Original Article

Evaluation of Safety of Spinal Anaesthesia in Patients Receiving Perioperative Antithrombotic Therapy Undergoing Infrainguinal Revascularisation Surgeries: A One-Year Prospective Clinical Research

Udita Naithani, M.D., Anjuri Goyal, M.D., Surendra Kumar Sethi, M.D.,

Rajeev Navaria, M.D., Riyaz Ahamed, M.D., Vandana Gakkhar, M.D.

Department of Anaesthesiology, R.N.T. Medical College, Udaipur, Rajasthan 313001, India.

Abstract:

Objective: To evaluate anaesthetic outcome, patient outcome and timing of perioperative antithrombotic therapy in relation to intrathecal injection in patients undergoing infrainguinal revascularisation surgery, for peripheral artery disease (PAD) in spinal anaesthesia.

Material and Methods: A one-year prospective observational study was conducted; from May 2019 to May 2020, in a tertiary care centre. This included all consecutive patients undergoing infrainguinal revascularisation surgery for PAD under spinal anaesthesia. Preoperative antithrombotics were stopped, as per standard guidelines, to achieve a normal coagulation profile before spinal anaesthesia. Perioperative data related to the patients, antithrombotics, anaesthesia, surgery, and complications were recorded. Primary outcomes measured were anaesthetic outcome in terms of spinal success and spinal safety. Secondary outcomes measured were timing of perioperative antithrombotic therapy in relation to intrathecal injection and patient outcomes defined as: good, morbidity or mortality.

Results: A total of 102 patients were evaluated, with a mean age of 54.69±16.36 years (91% males, 9% females): 58% had medical comorbidities. A single dose of intravenous (IV) unfractionated heparin (5,000–7,500 IU) was given intraoperatively at 24.97±3.69 minutes after intrathecal injection. Anaesthetic outcome was good in all patients; in terms of spinal safety (100%), as none of the patients developed spinal related complications. All had spinal success (100%), as no patient required conversion to general anaesthesia. Postoperatively, 98% (100) of patients had good outcomes, and mortality only occurred in 2% (2) of patients.

Contact: Dr. Rajeev Navaria, M.D.
Department of Anaesthesiology, R.N.T. Medical College, Udaipur, Rajasthan 313001, India.
E-mail: drrajeevnavaria@gmail.com

Conclusion: Spinal anaesthesia is safe and effective for infrainguinal revascularisation surgery. If the patient has a normal preoperative coagulation profile, and the timeline to stop antithrombotic therapy is strictly followed, administration of IV unfractionated heparin (5,000–7,500 IU); at approximately 25 minutes after intrathecal injection, was found to be safe.

Keywords: antithrombotics, heparin, peripheral artery disease, revascularisation, spinal anaesthesia, UFH

Introduction

Peripheral artery disease (PAD), also known as peripheral vascular disease (PVD), is an abnormal narrowing of arteries other than those that supply the heart or brain. It most commonly affects the lower limbs; however, other arteries may also be involved. Peripheral vascular revascularisation surgery remains the mainstay of treatment, if block is extensive and endovascular intervention is not feasible. Embolectomy, endarterectomy and bypass grafting are the commonly used surgical techniques[1]. There has been a global rise in the prevalence of PAD of more than 17% over a 5-year period (202 million in 2010, which increased to 236 million in 2015). This rise was 13% in high income countries and 29% in the low to middle income countries, resulting in an increase of related disease burden upon health care system worldwide[2]. Peripheral revascularisation surgery is classified as high risk by the recent American College of Cardiology and American Heart Association (ACC/AHA) guidelines on preoperative assessment[3]. PAD is a marker for severe multi-system atherosclerosis and for patients with critical limb ischaemia involving lower limb revascularisation presenting a significant challenge to the anaesthesiologist. These patients are usually elderly, with a high prevalence of hypertension, coronary artery disease, diabetes mellitus, cerebro-vascular, renal-vascular disease, and smoking-related respiratory diseases, which makes general anaesthesia more risky[4].

Both general anaesthesia (GA) and regional anaesthesia have been used for infrainguinal revascularisation surgery, and currently, there is insufficient evidence in favour of one technique over the other. This is because of distinct advantages and disadvantages of both, and no clinically significant differences have been found in long term survival with either technique[5–7]. In past decades, regional anaesthesia has drawn more interest for major vascular surgery, owing to its benefits; such as a reduction in stress response, thrombotic response, blood loss, pulmonary complications, improvement in myocardial supply–demand ratio, cardiovascular stability, vascular graft blood flow and superior pain relief[8,9]. Though there is always a risk of developing neuraxial haematoma in these patients, due to continuation of antithrombotic therapy. Hence, these drugs need to be mandatorily withhold prior to surgery; as per the guidelines, to achieve a normal preoperative coagulation profile before instituting neuraxial block. Moreover, these patients tend to receive heparin intraoperatively to prevent coagulation during cross-clamping of arterial vessels, and postoperatively to prevent further thrombotic events. Therefore, the timing of heparin in relation to the neuraxial block also needs to be titrated to avoid spinal or epidural hematoma[10]. The timing of neuraxial procedures related to heparin therapy has been much debated and the accepted practice currently advocates the institution of a block at least 4–6 hours after, or 1 hour before the administration of unfractionated heparin (UFH); and 12–24 hours after or 4 hours before the administration of low molecular weight heparin (LMWH)[11,12]. The estimated incidence of spinal hematoma is 1:150,000 for spinal anaesthesia (SA) and 1:100,000 for epidural anaesthesia (EA) when heparin was administered >1 hour after the neuraxial procedure.

However, when heparin is administered <1 hour after the neuraxial procedure, the estimated incidence was increased to 1:13,000 for SA and 1:8,700 for EA[12].

In the literature, many studies[5-9] are available in which revascularisation surgeries have been safely performed under SA or EA; however, the details of perioperative anticoagulants received by such patients, and timing of lumbar puncture in relation to intraoperative heparin administration, were not highlighted. So, this prospective study was conducted, involving all consecutive patients who underwent infrainguinal revascularisation surgery under SA over a one year period. The aim was to evaluate the anaesthetic outcome in terms of spinal safety and the success rate as its primary objective. Perioperative antithrombotic therapy along with its relation to the time of intrathecal injection and patient outcome (morbidity/mortality) were undertaken as secondary objectives.

Material and Methods

After obtaining institutional ethical committee clearance (RNT/STAT/IEC/2018/1834) and informed written consent from the patients, a one-year prospective cross-sectional non-comparative observational study was conducted at our tertiary institute. The study was registered under Clinical Trials Registry-India (CTRI/2019/04/018512), in accordance with the principles of the Declaration of Helsinki. All consecutive, chronic PAD patients with critical limb ischaemia undergoing infrainguinal lower limb revascularisation surgery in SA over a period of one year were enrolled for the study; which was the basis of sample size. Patients were selected for peripheral revascularisation surgery under SA only when their preoperative coagulation profile was normal (platelet count >150,000-400,000/mm^3, prothrombin time 11-14 seconds and international normalised ratio <1.5) and antithrombotic therapy was stopped before neuraxial puncture; as per standard international guidelines[12] (Ticlopidine-10 days, Clopidogrel-7

days, Warfarin-5 days, LMWH-12-24 hours and UFH-6 hours). A total of 102 patients underwent revascularisation surgery in SA; from May 2019 to May 2020.

Exclusion criteria were patients for revascularisation surgery in whom general anaesthesia was chosen by the attending anaesthesiologist, based on a deranged preoperative coagulation profile, stenotic valvular lesion, local site infection, pre-existing hypotension, patient refusal, or any other contraindication to subarachnoid block.

A thorough pre-anaesthetic evaluation including: history, physical examination and investigations, was conducted. All data were recorded in a proforma by an anaesthesiologist who was involved in the study. Preoperative data included: demographic characteristics, history, examination, investigations and treatment related to PVD illness and associated medical comorbidities of the patients. Preoperative antithrombotic drugs, their time of stoppage, coagulation profile and time from admission to surgery were recorded. Standard ASA monitoring was applied to all the patients, which included non-invasive blood pressure (NIBP), electrocardiography (ECG), and peripheral oxygen saturation (SpO$_2$). The baseline haemodynamic parameters i.e., heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and SpO$_2$ were recorded. SA was administered using a 25 gauge spinal needle having hyperbaric bupivacaine (12.5 mg) and fentanyl (25 µg) under all aseptic precautions. Surgery was allowed to start after achieving a desired sensory level L1 (first lumbar dermatome). All patients were given supplemental oxygen via facemask @ 5 litres/minute. As per cardiothoracic and vascular surgery (CTVS) department protocol, a single dose of UFH 80-100 IU/kg intravenously (IV) was given at the time of painting the surgical site. This was so that its anticoagulant effect would be achieved in 5-7 minutes before vascular manipulation. The time of heparin administration as of intrathecal injection was noted.

Revascularisation surgery was perfromed using the standard technique suitable for the patients. Intraoperative data; including details of SA, sensory-motor block characteristics, haemodynamic parameters, amount of fluid and blood given, urine output, surgical details with its duration, complications and management, were recorded. Sodium bicarbonate (1 ml/kg), after release of the cross clamp, was given to all patients to prevent re-perfusion injury.

Intraoperative hypotension was defined as a fall in MAP >20% of baseline and treated with IV mephentermine 6mg intermittent bolus for three episodes. If hypotension persisted thereafter, it was treated with IV vasopressor (noradrenaline) infusion. Any episode of bradycardia, arrythmia, myocardial ischaemic event, cardiac arrest, occuring were treated accordingly. If the desired sensory level was not achieved or the patient complained of intraoperative pain, the anaesthetic technique was converted into GA, which was defined as "failed spinal" when calculated the spinal success rate.

Postoperative data included: spinal block recovery, which was recorded as the time taken from lumbar puncture to first pain (duration of analgesia), sensory regression to S1 (first sacral dermatome) as assessed by return of sensation to the lateral side of the foot (duration of sensory block), return to Bromage score 0 (duration of motor block), complications and their management. As per CTVS protocol, once the patients achieved complete recovery from SA without surgical site bleeding, post-operative IV UFH infusion was given, via a syringe pump for 3 days; thereafter, this was switched over to oral warfarin and aspirin. The patients were followed up till discharge and length of stay was noted.

The primary outcome measured was anaesthetic outcome in terms of spinal success (when surgery was performed in SA without conversion to general anaesthesia) and spinal safety (absence of spinal related neurological i.e., sensory or motor deficit and significant cardiovascular complications; such as >3 episodes of hypotension/ intractable hypotension requiring IV noradrenaline infusion, arrhythmia, myocardial ischaemic event, or cardiac arrest). Secondary outcomes measured were perioperative antithrombotic therapy in relation to the time of intrathecal injection and patient outcome defined as good (if discharged uneventfully), morbidity (neurological and significant cardiovascular complications as mentioned above) and mortality.

Statistical analysis

Data were collected, compiled and tabulated as number (proportion), continuous variables as mean±standard deviation (S.D.) and ordinal data as median (interquartile range). Data were entered into MS Excel and analysed with Statistical Package of Software Sciences version 20.0 (IBM Corporation), with a p-value<0.05 as statistically significant.

Results

Out of 102 revascularisation surgeries, etiology in 68 patients (67%) was atherosclerosis and Buerger's disease in 34 patients (33%). Mean age of the patients was 54.69±16.36 years, mean weight was 61.84±7.5 kg; 93 patients were males and nine patients were females, with American society of Anesthesiologists (ASA) physical status (ASA I-46%, II-44%, III-10%). Fifty-nine patients (58%) had co-existing medical morbidity single or in combination; such as hypertension (36%), coronary artery disease (6%), chronic obstructive pulmonary disease (10%), asthma (4%) and diabetes mellitus (13%). Prior history of tuberculosis was present in 4%, only one patient had prior history of a cerebro-vascular accident i.e. left upper extremity hemiparesis three years back. History of smoking was present in 62% patients for 14.22±8.35 years and alcohol in 30% patients for 13.16±9.42 years, which were stopped at the time of admission. All patients had complaints of pain (100%), ischaemic ulcer or gangrene being present in

84% of patients (72% toe, 12% foot). History of previous surgery for PAD was present in 36% of cases (amputation 15%, embolectomy 4% and lumbar sympathectomy in 3% patients). Antithrombotic therapy was stopped in all patients; according to standard guidelines, as mentioned earlier, and all patients had a normal preoperative coagulation profile[12]. Mean time from admission to surgery was 6.00±5.17 days.

Surgery was performed in the supine position on the femoral artery in 64 patients (63%) and in the prone position on the popliteal artery in 38 patients (37%). Endarterectomy with embolectomy was performed in all patients, along with bypass grafting in 11 patients (10%). Duration of surgery was 83.17±19.18 minutes. Total intravenous fluid input was 2,030.0±185.6 ml, which included 1 unit of blood along with crystalloids in all patients. Mean urine output was 209.0± 60.5 ml.

Patients were given SA using hyperbaric bupivacaine (12.5 mg) with fentanyl (25 µg) and adequate sensory–motor block of sufficient duration was achieved in all patients (Table 1). IV UFH was given at a dose of 5,000 IU in 68% patients and 7,500 IU in 32% after a mean time of 24.97±3.69 minutes of intrathecal injection. After SA, a single episode of hypotension was observed in 13 patients (12.7%) that was easily treated with mephentermine 6 mg IV bolus; thereafter, they remained haemodynamically stable. None of the patients in this study required noradrenaline infusion for persistent hypotension. In addition, the mean values of MAP and HR remained within 20% of baseline at all time intervals, which is suggestive of intraoperative haemodynamic stability (Figure 1 and 2). None of the patients had bradycardia nor hypoxia. Patients were shifted to the intensive care unit or ward, and all patients recovered completely from sensory–motor block at a mean time of four hours (Table 1). Postoperative heparin infusion was started after 6 hours of surgery in 101 patients (99%). There was only one patient in whom post operatively heparin was not started, because of postoperative bleeding; for which he was reexplored under GA in the night, but succumbed to mortality the next day, in spite of all measures taken. Peri–operative anticoagulants data is shown in Table 2.

Table 1 Spinal anaesthesia characteristics

Block characteristics	Observed values
Peak sensory blockade level	
Median (IQR)	T10 (T8–T10)
Range	T6–T12
Maximum Bromage score	
(0–3)	Bromage 3 (complete motor block) in all patients
Duration of analgesia (min)	
Mean±S.D.	247.30±25.93 (~4 hours)
Range	175–300 min
Duration of sensory block (min)	
Mean±S.D.	205.13±22.02 (~3.5 hours)
Range	135–248 min
Duration of motor block (min)	
Mean±S.D.	178.33±21.06 (~3 hours)
Range	115–222 min

Data was presented as median (IQR), Range and mean±S.D.
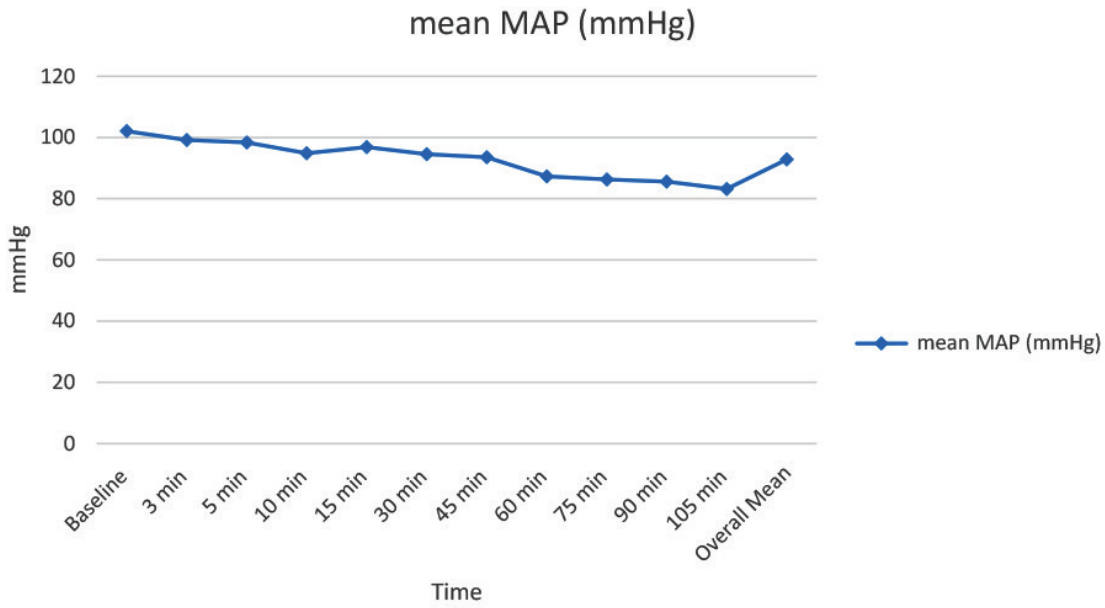IQR=interquartile range, S.D.=standard deviation

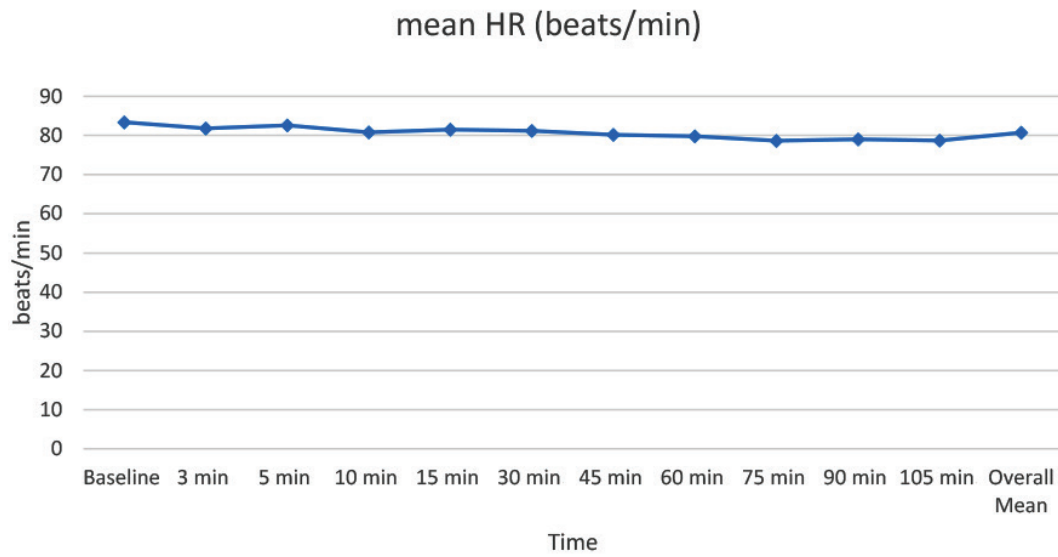**Figure 1** Intraoperative changes in mean arterial pressure (MAP)

Figure 2 Intraoperative changes in mean heart rate (HR)

Table 2 Perioperative anticoagulants/antithrombotic therapy

Variable	Distribution		Number (Proportion) (n=102)
Preoperative (n=102)	Not on prior antithrombotic therapy		20 (20%) [Trauma (ALI) cases]
	Prior antithrombotic therapy stopped as per timeline (Warfarin-5 days, Clopidogrel-7 days, Ticlopidine-10 days, UFH-6 hours, LMWH 12-24 hours)		82 (82%) [7 cases of them developed acute symptoms and IV UFH infusion (25,000 IU/24 hour @ 1,000 IU/hour) was given for it and stopped 6 hours before surgery]
Intraoperative (n=102)	Unfractionated Heparin dose (UFH)	5,000 IU	68 (67%)
		7,500 IU	34 (33%)
	Timing of UFH since intrathecal injection (min)	Mean±SD	24.97±3.69
		Range	21–40
Postoperative (n=101) [1 patient had postoperative haematoma, re-explored and heparin was not started]	IV UFH infusion for 3 days	25,000 IU/24 hours @ 1,000 IU/hour (body weight >50 kg)	82 (81%)
		12,500 IU/24 hours @ 500 IU/hour (body weight <50 kg)	19 (19%)
	On 3rd day and onwards	Tablet of warfarin 5 mg, aspirin 150 mg (body weight >50 kg)	82 (81%)
		Tablet of warfarin 3 mg, aspirin 75 mg (body weight <50 kg)	19 (19%)

Data was presented as number (proportion), range and mean±S.D. as appropriate
LMWH=low molecular weight heparin

Anaesthetic outcome was good in all the patients, as a 100% spinal success rate (no conversion to GA), and 100% spinal safety (no neurological and significant cardiovascular complications). Patient outcome was good in 100 patients (98%), and they were discharged after 7.69±1.82 days. Only two patients (2%) had mortality, which was not related to anaesthesia (first on the 6th day due to aspiration while feeding by an attendant in a lying position; 70-year-old male, and another on the next day due to post-operative bleeding: 60-year-old male).

Discussion

In this one-year prospective audit of 102 cases of infrainguinal revascularisation surgery, it was found that SA was a good choice as an adequate sensory and motor block of sufficient duration, as this was achieved and surgery was completed without conversion to GA in all of the patients. SA was also observed as a safe option, as no significant cardiovascular, respiratory or neurological complications occurred. Sensory as well as motor block recovery occurred in all the patients within four hours, signifying the absence of any spinal or epidural haematoma; even though all the patients received IV UFH (5,000–7,500 IU) around 25 minutes after intrathecal injection, and post-operative IV UFH infusion was started after 6 hours and continued for 3 days. This was then switched over to oral warfarin and aspirin. Such perioperative antithrombotic treatment is an established vascular surgery protocol to prevent thrombotic events[13,14].

The PAD population is at risk for major adverse cardiac events (MACE)[3] due to an increased atherosclerosis burden and associated medical comorbidities, which were also evident in this study (58% patients had medical diseases) as well as in other studies[7,8,15-17]. Hence, thorough pre-anaesthetic evaluation and optimisation involving a multidisciplinary approach is needed; however, care should be taken that life of the limb is not affected[18].

Both general and regional anaesthesia (spinal, epidural, nerve block) have been successfully used for revascularisation surgeries. The Cochrane Review (2013)[5] and other studies[6,7] have mentioned that the choice of anaesthesia does not significantly influence cardiac morbidity, overall mortality, 30 days graft patency, reoperation, amputation or length of hospital stay. In contrast, some authors have documented the superiority of SA and EA over GA. Singh et al.[8] conducted a prospective study in infrainguinal bypass surgery; from 1995-2003, in 14,788 patients (GA 9757, SA 2848, EA 2183) and reported that for GA a higher odds ratio was reported for graft failure (1.4), worsening of congestive heart failure or stroke (1.8), postoperative pneumonia (2.2), reoperation (1.4) and longer length of stay. This was compared to SA and EA patients, which were found to be comparable in all regards. Cook et al.[19] compared GA (n=51) and SA (n=50), and reported that GA was associated with higher incidence of hypertension (22% vs 0%), higher blood loss (792±440 ml vs 560±340 ml) and postoperative chest infections (33% vs 16%) as compared to SA, respectively.

In our institute, a single shot SA is preferred, rather than EA as there is less risk of neuraxial haematoma with it[11]. This has also been mentioned by Cook et al.[19]. This study only took patients for SA when their preoperative coagulation profile was normal, and antithrombotic treatment was stopped (clopidogrel-7 days, ticlopidine-10 days, warfarin-5 days, UFH-6 hours, LMWH-12 hours) to reverse any antithrombotic effect. In this study, mean time from admission to surgery was 6±5.17 days, which was taken for stoppage of antithrombotic drugs and optimisation of medical comorbid illness. As per standard guidelines, non-steroidal anti-inflammatory drugs did not appear to present a significant risk in the development of spinal or epidural haematoma, so cessation of aspirin before the neuraxial block is not recommended[12]. However, in our institute, as per CTVS protocol, aspirin was also stopped for 5 days in view of surgical haemostasis, because platelet function is affected following aspirin ingestion in addition to platelet aggregation being reported to normalise after 4-6 days of discontinuation[20]. Some case reports have also identified the concomitant use of other anticoagulants; such as aspirin, as a factor for increased risk of developing spinal or epidural haematoma[21,22]. Preoperative stoppage of aspirin might have contributed to no cases of neuraxial haematoma in this study. Previous studies[5-7] in revascularisation surgery have also highlighted the importance of stoppage of antithrombotic treatments and a normal coagulation profile before neuraxial blocks. However, the choice of anaesthesia should not jeopardise limb survival and GA should be given in case of emergency[17]. During the study period, two patients developed acute limb ischaemia as a complication of post-angiography femoral artery thrombus, and already received heparin. These patients were taken for emergency thromboembolectomy under GA, without delay, and the limb was saved. Charoensin et al.[24] also described that the patients undergoing coronary angiography and percutaneous coronary intervention received heparin during the procedure in a dose of 5,000-6,000 units.

It should be highlighted that the guidelines[12] state that UFH should be given after one hour of any neuraxial intervention, while in this study a single shot of IV heparin (5,000-7,500 IU UFH) was administered after 24.97± 3.69 minutes of intrathecal injection, and no neurological complications occurred. Similarly, previous studies[5-9], in which revascularisation surgeries were performed in SA or

EA, a single dose of heparin (80–100 IU/kg IV UFH) was used intraoperatively, and there was no case of neuraxial haematoma combined with complete sensory–motor block recovery occurring in all cases. However, the time of heparin administration after lumbar puncture was not mentioned in them.

In this study, the patient outcome was good in 100 patients (98%), and they were discharged after a mean length of stay of 7.69±1.82 days. Mortality occurred only in two patients (2%). The literature[18] mentions that maintenance of normovolemia, haemodynamic stability, avoidance of hypothermia, hypotension, and reperfusion injury are keys to successful outcomes in revascularisation surgeries, which was our aim also. Cook at al.[19] compared GA with SA for reversed vein femoropopliteal bypass graft surgery, and reported four deaths (4%) out of 101 patients (3 in GA, 1 in SA). Ghanami et al.[23] reported 157 deaths (3%) out of 5,462 infrainguinal bypass surgeries, and the mean and the median length of stay of surviving patients was 7.5±8.1 and 6 days, respectively.

There were some limitations of this study. No objective method; such as magnetic resonance imaging or computerised tomography scanning was used to exclude neuraxial haematoma. The activated clotting time was not measured to assess anticoagulation, which is in coherence to previous studies[5–9]. The success rate of graft and vessel patency after surgery was also not assessed, as the primary objective was to assess spinal anaesthetic outcome in vascular surgeries, with perioperative anticoagulation.

Conclusion

This study concludes that spinal anaesthesia is an effective and safe technique for infrainguinal revascularisation surgeries, if the preoperative coagulation profile is normal, and prior antithrombotics are stopped; as per standard guidelines. The administration of a single dose of IV UFH (5,000–7,500 IU) given at a mean time of around 25 min after lumbar puncture; therefore, implying it to be safe with no neurological sequelae.

It is also suggested that further multi–centric studies be conducted. These should include a large sample size in infrainguinal revascularisation surgery under spinal anaesthesia, in which the details of heparin dose and timing as of lumbar puncture could be recorded to prove its safety. Such studies would also provide a database for review of existing guidelines.

Conflict of interest

None

References

1. Vartanian SM, Conte MS. Surgical intervention for peripheral arterial disease. Circ Res 2015;116:1614–28.

2. Horváth L, Németh N, Fehér G, Kívés Z, Endrei D, Boncz I. Epidemiology of peripheral artery disease: narrative review. Life (Basel) 2022;12:1041.

3. Eagle KA, Berger PB, Calkins H, Chaitman BR, Ewy GA, Fleischmann KE, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery–executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). J Am Coll Cardiol 2002;39:542–53.

4. Golomb BA, Dang TT, Criqui MH. Peripheral arterial disease: Morbidity and mortality implications. Circulation 2006;114:688–99.

5. Barbosa FT, Jucá MJ, Castro AA, Cavalcante JC. Neuraxial anaesthesia for lower–limb revascularization. Cochrane Database of Systematic Reviews 2013;7:1–45. doi: 10.1002/14651858.CD007083.pub3.

6. Bode RH Jr, Lewis KP, Zarich SW, Pierce ET, Roberts M, Kowalchuk GJ, et al. Cardiac outcome after peripheral vascular surgery. Comparison of general and regional anesthesia. Anesthesiology 1996;84:3–13.

7. Pierce E, Pomposelli FB, Stanley GD, Lewis KP, Cass JL, LoGerfo FW, et al. Anesthesia type does not influence early

graft patency or limb salvage rates of lower extremity arterial bypass. J Vasc Surg 1997;25:226–33.

8. Singh N, Sidawy AN, Dezee K, Neville RF, Weiswasser J, Arora S, et al. The effects of the type of anesthesia on outcomes of lower extremity infrainguinal bypass. J Vasc Surg 2006;44: 964–70.

9. O'Toole DP, Cunningham AJ. Regional anesthesia for major vascular surgery. Yale J Biol Med 1993;66:447–56.

10. Wiersema AM, Watts C, Durran AC, Reijnen MM, van Delden OM, Moll FL, et al. The use of heparin during endovascular peripheral arterial interventions: a synopsis. Scientifica (Cairo) 2016;2016:1456298.

11. Horlocker TT. Regional anaesthesia in the patient receiving antithrombotic and antiplatelet therapy. Br J Anaesth 2011;107 (Suppl 1):i96–106.

12. Horlocker TT, Vandermeuelen, E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence–Based Guidelines (Fourth Edition). Reg Anesth Pain Med 2018;43:263– 309. doi: 10.1097/AAP.0000000000000763.

13. Foley TR, Waldo SW, Armstrong EJ. Antithrombotic therapy in peripheral artery disease. Vas Med 2016;21:156–69.

14. Weerasekera A, Gambhir RP. Antithrombotics in vascular surgery: current practice guidelines. Indian J Vasc Endovasc Surg 2017;4:85–91.

15. Brogneaux C, Sprynger M, Magnée M, Lancellotti P. 2011 ESC guidelines on the diagnosis and treatment of peripheral artery diseases. Rev Med Liege 2012;67:560–5.

16. Christopherson R, Beattie C, Frank SM, Norris EJ, Rock P, Parker SD, et al. Perioperative morbidity in patients randomized to epidural or general anesthesia for lower extremity vascular surgery. Anesthesiology 1993;79:422–34.

17. Goyal VD. Early intervention is an important factor in reducing mortality and morbidity after embolectomy/ thrombectomy for acute limb ischemia. Indian J Vasc Endovasc Surg 2015;2: 148–151.

18. Fraser K, Raju I. Anaesthesia for lower limb revascularization surgery. BJA Education 2015;15:225–30.

19. Cook PT, Davies MJ, Cronin KD, Moran P. A prospective randomized trial comparing spinal anaesthesia using hyperbaric cinchocaine with general anaesthesia for lower limb vascular surgery. Anaesth Intensive Care 1986;14:373–80.

20. Zisman E, Erport A, Kohanovsky E, Ballagulah M, Cassel A, Quitt M, et al. Platelet function recovery after cessation of aspirin: preliminary study of volunteers and surgical patients. Eur J Anaesthesiol 2010;27:617–623.

21. Vandermeulen EP, Aken HV, Vermylen J. Anticoagulants and spinal–epidural anesthesia. Anesth Analg 1994;79:1165–77.

22. Hyderally HA. Epidural hematoma unrelated to combined spinal– epidural anesthesia in a patient with ankylosing spondylitis receiving aspirin after total hip replacement. Anesth Analg 2005;100:882–3.

23. Ghanami RJ, Hurie J, Andrews JS, Harrington RN, Corriere MA, Goodney PP, et al. Anaesthesia based evaluation of outcomes of lower extremity vascular bypass procedures. Ann Vasc Surg 2013;27:199–207.

24. Charoensin C, Srichai R, Ingviya T. Vascular complications from coronary angiography/percutaneous coronary intervention: comparing day case patients and inpatients in a tertiary hospital in thailand: a retrospective cohort study. J Health Sci Med Res 2020;38:203–12.