The Effects of Steep Trendelenburg Positioning on Intraocular Pressure During Robotic Radical Prostatectomy

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BACKGROUND: Intraocular pressure (IOP) increases in steep Trendelenburg positioning, but the magnitude of the increase has not been quantified. In addition, the factors contributing to this increase have not been studied in robot-assisted prostatectomy cases. In this study, we sought to quantify the changes in IOP and examine perioperative factors responsible for these changes while patients are in the steep Trendelenburg position during robotic prostatectomy.
METHODS: In this prospective study, we measured IOP using a Tono-pen® XL in 33 patients undergoing robot-assisted prostatectomy. The IOP was measured before anesthesia while supine and awake (baseline T1), anesthetized and supine (T2), anesthetized after insufflation of the abdomen with carbon dioxide (CO_2) (T3), anesthetized in steep Trendelenburg (T4), anesthetized in steep Trendelenburg at the end of the procedure (T5), anesthetized supine before awakening (T6), and 1 hr after awakening in the supine position (T7).
RESULTS: On average, IOP was 13.3 ± 0.58 (mean ± SE) mm Hg higher at the end of the period of steep Trendelenburg position (T5) compared with supine position T1 ($P < 0.0001$). The least square estimates for each time point in mm Hg were as follows: T1 = 15.7, T2 = 10.7, T3 = 14.6, T4 = 25.2, T5 = 29.0, T6 = 22.2, T7 = 17.0. Using univariate mixed effects models for the T1–T5 time periods, peak airway pressure, mean arterial blood pressure, $ETco_2$, and time were significant predictors of the IOP increase, whereas age, body mass index, blood loss, volume of IV fluid administered, mean airway pressure, and desflurane concentration were not predictive. In T4–T5, which involved no significant positional or perioperative interventions, we performed a multivariate analysis to evaluate predictors of IOP increases. Surgical duration (in minutes) and $ETco_2$ were the only significant variables predicting changes in IOP during stable and prolonged Trendelenburg positioning. On average, IOP increased 0.21 mm Hg per mm Hg increase in $ETco_2$ after adjusting for time. An increase of 0.05 mm Hg in IOP per minute of surgery on average was observed during this period in the Trendelenburg position after adjusting for $ETco_2$.
CONCLUSIONS: IOP reached peak levels at the end of steep Trendelenburg position (T5), on average 13 mm Hg higher than the preanesthesia induction (T1) value. Surgical duration and $ETco_2$ were the only significant predictors of IOP increase in the Trendelenburg position (T4–T5).
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After skin cancer, prostate cancer is the most common cancer in men in the United States and the third leading cause of cancer death in this group.[1] There are many treatment options available, and robotic-assisted radical prostatectomy is one of the newest and most technically advanced. Its advantages include decreased blood loss and postoperative pain, shorter hospital stay, and faster recovery time.[2] Demand for the procedure is increasing worldwide.

Many urologic procedures, including robotic radical prostatectomy, require specific body positioning in which the patient must be placed in steep Trendelenburg position (25–45 degree head down).[3] This positioning uses gravity to pull the abdominal viscera away from the operative field, but is nonphysiologic and may have significant negative physiologic effects when maintained for long periods of time. Few studies have addressed the impact of placing surgical patients in this position for extended periods. Complications of radical robotic prostatectomy positioning were reported in two patients: postextubation respiratory distress attributed to laryngeal edema in one, and

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brachial plexus injury in another.[3] Serious ocular consequences, such as retinal detachment, have also been attributed to the Trendelenburg position, with cases being reported as early as 1952.[4] With an increasing number of procedures being performed using the robotic technique, other ocular complications have been reported. Posterior ischemic optic neuropathy followed minimally invasive prostatectomy in two patients, one having complete bilateral visual loss and the other permanent loss of inferior visual fields bilaterally after a da Vinci robotic-assisted procedure.[5] Positioning in steep Trendelenburg is a possible, but as yet uncertain, etiologic factor in this devastating complication.

The Trendelenburg position increases intraocular pressure (IOP); however, the magnitude of this increase is unknown, particularly during long procedures and in combination with carbon dioxide (CO_2) insufflation during laparoscopy in a typically older male population while positioned in steep Trendelenburg.[6,7] The aim of this study was to quantify the IOP changes in patients undergoing robotic radical prostatectomy at different time points and body positions throughout the procedure, and to explore the accompanying perioperative factors that influence IOP.

METHODS

After approval by the institutional review board, informed consent was obtained from 33 patients (ASA physical status I–II) scheduled for elective prostatectomy. All patients were recruited and had their procedures performed in a 4-week period. Patients with preexisting eye disease (glaucoma, diabetic retinopathy, cataracts, retinal detachment), history of eye surgery, elevated IOP (above 30 mm Hg), allergy to tetracaine or to latex, age older than 80 yr, and body mass index (BMI) >40 were excluded.

Both eyes were topically anesthetized with two drops of 0.5% tetracaine HCl (Bausch & Lomb, Tampa, FL). Baseline IOP was measured in the supine position with a Tono-pen XL handheld tonometer (Medtronic, Jacksonville, FL). The Tono-pen was selected as our instrument of measurement because of its speed, ability to make measurements on multiple patients secondary to its disposable latex tip covers, ease of use, accuracy in a variety of positions, and reliability.[8] The Tono-pen XL takes four separate readings and uses a microprocessor to calculate and display the mean and standard deviation. The tonometer was calibrated according to the manufacturer's guidelines before each reading. Measurements were repeated if the variability between sequential measurements exceeded 5%. We collected two sets of measurements for each eye (two IOP readings per eye, each of which represents the average of a series of four measurements as described previously). All measurements were performed by the same ophthalmology chief resident. Surgery was performed in the morning or early afternoon in all patients, thus avoiding diurnal variations in IOP.[9] The same urologist performed all operations.

The anesthesia protocol was standardized for drugs used during the procedure. After baseline IOP measurement, patients received 2 mg of midazolam for premedication. Anesthesia was induced with propofol (2–3 mg/kg), fentanyl (2–3 μg/kg), and cisatracurium (0.2 mg/kg). After tracheal intubation, we used desflurane in 50%/50% oxygen/air mixture and to maintain at 1–1.5 minimum alveolar concentration end-tidal concentration and keep the arterial blood pressure within 20% of its preinduction value. Cisatracurium was infused at 0.1 $mg \cdot kg^{-1} \cdot min^{-1}$ and was discontinued 25–30 min before the end of the procedure. A peripheral nerve stimulator was used to monitor neuromuscular transmission to maintain one twitch of the train-of-four. The lungs were mechanically ventilated. We maintained $ETco_2$ 30–40 mm Hg.

Pneumoperitoneum was created by intraperitoneal insufflation of CO_2 while the patient was in the supine position. Patients were then placed in the steep Trendelenburg position (25 degrees from horizontal), which was the maximal Trendelenburg angle of the Amsco 3085-SP surgical table. All operations were performed at the same angle on the same table. Throughout surgery, intraperitoneal pressure was maintained at 15 mm Hg, using CO_2 for insufflation. Lactated Ringer's solution was administered at 4–6 $mL \cdot kg^{-1} \cdot hr^{-1}$. A Capnomac respiratory in-line monitor (Datex-Ohmeda, GE Healthcare, Madison, WI) was used to monitor inspired and expired gases, ventilatory variables, and plethysmographic oxygen saturation. An automatic noninvasive monitor was used to monitor heart rate and arterial blood pressure (Datex-Ohmeda Aestiva/5, GE Healthcare).

Measurement/Instrumentation

We performed IOP measurements on each patient in both eyes at seven discrete time points (Table 1). Each patient served as his own control. After each pressure measurement, the time of procedure, arterial blood pressure, heart rate, peak airway pressure, plateau airway pressure, end-tidal desflurane concentration, $ETco_2$, IV fluid volume, and blood loss were recorded.

Statistical Analysis

We took two IOP measurements per eye per time point. Since measurements were taken over seven different time points (as a categorical variable), IOPs from the same patients are correlated. Therefore, mixed linear models were used to analyze these data over the time period T1–T7. The variables of age, BMI, blood loss, IV fluid intake, $ETco_2$, peak airway pressure, airway plateau pressure, and mean arterial blood pressure (MAP) were used as potential predictors of the changes in IOP over time and used in the model-building process. Those variables that were significant in the univariate models at the 0.20 α level were

Table 1. T1–T7 Time Points of Intraocular Pressure and Clinical Variable Measurements

Time point	Measurements	Event
T1	Blood pressure, heart rate, peak airway pressure, plateau airway pressure, end-tidal desflurane, $ETco_2$, IOP	Awake resting in supine position before anesthesia induction
T2	Same as T1	10 min after induction of general anesthesia, in the supine position
T3	Same as T1	After insufflation of the abdomen with CO_2 in the supine position
T4	Same as T1	In steep Trendelenburg[a] position with the abdomen still insufflated with CO_2
T5	Same as T1	In steep Trendelenburg[a] position at the end of procedure with CO_2 still insufflated
T6	Same as T1, plus intravenous fluid volume administered and estimated blood loss	Anesthetized before awakening in the supine position
T7	IOP only	45–60 min after awakening in the recovery room in the supine position

IOP = intraocular pressure.

[a] All patients remained at 25 degrees of Trendelenburg during T4–T5.

Table 2. Patient Demographics and Operative Variables Obtained from 33 Patients

Variable	Median (range)
Age (yrs)	61.5 (37–74)
BMI (kg/m^2),	28 (20–43)
ASA PS (range)	(1–2)[a]
Duration, total (min)	142.5 (105–210)
Duration, Trendelenburg (min)	68 (31–115)
Blood loss (mL)	80 (45–155)
Intravenous fluid (mL)	2000 (1600–3100)

BMI = body mass index.

[a] Only range is reported for this variable.

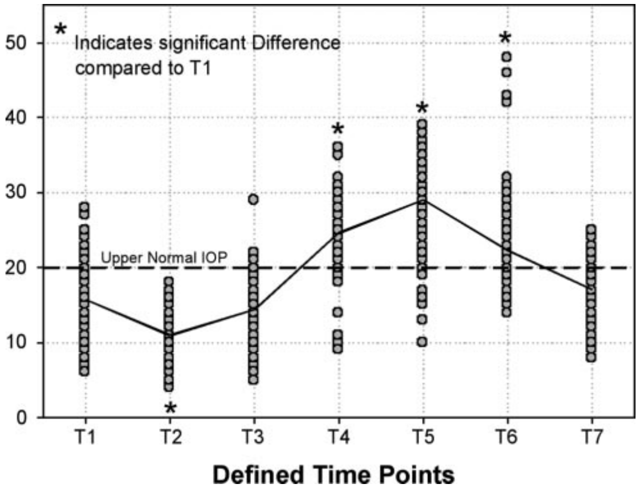

Figure 1. Scatter plot of the IOP with the overlaid line connecting the IOP least square estimates at each time point. The dotted line represents the upper normal IOP in adult patients. IOP = intraocular pressure.

included in the multivariate model. In the final multivariate model, only those significant at the 0.05 level were included. The autoregressive correlation structure in SAS version 9 (SAS v9.1, SAS Institute, [2002–2003] Cary, NC) was used to account for the autocorrelation among observations over time. Results from this analysis are shown in Figure 2 and Tables 3 and 4. We performed pairwise comparisons of IOP estimates between time points and the Holm's procedure was used to adjust for multiplicity. In addition, a model was fit using the same procedures as the model for T1–T5, however, just for the time period between T4 and T5, with the actual time in minutes (continuous variable), as the predictor variable.

RESULTS

Thirty-three patients were included in the analyses (two patients were excluded due to necessity to deviate from the standardized anesthesia regimen). The demographics of the study participants are summarized in Table 2. All patients were discharged the next day and returned to the Urology Clinic 4–5 days after surgery for Foley catheter manipulation. No eye complaints were reported. Transient conjunctival edema was observed in the postanesthesia care unit in seven patients, which resolved by the next day. None of the patients required blood transfusions, and all were satisfied with the surgical procedure. Two patients were advised to consult an ophthalmologist due to high IOP measurements at baseline and a family history of high IOP.

We found that IOP was 13.3 ± 0.58 mm Hg higher on average at the end of the period of steep Trendelenburg position (T5) compared with supine position T1 ($P < 0.0001$). IOP at time point T2 was significantly lower than IOP at T1 ($P < 0.0001$). IOP at T4, T5, and T6 were also significantly higher than T1 ($P < 0.0001$). One patient maintained significantly increased pressure at T6 and represented an outlier. The least square estimates for each time point are displayed in Figure 1.

On the basis of the univariate mixed effects models, $ETco_2$, peak airway pressure, MAP, plateau airway pressure, and surgical duration were significant predictors of changes in IOP over time periods T1–T5, as shown in Table 3. These significant predictors were all positively correlated (positive slope coefficients) with IOP. Age, BMI, blood loss, and IV fluid intake were

Table 3. *P* Values from Univariate Mixed Effects Models Using the Following Variables as Predictors for IOP Change, T1–T5

Variable	*P*	Slope coefficient
Age	0.5941	0.035
BMI	0.4754	−0.0857
Blood loss	0.0133	−0.0258
IV fluid intake	0.8945	0.0002
$ETco_2$	<0.0001	0.5560
Peak airway pressure	<0.0001	0.7787
Plateau airway pressure	<0.0001	2.1065
Mean arterial blood pressure	<0.0001	0.0916
Time		

BMI = body mass index; IOP = intraocular pressure.

Table 4. *P* Values from a Multivariate Model Using the Following Variables as Predictors for IOP Change, T2–T5

Variable	*P*	Slope coefficient
Peak airway pressure	<0.0001	0.38
$Esco_2$ (mm Hg)	<0.0001	0.17
Duration of procedure (min)	<0.0001	0.11
MAP	<0.0001	0.08

MAP = mean arterial blood pressure; IOP = intraocular pressure.

not significant predictors of changes in IOP. Only significant factors in explaining IOP changes were included in a multivariate model for this time period, T1–T5.

In the multivariate model for time period T1–T5, peak airway pressure, MAP, $ETco_2$, and surgical duration were significant predictors of IOP, as summarized in Table 4. We also examined the relationship between MAP and IOP at various concentrations of desflurane, as well as the relationship between MAP and end-tidal desflurane concentration. The relationship between MAP and IOP did not change at different end-tidal desflurane concentrations. There was no correlation between MAP and end-tidal desflurane concentration using Pearson correlation coefficient at 0.05 significance level ($r = 0.014$, $P = 0.73$).

We also examined univariate models over the time period T4–T5, when patients were in Trendelenburg position with CO_2 insufflation and with no positional or significant perioperative interventions that could affect measurements. Figures 2 and 3 are scatter plots of all the collected data for the period T4–T5, with the best line fit from a linear regression model of IOP as a function of time (Fig. 2) and $ETco_2$ (Fig. 3). We included all factors that had a $P < 0.15$ in a multivariate model. Only the significant factors were kept in the final model. Time and $ETco_2$ were the only significant covariates in the final model. The best linear fit from this mixed model analysis is: IOP = 7.95 + 0.21 ($ETco_2$) + 0.053 (time). For example, on average, IOP increased 0.21 mm Hg for every 1 mm Hg increase in $ETco_2$ after adjusting for time, and 0.05 mm Hg per minute between T4 and T5 after adjusting for $ETco_2$.

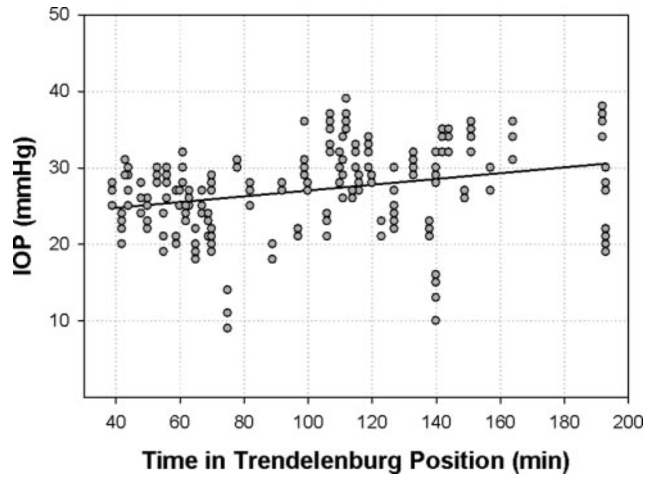

Figure 2. A linear regression model of IOP changes over time (as a continuous variable) over points T4 and T5, the time points at which patients were in Trendelenburg position with CO_2 insufflation of the abdomen. Each minute of time passing resulted in 0.05 mm Hg increase in IOP. IOP = intraocular pressure.

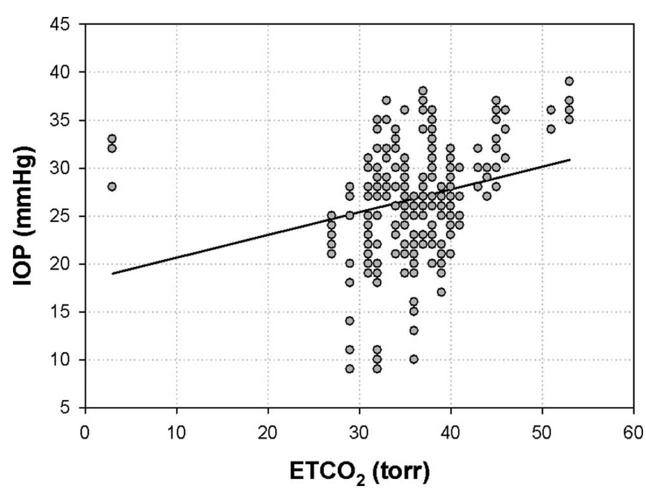

Figure 3. Linear regression model of IOP changes based on end-tidal CO_2 concentrations over time periods T4–T5. IOP = intraocular pressure.

DISCUSSION

This study shows that IOP increases significantly in anesthetized patients undergoing robotic prostatectomy in the steep Trendelenburg position. We were able to quantify the changes in IOP throughout the procedure, and we conclude that robotic prostatectomy patients reach IOP levels that are comparable with those observed in glaucoma patients who have temporarily stopped their medication and are placed in the steep Trendelenburg position.[10] The magnitude of this increase in IOP was also confirmed in an animal model of α-chymotrypsin-induced glaucoma in which a combination of CO_2 pneumoperitoneum and head down positioning were used.[11] IOP increases of this magnitude could be of concern in some elderly patients who have elevated IOP at baseline, and although definitive evidence is lacking, may be related to the occurrence of ischemic optic neuropathy in light of the two reported cases.[5]

The major determinants of IOP are aqueous humor flow, choroidal blood volume, central venous pressure (CVP), and extraocular muscle tone.[12] This study confirms the increase in IOP during Trendelenburg position; however, further research is required to determine which factor or combination of factors is responsible for producing this effect. Among the perioperative variables that we explored, $ETco_2$ and surgical duration contributed significantly to changes in IOP during time intervals T1–T5 and T4–T5. These were the only factors that were significant predictors in both periods. We believe that gravitational forces increase CVP, leading to increases in IOP. CVP is likely related to orbital venous pressure, which has been shown to change directionally with IOP under specific conditions in a rabbit model.[13] Our results also show that increases in $ETco_2$, which reflect increases in arterial CO_2, can lead to choroidal vasodilation and increases in IOP. Recently published data for robotic prostatectomy using continuous CVP monitoring in the steep Trendelenburg position with pneumoperitoneum for up to 4 hours show initial increases followed by a plateau of CVPs.[14] This leads us to believe that CVP is implicated in the initial increases in IOP in the steep Trendelenburg position; however, we believe the continuous increase of IOP in this position over time is related to other factors in addition to CVP, such as continuous aqueous humor production, which continues independently of increases in IOP.

There are multiple factors believed to contribute to increases in arterial CO_2 in robot-assisted laparoscopic surgery, which are related to increases in IOP. This increase could be due to continued absorption of intraperitoneal CO_2 and/or increased pressure on the diaphragm, resulting in lower delivered tidal volumes and in turn increased $ETco_2$. These increases in $ETco_2$ values cause increased arterial Pco_2 levels, leading to vasodilation in the choroid plexus and an increase in IOP. Based on the work by Kadam et al.,[15] CO_2 elimination increased in the first 30 min of CO_2 insufflation during laparoscopy, then reached a plateau for up to 4 hrs. Since we continued to observe increases in IOP over time despite the plateau of the CO_2 elimination, this raises the possibility that other factors contribute significantly, such as surgical duration.

The time-dependent increase in IOP in the steep Trendelenburg position is similar to previous work that showed time-dependent increases in IOP in the prone position.[16] We believe the time-dependent increase in IOP is likely secondary to the continued production of aqueous fluid by the ciliary body inside the eye. It is important to determine if these factors could have a functional outcome with regard to visual acuity after surgery.

Our data also show a positive relationship between IOP and MAP over the time period T1–T5. The exact physiologic basis of the relationship between IOP and MAP is not known.[17] It has been proposed that there is a positive correlation between MAP and IOP.[18] A possible mechanism for this response is that increases in mean blood pressure lead to increases in aqueous humor ultrafiltration by means of increased ciliary artery pressure, and thus an increase in IOP.[17] However, although there was a significant relationship between MAP and IOP from T1–T5, it was not significant in multivariate analysis during T4–T5 (time periods during which there were no perioperative positional or pharmacologic interventions that could confound this relationship in the Trendelenburg position). However, the change was very close to meeting the 0.05 criterion ($P = 0.06$), which suggests it may play a role in the increases in IOP.

Our data show a positive relationship between peak airway pressure and IOP over time period T1–T5, but not T4–T5. There have been conflicting data on whether peak airway pressure affects IOP. The effect of positive pressure ventilation on IOP has been studied both with continuous positive airway pressure masks and endotracheal mechanical ventilation.[19,20] Although these studies demonstrated a positive relationship between the peak airway pressure and IOP, other studies could not demonstrate the relationship between positive end-expiratory pressure and IOP.[21] A proposed mechanism for a relationship between these two factors is that an increase of intrathoracic pressure leads to increases in CVP which may reduce the aqueous humor outflow through the episcleral veins; this could explain the increase in IOP. Further study is needed to reexamine the relationship between peak airway pressure and IOP in the steep Trendelenburg position.

There are multiple perioperative factors involved in controlling the increase in IOP during robotic prostatectomy. Some of these factors, such as hemodynamic maintenance, ventilation strategy, and fluid management, may be controlled by the anesthesiologist. Other factors inherent in the procedure cannot be controlled, such as body positioning, CO_2 insufflation, and duration of the procedure in the Trendelenburg position. Future studies need to explore the contribution of each individual factor to the total increase in IOP and study whether visual function is impacted.

Although our procedures were completed relatively quickly by an experienced surgeon, there are currently no data available about the effects of sustained (4–6 hrs) elevation of IOP on visual outcome, as might occur during the initial surgical learning curve phase for robotic prostatectomy. A similar concern applies to procedures such as robotic cystectomy, in which the average operative times range from 3 to 11 hrs, and in which the Trendelenburg position may often be even longer than during robotic prostatectomy, especially in a high-risk population.[22–24]

More than half of all prostatectomy surgeries performed in the United States are robotic and this trend is expected to increase worldwide. In 2006 alone, 35,000 cases were performed robotically in the United States.[5] The advantages of this technique over the open procedure are well documented and patients typically prefer less invasive procedures; however, for robotic cases patients must be placed in steep Trendelenburg position during pneumoperitoneum. Patients who typically undergo this procedure often have higher rates of systemic comorbidities than younger patients and may have higher than average rates of ocular diseases. In light of our new findings, it might be important for the surgeon to ask ocular-specific questions to patients in the preoperative assessments and make appropriate referrals to ophthalmologists if concerns arise. This same information should also be evaluated by the anesthesiologists, especially if the patients have other systemic comorbidities, such as hypertension, diabetes mellitus and coronary artery disease, and the potential for significant surgical blood loss or fluid shifts. There has been no identifiable increased risk of perioperative ischemic optic neuropathy for procedures in the prone or Trendelenburg position in patients with glaucoma or other ocular diseases so far. There is a need for a larger prospective study with robotic prostatectomy to further evaluate the relationship between the steep Trendelenburg position and permanent ocular changes, as the pathogenesis of these changes remains unclear and the treatment elusive.[25] This is required before any recommendations or conclusions can be made regarding prevention and/or treatment of increased intraoperative IOP. Considering the cases of permanent ocular damage in previously healthy patients during robotic prostatectomy cases, the clinical and perioperative variables specific for these cases, such as degree of Trendelenburg and duration of this position, as well as the amount of insufflation of CO_2, should be documented in the ASA database of Postoperative Vision Loss registry for nonocular surgeries.[26]

In summary, IOP reached peak levels at the end of Trendelenburg position (T5), with an average of 13 mm Hg higher than the preinduction value in awake, supine patients (T1). During this period (T1–T5), peak airway pressure, MAP, $ETco_2$, and surgical duration were significant predictors of IOP changes. Time and $ETco_2$ were the only significant predictors of IOP increase in the Trendelenburg position (T4–T5) in patients undergoing robotic prostatectomy.

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