Orthostatic intolerance during early mobilization after fast-track hip arthroplasty

Ø. Jans1,2*, M. Bundgaard-Nielsen1, S. Solgaard3, P. I. Johansson4 and H. Kehlet1,2

1 Section of Surgical Pathophysiology, 407A, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark
2 Lundbeck Centre for Fast-track Hip and Knee Arthroplasty, Denmark
3 Department of Orthopaedic Surgery, Hørsholm Hospital, Denmark
4 Capital Region Blood Bank, Rigshospitalet, Denmark
* Corresponding author. E-mail: oeivind.jans@rh.regionh.dk

Editor’s key points

- Haemodynamic responses during orthostatic intolerance (OI) after hip surgery were studied.
- Up to 20% patients had OI 24 h after surgery.
- Patients with intolerance showed impaired haemodynamic responses to changes in position.
- The study shows how common orthostatic hypotension after hip surgery is, and it attempts to evaluate the underlying mechanisms.

Background. Early postoperative mobilization is a cornerstone in fast-track total hip arthroplasty (THA), but postoperative orthostatic intolerance (OI) may delay early recovery or lead to fainting, falls, and prosthesis dislocation or fracture. However, the prevalence and pathophysiology of OI has not been established after THA. This study evaluated the cardiovascular response and tissue oxygenation to mobilization before and after surgery in relation to OI in fast-track THA patients.

Methods. OI and the cardiovascular response to standing were evaluated with a standardized mobilization protocol, before, 6, and 24 h after surgery in 26 patients undergoing THA with spinal anaesthesia and an opioid-sparing analgesic regime. Haemoglobin, fluid balance, and opioid use were recorded. Systolic (SAP) and diastolic (DAP) arterial pressure, heart rate (HR), stroke volume (SV), cardiac output (CO), and systemic vascular resistance were measured non-invasively (Nexfin®) and cerebral (ScO2) and muscle tissue oxygenation by non-infrared spectroscopy.

Results. No patients demonstrated OI before surgery, whereas 11 (42%) and five (19%) patients experienced OI 6 and 24 h after surgery, respectively. OI was associated with decreased orthostatic responses in SAP, DAP, SV, CO, and ScO2 compared with orthostatic tolerant patients (P<0.05). There was no difference in postoperative haemoglobin concentrations or opioid use between orthostatic intolerant and tolerant patients.

Conclusions. Early postoperative OI is common in patients undergoing THA and is associated with an impaired cardiovascular orthostatic response and decreased cerebral oxygenation.

Keywords: arthroplasty, replacement, hip; orthostatic intolerance; postoperative period

Accepted for publication: 3 October 2011

Early postoperative mobilization is essential for rapid functional recovery after surgery and is considered a cornerstone in the so-called fast-track multimodal perioperative approach which includes early ambulation and oral nutrition, multimodal opioid-sparing analgesia, and optimized fluid therapy. This strategy has improved patients outcome after surgery and reduced length of hospital stay. However, postoperative orthostatic intolerance (OI) may delay ambulation and is characterized by symptoms of dizziness, nausea, blurred vision, or syncope due to failed orthostatic cardiovascular regulation, a decrease in arterial pressure, and cerebral hypoperfusion during standing. Transient inability to ambulate has been observed after ambulatory surgery and remains a cause of prolonged hospital stay. Additionally, a high (50%) incidence of OI during early postoperative mobilization has been reported in patients undergoing radical prostatectomy, whereas intact orthostatic cardiovascular regulation was observed 30 min after mastectomy in a fast-track setting.

Patients undergoing fast-track total hip arthroplasty (THA) are often mobilized on the day of surgery and are required to participate in physiotherapy sessions in the early postoperative period. Thus, OI may delay recovery and cause symptoms of cerebral hypoperfusion and syncope, leading to potential serious complications such as falls with a risk of prosthesis dislocation and fracture in this often elderly group of patients. However, the incidence of OI during early mobilization in orthopaedic surgery is unknown and the predisposing factors and cardiovascular mechanisms involved in failed orthostasis are not fully understood.

The primary aim of this study was to determine the incidence of OI during early postoperative mobilization in
fast-track THA and secondary aims were to describe the changes in cerebral oxygenation and cardiovascular variables involved in the pathophysiology of OI. In addition, we examined whether bleeding, postoperative anaemia, or opioid use was associated with OI.

**Methods**

Twenty-six patients (17 females) undergoing unilateral primary THA were included in the period of March–July 2010. Exclusion criteria were history of OI, diabetes mellitus, atrial fibrillation, ASA score ≥ III, or a history of alcohol abuse (>40 units week⁻¹). All patients gave informed consent and the trial was approved by the local ethics committee (H-D-2009-067) and registered by the Danish data protection agency and on ClinicalTrials.gov under the US national library of medicine (NCT01089946).

**Anaesthesia, pain management, and surgery**

Patients were anaesthetized with spinal anaesthesia (12.5–15 mg bupivacaine) and received propofol sedation at the discretion of the attending anaesthesiologist.

The preoperative fasting period was 6 and 2 h before surgery for solid food and clear fluids, respectively. To cover basal and surgical fluid losses, a fixed volume fluid regimen of 12 ml kg⁻¹ isotonic saline the first hour of surgery was administered, followed by 6 ml kg⁻¹ h⁻¹ until end of surgery. Blood loss was replaced 1:1 with 6% hydroxyethyl starch (Voluven; 130/0.4 Fresenius Kabi AB, Uppsala, Sweden). For the first 6 h after surgery, patients received saline 2 ml kg⁻¹ h⁻¹ with no restrictions on oral fluid intake. Criteria for blood transfusion were haemoglobin (Hb) <7.5 g dl⁻¹ or Hb <10.0 g dl⁻¹ in patients with severe ischaemic heart disease according to guidelines published by the Danish National Board of Health.

Perioperative pain management was standardized as follows: acetaminophen 2 g and gabapentin 600 mg before operation, continuing with gabapentin 900 mg and acetaminophen 4 g daily for the duration of hospital stay. During the first 24 h after surgery, high volume local infiltration analgesia with ropivacaine 2% was administered intraoperatively and 8 and 24 h after surgery using an 18 G epidural catheter placed in the incision by the surgeon.

Pain scores were graded on a verbal rating scale (0–10) and if they exceeded 3 at rest or 5 during movement, patients received supplemental oxycodone.

**Orthostatic challenge**

A standardized mobilization procedure was performed ~1 h before surgery and was repeated 6 and 24 h after the operation, defined from the time of wound closure. Mobilization included supine rest (5 min), followed by 30° passive leg raise (3 min), supine rest (5 min), sitting on the bed with the feet on the floor (3 min), followed by standing while the patient was verbally encouraged to stand on the toes and shift body weight from one leg to the other in order to activate the muscle pump and attenuate venous pooling in the legs (3 min). The mobilization procedure ended with recovery at supine rest (5 min). The procedure was terminated if the patients reported symptoms of OI (dizziness, nausea, blurred vision) or upon a decrease in systolic arterial pressure (SAP) >30 mm Hg. During the test, the muscle and cerebral (frontal lobe cortex) oxygenation were assessed with intervals of 10 s by near-infrared spectroscopy (NIRS, Somanetics, INVOS, cerebral oximeter, Troy, OH, USA) with optodes placed on the biceps brachii muscle and on the forehead. NIRS has been validated as a measure of tissue oxygenation in both surgical and non-surgical settings.

Continuous arterial pressures were measured by a finger cuff applied on the middle part of the third finger. From the arterial pressure wave, an aortic flow waveform is computed by simulating a non-linear, time-varying model of the aortic input impedance (Nexfin, BMeve, Amsterdam, The Netherlands) and integrating the computed aortic flow waveform per beat provides stroke volume (SV). Cardiac output (CO) was calculated as SV times heart rate (HR) and total peripheral resistance (TPR) from the ratio of mean arterial pressure to CO. During each postoperative mobilization test, fluid status and Hb were recorded and pain was graded for each body position. Before the 6 h test, remaining motor blockade was ruled out using a modified Bromage scale.

**Orthostatic classification**

During the mobilization challenge, patients were classified as having OI if they experienced signs of cerebral hypoperfusion such as dizziness, nausea, blurred vision, feeling of heat or syncope, or a decrease in SAP >30 mm Hg. Regardless of symptoms, patients with a >20 mm Hg decrease in SAP or a >10 mm Hg decrease in diastolic arterial pressure (DAP) upon standing were classified as having orthostatic hypotension.

**Data analyses**

The finger arterial pressure curve and the derived cardiovascular values were analysed using the Nexfin@PC 1.0 software package (BMeve, Amsterdam, The Netherlands). Each curve was visually inspected for artifacts, and such data were excluded. For both Nexfin and NIRS variables, estimates representing the supine rest periods were averaged over 5 min, while estimates representing the mobilization periods of sitting and standing were averaged over the last 10 s before termination of each posture, both for patients completing the mobilization procedure and patients terminating the mobilization procedure prematurely due to OI.

Normally distributed data are presented as mean (SD), while data not normally distributed are presented as median (inter-quartile range, IQR). A mixed-model analysis of variance for repeated measures was used for comparison of cardiovascular and oxygenation variables between and within each test session and between orthostatic tolerant (OT) and intolerant patients. CO and TPR were included in the model as covariates in order to explain differences in...
SAP between sessions. Differences in patient characteristics between OT and OI patients were identified using an unpaired t-test or the Mann–Whitney U-test where appropriate and logistic regression analyses were performed to evaluate the correlation between the postoperative Hb concentration or opioid use and the occurrence of OI. While no data on OI after THA existed, previous data from an evaluation of OI after prostatectomy found a 17 (SD 16.5) mm Hg difference between the SAP response before and 6 h after surgery. Based on these data, a sample size of 21 patients was required in order to detect a difference of 10 mm Hg in the orthostatic SAP response before and after surgery with a power of 0.8 (1 − β) and an α of 0.05 in a paired analysis. Thus, 26 patients were, therefore, enrolled in the study. Statistical analyses were performed using SAS 9.1.3 (SAS Institute Inc., Cary, NC, USA) with a P-value of <0.05 representing statistical significance.

**Results**

**Patient characteristics and perioperative management**

Patients had a median (range) age of 64 (43–80) yr, weight 82 (52–125) kg, height 168 (152–193) cm, and 12 (46%) patients received oral antihypertensives. Patient characteristics did not differ between OT and intolerant patients at 6 and 24 h after surgery.

Patients received a median (IQR) dose of 15 (14.5–15) mg bupivacaine 5 mg ml−1 for spinal anaesthesia with surgery lasting 49 (40–57) min (cut to last suture). Fluid administration and losses are shown in Table 1.

**OI and hypotension**

No patients demonstrated OI or orthostatic hypotension during the preoperative mobilization procedure, while 11 (42%) and five (19%) patients had OI 6 and 24 h after surgery, respectively. Of the 11 patients experiencing OI at 6 h after surgery, nine were classified as having OI due to both subjective symptoms and objective criteria (SAP decrease >20 mm Hg) at 6 and 24 h after surgery, respectively.

**Cardiovascular responses and changes in tissue oxygenation**

Table 2 shows cardiovascular variables and tissue oxygenation during mobilization before, 6, and 24 h after surgery. Before surgery, upon 30° leg raise, all cardiovascular variables remained stable. However, from the supine to standing position, SAP increased by mean (95% confidence interval) 18 (11–26) mm Hg, DAP by 12 (9–15) mm Hg, HR by 9 (7–11) beats min−1, and systemic vascular resistance (SVR) by 315 (208–423) dyn s cm−5. CO remained stable while SV decreased by 12 (9–15) ml and cerebral and muscle tissue oxygenation decreased by 2 (1–3)% and 8 (7–10)%, respectively (Fig. 1).

At 6 h after surgery, the responses in SAP, DAP, CO, SV, and SCO2 from supine to standing were significantly decreased in OI patients compared with OT patients (P<0.01; Table 3). The responses to standing were impaired for SAP, DAP, SVR, and SCAO2, compared with the preoperative evaluation for both OT and OI patients. In addition, for OI patients, the SV and CO responses were also impaired compared with before operation (P<0.05; Fig. 1).

At 24 h, the responses from supine to standing were impaired for SAP, DAP, CO, SVR, and SCAO2, in OI vs OT patients (P<0.01; Table 3). Compared with the preoperative evaluation, orthostatic responses in DAP and SVR were attenuated for both OT and OI patients, while SAP responses were attenuated for OI patients only (P<0.05; Fig. 2). At 6 and 24 h after surgery, neither CO nor SVR alone explained the differences in the arterial pressure response from the preoperative evaluation. However, when both CO and SVR were included as covariates, they accounted for the differences from the preoperative evaluation.

**Bleeding, postoperative haemoglobin concentration, and opioid use**

The Hb concentration was mean (SD) 14.1 (1.3) g dl−1 before surgery and 11.1 (1.3) and 11.2 (0.9) g dl−1 at 6 and 24 h after surgery, respectively. The estimated amount of bleeding and the postoperative Hb concentration did not differ between OT and intolerant patients and were not associated with OI in logistic regression analyses (Table 3). No patients received blood transfusion during the study period.

At 6 h after surgery, patients had received a median (IQR) oxycodone dose of 9 (5–13.5) mg and pain scores were 3 (2–4), 4 (2–5), and 3 (2–4) at rest, sitting, and standing, respectively. At 24 h, oxycodone dose was 16.5 (12.3–25), while pain scores were 2 (0–3), 2 (2–3), and 2 (2–3) at rest, sitting, and standing, respectively. At 6 and 24 h, there were no differences in pain scores or opioid dose administered between

---

**Table 1** Cumulative fluid administration and losses intraoperative, 6 and 24 h after surgery (n=26). Data presented as median (IQR) or mean (SD). 6 h, 6 h after surgery; 24 h, 24 h after surgery; NaCl, isotonic saline; HES, hydroxethyl starch 130/0.4; Hb, haemoglobin. *Preoperative Hb

<table>
<thead>
<tr>
<th></th>
<th>Intraoperative</th>
<th>6 h</th>
<th>24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl (ml)</td>
<td>900 (300)</td>
<td>2050 (400)</td>
<td>2725 (800)</td>
</tr>
<tr>
<td>HES (ml)</td>
<td>500 (100)</td>
<td>500 (200)</td>
<td>550 (500)</td>
</tr>
<tr>
<td>Oral (ml)</td>
<td>—</td>
<td>945 (425)</td>
<td>2324 (700)</td>
</tr>
<tr>
<td>Diuresis (ml)</td>
<td>300 (160)</td>
<td>725 (400)</td>
<td>2250 (800)</td>
</tr>
<tr>
<td>Bleeding (ml)</td>
<td>460 (238)</td>
<td>473 (250)</td>
<td>487 (256)</td>
</tr>
<tr>
<td>Hb (g dl−1)</td>
<td>14.1 (1.3)*</td>
<td>11.1 (1.3)</td>
<td>11.2 (0.9)</td>
</tr>
</tbody>
</table>
OT and intolerant patients (Table 3), and opioid dose was not associated with OI in the logistic regression analysis.

Discussion

The main finding of this study is the high incidence of OI of 42% and 19% at 6 and 24 h after THA, respectively. In addition, this study found an attenuated arterial pressure response to mobilization after surgery compared with the preoperative evaluation in both patients with and without OI. The impaired responses were aggravated in OI patients, where orthostatic hypotension and decreased cerebral frontal lobe oxygenation occurred. Furthermore, we found no association between OI and bleeding, postoperative Hb concentration, or opioid use.

The high incidence of OI in the early postoperative period may have serious clinical implications. The ability to maintain an upright posture early after surgery is considered essential as patients are enrolled in various rapid recovery regimens where mobilization on the day of surgery is considered a cornerstone.22 Furthermore, OI may lead to syncope during mobilization, where it may cause falls with a risk of prosthesis dislocation or even fracture.9

The findings from the present study are in agreement with the only other detailed study evaluating orthostatic function during early mobilization after major surgery, which found a high incidence (50%) of OI after radical prostatectomy.6 In contrast to these findings, the presence of OI after minor surgery appears to be low.7 The present study also evaluated changes in cerebral and muscle oxygenation during early mobilization and found a significant decrease in frontal lobe oxygenation in OI patients. The decrease deviated significantly, both from the preoperative response and from the response of OT patients, and followed the decrease in arterial pressure, suggesting an association between cerebral hypoperfusion and OI during early postoperative mobilization. The present study found an altered response in arterial pressures and SVR compared with the preoperative evaluation, even in patients completing the mobilization procedure. This is in agreement with previous findings,8 and may represent a general dysfunction in orthostatic cardiovascular regulation in the early postoperative period after major surgery. Although the precise pathophysiological mechanisms remain to be elucidated, they may involve factors such as impaired reflex vasoconstriction or baroreflex dysfunction. This ultimately leads to reduced cardiac preload and a decrease in arterial pressure causing reduced cerebral perfusion and cerebral deoxygenation as observed by the cerebral NIRS measurements in this study.23 Some patients developed no symptoms of OI despite orthostatic hypotension, which may reflect individual tolerances to hypotension due to differences in the lower limit of cerebral autoregulation.26 In agreement with a previous study in open radical prostatectomy, both CO and SVR had to be included in the statistical model in order to explain the impaired orthostatic arterial pressure responses after surgery.6 Although CO and SVR
are interrelated, this finding may suggest that a combination of these factors contribute to the impaired orthostatic arterial pressure response or that mechanisms involved in OI may vary between patients.

The high incidence of OI found in the present study may be related to postoperative hypovolaemia or impaired fluid balance which may have aggravated the reduction in central blood volume caused by the transition from the supine to the upright position. However, all patients received liberal fluid therapy and did not respond to 30° passive leg raise during the postoperative measurements arguing against functional hypovolaemia. Furthermore, there were no differences in postoperative fluid status between OT and intolerant patients.

The presence of dizziness and OI after surgery might be explained by postoperative anaemia, which could potentially contribute to the high incidence of OI found in the present study. The mean perioperative blood loss in THA has been established to be of a magnitude of ~1 litre leading to a reduction in Hb of ~3 g dl⁻¹ which is comparable with the blood loss found in the present study. However, we found no association in the statistical analyses between OI and the postoperative Hb concentration or estimated bleeding in the early postoperative period and all OI events occurred in patients having a Hb concentration of >10 g dl⁻¹ which is above even liberal transfusion triggers, according to international guidelines. As postoperative dizziness and OI may trigger the clinical decision to transfuse, our findings suggest...
that other causes of OI should be considered before transfusing the patient with moderate postoperative anaemia, thus avoiding unnecessary transfusions that may per se worsen outcome.28 29

The administration of opioids and pain during mobilization are additional factors that potentially may contribute to OI in the postoperative period. While the patients in the present study received a multimodal opioid-sparing analgesic regimen, supplemental oxycodone was administered as a rescue analgesic, which may have contributed to the occurrence of OI. However, the administered doses were small and not associated with OI in the regression analyses. In addition, gabapentin, which was administered for postoperative analgesia, may cause dizziness which potentially might have contributed to OI in the present study.28 30 However, in a previous study in mastectomy patients including gabapentin, we did not find postoperative OI.7

Previous studies have evaluated orthostatic function after general anaesthesia,6 7 nevertheless, the present study is the first study to evaluate orthostatic function during early mobilization after spinal anaesthesia. While remaining motor blockade was ruled out before performing the 6 h mobilization procedure, we cannot exclude any remaining effect on vasomotor function. This may have contributed to the high incidence of OI observed 6 h after surgery. However, OI was common even 24 h after surgery when no remaining effect of spinal anaesthesia is expected.

We used Modelflow (Nexfin)5 to measure arterial pressure and calculate haemodynamic variables. Modelflow is a non-invasive approach to estimate cardiovascular variables but correlates well with a thermodilution-based determination of CO and has been validated in cardiac surgery and in determination of the pathology of orthostatic intolerant patients in non-surgical settings.32 33 To estimate tissue oxygenation, we used NIRS. Although the absolute values observed with NIRS may be variable between individuals, we evaluated intra-individual changes in oxygenation which correlates well with several other measures of cerebral oxygenation and perfusion, when used in a number of non-surgical and surgical settings, including cardiovascular surgery.16–18

During mobilization, we averaged cardiovascular data over 10 s before termination of the mobilization procedure both in OI patients and in patients completing the mobilization procedure. Although a different averaging period might have altered our findings, this approach evaluates the cardiovascular state preceding the appearance of OI symptoms and allows for comparisons between OT and intolerant patients using similar averaging periods.

In conclusion, the present study found a high (42%) incidence of OI during early mobilization after fast-track THA.
OI was related to attenuated CO and SVR responses to standing and cerebral hypoperfusion. However, OI was not explained by the degree of postoperative anaemia or the amount of opioid administered in the early postoperative period. Future studies should elucidate the mechanisms of failed postoperative cardiovascular regulation in order to evaluate interventions to reduce the incidence of OI after major surgery.

Declaration of interest
None declared.

Funding
This work was supported by The Lundbeck Foundation.

References

Fig 2 Changes in cardiovascular variables before (Pre) and 24 h after surgery (Post) in orthostatic tolerant (OT) and intolerant (OI) patients during a standardized mobilization procedure. PLR, 30° leg elevation. *P*<0.05 compared with preoperative evaluation; #*P*<0.05 compared with OT patients 24 h after surgery.
Orthostatic intolerance after hip arthroplasty


8 Husted H, Holm G. Fast track in total hip and knee arthroplasty—experiences from Hvidovre University Hospital, Denmark. Injury 2006; 37(Suppl. 5): S31–5


10 Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology 2011; 114: 495–511


24 Secher NH, Van Lieshout JJ. Dynamic cerebral autoregulation and monitoring cerebral perfusion. Hypertension 2010; 56: 189–90


26 Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology 2010; 113: 482–95


31 Mathiesen O, Moiniche S, Dahl JB. Gabapentin and postoperative pain: a qualitative and quantitative systematic review, with focus on procedure. BMC Anesthesiol 2007; 7: 6

32 de Wilde RB, Schreuder JJ, van den Berg PC, Jansen JR. An evaluation of cardiac output by five arterial pulse contour techniques during cardiac surgery. Anesthesia 2007; 62: 760–8