Propofol TCI Reductions Do Not Attenuate Significant Falls in Cardiac Output Associated With Anesthesia Induction and Knee-Chest Positioning in Spinal Surgery

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Background: Induction of anesthesia and the knee-chest position are associated with hemodynamic changes that may impact patient outcomes. The aim of this study was to assess whether planned reductions in target-controlled infusion propofol concentrations attenuate the hemodynamic changes associated with anesthesia induction and knee-chest position.

Materilas and Methods: A total of 20 patients scheduled for elective lumbar spinal surgery in the knee-chest position were included. In addition to standard anesthesia monitoring, bispectral index and noninvasive cardiac output (CO) monitoring were undertaken. The study was carried out in 2 parts. In phase 1, target-controlled infusion propofol anesthesia was adjusted to maintain BIS 40 to 60. In phase 2, there were 2 planned reductions in propofol target concentration: (1) immediately after loss of consciousness—reduction calculated using a predefined formula, and (2) before positioning—reduction equal to the average percentage decrease in CO after knee-chest position in phase 1. Changes from baseline in CO and other hemodynamic variables following induction of anesthesia and knee-chest positioning were compared.

Results: Induction of anesthesia led to decreases of 25.6% and 19.8% in CO from baseline in phases 1 and 2, respectively ($P < 0.01$). Knee-chest positioning resulted in a further decrease such that the total in CO reduction from baseline to 10 minutes after positioning was 38.4% and 46.9% in phases 1 and 2, respectively ($P < 0.01$). There was no difference in CO changes between phases 1 and 2, despite the planned reductions in propofol during phase 2. There was no significant correlation between changes in CO and mean arterial pressure.

Conclusions: Planned reductions in propofol concentration do not attenuate anesthesia induction and knee-chest position-related decreases in CO. The knee-chest position is an independent risk factor for decrease in CO. Minimally invasive CO monitors may aid in the detection of clinically relevant hemodynamic changes and guide management in anesthetized patients in the knee-chest position.

Key Words: cardiac output, anesthesia induction, spinal surgery, knee-chest position, hemodynamic variation, propofol TCI anesthesia, minimally invasive CO monitors

following induction of anesthesia and knee-chest positioning were compared.

I nduction of anesthesia is associated with important hemodynamic changes, but previous studies have mostly been limited to assessment of blood pressure effects.[1–3] In recent years there have been significant technological advances in perioperative monitoring,[4] particularly in the development of minimally invasive cardiac output (CO) monitors such as the LIDCO *rapid* (LiDCO Ltd, Cambridge, UK).[5–11] Unlike previous devices, the LIDCO *rapid* requires neither lithium dilution nor calibration; it uses nomograms based on an individual patient's biometrics to estimate CO and stroke volume. This technology has seldom been used to assess comprehensive hemodynamic changes during anesthesia-induced loss of consciousness (LOC).[12,13] Modern target-controlled infusion (TCI) systems allow more precise titration of induction and maintenance of intravenous anesthesia, as well as modeling of plasma and cerebral drug concentrations.[14,15] Together, these technological advances allow a more accurate

and comprehensive assessment of the hemodynamic changes associated with induction of anesthesia and patient positioning.

Even short durations of arterial hypotension during anesthesia, and the subsequent ischemia-reperfusion, have been associated with acute kidney injury, cardiac complications, stroke, and increased 30-day and 1-year mortality after noncardiac surgery.[16–18] In procedures where the surgical position may also cause reductions in blood pressure and CO, patients may be exposed to an increased risk of intraoperative hypotension that is sufficient to precipitate critical tissue ischemia.

The knee-chest is a variant of the prone position (Supplementary Digital Content 1, http://links.lww.com/JNA/A96), and it may be a particular problem, as it reduces venous return and CO.[19,20] Physiological changes and complications associated with surgical positioning, including standard prone[21] and knee-chest position, have been studied since the 1930s and extensively reviewed elsewhere.[22,23] The prone position and its variants are currently used in a large number of surgical procedures.[24,25] Anesthesiologists must be aware of the risks that they pose of substantial hemodynamic variation and be prepared to anticipate and minimize such changes.

We have previously observed that lower propofol concentrations are required in patients in the prone position compared with similar individuals in the supine position. Thus, in the present study, we hypothesized that the reduction in blood pressure and CO associated with the knee-chest position could be attenuated by reducing the dose of propofol administered after induction of anesthesia but before positioning. We also hypothesized that the use of TCI propofol would allow more controlled reductions in propofol dose. The main aim of the study was to assess whether reductions in TCI propofol concentrations applied promptly after LOC but before positioning would attenuate the hemodynamic changes associated with anesthesia induction and knee-chest positioning.

MATERIALS AND METHODS

A 2-phase prospective cohort study of patients undergoing elective lumbar spine surgery in the knee-chest position with TCI propofol anesthesia was conducted following Research Ethics Board approval and after receiving written informed consent. Patients with severe ischemic heart disease, congestive cardiac failure, atrial fibrillation or flutter, body mass index $> 35 \, kg/m^2$, Glasgow Coma Scale <15, dementia, history of drug abuse or addiction, and chronic opioid consumption, and those who were administered preoperative midazolam were excluded.

Anesthesia, Monitoring, and Equipment

All patients received a crystalloid intravenous infusion at 400 mL/h from arrival in the operating room until the end of anesthesia induction, and, thereafter, at 200 mL/h until the end of surgery. Routine monitoring—ECG, heart rate, peripheral arterial oxygen saturation measured by pulse oximetry, invasive blood pressure,

bispectral index (BIS brain monitoring; Medtronic, Minneapolis, Minnesota), peripheral body temperature, and neuromuscular block monitoring—was undertaken in all patients. A left radial artery catheter was placed under local anesthesia before induction of anesthesia. The LiDCO *rapid* monitor was connected via this cannula, and the following hemodynamic data were collected every second: CO, cardiac index, stroke volume, stroke volume index, systemic vascular resistance, invasive systolic, diastolic, and mean arterial blood pressure, heart rate, pulse pressure variation, and stroke volume variation. A separate computer connected via the patient monitor (Aisys; GE Healthcare, Chicago, Illinois), RugLoopII software (DEMED website; Temse, Belgium) was used to drive the propofol and remifentanil infusion pumps (Alaris; Asena, BD, UK) and to collect data every 5 minutes.

Immediately before induction of anesthesia, baseline clinical and hemodynamic parameters were recorded; this was defined as moment 0 (M0). Anesthesia was then induced with TCI remifentanil (20 µg/mL) to achieve and maintain an effect-site concentration target (Ce) of 2.5 ng/mL (Minto pharmacokinetic model) and propofol (1%) at 200 mL/h until LOC, determined as the moment when the patient failed to open his/her eyes after being called by name and tapped on the forehead. At the moment of LOC, propofol infusion was stopped, and the estimated Ce noted. The infusion pump was then immediately switched to TCI mode using Schnider's pharmacokinetic model. From this moment onwards, the propofol administration protocols were different during phases 1 and 2. These are outlined in detail below and illustrated in the Figure 1.

Following induction of anesthesia and administration of muscle relaxants (rocuronium, 0.6 mg/kg), all patients were intubated. Mechanical ventilation (tidal volume, 8 mL/kg) with an O_2/air mixture to achieve $SpO_2 > 98\%$ was adjusted to maintain normocapnic end-tidal carbon dioxide. Remifentanil Ce was switched to 1 ng/mL after intubation and before surgical incision. Ephedrine boluses (5 mg) were allowed if CO or systolic blood pressure decreased by $> 30\%$ from baseline in all patients.

After placement in the knee-chest position, a ProneView platform was used to support the head, and compression points were carefully protected. All monitoring and anesthetic infusions were continued during positioning.

Experimental Protocol

The study was carried out in 2 parts. In phase 1, the reductions in propofol Ce were not protocolized but targeted to maintain BIS 40 to 60. The reductions in CO following induction of anesthesia and knee-chest positioning were quantified. In a second group of patients—phase 2—two planned reductions in propofol Ce were applied, one immediately after LOC and the other before patient positioning. Hemodynamic variables were compared within individuals and also between the 2 phases. All hemodynamic variables were collected with drugs in
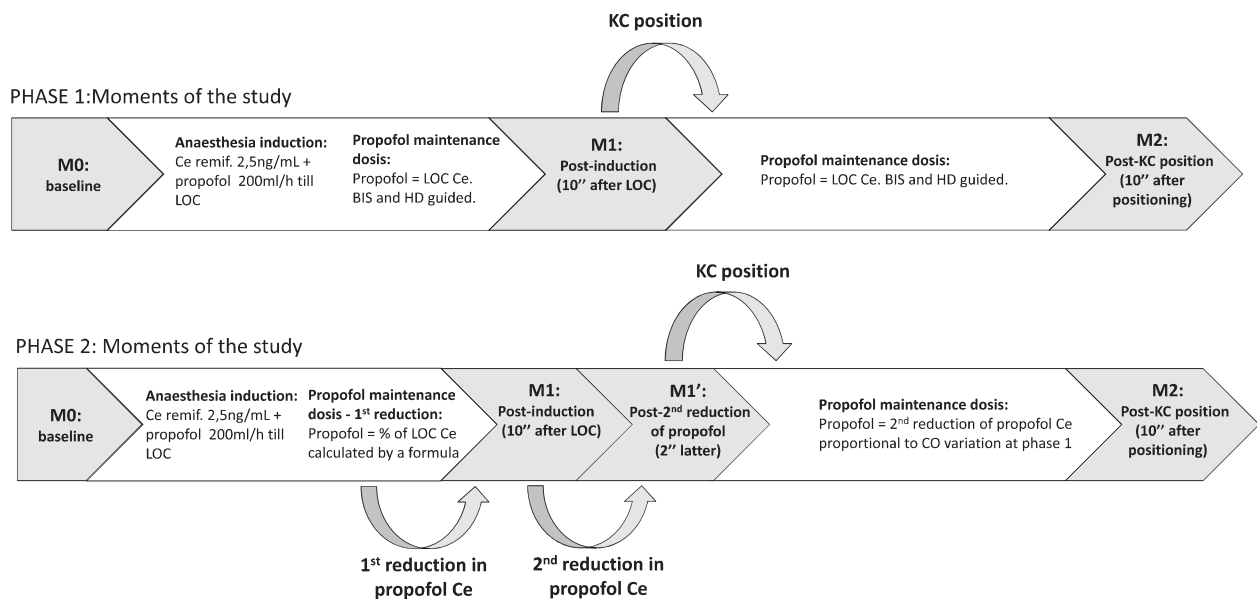
FIGURE 1. Moments of the study. Phase 1 included three moments—M0, M1, and M2. Phase 2 included four moments—M0, M1, M1′, M2. BIS indicates bispectral index; Ce, effect-site concentration; CO, cardiac output; HD, hemodynamic; KC, knee-chest position; LOC, loss of consciousness; remif, remifentanil.

the steady-state and when the signal of the LiDCO *rapid* was quantified as "good."

Phase 1

After LOC, propofol administration was switched to TCI mode at a target Ce equal to the Ce recorded at LOC. Subsequent propofol administration was targeted to maintain BIS 40 to 60 and stable hemodynamic parameters. Data were recorded 10 minutes after LOC (before positioning the patient), and this was defined as moment 1 (M1). Further data were recorded 10 minutes after the patient was placed in the knee-chest position but before skin incision, and this was defined as moment 2 (M2).

Phase 2

In phase 2, propofol was also switched to TCI mode after LOC, but with a lower Ce target than in phase 1, calculated using a formula previously developed by our group (Supplemental Digital Content 2, http://links.lww.com/JNA/A97). This formula relates the Ce at LOC with the Ce that maintains BIS between 40 and 60, as follows:

$$\text{Propofol Reduction}\,(\%) = 0.75\,(100 - [95.2 - 7.6 \times ID]),$$

where ID = induction dose (ie, Ce at LOC)

A second reduction in propofol Ce was implemented after M1. The magnitude of this reduction was equal to the percentage decrease in CO during knee-chest positioning measured in phase 1. Further data were collected 2 minutes after the second reduction in propofol Ce in phase 2, and this was defined as moment M1′ (M1′). As in phase 1, data were recorded 10 minutes after patients were placed in the knee-chest position (M2).

Data Analysis

In phase 1, a decrease in CO between supine and knee-chest positions of 30% was expected on the basis of data from a previous study.[19] In phase 2, we anticipated a reduction of half the CO variation quantified in phase 1, that is, 15%, similar to that in awake volunteers.[26] On the basis of a statistical significance of 5% and power of 80%, the power analysis determined that 20 patients were required.

Data were collected from the LiDCO *rapid* and RugLoopII software independently and at different sampling frequencies. Synchronization between the 2 data sets was, therefore, required before the analysis. Dedicated software was developed in Matlab for this task. The delay between the LiDCO *rapid* and RugLoopII data were estimated by the lag of the maximum cross-correlation value between simultaneous systolic blood pressure values acquired from both sources. The optimum resampling of RugLoopII data were placed in the same timeline as those from the LiDCO *rapid*, achieving the highest maximum cross-correlation value. Data synchronization was successful in all recordings. Normalized cross-correlations between systolic blood pressure time series acquired by both devices were above 0.9 for all recordings. For data analysis, 1-minute duration windows around each of the above-defined study moments were utilized, and the average of the observed values computed for each window.

Statistical analysis incorporated a full factorial model in a 2-way mixed analysis of variance (ANOVA) analysis to compare the mean differences of the measured variables, considering the main effect moment (between subjects), the main effect phase (within subjects), and their interactions. The normality assumption was tested by the Shapiro-Wilk test of normality, and the sphericity

assumption was investigated by the Mauchly's Test of sphericity. Further post hoc testing (ANOVA and *t* test with Bonferroni correction) was conducted to compare moments and phases. The assumption of homogeneity of variances was investigated using Levene's test. Alternative nonparametric testing (Friedman, Wilcoxon Signed-Rank, and Mann-Whitney *U*) was also conducted in order to investigate the impact of any deviation from the assumptions of the parametric tests. In this analysis, the statistical conclusions at the 5% level from parametric and nonparametric tests were concordant. Data for moment and phases are expressed as mean ± SD. All statistical analyses were conducted in SPSS software (version 25) (IBM, New York). *P*-values <0.05 were considered statistically significant.

RESULTS

Twenty patients were included in the study: 9 in phase 1 and 11 in phase 2. Patient demographics and baseline values are shown in Table 1. There were no significant differences in patient demographics or American Society of Anesthesiologists' status between the 2 phases. There was also no statistically significant difference in baseline CO before induction of anesthesia, or in the estimated propofol Ce at LOC between phases 1 and 2.

Phase 1 Results

Anesthesia induction reduced CO by 25.6% (averaged percentage reduction for all patients with respect to the baseline—M0 to M1), from 7.37 ± 1.85 to 5.39 ± 1.33 L/min ($P < 0.01$). Positioning patients from supine to knee-chest caused a further average decrease in CO of 17.2% (M1 to M2), from 5.39 ± 1.33 to 4.39 ± 1.17 L/min ($P = 0.026$). The total decrease in CO from baseline (M0) to after knee-chest positioning (M2) was, on average, 38.4%, from 7.37 ± 1.85 to 4.39 ± 1.17 L/min ($P < 0.01$) (Table 2).

There was no statistically significant association between CO changes and age, weight, sex, initial CO, or propofol Ce at LOC at any moment in phase 1. Systolic, diastolic, and mean arterial blood pressure decreased significantly from baseline at both M1 and M2 ($P < 0.01$). From M0 to M1, on average, systolic blood pressure decreased by 30.7%, diastolic pressure by 28.9%, and mean

pressure by 30.3%. From M0 to M2, systolic blood pressure decreased by 42.4%, diastolic pressure by 39%, and mean pressure by 33.1%. Stroke volume was also reduced from baseline (M0) to M1 by 16% and from baseline to M2 by 37% (both $P < 0.01$). Systemic vascular resistance and heart rate decreased from M0 to M1 by 4.4% and 11.7%, respectively, and increased from M1 to M2 by 7.3% and 11.8%, respectively. Pulse pressure and stroke volume variability increased significantly from M1 to M2, from 9% to 21% and 13% to 21%, respectively (Fig. 2). Ephedrine boluses of 5 mg were required in 4 patients: 1 bolus per patient after induction and one bolus after positioning in 2. BIS values did not differ between M1 and M2. Propofol Ce at LOC was 5.03 ± 0.75 µg/mL (Table 1).

Phase 2 Results

The average decrease in propofol Ce following LOC was 27.5% (maximum decrease 43% (7.0 µg/mL), minimum decrease 19% (2.7 µg/mL). At M1 (10 min after LOC), CO decreased by 19.8% (average percentage of all subjects with respect to the baseline, from M0 to M1), from 7.24 ± 2.34 to 5.64 ± 1.65 L/min ($P < 0.01$). After M1, the planned second reduction in propofol target Ce was 17.2% (the percentage decrease in CO identified during positioning in phase 1). Following this second reduction at M1', CO was 5.56 ± 1.74 L/min, which was not significantly different from that at M1. From M1' to M2 (10 min after KC position), CO decreased on average by 31% (from 5.56 ± 1.74 to 3.91 ± 1.89 L/min, $P < 0.01$), and from M0 to M2 by 46.9% (7.24 ± 2.34 to 3.91 ± 1.89 L/min, $P < 0.01$) (Table 2). There was no statistically significant association between CO changes and age, weight, sex, initial CO, or propofol Ce at LOC, at any moment in phase 2. Ephedrine was not administered in any patient.

Systolic, diastolic, and mean blood pressure were decreased significantly from baseline at all moments ($P < 0.01$). From M0 to M1, on average, systolic blood pressure decreased by 22.2%, diastolic blood pressure by 15.1%, and mean pressure by 19%. From M2 to M0, systolic blood pressure decreased by 42.5%, diastolic pressure by 24.6%, and mean pressure by 34.3%. Stroke volume was also reduced significantly from baseline, on average, by 18.6% from M0 to M1, and 47% from M0 to M2 (both $P < 0.01$).

Systemic vascular resistance was slightly increased after induction of anesthesia (by 1.9%) and significantly so (23.9%) after knee-chest positioning ($P < 0.05$). There was no change in heart rate. Changes in pulse pressure variation (26% vs. 29%) and stroke volume variation (23% vs. 24%) after knee-chest positioning were similar (Fig. 3). In phase 2, propofol Ce at LOC was 4.34 ± 1.52 µg/mL (Table 1).

Phase 1 Versus Phase 2 Results

The reduction in CO following induction of anesthesia was not significantly different between phases: a 25.6% reduction during phase 1 and 19.8% during phase 2. There was also no difference in the reductions in CO following the knee-chest position between the 2 phases: 17.2% and 31% in phases 1 and 2, respectively. Only

TABLE 1. Patients' Demographics and Baseline Values

Characteristics	Phase 1	Phase 2
Age (y)	49.3 ± 8.7	59.7 ± 13.5
Sex (F/M) (n)	6/3	6/5
Height (cm)	161.6 ± 9.0	167.8 ± 12.4
Weight (kg)	70.9 ± 13.9	77.3 ± 11.6
Body mass index (Kg/m²)	27.0 ± 3.5	27.4 ± 3.0
ASA classification I/II (n)	3/6	2/9
Cardiac output (baseline) (L/min)	7.4 ± 1.8	7.2 ± 2.3
Propofol Ce at LOC (µg/mL)	5.03 ± 0.75	4.34 ± 1.52

Demographics and baseline values of the patients for phase 1 and phase 2. Values are expressed as mean ± SD or number (n).

ASA indicates American Society of Anesthesiologists; Ce, effect-site concentration; LOC, loss of consciousness.

TABLE 2. Hemodynamic Variables, Bispectral Index Values, and Effect-Site Concentration (Ce) of the Drugs

Variables (Units)	Phase 1 (N=9)					Phase 2 (N=11)						Two-way ANOVA (P)		
	Moment 0 (M0)	Moment 1 (M1)	Moment 2 (M2)	Variation M0 to M1 (%)	Variation M0 to M2 (%)	Moment 0 (M0)	Moment 1 (M1)	Moment 1' (M1')	Moment 2 (M2)	Variation M0 to M1 (%)	Variation M0 to M2 (%)	Moment	Phase	Moment× Phase
Cardiac output (L/min)	7.4±1.8	5.4±1.3$	4.4±1.2¥	−25.6	−38.4	7.2±2.3	5.6±1.6$	5.6±1.7	3.9±1.9¥#	−19.8	−46.9	<0.001	0.867	0.514
Cardiac index (L/min/m²)	4.2±1.0	3.0±0.6$	2.5±0.5¥	−25.6	−38.4	3.9±1.1	3.0±0.9$	3.0±0.8	2.1±1.0¥#	−19.8	−46.9	<0.001	0.479	0.516
SVR (dynes s/cm⁻⁵)	1077.4±208.1	1011.2±141.9	1095.1±385.5	−4.4	4.3	1263.0±511.9	1230.2±417.3	1285.8±444.7	1518.3±621.8#	1.9	23.9	0.043	0.133	0.209
Systolic pressure (mm Hg)	153.2±16.4	106.7±18.2$	87.1±13.0¥	−30.7	−42.4	170.1±23.0	131.5±23.1$	129.7±32.2	95.9±24.6¥#	−22.2	−42.5	<0.001	0.018	0.363
MAP (mm Hg)	105.7±15.5	74.0±14.5$	63.2±10.0¥	−30.3	−39.0	108.4±15.7	86.7±12.0$	89.1±21.7	69.6±14.5¥#	−19.0	−34.3	<0.001	0.099	0.427
Diastolic pressure (mm Hg)	77.3±13.7	55.0±10.6$	50.6±9.9¥	−28.9	−33.1	75.7±10.1	63.2±7.7$	65.0±14.2	56.0±10.3¥	−15.1	−24.6	<0.001	0.22	0.246
Stroke volume (mL/beat)	97.0±19.6	81.2±16.6$	59.7±14.8¥,#	−16.0	−37.1	99.8±20.8	81.7±24.0$	76.7±23.9	54.4±24.2¥#	−18.6	−47.0	<0.001	0.939	0.453
Heart rate (beats/min)	77.0±15.4	66.9±12.4	74.5±13.8	−11.7	−2.5	72.6±18.4	70.5±16.1	73.3±13.1	72.3±15.3	−0.7	1.5	0.035	0.879	0.208
SVV (%)	—	9.4±5.9	21.1±8.6¥	—	—	—	17.1±10.8	23.2±13.3	24.5±9.9	—	—	<0.001	0.295	0.235
PPV (%)	—	13.6±5.2	27.9±11.2#	—	—	—	20.3±14.6	26.4±15.7	29.2±21.1	—	—	<0.001	0.636	0.293
BIS	94.0±2.2	61.8±15.2$	42.3±15.1#	−34.2	−55.5	95.3±2.6	49.9±9.8$	46.5±7.5	37.7±8.7¥#	−48.0	−22.7	<0.001	0.056	0.165
Propofol Ce (µg/mL)	—	3.84±0.63	2.53±0.79#	—	−34.1 (M1 to M2)	—	2.63±0.54	2.47±0.57	2.13±0.47#	—	−19.0 (M1 to M2)	<0.001	0.018	0.003
Remifentanil Ce (ng/mL)	—	2.36±0.42	1.11±0.35#	—	−51.2 (M1 to M2)	—	1.85±0.66	1.12±0.20	1.15±0.48#	—	−21.3 (M1 to M2)	0.001	0.132	0.107

Results are presented as mean ± SD.
ANOVA indicates analysis of variance; BIS, bispectral index; MAP, mean arterial pressure; PPV, pulse pressure variation; SVR, systemic vascular resistance; SVV, stroke volume variation.
The significant differences (5% level) were calculated based on repeated measures of ANOVA post hoc pairwise testing with Bonferroni correction. There were no significant differences between M1 and M1'. The percentage of variation is computed as (Mi/Mj−1)×100. For example (M1/M0−1)×100 is the percentage of each variable increase/reduction from M0 to M1. Phase comparison presents the P-value of the 2-way ANOVA analysis with regard to between-subjects effect (phase) and the moment(s) exhibiting significant differences at 5% level.
$significant differences between M0 and M1.
¥significant differences between M0 and M2.
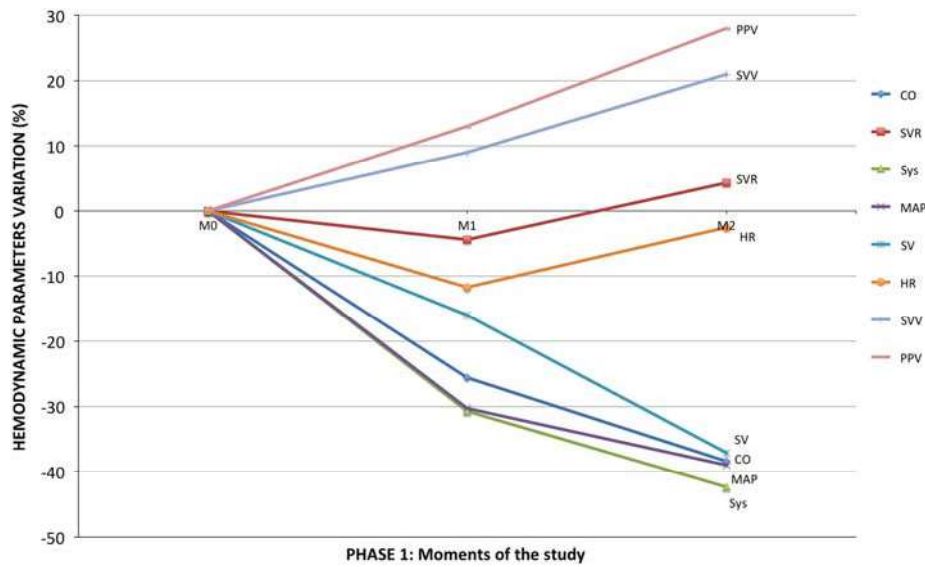#significant differences between M1 and M2.

FIGURE 2. Hemodynamic changes (% from baseline) from M0 to M1 and M2 during phase 1. CO indicates cardiac output; HR, heart rate; MAP, mean arterial blood pressure; PPV, pulse pressure variation; SV, stroke volume; SVR, systemic vascular resistance; SVV, stroke volume variation; Sys, invasive systolic blood pressure.

postinduction changes in systolic blood pressure were significantly different between the 2 phases, being higher in phase 2 compared with phase 1 ($P < 0.001$) (Table 2). There was a nonsignificant trend toward higher systemic vascular resistance increases from baseline in phase 2 (Table 2 and Fig. 4). There were no differences in BIS between phases (Table 2).

The relationship between CO and mean arterial pressure variation in both phases of the study were assessed using correlation coefficients: In phase 1, $r = 0.34$ for variation between M0 and M1, and $r = 0.004$ for variation between M0 and M2 (not significant). For phase 2, $r = 0.56$ for variation between M0 and M1 (not significant) and $r = 0.76$ between M0 and M2 ($P < 0.01$).

Comparing drug concentrations between the 2 phases, propofol Ce was significantly lower in phase 2 at M1, but there were no significant differences for remifentanil Ce (Table 2). In order to test for any interaction between age and
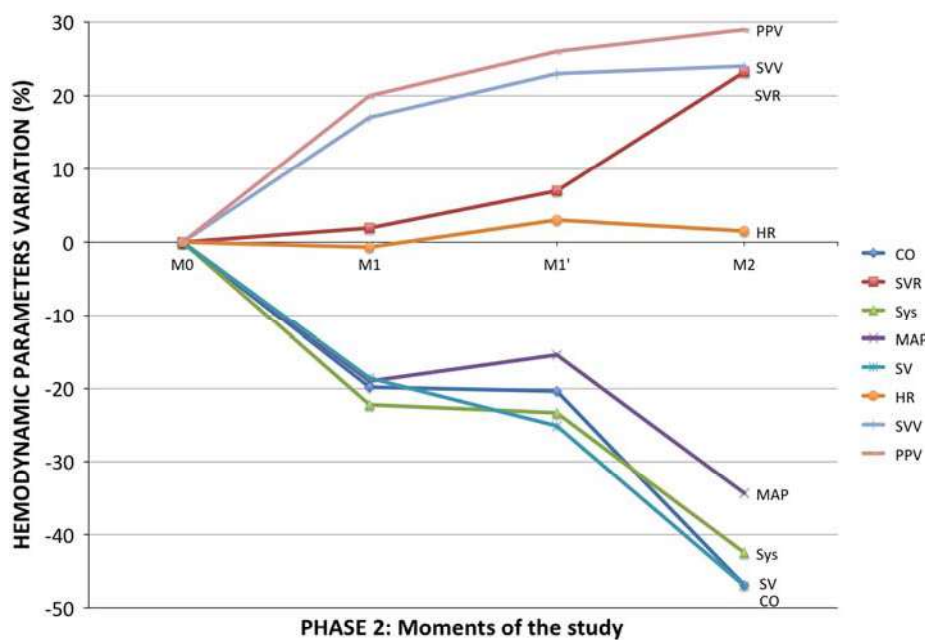

FIGURE 3. Hemodynamic changes (% from baseline) from M0 to M1, M1′, and M2 in phase 2. CO indicates cardiac output; HR, heart rate; MAP, mean arterial blood pressure; PPV, pulse pressure variation; SV, stroke volume; SVR, systemic vascular resistance; SVV, stroke volume variation; Sys, invasive systolic blood pressure.
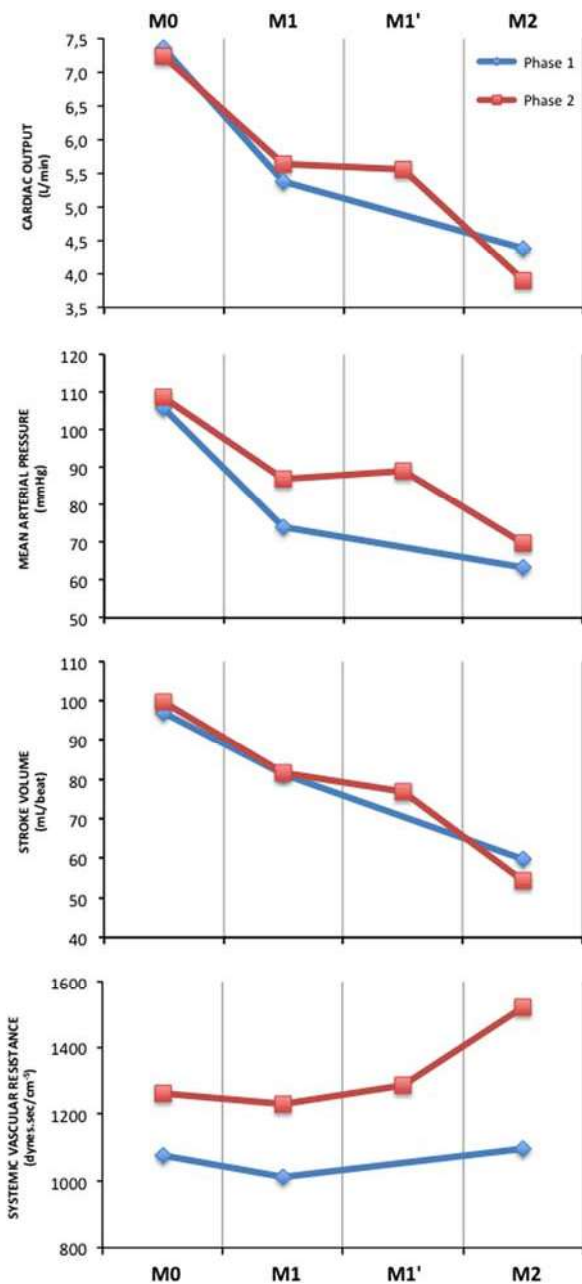
FIGURE 4. Changes in cardiac output, mean arterial pressure, stroke volume, and systemic vascular resistance during phases 1 and 2.

response to changes in propofol Ce, we further considered the ANOVA adjusted for age and found no significant age interaction terms for all the variables reported in Table 2. Furthermore, adjustment for age did not impact the significance of the differences between moments and phases.

DISCUSSION

In this study, induction of anesthesia was associated with significant reductions in CO. In phase 1, CO decreased by 25.6% and, in phase 2, by 19.8% despite the predefined reduction in propofol following LOC. Despite this, systolic blood pressure was higher at M1 (after induction of anesthesia) in phase 2 compared with phase 1 ($P = 0.018$). Hypotension after induction of anesthesia is relatively common, and it is more prevalent during the late postinduction period and before skin incision (5 to 10 min after).[2,13] Although this is often believed to be clinically inconsequential, there is some evidence that even small reductions in blood pressure can be associated with poor patient outcomes.[4,5,27] Intraoperative management of hypotension is usually guided by conventional hemodynamic monitoring (systolic and mean blood pressures), but these variables might not identify low levels of blood flow and oxygen delivery, which, even if time limited, may lead to major perioperative complications and longer hospital lengths of stay.[17,28] In our study, there was no correlation between mean arterial pressure and CO, especially during phase 1. Therefore, it appears that arterial pressure might not be the best variable to guide anesthesia management, and vasoactive drug or fluid therapy.

Placing anesthetized patients in the knee-chest position resulted in further decreases in CO in both phases of our study. It had been expected that the preplanned propofol reduction of 17% before positioning would attenuate any further reduction in CO, but, in the event, it did not, there was a 31% reduction in CO associated with knee-chest positioning in phase 2. Possibly the measured reduction in CO (17%) during knee-chest positioning identified in phase 1, which was the basis for the second planned reduction in propofol Ce during phase 2, was impacted by the ephedrine boluses administered in some patients to maintain blood pressure within predetermined targets. Using an esophageal Doppler in anesthetized patients after knee-chest positioning, Bennarosh et al[19] reported a 35% reduction in CO, although the change after anesthesia induction was not quantified. That study also indicated that propofol target plasma concentrations to maintain BIS values constant were reduced (by 30%), but there was no intervention in the anesthesia protocol. A study in awake volunteers reported a 15% to 20% reduction in CO after the knee-chest position,[26] likely related to a decrease in venous return due to blood sequestration in lower limbs.

In our study, assessment at M1′ in phase 2 allowed us to interpret the hemodynamic changes in more detail. The only intervention between M1′ and M2 was positioning, confirming that the knee-chest position is an independent factor for CO reduction. Our data suggest that this likely occurred because of decreased venous return, because the reduction in stroke volume we observed was not compensated by an increase in heart rate. The absence of a heart rate response may be related to propofol's action on the baroreflex.[1,29] In addition, the changes in systemic vascular resistance in phase 2 were not sufficient to compensate for the decrease in stroke volume.

Pulse pressure variation and stroke volume variation are hemodynamic markers of hypovolemia in mechanically ventilated patients, and they might also be useful in the standard prone or knee-chest positions; Biais et al[30] demonstrated that fluid responsiveness could be predicted

in the prone position. In our study, increases in pulse pressure and stroke volume variations suggest that anesthetized patients in the knee-chest position behave as if they are hypovolemic. Stroke volume decreased from M1 to M2 by 24.6% in phase 1 and by 30.1% in phase 2. We believe that this represents a relative hypovolemia because of reduction in venous return secondary to accumulation of the intravascular volume in the lower extremities. These findings suggest that vasopressor and chronotropic drugs, such as ephedrine, may be the best treatment for the decrease in CO caused by the knee-chest position in anesthetized patients.

As expected, propofol Ce was significantly lower in phase 2 compared with phase 1 because of the planned reductions. There were no differences in remifentanil Ce, BIS values, or hemodynamic parameters except for systolic blood pressure. Thus, we can conclude that, in the knee-chest position, patients may require a lower propofol Ce to maintain anesthesia. Importantly, there were no cases of awareness in our study. These findings suggest that plasma concentrations might be higher than estimated by the models we used,[14,15] and influenced by CO variations, as previously observed by Keyl et al.[31] The increased plasma propofol concentrations may be due to a reduction in propofol distribution or due to reduced hepatic clearance during hypotensive episodes.[32,33] The effects of the prone position and its variants on cerebral blood flow and cerebral oxygenation are also not well quantified.[34] Although cerebral oxygenation in anesthetized patients in the prone position can be maintained within safe margins, there is evidence of impairment of autoregulation,[35] and this might be reflected in low BIS values. However, our hypothesis that reducing propofol Ce promptly after LOC and immediately before knee-chest positioning could attenuate the fall in CO and thereby minimize adverse effects, including cerebral effects, was not supported by the findings of our study.

Nevertheless, our study does confirm that hemodynamic changes in anesthetized patients do not necessarily result from excessive anesthesia, as BIS was similar in both phases. Further, because our study was conducted in healthy patients (American Society of Anesthesiologists classification I and II) scheduled for an elective procedure for either lumbar disc herniation or lumbar spinal canal stenosis, the hemodynamic changes we identified could not be attributed to blood loss, hypovolemia, or cardiac disease. Many authors have highlighted the need to optimize high-risk patients during the perioperative period, guided by advanced hemodynamic monitoring.[5,7,36,37] We believe that anesthetized patients in the knee-chest position could also benefit from such monitoring, including before induction of anesthesia, when it is possible to establish a baseline for trend evaluation during the entire surgical procedure.[38]

The present study has several limitations. The sample size may be considered small. However, the ANOVA analysis was comprehensive, with 3 measures compared in each individual and between the 2 phases. The definition of the moments of data analysis presented quite a challenge, but we defined the 10-minute period of stabilization following induction of anesthesia and KC positioning

according to previous literature.[2,19] The fact that this was a nonrandomized study may also be considered a limitation. However, data from phase 1 was essential to quantify the interventions during phase 2. Finally, as this was a short duration study limited to the early intraoperative period, it was not possible to determine whether any of the hemodynamic changes we identified might impact patient outcomes.

CONCLUSIONS

Induction of anesthesia and the knee-chest position are associated with significant reductions in CO. Physicians should be aware that the knee-chest position is an independent risk factor for hemodynamic changes, and that reductions in propofol concentration immediately after LOC and before positioning do not attenuate them. We found no correlation between mean arterial pressure and changes in CO, suggesting that blood pressure alone may not be a useful variable to guide anesthesia management or vasoactive drug or fluid therapy in this context. The use of minimally invasive CO monitors in anesthetized patients may aid in the detection of important hemodynamic changes in the knee-chest position and guide therapy in order to minimize predictable risks. We plan further work using a simulation program to educate clinical teams in a structured approach with regard to the anesthesia management of patients scheduled for surgery in the knee-chest position.

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