No significant retinal damage induced by major orthopedic surgery – a pilot study

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Background. Perioperative visual loss is one of the rare but devastating complications of anesthesia and surgery. The incidence of less severe or even subclinical postoperative visual dysfunction is unknown. Therefore, we decided to perform a pilot prospective observational clinical study to evaluate whether structural changes of the retina can be detected in patients undergoing elective orthopaedic surgery by optical coherence tomography (OCT).
Methods. Adult patients indicated for elective knee replacement surgery with the absence of known retinal or optic nerve disease were included. Each patient underwent baseline OCT examination of the eyes one day before surgery and it was repeated 4-7 days after the surgery. The surgery was done under general and epidural anesthesia.
Results. A total of 18 patients (6 men and 12 women) at the age of 70.8±7.1 years were enrolled. We found statistically significant changes in the Macular central thickness and in a few areas of the Retinal Nerve Fiber Layer between the baseline and postoperative measurements.
Conclusions. Even though we found significant changes in some parameters, we did not confirm that general anesthesia and/or surgical damage causes significant damage of the retina using OCT measurement.
Trial Registration: ClinicalTrials.gov (NCT 04311801)

Key words: anesthesia, optical coherence tomography, orthopedic surgery

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INTRODUCTION

Perioperative visual loss is one of the rare but devastating complications of surgery under general anesthesia with a reported incidence of 1 case for 60000–125000 anesthesia[1]. The incidence of less severe or subclinical postoperative visual dysfunction (POVD) and etiology of this complication has not been recognized yet. One of the structures that can be potential target of induced damage is the retina. However, on our best knowledge, the influence of surgery and general anaesthesia on retina`s structure has never been investigated. This contrasts with that visual impairment, although subclinical, may significantly affect the subsequent quality of life of patients undergoing surgery. Therefore, this problem needs to be addressed.

One way to investigate potential induced retinal damage is by Optical Coherence Tomography (OCT). The OCT is a non-contact, non-invasive transpupillary diagnostic method which can easily assess retina`s layers with high resolution[2]. This enables identification of microscopic structural changes of retina and optic nerve. In clinical practice, OCT is useful in diagnosing many eye conditions, including diabetic retinopathy, macular edema, macular hole, macular pucker, glaucoma etc[3]. It is also a potentially suitable method for POVD research.

Therefore, we decided to perform a pilot prospective observational clinical study to evaluate whether any postoperative retinal damage recognized by the OCT investigation may be detected in the patients undergoing elective knee replacement surgery under combined general and epidural anesthesia.

METHODS

We carried a prospective observational clinical study of adult patients undergoing elective knee replacement surgery under combined general and epidural anesthesia. It was approved by the ethics committee (Ethics Committee, Masaryk Hospital Usti and Labem, Czech Republic, reference code 236/59). The study was conducted in accordance with the Helsinki Declaration and good clinical practice. Informed consent was required for all patients to sign before inclusion to the study. The study has been retrospectively registered and assigned by trial registration number NCT 04311801.

Selection of Participants

Adult patients undergoing elective knee replacement surgery from January to June 2018 were evaluated for eligibility for inclusion to the study. Inclusion criteria were awake adult patient indicated for elective knee replacement surgery under combined general and epidural anesthesia at the Masaryk Hospital in Usti and Labem, the Czech Republic with the absence of known retinal or optic nerve disease. The exclusion criteria were as follows: Glasgow coma scale score <15, age <18 years, the absence of known structural eye disease excluding refractive disorder, inability to undergo OCT examination and refusal to sign informed consent.

Protocol

The patients were screened for eligibility during pre-anesthetic visit that took place one day before planned surgery. After obtaining informed consent, they were referred to OCT examination in the Ophthalmology clinic at the same day. The result of OCT examination was blinded to the anesthetist and to the patient unless it could potentially have an impact on the anesthesia and surgery at the discretion of the investigating ophthalmologist. Anesthesia, surgery and postoperative care were performed in accordance with the recent guidelines[4]. Between the fourth and the seventh postoperative day, the patients underwent control OCT examination. Their participation in the study was then terminated. Baseline medical history and clinical data, the data on the course of anesthesia, surgery and postoperative care and the results of OCT examinations were recorded for further analysis.

Surgery and Anesthesia

Complete pre-anesthetic assessment including discussing the plan of anesthesia was performed in the anesthesia ambulance. According to our standards, no premedication was administered. All patients received combined general and epidural anesthesia for the surgery. In the operating room, epidural catheter was placed by loss of resistance technique at the level of L2-L3 or L3-L4 disc level and epidural infusion of Bupivacaine Hydrochloride 0.25% solution and sufentanil was maintained during the surgery. General anesthesia was initiated with propofol 2% solution (2 mg/kg) and sufentanil (0.2 ug/kg) and maintained with sevoflurane. Airways were secured with laryngeal mask LMA® Supreme™ (Teleflex Inc., Triangle Park, NC, USA). All patients underwent total knee replacement surgery following the recent guidelines[4]. Duration of surgery was defined as the time interval from skin incision to closure in minutes. After the surgery, all patients were recovered from anesthesia at the post-anesthesia care unit and then transported to surgical intensive care unit to stay there at least for 2 days. Thereafter, the patients were transferred to a ward where they stayed until hospital discharge.

Optical coherence tomography

OCT is an imaging diagnostic method that depicts in detail sections of the retina and optic nerve that may change due to ocular disease. It uses low-coherence light to capture high-resolution images of investigated tissues. The parameters we measured to evaluate status and potential structural changes of macula were Macular Total Volume (MTV, mm3), Macular Center Volume (MCV, mm3) and Macular Total Thickness (MTT, μm) (ref.[5,6]). The Retinal Nerve Fiber Layer (RNFL, μm) formed by the expansion of the axons of the optic nerve was also measured. Its thickness was evaluated as global thickness (RNFL G) and regional thickness in several segments of ocular fundus: superior-temporal (RNFL TS), superior-nasal (RNFL NS), inferior-nasal (RNFL NI), inferior-temporal (RNFL TI), temporal quadrant (RNFL T), nasal quadrant (RNFL N) (ref.[7]).

Statistical calculations

While there are no relevant data available to calculate the sample size for this specific purpose, we considered this study to be a pilot and carried it out without sample size calculation.

Mean values ± SD or percentages were calculated, as necessary. Normality of continuous variables was assessed using Kolmogorov-Smirnov tests. Comparisons of continuous variables were made using paired Student´s t-test for dependent samples. In all cases a p-value of less than 0.05 was considered significant. All computations were performed using STATISTICA 13.5 software (TIBCO Software Inc., Palo Alto, CA, USA) and Microsoft Excel 2010 (Microsoft, Redmond, WA, USA).

RESULTS

Characteristic of patients

A total of 30 patients were enrolled to the study. Two patients actively refused to undergo postoperative OCT examination. Nine patients were discharged from the hospital before the predefined period for control OCT examination or were discharged during weekend when OCT examination was not available. In one patient, OCT postoperative examination was not performed for technical difficulties. Complete data were collected from 18 patients and these are included in the subsequent analysis. There were 6 men and 12 women included, average age was 70.8 ± 7.1 years. All were indicated for elective knee replacement surgery for gonarthrosis. Table 1 summaries baseline medical history of the patients and Table 2

Table 1. Baseline medical history of the patients.

Baseline medical history	n (%)
Arterial hypertension	17 (94.4)
Diabetes mellitus	7 (38.9)
Active smokers	4 (22.2)
Hyperlipoproteinemia	9 (50.0)
Ischemic heart disease	4 (22.2)
Congestive heart failure	1 (5.6)
Atrial fibrillation	1 (5.6)
Peripheral vascular disease	1 (5.6)
Chronic pulmonary disease	5 (27.7)
Chronic kidney disease	3 (16.7)
Endocrine disease	3 (16.7)
Gastrointestinal disorder	1 (5.6)
Malignancy	1 (5.6)
Osteoporosis	1 (5.6)
History of psychiatric disease or drug abuse	3 (16.7)

their pre-operative assessment by American Society of Anesthesiologist Physical Status Classification System[8].

Anesthesia and surgery

All patients received combined general and epidural anesthesia. Anesthesia and surgery were performed without complications in all patients. Four patients needed blood derivatives during the surgery. Table 3 shows characteristics of anesthesia, surgery and postoperative care including recorded postoperative complications.

OCT measurements

Table 4 demonstrates the results of repeated OCT measurements. All patients exhibited normal values of all investigated parameters in pre-operative examination.

We identified statistically significant changes in MCT, RNFL TS, RNFL TI, RNFL NI between the baseline and postoperative measurements.

At the follow up examination no patient reported subjective worsening of visual functions.

Table 2. Preoperative ASA classification of the patients.

ASA Physical Status Classification	n
ASA I	0
ASA II	12
ASA III	3
ASA IV	3
ASA V	0
ASA VI	0

Table 3. Characteristics of anesthesia, surgery, and postoperative care.

Anesthesia and surgery	
Duration of surgery (min±SD)	64.44 ± 24.60
Need for vasopressors during anesthesia (n±SD)	0
Number of blood units during surgery (n±SD)	0.2 ± 0.5
Postoperative care and complications	
Number of ICU days (days±SD)	2.2 ± 0.5
Number of days in the ward (days±SD)	10.6 ± 5.3
Postoperative atrial fibrillation (n)	2
Deep venous thrombosis (n)	1
Nosocomial infection (n)	1

ICU, intensive care unit

DISCUSSION

The main finding of presented study is that a total knee replacement surgery under combined general and epidural anesthesia was not associated with any retinal damage detectable by repeated OCT measurement.

It has been reported that one of the complications of major surgery under general anesthesia may be a vision loss[1,9-11]. To the best of our knowledge, clear evidence explaining pathophysiological mechanism, incidence and outcome of the visual loss and its relation to the technique of anesthesia or the surgical procedure does not exist. Moreover, we believe that apparent vision loss represents massive clinical damage, which may represent the imaginary tip of the iceberg of potentially more frequent sub-

Table 4. Results of repeated OCT measurements.

Parameter	Baseline measurement	Postoperative measurement	*P*
MTV (mm^3±SD)	8.39 ± 0.6	8.38 ± 0.6	0.400
MCT (μm±SD)	273.89 ± 30.72	271.72 ± 29.46	0.004
MCV (mm^3±SD)	0.22 ± 0.03	0.21 ± 0.02	0.180
RNFL TS (μm±SD)	132.53 ± 20.99	135.69 ± 20.66	0.008
RNFL NS (μm±SD)	105.64 ± 22.61	108.89 ± 20.94	0.040
RNFL T (μm±SD)	71.55 ± 14.57	72.63 ± 15.65	0.144
RNFL G (μm±SD)	98.33 ± 13.5	99.36 ± 14.99	0.300
RNFL N (μm±SD)	76.52 ± 14.93	77.36 ± 14.65	0.100
RNFL TI (μm±SD)	135.92 ± 31.75	139.22 ± 32.45	<0.001
RNFL NI (μm±SD)	116.89 ± 25.89	119.14 ± 26.78	<0.001

clinical vision damage induced by surgery under general anesthesia. POVD can potentially occur at any level of the oculocerebral pathway, however, the most sensitive part of the system is probably the retina[12,13].

Therefore, we decided to evaluate the presence of potential morphological postoperative retinal damage in our study. OCT examination is an established and reliable non-invasive method that can detect even exceptionally fine retinal damage and that is why we used this method[5].

Facing the idea that a typical manifestation of perioperative retinal damage is retinal edema, we mostly concentrated on the MTV, MCT and MCV parameters. Out of these, we identified a statistically significant change only in MCT in terms of reduction. However, a typical OCT finding of retinal edema is retinal thickening and generally, it is reflected by all parameters[6,14,15]. Moreover, the MT reduction observed in our study was not clinically relevant and occurred only in right eyes. Thus, we conclude, that no postoperative morphological retinal damage was found in our study.

We also evaluated the RNFL thickness map to detect the presence of potential defects in axonal layer of optic nerve. This is represented by changes in central and general RNFL parameters, but we did not identify any differences between pre- and post-operative evaluation[6,14,16]. On the contrary, we detected a statistically significant changes in peripheral RNFL zones (RNFL TS, RNFL NS, RNFL TI, RNFL NI). Changes in these segments are related mainly to the retinal vessels which run in these zones. Their volume may physiologically fluctuate, and this may be recognized by OCT measurements[17,18]. Thus, we did not identify any defects in retinal nerve fiber layer which could represent the damage induced by major surgery under combined general and epidural anesthesia.

Study limitations

There are several study limitations in our study. First, this is the first study evaluating this topic. Therefore, we did not calculate sample size for the absence of relevant input data. The results of this feasibility preliminary study will be used for sample size calculation of the subsequent studies targeting to the OCT examination. Second, several patients did not complete the study, but this was mainly for technical reasons. Third, we evaluated only morphological, but not functional parameters of the eye.

CONCLUSION

In the presented study evaluating patients who underwent a total knee replacement surgery we did not find any morphological retinal changes induced by surgery or combined general and epidural anesthesia. These results do not explain the mechanism of POVD and indicate, that morphological OCT examination as the sole investigative procedure may not be a suitable approach for POVD research. In further studies, also functional characteristics must be evaluated.

ABBREVIATIONS

ICU, Intensive care unit; MCV, Macular central volume; MTV, Macular total volume; MTT, Macular total thickness; OCT, Optical coherence tomography; POVD, Postoperative visual dysfunction; RNFL, Retinal nerve fiber layer; RNFL G, Retinal nerve fiber layer global thickness; RNFL N, Retinal nerve fiber layer nasal quadrant; RNFL NI, Retinal nerve fiber layer inferior-nasal quadrant; RNFL NS, Retinal nerve fiber layer superior-nasal quadrant; RNFL T, Retinal nerve fiber layer temporal quadrant; RNFL TI, Retinal nerve fiber layer inferior-temporal quadrant; RNFL TS, Retinal nerve fiber layer superior-temporal quadrant.

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