

KNEE

Orthostatic intolerance following total joint arthroplasty remains a significant barrier to successful same-day discharge: a narrative review of an underreported complication

Papa Kyei¹, Mabua Chuene, Jurek RT Pietrzak, Allan Roy Sekeitto, Nkhodiseni Sikhauli, Lipalo Mokete and Collen Nkosi

Division of Orthopaedic Surgery, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa

Correspondence should be addressed to P Kyei: Pko.kyei@gmail.com or to 456652@students.wits.ac.za

- Early mobilisation following total joint arthroplasty is crucial in considering patients for successful same-day discharge (SDD).
- Recent years have seen an increase in SDD after total joint arthroplasty, with complication rates comparable to those with prolonged hospital stays.
- Orthostatic intolerance (OI) is a significant barrier to successful SDD after total hip and knee arthroplasties, with up to 52% of patients experiencing it.
- Patient-related factors include being female, being elderly, having multiple comorbidities, possessing a higher American Society of Anesthesiologists (ASA) status, experiencing pain levels exceeding 5/10, and using gabapentin.
- Surgery-related risk factors identified were spinal anaesthesia versus general anaesthesia, hip replacement versus knee replacement, and postoperative opioid use.
- Non-pharmacological and pharmacological approaches can be used to categorise management strategies. However, no treatment has conclusively proven to address OI fully.

Keywords: orthostatic intolerance; hip arthroplasty; knee arthroplasty; orthostatic hypotension

Introduction

Hip and knee arthroplasties are successful surgical treatments to relieve pain, restore limb function, and improve the quality of life in patients with degenerative joint disease (1). Early postoperative mobilisation is one cornerstone of enhanced recovery after joint replacement surgery (2, 3). Early ambulation benefits include a decreased length of stay (LOS), improved patient satisfaction outcomes, and reduced perioperative morbidity and mortality (2, 3). Orthostatic intolerance (OI) has been identified as one hindrance to early postoperative

mobilisation (4). Up to 52% of patients experience postoperative OI after hip and knee arthroplasties (5).

Same-day discharge (SDD) after total joint arthroplasty (TJA) has shown success in recent years and is on the rise (6). Debbi *et al.* showed that from 2010 to 2017, the annual increase in SDD was approximately 11% after total knee arthroplasty (TKA) and 16% after total hip arthroplasty (THA) (6). Keulen *et al.* showed that the complications and readmission rates after SDD were

equivalent to those of a prolonged hospital stay after TJA (7). However, OI is one hindrance to SDD (8).

Definition and impact

Orthostatic intolerance can be described as symptoms of dizziness, blurry vision, tremulousness, nausea, vomiting, palpitations, and/or a syncopal episode when transitioning from a recumbent position to sitting or standing (5, 9, 10, 11). It is primarily because of autonomic nervous system dysfunction, which results in dysregulation of the cardiovascular system, a reduction in arterial blood pressure, and a decrease in cerebral perfusion (4, 9). Blood pools in the lower limbs and abdominal vasculature in the upright position, resulting in a reduction in central blood volume and cardiac output (8). The baroreceptor reflex, coupled with vasoconstriction, should increase total peripheral resistance and, therefore, blood pressure. However, this vasopressor response is attenuated in intolerant patients (4, 10, 12). Orthostatic hypotension (OH), defined as a decrease in systolic arterial pressure of more than 20 mmHg or a reduction in diastolic arterial pressure greater than 10 mmHg, is one of the primary mechanisms underlying the symptoms experienced in OI (4, 9, 10). When OI symptoms occur without hypotension, combined with a sustained increase in pulse rate of more than 30 beats per minute (bpm) or a heart rate above 120 bpm within 10 min of a head-up tilt test or upon standing, it is considered postural orthostatic tachycardia syndrome (POTS) (13, 14, 15). POTS is a chronic form of OI with symptoms persisting for at least six months (13, 14). Serum norepinephrine levels are elevated in these patients upon standing (>600 ng/mL) (14, 15). This indicates dysregulation of the autonomic nervous system in OI, with one group exhibiting decreased sympathetic activity and another exhibiting increased sympathetic activity, yet both groups present with similar symptoms (15).

Orthostatic intolerance (OI) is common after hip and knee arthroplasties (5). Studies show that OI is more common at 6 h postoperatively than at 24 h postoperatively (5). After total hip arthroplasty (THA), OI is experienced in approximately 40% of patients 6 h after surgery (9). At 24 h post-THA, that figure drops to 20% (9, 12). Hristovska *et al.* showed similar figures for patients who experience OI post-total knee arthroplasty (TKA) (16). In their study, 44% of patients developed OI post-TKA at 6 h postoperatively, and 22% had OI at the 24-h mark post-surgery (16). However, in unicompartmental knee arthroplasty (UKA), OI was only noted in 14% of patients 6 h postoperatively (17). Kurkis *et al.* showed that OI occurred more commonly post-THA, followed by TKA, and finally, UKA (18).

Risk factors

Several factors have been proposed to cause postoperative development of OI, such as the response to the surgical insult, use of opioids, pain-related issues, after-effects of anaesthesia, blood loss, and a history of

Table 1 Risk factors for OI.

Patient-related	Surgery-related
Female	Spinal anaesthesia > general anaesthesia
Elderly	Spinal anaesthesia: ropivacaine > bupivacaine
Multiple comorbidities	THA > TKA > UKA
ASA ≥ 3	Approach: posterior > direct anterior > anterolateral
Pain ≥ 5/10	Postoperative opioid administration
Gabapentin use	

preoperative OI (4, 18). These proposed OI risk factors can be categorised into patient-related and surgery-related factors (Table 1).

Patient-related risk factors

Gender

Female gender is a significant patient-related risk factor for OI after hip and knee arthroplasties (12, 18). In the study by Kurkis *et al.*, females developed OI two times more than males after THA and TKA (18). Studies done post-gastrectomy and video-assisted thoracic surgery (VATS) corroborated this finding and identified the female gender as an independent risk factor for OI (19, 20). Reulecke *et al.* illustrated that males mount an increased sympathetic response when challenged to stand (21). This sympathetic response has a delayed onset in females, accompanied by a slight increase in the parasympathetic response (21). This is further exacerbated by females being prone to increased blood pooling in the lower limbs due to increased venous capacitance (22). Lamo-Espinosa *et al.* showed that females were at a higher risk of failing same-day discharge post-THA and TKA (23).

Age

OI in arthroplasty is typically present over the age of 60 years (9, 16, 18, 24). Hip and knee arthroplasty surgery is commonly performed in the older population (9, 16, 18, 24). The literature supports that advancing age increases the prevalence of OH and OI (25, 26). Those who had OI in the study by Kurkis *et al.* had a mean age of 67 (18). However, Skarin *et al.* and Hristovska *et al.* did not note a relationship between age and OI after THA and TKA, respectively (12, 16). In their systematic review, Sumbal *et al.* identified elderly patients as being at risk of failing same-day discharge after total joint arthroplasty (27). Older persons have an attenuated vagal tone control coupled with increased vessel wall stiffness of the baroreceptors, thereby increasing the likelihood of postural hypotension and intolerance (26).

Comorbidities

The presence of multiple medical conditions, such as neurodegenerative diseases, chronic heart failure,

hypertension, diabetes, renal failure, and autoimmune diseases, has been documented to be associated with OH and OI (28). The effect of these comorbidities is aggravated by their medications, such as antihypertensive and hypoglycaemic agents (28). Roach *et al.* evaluated the safe resumption of antihypertensives after THA and TKA and found that 35% of their patients developed hypotension on the resumption of their medication (29). They identified diuretics to be associated with the highest number of hypotensive episodes on resumption. They also did not note a relationship between the type of surgery (THA or TKA), gender, age, or type of antihypertensive regimen and the likelihood of postoperative hypotension (29). What they, however, recommended on days 1 and 2 post-surgery is that if a patient is a known hypertensive, the patient's blood pressure (BP) should be evaluated 15 min before receiving their boarded antihypertensives (29). If the systolic BP is less than 100 mmHg, the antihypertensives should be withheld and reviewed with the physician (29). If the systolic BP is less than 120 mmHg, the reading should be repeated with the patient in a seated position (29). If the reading is still below 120 mmHg, the antihypertensive should be postponed to after the patient's physiotherapy session and the BP should be reevaluated (29). Suppose the systolic BP is between 120 and 130 mmHg. In that case, one antihypertensive is administered, and depending on the number of agents the patient is already taking, the other drugs are given after the session (28). If the systolic BP is more than 130 mmHg, the appropriate antihypertensive(s) should be administered (29). Their patients had their blood pressures routinely measured every 4 h for 72 h postoperatively (29). More large-scale studies are needed to evaluate the appropriate resumption of antihypertensives after total joint arthroplasty and their applicability in patients being considered for same-day discharge. Kurkis *et al.* and Skarin *et al.* did not find a relationship between medical comorbidities, their associated treatment regimens, and OI (12, 18).

ASA class

An ASA class of more than 1, according to the American Society of Anesthesiologists (ASA), is a well-established risk factor for intolerance after gastrointestinal surgery (30). A study conducted in Ethiopia also identified that patients with an ASA class of 2 or more were associated with postoperative OI (31). However, in a study comparing THA and TKA, Kurkis *et al.* reported that patients with a lower ASA classification of 1 or 2 were more likely to develop postoperative orthostasis than those with an ASA classification of 3 or 4 (18). They speculated that lower ASA-classed patients were mobilised more aggressively earlier than higher ASA-classed patients (18). However, bias could have played a role in this finding. Patients who may have had a prior history of intolerance and those who had comorbidities had their perioperative management tweaked to avoid subsequent episodes of intolerance (18). Skarin *et al.* and Hristovska *et al.* did not,

however, identify a relationship between ASA class and OI or OH (12, 16). ASA class ≥ 3 was shown to be a risk factor for failing same-day discharge (SDD) after THA and TKA in the study by Lamo-Espinosa *et al.* (23). Sumbal *et al.* corroborated that finding in their systematic review, which showed that patients who have an ASA class of 3 and higher were at risk of failing SDD (27).

Surgery-related factors

Anaesthesia

To our knowledge, there is currently no randomised controlled trial (RCT) study that directly compares the use of general anaesthesia (GA) vs spinal anaesthesia (SA) as a risk factor for OI. OI was experienced in both spinal and general anaesthesia groups in patients who underwent major surgery such as THA or TKA (9, 10, 31, 32, 33). However, Kurkis *et al.* found that the use of SA with sedation produced more intolerance as compared to those who received GA (18). Specifically, the use of bupivacaine over ropivacaine led to more OI (18). Studies show that bupivacaine provides motor and sensory blockade longer than ropivacaine (34, 35). Therefore, patients recover earlier after ropivacaine blockade (34, 35). Ropivacaine also has a better cardiac and central nervous system profile regarding side effects compared to bupivacaine (34, 35).

Harsten *et al.*, in their study on recovery of patients, post-TKA, illustrated that those who received GA had less dizziness, postoperative nausea and vomiting (PONV), and shorter LOS than those who received SA (36). The GA group could walk 5 metres significantly better than the SA group at 6 and 10 h postoperatively (36). Similarly, another study of 120 THA patients who received either GA or SA showed that the GA group exhibited more favourable outcomes regarding LOS, PONV, dizziness, and orthostatic function (37). Both studies also showed that the GA group had higher pain scores 2 h postoperatively; however, the pain scores were significantly higher in the SA group 6 h postoperatively (36, 37). Fewer patients in the GA group required more analgesia than those in the SA group (36, 37).

Post-op pain and analgesia

Skarin *et al.* demonstrated that peak pain scores were recorded post-THA during mobilisation (12). A pain score grading of more than 5 out of 10 was shown to be a risk factor for OI (12). Pain not only is associated with fear and anxiety during mobilisation but can also stimulate a vasovagal response by triggering the hypothalamus (12, 38). This, in turn, can lead to the activation of cardiovascular centres within the medulla (12, 38). Two studies showed that there was no difference in pain scores in the tolerant versus intolerant groups and, therefore, the use of opioids (9, 16). Contrastingly, Kurkis *et al.* found a significant association between OI and the use of tramadol and oxycodone postoperatively (18). Hristovska *et al.* noted that patients developed OI 30 min after the administration

of 0.1 mg /kg morphine when posturally challenged (39). Skarin *et al.* identified the use of gabapentin post-THA as a risk factor for OI (12). A known side effect of gabapentin is dizziness (12). This may have contributed to the development of OI in their study (12).

THA vs TKA

THA is shown to have a higher association with OI, followed by TKA and then unicompartmental knee arthroplasty (UKA) (18). In the study by Kurkis *et al.*, the posterolateral approach to the hip showed an increased likelihood for OI, followed by the direct anterior and anterolateral approaches (18). De Campos *et al.*, in their meta-analysis, also noted that the posterolateral approach had a higher incidence of OI. Studies have shown that the C-reactive protein levels are higher post-aseptic hip arthroplasty when using the posterolateral approach compared to the direct anterior approach (40). This illustrates an elevated inflammatory response in the posterolateral approach compared to the other hip approaches (40). Jans *et al.* speculated that the post-inflammatory response may be related to the magnitude of the surgical procedure performed, which could be an essential mechanism of OI (9). This is the proposed reason why OH and, therefore, OI are more prevalent in THA than in TKA (41). Huston *et al.* illustrated that an 'inflammatory reflex' occurred post-surgery, which leads to a systemic inflammatory response whereby the vagus nerve is stimulated (42). This reflex leads to a cholinergic sequence of events, which produces bradycardia, vasodilation, and a dysregulation of blood pressure (42).

Blood loss

Sehat *et al.* showed that the total blood loss from both THA and TKA is very similar when hidden blood loss is considered (43). Although a tourniquet is used in TKA intraoperatively and, therefore, minimises blood loss, most of the blood loss occurs postoperatively (43). The average drop in haemoglobin levels is about 3 g/dL, which is similar to that reported by Jans *et al.* (9, 43). Kurkis *et al.* found an association between orthostasis and lower postoperative haemoglobin levels in THA (18). However, three other studies found no association with haemoglobin levels in intolerant and tolerant groups in TKA and THA (9, 12, 16). This is despite previous reports that up to 70% of intolerant patients have hypovolaemia (15).

Orthostatic challenge and therapeutic measures for OI postoperatively

The therapeutic measures available to address OI are divided into non-pharmacological and pharmacological approaches (Table 2). Non-pharmacological approaches include repeated orthostatic challenges, patient education, and the prevention of hypovolaemia. Pharmacological strategies against OI are the use of perioperative steroids, midodrine administration, and judicious postoperative opioid administration.

Table 2 Treatment strategies that could prevent OI.

Treatment strategy
Non-pharmacological options
• Repeated orthostatic challenges
• Patient education
• Preventing hypovolaemia
Pharmacological options
Preoperatively
Midodrine 5 mg orally 90 min prior to spinal anaesthesia
Postoperatively
Midodrine 10 mg orally 8 hourly for 24 h
Dexamethasone 4 mg intravenously 8 hourly for 24 h
Avoid gabapentin
Limit opioid analgesia

Orthostatic challenge

The orthostatic challenge that has been employed is as follows: the patient would rest in the supine position for 5 min, followed by a 30-degree passive leg raise for 3 min, and then rest again in the supine position for 5 min, followed by sitting on the edge of the bed with the patient's feet on the floor for 3 min; next, the patient is then asked to stand and then encouraged to tiptoe and shift weight from one leg to another for 3 min (9, 16). The patient then rests in the supine position after mobilisation (9, 16).

Repeated mobilisation or orthostatic challenges have been another modality in managing orthostatic intolerance (11). Frandsen *et al.* challenged their patients 4 and 6 h post-total hip replacement (44). They found that after their repeated mobilisation procedure, the prevalence of OI decreased from 30% at 4 h postoperatively to 0% at 6 h (44). The proposed theory for the benefit of repeated orthostatic challenges is that it reduces the duration of OI post-surgery (44). Patients should be encouraged to contract muscles in their lower limbs for 30 s at a time when recumbent. Quadriceps contractions, calf muscles contractions, and ankle and toe plantar and dorsiflexion, as well as leg raises, are all manoeuvres that can assist in improving venous return and, therefore, improving the preload (45).

Patient education and counselling

Patients need to be informed, be guided, and have their expectations clarified to improve outcomes after total joint arthroplasty (46). One of the main strategies of enhanced recovery after surgery (ERAS) is a multidisciplinary approach and patient education, which can improve adherence and the effectiveness of the ERAS programme (47). Crawford *et al.* emphasised the need for a team-based approach to achieve successful same-day discharge after total joint arthroplasty (TJA) in patients who were appropriately selected (48). Since implementing their multidisciplinary approach, they have seen over 150 patients who have been successfully discharged on the same day (45). Patients should be educated and counselled on the symptoms of OI (45). Emphasis should be placed on rising slowly from a recumbent position (45).

Fluids

Intravenous (IV) fluid administration is another preventative modality to consider in tackling OI (11, 32). Orthostatic intolerance was evaluated in patients who received goal-directed fluid therapy post-radical prostatectomy, and it was found that there was no reduction in OI incidence against a control group (32). Both groups received both colloids and crystalloids, with the control group receiving fluids according to international standards (32). They, however, showed that there was an impaired response in their patients' noradrenaline and haemodynamic statuses when asked to mobilise, alluding to the necessity of an appropriate vasomotor tone response and an acceptable cardiac preload to prevent OI (32). Hristovska *et al.* attempted to identify patients in their cohort post-TKA who were possibly hypovolaemic by conducting a passive leg raise to determine which patients had a more than 10% increase in their cardiac output and stroke volume (16, 17). They found that the patients who showed that response did not predict the development of OI (16). They also found that there was no difference in perioperative fluid status between those who were tolerant and those who were intolerant (16). It is, however, suggested that the prevention of orthostatic intolerance should begin with avoiding hypovolaemia (11). In a patient where OI is a concern, a 500 mL bolus of water can be given orally, or a bolus of crystalloid can be administered intravenously (45). This bolus can expand plasma volume and, therefore, the blood pressure, which can improve the patient's symptoms (45).

Midodrine

Jans *et al.* conducted an RCT using midodrine hydrochloride, an oral alpha-1 agonist, and hypothesised that it would offer an effective vasopressor response postoperatively (33). The idea is that the drug may prevent OI and OH by increasing vascular resistance (33). The drug was administered an hour before mobilisation at 6 h and 24 h post-THA (33). There was no difference in the prevalence of OI in the placebo and treatment groups (33). Smits *et al.* then conducted a pilot study using midodrine hydrochloride in patients after TKA and THA to evaluate the blood pressure response in three different dosing groups (49). The drug was administered three times a day for 72 h postoperatively (49). The high-dose group, who received 10 mg of the drug three times over 24 h, showed a significant increase in systolic blood pressure of 14 mmHg 2 h post-administration, compared to the groups who received 2.5 and 5 mg (49). Smits *et al.* demonstrated that OI/OH was reduced to 22.5% with the use of high-dose midodrine, compared to 40% reported by Jans *et al.* using only half the dose (33, 49).

Amin *et al.* conducted a randomised controlled trial using prophylactic oral midodrine to prevent post-spinal

anaesthesia hypotension in elderly patients undergoing a total hip replacement (50). They found that 5 mg of midodrine, administered 90 min before spinal anaesthesia, was sufficient to decrease the incidence of hypotension and the requirements for vasopressor use intraoperatively (50). They did, however, highlight inconsistencies in different population groups' responses to the drug (50). This then poses a challenge in recommending the drug for use in various clinical scenarios (50). Therefore, more large-scale studies need to be conducted on the use of midodrine to safely consider its routine use for preventing OI.

Perioperative steroid use

Steroids, especially when administered intravenously, have been evaluated for preventing OI perioperatively (40, 48). Linberg-Larsen *et al.*, in their RCT, used IV methylprednisone preoperatively in patients undergoing THA and showed no significant difference between the treatment and control groups (51). They concluded that administering IV methylprednisone did not reduce the incidence of OH or OI in THA (51).

In contrast, Cheng *et al.* used IV dexamethasone post-TKA, administered to patients over 24 h in three divided doses (41). Seventy-eight patients out of 149 who received dexamethasone postoperatively were statistically less likely to develop orthostatic hypotension and PONV (41). They deduced that 12 mg dexamethasone was an adequate dose over 24 h to lower the risk of OH and PONV compared to 24 mg over the same duration (41). The patients were also more likely to participate in postoperative physiotherapy, although this was statistically insignificant in their findings (41).

Postoperative analgesia

The type of postoperative analgesia is another area where OI can be mitigated (11, 12, 39). Gabapentin and morphine have been associated with OI in patients postoperatively (12, 39). Non-opioid analgesia should be a consideration in preventing OI (11). Vu *et al.* implemented an enhanced recovery after surgery (ERAS) protocol in their setting following hip arthroplasty (47). The improvements they observed were a reduction in complications and a shorter length of hospital stay (47). The postoperative analgesia they administered entailed paracetamol, pregabalin, and a non-steroidal anti-inflammatory drug (47). Intravenous opioids, such as tramadol and morphine, were reserved as rescue analgesia (47).

Conclusion

Orthostatic intolerance is a significant barrier to same-day discharge, early mobilisation, and recovery following hip and knee arthroplasties. It is multifactorial, with risk factors related to the patient, the type of anaesthesia used, and the type of surgery undergone. To prevent and manage this complication, a multidisciplinary team

is necessary. Patient education, repeated orthostatic challenges, and prevention of hypovolaemia are non-pharmacological methods to mitigate against OI. The pharmacological routes that could minimise OI are the use of midodrine pre- and postoperatively, the use of dexamethasone postoperatively, and limiting the use of opioids for analgesia after surgery.

ICMJE Statement of Interest

No grant, equipment, or other items to disclose. The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Funding Statement

This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector. The authors, their immediate families, and any research foundation with which they are affiliated did not receive any financial payments or other benefits from any commercial entity related to the subject of this article.

Author contribution statement

PK contributed to study conceptualisation, data capture, data analysis, manuscript preparation, revision, and approval of the final manuscript. MC was involved in study conceptualisation, analysis, manuscript drafting, critical revision, and final approval of the manuscript. JRTP, ARS, NS, and LM participated in manuscript revision and approved the final manuscript. CN contributed to manuscript design, preparation, revision, and approval of the final manuscript.

Acknowledgements

We would like to thank Prof Ramokgopa, Prof Robertson and Dr Ukunda for permitting research to be performed in their departments.

References

- Singh JA. Epidemiology of knee and hip arthroplasty: a systematic review. *Open Orthop J* 2011 **5** 80–85. (<https://doi.org/10.2174/1874325001105010080>)
- Wainwright TW, Gill M, McDonald DA, *et al.* Consensus statement for perioperative care in total hip replacement and total knee replacement surgery: enhanced recovery after surgery (ERAS®) society recommendations. *Acta Orthop* 2020 **91** 3–19. (<https://doi.org/10.1080/17453674.2019.1683790>)
- Chua MJ, Hart AJ, Mittal R, *et al.* Early mobilisation after total hip or knee arthroplasty: a multicentre prospective observational study. *PLoS One* 2017 **12** e0179820. (<https://doi.org/10.1371/journal.pone.0179820>)
- Jans Ø & Kehlet H. L'intolérance orthostatique postopératoire: malgré un problème périopératoire fréquent, peu de solutions. *Can J Anesth* 2017 **64** 10–15. (<https://doi.org/10.1007/s12630-016-0734-7>)
- De Campos TF, Vertzyas N, Wolden M, *et al.* Orthostatic intolerance-type events following hip and knee arthroplasty: a systematic review and meta-analysis. *J Bone Joint Surg* 2023 **105** 239–249. (<https://doi.org/10.2106/jbjs.22.00600>)
- Debbi EM, Mosich GM, Bendich I, *et al.* Same-day discharge total hip and knee arthroplasty: trends, complications, and readmission rates. *J Arthroplast* 2022 **37** 444–448.e1. (<https://doi.org/10.1016/j.arth.2021.11.023>)
- Keulen MHF, Schotanus MGM, van Haaren EH, *et al.* Rates and causes of 90-day complications and readmissions following outpatient hip and knee arthroplasty: a retrospective analysis of 525 patients in a single institution. *J Arthroplast* 2021 **36** 863–878. (<https://doi.org/10.1016/j.arth.2020.09.019>)
- Gong MF, McElroy MJ, Li WT, *et al.* Reasons and risk factors for failed same-day discharge after total joint arthroplasty. *J Arthroplast* 2024 **39** 1468–1473. (<https://doi.org/10.1016/j.arth.2023.11.032>)
- Jans Ø, Bundgaard-Nielsen M, Solgaard S, *et al.* Orthostatic intolerance during early mobilization after fast-track hip arthroplasty. *Br J Anaesth* 2012 **108** 436–443. (<https://doi.org/10.1093/bja/aer403>)
- Bundgaard-Nielsen M, Jørgensen CC, Jørgensen TB, *et al.* Orthostatic intolerance and the cardiovascular response to early postoperative mobilization. *Br J Anaesth* 2009 **102** 756–762. (<https://doi.org/10.1093/bja/aep083>)
- Joshi GP, Lobo DN & Kehlet H. Early postoperative orthostatic intolerance: pathophysiology and clinical implications. *Br J Surg* 2025 **112** znaf109. (<https://doi.org/10.1093/bjs/znaf109>)
- Skarin MU, Rice DA, McNair PJ, *et al.* Orthostatic intolerance following hip arthroplasty: incidence, risk factors and effect on length of stay: a prospective cohort study. *Eur J Anaesthesiol* 2019 **36** 123–129. (<https://doi.org/10.1097/eja.0000000000000940>)
- Fedorowski A. Postural orthostatic tachycardia syndrome: clinical presentation, aetiology and management. *J Intern Med* 2019 **285** 352–366. (<https://doi.org/10.1111/joim.12852>)
- Novak P. Autonomic disorders. *Am J Med* 2019 **132** 420–436. (<https://doi.org/10.1016/j.amjmed.2018.09.027>)
- Ruzieh M & Grubb BP. Orthostatic intolerance and postural tachycardia syndrome: new insights into pathophysiology and treatment. *Herzschrittmacherther Elektrophysiol* 2018 **29** 183–186. (<https://doi.org/10.1007/s00399-018-0563-1>)
- Hristovska AM, Andersen LB, Grentoft M, *et al.* Orthostatic intolerance after fast-track knee arthroplasty: incidence and hemodynamic pathophysiology. *Acta Anaesthesiol Scand* 2022 **66** 934–943. (<https://doi.org/10.1111/aas.14098>)
- Hristovska AM, Andersen LB, Uldall-Hansen B, *et al.* Postoperative orthostatic intolerance following fast-track unicompartmental knee arthroplasty: incidence and hemodynamics—a prospective observational cohort study. *J Orthop Surg Res* 2024 **19** 214. (<https://doi.org/10.1186/s13018-024-04639-6>)
- Kurkis GM, Dennis DA, Johnson RM, *et al.* Incidence and risk factors of orthostasis after primary hip and knee arthroplasty. *J Arthroplast* 2022 **37** S70–S75. (<https://doi.org/10.1016/j.arth.2022.01.035>)
- Mizota T, Iwata Y, Daijo H, *et al.* Orthostatic intolerance during early mobilization following video-assisted thoracic surgery. *J Anesth* 2013 **27** 895–900. (<https://doi.org/10.1007/s00540-013-1634-4>)
- Park KO & Lee YY. Orthostatic intolerance ambulation in patients using patient controlled analgesia. *Korean J Pain* 2013 **26** 277–285. (<https://doi.org/10.3344/kjp.2013.26.3.277>)
- Reulecke S, Charleston-Villalobos S, Voss A, *et al.* Dynamics of the cardiovascular autonomic regulation during orthostatic challenge is more relaxed in women. *Biomed Tech* 2018 **63** 139–150. (<https://doi.org/10.1515/bmt-2016-0150>)
- Lindenberger M & Länne T. Sex-related effects on venous compliance and capillary filtration in the lower limb. *Am J Physiol Regul Integr Comp*

- Physiol* 2007 **292** 852–859.
<https://doi.org/10.1152/ajpregu.00394.2006>
- 23 Lamo-Espinosa JM, Mariscal G, Gómez-Álvarez J, *et al.* Causes and risk factors for same-day discharge failure after total hip and knee arthroplasty: a meta-analysis. *Sci Rep* 2024 **14** 12627.
<https://doi.org/10.1038/s41598-024-63353-9>
 - 24 Bayliss LE, Culliford D, Monk AP, *et al.* The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. *Lancet* 2017 **389** 1424–1430. [https://doi.org/10.1016/s0140-6736\(17\)30059-4](https://doi.org/10.1016/s0140-6736(17)30059-4)
 - 25 Low PA. Prevalence of orthostatic hypotension. *Clin Auton Res* 2008 **18** 8–13. <https://doi.org/10.1007/s10286-007-1001-3>
 - 26 Goswami N, Blaber AP, Hinghofer-Szalkay H, *et al.* Orthostatic intolerance in older persons: etiology and countermeasures. *Front Physiol* 2017 **8** 803. <https://doi.org/10.3389/fphys.2017.00803>
 - 27 Sumbal R, Ashkar A, Sumbal A, *et al.* Reasons and risk factors for same-day discharge following total joint arthroplasty: a systematic review. *Arthroplast Today* 2024 **27** 101363.
<https://doi.org/10.1016/j.artd.2024.101363>
 - 28 Ricci F, De Caterina R & Fedorowski A. Orthostatic hypotension epidemiology, prognosis, and treatment. *J Am Coll Cardiol* 2015 **66** 848–860. <https://doi.org/10.1016/j.jacc.2015.06.1084>
 - 29 Roach J, George C, John L, *et al.* Assessing the safe resumption of antihypertensive medications following total hip or knee arthroplasty surgery. *Orthop Nurs* 2009 **28** 176–182.
<https://doi.org/10.1097/nor.0b013e3181ada7e4>
 - 30 Eriksen JR, Munk-Madsen P, Kehlet H, *et al.* Orthostatic intolerance in enhanced recovery laparoscopic colorectal resection. *Acta Anaesthesiol Scand* 2019 **63** 171–177.
<https://doi.org/10.1111/aas.13238>
 - 31 Gobeze NZ, Endalew NS, Tawuye HY, *et al.* Prevalence and associated factors of postoperative orthostatic intolerance at University of Gondar Comprehensive specialized Hospital, Northwest Ethiopia, 2022: cross sectional study. *BMC Surg* 2023 **23** 108.
<https://doi.org/10.1186/s12893-023-02015-5>
 - 32 Bundgaard-Nielsen M, Jans Ø, Müller R, *et al.* Does goal-directed fluid therapy affect postoperative orthostatic intolerance? *Anesthesiology* 2013 **119** 813–823. <https://doi.org/10.1097/aln.0b013e31829ce4ea>
 - 33 Jans Ø, Mehlsen J, Kjærsgaard-Andersen P, *et al.* Oral midodrine hydrochloride for prevention of orthostatic hypotension during early mobilization after hip arthroplasty. *Anesthesiology* 2015 **123** 1292–1300. <https://doi.org/10.1097/aln.0000000000000890>
 - 34 Bhat S, Himaldev UM & Upadya M. Comparison of efficacy and safety of ropivacaine with bupivacaine for intrathecal anesthesia for lower abdominal and lower limb surgeries. *Anesth Essays Res* 2013 **7** 381.
<https://doi.org/10.4103/0259-1162.123252>
 - 35 Kaur A, Singh RB, Tripathi RK, *et al.* Comparison between bupivacaine and ropivacaine in patients undergoing forearm surgeries under axillary brachial plexus block: a prospective randomized study. *J Clin Diagn Res* 2015 **9** UC01-UC06.
<https://doi.org/10.7860/jcdr/2015/10556.5446>
 - 36 Harsten A, Kehlet H & Toksvig-Larsen S. Recovery after total intravenous general anaesthesia or spinal anaesthesia for total knee arthroplasty: a randomized trial. *Br J Anaesth* 2013 **111** 391–399.
<https://doi.org/10.1093/bja/aet104>
 - 37 Harsten A, Kehlet H, Ljung P, *et al.* Total intravenous general anaesthesia vs. spinal anaesthesia for total hip arthroplasty: a randomised, controlled trial. *Acta Anaesthesiol Scand* 2015 **59** 298–309.
<https://doi.org/10.1111/aas.12456>
 - 38 Van Lieshout JJ, Wieling W, Karemaker JM, *et al.* The vasovagal response. *Clin Sci* 1991 **81** 575–586.
<https://doi.org/10.1042/cs0810575>
 - 39 Hristovska AM, Uldall-Hansen B, Mehlsen J, *et al.* Orthostatic intolerance after intravenous administration of morphine: incidence, haemodynamics and heart rate variability analysis. *Anaesthesia* 2023 **78** 526–528. <https://doi.org/10.1111/anae.15945>
 - 40 De Berardinis L, Senarighi M, Farinelli L, *et al.* In primary total hip arthroplasty, the direct anterior approach leads to higher levels of creatine kinase and lower levels of C-reactive protein compared to the posterolateral approach: a propensity score matching analysis of short-term follow-up data. *J Orthop Surg Res* 2023 **18** 594.
<https://doi.org/10.1186/s13018-023-04084-x>
 - 41 Cheng GHM, Tan GKY, Kamarudin MFB, *et al.* Steroids significantly decrease postoperative postural hypotension in total knee replacement. *J Knee Surg* 2023 **36** 208–215.
<https://doi.org/10.1055/s-0041-1731722>
 - 42 Huston JM & Tracey KJ. The pulse of inflammation: heart rate variability, the cholinergic anti-inflammatory pathway and implications for therapy. *J Intern Med* 2011 **269** 45–53.
<https://doi.org/10.1111/j.1365-2796.2010.02321.x>
 - 43 Sehat KR, Evans RI & Newman JH. Hidden blood loss following hip and knee arthroplasty. *J Bone Joint Surg* 2004 **86** 469–479.
<https://doi.org/10.1302/0301-620X.86B4.14508>
 - 44 Frandsen MN, Mehlsen J, Varnum C, *et al.* Feasibility of repeated early mobilization in orthostatic intolerance after total hip arthroplasty. *Int J Orthop Trauma Nurs* 2025 **57** 101187.
<https://doi.org/10.1016/j.ijotn.2025.101187>
 - 45 Swope R & Adams A. Prevention and treatment of orthostatic hypotension in the orthopedic patient population. *Orthopedics* 2012 **35** 600–603. <https://doi.org/10.3928/01477447-20120621-07>
 - 46 Pelt CE, Gililland JM, Erickson JA, *et al.* Improving value in total joint arthroplasty: a comprehensive patient education and management program decreases discharge to post-acute care facilities and post-operative complications. *J Arthroplast* 2018 **33** 14–18.
<https://doi.org/10.1016/j.arth.2017.08.003>
 - 47 Vu PTN, Khanh BHT, Hung HQ, *et al.* Effectiveness of an enhanced recovery after surgery (ERAS) program in hip arthroplasty in a developing country: a propensity score-matched study from Vietnam. *J Multidisc Healthc* 2025 **18** 2731–2747.
<https://doi.org/10.2147/jmdh.s521828>
 - 48 Crawford AM, Chen AF, Sabeti A, *et al.* Team approach: same-day discharge of patients undergoing total joint arthroplasty. *JBJS Rev* 2020 **8** e0176. <https://doi.org/10.2106/jbjs.rvw.19.00176>
 - 49 Smits M, Lin S, Rahme J, *et al.* Blood pressure and early mobilization after total hip and knee replacements A pilot study on the impact of midodrine hydrochloride. *JBJS Open Access* 2019 **4** e0048.
<https://doi.org/10.2106/jbjs.oe.18.00048>
 - 50 Amin S, Hasanin A, Mansour R, *et al.* Oral midodrine for prophylaxis against post-spinal anesthesia hypotension during hip arthroplasty in elderly population: a randomized controlled trial. *BMC Anesthesiol* 2024 **24** 64. <https://doi.org/10.1186/s12871-024-02442-8>
 - 51 Lindberg-Larsen V, Petersen PB, Jans Ø, *et al.* Effect of pre-operative methylprednisolone on orthostatic hypotension during early mobilization after total hip arthroplasty. *Acta Anaesthesiol Scand* 2018 **62** 882–892. <https://doi.org/10.1111/aas.13108>