



Systematic review and meta-analysis of Trendelenburg position on intraocular pressure in adults undergoing surgery

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Background: Because of the increase in intraocular pressure (IOP) that occurs in the Trendelenburg position, patients undergoing surgery in this position may be at risk for postoperative vision loss and other ocular complications. IOPs higher than 21 millimeters of mercury (mmHg) pose a risk for glaucoma, detached retina, and postoperative vision loss. The purpose of this systematic review and meta-analysis is to estimate the magnitude of the increase in IOP in adult patients undergoing surgery in the Trendelenburg position.

Methods: Comprehensive search strategies were used to identify 18 eligible studies (n=762). Standardized mean difference effect sizes were calculated for nine intraoperative time points. Time points for meta-analysis were selected to achieve the greatest number of comparisons for analysis at each time point. Prediction intervals for each time point were also calculated.

Results: Using a random effects model, meta-analysis showed that IOP increased significantly after abdominal insufflation (T2: $d=1.89$, $P<0.001$) and during Trendelenburg position (T3: $d=1.34$, $P<0.001$; T4: $d=0.91$, $P<0.001$; T6: $d=0.30$, $P<0.001$; T8: $d=0.38$, $P<0.001$). In total, IOP increases significantly by 13.6 mmHg. Based on the upper limits of the prediction intervals, in 95% of all populations IOP could increase by as much as 28.1 mmHg.

Conclusions: IOP increases of this magnitude demonstrate the need for implementing intraoperative interventions to reduce the risk for postoperative vision loss and other ocular complications in patients undergoing surgery in the Trendelenburg position.

Keywords: Intraocular pressure (IOP); Trendelenburg position; head-down tilt; pneumoperitoneum

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Introduction

In the Trendelenburg position, the patient's feet are higher than the patient's head by 15 to 30 degrees (1). Many surgeons use a steep Trendelenburg position of 30 to 45 degrees, particularly during laparoscopic and robotic surgery. The benefit of the Trendelenburg position is that it moves the abdominal viscera cephalad to improve visibility and surgical access to the abdominal and pelvic organs. However, there are potential harms associated with the Trendelenburg position. The Trendelenburg position increases intraocular pressure (IOP) (2-10). According to the American Academy of Ophthalmology (11), normal IOP is 10 millimeters of mercury (mmHg) to 21 mmHg. IOPs

higher than 21 mmHg pose a risk for glaucoma, detached retina, and postoperative vision loss (3,5,10,12-18).

Pathogenesis of postoperative vision loss

The specific pathogenesis of postoperative vision loss associated with increased IOP is unclear; however, it is known that elevated IOP can lead to optic nerve injury and decreased ocular perfusion pressure resulting in ischemic optic neuropathy (8,19). Ischemic optic neuropathy is the most common cause of postoperative vision loss (8,19). The ischemic process can occur as a direct result of decreased blood supply from the arteries of the optic

nerve or by venous stasis that occurs as a result of decreased venous outflow (8,14,20). Periorbital swelling and venous congestion resulting from the Trendelenburg position can lead to a compartment syndrome in the orbital space that compromises blood flow to the eye, retina, and optic nerve (20,21). The amount of subsequent postoperative vision loss can range from temporary blurring to partial to complete blindness; however, once a loss of vision occurs, it is an irreversible complication (12,18).

Some researchers have found that increased IOP associated with the Trendelenburg position poses a greater risk for postoperative vision loss in patients who have existing ocular disease compared with patients without ocular disease (3,5,9,10,17,22). Older patients with elevated baseline IOPs are also at greater risk for ischemic optic neuropathy than younger patients with normal baseline IOPs (7-9,16,23). Likewise, patients with cardiovascular deficits may be at greater risk for postoperative vision loss than patients without cardiovascular deficits (5). The increase in IOP and subsequent risk for postoperative vision loss is related to the amount of time the patient is in the Trendelenburg position (21,24-27).

Incidence of postoperative vision loss

The incidence of postoperative vision loss following non-ocular surgery has been estimated to be as low as 0.0002% and as high as 0.2% (19,28); however, the incidence of postoperative vision loss specific to patients undergoing surgery in the Trendelenburg position remains unknown. To identify cases of ischemic optic neuropathy associated with prostatectomy procedures performed in the Trendelenburg position, Lee (29) reviewed the American Society of Anesthesiologists Postoperative Vision Loss Registry, a database of 175 cases of postoperative vision loss occurring between 1987 and 2010, and found six cases. A number of reports of postoperative vision loss following surgical procedures where the patient was in the Trendelenburg position have also been published (20,30-33).

Purpose

Although some researchers have studied the quantitative increase of IOP in surgical patients in the Trendelenburg position (3-5,9,10,17,20), there is a need for systematic review and meta-analyses of these studies to demonstrate the overall effect size and provide high-quality evidence supporting, or negating the need for, implementing

intraoperative interventions designed to mitigate the increase of IOP and reduce the risk for postoperative vision loss. Meta-analysis research methods provide increased power compared to individual studies, improve estimates of effect size, and help resolve uncertainty when the results of individual studies disagree (34). Because all of the evidence pertaining to a particular phenomenon is included in the analysis, meta-analysis research provides a high level of objectivity, precision, and generalizability (35). Currently, there has been no quantitative meta-analytic synthesis of the existing studies examining the increase in IOP in adult patients undergoing surgery in the Trendelenburg position. The purpose of this systematic review and meta-analysis is to estimate the magnitude of the increase in IOP at selected perioperative time points in adult patients (i.e., individuals 18 years and older) undergoing any type of surgery in the Trendelenburg position.

Methods

To ensure rigorous and transparent presentation of the methods and results of this systematic review and meta-analysis, the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines have been followed (36).

Search strategies

An expert health sciences reference librarian was consulted to identify the most appropriate search terms and databases and to assist with refining search strategies for an exhaustive literature search. Keywords or medical subject headings included intraocular pressure or ocular tension, and Trendelenburg position or head-down tilt. Search strategies included online searching of the PubMed, Cumulative Index of Nursing and Allied Health Literature, and Scopus databases, and the Cochrane Database of Systematic Reviews for published and unpublished literature; ancestry searching of references from relevant reports to locate additional applicable references; author searching of individuals identified in the literature as experts in the field; and a dissertation search of the ProQuest database. The author reviewed abstracts for eligibility and obtained full-text copies of potentially eligible reports.

Inclusion and exclusion criteria

Criteria for inclusion in the meta-analysis were reports

written in English; studies reported between January 01, 1990 and September 30, 2018; published or unpublished reports of primary studies that encompassed dissertations, conference abstracts, and presentations; studies that used either a one-group, pretest posttest design or a multiple-group, pretest posttest design; reports where the minimum age of the study participants was 18-year or older; studies that included a specific measured outcome of IOP using any type of tonometer; studies where the participants received any type of general anesthesia; and reports of studies that included sufficient data to calculate an effect size. The year 1990 was selected as the initial searching date because the first laparoscopic cholecystectomy was performed in 1987 (37). The use of steep Trendelenburg position has increased dramatically with the use of laparoscopic and robotic-assisted laparoscopic surgery. When reports did not include sufficient data to calculate an effect size, the author contacted the researchers on at least two separate occasions 2 to 3 weeks apart to obtain missing data.

Reports were excluded if the IOP was measured in adults not undergoing surgery. Reports were also excluded if data from only one time point of IOP measurement were present. Participant groups were additionally excluded if they were receiving an intervention specifically intended to mitigate IOP; however, participant groups representing control arms receiving placebos or no interventions were included in the systematic review and meta-analysis.

Risk of bias within individual studies

To assess the risk of bias within individual studies, the Association of periOperative Registered Nurses Research Evidence Appraisal Tool – Study, available on the Association’s website (<https://www.aorn.org/guidelines/about-aorn-guidelines/evidence-rating>) was used by the author and an experienced evidence reviewer to independently evaluate and critically appraise each study for its level of strength and quality. When using the appraisal tool, strong study designs (e.g., randomized controlled trials) are assigned the highest level of strength (i.e., experimental). Non-experimental designs (e.g., observational studies) are assigned the lowest level of strength, and quasi-experimental designs (e.g., non-randomized) are assigned a moderate level of strength. Measures such as sample size, generalizability, bias, reliability, and validity are assessed to determine whether the study quality is high, good, or low. The author and evidence reviewer participated in

conference calls to discuss their independent appraisals until 100% consensus was achieved on study design and quality levels for each of the included studies.

Risk of bias across studies

Risk of bias that may affect cumulative evidence was managed using several strategies. To avoid bias due to a narrow or limited search, a comprehensive and diverse literature search was conducted. Only research studies were included in the systematic review and meta-analysis to ensure the included studies were of sufficient strength and quality. As well, studies that included objective measurements of IOP at less than two perioperative time points were excluded. An analysis of publication bias was also conducted to determine whether unpublished research was unintentionally excluded.

Coding and data extraction

An iterative process that included studying codebooks used by experienced meta-analysts for data extraction and coding of their research studies was used to develop the codebook. The relevant literature was also reviewed. The codebook was pilot tested by the author using 10 randomly selected studies before being used to code and extract data from all eligible reports to identify missed coding categories and verify fit between coding categories and study characteristics.

Effect size data for each of the reports included in the systematic review and meta-analysis was independently coded by a trained researcher. The author and independent researcher discussed coding discrepancies until 100% consensus was achieved on effect size data for each of the eligible studies.

Data collected from each eligible study included study characteristics (i.e., authors, year of publication, publication status, geographic location, reported funding) and data related to study design (i.e., type of study, study quality, type of tonometer, inclusion of ophthalmologic exams by participants). When available, data related to participant and surgery characteristics [i.e., age; gender; American Society of Anesthesiologists Physical Status Classification (38); body mass index (BMI); comorbidities; type of surgery; degree of Trendelenburg; intra-abdominal pressure; type of anesthesia; duration of anesthesia, pneumoperitoneum, Trendelenburg position, and surgery; estimated blood

Box 1 Time points analyzed for changes in IOP

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- T1: Before induction of anesthesia to 0 to 5 minutes after induction of anesthesia
- T2: 0 to 5 minutes after induction of anesthesia to 0 to 5 minutes after abdominal insufflation
- T3: 0 to 5 minutes after abdominal insufflation to 0 to 5 minutes after Trendelenburg position
- T4: 0 to 5 minutes after Trendelenburg position to 30 to 60 minutes after Trendelenburg position
- T5: 30 to 60 minutes after Trendelenburg position to before arousal from general anesthesia
- T6: 30 to 60 minutes after Trendelenburg position to 120 to 150 minutes after Trendelenburg position
- T7: 120 to 150 minutes after Trendelenburg position to before arousal from general anesthesia
- T8: 120 to 150 minutes after Trendelenburg position to 180 to 240 minutes after Trendelenburg position
- T9: 180 to 240 minutes after Trendelenburg position to before arousal from general anesthesia
-

IOP, intraocular pressure; T, time point.

loss] were collected. Data necessary to calculate effect sizes were extracted for the multiple time points recorded by the researchers during the perioperative phases of the procedures included in their studies.

Analyses

Meta-analyses were conducted using Comprehensive Meta-Analysis, Version 3, a statistical software developed specifically for meta-analysis research (39). Time points for meta-analysis were selected from the time points recorded by the researchers to achieve the greatest number of comparisons for analysis at each time point and to allow for similarity with the order of events as they occur during surgery. Analyses were conducted for the nine time points described in *Box 1*. Standardized mean difference effect sizes were calculated for each participant group at each measured time point.

To account for sample size and adjust for bias, effect size values were weighted by the inverse of the variance. To account for between- and within-study variation, and because heterogeneity was observed among study designs, sample attributes, and outcome measures, a random effects model was selected a priori to synthesize effect sizes. Using

a random effects model assumes that the true effect size varies from one study to the next (40). A random effects model was used for seven analyses (T1, T2, T3, T5, T6, T7, T8). A fixed effect model was used to synthesize effect sizes for two analyses (T4, T9) because the number of included studies at these time points was limited. Using a fixed effect model assumes that the true effect size is the same for all studies (40). Borenstein *et al.* (40) suggest using a fixed effect analysis when the number of included studies is limited, even when heterogeneity among the studies is observed, because when using a random effects analysis, the estimate of between-studies variance may have poor precision. Relative to the interpretation of effect sizes, Cohen (41) recommended that 0.2 be considered a small effect size, 0.5 be considered a medium effect size, and 0.8 or greater be considered a large effect size. Following the procedures described by Lipsey and Wilson (42), the calculated effect sizes were converted to the metric used to measure IOP (i.e., mmHg) to facilitate interpretation of effect size findings.

The extent of publication bias for the meta-analysis was assessed by constructing a funnel plot. Notably, a funnel plot may suggest publication bias, but does not eliminate the bias (43). In order to create a funnel plot, there must be a minimum of three studies (39). An Egger's test using linear regression was also conducted to measure asymmetry of the funnel plot (39,44,45). Using an Egger's test is not advised when there are less than 10 studies included in the meta-analysis because the power of the test may be too low to distinguish true asymmetry from chance (44). Therefore, when the time point analysis included 10 or more participant groups (T1, T2, T6), a funnel plot was constructed and an Egger's test conducted.

After deciding on the model and calculating effect sizes, the studies included in the meta-analysis were assessed for heterogeneity [i.e., variability among the studies (46)]. Heterogeneity testing explores the null hypothesis (i.e., that the same effect is being evaluated by all studies) (47). Heterogeneity among the included studies in a meta-analysis is very common and should be anticipated, not regarded as the exception (34).

Homogeneity of variance among effect sizes was tested using Cochran's Q, which estimates statistical significance; Tau-squared, which estimates the absolute value of the true variance between studies, but not the proportion of the variance; and I-squared, which estimates the proportion of true variance, but not the absolute value of

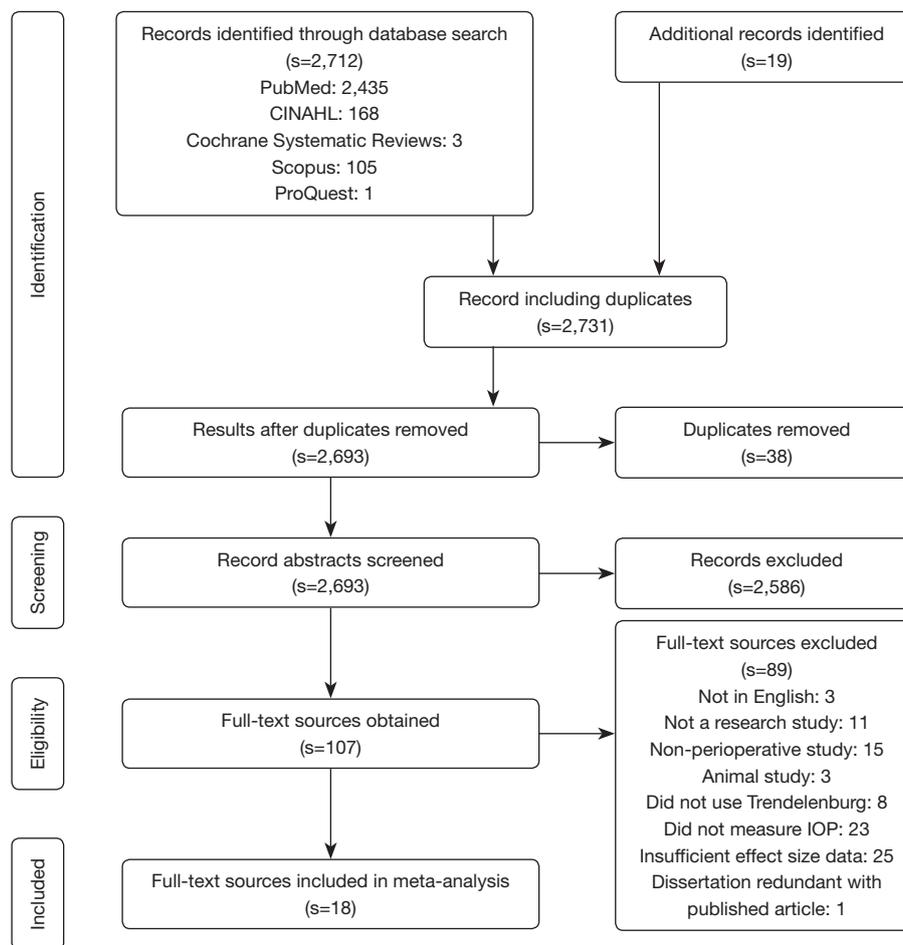


Figure 1 Flow diagram of study selection. Adapted from (36). s, studies.

the variance (48). Prediction intervals for each time point were also calculated to show the dispersion of true effect sizes around the mean (49).

Results

The flow of study selection is depicted in *Figure 1*. In total, 2,693 records were identified for possible inclusion, and of these, 18 studies were included in the systematic review and meta-analysis. Four non-experimental studies had multiple participant groups (50-53), resulting in a total of 24 participant groups and 762 participants for analysis. *Table 1* contains a summary of the studies included in this review and meta-analysis.

Study characteristics

All 18 studies included in the systematic review and meta-analysis were obtained from peer-reviewed journals. The researchers of six studies (33.3%) reported receiving some type of funding or donated supplies (53-56,66,61). Although the literature was searched from 1990 through 2018, studies included in the systematic review and meta-analysis were published between 2011 and 2018 (*Figure 1* and *Table 1*). Some earlier studies were located during the literature search (4,63,64); however, these were excluded because of insufficient effect size data. As shown in *Table 1*, the greatest number of studies were published in 2015 (9,10,53,62) (s=4) and 2018 (51,56-58) (s=4), but the greatest number of participants occurred in 2013 (5,16,50) (n=147). The

Table 1 Summary of studies included in the systematic review and meta-analysis (s=18)

First author, [year], country	Study design, (quality) ^a	Participant groups and observations/interventions	IOP measures, (tonometer)	Outcome measures	Effect sizes (Cohen's d)
Adisa (54), [2016], Nigeria	Non-experimental, (Good)	<ul style="list-style-type: none"> 20 patients undergoing laparoscopic surgery in a 15-degree to 20-degree Trendelenburg position 20 patients undergoing laparoscopic surgery in a 15- to 20-degree reverse Trendelenburg position^b <p>Note: patients with BMI ≥ 35 kg/m² excluded. Patients with a preoperative IOP < 20 mmHg, a known diagnosis of glaucoma, or acute or chronic eye infection excluded</p>	Measurement of IOP at seven different time points, (Perkins)	Differences in IOP levels at each time point	T1: -1.043; T2: 0.013; T3: 0.839
Agrawal (50), [2013], India	Non-experimental, (Good)	<ul style="list-style-type: none"> 30 women undergoing laparoscopic gynecologic procedures in a 20-degree Trendelenburg position with anesthesia using propofol for induction and propofol for maintenance (A) 30 women undergoing laparoscopic gynecologic procedures in a 20-degree Trendelenburg position with anesthesia using propofol for induction and 1% isoflurane for maintenance (B) 30 women undergoing laparoscopic gynecologic procedures in a 20-degree Trendelenburg position with anesthesia using thiopentone for induction and propofol for maintenance (C) 30 women undergoing laparoscopic gynecologic procedures in a 20-degree Trendelenburg position with anesthesia using thiopentone for induction and 1% isoflurane for maintenance (D) <p>Note. Patients with weight > 70 kg excluded. Patients suffering from acute or chronic disorders of eye excluded</p>	Measurement of IOP at six different time points, (Schiotz)	Differences in IOP levels at each time point	T1(A): -5.047; T1(B): -2.533; T1(C): -2.412; T1(D): -2.027; T2(A): 1.231; T2(B): 1.131; T2(C): 0.859; T2(D): 1.559; T3(A): 1.327; T3(B): 1.523; T3(C): 1.671; T3(D): 2.419
Blecha (55), [2017], Germany	Non-experimental, (High)	<ul style="list-style-type: none"> 51 men undergoing robotic-assisted laparoscopic prostatectomy in a 45-degree Trendelenburg position <p>Note: patients > 80 years, ASA Class $> III$, or BMI > 40 kg/m² excluded. Patients with pre-existing eye disease (diabetic retinopathy, glaucoma, retinal detachment), history of eye surgery excluded</p>	Measurement of IOP at six different time points, (Icare PRO)	Differences in IOP levels at each time point	T5: -1.650
Borahay (5), [2013], USA	Non-experimental, (Good)	<ul style="list-style-type: none"> 10 women undergoing elective robotic-assisted or laparoscopic-assisted hysterectomy procedures in a 30-degree Trendelenburg position <p>Note: patients with a history of eye disease or previous intraocular surgery excluded</p>	Measurement of IOP at five different time points, (Tono-Pen XL)	Differences in IOP levels at each time point	T6: 0.132

Table 1 (continued)

Table 1 (continued)

First author, [year], country	Study design, (quality) ^a	Participant groups and observations/interventions	IOP measures, (tonometer)	Outcome measures	Effect sizes (Cohen's d)
Grosso (16), [2013], Italy	Non-experimental, (Good)	<p>Participant groups and observations/interventions</p> <ul style="list-style-type: none"> 17 patients undergoing colorectal laparoscopic surgery in a 30-degree Trendelenburg position 12 patients undergoing colorectal laparoscopic surgery in supine position^b <p>Note: patients >45 years, ASA Class > III, or BMI >35 kg/m² excluded. Patients with an established diagnosis of glaucoma with topical therapy, a documented increase in IOP, and recent (≤6 months) eye infections excluded</p>	Measurement of IOP at eight different time points, (Icare PRO)	Differences in IOP levels at each time point	T2: 0.975; T3: 0.204; T4: 0.010
Hirooka (56), [2018], Japan	Non-experimental, (Good)	<p>Participant groups and observations/interventions</p> <ul style="list-style-type: none"> 20 men undergoing robotic-assisted laparoscopic radical prostatectomy in a 30-degree Trendelenburg position <p>Note: patients with previous abnormal visual field test results or ocular hypertension (IOP >21 mmHg) excluded</p>	Measurement of IOP at six different time points, (Tono-Pen XL)	Differences in IOP levels at each time point	T4: 0.964; T6: 0.091; T8: 0.539
Kaur (51), [2018], India	Non-experimental, (High)	<p>Participant groups and observations/interventions</p> <ul style="list-style-type: none"> 30 patients undergoing lower abdominal laparoscopic surgery in a 25- to 30-degree Trendelenburg position with anesthesia using intravenous propofol (P) 30 patients undergoing lower abdominal laparoscopic surgery in a 25-degree to 30-degree Trendelenburg position with anesthesia using inhaled sevoflurane (S) <p>Note: patients with extreme obesity excluded. Patients with a history of eye disease, baseline IOP >21 mmHg, difference in IOP of >8 mmHg between two eyes, diabetic retinopathy, cataract, who have received medication or surgery for previously diagnosed glaucoma or who are taking any medication that can alter IOP excluded</p>	Measurement of IOP at seven different time points, (Schiotz)	Differences in IOP levels at each time point	T1(P): -4.087; T1(S): -4.134; T2(P): 2.275; T2(S): 4.508
Kitamura (57), [2018], Japan	Experimental, (High)	<p>Participant groups and observations/interventions</p> <ul style="list-style-type: none"> 20 patients undergoing robotic-assisted laparoscopic radical prostatectomy in a 25-degree Trendelenburg position and receiving a placebo (saline) 20 patients undergoing robotic-assisted laparoscopic radical prostatectomy in a 25-degree Trendelenburg position and receiving dexmedetomidine^b <p>Note: patients with BMI >35 kg/m² excluded. Patients with glaucoma, a history of ophthalmic surgery or those receiving any medication known to alter IOP excluded</p>	Measurement of IOP at eight different time points, (Icare PRO)	Differences in IOP levels at each time point	T1: -1.466; T6: 0.165; T8: 0.611

Table 1 (continued)

Table 1 (continued)

First author, [year], country	Study design, (quality) ^a	Participant groups and observations/interventions	IOP measures, (tonometer)	Outcome measures	Effect sizes (Cohen's d)
Mathew (58), [2018], Canada	Experimental, (High)	<ul style="list-style-type: none"> 15 men undergoing robotic-assisted laparoscopic radical prostatectomy in a 33-degree Trendelenburg position and receiving a placebo (artificial tears) 11 men undergoing robotic-assisted laparoscopic radical prostatectomy in a 33-degree Trendelenburg position and receiving brimonidine tartrate 0.2%^b <p>Note: patients who underwent any ophthalmic surgical procedure within 6 months of study enrollment, or those with a diagnosis of glaucoma or ocular hypertension excluded</p>	Measurements of IOP at six different time points, (Tono-Pen AVIA)	Differences in IOP levels at each time point	T1: -1.654 T6: 0.068 T8: 0.282
Molloy (20), [2011], USA	Non-experimental, (High)	<ul style="list-style-type: none"> 37 patients undergoing laparoscopic surgery in a 32- to 37-degree Trendelenburg position <p>Note: patients with a history of eye disease or eye surgery excluded</p>	Measurements of IOP at six different time points, (Tono-Pen XL)	Differences in IOP levels at each time point	T5: -1.589 T6: 0.029 T7: -1.638
Molloy (59), [2012], USA	Quasi-experimental, (High)	<ul style="list-style-type: none"> 37 patients undergoing laparoscopic surgery in a 32- to 37-degree Trendelenburg position 29 patients undergoing laparoscopic surgery in a 32- to 37-degree Trendelenburg position and receiving a level supine intervention^b <p>Note: patients with a history of eye disease or eye surgery excluded</p>	Measurement of IOP at six different time points, (Tono-Pen XL)	Differences in IOP levels at each time point	T5: -1.497; T6: 0.330; T7: -1.855
Molloy (60), [2014], USA	Quasi-experimental, (High)	<ul style="list-style-type: none"> 131 patients undergoing robotic-assisted laparoscopic radical prostatectomy or pelvic gynecologic procedures in a 32- to 40-degree Trendelenburg position 63 patients undergoing robotic-assisted laparoscopic prostatectomy or pelvic gynecologic procedures in a 32- to 40-degree Trendelenburg position receiving dorzolamide-timolol when IOP exceeds 40 mmHg^b <p>Note: no exclusions</p>	Measurements of IOP at eight different time points, (Tono-Pen XL)	Differences in IOP levels at each time point	T5: -0.793; T6: 0.352; T7: -1.082; T8: 0.188; T9: -1.165
Molloy (61), [2016], USA	Experimental, (High)	<ul style="list-style-type: none"> 44 patients undergoing laparoscopic procedures in a 32- to 40-degree Trendelenburg position and receiving an ophthalmic placebo (balanced salt solution) after induction of anesthesia 63 patients undergoing laparoscopic procedures in a 32- to 40-degree Trendelenburg position receiving dorzolamide-timolol after anesthesia induction and when IOP exceeded 40 mmHg^b <p>Note: no exclusions</p>	Measurements of IOP at eight different time points, (Tono-Pen XL)	Differences in IOP levels at each time point	T5: -1.519; T6: 0.497; T7: -1.922; T8: 0.536; T9: -2.758

Table 1 (continued)

Table 1 (continued)

First author, [year], country	Study design, (quality) ^a	Participant groups and observations/interventions	IOP measures, (tonometer)	Outcome measures	Effect sizes (Cohen's d)
Mondzelewski (9), [2015], USA	Non-experimental, (Good)	<ul style="list-style-type: none"> 18 patients undergoing robotic-assisted laparoscopic procedures in a 30-degree Trendelenburg position; 9 patients undergoing laparoscopic procedures in supine position^b; 12 patients undergoing open procedures in supine position^b <p>Note: patients with a history of glaucoma, macular degeneration, previous eye trauma, nonrefractive eye surgery, or diabetic retinopathy excluded</p>	Measurements of IOP at 11 different time points, (Tono-Pen AVIA)	Differences in IOP levels at each time point	
Nishikawa (52), [2017], Japan	Non-experimental, (Good)	<ul style="list-style-type: none"> 15 men undergoing robotic-assisted laparoscopic radical prostatectomy in a 25° Trendelenburg position (25); 15 men undergoing robotic-assisted laparoscopic radical prostatectomy in a 30° Trendelenburg position (30) <p>Note: patients with pre-existing glaucoma, retinal vascular diseases, or a history of eye surgery excluded</p>	Measurement of IOP at six different time points, (Tono-Pen XL)	Differences in IOP levels at each time point	T1[25]: -1.934; T1[30]: -1.076; T5[25]: -2.103; T5[30]: -2.584; T6[25]: 0.555; T6[30]: 0.895; T7[25]: -2.887; T7[30]: -3.744
Raz (62), [2015], Australia	Experimental, (Good)	<ul style="list-style-type: none"> 21 men undergoing robotic-assisted laparoscopic radical prostatectomy in a 23-degree Trendelenburg position; 29 men undergoing robotic-assisted laparoscopic radical prostatectomy in a modified-Z 23-degree Trendelenburg position^b <p>Note: patients with a history of eye surgery in the last three months excluded</p>	Measurement of IOP at 18 different time points, (Tono-Pen AVIA)	Differences in IOP levels at each time point	T4: 1.238; T5: -1.093; T6: 0.135; T7: -1.593
Taketani (10), [2015], Japan	Non-experimental, (Good)	<ul style="list-style-type: none"> 25 men undergoing robotic-assisted laparoscopic radical prostatectomy in a 25- to 30-degree Trendelenburg position <p>Note: no exclusions</p>	Measurement of IOP at eight different time points, (Tono-Pen XL)	Differences in IOP levels at each time point	T6: 0.386; T8: 0.161
Yoo (53), [2015], Korea	Non-experimental, (High)	<ul style="list-style-type: none"> 32 patients undergoing robotic-assisted laparoscopic radical prostatectomy in a 29-degree Trendelenburg position with anesthesia using moderate neuromuscular blockade (M); 34 patients undergoing robotic-assisted laparoscopic radical prostatectomy in a 29-degree Trendelenburg position with anesthesia using deep neuromuscular blockade (D) <p>Note: patients with BMI >30 kg/m² excluded. Patients who had undergone previous ophthalmic surgery or were taking medications for glaucoma, those with current ophthalmic disease (glaucoma, diabetic retinopathy, cataract, and retinal detachment), and those with a baseline IOP of >30 mmHg excluded</p>	Measurement of IOP at eight different timepoints, (Tono-Pen XL)	Differences in IOP levels at each time point	T1(M): -2.952; T1(D): -3.954; T2(M): 3.262; T2(D): 3.389

^a, study design and quality ratings are based on the Association of perOperative Registered Nurses (AORN) Research Evidence Appraisal Tool - Study; ^b, this group was not eligible for inclusion in the meta-analysis; ASA, American Society of Anesthesiologists Physical Classification Status; BMI, body mass index; IOP, intraocular pressure; kg, kilograms; kg/m², kilograms/meter-squared; mmHg, millimeters of mercury; s, studies.

majority of studies ($s=14$) were conducted in Asia (10,50-53, 56,57) ($s=7$) or North America (5,9,20,58-61) ($s=7$), with the majority of participants also from Asia ($n=361$) or North America ($n=292$).

Participant and surgery characteristics

Participant and surgery characteristics are shown in *Table 2*. Participant race was only reported by two researchers (5,54). Socioeconomic status was not reported by any researchers. Participants were slightly overweight with a mean BMI of 27.5 kg/m^2 (± 2.3) (65). Notably, some researchers had exclusion criteria for participant age, BMI, ocular disease, and American Society of Anesthesiologist's classification (*Table 1*).

Study design characteristics

As shown in *Table 1*, the 18 reports included in the systematic review and meta-analysis comprised four experimental (57,58,61,62) ($n=100$), two quasi-experimental (59,60) ($n=168$), and 12 non-experimental (5,9,10,16,20,50-56) ($n=494$). Nine were high quality (20,51,53,55,57-61) ($n=461$) and nine were good quality (5,9,10,16,50,52,54,56,62) ($n=301$). The researchers used five different types of tonometers to measure IOP, the Tono-Pen XL was used most frequently (5,10,20,52,53,56,59-61) ($s=9$; $n=420$). The researchers reported having 195 participants undergo preoperative ophthalmologic examinations (9,10,16,50,54,56,58) ($s=7$), and 100 participants undergo postoperative ophthalmologic examinations (9,10,56,58) ($s=4$). Notably, all participants who received postoperative ophthalmologic examinations also received preoperative examinations ($n=100$).

Effect sizes

Results of the synthesized effect sizes, prediction intervals, and meta-analyses for each time point of IOP measurement are shown in *Table 3*. A graphical representation of the magnitude of change in IOP for T0 through T9 is shown in *Figure 2*. In total, between abdominal insufflation in supine position (T2) and 5 minutes (T3), 60 minutes (T4), 150 minutes (T6), and 240 minutes (T8) of Trendelenburg position, IOP increases significantly by 13.6 mmHg (i.e., $3.5+4.4+2.6+1.5+1.6=13.6 \text{ mmHg}$). Based on the upper limits of the prediction intervals (*Figure 3*), in 95% of all

populations IOP could increase by as much as 28.1 mmHg (i.e., $7.6+8.5+6.6+2.3+3.1=28.1 \text{ mmHg}$). The greatest increase in IOP occurs after the patient is placed into the Trendelenburg position (*Figure 2*; T3: $+4.4 \text{ mmHg}$). The IOP continues to increase significantly while the patient is in Trendelenburg position, but to a lesser degree (T4: $+2.6 \text{ mmHg}$; T6: $+1.5 \text{ mmHg}$; T8: $+1.6 \text{ mmHg}$). IOP decreases significantly after induction of anesthesia in supine position (T1: -5.2 mmHg) and after a return to supine position for arousal from anesthesia (T5: -7.5 mmHg ; T7: -8.2 mmHg ; T9: -6.0 mmHg). The forest plot of effect sizes for each participant group included in the meta-analysis for T6 is shown in *Figure 4*. The funnel plot for publication bias for T6 is shown in *Figure 5*.

Discussion

The results of this systematic review and analysis have shown that IOP increases significantly for adult patients undergoing surgery in the Trendelenburg position. As shown in *Figure 2*, if an individual had a baseline IOP of 16.5 mmHg before induction of anesthesia (as indicated by the pooled mean calculated for T0), after 180 to 240 minutes in the Trendelenburg position, the patient's IOP could increase to 24.9 mmHg ($16.5-5.2+3.5+4.4+2.6+1.5+1.6=24.9 \text{ mmHg}$). Based on the upper limits of the prediction intervals (*Figure 3*), after 180 to 240 minutes in the Trendelenburg position, IOP could increase to 35 mmHg ($16.5-9.6+7.6+8.5+6.6+2.3+3.1=35 \text{ mmHg}$). An IOP of 24.9 to 35 mmHg is above the highest parameter of normal IOP (i.e., 21 mmHg). As shown in *Table 2*, the mean duration of Trendelenburg position for the studies included in this systematic review and meta-analysis was 104.8 minutes (± 58.2) with a range of 68 to 207 minutes. The greatest increases in IOP occur during abdominal insufflation and within the first 60 minutes after Trendelenburg position (*Figure 2*); however, based on the collective range of 68 to 207 minutes for duration of Trendelenburg position, a Trendelenburg time of 180 to 240 minutes is not implausible. Another important consideration regarding the findings of this systematic review and meta-analysis is that the mean degree of Trendelenburg position was 28.4 (*Table 2*). Steep Trendelenburg is generally considered to be a head-down tilt of 30 to 45 degrees (7,15,66); thus, it is likely that Trendelenburg positions greater than 28.4 degrees would have produced even greater increases in IOP.

Table 2 Participant and surgery characteristics (s=18; n=762)

Category	Number of participants, (number of studies)	Mean \pm SD, (range) or percent
Age (years)	612 [16]	55.2 \pm 11.9 (30.5–66.9)
Gender	624 [16]	
Women	209	33.0
Men	415	67.0
BMI (kg/m ²)	287 [12]	27.5 \pm 2.3 (23.6–30.7)
ASA	308 [8]	
Class I	107	34.7
Class II	180	58.4
Class III	21	6.9
ASA		
Class I or II	145 [2]	100
Comorbidities	300 [7]	
Asthma	76 [2]	2.6
Diabetes	107 [3]	7.5
Hypertension	117 [4]	37.6
Surgery type	762 [18]	
Laparoscopic	292	38.3
Colorectal	47	6.2
Gynecologic	151	19.8
Prostatectomy	14	1.8
Unspecified	80	10.8
Laparoscopic/Robotic	44	5.8
Unspecified	44	5.8
Robotic	426	55.9
Hysterectomy	8	1.0
Pelvic node	1	0.1
Prostatectomy	335	44.0
Vaginal repair	82	10.8
Anesthesia	762 [18]	
General-inhalation	298	39.1
General-propofol	242	31.8
General-unspecified	222	29.1
Intra-abdominal pressure (mmHg)	536 [12]	13.6 \pm 1.3 [12–15]
Trendelenburg degree	762 [18]	28.4 \pm 6.5 (17.5–45)

Table 2 (continued)

Table 2 (continued)

Category	Number of participants, (number of studies)	Mean \pm SD, (range) or percent
Duration (min)		
Anesthesia	66 [1]	158.0 \pm 2.8 [156–160]
Pneumoperitoneum	126 [2]	94.5 \pm 15.1 (80–109.4)
Trendelenburg	159 [3]	104.8 \pm 58.2 [68–207]
Surgery	484 [10]	197.9 \pm 64.4 [111–318]
Estimated blood loss (mL)	444 [11]	252.4 \pm 113.3 (69.4–467)

ASA, American Society of Anesthesiologists Physical Classification Status; BMI, body mass index; s, studies; SD, standard deviation.

Table 3 Effect sizes and magnitude of change in IOP for T1 through T9 (Box 1; s=18; n=762)

Time points	s	k	n	Model	d	95% CI		Q	I ²	Mean change in IOP ^a	Prediction interval ^b
						LL	UL				
T1	7	13	331	R	-2.45*	-1.70	-0.30	109.82*	89.07	-5.2 mmHg	-0.9 to -9.6 mmHg
T2	5	10	283	R	1.89*	1.14	2.63	121.56*	92.60	+3.5 mmHg from T1	-0.7 to +7.6 mmHg
T3	3	6	157	R	1.34*	0.78	1.90	24.90*	79.92	+4.4 mmHg from T2	+0.4 to +8.5 mmHg
T4	3	3	78	F	0.91*	0.57	1.25	12.96**	84.57	+2.6 mmHg from T3	-1.5 to +6.6 mmHg
T5	7	8	351	R	-1.54*	-1.93	-1.16	30.71*	77.20	-7.5 mmHg from T4	-3.1 to -12.0 mmHg
T6	11	12	410	R	0.30*	0.16	0.44	7.06	0.00	+1.5 mmHg from T4	+0.9 to +2.3 mmHg
T7	6	7	300	R	-1.94*	-2.47	-1.41	33.52*	82.10	-8.2 mmHg from T6	-3.1 to -13.3 mmHg
T8	6	6	275	R	0.38*	0.12	0.65	1.90	0.00	+1.6 mmHg from T6	+0.5 to +3.1 mmHg
T9	2	2	175	F	-1.58*	-2.06	-1.11	8.46**	88.18	-6.0 mmHg from T8	-13.9 to +1.7 mmHg

*, P<0.001; **, P<0.005; ^a, mean effect sizes were converted to the metric used to measure IOP (i.e., mmHg) following the procedures described by Lipsey and Wilson (42); ^b, in 95% of all populations, the true effect size will fall within this range. CI, confidence interval; d, standardized mean difference; F, fixed effect; I², heterogeneity statistic; IOP, intraocular pressure; k, comparisons; LL, lower limit; mmHg, millimeters of mercury; Q, Cochran's Q; R, random effects; s, studies; T, time point; UL, upper limit.

Implications for practice

Increased IOP puts the patient at risk for glaucoma, detached retina, or partial to complete vision loss (3,5,7,10,12,14,18). IOP increases of the magnitude found in this systematic review and meta-analysis clearly demonstrate the need for implementing intraoperative interventions to mitigate the increase in IOP and reduce the potential for serious ocular complications in patients undergoing surgery in the Trendelenburg position. These intraoperative interventions may include monitoring IOP at established intervals or continuously (17,67,68), reducing the degree of Trendelenburg position (7,62,69,70), implementing a modified Trendelenburg position (62),

providing periodic position changes or rest periods (5,14,15,23,55,59) and administering specific medications or anesthetics (8,50,51,58,64,71-74).

Because IOP increases during abdominal insufflation and Trendelenburg position, intraoperative monitoring of IOP either continuously or at established intervals or time points (e.g., after abdominal insufflation, after initiation of Trendelenburg position, after 60 minutes of Trendelenburg position, etc.) seems prudent. Elevated IOPs can be an indication of ocular venous congestion and decreased perfusion of the optic nerve (21). Monitoring IOP can provide a baseline IOP and an objective measurement that can help the surgical team maintain awareness of the patient's IOP, implement interventions to reduce

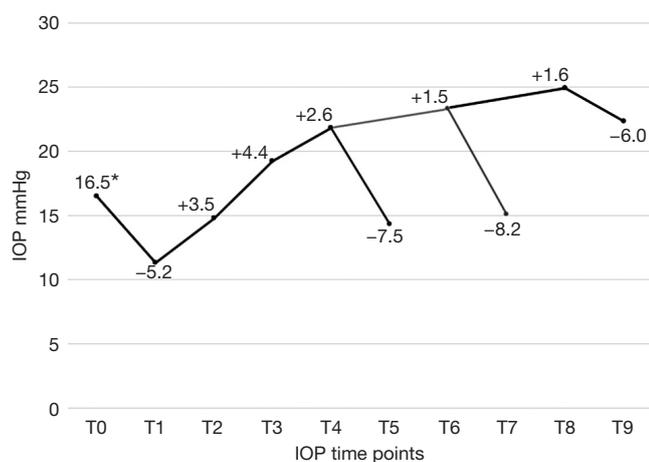


Figure 2 Magnitude of mean change in IOP for T0 through T9 (Box 1). IOP increases significantly after abdominal insufflation in the supine position (T2: +3.5 mmHg, $P < 0.001$), when the patient is placed in Trendelenburg position (T3: +4.4 mmHg, $P < 0.001$), and with extended time in the Trendelenburg position (T4: +2.6 mmHg, $P < 0.001$; T6: +1.5 mmHg, $P < 0.001$; T8: +1.6 mmHg, $P < 0.001$). IOP decreases significantly after induction of anesthesia (T1: -5.2 mmHg, $P < 0.001$) and before arousal from anesthesia (T5: -7.5 mmHg, $P < 0.001$; T7: -8.2 mmHg, $P < 0.001$; T9: -6.0 mmHg, $P < 0.001$) when the patient is in the supine position. *, Pooled mean at T0—Before induction of anesthesia. IOP, intraocular pressure; mmHg, millimeters of mercury; T, time point.

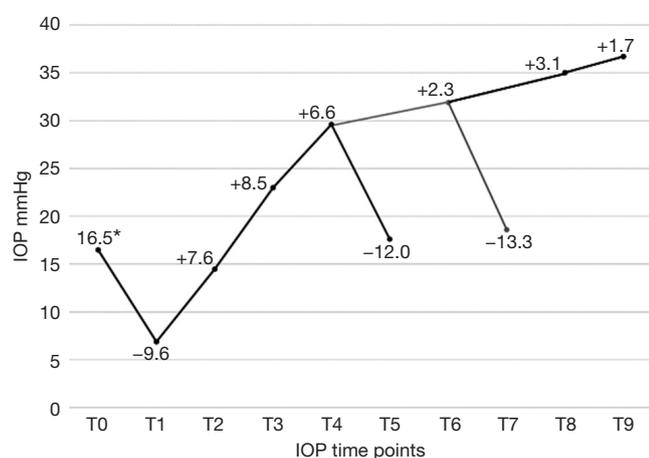


Figure 3 Magnitude of change in upper prediction intervals of IOP for T0 through T9 (Box 1). After 180 to 240 minutes in the Trendelenburg position, in 95% of all populations, IOP could increase to 35 mmHg ($16.5 - 9.6 + 7.6 + 8.5 + 6.6 + 2.3 + 3.1 = 35$ mmHg). *, pooled mean at T0—before induction of anesthesia. IOP, intraocular pressure; mmHg, millimeters of mercury; T, time point.

IOP as needed, and thus reduce the potential for ocular complications and postoperative vision loss (17,67).

Steeper degrees of Trendelenburg increase the risk for postoperative complications because they place greater physiologic stress on the patient's body (7,15,70). Ghomi *et al.* (7) found that robotic-assisted gynecologic surgery could be performed successfully with a modest head-down tilt of 16.4 degrees. In a study to determine the head-down tilt necessary to provide adequate surgical access and visibility, Gould *et al.* (15) found the mean head-down tilt most often selected by the participating surgeons was 28.1 degrees, which was much less than the 40-degree head-down tilt the surgeons were using.

Raz *et al.* (62) found that modifying the Trendelenburg position so that the patient's head and shoulders remained level significantly decreased IOP and accelerated its return to baseline levels. Implementing periodic intraoperative position changes or rest periods in supine position (or positions where the ocular level is above the heart) can help to reduce IOP. In a quasi-experimental study, Molloy and Watson (59) implemented a 5-to-7-minute level supine intervention after 60 minutes of 32- to 40-degree Trendelenburg position and found there was a significant decrease in IOP after 120 minutes (Intervention: 18.7 ± 5.22 mmHg; Control: 35.7 ± 10.56 mmHg; $P < 0.001$). The dramatic and significant decrease in IOP that occurs before arousal from anesthesia found in this systematic review and meta-analysis (T5: -7.5 mmHg, $P < 0.001$; T7: -8.2 mmHg, $P < 0.001$; T9: -6.0 mmHg, $P < 0.001$) also supports the implementation of periodic intraoperative position changes or rest periods as a mechanism to help reduce IOP.

Administering specific medications or anesthetics may also be effective in reducing IOP or mitigating the intraoperative increase in IOP (50,51,58,64,67,71-74). Agrawal *et al.* (50) found that induction and maintenance of anesthesia with propofol was the most effective option for mitigating the increase in IOP in adult patients undergoing surgery in the Trendelenburg position. Likewise, Kaur *et al.* (51) found that propofol-based total intravenous anesthesia was more effective than inhalational anesthesia with sevoflurane in mitigating the increase in IOP in patients undergoing laparoscopic surgery in the Trendelenburg position. Kitamura *et al.* (57) found that continuous administration of dexmedetomidine in combination with propofol-based total intravenous anesthesia decreased IOP in patients undergoing robotic-assisted laparoscopic radical prostatectomy. Molloy and Cong (60) found that intraoperative treatment with

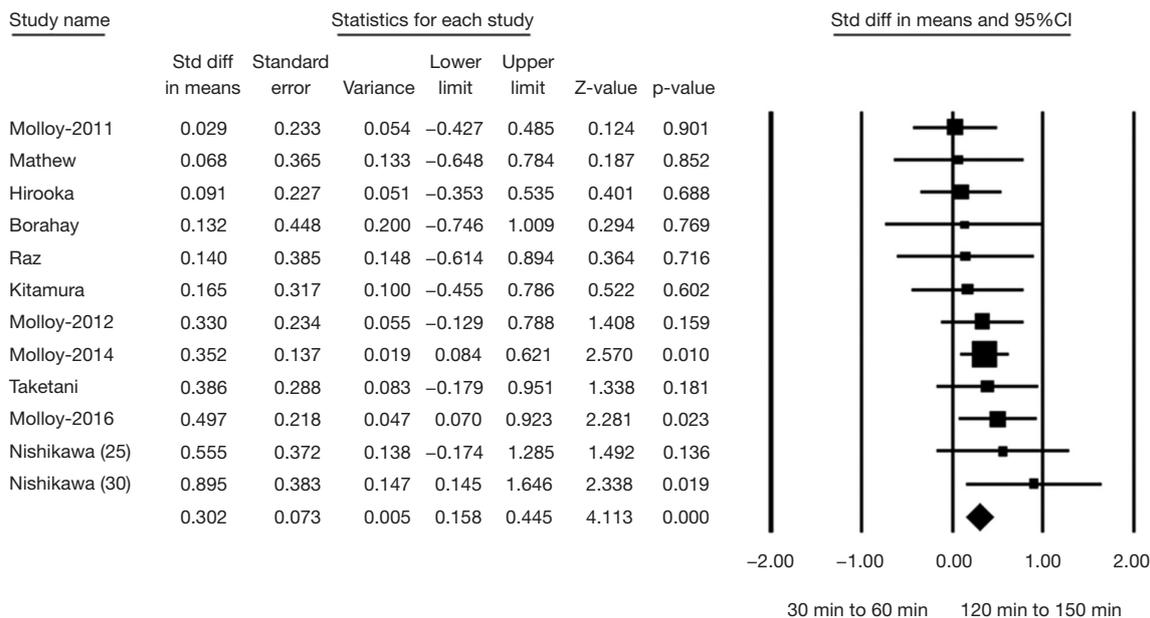


Figure 4 Forest plot of meta-analysis of T6. Abbreviations: min, minutes; Std, standard; T, time point. This analysis included 11 studies representing 12 participant groups (n=410). Effect sizes were calculated using a random effects model. The area of each square is proportional to study weight.

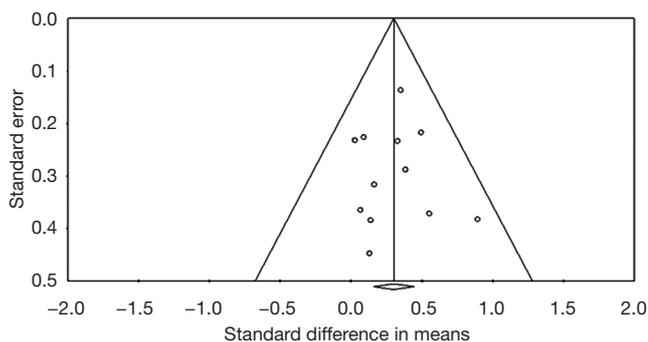


Figure 5 Funnel plot of publication bias for T6. Larger studies are shown at the top of the funnel. Positive smaller studies are shown at the right of the mean effect size (i.e., center line). The symmetrical distribution of studies (i.e., data points) around the mean effect size indicates a lack of publication bias. The non-significant Egger’s regression intercept for this funnel plot (bias = -0.05; P=0.47) is also indicative of the absence of apparent bias in the studies included in the meta-analysis for this time point. T, time point.

dorzolamide-timolol eyedrops significantly reduced elevated IOP in patients undergoing lengthy laparoscopic procedures in the Trendelenburg position, while Molloy

et al. (61) found that prophylactic therapy with dorzolamide-timolol eyedrops significantly reduced IOP in patients undergoing robotic-assisted laparoscopic prostate and gynecologic procedures.

Another important consideration for practice is the need to evaluate whether patients undergoing surgery in the Trendelenburg position should receive a preoperative ophthalmologic examination to reduce the risk for ocular injury (5,67). Preoperative ophthalmologic examinations may be helpful in identifying patients at risk for postoperative vision loss or other ocular complications. Increases in IOP may be more harmful in older patients or patients who are predisposed to developing glaucoma than in younger, healthier patients (5,9,10,16).

Grosso *et al.* (75), recommend developing a risk assessment model to help identify individuals who may be at risk for ocular complications following prolonged laparoscopic or robotic-assisted laparoscopic procedures. In selected patients (e.g., individuals with a diagnosis of glaucoma or those who are currently using glaucoma medications, individuals with a history of ocular trauma or surgery, individuals undergoing minimally invasive or robotic-assisted laparoscopic surgery anticipated to last longer than 1 hour), collaboration with an ophthalmologist

Table 4 Summary of anesthetic agents used in the studies included in the systematic review and meta-analysis (s=18)

First author	Induction	Maintenance	Muscle relaxants
Adisa (54)	Propofol	Isoflurane	Pancuronium
	Succinylcholine	Fentanyl	
Agrawal (50)	Group A and B: Propofol, Atracurium; Group C and D: Pentothal, Atracurium	Group A and C: Propofol; Group B and D: Isoflurane	Atracurium
Blecha (55)	Propofol	Propofol	Rocuronium
	Rocuronium	Remifentanyl	
Borahay (5)	Propofol	Isoflurane	Cisatracurium
	Cisatracurium	Fentanyl	
Grosso (16)	Propofol	Sevoflurane	Rocuronium
	Rocuronium	Sufentanil	
Hirooka (56)	Propofol or Desflurane	Remifentanyl	Rocuronium
	Rocuronium	Fentanyl	
Kaur (51)	Propofol	Group A: Propofol	Atracurium
	Atracurium	Group B: Sevoflurane	
Kitamura (57)	Propofol	Remifentanyl	Rocuronium
	Rocuronium		
Mathew (58)	Propofol	Sevoflurane	Rocuronium
	Rocuronium	Fentanyl or Hydromorphone	
Molloy (2011) (20)	Not described	Not described	Not described
Molloy (2012) (59)	Propofol	Sevoflurane or Desflurane	Rocuronium or Vecuronium
	Rocuronium or Vecuronium	Fentanyl	
Molloy (2014) (60)	Propofol	Sevoflurane or Desflurane	Rocuronium or Vecuronium
	Rocuronium or Vecuronium	Fentanyl	
Molloy (2016) (61)	Propofol	Sevoflurane or Desflurane	Rocuronium or Vecuronium
	Rocuronium or Vecuronium	Fentanyl	
Mondzelewski (9)	Propofol	Sevoflurane	Rocuronium
	Rocuronium	Fentanyl	
Nishikawa (52)	Propofol	Fentanyl	Rocuronium
	Rocuronium	Remifentanyl	
Raz (62)	Propofol	Propofol	Cisatracurium
	Cisatracurium		
Taketani (10)	Propofol or Desflurane	Remifentanyl	Rocuronium
	Rocuronium		
Yoo (53)	Propofol	Sevoflurane	Group D: Rocuronium;
	Rocuronium or Atracurium	Remifentanyl	Group M: Atracurium

s, studies.

to monitor intraoperative IOP and recommend treatment for increases in IOP is prudent.

Implications for future research

Further research relative to the magnitude of IOP increases in patients undergoing surgery in the Trendelenburg position is warranted. To allow for consistent data collection, comparison, meta-analysis, and reporting, researchers of future studies should use standardized time points for measurement (i.e., before arousal, after arousal, after abdominal insufflation, after change to Trendelenburg position and every 30 to 60 minutes thereafter, after return to supine position, before arousal, and postoperatively). Further, researchers should present data in a consistent format for each time point (i.e., sample size, mean, standard deviation). Additionally, to determine whether certain variables affect the strength of the relationship between Trendelenburg position and IOP, researchers should include patients of all ages (e.g., children, older adults), without restricting patients based on BMI or comorbidities.

Limitations

This systematic review and meta-analyses have several limitations. The literature search yielded 107 potentially eligible studies. Studies were excluded for a variety of reasons (Figure 1); however, 25 studies were excluded from the analyses because of a lack of data necessary to calculate an effect size. The researchers were contacted a minimum of two times to obtain missing data, but most did not respond. Some of the researchers excluded participants based on age, BMI, and comorbidities; therefore, the mean values for these variables may not fully reflect the characteristics of all adult surgical patients. Because researchers measured IOP at different intraoperative time points, all studies could not be included at all time points examined in the meta-analysis. Likewise, there were not enough studies included at each time point to allow for moderator analyses. With the exception of T6 and T8, heterogeneity was significant, indicating that variation across studies was substantial, potentially limiting generalizability. The non-significant Egger's regression intercept (bias = -0.05; P=0.47) is indicative of the absence of bias in the studies included in the meta-analysis for T6 (s=12); however, the Egger's test has low power for meta-analyses containing small to moderate numbers of studies (43).

IOP can be affected by a number of factors (e.g., age,

gender, blood pressure, BMI, total cholesterol, low-density lipoprotein, high-density lipoprotein, blood glucose, diabetes, smoking) (76). Although the researchers conducting each study included in the meta-analysis attempted to control for factors other than the effect of Trendelenburg position on IOP, it is possible that the increase in IOP was affected by factors other than patient position.

There is a potential for IOP to be affected by anesthetic agents and positive end-expiratory pressure (PEEP) greater than 15 cmH₂O (77). In all of the studies except one (20), a standardized protocol for anesthetic administration was used as a mechanism to help control potentially confounding variables. Succinylcholine is an anesthetic agent known to increase IOP (77). This agent was used for induction by only one researcher (54). Propofol, pentothal, opiates, and volatile anesthetic agents are known to reduce IOP (77). Rocuronium has no effect on IOP (78). Therefore, the primary confounding effect of these anesthetic agents, if present, would be to either lower or have no effect on IOP. This means that the actual increase in IOP could be even greater than the increase shown in the meta-analysis. As well, the variety of anesthetic agents used by the researchers reduces the likelihood of the anesthetic agents being a confounding factor in the meta-analysis (Table 4).

None of the studies included in the meta-analysis discuss the PEEP levels used during general anesthesia, so there is no way to know if these levels were greater than 15 cmH₂O. Notably, Blecha *et al.* (55) found that IOP doubled and the optic nerve sheath diameter increased to values indicative of increased intracranial pressure when the patient was in a 45-degree Trendelenburg position during robotic-assisted laparoscopic prostatectomy. The researchers concluded that this nonsignificant increase in IOP could be due to the effect of PEEP.

Pneumoperitoneum can also cause an increase in IOP (75,79). Uno *et al.* (79) found there was a profound increase in IOP during abdominal insufflation with Trendelenburg position. The researchers speculated this was due to the effect of increased central venous pressure, abdominal insufflation, and position change. In the studies included in this meta-analysis, abdominal insufflation occurred while the patient was in the supine position. After abdominal insufflation, the trocars were inserted and the patient was moved to a Trendelenburg position.

Grosso *et al.* (75) conducted a prospective study to determine the effects of pneumoperitoneum used during colorectal procedures performed in Trendelenburg and reverse Trendelenburg positions (degree of Trendelenburg

not specified). The researchers measured IOP at eight different intraoperative timepoints and used optical coherence tomography to measure the thickness of the peripapillary retinal nerve fiber layer (RNFL) before and after surgery. They found that pneumoperitoneum (12 to 14 mmHg CO₂) resulted in a mean increase of 4 mmHg in IOP. Notably, there was no statistically significant difference in the increase in IOP during surgery between the two groups ($P>0.05$), and no statistically significant difference in RNFL thickness before or after surgery ($P>0.05$). Additionally, there were no statistically significant associations between time in the Trendelenburg position and an increase in IOP (right eye $P=0.786$; left eye $P=0.668$). The researchers emphasized the importance of this finding because it demonstrates that the increase in IOP caused by pneumoperitoneum is a temporary, reversible occurrence.

The results of this meta-analysis showed there was a significant increase in IOP after insufflation in the supine position (+3.5 mmHg, $P<0.001$). There is no way to separate the effect of maintaining pneumoperitoneum from the effect of Trendelenburg position on IOP and it is likely that some of the increase in IOP was due to maintaining abdominal insufflation. However, the greatest increase in IOP occurred immediately after the patient was placed into the Trendelenburg position (Figure 2; T3: +4.4 mmHg). The IOP continues to increase significantly while the patient is in Trendelenburg position, but to a lesser degree (T4: +2.6 mmHg; T6: +1.5 mmHg; T8: +1.6 mmHg). This supports the concept that the increase in IOP is primarily due to the Trendelenburg position. The meta-analysis included both laparoscopic and robotic-assisted laparoscopic procedures. Some surgeons may use much steeper degrees of Trendelenburg during robotic-assisted laparoscopic procedures, leading to a greater increase in IOP for these procedures than for laparoscopic procedures. Only one study of robotic-assisted laparoscopic procedures included in the meta-analysis used a steep 45-degree Trendelenburg position (55). The mean degree of Trendelenburg for all studies was 28.4 (± 6.5 ; range, 17.5–45). The mean degree of Trendelenburg for laparoscopic procedures was 28.1 (± 6.3 ; range, 17.5–36). The mean degree of Trendelenburg for robotic-assisted laparoscopic procedures was only minimally greater at 31.2 (± 6.3 ; range, 23–45), and therefore, the difference in the degree of Trendelenburg used for laparoscopic compared with robotic-assisted laparoscopic procedures was not likely to substantively influence IOP levels.

Conclusions

IOP increases significantly between abdominal insufflation in supine position and 240 minutes of Trendelenburg position. The greatest increase in IOP occurs within 5 minutes of placing the patient into the Trendelenburg position. The IOP continues to increase significantly while the patient is in Trendelenburg position, but to a lesser degree. IOP increases of the magnitude found in this systematic review and meta-analysis demonstrate the need for implementing intraoperative interventions to mitigate the increase in IOP and reduce the risk for postoperative vision loss and other ocular complications in patients undergoing surgery in the Trendelenburg position.

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Footnote

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/ales.2019.07.09>). The author has no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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