Changes in the augmentation index and postoperative orthostatic intolerance in orthopedic surgery: a prospective cohort study

Modifications de l'indice d'augmentation et intolérance orthostatique postopératoire en chirurgie orthopédique: étude prospective de cohorte

Stavros G. Memtsoudis, MD, PhD · Eva E. Mörwald, MD · Kara Fields, MS ·
Crispiana Cozowicz, MD · Nigel E. Sharrock, BMedSci, MB, ChB · Mathias Opperer, MD ·
Ottokar Stundner, MD · Angie Zhang, BA · George Go, BS · Thomas Danninger, MD

Received: 29 October 2017 / Revised: 12 March 2018 / Accepted: 19 March 2018 / Published online: 22 May 2018
© Canadian Anesthesiologists' Society 2018

Abstract

Background Postoperative orthostatic intolerance (OI) can be a major obstacle to early ambulation and its determinants are poorly understood. We aimed to study postoperative changes in vascular tone and their potential association with OI in various orthopedic surgical settings. **Methods** In this prospective cohort study, 350 patients undergoing total joint arthroplasty under neuraxial anesthesia or spine surgery under general anesthesia were enrolled. We determined the augmentation index (AI) as a measure of vascular tone and studied symptoms of OI using a validated questionnaire at various postoperative time points.

Results The AI was significantly reduced postoperatively (at spinal resolution in patients with neuraxial anesthesia or two hours postoperatively in general anesthesia) compared with baseline values in all procedures and did not subsequently return to baseline throughout the postoperative period in the majority of patients [252/335 (75.2%); $P < 0.001$]. The majority [260/342 (76.0%); $P < 0.001$] of patients had postoperative symptoms of OI. Nevertheless, no association was found between postoperative change in AI from baseline and postoperative symptoms of OI.

Conclusions A significantly prolonged decrease in AI and symptoms of OI are common after orthopedic surgery. Nevertheless, an association between the two measures was not observed. While compensatory mechanisms may limit the influence of an AI decrease on symptoms of OI, more research is needed to understand the contributing factors and aid in the identification of patients at risk of OI.

Abstract presentation: ASRA 2013 spring meeting. Poster: Postoperative Dizziness and Arterial Tone in Patients undergoing Total Joint Arthroplasty.

S. G. Memtsoudis, MD, PhD (✉) · E. E. Mörwald, MD ·
C. Cozowicz, MD · N. E. Sharrock, BMedSci, MB, ChB ·
A. Zhang, BA · G. Go, BS
Department of Anesthesiology, Critical Care and Pain
Management, Hospital for Special Surgery, Weill Cornell
Medical College, 535 E 70th Street, New York, NY 10021, USA
e-mail: memtsoudiss@hss.edu

S. G. Memtsoudis, MD, PhD · E. E. Mörwald, MD ·
C. Cozowicz, MD · M. Opperer, MD · O. Stundner, MD ·
T. Danninger, MD
Department of Anesthesiology, Perioperative Medicine and
Intensive Care Medicine, Paracelsus Medical University,
Salzburg, Austria

K. Fields, MS
Healthcare Research Institute, Hospital for Special Surgery, New
York, NY, USA

Résumé

Contexte L'intolérance orthostatique (IO) postopératoire peut être un obstacle majeur à la déambulation précoce et ses déterminants sont mal compris. Nous avons cherché à étudier les modifications postopératoires du tonus vasculaire et leurs associations potentielles avec l'IO dans différents types de chirurgie orthopédique.

Méthodes Cette étude de cohorte prospective a inclus 350 patients subissant une arthroplastie sous anesthésie neuraxiale ou une chirurgie de la colonne sous anesthésie générale. Nous avons choisi l'indice d'augmentation (IA) comme mesure du tonus vasculaire et étudié les symptômes de l'IO en utilisant un questionnaire validé à différentes étapes de la période postopératoire.

Résultats L'IA a été significativement abaissé en postopératoire (à la résolution du bloc des patients ayant eu une anesthésie neuraxiale ou deux heures postopératoires en cas d'anesthésie générale) par rapport aux valeurs de référence pour toutes les procédures et n'est pas revenu à la valeur de référence pendant toute la période postopératoire chez la majorité des patients (252/335 [75,2%]; $P < 0,001$). La plupart (260/342 [76,0%]; $P < 0,001$) des patients ont présenté des symptômes postopératoires d'IO. Néanmoins, aucune association n'a été mise en évidence entre la modification postopératoire de l'IA par rapport aux valeurs de référence et les symptômes postopératoires d'IO.

Conclusions Une diminution significative et prolongée de l'IA, de même que des symptômes d'IO sont fréquents après la chirurgie orthopédique. Néanmoins, aucune association entre les deux mesures n'a été observée. Bien que des mécanismes compensatoires puissent limiter l'influence de la baisse de l'IA sur les symptômes d'IO, de nouvelles études seront nécessaires pour comprendre les facteurs contributifs et aider à identifier les patients présentant un risque d'IO.

Safe ambulation and rehabilitation are critical to success in orthopedic surgery. Thus, postoperative orthostatic intolerance (OI) and associated symptoms, including dizziness, present major obstacles by potentially driving in-hospital falls and delayed functional recovery.¹ While the underlying pathophysiology is not fully explored, multiple factors, including hypovolemia, anemia, opioids, and residual neuraxial blockade, may influence the development of OI.²⁻⁴ Nevertheless, in a study by Jan *et al.*³ these factors could not sufficiently explain the high incidence of OI after total hip arthroplasty (THA), suggesting the presence of additional drivers, including perioperative metabolic injury, mediated by systemically active metabolites and cytokines with significant impact on postoperative vascular tone.^{3,5} Recently, the impact of other perioperative factors on vascular tone, such as regional anesthesia, was studied in THA⁶ by investigating the augmentation index (AI), a measure of the overall stiffness of large arterial vessels. Interestingly, a postoperative substantial and sustained reduction in AI, outlasting neuraxial and peripheral nerve blockade, was observed, indicating an impact of postoperative metabolic changes on vascular tone. Currently, however, there is a lack of studies investigating associations between AI and perioperative outcomes such as OI. Therefore, this study aimed to investigate 1) changes in AI over time, 2) possible associations of OI related symptoms with AI, and 3)

potential differences in AI changes and OI symptoms in various orthopedic procedures.

Methods

This prospective cohort study was approved by the Institutional Review Board of the Hospital for Special Surgery (New York, NY, USA, IRB #2012-030). Enrolment took place between 8 April 2013 and 8 July 2015 at the Hospital for Special Surgery, and written informed consent was obtained from all patients.

Study sample

We enrolled 200 patients (18-90 yr) undergoing primary total hip or knee arthroplasty (THA, TKA) as our primary study cohort. To study the impact of higher surgical invasiveness and differences in respect to regional and general anesthesia on AI and OI symptoms, the study sample was expanded to include 50 patients with bilateral knee arthroplasty (BKA) (regional anesthesia/higher invasiveness), 50 cases of single-level microdiscectomies (SLMD) or laminectomies (SLML) (general anesthesia/lower invasiveness), and 50 cases of posterior lumbar fusion with instrumentation (PLF) (general anesthesia/higher invasiveness). Patients with an American Society of Anesthesiologists physical status $> III$, with contraindications to sphygmomanometric blood pressure measurement (lymphedema), severe cardiorespiratory disease, cardiac insufficiency, atrial fibrillation, valvular disease, significant cardiac arrhythmia, diabetes mellitus (type I and II), pronounced preoperative anemia (hemoglobin $< 10.5 \text{ mg-dl}^{-1}$), and alcohol abuse were excluded. Further exclusion criteria included postoperative use of patient controlled intravenous anesthesia and vasopressors or same day hospital discharge.

Changes in AI over time

The AI is a measure of arterial vascular tone derived from the late systolic shoulder of the peripheral arterial waveform.⁷ To characterize changes in AI over time, it was measured at several perioperative time points using the PulseCor Ltd. CardioScope II (PulseCor Ltd., Auckland, New Zealand), which uses a sphygmomanometer to non-invasively measure various hemodynamic parameters by analyzing low-frequency suprasystolic waveforms at the brachial artery level.⁸ Baseline AI measurements were taken preoperatively in the holding area and served as reference. Postoperatively, AI was measured at postanesthesia care unit (PACU) admission, after resolution of neuraxial motor blockade in joint surgery,

Fig. 1 Flow chart

or two hours after PACU admission in spine cases as well as every 24 hr thereafter until hospital discharge. At every time point, AI was measured in the supine position and when feasible also in the seated position, while positional alterations were analyzed (according to hospital practice patients remain in the supine position until spinal resolution to avoid hypotension due to venous pooling). In 25 cases (BKA, PLF, SLML, SLMD), a last AI measurement at six weeks postoperatively was performed during follow-up visits to determine if AI had returned to baseline.

Association of symptomatic postoperative OI with AI

Symptoms of OI were measured by clinical assessment and the Orthostatic Hypotension Questionnaire (OHQ). The OHQ is a validated questionnaire, which includes an Orthostatic Hypotension Symptom Assessment (OHSA) scale and an Orthostatic Hypotension Daily Activity Scale (OHDAS).⁹ The OHSA scale assesses the severity of six acute symptoms of orthostatic hypotension using 11-point scales from 0 to 10 (0 = no symptoms; 10 = worst symptoms imaginable). These symptoms include: dizziness, problems with vision, weakness, fatigue, trouble concentrating, and head/neck discomfort. The OHDAS relates to chronic aspects of OI by measuring to which extent daily activities are limited because of OI. It consists of four items with 11-point scales (0 = no interference, 10 = strongest interference imaginable) assessing activities that require standing for a short time, standing for a long time, walking for a short time, and

walking for a long time. The OHDAS part also provides the option to state that an activity is not accomplishable for other reasons besides OI. Originally developed for neurogenic orthostatic hypotension, it readily assesses the severity of symptoms of orthostatic intolerance postoperatively. The OHDAS was evaluated for each patient preoperatively at baseline. The OHDAS and additional clinical assessment questions were repeatedly utilized at the same time points as AI was obtained to investigate potential associations between OI and AI.

Study protocol

Baseline AI and symptoms of OI were assessed preoperatively, while intraoperatively all patients received standard of care. This included neuraxial anesthesia for THA, TKA, and BKA and the addition of peripheral nerve blocks in the latter two groups. Patients undergoing PLF, SLMD, or SLML received general balanced anesthesia. Patients were monitored in the PACU until discharge, while ambulation was initiated when deemed appropriate by physical therapy or at patient request. Data on analgesic consumption, administration route, hematocrit, and invasive and non-invasive peripheral and central blood pressure were tabulated as potential drivers of dizziness.

Statistical analysis

Continuous variables are presented as means (standard deviation [SD]) or medians [interquartile range (IQR)], depending on the distribution of data. Categorical variables

Table 1 Baseline characteristics

Procedure, <i>n</i> (%)	
THA	100 (28.6)
TKA	100 (28.6)
BKA	50 (14.3)
PLF	50 (14.3)
SLMD/SLML	50 (14.3)
Age, year/mean (SD)	62.8 (11.8)
BMI, kg·m ⁻² /mean (SD)	28.7 (5.7)
Race, <i>n</i> (%)	
White	318 (90.9)
Black	14 (4.0)
Other	8 (2.3)
Asian	6 (1.7)
Hispanic	4 (1.1)
Female, <i>n</i> (%)	209 (59.7)
AI, %/mean (SD)	
Supine	111 (49)
Seated	110 (49)
Difference between seated and supine	−1 (21)
MAP, mmHg/mean (SD)	
Supine	94 (10)
Seated	95 (10)
Difference between seated and supine	2 (4)
HR, beats·min ⁻¹ /mean (SD)	
Supine	69 (11)
Seated	70 (10)
Difference between seated and supine	1 (6)
ACE inhibitor, <i>n</i> (%)	
Yes	6 (1.7)
Temporarily withheld	33 (9.4)
No	311 (88.9)
Angiotensin II blocker, <i>n</i> (%)	
Yes	5 (1.4)
Temporarily withheld	43 (12.3)
No	302 (86.3)
Beta blocker, <i>n</i> (%)	
Yes	32 (9.1)
Temporarily withheld	11 (3.1)
No	307 (87.7)
Calcium channel blocker, <i>n</i> (%)	
Yes	22 (6.3)
Temporarily withheld	25 (7.1)
No	303 (86.6)
Diuretic, <i>n</i> (%)	
Yes	1 (0.3)
Temporarily withheld	40 (11.4)

Table 1 continued

No	309 (88.3)
ACE = angiotensin converting enzyme; AI = augmentation index; BKA = bilateral knee arthroplasty; BMI = body mass index; HR = heart rate; MAP = mean arterial pressure; PLF = posterior lumbar fusion; SD = standard deviation; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; THA = total hip arthroplasty; TKA = total knee arthroplasty	

are presented as frequencies and percentages. The minimally important difference (MID) in AI was estimated as one half the SD of the mean baseline (i.e., holding area) AI.¹⁰ One-sided Z tests were used to test whether the proportions of patients with postoperative reduced AI or symptoms of OI were > 0.5. All other statistical hypothesis tests were two-sided. Linear mixed-effects models¹¹ with Gaussian random intercepts and unstructured covariance structures were used to model change and percentage change in AI from baseline (holding area) over time. Mixed-effects modeling accounts for the correlation between repeated measurements on the same patient, where the unstructured covariance structure does not assume a pattern in the covariance matrix. To ensure model stability, time points in which < 15 patients were measured were excluded from the longitudinal data analysis. Histograms and quantile-quantile plots indicated approximately normally distributed model residuals. Multivariable linear regression was used to assess potential predictors of the minimum change (i.e., maximum decrease) in AI from baseline. Multivariable Cox proportional hazards regression was used to assess potential predictors of the time until a dizziness score > 0 and the time until a total OHSA score > 0. Change in supine AI from baseline, opioid consumption, and hematocrit were included in the models as time-varying covariates. Model covariates were chosen by the study authors *a priori* based on clinical relevance. Given the large number of comparisons performed, all point estimates are presented along with their 99.9% confidence interval (CI). Statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA).

Results

Of 1,668 screened cases, *n* = 350 patients were enrolled (*n* = 100 THA, *n* = 100 TKA, *n* = 50 BKA, *n* = 50 PLF, and *n* = 50 SLMD/ SLML, respectively) (Fig. 1). Table 1 presents the baseline data.

Table 2 Change in supine AI over time

	<i>n</i>	Difference in means from baseline (99.9% CI)	<i>P</i> value	Percentage difference in means from baseline (99.9% CI)	<i>P</i> value
THA					
PACU admission	97	0 (−13 to 13)	0.93	6% (−4.4 to 16.3)	0.06
Spinal resolution	95	−39 (−52 to −26)	< 0.001	−30% (−40.4 to −19.5)	< 0.001
POD 1	93	−68 (−81 to −55)	< 0.001	−59.2% (−69.7 to −48.6)	< 0.001
POD 2	88	−62 (−76 to −49)	< 0.001	−52.8% (−63.6 to −42)	< 0.001
POD 3	56	−53 (−69 to −38)	< 0.001	−45% (−58.3 to −31.7)	< 0.001
POD 4	13	—	—	—	—
6 weeks	0	—	—	—	—
Minimum	100	−75 (−87 to −63)	< 0.001	−64.7% (−70.9 to −58.5)	< 0.001
TKA					
PACU admission	98	4 (−12 to 20)	0.36	8.7% (−3.4 to 20.9)	0.02
Spinal resolution	97	−40 (−56 to −24)	< 0.001	−27.2% (−39.4 to −15)	< 0.001
POD 1	97	−57 (−73 to −41)	< 0.001	−45.2% (−57.4 to −33)	< 0.001
POD 2	93	−57 (−73 to −41)	< 0.001	−43.2% (−55.7 to −30.8)	< 0.001
POD 3	89	−58 (−74 to −41)	< 0.001	−44.9% (−57.5 to −32.2)	< 0.001
POD 4	36	−59 (−82 to −36)	< 0.001	−46% (−65 to −27)	< 0.001
6 weeks	0	—	—	—	—
Minimum	100	−79 (−93 to −65)	< 0.001	−65% (−71.1 to −58.9)	< 0.001
BKA					
PACU admission	44	5 (−16 to 25)	0.45	18% (−4 to 40)	0.007
Spinal resolution	38	−29 (−51 to −8)	< 0.001	−24.6% (−47.7 to −1.4)	< 0.001
POD 1	40	−53 (−74 to −32)	< 0.001	−47% (−70 to −24)	< 0.001
POD 2	38	−55 (−76 to −34)	< 0.001	−51% (−74 to −28)	< 0.001
POD 3	34	−55 (−78 to −33)	< 0.001	−51.5% (−75.7 to −27.3)	< 0.001
POD 4	32	−46 (−69 to −23)	< 0.001	−45.3% (−70.1 to −20.5)	< 0.001
6 weeks	7	—	—	—	—
Minimum	48	−68 (−87 to −50)	< 0.001	−64.9% (−76.5 to −53.3)	< 0.001
PLF					
PACU admission	32	−27 (−50 to −5)	< 0.001	−20.2% (−40.3 to −0.1)	< 0.001
2 hr after PACU admission	29	−52 (−75 to −29)	< 0.001	−47.1% (−68.0 to −26.1)	< 0.001
POD 1	26	−55 (−78 to −31)	< 0.001	−50.5% (−72.3 to −28.6)	< 0.001
POD 2	25	−61 (−85 to −37)	< 0.001	−58.5% (−80.7 to −36.3)	< 0.001
POD 3	30	−56 (−78 to −33)	< 0.001	−47.0% (−67.6 to −26.3)	< 0.001
POD 4	22	−58 (−82 to −33)	< 0.001	−49.6% (−73.1 to −26.2)	< 0.001
6 weeks	8	—	—	—	—
Minimum	50	−63 (−84 to −41)	< 0.001	−58.5% (−71.6 to −45.3)	< 0.001
SLMD/SLML					
PACU admission	46	−1 (−22 to 20)	0.84	−1.2% (−20.6 to 18.2)	0.84
2 hr after PACU admission	40	−27 (−49 to −5)	< 0.001	−27.5% (−48 to −6.9)	< 0.001
POD 1	34	−35 (−59 to −11)	< 0.001	−32.6% (−54.5 to −10.7)	< 0.001
POD 2	4	—	—	—	—
POD 3	4	—	—	—	—
POD 4	1	—	—	—	—
6 weeks	11	—	—	—	—
Minimum	50	−44 (−62 to −26)	< 0.001	−44.8% (−57.5 to −32.1)	< 0.001

Table 2 continued

	<i>n</i>	Difference in means from baseline (99.9% CI)	<i>P</i> value	Percentage difference in means from baseline (99.9% CI)	<i>P</i> value
All					
PACU admission	317	−1 (−9 to 7)	0.74	4.7% (−2.0 to 11.5)	0.02
PACU stay*	299	−38 (−46 to −30)	< 0.001	−29.9% (−36.8 to −23)	< 0.001
POD 1	290	−58 (−66 to −49)	< 0.001	−49.4% (−56.4 to −42.4)	< 0.001
POD 2	248	−58 (−66 to −49)	< 0.001	−49.4% (−56.9 to −41.9)	< 0.001
POD 3	213	−54 (−63 to −45)	< 0.001	−46% (−54 to −38)	< 0.001
POD 4	104	−53 (−65 to −41)	< 0.001	−46.1% (−57.1 to −35.1)	< 0.001
6 weeks	26	−34 (−57 to −11)	< 0.001	−22.7% (−44.3 to −1.1)	< 0.001
Minimum	358	−69 (−76 to −62)	< 0.001	−61.1% (−65 to −57.1)	< 0.001

Time points when < 15 patients were measured were excluded from the analysis

AI = augmentation index; BKA = bilateral knee arthroplasty; CI = confidence interval; PACU = postanesthesia care unit; PLF = posterior lumbar fusion; POD = postoperative day; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; THA = total hip arthroplasty; TKA = total knee arthroplasty

*PACU stay corresponds to spinal resolution for THA, TKA, and BKA and two hours after PACU admission for PLF and SLMD/SLML

Changes in AI

The MID was estimated to be 25, 25, and 10 percentage points for supine, seated, and difference between seated and supine AI, respectively. Table 2 presents changes and percentage changes in supine AI over time in relation to baseline. Changes and percentage changes in seated AI and difference between seated and supine AI over time in relation to baseline are shown in the Appendix (Tables 5 and 6). Raw supine, seated, and difference between supine and seated AI, heart rate, and mean arterial pressure values over time are also presented in the Appendix (Figs. 3, 4, and 5). The AI significantly decreased postoperatively from baseline for all procedures. The decrease in AI was observed at spinal resolution or at first measurement in the PACU among PLF cases of spine surgery. The AI did not return to baseline from spinal resolution throughout the postoperative period in 252 of 335 (75.2%) of patients ($P < 0.001$).

Table 3 presents multivariable regression models of minimum change (i.e., maximum decrease) in supine AI from baseline. Based on an MID of 25 percentage points, the possibility of an association between the included predictors and an MID in AI could not be ruled out for any covariate besides age and body mass index (BMI).

Changes in symptoms OI (OHSA score) including dizziness

Figure 2 shows symptoms of OI and dizziness over time. The majority [260/342 (76.0%); $P < 0.001$] of patients

reported postoperative symptoms of OI, with 198 of 342 (57.9%) reporting dizziness specifically.

Association between changes in AI and symptomatic OI and dizziness

As shown in Table 4, there was no consistent evidence of an association between included covariates and symptoms of orthostatic intolerance besides a potential increase in probability associated with female sex.

Discussion

The AI significantly decreased postoperatively, outlasting immediate, direct effects of surgery and anesthesia. In the majority of patients (75.2%; $P < 0.001$), supine AI did not return to baseline from spinal resolution throughout the subsequent postoperative period. Despite significant decreases in AI amongst study subjects and the presence of OI symptoms in the majority of patients, no association could be established between AI and OI.

The AI is a measure of the relative amplitudes of the incident wave caused by ventricular contraction and the late systolic augmentation of the reflection wave that travels back to the central circulation from the bifurcation of the abdominal aorta. The Pulsecor device uses a standard blood pressure cuff and measures the ascending aortic pressure waveform (sum of the incident and reflected wave), while the augmentation index is derived as the ratio of augmented ascending aortic pressure and pulse pressure.

Table 3 Multivariable linear regression models of change in supine AI from baseline

	Difference in means (99.9% CI)	<i>P</i> value
Model 1 (<i>n</i> = 148)		
BKA vs TKA	6 (−17 to 29)	0.41
BMI (per 1 SD = 5.7 kg·m ^{−2})	4 (−7 to 15)	0.22
Age (per 1 SD = 11.8 yr)	−11 (−24 to 3)	0.01
Female vs male	−14 (−36 to 8)	0.04
ACE inhibitor and/or angiotensin II blocker	4 (−20 to 28)	0.60
Beta blocker	−25 (−58 to 9)	0.02
Calcium channel blocker	−1 (−32 to 30)	0.92
Diuretic	−12 (−45 to 21)	0.23
Model 2 (<i>n</i> = 200)		
PLF vs SLMD/SLML	−17 (−45 to 12)	0.05
BMI (per 1 SD = 5.7 kg·m ^{−2})	−7 (−23 to 10)	0.17
Age (per 1 SD = 11.8 yr)	−9 (−22 to 4)	0.03
Female vs male	−1 (−29 to 27)	0.90
ACE inhibitor and/or angiotensin II blocker	8 (−35 to 50)	0.54
Beta blocker	−11 (−64 to 42)	0.49
Calcium channel blocker	25 (−36 to 86)	0.16
Diuretic	5 (−44 to 54)	0.74
Model 3 (<i>n</i> = 348)		
Spine vs joint	12 (−4 to 29)	0.02
BMI (per 1 SD = 5.7 kg·m ^{−2})	0 (−7 to 7)	0.87
Age (per 1 SD = 11.8 yr)	−9 (−16 to −2)	< 0.001
Female vs male	−12 (−26 to 2)	0.006
ACE inhibitor and/or angiotensin II blocker	1 (−15 to 18)	0.80
Beta blocker	−18 (−39 to 4)	0.006
Calcium channel blocker	0 (−20 to 21)	0.97
Diuretic	0 (−23 to 22)	0.96

Changes in supine AI relate to minimum change (i.e., maximum decrease)

ACE = angiotensin converting enzyme; AI = augmentation index; BKA = bilateral knee arthroplasty; BMI = body mass index; CI = confidence interval; PLF = posterior lumbar fusion; SD = standard deviation; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; THA = total hip arthroplasty; TKA = total knee arthroplasty

The stiffer the aortic and iliac arteries are, the greater the amplitude of the reflection wave and measure of AI. While the stiffness of these large vessels can be due to degenerative disease with calcification and atheroma, it is also influenced by smooth muscle tone in the wall of the arteries. Thus, changes in AI over the years may be due to atheromatous disease; however, short-term changes, as measured in this current study, reflect changes in vascular tone. The physiology and medical significance of AI have been extensively studied in the hypertension literature, where reductions in AI show improved outcome.¹² Particularly in the perioperative setting, with multiple factors affecting the cardiovascular physiology,¹³ the level of vascular tone is essential for the maintenance of orthostasis and therefore brain and organ perfusion.¹⁴

While other more elaborate ways to measure vascular tone, such as pulse wave velocity exist, AI renders a feasible, non-invasive method for repeated measurements in the perioperative setting.

Changes in AI

The AI analysis was based on measurements taken at predefined postoperative time points in relation to preoperative baseline AI, aiming to determine acute changes in vascular tone rather than potential chronic alterations due to cardiovascular disease or inflammation.¹⁵ Notably, throughout all procedures a significant and persistent decrease in AI was observed postoperatively. Interestingly, the significant decrease in AI occurred hours

Fig. 2 Dizziness and total Orthostatic Hypotension Symptom Assessment scores over time. In this box plot, the upper and lower edges of the boxes represent the 1st and 3rd quartiles. The horizontal line represents the median while the diamond represents the mean. The whiskers represent observations within 1.5 times the interquartile range. *PACU stay corresponds to spinal resolution for THA, TKA,

and BKA and two hours after PACU admission for PLF and SLMD/SLML. BKA = bilateral knee arthroplasty; PACU = postanesthesia care unit; PLF = posterior lumbar fusion; POD = postoperative day; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; THA = total hip arthroplasty; TKA = total knee arthroplasty

Table 4 Multivariable Cox proportional hazards models of time to dizziness score > 0 and time to total OHSA score > 0

	Outcome: time to dizziness score > 0		Outcome: time to total OHSA score > 0	
	Hazard ratio (99.9% CI)	P value	Hazard ratio (99.9% CI)	P value
Model 1 (n = 147)				
BKA vs TKA	0.57 (0.19 to 1.73)	0.10	0.76 (0.29 to 1.95)	0.34
BMI (per 1 SD = 5.7 kg·m ⁻²)	1.02 (0.68 to 1.51)	0.88	0.99 (0.68 to 1.44)	0.93
Age (per 1 SD = 11.8 yr)	1.04 (0.59 to 1.84)	0.81	0.95 (0.56 to 1.62)	0.75
Female vs male	1.49 (0.55 to 4.03)	0.19	1.35 (0.56 to 3.26)	0.26
Change in supine AI (per 1 SD = 49 percentage points)	1.04 (0.63 to 1.74)	0.78	0.89 (0.55 to 1.43)	0.41
Opioid consumption (per 1 SD = 40 mg OME)	1.07 (0.78 to 1.46)	0.48	1.15 (0.84 to 1.56)	0.14
Hematocrit (per 1 SD = 4.2 percentage points)	1.00 (0.63 to 1.59)	0.99	0.92 (0.62 to 1.35)	0.47
Model 2 (n = 97)				
PLF vs SLMD/SLML	1.00 (0.04 to 28.37)	0.99	0.87 (0.05 to 15.17)	0.88
BMI (per 1 SD = 5.7 kg·m ⁻²)	0.54 (0.14 to 2.18)	0.15	0.91 (0.34 to 2.4)	0.5
Age (per 1 SD = 11.8 yr)	1.82 (0.47 to 7.12)	0.15	1.08 (0.33 to 3.46)	0.84
Female vs male	3.15 (0.46 to 21.64)	0.05	1.91 (0.31 to 11.71)	0.24
Change in supine AI (per 1 SD = 49 percentage points)	1.88 (0.46 to 7.77)	0.14	0.86 (0.23 to 3.21)	0.71
Opioid consumption (per 1 SD = 40 mg OME)	1.19 (0.55 to 2.58)	0.46	0.92 (0.53 to 1.57)	0.60
Hematocrit (per 1 SD = 4.2 percentage points)	1.27 (0.39 to 4.17)	0.50	1.10 (0.37 to 3.28)	0.77
Model 3 (n = 342)				
Spine vs joint	0.57 (0.19 to 1.73)	0.10	1.32 (0.55 to 3.16)	0.29
BMI (per 1 SD = 5.7 kg·m ⁻²)	1.02 (0.68 to 1.51)	0.88	1.00 (0.76 to 1.31)	0.99
Age (per 1 SD = 11.8 yr)	1.04 (0.59 to 1.84)	0.81	1.00 (0.69 to 1.43)	0.97
Female vs male	1.49 (0.55 to 4.03)	0.19	1.39 (0.72 to 2.68)	0.10
Change in supine AI (per 1 SD = 49 percentage points)	1.04 (0.63 to 1.74)	0.78	0.93 (0.63 to 1.36)	0.51
Opioid consumption (per 1 SD = 40 mg OME)	1.07 (0.78 to 1.46)	0.48	1.03 (0.82 to 1.28)	0.70
Hematocrit (per 1 SD = 4.2 percentage points)	1.00 (0.63 to 1.59)	0.99	0.94 (0.69 to 1.28)	0.51

BKA = bilateral knee arthroplasty; BMI = body mass index; CI = confidence interval; OHSA = Orthostatic Hypotension Symptom Assessment; OME = oral morphine equivalent; PLF = posterior lumbar fusion; SD = standard deviation; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; TKA = total knee arthroplasty

after PACU admission in all procedures except in spine cases of PLF, where AI was decreased at first measurement in PACU.

Based on multivariable regression models of the minimum change (i.e., maximum decrease) in supine AI from baseline, the possibility of an association between the included predictors and an MID in AI could not be ruled out for any covariate besides age and BMI. Specifically, the 95% CI for the β coefficients corresponding to all predictors besides age and BMI included the estimated supine AI MID (-25 or 25 percentage points). Therefore, future studies with larger sample sizes are required to estimate β coefficients with enough precision to definitively identify strong predictors of change in AI.

Similar to our results, Goytizolo *et al.*⁶ found a prolonged postoperative reduction in AI past the effects of regional anesthesia in THA under neuraxial anesthesia, which however did not differ with or without the addition

of a peripheral nerve block. In contrast to our analysis, however, Goytizolo *et al.*⁶ did not compare AI between different procedures and anesthetic techniques.

Most previous studies measured AI only up to 48 hr postoperatively; thus, our aim was to investigate AI until hospital discharge to enable a longer observation of the natural postoperative course of changes in vascular tone. Our results show that in the majority of patients, AI did not return to baseline from spinal resolution through the last AI measurement. Overall, these results suggest that events surrounding surgery confer a prolonged decrease in vascular tone of unknown duration, while the severity may depend on the type of anesthesia technique or surgical procedure, potentially reflecting differences in the metabolic and neuroendocrine stress response to surgical injury with varying impact on vascular tone.

Association between AI and symptoms of OI

Only a few studies have investigated potential associations between postoperative OI and measures of cardiovascular function. Nevertheless, no other study has investigated a potential association between changes in postoperative AI and symptoms of OI, including dizziness or lightheadedness. We did not find a consistent direction of association between change in supine AI from baseline and the presence of symptoms of OI across regression models (range of adjusted hazard ratio point estimates: 0.86–1.88). Nevertheless, the 99.9% CI for these hazard ratios were wide, so future studies with larger sample sizes must be undertaken to confirm this finding. Although Jans *et al.*¹⁶ found a significant association between postoperative OI and heart rate variability among patients undergoing THA under neuraxial anesthesia, they could not find an association with other cardiovascular parameters in a separate investigation.³ Nevertheless, in critically ill patients Hughes *et al.*¹⁷ showed that vascular tone was associated with changes in systemic endothelial function and acute brain dysfunction, highlighting the clinical significance of this parameter. Nevertheless, varying findings may be due to inter-individual differences in the ability to autoregulate brain perfusion, potentially causing bias in smaller sample sizes, or possibly due to erratic self-reporting of OI symptoms. Furthermore, the lack of association between AI and OI in our analysis may be due to the application of standard of care, and therefore the utilization of resuscitative measures, including intravenous fluids and blood transfusions as needed. This could have counteracted hemodynamic changes, potentially otherwise more prevalent in decreased AI.

In contrast to change in supine AI from baseline, the adjusted hazard ratio point estimates for female vs. male sex were consistently > 1.00 (range, 1.35–3.15) for all regression models. Nevertheless, the *P* values associated with these coefficients were much greater than 0.001. In the context of literature suggesting a positive association between female sex and risk of dizziness in other settings, these *P* values may indicate a type II error (a false negative) due to a limited sample size.^{18–20}

Changes in symptoms of OI

Postoperative OI can hinder recovery and is a major reason for prolonged hospital stay.¹ Our results showed that the majority of the patients undergoing orthopedic surgery developed postoperative OI to some extent, although for most patients the severity of symptoms was not very pronounced. This finding may again have been modulated by adequate routine resuscitative clinical and intrinsic measures. The incidence of dizziness in our patient sample

(57.9%) was comparable to Bundgaard-Nielsen *et al.*²¹ in radical prostatectomy under general anesthesia (50% at six hours after surgery) and Jans *et al.*³ in THA under neuraxial anesthesia (42% at six hours after surgery). In contrast, Müller *et al.*⁴ reported a postoperative OI incidence of only 4% in breast cancer surgery under general anesthesia. They concluded that general anesthesia did not necessarily have a negative impact on the prevalence of postoperative OI, whereas the invasiveness of surgery seemed to have relevant influence. Nevertheless, Müller *et al.*⁴ evaluated OI only once, at 30 min after surgery, while our study directly compared symptoms of OI and changes in AI in different orthopedic surgeries at multiple time points. Furthermore, the aforementioned studies^{3,4,21} assessed OI by utilizing clinical parameters in combination with blood pressure changes, while we employed a validated questionnaire, specifically designed for the evaluation of OI.⁹

Limitations of our analysis should be addressed. The observational nature does not allow for causal conclusions, while interpretations require cautious consideration of potential residual confounding factors that could not be entirely accounted for. Despite the application of rigorous exclusion criteria including cardiovascular disease and the provision of analysis of baseline characteristics including age, BMI, and consumption of various medications, potential residual confounding factors on OI and AI cannot be entirely ruled out. Potential factors to consider include other comorbidities, postoperative cognitive dysfunction, neuro-inflammatory reaction, hypotension, use of pregabalin and gabapentin, and the fact that the questionnaires for the measures OI and dizziness were subjectively answered.^{22,23} Additionally, the use of especially angiotensin converting enzyme inhibitors has been linked to perioperative hemodynamic derangements. Further, the holding of antihypertensives on the day of surgery may also influence a patient's cardiovascular status. Similarly, despite referencing AI to baseline values, other potential drivers of AI include heart rate, body height, and additional medications and comorbidities that cannot be entirely excluded as potential confounders.¹⁵ The benefit of comparability among different procedures bears the risk that surgeries varied in more aspects than surgical invasiveness and anesthesia technique; thus, the identified differences in AI and OI potentially also reflected other factors. Furthermore, this study is reflective of a single specialized high-volume orthopedic setting, potentially differing in practice from other clinical settings. Finally, investigation of the impact of AI and OI on other outcomes including length of stay, morbidity, functional recovery, or patient satisfaction was beyond the study scope and requires further investigation.

In conclusion, vascular tone, as measured by AI, significantly decreased after orthopedic surgery and

outlasted the immediate postoperative period. While the majority of patients developed some extent of postoperative OI, an association between symptoms of AI and OI was not found. The high prevalence of OI and its significance in terms of early recovery require further research into potential drivers.

Conflict of interest None declared.

Disclosures Stavros G. Memtsoudis is funded by the Anna Maria and Stephen Kellen Career Development Award, New York. Dr. Memtsoudis is a director on the boards of the American Society of Regional Anesthesia and Pain Medicine (ASRA) and the Society of Anesthesia and Sleep Medicine (SASM). He is a one-time consultant for Sandoz Inc. and the holder US Patent Multicatheter Infusion System (US-2017-0361063). He is the owner of SGM Consulting, LLC and co-owner of FC Monmouth, LLC. None of the above relations influenced the conduct of the present study. Nigel E. Sharrock has stock options in Uscom Ltd., which owns the PulseCor monitor.

Editorial responsibility This submission was handled by Dr. Gregory L. Bryson, Deputy Editor-in-Chief, *Canadian Journal of Anesthesia*.

Author contributions Stavros G. Memtsoudi, Nigel E. Sharrock, and Thomas Danninger helped design the study, conduct the study, analyze the data, and write the manuscript and have given final approval of the version to be published. Eva E. Mörwald helped analyze the data and write the manuscript and has given final approval of the version to be published. Kara Fields helped analyze the data and draft the article and has given final approval of the version to be published. Crispiana Cozowicz, Mathias Opperer, Ottokar Stundner, and Angie Zhang helped conduct the study, analyze the data, and write the manuscript and have given final approval of the version to be published. George Go helped to conduct the study and write the manuscript and has given final approval of the version to be published.

Funding This study was funded by the Department of Anesthesiology at the Hospital for Special Surgery New York, New York. Research reported in this publication was supported by the National Center For Advancing Translational Science of the National Institute of Health under award number UL1TR000457.

Appendix

See Tables 5 and 6 and Figs. 3, 4, and 5.

Table 5 Change in seated AI over time

	<i>n</i>	Difference in means from holding area (99.9% CI)	<i>P</i> value	Percentage difference in means from holding area (99.9% CI)	<i>P</i> value
THA					
PACU admission	4	—	—	—	—
Spinal resolution	94	−43 (−57 to −29)	< 0.001	−33.1% (−41.3 to −24.9)	< 0.001
POD 1	90	−66 (−80 to −52)	< 0.001	−56.2% (−64.6 to −47.8)	< 0.001
POD 2	87	−63 (−77 to −49)	< 0.001	−52.7% (−61.2 to −44.2)	< 0.001
POD 3	56	−58 (−73 to −42)	< 0.001	−48.6% (−59 to −38.3)	< 0.001
POD 4	13	—	—	—	—
6 weeks	0	—	—	—	—
Minimum	99	−75 (−89 to −61)	< 0.001	−64% (−70.2 to −57.7)	< 0.001
TKA					
PACU admission	1	—	—	—	—
Spinal resolution	95	−42 (−58 to −25)	< 0.001	−28.6% (−40.3 to −17.0)	< 0.001
POD 1	94	−57 (−74 to −41)	< 0.001	−44.8% (−56.5 to −33.1)	< 0.001
POD 2	93	−59 (−76 to −43)	< 0.001	−47.6% (−59.4 to −35.8)	< 0.001
POD 3	89	−59 (−76 to −43)	< 0.001	−45.8% (−57.7 to −33.8)	< 0.001
POD 4	37	−52 (−73 to −30)	< 0.001	−41.5% (−59.1 to −23.8)	< 0.001
6 weeks	0	—	—	—	—
Minimum	100	−79 (−94 to −63)	< 0.001	−65.2% (−71.4 to −58.9)	< 0.001
BKA					
PACU admission	6	—	—	—	—
Spinal resolution	32	−31 (−51 to −12)	< 0.001	−27.7% (−47.5 to −7.8)	< 0.001
POD 1	37	−50 (−69 to −31)	< 0.001	−46.2% (−65.1 to −27.4)	< 0.001
POD 2	34	−56 (−75 to −36)	< 0.001	−53.7% (−73.2 to −34.3)	< 0.001
POD 3	32	−55 (−75 to −35)	< 0.001	−54.6% (−74.6 to −34.7)	< 0.001
POD 4	30	−51 (−71 to −31)	< 0.001	−50.7% (−71.2 to −30.3)	< 0.001
6 weeks	7	—	—	—	—

Table 5 continued

	<i>n</i>	Difference in means from holding area (99.9% CI)	<i>P</i> value	Percentage difference in means from holding area (99.9% CI)	<i>P</i> value
Minimum	49	−63 (−81 to −46)	< 0.001	−63.3% (−76.5 to −50.1)	< 0.001
PLF					
PACU admission	4	—	—	—	—
2 hr after PACU admission	19	−50 (−75 to −25)	< 0.001	−43.7% (−66.1 to −21.3)	< 0.001
POD 1	29	−56 (−80 to −33)	< 0.001	−55.2% (−74.2 to −36.1)	< 0.001
POD 2	23	−62 (−86 to −38)	< 0.001	−58.5% (−79.3 to −37.8)	< 0.001
POD 3	26	−54 (−78 to −31)	< 0.001	−49.3% (−69.1 to −29.5)	< 0.001
POD 4	19	−52 (−77 to −27)	< 0.001	−46.7% (−69.1 to −24.3)	< 0.001
6 weeks	7	—	—	—	—
Minimum	50	−60 (−81 to −39)	< 0.001	−57% (−71.1 to −43.0)	< 0.001
SLMD/SLML					
PACU admission	6	—	—	—	—
2 hr after PACU admission	29	−25 (−50 to 0)	< 0.001	−23.5% (−49.6 to 2.5)	0.002
POD 1	32	−39 (−63 to −15)	< 0.001	−36.4% (−61.3 to −11.5)	< 0.001
POD 2	4	—	—	—	—
POD 3	4	—	—	—	—
POD 4	0	—	—	—	—
6 weeks	11	—	—	—	—
Minimum	50	−41 (−59 to −23)	< 0.001	−40.3% (−54.0 to −26.7)	< 0.001
All					
PACU admission	21	−20 (−42 to 2)	0.002	−17.2% (−37.6 to 3.2)	0.006
PACU stay*	269	−39 (−47 to −31)	< 0.001	−30.6% (−36.8 to −24.3)	< 0.001
POD 1	282	−57 (−65 to −49)	< 0.001	−48.8% (−55.0 to −42.7)	< 0.001
POD 2	241	−59 (−67 to −50)	< 0.001	−51% (−57.5 to −44.4)	< 0.001
POD 3	207	−56 (−65 to −47)	< 0.001	−47.9% (−54.9 to −40.9)	< 0.001
POD 4	99	−51 (−63 to −40)	< 0.001	−45% (−54.7 to −35.3)	< 0.001
6 weeks	25	−48 (−68 to −27)	< 0.001	−37.2% (−56.2 to −18.3)	< 0.001
Minimum	348	−67 (−75 to −60)	< 0.001	−59.8% (−64.1 to −55.5)	< 0.001

Time points when < 15 patients were measured were excluded from the analysis

AI = augmentation index; BKA = bilateral knee arthroplasty; PACU = postanesthesia care unit; PLF = posterior lumbar fusion; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; THA = total hip arthroplasty; TKA = total knee arthroplasty

*PACU stay corresponds to spinal resolution for THA, TKA, and BKA and two hours after PACU admission for PLF and SLMD/SLML

Table 6 Change in difference between seated and supine AI over time

	<i>n</i>	Difference in means from holding area (99.9% CI)	<i>P</i> value	<i>n</i>	Percentage difference in means from holding area (99.9% CI)	<i>P</i> value
THA						
PACU admission	4	—	—	4	—	—
Spinal resolution	94	−4 (−11 to 4)	0.10	92	−13.6% (−232.7 to 205.5)	0.84
POD 1	90	3 (−5 to 10)	0.22	88	−158% (−382 to 66.1)	0.02
POD 2	87	0 (−7 to 8)	0.83	86	−116.6% (−343.2 to 110.1)	0.09
POD 3	55	−5 (−13 to 3)	0.06	55	45.4% (−238 to 328.8)	0.59
POD 4	13	—	—	13	—	—
6 weeks	0	—	—	0	—	—
Minimum	99	−13 (−20 to −7)	< 0.001	97	−375.3% (−588.2 to −162.5)	< 0.001

Table 6 continued

	<i>n</i>	Difference in means from holding area (99.9% CI)	<i>P</i> value	<i>n</i>	Percentage difference in means from holding area (99.9% CI)	<i>P</i> value
TKA						
PACU admission	1	—	—	1	—	—
Spinal resolution	95	0 (−10 to 10)	0.96	94	−38.9% (−433.5 to 355.7)	0.74
POD 1	94	1 (−9 to 11)	0.77	93	−121.7% (−518.4 to 275.1)	0.31
POD 2	92	−2 (−12 to 8)	0.54	91	−34.7% (−435.8 to 366.3)	0.77
POD 3	89	−1 (−11 to 9)	0.69	89	−45.3% (−450.8 to 360.2)	0.71
POD 4	36	8 (−6 to 21)	0.07	36	388.4% (−247.9 to 1024.6)	0.04
6 weeks	0	—	—	0	—	—
Minimum	100	−20 (−27 to −12)	< 0.001	99	−367.3% (−537.6 to −197)	< 0.001
BKA						
PACU admission	6	—	—	6	—	—
Spinal resolution	31	−4 (−19 to 11)	0.40	31	42.3% (−172 to 256.7)	0.51
POD 1	35	1 (−14 to 15)	0.87	35	−100% (−301.8 to 101.7)	0.10
POD 2	33	2 (−12 to 17)	0.57	33	−171.3% (−379.1 to 36.5)	0.006
POD 3	31	4 (−10 to 19)	0.31	31	−125.2% (−339.5 to 89.2)	0.05
POD 4	29	−3 (−18 to 12)	0.51	29	−194.5% (−416.1 to 27.1)	0.004
6 weeks	6	—	—	6	—	—
Minimum	48	−17 (−33 to −1)	< 0.001	48	−296% (−532.5 to −59.4)	< 0.001
PLF						
PACU admission	1	—	—	1	—	—
2 hr after PACU admission	11	—	—	11	—	—
POD 1	19	4 (−9 to 18)	0.27	19	−35% (−534.8 to 464.7)	0.81
POD 2	20	4 (−10 to 17)	0.32	20	−56.7% (−543.7 to 430.4)	0.68
POD 3	25	5 (−7 to 18)	0.15	25	33.9% (−401.7 to 469.5)	0.78
POD 4	17	3 (−11 to 17)	0.52	17	14.6% (−513.7 to 542.9)	0.92
6 weeks	7	—	—	7	—	—
Minimum	50	−7 (−12 to −1)	< 0.001	50	−223.3% (−389.3 to −57.2)	< 0.001
SLMD/SLML						
PACU admission	5	—	—	5	—	—
2 hr after PACU admission	28	0 (−19 to 20)	0.93	28	−129.1% (−355.7 to 97.5)	0.04
POD 1	30	−6 (−25 to 13)	0.26	30	−134.4% (−353.3 to 84.5)	0.03
POD 2	4	—	—	4	—	—
POD 3	4	—	—	4	—	—
POD 4	0	—	—	0	—	—
6 weeks	11	—	—	11	—	—
Minimum	50	−14 (−26 to −2)	< 0.001	50	−236.7% (−385.8 to −87.5)	< 0.001
All						
PACU admission	17	−9 (−24 to 6)	0.06	17	−45.6% (−703.5 to 612.4)	0.82
PACU stay*	259	−2 (−7 to 3)	0.28	256	−27.6% (−197.3 to 142)	0.59
POD 1	268	1 (−4 to 6)	0.44	265	−125.8% (−292.6 to 41)	0.013
POD 2	236	0 (−6 to 5)	0.84	234	−91.8% (−269.3 to 85.7)	0.09
POD 3	204	−1 (−6 to 5)	0.64	204	−27.9% (−218 to 162.2)	0.63
POD 4	95	2 (−5 to 9)	0.34	95	54.8% (−223.7 to 333.2)	0.52
6 weeks	24	−10 (−24 to 3)	0.01	24	−101.5% (−655.4 to 452.4)	0.55
Minimum	347	−15 (−19 to −11)	< 0.001	344	−319.7% (−407.5 to −231.9)	< 0.001

Time points when < 15 patients were measured were excluded from the analysis

CI = confidence interval; BKA = bilateral knee arthroplasty; PACU = postanesthesia care unit; PLF = posterior lumbar fusion; POD = postoperative day; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; THA = total hip arthroplasty; TKA = total knee arthroplasty

*PACU stay corresponds to spinal resolution for THA, TKA, and BKA and two hours after PACU admission for PLF and SLMD/SLML

Fig. 3 Supine, seated, and difference between seated and supine AI over time. In this box plot, the upper and lower edges of the boxes represent the 1st and 3rd quartiles. The horizontal line represents the median while the diamond represents the mean. The whiskers represent observations within 1.5 times the interquartile range. *PACU stay corresponds to spinal resolution for THA, TKA, and BKA and 2 hr after PACU admission for PLF and SLMD/SLML. BKA = bilateral knee arthroplasty; PACU = postanesthesia care unit; PLF = posterior lumbar fusion; POD = postoperative day; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; THA = total hip arthroplasty; TKA = total knee arthroplasty

Fig. 4 Supine, seated, and difference between seated and supine MAP over time. In this box plot, the upper and lower edges of the boxes represent the 1st and 3rd quartiles. The horizontal line represents the median while the diamond represents the mean. The whiskers represent observations within 1.5 times the interquartile range. *PACU stay corresponds to spinal resolution for THA, TKA, and BKA and two hours after PACU admission for PLF and SLMD/SLML. BKA = bilateral knee arthroplasty; PACU = postanesthesia care unit; PLF = posterior lumbar fusion; POD = postoperative day; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; THA = total hip arthroplasty; TKA = total knee arthroplasty

Fig. 5 Supine, seated, and difference between seated and supine heart rate over time. In this box plot, the upper and lower edges of the boxes represent the 1st and 3rd quartiles. The horizontal line represents the median while the diamond represents the mean. The whiskers represent observations within 1.5 times the interquartile range. *PACU stay corresponds to spinal resolution for THA, TKA, and BKA and two hours after PACU admission for PLF and SLMD/SLML. BKA = bilateral knee arthroplasty; PACU = postanesthesia care unit; PLF = posterior lumbar fusion; POD = postoperative day; SLMD = single-level microdiscectomies; SLML = single-level microlaminectomies; THA = total hip arthroplasty; TKA = total knee arthroplasty

References

1. Husted H, Lunn TH, Troelsen A, Gaarn-Larsen L, Kristensen BB, Kehlet H. Why still in hospital after fast-track hip and knee arthroplasty? *Acta Orthop* 2011; 82: 679-84.
2. Bundgaard-Nielsen M, Jans O, Muller RG, et al. Does goal-directed fluid therapy affect postoperative orthostatic intolerance? A randomized trial. *Anesthesiology* 2013; 119: 813-23.
3. Jans O, Bundgaard-Nielsen M, Solgaard S, Johansson PI, Kehlet H. Orthostatic intolerance during early mobilization after fast-track hip arthroplasty. *Br J Anaesth* 2012; 108: 436-43.
4. Muller RG, Bundgaard-Nielsen M, Kehlet H. Orthostatic function and the cardiovascular response to early mobilization after breast cancer surgery. *Br J Anaesth* 2010; 104: 298-304.
5. 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.
6. Goytizolo EA, Stundner O, Rua SH, et al. The effect of regional analgesia on vascular tone in hip arthroplasty patients. *Hss J* 2016; 12: 125-31.
7. Munir S, Guilcher A, Kamalesh T, et al. Peripheral augmentation index defines the relationship between central and peripheral pulse pressure. *Hypertension* 2008; 51: 112-8.
8. Lin AC, Lowe A, Sidhu K, Harrison W, Ruygrok P, Stewart R. Evaluation of a novel sphygmomanometer, which estimates central aortic blood pressure from analysis of brachial artery suprasystolic pressure waves. *J Hypertens* 2012; 30: 1743-50.
9. Kaufmann H, Malamut R, Norcliffe-Kaufmann L, Rosa K, Freeman R. The Orthostatic Hypotension Questionnaire (OHQ): validation of a novel symptom assessment scale. *Clin Auton Res* 2012; 22: 79-90.
10. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003; 41: 582-92.
11. Ma Y, Mazumdar M, Memtsoudis SG. Beyond repeated-measures analysis of variance: advanced statistical methods for the analysis of longitudinal data in anesthesia research. *Reg Anesth Pain Med* 2012; 37: 99-105.
12. Williams B, Lacy PS, Thom SM, et al. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. *Circulation* 2006; 113: 1213-25.
13. Park S, Lakatta EG. Role of inflammation in the pathogenesis of arterial stiffness. *Yonsei Med J* 2012; 53: 258-61.
14. Stewart JM. Mechanisms of sympathetic regulation in orthostatic intolerance. *J Appl Physiol* 1985; 2012(113): 1659-68.
15. Nichols WW, Singh BM. Augmentation index as a measure of peripheral vascular disease state. *Curr Opin Cardiol* 2002; 17: 543-51.
16. Jans O, Brinth L, Kehlet H, Mehlsen J. Decreased heart rate variability responses during early postoperative mobilization—an observational study. *BMC Anesthesiol* 2015; 15: 120.
17. Hughes CG, Morandi A, Girard TD, et al. Association between endothelial dysfunction and acute brain dysfunction during critical illness. *Anesthesiology* 2013; 118: 631-9.
18. Bosner S, Schwarm S, Grevenrath P, et al. Prevalence, aetiologies and prognosis of the symptom dizziness in primary care - a systematic review. *BMC Fam Pract* 2018; 19: 33.
19. Maarsingh OR, Dros J, Schellevis FG, van Weert HC, Bindels PJ, Horst HE. Dizziness reported by elderly patients in family practice: prevalence, incidence, and clinical characteristics. *BMC Fam Pract* 2010; 11: 2.
20. Chang J, Hwang SY, Park SK, et al. Prevalence of dizziness and associated factors in South Korea: a cross-sectional survey from 2010 to 2012. *J Epidemiol* 2010. DOI: <https://doi.org/10.2188/jea.JE20160113>.
21. Bundgaard-Nielsen M, Jorgensen CC, Jorgensen TB, Ruhnau B, Secher NH, Kehlet H. Orthostatic intolerance and the cardiovascular response to early postoperative mobilization. *Br J Anaesth* 2009; 102: 756-62.
22. Krenk L, Kehlet H, Baek Hansen T, Solgaard S, Soballe K, Rasmussen LS. Cognitive dysfunction after fast-track hip and knee replacement. *Anesth Analg* 2014; 118: 1034-40.
23. Riedel B, Browne K, Silbert B. Cerebral protection: inflammation, endothelial dysfunction, and postoperative cognitive dysfunction. *Curr Opin Anaesthesiol* 2014; 27: 89-97.