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CLINICAL RESEARCH

Changes in intraocular pressure during coronary artery bypass graft surgery: an observational study

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Abstract
Background: In this study, the effects of pulsatile and non-pulsatile on-pump Coronary Artery Bypass Graft surgery (CABG) and off-pump CABG techniques on the intraocular pressure were investigated.
Methods: Forty-five patients who planned to elective coronary artery bypass surgery with on-pump pulsatile (n = 15), non-pulsatile (n = 15), or off-pump (n = 15) were included. Intraocular Pressure (IOP) measurements were performed on both eyes at nine time-points: 1) Before the operation, 2) After anesthesia induction, 3) 3 minutes after heparin administration Left Internal Mammary Artery (LIMA) harvesting, 4) End of the first anastomosis, 5) End of LIMA anastomosis, 6) 3 minutes after protamine administration, 7) End of the operation, and 8) Second hour in Intensive Care Unit (ICU), 9) Fifth hour in ICU. Mean Arterial Pressure (MAP) and Central Venous Pressure (CVP) were also recorded at the same time points as IOP.
Results: In Cardiopulmonary Bypass (CPB) groups (pulsatile or non-pulsatile CPB) with the beginning of CPB, there were significant decreases in IOP values when compared to baseline ($p = 0.012$). This decrease was more prominent in the non-pulsatile group when compared to the pulsatile group (T_4 IOP values: pulsatile, 9.7 ± 2.6; non-pulsatile, 6.8 ± 1.9; $p = 0.002$; T_5 IOP values: pulsatile, 9.5 ± 1.9; non-pulsatile, 6.7 ± 2.1; $p = 0.004$). At the end of the surgery (T_7), IOP values returned to the baseline and stayed stable at the remaining time-points. In-off pump group, IOP values significantly increased with a head-down position (T_4 IOP values: off-pump surgery, 19.7 ± 5.2; $p = 0.015$). IOP values remained high until the normalization of head-down position (T_6) and stayed stable through the rest of all remaining time-points.
Conclusion: During cardiac surgery regardless of the technique (on-pump CABG, off-pump CABG), intraocular pressures remain in the normal ranges. It should be kept in mind that patients should be avoided from long and extreme Trendelenburg position, low CVP, and MAP levels during cardiac surgery to prevent eye-related complications.

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Introduction

Cardiac surgery and cardiopulmonary bypass cause some important physiological changes in organ systems.[1] Extracorporeal perfusion is generally established by the on-pump non-pulsatile technique that provides a linear blood pressure. The other technique is the on-pump, pulsatile perfusion. In this system, a pump produces pulsatile blood pressure. There is also another option, the off-pump technique, in which the surgery is performed without arresting the heart.[2]

The eye can be considered as a hollow sphere having a rigid wall. Intraocular pressure (IOP) helps to maintain the shape and the optical properties of the eye. The normal range of IOP is 10–20 mmHg and it is constantly maintained between these values. However, there is some diurnal and seasonal variation. IOP variation may be affected by many factors. These factors may be local (Intraglobal: aqueous humor volume, blood volume, foreign bodies, etc. Extraglobal: anesthetic regional blocks, extraocular compression device, extraocular muscle tone, etc.) or systemic (blood pressure, central venous pressure, etc.).[3]

Reported rates of postoperative ophthalmological complications following on-pump cardiac surgery are between 0.06% and 25.6%.[1] These are mainly caused by multiple physiologic changes that occur during CPB such as cerebral hypoperfusion, systemic hypotension, arterial embolism, and hypothermia.[1] The maintenance of IOP between normal ranges is important. Although there is an autoregulation mechanism for keeping the IOP between normal ranges, during surgical procedure IOP levels may reach exceedingly low or high values. Increased IOP was evaluated as a risk factor for optic nerve damage in decreased perfusion pressure and ischemic optic neuropathy may occur as a result.[4] Low IOP ($\leq$ 5 mmHg) can be asymptomatic or it can be associated with clinically visible choroidal expansion and shallowing of the anterior chamber. Furthermore, low IOP may produce retinal and choroidal folds in some eyes.[5]

During cardiac surgery, steep changes in the arterial blood pressure and central venous pressure can be observed. These changes may also cause effects in IOP. Since cardiac surgery is mostly performed in elderly people, steep and prolonged unpredicted changes in IOP may cause significant problems after surgery especially in patients with undiagnosed eye problems such as glaucoma.

The current study has investigated the effects of cardiopulmonary bypass (pulsatile or non-pulsatile) versus the off-pump technique in the IOP of patients undergoing Coronary Artery Graft Bypass surgery (CABG).

Methods

The institutional ethical committee approved the study and written informed consent was obtained from all patients. Forty-five patients scheduled to undergo CABG surgery with pulsatile CPB (n = 15), non-pulsatile CPB (n = 15), or off-pump surgery (n = 15) were included. Patients with preoperative glaucoma, carotid and/or vertebral artery stenosis, or who underwent intraoperative deep hypothermic circulatory arrest (<28 °C) and selective cerebral perfusion, and patients with preoperative and perioperative inotrope support were excluded.

Preoperative cardiac medications except for angiotensin-converting enzyme inhibitors, angiotensin II antagonists, and acetylsalicylic acid were continued until the morning of surgery. All patients were premedicated with 10 mg oral diazepam (Nervium®, Saba AS, Istanbul, Turkey) 12 hours before surgery.

In the operating room patients were monitored with 5-lead-electrocardiogram, radial and pulmonary artery catheters (Swan Ganz, Edwards Lifesciences, Irvine, California, USA), pulse oximetry, capnography, and temperature monitoring (Philips Intellivue MP70 Patient Monitor, Koninklijke Philips N.V., Eindhoven, Netherlands).

Anesthesia was induced with propofol (Propofol®; Fresenius Kabi, Bad Homburg, Germany), remifentanil (Ultiva®; Glaxo-Smithkline, Genval, Belgium), midazolam (Dormicum®; Roche, Gaillard, France). Muscle relaxation was obtained with vecuronium bromide (Norcuron®; Organon, Oss, Holland). Maintenance of anesthesia was provided with remifentanil and sevoflurane with neuromuscular blockade. Following tracheal intubation, semiclosed circuit mechanical ventilation was set to maintain the partial pressure of end-tidal carbon dioxide tension between 35 and 45 mmHg, with a tidal volume adjusted to 8–10 mL kg^{-1} and a rate of 8–12 breaths/min. Air (50%) and oxygen (50%) mixture were administrated. Intraoperative fluids in each group were given according to the discretion of the anesthesiologist. Blood cardioplegia was used in on-pump groups. Induction and maintenance cardioplegic solutions were cold to tepid. The ratio of blood-to-crystalloid was 4:1.

Off-pump technique

Following median sternotomy, patients were anticoagulated with 100–200 IU kg^{-1} of heparin to have an Activated Clotting Time (ACT) of more than 250 seconds. Before anastomosis, a Trendelenburg positioning to 20° head down was given to improve preload and increase cardiac output. Octopus tissue stabilizer (Medtronic Inc., Minneapolis, MN, USA) was used for immobilization during distal anastomoses. The heart was positioned using deep pericardial traction sutures and revascularization was performed.

Pulsatile and non-pulsatile CPB technique

Before the cannulations of the aorta and the right atrium, patients were anticoagulated with 300–400 IU kg^{-1} of heparin to have an ACT level for more than 400 seconds. Roller pump (Sarns Perfusion System 9000, Baxter Healthcare, Ann Arbor, MI, USA) and a membrane oxygenator (Dideco Compact Flo Evo, Sorin Group, Mirandola, Italy) were used. The prime solution contained lactated Ringer's solution (1000–1500 mL) to reach a hematocrit level of 26% ± 2%. Pump flow was set at 2.2–2.4 $L.m^{-21}$ to maintain the Mean Arterial Pressure (MAP) between 50–70 mmHg. The body temperatures of the patients were cooled down to 30 °C. Intermittent cardioplegia technique (repeated in every 20 minutes) for used for myocardial protection, and additionally cold (4 °C), a topical isotonic solution was applied to the surface of the heart with the same intervals. Cross-clamp

time (minutes) and CPB time (minutes) were recorded. In the pulsatile group, pulsation was achieved by creating temporary changes on the roles of the arms' rates.

IOP measurement

IOP was measured using a hand-held TonoPen®XL (Carleton Optical Equipment Ltd, Chesham, UK). Calibration of the TonoPen was carried out in the operating room before each case. IOP measurements were performed on both eyes at the following time-points: 1) Before operation (when patients lay down on to the operation table), 2) After anesthesia induction (at the fifth minute after induction of anesthesia), 3) 3 minutes after heparin administration – Left Internal Mammary Artery (LIMA) harvesting, 4) End of the first anastomosis, 5) End of LIMA anastomosis, 6) 3 minutes after protamine administration, 7) At the end of the operation, and 8) Second hour in ICU, 9) Fifth hour in ICU. Mean arterial pressure and CVP, were also recorded at the same time points as IOP.

Statistical analysis

The Shapiro-Wilk test was used to determine to detect the normal and abnormal distribution of data. While analysis of variance (ANOVA) used for normally distributed variables, Kruskal-Wallis one-way analysis of variance test used for abnormally distributed variables. The comparison of time-dependent changes was performed by the repeated measures ANOVA for normally distributed and by the Friedman test for abnormally distributed variables. Due to intra-group and inter-group comparisons, Bonferroni correction was performed for each time point. While the comparison of two dependent groups was performed by the Wilcoxon test, a comparison of rates in two independent groups was assessed by the Chi-square test.

Results

There were no significant differences in patient characteristics, which were summarized in Table 1. Complete revascularization was performed, and surgery was uneventful in all groups. None of the patients developed myocardial infarction perioperatively. The LIMA was used, and a left chest tube was inserted for all patients. No significant difference was determined between the drainage amount and transfusion rates in three groups.

The comparison of the three groups for measured nine time-points was summarized in Figure 1. In CPB groups (pulsatile, non-pulsatile) with the beginning of CPB, there were significant decreases in IOP values when compared to baseline ($p = 0.012$). These decreases were significant in the non-pulsatile group when compared to the pulsatile group (T_4 IOP values: pulsatile, 9.7 ± 2.6; non-pulsatile, 6.8 ± 1.9; $p = 0.002$; T_5 IOP values: 9.5 ± 1.9; non-pulsatile, 6.7 ± 2.1; $p = 0.004$). With the cessation of CPB, IOP values began to return baseline measurements. Although there were differences between pulsatile and non-pulsatile groups at time-point 6, this was not statistically different ($p = 0.054$).

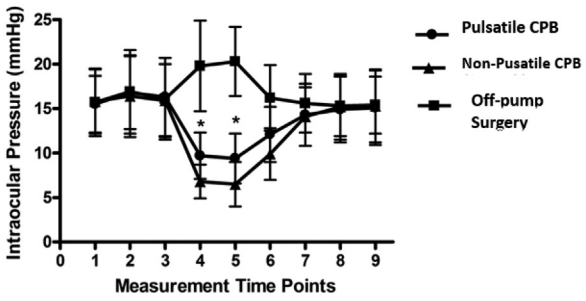

Figure 1 Diagram showing the intraocular pressure changes at the nine measured time-points (*$p < 0.05$). Time-points: 1, before operation; 2, after anesthesia induction; 3, 3-minutes after heparin administration – LIMA harvesting; 4, end of first anastomosis; 5, end of LIMA anastomosis; 6, 3-minutes after protamine administration; 7, end of operation; 8, ICU-2-hour; 9, ICU-5-hours.

At the end of the surgery (T_7), IOP values returned to the baseline and stayed stable at the remaining time-points.

In-off pump group, IOP values significantly increased with a head-down position (T_4 IOP values: off-pump surgery, 19.7 ± 5.2; $p = 0.015$) (Figure 1). IOP values remained high until the normalization of head-down position (T_6) and stayed stable through the rest of all remaining time-points (T_6 IOP values: off-pump surgery, 16.6 ± 3.4) (Figure 1).

CVP and MAP values are shown in Table 2. In patients with CPB, CVP levels were significantly decreased with the introduction of CPB. CVP increased with the head-down position in the off-pump group but returned to their baseline value with normalization of the head-down position at the end of surgery. Changes in MAP were also parallel to the CVP values in pulsatile CPB and non-pulsatile CPB groups. However, MAP levels did not significantly change throughout the surgery in the off-pump group.

Discussion

In our study, we aimed to investigate out the effects of pulsatile CPB, non-pulsatile CPB, and off-pump CABG on the intraocular pressure. There were alterations of CVP and MAP levels during and after cardiac surgery and these alterations may vary according to different techniques. We claimed that CVP and MAP alterations could affect IOP in cardiac surgery.

Normal Intraocular Pressure (IOP) is approximately 10 to 20 mmHg. The main physiological determinant of IOP is the dynamic balance between the production of aqueous humor and its eventual elimination into the episcleral venous system via spaces of Fontana and the canal of Schlemm at the iridocorneal angle.[6] Most of the aqueous humor is actively secreted at the ciliary process of the posterior chamber and circulates freely around the iris into the anterior chamber. Any increase in venous pressure or decrease in the cross-sectional area of the spaces of Fontana increases resistance to the outflow of aqueous humor and increases IOP. Mydriatic drugs relax ciliary muscles, close the iridocorneal angle at Fontana spaces and thereby increase IOP. Coughing, straining, and Valsalva maneuvers significantly increase central venous pressure, decrease the outflow of aqueous humor

Table 1 Patient characteristics and operative data.

	Pulsatile CPB (n = 15)	Non-pulsatile CPB (n = 15)	Off-pump (n = 15)	*p*-value
Preoperative data				
Gender, M/F	9/6	8/7	8/7	0.792
Age, y	66 ± 9	68 ± 10	68 ± 11	0.595
BSA, m^2	1.91 ± 0.19	1.92 ± 0.17	1.89 ± 0.18	0.571
EF, %	47 ± 4	50 ± 6	45 ± 5	0.613
Diabetes	3	2	2	0.586
COPD	2	3	2	0.314
Intraoperative data				
Average number of grafts	3 (3–5)	3 (2–5)	3 (2–3)	0.251
Anastomosis time, min	60 ± 11	59 ± 17	55 ± 15	0.412
Anesthesia time, min	322 ± 61	341 ± 59	296 ± 64	0.549
Surgery time, min	219 ± 58	237 ± 63	208 ± 56	0.548
Postoperative data				
Mechanical ventilation, h	4.6 ± 0.7	4.2 ± 0.5	3.4 ± 0.5	0.297
ICU stay, h (min–max)	18 (17–25)	19 (17–26)	16 (15–24)	0.437
30-day mortality, n	0	0	0	

CPB, Cardiopulmonary Bypass; BSA, Body Surface Area; EF, Ejection Fraction; COPD, Chronic Obstructive Pulmonary Disease; ICU, Intensive Care Unit.

Table 2 Changes in CVP, MAP in three groups.

Time point	CVP (mmHg)			MAP (mmHg)		
	Pulsatile CPB (n = 15)	Non-pulsatile CPB (n = 15)	Off-pump (n = 15)	Pulsatile CPB (n = 15)	Non-pulsatile CPB(n = 15)	Off-pump (n = 15)
T1	8.7 ± 3.1	8.8 ± 4.5	8.5 ± 3.3	72.4 ± 9.2	70.3 ± 11.6	73.6 ± 8.7
T2	9.1 ± 4.3	8.6 ± 3.7	10.8 ± 4.1	73.9 ± 8.4	72.5 ± 10.3	72.7 ± 9.2
T3	9.3 ± 3.2	10.2 ± 4.1	9.6 ± 4.4	69.3 ± 7.1	71.8 ± 7.7	75.9 ± 8.4
T4	3.4 ± 2.5[a]	3.3 ± 3.1[a]	16.2 ± 3.2	47.4 ± 8.2[a]	45.1 ± 6.4[a]	69.3 ± 8.5
T5	5.1 ± 3.2[a]	4.2 ± 3.4	15.6 ± 3.4	51.5 ± 8.3[a]	50.5 ± 7.3[a]	68.7 ± 9.1
T6	7.3 ± 4.4	6.3 ± 3.5	10.1 ± 4.1	63.7 ± 7.6	65.6 ± 8.2	72.4 ± 8.7
T7	9.6 ± 4.0	9.4 ± 4.8	10.2 ± 4.8	70.2 ± 10.1	69.5 ± 11.4	70.1 ± 7.5
T8	8.8 ± 3.5	8.6 ± 3.5	9.6 ± 3.7	71.7 ± 8.3	70.8 ± 7.1	71.6 ± 8.8
T9	9.2 ± 4.6	9.4 ± 3.7	10.3 ± 3.4	70.6 ± 9.1	71.9 ± 9.8	69.3 ± 7.4

CVP, Central Venous Pressure; MAP, Mean Arterial Pressure; CPB, Cardiopulmonary Bypass. [a] $p < 0.05$.
Time-points: T1, Before operation; T2, After anesthesia induction; T3, 3 minutes after heparin administration – LIMA harvesting; T4, End of first anastomosis; T5, End of LIMA anastomosis; T6, 3 minutes after protamine administration; T7, End of operation; T8, ICU-2 hours; T9, ICU-5 hours.

from the Schlemm canal into the episcleral venous system, and thus increase IOP.[7,8]

Choroidal Blood Volume (CBV) changes also significantly affect IOP. The choroid is a vascular meshwork of arterial anastomoses located in the posterior chamber.[7] Choroidal blood flow is usually autoregulated over a range of perfusion pressure to keep IOP stable.[7] A sudden increase in systolic arterial blood pressure causes a transient swelling of CBV; a subsequent temporary outflow adjusts IOP toward normal. Hypotension (systolic arterial blood pressure <90 mmHg) may reduce IOP as CBV decreases.[9] Sudden increases in CBV can force vitreous gel forward into the anterior chamber during open eye surgery or can increase IOP in the intact eye. Coughing, bucking, emesis, and the Valsalva maneuver increase CBV by increasing central venous pressure and thus increase IOP. Coughing can increase IOP to 30 or 40 mmHg.[10] CBV, and therefore IOP, will also increase in response to respiratory acidosis and hypercarbia.[9] Choroidal circulation is also sensitive to changes in the partial pressure of oxygen. Hypoxia induces choroidal vasodilation and increases IOP.[8]

Murphy[9] reviewed factors affecting intraocular blood volume and concluded that arterial blood pressure has a small effect over IOP. A more direct relationship exists between CVP and IOP. A slight head-up position during intraocular surgery helps to counteract the effects of central venous pressure.

Anesthesia and anesthetic drugs also affect IOP. All induction agents and all inhalational anesthetic drugs reduce IOP.[3] The observed fall in IOP is more likely to be direct action on central control mechanisms. Opioids do not have a direct effect on IOP but attenuate the elevation in pressure due to intubation. Non-depolarizing muscle relaxants have a mini-

mal effect on IOP.[3] In our study, we used the same anesthetic regimen in all groups, and we avoided the effects of anesthetic agents over IOP.

Our results showed that intraocular pressure values in CPB groups were significantly decreased when compared to off-pump group patients. Off-pump cardiac surgery is more physiological surgery than pulsatile or non-pulsatile CPB. Although statistically not significant, the decrease in non-pulsatile flow was more prominent than pulsatile flow. This small difference may be explained by the parallel changes that were observed in CVP and MAP levels. We thought that pulsatile flow was more physiological than non-pulsatile flow.

Although there are developments in the equipment and applied techniques in open-heart surgery, postoperative complications related to respiratory failure, neurological damage, and inflammatory system activation during extracorporeal circulation and reperfusion have emerged research for new solutions. Off-pump CABG surgery has been performed increasingly in recent years. This technique aims to avoid the negative consequences of extracorporeal perfusion and cooling methods. The off-pump technique was superior in older patients (>70 years old), patients with poor ventricle function, redo cases, and patients with systemic diseases (cerebrovascular, liver, bleeding disorder), and with severe aortic calcifications.[11]

There is still a contradiction about the beneficial and detrimental effects of the pulsatile CPB technique. Hemolysis is one of the important issues, however, it was mainly solved with the introduction of centrifugal pumps and new technology. The other question is about the capability of non-pulsatile perfusion technique to produce more beneficial effects than pulsatile perfusion technique for human organ systems.[11]

Hypotension itself may decrease ocular perfusion pressure. Deliberate hypotension may decrease intraocular pressure, but this was not demonstrated in a porcine model.[12] MAP was maintained within the normal range in the off-pump group. However, mean arterial pressures decreased with the introduction of CPB in pulsatile and non-pulsatile groups. The decrease in IOP was also parallel to the decrease in MAP levels.

In the literature, there are few papers investigating the relationship between CABG and IOP. In a recent study effects of pulsatile CPB and non-pulsatile CPB on the IOP were investigated, a comparison of two groups demonstrated that there were significant differences at before CPB and after CPB 5th-minute measurements.[13] Our study also revealed CPB decreased the IOP and additionally assured that off-pump CABG had not affected the IOP.

In the current study, the mean IOP levels in all groups were maintained between 6.5 ± 2.5 and 20.3 ± 3.9 mmHg throughout the study time points. Our results were similar to the findings of Hayashi et al.[1] In our study, the lowest and the highest IOP levels were 5.5 ± 4.3 and 19.9 ± 4.9 mmHg respectively. Changes in the balance of aqueous humor production and drainage and reduction of choroidal blood volume were shown as possible responsible mechanisms that were also affected by the changes mainly in central venous pressure.[1] As a conclusion of this study, they could not make an exact comment on the clinical importance of these IOP changes in cardiac surgery.[1] More recently, Hoshikawa et al.[4] tried to show the effect of steep Trendelenburg position on IOP during robotic-assisted radical prostatectomy. In their study, the maximum detected IOP level was 36 mmHg. They concluded that IOP increased in a time-dependent manner in study patients due to the steep Trendelenburg position. Despite this increase in IOP levels, there were no significant changes in visual function and no complications.

However, there is no previously published data regarding the safe limits for transient IOP decreases and elevations. Several glaucoma studies have demonstrated that optic nerve damage depends on IOP, but there are other important factors such as optic nerve circulation, age, race, and genetics. Compared to other surgery types, ocular changes in cardiac surgery have not been studied in detail.[14]

In the literature, there are some cases of ischemic optic neuropathy after a minimally invasive prostatectomy with a longer duration than 6 hours and with a blood loss greater than 1000 mL.[12] There is no guarantee that complications can occur after any standard surgical procedure. Ischemic optic neuropathy and vision loss are complications of CABG. Awareness of these complications is important to early diagnosis, appropriate treatment, and developing safer surgical techniques.[15]

Although it may go asymptomatic, low IOP may be associated with clinically visible choroidal expansion and shallowing of the anterior chamber. In some eyes, low IOP produces hypotony maculopathy.[5] However, in the current study, IOP levels of the patients did not decrease as low as 5 mmHg, corroborating the results of Hayashi et al.

Conclusion

This study has demonstrated that intraocular pressures remain in the normal ranges during CABG surgery regardless of the technique (pulsatile/non-pulsatile on-pump or off-pump surgery). Transient fluctuations in IOP levels during several surgery types may be safe. Although there is autoregulation, we still do not have any information on the factors that affect this regulation system and its clinical implications. In patients with clinically proven glaucoma, we may take some precautions to prevent postoperative complications, but in patients with no previous diagnosis unexpected complications may be observed. Therefore, it should be kept in mind that patients should be avoided from long and extreme Trendelenburg positions and low CVP-MAP levels during cardiac surgery to prevent eye-related complications.

Conflicts of interest

The authors declare no conflicts of interest.

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