to Bromage 2), motor blockade duration (300 min [5.0 h]), and effective postoperative analgesia duration (300–360 min [5.0–6.0 h], mean 330.0 ± 24.5 min) are close to international trials of 5–10 µg intrathecal DXM. Those trials report motor block durations of 280–310 minutes and postoperative analgesia of 330–420 minutes. Our motor onset was far faster than with 3–5 µg regimens (11–13 minutes), and analgesia (300 to 360 minutes) was longer than the published median of 204 minutes for local anesthetic alone, as detailed in Table 5. Several cited studies differ from this series in population, route, dose, and design.

Table 5. Comparison of the Present Series With Published Studies of Intrathecal, Perineural, and Intravenous Dexmedetomidine.

Study (Reference) and Design	Population and Sample Size	Regimen	Block Onset	Block and Analgesia Duration	Hemodynamic and Safety Findings
Present series (Adiwibowo & Yusuf, 2026), case series	n = 4 females (29–73 y): subtrochanteric ORIF (post-stroke), femoral lesion curettage with IM nail and cement (lymphoma), hysterectomy (T2DM), TAH-BSO for a 14 cm ovarian cystoma (Parkinson's disease)	Hyperbaric bupivacaine 0.5% 15–20 mg + intrathecal DXM 10 µg (RA-SAB in 3; CSE with epidural ropivacaine in 1)	Sensory T10 ≤ 1 min; Bromage 2 at 3 min in 4/4	Motor block 300 min; recovery 360 min; analgesia 300–360 min; NRS 0–2 (0–4 h), 3–4 (5–6 h)	Case 1 MAP 70 mmHg (90/63 mmHg, HR 78 bpm); Case 2 drop to 50/30 mmHg reversed with 1,000 mL fluid + ephedrine; SpO_2 97–99%; no shivering or PONV recorded
Mo et al. (2023)[1], prospective double-blind up-down sequential allocation RCT	n = 60 parturients, elective cesarean section, spinal anesthesia	Plain ropivacaine 8 or 10 mg + intrathecal DXM, starting at 5 µg	ED_{50} of DXM (T6 block within 10 min): 5.9 µg with 8 mg and 3.1 µg with 10 mg ropivacaine	Not an analgesia-duration study	Not summarized in the abstract
Bao et al. (2022)[24], prospective double-blind RCT	n = 60 hand-surgery patients, mid-forearm triple-nerve blocks	Ropivacaine; perineural vs intravenous DXM vs control	Not summarized in the abstract	Longer analgesia and sensory block with perineural DXM; mainly a perineural mechanism	Not summarized in the abstract
Sangkum et al. (2024)[2], prospective RCT	n = 38 elderly patients (60–80 y), TURP under spinal anesthesia	Intravenous DXM 0.4 µg/kg vs saline after the spinal block (not intrathecal)	Not applicable	Two-dermatome regression 104.4 ± 17.0 vs 80.6 ± 15.6 min; postoperative analgesia not different	Hemodynamic stability without more side effects
Shukla et al. (2024)[19], prospective randomized double-blind study	Lower-limb orthopedic surgery, n = 60	Hyperbaric bupivacaine 15 mg + intrathecal DXM 5 µg vs fentanyl 25 µg	Sensory block to T6: 2.40 vs 5.03 min	Longer sensory and motor block than with fentanyl	Stable hemodynamics; bradycardia was common
Kalbande et al. (2022)[20], randomized comparative study	Lower-limb surgery, ASA I–II, n = 60	Hyperbaric bupivacaine 12.5 mg + intrathecal DXM 5 µg vs fentanyl 25 µg	Earlier onset with DXM	Prolonged block with DXM	Not summarized in the abstract
Asghar et al. (2025)[25], quasi-experimental study	Hysterectomy, n = 220	Spinal DXM vs tramadol	Not summarized in the abstract	Longer time to first rescue analgesic, less rescue analgesic, lower VAS	Side effects comparable
Madhav et al. (2026)[26], randomized trial	Lower abdominal and lower-limb surgery, n = 60	Hyperbaric bupivacaine 15 mg + intrathecal DXM 10 µg vs nalbuphine 0.8 mg	Sensory 3.0 min; motor 5.1 min	Analgesia 353 vs 299 min	Hemodynamics comparable
Geng et al. (2025)[23], placebo-controlled double-blind RCT	Elderly hip-fracture patients under spinal anesthesia, n = 248	Overnight preoperative low-dose DXM (intravenous) vs placebo	Not applicable	Not applicable (primary outcome: delirium)	Postoperative delirium 10.3% vs 22.2%; better preoperative sleep

Note: ASA, American Society of Anesthesiologists; CSE, combined spinal-epidural anesthesia; DXM, dexmedetomidine; ED_{50}, median effective dose; IM, intramedullary; NRS, Numerical Rating Scale; ORIF, open reduction and internal fixation; PONV, postoperative nausea and vomiting; RA-SAB, subarachnoid block; RCT, randomized controlled trial; T2DM, type 2 diabetes mellitus; TAH-BSO, total abdominal hysterectomy and bilateral salpingo-oophorectomy; TURP, transurethral resection of the prostate; VAS, visual analog scale.

4. Discussion

4.1. Onset and the Sensory-Motor Recovery Window

In this case series, adding 10 µg of preservative-free intrathecal dexmedetomidine to 0.5% hyperbaric bupivacaine (15–20 mg) gave a rapid and sufficient neuraxial block in four high-risk orthopedic and gynecological patients. Two findings stand out. Blockade began very quickly: T10 pinprick sensory analgesia appeared within ≤ 1.0 minute and Modified Bromage 2 motor blockade within 3 minutes in all four patients. Recovery then showed analgesia that outlasted motor block in three patients, between 5 and 6 hours after injection. When hyperbaric bupivacaine is given alone into the subarachnoid space, onset and duration depend on passive diffusion across neural membranes and on reversible binding to the intracellular S6 segment of voltage-gated sodium channels (Nav1.7 and Nav1.8). Adding 10 µg of intrathecal DXM may change this pharmacodynamic profile. DXM binds spinal α_2-adrenoceptors with high affinity (α_2:α_1 selectivity ratio 1,620:1), and these receptors are concentrated in the superficial laminae (substantia gelatinosa) of the dorsal horn. At physiological CSF pH DXM is highly lipid soluble, so it should enter dorsal horn grey matter and intrathecal nerve rootlets within seconds of the L4–L5 injection. There it suppresses presynaptic voltage-gated Ca^{2+} influx and stops the release of the excitatory neurotransmitters glutamate and substance P from primary afferent C-fibers. At the same time it opens postsynaptic GIRK

K^+ channels and hyperpolarizes dorsal horn wide-dynamic-range (WDR) projection neurons. This presynaptic and postsynaptic hyperpolarization lowers the bupivacaine concentration needed to stop action potential propagation. These mechanisms could explain the ≤ 1.0-minute sensory onset and the 3.0-minute motor onset seen here. None of them was measured in this series.

The cellular basis for the low postoperative Numerical Rating Scale (NRS) pain scores also matters for enhanced recovery. Scores stayed at 0–2 during hours 0–4 and at 3–4 during hours 5–6, even after lower-extremity motor function began to recover at 5 hours (300 minutes) and resolved completely by 6 hours (360 minutes). Neurophysiological work has shown that DXM acts beyond Gi/o-coupled α_2-adrenoceptor signaling. It also inhibits hyperpolarization-activated cyclic nucleotide-gated (Ih) cation channels in dorsal root ganglion neurons,[11] which generate the inward pacemaker current that restores resting membrane potential after an action potential. Ih channel expression and DXM sensitivity may be higher in unmyelinated nociceptive C-fibers and lightly myelinated Aδ-fibers than in large-diameter, heavily myelinated Aα motor axons, but this has not been shown directly. DXM may hold unmyelinated C-fibers in a prolonged hyperpolarized state while myelinated Aα motor fibers repolarize and resume saltatory conduction at 5 hours. If this holds, 10 µg of intrathecal DXM could create a functional window of up to 60 minutes (between 300 and 360 minutes). Here the window was 30, 30, 0, and 60 minutes in Cases 1 to 4, and the postoperative analgesic regimens may also have contributed. During that interval patients regained voluntary lower-limb movement without recorded incisional or periosteal pain spikes. The full five-tier neuropharmacological, ion-channel, and autonomic cascade is summarized in Figure 5 as a hypothesis.

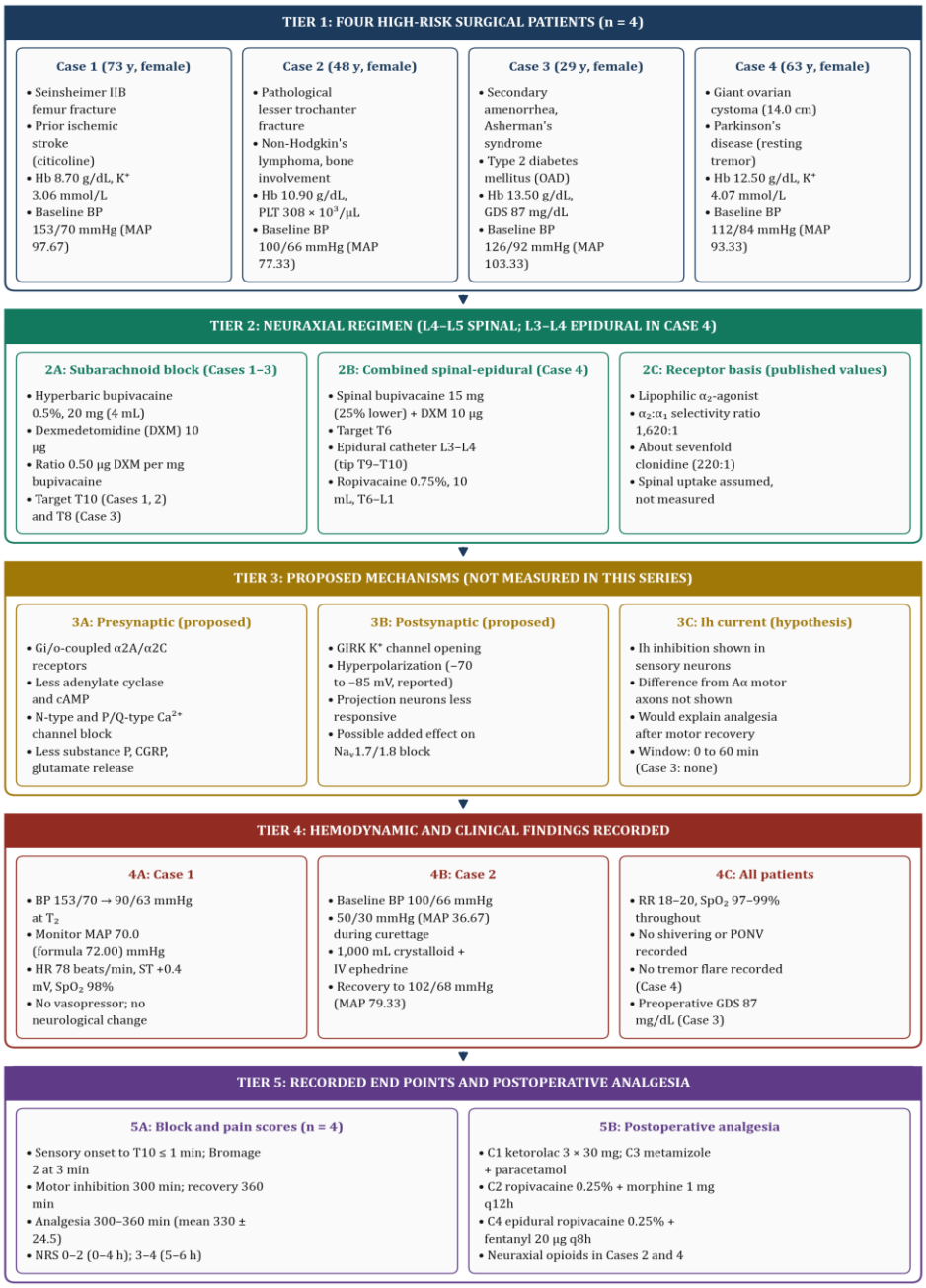


Figure 5. Proposed Mechanisms and Recorded Findings After 10 µg of Intrathecal Dexmedetomidine in Four High-Risk Patients (Hypothesis Schematic). Tiers 1, 2, 4, and 5 show recorded data; tier 3 shows mechanisms proposed in the literature that were not measured in this series.

4.2. Dose and Comparison With Published Studies

Comparing our 10 µg intrathecal DXM dosing kinetics with international dose-finding studies suggests a possible dose-response relationship for onset latency and block density. In randomized trials of lower intrathecal DXM doses (3 to 5 µg) combined with hyperbaric bupivacaine, motor onset latency to Bromage 3 typically ranges from 11 to 13 minutes, with a benchmark mean of 11.6 minutes. Sensory onset to T10 takes 4 to 6 minutes. In our cohort, 10 µg of intrathecal DXM was followed by motor onset at 3 minutes (to Modified Bromage 2, against 11.6 minutes to Bromage 3 in the benchmark trials) and sensory onset at ≤ 1.0 minute in all four patients. Surgical positioning and skin incision could therefore proceed quickly, without supplemental intravenous sedatives or opioids. Our analgesia duration of 300 to 360 minutes (5–6 hours; mean 330.0 ± 24.5 minutes) lies within the range reported in meta-analytic evidence. In that evidence, median analgesia duration was 363.6 minutes (range 252.3–824 minutes) with intrathecal DXM against 204 minutes (range 68.9–406 minutes) with local anesthetic alone, and a pooled mean prolongation of 191.3 minutes was reported.[22] Our mean of 330 minutes is 126 minutes (62%) longer than the published median of 204 minutes, but without a control group this cannot be attributed to DXM. Orthopedic and hysterectomy trials have compared other intrathecal adjuvants head to head: magnesium sulfate (50 mg), dexamethasone (4–8 mg), fentanyl (25 µg), nalbuphine (0.8–1.6 mg), and tramadol (20–25 mg). In several of them dexmedetomidine was reported to give faster sensory onset and better pain scores. This series has no comparator and cannot add to that comparison.

4.3. Hemodynamic Response in the Post-Stroke Patient

A main clinical contribution of this case series is its detailed description of autonomic and hemodynamic responses to 10 µg intrathecal DXM in contrasting cardiovascular phenotypes. Case 1 had geriatric post-stroke arterial stiffness. Case 2 had bone curettage for a lymphomatous lesion with a borderline baseline preload.[27,28] In theory, systemic or high-dose neuraxial α_2-agonists produce a biphasic hemodynamic response. The first phase is a transient hypertensive response, mediated by α2B-adrenoceptor vasoconstriction in peripheral vascular smooth muscle and seen mainly after a rapid intravenous bolus. The second phase is sustained arterial hypotension with sinus bradycardia. It is driven by central locus coeruleus and intermediolateral column (T1–L2) preganglionic sympatholysis, reduced norepinephrine overflow, and greater cardiac vagal baroreflex sensitivity. At an intrathecal microgram dose of 10 µg (the dose used in this series), however, plasma systemic absorption is expected to be small. Hemodynamic shifts are then governed mainly by the cephalad spread of subarachnoid local anesthetic sympathectomy.[29] Case 1 was a 73-year-old female with a 2024 ischemic stroke, residual left leg paresis, thoracic dextroscoliosis, aortosclerosis, and preoperative anemia (Hb 8.70 g/dL, Hct 25.60%). Preserving cerebral perfusion pressure (CPP = MAP − ICP) was essential for her, because chronic cerebrovascular disease shifts the lower limit of cerebral blood flow autoregulation to the right, toward a mandatory safety floor of MAP ≥ 70 mmHg.[30,31] The cephalad block was limited to T10, which spares T1–T4 cardioaccelerator fibers and upper splanchnic vasomotor tone. Case 1 then moved smoothly from a hypertensive, wide-pulse-pressure baseline (153/70 mmHg; MAP 97.67 mmHg; PP 83 mmHg; HR 100 beats/min) to an intraoperative equilibrium on the GE B40i monitor of 90/63 mmHg (MAP 70 mmHg; PP 27 mmHg; HR 78 beats/min; Lead II ST +0.4 mV; SpO_2 98%). MAP was kept at the 70 mmHg threshold throughout subtrochanteric femur fixation. Cerebral perfusion was not measured. No vasopressor rescue, neurological change, or postoperative delirium was recorded.

4.4. Hypotension During Femoral Curettage

Cases 1, 3, and 4 had smooth hemodynamic equilibrium. Case 2 differed: she had a marked but rapidly reversible intraoperative hypotensive episode (BP dropping to 50/30 mmHg; MAP 36.67 mmHg; ΔMAP = −52.58%). It occurred during surgical curettage of her osteolytic left lesser trochanter lesion, before intramedullary nailing and polymethylmethacrylate (PMMA) bone cement augmentation.[32] Clinical and pharmacovigilance analysis (Naranjo ADR score +3 ['Possible']; WHO-UMC 'Conditional/Possible') suggests that this nadir was probably not a primary toxic reaction to 10 µg of intrathecal DXM. It may reflect three stressors acting together. The first was a borderline-low preoperative blood pressure of 100/66 mmHg (MAP 77.33 mmHg) with mild oncological anemia (Hb 10.90 g/dL, Hct 32.30%), which means narrow intravascular preload reserve. The second was T10 preganglionic sympathetic venodilation, which reduced venous return from the lower limbs to the right atrium. The third was a possible acute surgical visceral/periosteal vasovagal reflex, including the Bezold-Jarisch mechanoreceptor reflex in an underfilled left ventricle. Forceful mechanical curettage and decompression of a highly vascularized Non-Hodgkin's Lymphoma lesion in the femoral medullary canal may have triggered it, and blood loss and anemia may also have contributed.[33]

Patients who have intramedullary curettage, reaming, and PMMA cementation for femoral metastatic bone disease are also prone to sudden intramedullary pressure surges, fat/marrow microembolization, and mediator-driven vasodilation, the features of early Bone Cement Implantation Syndrome (BCIS).[34,35] Venous return can fall abruptly in a patient under spinal sympathetic blockade. The partly empty left ventricle may then contract vigorously and activate unmyelinated C-fiber mechanoreceptors in the inferoposterior myocardial wall (the Bezold-Jarisch reflex arc). Vagal efferent tone could then rise and residual sympathetic vasoconstriction be withdrawn, which could give sudden hypotension (50/30 mmHg) with a heart rate of 62 beats/min. The event occurred during curettage, before nailing and cementation, so bone cement implantation syndrome is unlikely to explain it. Case 2 recovered promptly and completely after a rapid 1,000 mL crystalloid preload and a direct intravenous ephedrine bolus. Ephedrine is a mixed α_1- and β_1-adrenergic agonist that restores venous capacitance tone and myocardial inotropy/chronotropy. This recovery is compatible with a preload-dependent mechanism, but it does not identify the cause of the hypotension. It also points to the value of fluid co-loading and ready vasopressors during oncological femoral curettage and cementation under neuraxial anesthesia.

4.5. Respiratory, Glycemic, and Neurological Observations

In all four patients, peripheral oxygen saturation (SpO_2 97–99%) and spontaneous respiratory rate (18–20 breaths/min) stayed completely stable during the intraoperative and postoperative periods. No respiratory depression was recorded after 10 µg of intrathecal DXM; ventilatory drive itself was not measured. Intrathecal morphine or fentanyl behaves differently. These drugs diffuse rostrally in the CSF, bind µ-opioid receptors in the ventrolateral medulla and pre-Bötzinger complex, and blunt

CO_2 chemosensitivity. Dexmedetomidine acts on locus coeruleus α_2-adrenoceptors and produces a state of physiological 'cooperative sedation' that resembles non-rapid eye movement (NREM) stage 2 sleep. Respiratory drive is generally less affected than with opioids. Central α_2-adrenoceptor activation also lowers the hypothalamic thermoregulatory vasoconstriction and shivering thresholds by approximately 0.5°C. No shivering was recorded in our four patients (0/4), although body temperature was reported only at baseline. Shivering would matter for geriatric and oncological patients, in whom it can raise systemic oxygen consumption by 200% to 400% and precipitate myocardial ischemia.

The two gynecological laparotomy patients (Cases 3 and 4) had complex endocrine and neurodegenerative comorbidities, and they also benefited from 10 µg of intrathecal DXM.[25,36] Case 3 was a 29-year-old female with secondary amenorrhea from Asherman's syndrome and a 2-year history of Type 2 Diabetes Mellitus (preoperative GDS 87 mg/dL on OAD). She had had two uterine curettages under general anesthesia (GA-TIVA). Moving to RA-SAB (20 mg hyperbaric bupivacaine + 10 µg DXM to T8) avoided airway instrumentation and systemic opioid exposure.[37,38] Intraoperative glucose values were not reported, so an effect on the hyperglycemic response cannot be assessed. Case 4 was a 63-year-old female with a 14 cm giant ovarian cystoma and Parkinson's disease (right-hand resting tremor). General anesthesia carries substantial hazards for her. Intravenous opioids (fentanyl/remifentanil) can worsen nigrostriatal extrapyramidal rigidity. Dopamine-antagonist antiemetics (metoclopramide or droperidol) can precipitate an acute dystonic crisis. Autonomic orthostatic instability and pharyngeal dysphagia with aspiration pneumonia are further risks.[39,40] A tailored Combined Spinal-Epidural (CSE) regimen was used instead. The intrathecal hyperbaric bupivacaine dose was reduced by 25% to 15 mg, with 10 µg DXM at L4–L5 (T6 block). An L3–L4 epidural catheter (tip at T9–T10) supplemented the block with 0.75% ropivacaine (10 mL) intraoperatively and with 0.25% ropivacaine plus 20 µg fentanyl every 8 hours postoperatively. Under this regimen Case 4 had comprehensive surgical staging (TAH-BSO) with hemodynamic stability (MAP 93.33 → 83.33 mmHg; ΔMAP −10.71%). No PONV or rescue antiemetic was recorded, and her baseline neurological status was unchanged.[41,42]

4.6. Strengths, Limitations, and Practical Suggestions

The strengths of this series are its detailed longitudinal profile of four complex surgical phenotypes that are rarely included in homogeneous randomized trials, its use of a structured pharmacovigilance instrument (Naranjo/WHO-UMC) for the one adverse event, and its report of hematological, biochemical, radiological, and multiparameter hemodynamic data at each perioperative timepoint (T_0 to T_4). The limitations follow from the design. There are four patients and no comparator, so no effect of the adjuvant can be separated from the effect of the bupivacaine, the surgical stimulus, or the postoperative analgesia. Mechanisms (α_2, GIRK, Ih) and cerebral perfusion were not measured. Postoperative analgesia included scheduled ketorolac, metamizole, paracetamol, an epidural ropivacaine–fentanyl infusion in Case 4, and a ropivacaine–morphine infusion in Case 2, so analgesic duration is confounded. Onset and duration values are identical across patients, and exact times were not recorded for each patient. Published values used for comparison differ in endpoint (Bromage 3 versus Bromage 2), dose, and population. Temperature, glucose, fluid balance, and blood loss were not reported after induction. Prospective, multicenter randomized controlled trials should refine the best intrathecal α_2-adrenergic dose for high-risk surgical populations. Useful features would be parallel dose-comparison arms, continuous 15-minute dermatomal two-segment regression mapping, standardized Richmond Agitation-Sedation Scale (RASS) profiling, and extended post-discharge neurocognitive surveillance.

On the basis of these four patients we offer five practical suggestions for intrathecal DXM adjuvant therapy in high-risk surgical patients. They are hypotheses that need testing in controlled studies, not a protocol. (1) Restrict intrathecal DXM to ≤ 10 µg (specifically 5–10 µg of preservative-free solution) when it is combined with 15–20 mg of 0.5% hyperbaric bupivacaine. (2) Use Combined Spinal-Epidural (CSE) anesthesia with a 25% intrathecal local anesthetic dose reduction (15 mg bupivacaine + 10 µg DXM) whenever high thoracoabdominal dermatomal coverage (T6) is needed in elderly or neurodegenerative patients. (3) Consider an intraoperative MAP floor of ≥ 70 mmHg in patients with prior stroke or carotid/aortic atherosclerosis. (4) Give preemptive crystalloid co-loading (500–1,000 mL) and keep syringe-ready ephedrine and atropine at hand during orthopedic intramedullary curettage, reaming, and bone cementation, to counter visceral/periosteal vasovagal reflexes.[43,44] (5) Start scheduled multimodal non-opioid or low-dose epidural analgesia before the 5.0-hour motor recovery mark, to bridge the 5–6 hour sensory regression transition; dexmedetomidine adjuvants have prolonged the time to the first opioid request in multimodal regimens.[45]

5. Conclusion

In these four high-risk women, 10 µg of intrathecal dexmedetomidine was given with 0.5% hyperbaric bupivacaine (15–20 mg). The route was single-shot subarachnoid block (L4–L5) or combined spinal-epidural anesthesia (L4–L5 spinal with L3–L4 epidural catheter). It was followed by rapid sensory blockade to T6–T10 within ≤ 1.0 minute and Modified Bromage 2 motor blockade within 3 minutes. The patients were a 73-year-old ischemic stroke survivor with a Seinsheimer Type IIB subtrochanteric femur fracture and a 48-year-old patient with a pathological lesser trochanter fracture from Non-Hodgkin's Lymphoma. The others were a 29-year-old patient with Asherman's syndrome and Type 2 Diabetes Mellitus who had a hysterectomy, and a 63-year-old patient with a 14 cm giant ovarian cystoma and Parkinson's disease who had staging TAH-BSO. Motor inhibition lasted 5 hours (300 minutes), with complete motor recovery at 6 hours (360 minutes). Analgesia lasted 5 to 6 hours (300–360 minutes; NRS 0–2 initially, rising gradually to 3–4). Postoperative analgesia also included scheduled non-opioid drugs and, in two patients, neuraxial opioids.

No respiratory depression (SpO_2 97–99%, RR 18–20 breaths/min), shivering, or PONV was recorded, MAP was kept at or above 70 mmHg in the post-stroke patient, and no extrapyramidal or glycemic problem was noted in the patients with Parkinson's disease and diabetes mellitus. Surgical curettage of a vascularized femoral lesion was followed by a transient hypotensive episode (50/30 mmHg) in a patient with borderline preload under spinal sympathectomy, and it resolved with crystalloid (1,000 mL) and intravenous ephedrine. With four patients and no comparator, these observations cannot establish an effect of the adjuvant or its mechanism. Prospective, multicenter randomized dose-finding trials, stratified by geriatric frailty and surgical risk, are warranted.

Declarations

Ethics Approval and Consent to Participate

This case series was approved by the CMHC Research Center, Ethics Committee, Indonesia (Protocol Approval Number: 2025/0814) and conducted in accordance with the Declaration of Helsinki. Written informed consent for care and study participation was obtained from all four patients and their legally authorized family representatives.

Consent for Publication

Written informed consent for publication of de-identified clinical data, monitoring records, and diagnostic and clinical images was obtained from all four patients.

Availability of Data and Materials

All datasets generated and analyzed during this study are included in the article (Tables 1–5 and Figures 1–5).

Competing Interests

The authors declare that they have no competing interests.

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None.

Authors' Contributions

M.A.: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Visualization, Writing - original draft. M.F.Y.: Supervision, Validation, Resources, Writing - review & editing.

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Use of Artificial Intelligence

None.

6. References

1. Mo X, Huang F, Wu X, et al. Intrathecal dexmedetomidine as an adjuvant to plain ropivacaine for spinal anesthesia during cesarean section: a prospective, double-blinded, randomized trial for ED50 determination using an up-down sequential allocation method. BMC Anesthesiol. 2023;23(1):325. doi: 10.1186/s12871-023-02275-x..
2. Sangkum L, Termpornlert S, Tunprasit C, et al. Effect of low-dose dexmedetomidine to prolong spinal anesthesia in elderly patients: a prospective randomized controlled study. BMC Anesthesiol. 2024;24(1):427. doi: 10.1186/s12871-024-02815-z..
3. Sun Y, Yao Y, Li Y, et al. Dexmedetomidine for opioid-sparing postoperative analgesia: a systematic review and meta-analysis. BMC Anesthesiol. 2026;26(1):103. doi: 10.1186/s12871-025-03606-w..
4. Kumar S, Choudhury B, Varikasuvu SR, et al. A systematic review and meta-analysis of efficacy and safety of dexmedetomidine combined with intrathecal bupivacaine compared to placebo. Cureus. 2022;14(12):e32425. doi: 10.7759/cureus.32425.
5. Boshoff J, Fourtounas M, Pegu K, et al. Effectiveness of intrathecal dexmedetomidine versus fentanyl as additives to hyperbaric bupivacaine on postoperative analgesia in patients undergoing Cesarean section: a systematic review and meta-analysis. JBI Evid Synth. 2025;23(12):2379-2418. doi: 10.11124/jbies-24-00418..
6. Gibson AW, Cooper NE, Albrecht E, et al. Intrathecal morphine versus other techniques for postoperative pain management in the context of multimodal analgesia: a meta-analysis. Pharmaceuticals (Basel). 2025;18(4):512. doi: 10.3390/ph18040512..
7. Wang X, Zhang S, Wang C, et al. Real-time evaluation of the independent analgesic efficacy of dexmedetomidine. BMC Anesthesiol. 2023;23(1):68. doi: 10.1186/s12871-023-02022-2..
8. Liu W, Guo J, Zheng J, et al. Low-dose dexmedetomidine as a perineural adjuvant for postoperative analgesia: a randomized controlled trial. BMC Anesthesiol. 2022;22(1):249. doi: 10.1186/s12871-022-01791-6..
9. Weerink MAS, Struys MMRF, Hannivoort LN, et al. Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. Clin Pharmacokinet. 2017;56(8):893-913. doi: 10.1007/s40262-017-0507-7.
10. Schwerin S, Westphal C, Klug C, et al. Sedative properties of dexmedetomidine are mediated independently from native thalamic hyperpolarization-activated cyclic nucleotide-gated channel function at clinically relevant concentrations. Int J Mol Sci. 2022;24(1):519. doi: 10.3390/ijms24010519..
11. Zhang T, Liao X, Chen Y, et al. Dexmedetomidine prolongs lidocaine intravenous regional anesthesia in rats by blocking the hyperpolarization-activated cation current. Drug Des Devel Ther. 2024;18:1103-14. doi: 10.2147/DDDT.S450971.
12. Zhang Q, Xia L, Liang W, et al. Intrathecal dexmedetomidine combined with ropivacaine in cesarean section: a prospective randomized double-blind controlled study. Front Med (Lausanne). 2022;9:922611. doi: 10.3389/fmed.2022.922611..
13. Yadav I, Aggarwal A, Lakhanpal M, et al. Comparison of clinical efficacy of intrathecal ropivacaine versus ropivacaine with dexmedetomidine in patient posted for infraumbilical surgeries under spinal anesthesia. Asian J Med Sci. 2022;13(5):62-68. doi: 10.3126/ajms.v13i5.42270..
14. Singh S, Rathore P, Kumar U, et al. Comparison of two doses of intrathecal dexmedetomidine as an adjuvant to hyperbaric ropivacaine in infraumbilical surgeries: a double-blinded randomised clinical study. J Clin Diagn Res. 2026;20(2):UC01-UC05. doi: 10.7860/jcdr/2026/90029.24755..
15. Abd El-Hamed Hassan A, Abd-Allah Al-Kumity A, El-Deen Mahmoud Sayed Ahmed A, et al. Clinical comparative study between intrathecal dexmedetomidine and dexamethasone on prolonging the duration of intrathecal blockade in lower limb orthopedic surgery. Al-Azhar Med J. 2021;50(2):1467-1478. doi: 10.21608/amj.2021.158633..
16. Hazra S, Barua D, Mondal S, et al. Comparisons of effects of different doses of dexmedetomidine as additive in intrathecal blockade with 0.5% hyperbaric bupivacaine in lower limb orthopedic surgeries. Int J Sci Res. 2021;10(6):21-23. doi: 10.36106/ijsr/7606385..
17. Alshawadfy A, Elsadany MA, Elkeblawy AM, et al. Intravenous versus intrathecal dexmedetomidine as an additive to hyperbaric bupivacaine in spinal anesthesia for hip arthroplasty: a randomized controlled trial. Egypt J Anaesth. 2022;38(1):342-348. doi: 10.1080/11101849.2022.2085974..
18. Agha RA, Sohrabi C, Mathew G, et al. The PROCESS 2020 guideline: updating consensus Preferred Reporting Of CasE Series in Surgery (PROCESS) guidelines. Int J Surg. 2020;84:231-5. doi: 10.1016/j.ijsu.2020.11.005.
19. Shukla U, Singh RB, Mishra K, et al. A comparative study of intrathecal hyperbaric bupivacaine with fentanyl versus intrathecal hyperbaric bupivacaine with dexmedetomidine administered sequentially for lower limb orthopaedic surgeries: a prospective randomised double-blind study. Cureus. 2024;16(11):e73672. doi: 10.7759/cureus.73672..
20. Kalbande JV, Deotale KD, N AK, et al. Addition of dexmedetomidine and fentanyl to intrathecal hyperbaric bupivacaine for lower limb surgeries: a randomized, comparative study. Cureus. 2022;14(8):e28276. doi: 10.7759/cureus.28276..
21. Riaz MA, Qamar SB, Siddiqi A, et al. Comparison of duration of action in spinal anesthesia of 0.5% bupivacaine and 0.5% bupivacaine with dexmedetomidine. J Health Rehabil Res. 2024;4(3):1-5. doi: 10.61919/jhrr.v4i3.1459..
22. Paramasivan A, Lopez-Olivo MA, Foong TW, et al. Intrathecal dexmedetomidine and postoperative pain: a systematic review and meta-analysis of randomized controlled trials. Eur J Pain. 2020;24(7):1215-27. doi: 10.1002/ejp.1575.
23. Geng P, Shang Z, Cheng F, et al. Preoperative low-dose dexmedetomidine reduces postoperative delirium in elderly patients with hip fracture under spinal anesthesia: a randomized, double blind, controlled clinical study. J Clin Anesth. 2025;105:111897. doi: 10.1016/j.jclinane.2025.111897..
24. Bao N, Shi K, Wu Y, et al. Dexmedetomidine prolongs the duration of local anesthetics when used as an adjuvant through both perineural and systemic mechanisms: a prospective randomized double-blinded trial. BMC Anesthesiol. 2022;22(1):176. doi: 10.1186/s12871-022-01716-3..
25. Asghar HF, Bashir M, Sabir S, et al. Comparison of the effectiveness of tramadol and dexmedetomidine as adjuvants in spinal anesthesia for prolonging postoperative analgesia in patients undergoing hysterectomy. Pak J Health Sci. 2025;6(11):142-147. doi: 10.54393/pjhs.v6i11.3549..
26. Madhav BR, Kumar AS, Khan MAA, et al. Intrathecal dexmedetomidine versus nalbuphine as an adjuvant to 0.5% hyperbaric bupivacaine in lower abdominal and lower limb surgeries. Acta Med Int. 2026;13(1):414-419. doi: 10.21276/amit.2026.v13.i1.362..
27. Xu Z, Tang Z, Yao J, et al. Comparison of low-dose morphine intrathecal analgesia and sufentanil PCIA in elderly patients with hip fracture undergoing single spinal anesthesia: a randomized clinical trial. BMC Anesthesiol. 2022;22(1):124. doi: 10.1186/s12871-022-01677-7..
28. Çağıran Z, Vahabi A, Özgül KK, et al. Unilateral spinal anesthesia in hip fracture surgery for geriatric patients with high cardiovascular risk due to aortic stenosis is safe and effective. Geriatr Orthop Surg Rehabil. 2024;15:21514593241280908. doi: 10.1177/21514593241280908.
29. Zeng W, Shi Y, Zheng Q, et al. Ultrasound-assisted modified paramedian technique for spinal anesthesia in elderly. BMC Anesthesiol. 2022;22(1):242. doi: 10.1186/s12871-022-01751-0..
30. Komarov AS, Sokolov DA, Ganert AN, et al. Myocardial injury in patients with hypertonic disease at osteosynthesis of the hip and spinal anesthesia. Reg Anesth Acute Pain Manag. 2022;16(1):79-86. doi: 10.17816/1993-6508-2022-16-1-79-86..

31. Claassen JAHR, Thijssen DHJ, Panerai RB, et al. Regulation of cerebral blood flow in humans: physiology and clinical implications of autoregulation. Physiol Rev. 2021;101(4):1487-559. doi: 10.1152/physrev.00022.2020.
32. Klahs KJ, Heh E, Yousaf M, et al. Operative challenges of intramedullary nailing for subtrochanteric blastic pathological femur fracture: a case report. J Surg Case Rep. 2023;2023(1):rjac630. doi: 10.1093/jscr/rjac630..
33. Ladegaard TH, Stensballe J, Petersen MM, et al. Bone cement implantation syndrome in patients with cemented endoprostheses for metastatic bone disease in the femur. J Bone Oncol. 2025;52:100677. doi: 10.1016/j.jbo.2025.100677..
34. Qin Z, Deng Y, Li X, et al. Bone cement implantation syndrome induced by antibiotic-loaded bone cement covering the infected bone surface. Int J Surg Case Rep. 2021;89:106627. doi: 10.1016/j.ijscr.2021.106627..
35. Olsen F, Hård af Segerstad M, Nellgård B, et al. The role of bone cement for the development of intraoperative hypotension and hypoxia and its impact on mortality in hemiarthroplasty for femoral neck fractures. Acta Orthop. 2020;91(3):293-8. doi: 10.1080/17453674.2020.1745510.
36. Sinha M, Kumar M, Dubey I, et al. Comparison of morphine and dexmedetomidine as adjuvants to isobaric levobupivacaine for spinal anesthesia in patients undergoing abdominal hysterectomy. Anesth Essays Res. 2021;15(2):188-93. doi: 10.4103/aer.aer_88_21.
37. Hazarika P, Talukdar TK, Basumatary J, et al. Hemodynamic and analgesic effect of intrathecal dexmedetomidine with low dose hyperbaric bupivacaine in spinal anaesthesia, caesarean section: a randomized controlled trial. New Indian J OBGYN. 2023;10(1):93-98. doi: 10.21276/obgyn.2023.10.1.16..
38. Abdelrahman RAA, Abdel-Barr TMF, El-Sonbati MA, et al. Intrathecal bupivacaine-dexmedetomidine compared to intrathecal bupivacaine-neostigmine in elective caesarian section: a randomized controlled trial. SVU Int J Med Sci. 2025;8(1):576-585. doi: 10.21608/svuijm.2025.357051.2103..
39. Lenka A, Mittal SO, Lamotte G, et al. A pragmatic approach to the perioperative management of Parkinson's disease. Can J Neurol Sci. 2021;48(3):299-307. doi: 10.1017/cjn.2020.211.
40. Tao B, Liu K, Ding M, et al. Ultrasound increases the success rate of spinal needle placement through the epidural needle during combined spinal-epidural anesthesia. Obstet Anesth Dig. 2022;42(1):43-44. doi: 10.1097/01.aoa.0000816912.20159.28..
41. Gautam B, Tabdar S, Shrestha U. Comparison of fentanyl and dexmedetomidine as intrathecal adjuvants to spinal anaesthesia for abdominal hysterectomy. JNMA J Nepal Med Assoc. 2018;56(213):848-55. doi: 10.31729/jnma.3739.
42. Gautam B, Niroula S, Sharma M, et al. Effects of intrathecal dexmedetomidine as an adjuvant to hyperbaric bupivacaine for spinal anaesthesia in adults undergoing elective infra-umbilical surgery. JNMA J Nepal Med Assoc. 2017;56(208):379-87. doi: 10.31729/jnma.3394.
43. Kang S, Chae YJ, Park SK, et al. Prevention of bradycardia during spinal anesthesia under dexmedetomidine sedation in older adults. J Clin Med. 2022;11(21):6349. doi: 10.3390/jcm11216349..
44. Tan C, Yan S, Shen J, et al. Effects of dexmedetomidine on cardiac electrophysiology in patients undergoing general anesthesia during perioperative period: a randomized controlled trial. BMC Anesthesiol. 2022;22(1):271. doi: 10.1186/s12871-022-01811-5..
45. Wang Y, Wang L, Wang Y, et al. Dexmedetomidine as adjuvant of transversus abdominal plane block for cesarean delivery under multimodal analgesia: a randomized clinical trial. BMC Anesthesiol. 2026;26(1):147. doi: 10.1186/s12871-026-03642-0..