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Original Article

Impact of hypoxic and mesopic environments on visual acuity, contrast sensitivity and accommodation in subjects with LASIK surgery and aircrew candidate

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Abstract

Background: The safety of Laser-assisted in situ keratomileusis (LASIK) in aircrew was unclear, in addition, LASIK was not yet approved for aircrew of Taiwan Air Force. This study was aimed to evaluate visual performance in LASIK eyes in hypoxic and twilight environment.
Methods: 48 myopic eyes of 24 subjects enrolled in this study were divided into LASIK group and control group. Subjects were exposed in hypoxic (15% O_2) and mesopic (3 cd/m^2) environment. Visual performance was evaluated using the Early Treatment of Diabetic Retinopathy Study (ETDRS) visual chart, and Functional Acuity Contrast Test (FACT) before and after the expirement. Physiological parameters of all subjects were measured and recorded throughout the experiment.
Results: There was no significant difference of the two groups regarding their age, height, weight, and BMI. There is significant difference of preoperative spherical refractive error between the two groups. The results of physiological parameters were similar between two groups. Under normoxic conditions, there were no significant difference regarding distant vision in photopic and mesopic environments, so as for near vision. As a whole, the contrast sensitivity of the LASIK group were lowered than that of the control group about 35%, under whether normoxic or hypoxic conditions; photopic or mesopic circumstances. Under normoxic conditions, the measured accommodation of the LASIK group were 21% lowered than that of the control group and 31% lowered under hypoxic circumstances.
Conclusion: There was no significant difference of visual acuity between the two groups regarding hypoxic and mesopic environment, but reduced contrast sensitivity was significant in LASIK group as compared to those of the control group. Accommodation was significantly lowered in LASIK group, compared with control group, in hypoxic environment. Whether postoperative visual performance after LASIK in aircrew during flying duty is safe might need further investigation.

Keywords: Accommodation; Aircrew safety; Contrast sensitivity; Hypoxic; LASIK surgery; Mesopic environment; Visual acuity

1. Introduction

In high altitude environment, pilots have to tolerate a variety of high-altitude environmental pressures, including hypoxia, low pressure and low brightness, etc. The atmospheric pressure falls as going higher altitude and decreases the partial pressure of oxygen inspired by the lungs, which ultimately leads to hypoxia. During flying at high altitude, pilots have a relatively hypoxic state inside the Cockpit despite the cockpit pressurization system. With increasing altitude, the visual sense is the first to receive hypoxic damage, thus, hypoxia related visual disturbances are important in aviation medicine. Previous studies reported that a pilot's hypoxia may

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affect contrast sensitivity, field of vision, color vision and even affect the rate of dark adaptation.[1−4]

The nighttime flight environment is also a disadvantage for pilots. A pilot with vision 1.0, diopter −0.25D during normal daylight could reduce his vision to 0.5 to 0.7 and refraction to −0.5 to −0.75 D if flying at night.[5] Visual performance in low-light conditions (dark vision) is mediated by the cone-rod cells of the retina without assistance of most retinal cells, so the visual quality in low-light conditions is poorer than in photopic environments.[6]

Although there are many previous studies on the pilot's visual performance in hypoxia and low light conditions, there is no conclusive evidence of changes in accommodation power during flight. The increasing prevalence of myopia in general population lead to shortage of national army flight students in near future. So it is necessary to standardize the vision correction procedures that does not affect the combat effectiveness and flight safety.

Currently, laser-assisted in-situ keratomileusis (LASIK) is the most common and safest surgical method in refractive eye surgery. It restores rapid recovery, high accuracy and less pain, and most importantly, with no frame glasses and contact lenses ever.

Although some studies revealed visual acuity under dark conditions is slightly impaired after the LASIK surgery[7,8]; other studies suggested that visual acuity after LASIK did not change much (including contrast, corneal curvature, and refractive error, etc.).[9] Further, most studies evidenced that myopic shift and related vision loss[10] occur under hypoxic conditions. The visual conditions (including visual acuity, contrast sensitivity and regulatory capacity) after LASIK surgery are still controversial, and the current visual performance in the flying environment after LASIK surgery is also not clear. Therefore, the purpose of this research is to evaluate whether there exist significant difference of visual performance post LASIK (including vision, contrast sensitivity and accommodation), under separately the condition of altitude hypoxia (about 8000 feet, oxygen concentration 15% O2) and mesopic environment (3 cd/m2) in a stimulated aircraft cabin environment, in comparison with the visual performance from normal eyes, anticipating it would provide our air force a reference for whether LASIK should be open for vision correction in the future.

2. Methods

This research prospectively recruited subjects from Ophthalmology Clinics and had passed the verification from Institutional Review Boards from Tri-Service General Hospital (TSGHIRB No 2-101-05-087). Subjects were divided into two groups: those who had undergone LASIK surgery (the experiment group) at least 1 month, and those who had not undergone LASIK surgery (the control group).

All subjects aged between 20 and 35, gender not restricted, with signed informed consent required. Subjects should have no known remarkable medical history (including respiratory, cardiovascular disease), and no other ocular diseases (including cataract, glaucoma, impaired accommodation/oculomotor/contrast/color sensation/visual field, uncorrectable refractive error). Subjects who were pregnant, coincided with ocular infection, or under other Ophthalmology clinical trial were excluded from the experiment. The spherical equivalent refractive error of the control group should be less than −6.00 diopters, astigmatism rating less than −1.00 diopters. And the spherical equivalent refractive error of experiment group should also be less than −6.00 diopters, astigmatism rating less than −1.00 diopters, at least three months post LASIK surgery, and corneal flap was verified to be stabilized. Monocular visual acuity of the control group should reach at least 20/20 vision after corrected by soft (hydrophilic) contact lens; monocular visual acuity of the experiment group should reach bare eye sight at least 20/20 vision. If any self-discomfort (including palpitations, dizziness, red, swollen, itchy or overproduction of secretions of eyes) was noted, subjects should stop participating the project immediately.

2.1. The control group

28 myopic eyes of 14 subjects were enrolled in the control group, including 7 males and 7 females. The mean age was 27.86 ± 1.11 yr. The mean body mass index (BMI) was 21.69 ± 0.72, with mean height 167.79 ± 2.59 cm and mean weight 61.71 ± 3.30 kg. The mean spherical equivalent refractive error was −4.68 ± 0.47 D, with the mean myopia −4.23 ± 0.46 D and the mean astigmatism −0.96 ± 0.10 D.

2.2. The experiment group (the LASIK group)

20 myopic eyes of 10 subjects were enrolled in the LASIK group, including 2 males and 8 females. The mean age was 31.10 ± 1.08 yr. The mean BMI was 22.21 ± 0.73, with mean height 163.40 ± 2.24 cm and mean weight 59.50 ± 2.66 kg. Before LASIK, the mean spherical equivalent refractive error was −5.66 ± 0.18 D, with the mean myopia −5.28 ± 0.17 D and the mean astigmatism −0.75 ± 0.05 D. The mean post-surgery time was 3.60 ± 0.48 yr. After LASIK, the mean spherical equivalent refractive error was −0.69 ± 0.18 D, with the mean myopia −0.50 ± 018 D and the mean astigmatism −0.45 ± 0.05 D.

2.3. SofLens daily disposable (hilafilcon B) visibility tinted contact lenses

The brand name was Bausch & Lomb, country of origin is England, Department of Health approved ID number 018,385, the component part was hydrogel, with 41% hilafilcon B and 59% water, preserved in phosphoric acid buffered normal saline. Reactive Blue Dye 246 was added to the contact lenses which provide the light-blue appearance of lenses and contribute to its convenience. This was daily disposable kind of contact lens, and should be removed before bedtime, and replaced with new one each day.

2.4. iTrace ray tracing wavefront aberrometer and corneal topography

The brand name was Tracey Technologies, country of origin was the United States. iTrace, with the combination of Wavefront aberrometer and corneal topographer, was capable of measuring aberration and corneal curvature respectively. Wavefront aberrometer projects 168 spotted onto the retina with a Matrix Beam, and extracted the image produced by the Matrix Beam, the difference between both was the aberration. Therefore, Wavefront aberrometer was utilized to measure low order (refraction of eye) and high order aberration.[11] During our experiment, the aberration of the subjects were conversed to spherical equivalent in order to select appropriate contact lenses. Wavefront aberrometer also utilized the image difference from reflected beam and conversed to accommodation needs [unit: diopter (D)] while the subjects were asked to stared at sight markers of varied distance. When evaluating the amplitude of accommodation with iTrace, the set distance of close range sight markers could be chosen from 60 cm, 50 cm, 40 cm, 33 cm, and 25 cm, with the corresponding accommodation needs as 1 D, 2 D, 2.5 D, 3 D, and 4 D, due to the limitation of experimental environment and illumination, the sight markers were set at 4 m and 33 cm, with the corresponding accommodation needs as 0.25 D and 3 D, therefore, amplitude of accommodation of this experiment is 2.75 D.

2.5. Functional vision analyzer

The brand was Stereo Optical, country of origin was the United States. Multifunction vision analyzer was provided with 12 sets of pictures (total of 150 sets of pictures for select and interchange), to test monocular or binocular functional vision evaluation (including contrast sensitivity, stereoscopic sense, color vision, potential vision, visual field) by day or night, under situations with or without glare and corrected vision; it was also capable of making comparisons between the image that patients observe and the original ones (mainly by color resolution of the two pictures, clarity of the objects' edges, and contrast of the objects' color) under following five stimulated scenes: eye chart, streetscape, newspaper, distant view and driving at night. It was mainly used for evaluating daytime/nighttime vision and contrast sensitivity.[12]

2.5.1. Visual acuity

Utilizing Early Treatment Diabetic Retinopathy Study (ETDRS) could measure vision acuity at distant and near distance at 20 ft and 40 cm, in photopic environment (85 cd/m2), and in mesopic environment (3 cd/m2), monocularly or binocularly.

2.5.2. Contrast sensitivity

Utilizing Functional Acuity Contrast Test (FACT), distance set at 20 ft, could measure contrast sensitivity in photopic environment (85 cd/m2), and in mesopic environment (3 cd/m2), monocularly or binocularly. This test was composed of 5 sets of circular figures with black and white lines, directions of lines can be right, up or left. The spatial frequency represented by each group were categorized into group A (1.5 cpd), group B (3 cpd), group C (6 cpd), group D (12 cpd), and group E (18 cpd), each group containing 9 contrast degrees.

2.6. Mercury sphygmomanometer

The brand was Spirit, country of origin was Taiwan. The mercurial sphygmomanometer was mainly used for monitoring tested subjects blood pressure before, during and after exposed to a hypoxic environment.

2.7. Pulse oximeter

The brand was Risung Medical Equipment, product model RPO-50 E, country of origin China. The oximeter could measure blood oxygen saturation (SpO2) and pulse simultaneously, it was utilized in this experiment mainly to monitor the change of SpO2 and pulse of the subjects before, during and after exposed to a hypoxic environment, also to verify the status of decreasing blood oxygen while the subjects were under hypoxic environment.

2.8. Photometer

The brand was SEKONIC, product model L-398 A, made in Philippines. Illuminometer was used in this experiment mainly before the start of project, to measure the brightness of environment, and to make sure it belonged to either mesopic (3 cd/m2) or photopic (85 cd/m2) environment.

2.9. Hypoxic environment

15% oxygen (O2) post inspection and verification, the brand was TOYO GAS, country of origin Taiwan. It went with breathing tube, air bag, deflator valve, nasal clip and enabled the subjects to be exposed to a hypoxic environment which was similar to the aircraft cabin environment in order to measure the variation of their visual performances. Different from the normal 21% O2 which was inhaled in normal condition, the 15% O2 which was inhaled by the subjects was a stimulation to a 8000 feet (2438 m) high altitude (correspond to the oxygen concentration in a cabin of an ordinary transport aircraft).[1]

2.10. Protocol

This experiment took the methods from past research of hypoxic and mesopic environment,[1,2] as further research for associated documents.The refractive state of the subjects were measured by iTrace Wavefront aberrometer, including spherical correction, cylinder correction and axis of astigmatism, in order to select appropriate subjects. Regarding physiological parameters measurement, 10 min after the subjects have entered the laboratory, the physiological parameters, including

blood pressure (BP), heart rate (HR), and oxyhemoglobin saturation by pulse oximetry (SpO2) were measured in sitting position. The measured lens power of the subjects from the control group were first converted into the lens power of the contact lenses, then these subjects were asked to wear the appropriate contact lenses. After the subjects from the control group had worn the contact lenses, they should adapted for about 3 min. The two groups of subjects should be instructed of ETDRS eye chart and FACT scale before the experiment started, far-sight vision (4 m) and near sight vision (33 cm) are checked after 3–5 min. The eyesight of the control group after wearing contact lenses, and bare eyesight of the experiment group after surgery were made sure to be equal or greater than 20/20. In order to examine visual performance, subjects were divided into two groups: normal oxygen level of flow and low oxygen level of flow, the order of priority of which were chosen randomly. Similar to the previous research flow, before checking the vision, all subjects should wear eye cover and go through 10 min of dark adaptation at a dark room, 5 min of low light level environment adaptation (3 cd/m2) before measuring the visual performance at a low light level environment, then went through 5 min of light adaptation (85 cd/m2) before measuring the visual performance at a light environment. The tested items of visual function included visual acuity, contrast sensitivity, and accommodation. Not only should the subjects' physiological parameters (including blood pressure, heart rate and oxyhemoglobin saturation by pulse oximetry, to make sure that the tested subjects is under physiologically hypoxemic state while inhaling 15% O2) be measured 10 min after they enter the laboratory, these physiological parameters should also be measured before (pre-), during (mid-), after (post-) the exposure to the hypoxic flow, and 10 min after all of experimental processes had been completed.

2.11. Data analysis

Visual function data were converted and exported by Eye View®. VA value went through logarithmic transformation, and was statistically analyzed by log MAR. All data were expressed in Mean ± Standard error. The data were analyzed by SAS 9.4. Comparisons between LASIK group and control group were analyzed by Wilcoxon signed-rank test if within group comparison and Mann–Whitney U test if between groups comparisons. Figures were made by R 3.3.1.

3. Results

3.1. Basic information

The 14 subjects from the control groups include 7 male and 7 female, 28 eyes in total. The mean age was 27.86 ± 1.11 years old (24–35 years old), mean height was 167.79 ± 2.59 cm, mean weight was 61.71 ± 3.30 kg, and mean BMI was 21.69 ± 0.72 (Table 1). The mean spherical refractive error was −4.23 ± 0.46 D, mean cylindrical refractive error −0.96 ± 0.10 D, mean spherical equivalent −4.68 ± 0.47 D (Table 2). The 10 tested subjects from the LASIK groups include 2 male and 8 female, 20 eyes in total. The mean age was 31.10 ± 1.08 years old (25–35 years old), mean height was 163.40 ± 2.24 cm, mean weight was 59.50 ± 2.66 kg, and mean BMI was 22.21 ± 0.73 (Table 1). The mean preoperative spherical refractive error in the LASIK group was −5.28 ± 0.17 D, mean cylindrical refractive error −0.75 ± 0.05 D, mean spherical equivalent −5.66 ± 0.18 D; the mean postoperative period was 3.60 ± 0.48 years (1–7 years), the mean postoperative spherical refractive error was 0.50 ± 0.18 D, mean cylindrical refractive error −0.45 ± 0.05 D, and mean spherical equivalent −0.69 ± 0.18 D (Table 2).

Table 1
Demographic data of gender, age, body height, body weight, and BMI in the KASIK and control group. There is no significant difference between the two groups.

Characteristic	Control Group	LASIK Group
Sex (male)	7 (50%)	2 (25%)
Age	27.86 ± 1.11	31.10 ± 1.08
Height	167.79 ± 2.59	163.40 ± 2.24
Weight (kg)	61.71 ± 3.30	59.50 ± 2.66
BMI (kg/m^2)	21.69 ± 0.72	22.21 ± 0.73

There was no significant difference of the two groups regarding their basic information, including age ($p = 0.06$), height ($p = 0.24$), weight ($p = 0.63$), and BMI ($p = 0.63$). Regarding of their refractive status, significant difference of preoperative spherical refractive error did exist between the control group and the experimental group ($p = 0.04$), but no significant difference was observed in the aspect of preoperative mean cylindrical refractive error and mean spherical equivalent ($p = 0.08$ and 0.06).

3.2. Physiological change

3.2.1. Control group

The baseline physiological parameters of the control Group 5 min after entering the laboratory were as follows: mean systolic blood pressure (SBP) 106.1 ± 4.2 mmHg, mean diastolic blood pressure (DBP) 69.3 ± 3.0 mmHg, mean heart rate 78.9 ± 2.1 bpm, mean saturation of peripheral oxygen (SpO2) 97.3 ± 0.2%; the measured pre-hypoxia data were as follows: mean SBP 107.1 ± 4.3 mmHg, mean DBP 69.6 ± 3.0 mmHg, mean heart rate 79.0 ± 2.2 bpm, mean saturation of peripheral oxygen (SpO2) 97.2 ± 0.2%; the measured mid-hypoxia data as follows: mean SBP 105.4 ± 4.6 mmHg, mean DBP 69.6 ± 3.5 mmHg, mean heart rate 85.3 ± 3.8 bpm, mean saturation of peripheral oxygen (SpO2) 90.9 ± 0.5%; the measured post-hypoxia data as follows: mean SBP 106.1 ± 3.8 mmHg, mean DBP 70.4 ± 3.1 mmHg, mean heart rate 85.1 ± 3.4 bpm, mean saturation of peripheral oxygen (SpO2) 90.7 ± 0.5%; The measured parameters 5 min after completion of the experimental processes as follows: mean SBP 105.7 ± 4.1 mmHg, mean DBP 68.6 ± 3.1 mmHgmean heart rate 78.9 ± 2.0 bpm, mean saturation of peripheral oxygen (SpO2) 97.3 ± 0.2%.

Table 2
The comparisons of mean spherical refractive error, mean cylindrical refractive error and mean spherical equivalent between LASIK (20 myopic eyes in 10 subjects)and control groups (28 myopic eyes in 14 subjects) and postoperative time in LASIK group.

Characteristic	Control Group (N = 14)	LASIK Group	
		Preoperative (N = 10)	Postoperative (N = 10)
spherical refractive error	−4.23 ± 0.64	−5.28 ± 0.18**	−0.50 ± 0.24
cylindrical refractive error	−0.96 ± 0.11	−0.75 ± 0.07**	−0.45 ± 0.05
spherical equivalent	−4.68 ± 0.66	−5.66 ± 0.18**	−0.69 ± 0.22
postoperative time	–	–	3.60 ± 0.7 (1–9 years)

** Notation** means that the p-value is < 0.01 of comparisons between preoperative of LASIK group and control group under the Mann–Whitney U test.

As expected, for the control group, compensatory increase of heart rate were noted under 15% O2 (mid-hypoxia) and post-hypoxia condition, with significant difference ($p = 0.02$ and 0.03); so were the lowered saturation of peripheral oxygen (SpO2) under 15% O2 (mid-hypoxia) and post-hypoxia condition, with significant difference ($p = 0.00$ and 0.00)). (data not shown)

3.2.2. LASIK group

The measured parameters of the LASIK Group 5 min after entering the laboratory were as follows: mean SBP 100.2 ± 2.9 mmHg, mean DBP 64.5 ± 2.0 mmHg, mean heart rate 80.3 ± 4.8 bpm, mean SpO2 97.4 ± 0.3%; the measured pre-hypoxia data were as follows: mean SBP 98.5 ± 3.0 mmHg, mean DBP 65.5 ± 2.2 mmHg, mean heart rate 76.4 ± 2.8 bpm, mean SpO2 97.3 ± 0.3%; the measured mid-hypoxia data as follows: mean SBP 101.3 ± 2.3 mmHg, mean DBP 67.5 ± 2.1 mmHg, mean heart rate 79.9 ± 2.4 bpm, mean SpO2 91.0 ± 0.5%; the measured post-hypoxia data as follows: mean SBP 101.0 ± 2.7 mmHg, mean DBP 68.0 ± 2.0 mmHg, mean heart rate 82.4 ± 2.3 bpm, mean SpO2 91.0 ± 0.6%; the measured parameters 5 min after completion of the experimental processes were as follows: mean SBP 99.0 ± 2.8 mmHg, mean DBP 65.5 ± 2.4 mmHg, mean heart rate 76.5 ± 2.0 bpm, mean SpO2 97.3 ± 0.2%.

The results were similar among the LASIK group and the control group, there were a compensated raise of heart rate noted under a hypoxic 15% O2 condition (mid-hypoxia) and post-hypoxia condition, with statistical significant difference (p value equals to 0.05 and 0.00); the SpO2 also declined as expected under a hypoxic 15% O2 condition (mid-hypoxia) and post-hypoxia condition, with statistical significant difference ($p < 0.01$). (data not shown).

3.3. Visual acuity

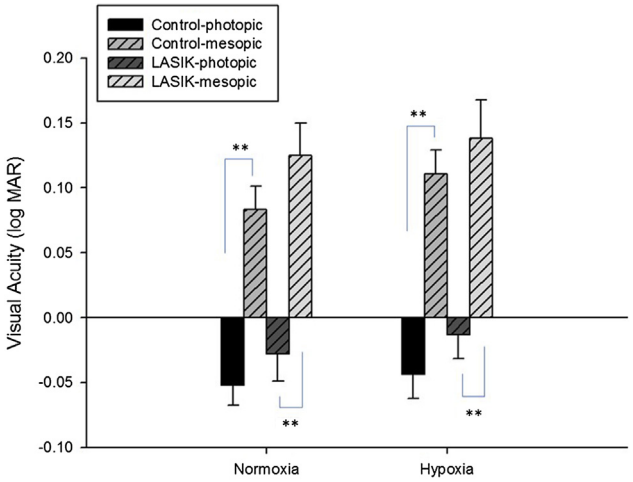
3.3.1. Control group

The VA value went through logarithmic transformation, were expressed in log MAR value then statistically analyzed. Under normoxic conditions, the measured distant vision were −0.05 ± 0.02, and near vision were −0.07 ± 0.01 for photopic environments; distant vision were 0.08 ± 0.02 in a mesopic environment, there exists statistical significant difference ($p = 0.00$) between the two measured distant vision values. Under hypoxic conditions, the measured distant vision were −0.04 ± 0.02, and near vision were −0.05 ± 0.02 for photopic environments; distant vision were 0.11 ± 0.02 for mesopic environment, statistical significant difference (p = 0.00) also exists between the two measured distant vision values (Fig. 1).

3.3.2. LASIK group

The VA value went through logarithmic transformation, were expressed in log MAR value then statistically analyzed. Under normoxic conditions, the measured distant vision were −0.03 ± 0.02, and near vision were −0.01 ± 0.02 in photopic environments; distant vision were 0.13 ± 0.02 in mesopic environments, there exists statistical significant difference ($p = 0.00$) between the two measured distant vision values.

Under hypoxia environments, the measured distant vision were −0.01 ± 0.02, and near vision were −0.09 ± 0.02 for photopic environments; distant vision were 0.14 ± 0.03 in mesopic environment, statistical significant difference ($p = 0.00$) also exists between the two measured distant vision values. When both were exposed under a photopic environment, in normoxic or hypoxic conditions, there were no statistical significant difference ($p = 0.30$) between the distant vision, or the near vision ($p = 0.50$). And when both were exposed under a mesopic environments, in normoxic or



**p<0.01, photopic vs mesopic under normoxia, control group; photopic vs mesopic under normoxia, LASIK group; photopic vs mesopic under hypoxia, control group; photopic vs mesopic under hypoxia, LASIK group; Wilcoxon signed-rank test

Fig. 1. Comparisons of visual acuity under photopic and mesopic condition regarding normoxia and hypoxia status within and between LASIK and control groups.

hypoxic conditions, there were no statistical significant difference ($p = 0.59$) between the distant vision (Fig. 1).

3.3.3. Intergroup difference

Under normoxic conditions, there were no statistical significant difference regarding distant vision in photopic and mesopic environments ($p = 0.41$, $p = 0.28$). The results from hypoxia environments were similar, no statistical significant difference existed regarding distant vision in photopic and mesopic environments ($p = 0.17$, $p = 0.56$), and no statistical significant difference as well regarding near vision ($p = 0.09$). (Fig. 1).

3.4. Contrast sensitivity

3.4.1. Control group

Utilizing 5 spatial frequency A (1.5 cycle/degree), B (3 cycle/degree), C (6 cycle/degree), D (12 cycle/degree), and E (18 cycle/degree) as measurement models for contrast sensitivity. The results were as follows: under normoxic conditions, the contrast sensitivity were 54.29 ± 3.67, 108.00 ± 5.40, 136.75 ± 6.91, 55.61 ± 5.99, and 20.36 ± 1.57 when tested in photopic environments; and the contrast sensitivity were 59.25 ± 4.14, 91.07 ± 4.88, 90.79 ± 7.08, 22.29 ± 3.12, and 6.96 ± 0.82 in mesopic environments, there were marginal significance (p = 0.053) at A (1.5 cpd), and statistical significance existed at B (3 cpd), C (6 cpd), D (12 cpd), and E (18 cpd) ($p = 0.01$, 0.00, 0.00, and 0.001), which were lowered 16%, 34%, 60%, and 66% respectively.

Under hypoxic situations, the contrast sensitivity were 46.07 ± 3.85, 91.71 ± 6.42, 122.18 ± 7.63, 47.43 ± 4.62, and 22.96 ± 3.00 when tested in photopic environments; and the contrast sensitivity were 53.61 ± 4.52, 78.00 ± 4.38, 73.71 ± 6.30, 18.54 ± 2.01, and 5.39 ± 0.80 in mesopic environments, there were no statistical significance ($p = 0.14$) at A (1.5 cpd), but statistical significance at B (3 cpd), C (6 cpd), D (12 cpd), and E (18 cpd) ($p = 0.01$, 0.00, 0.00, and 0.00), which were lowered 15%, 40%, 61%, and 77% respectively.

When both were exposed in a photopic environment, under normoxic or hypoxic conditions, there were statistical significance regarding contrast sensitivity at A (1.5 cpd), B (3 cpd), and C (6 cpd), ($p = 0.02$, 0.02, 0.01, 0.22, and 0.39) and were lowered 15%, 15%, and 11% respectively. When both were exposed in a mesopic environments, under normoxic or hypoxic conditions, there were statistical significance regarding contrast sensitivity at B (3 cpd) and C (6 cpd), ($p = 0.21$, 0.01, 0.01, 0.28, and 0.08) and were lowered 14% and 19% respectively. In spatial frequency C (6 cpd), the contrast sensitivity was lowered 11% when exposed under a 15% O2 hypoxia circumstance; lowered 34% when exposed under a mesopic environments; and lowered significantly about 46% when exposed under both hypoxia and mesopic circumstances simultaneously (Fig. 2).

3.4.2. LASIK group

Utilizing 5 spatial frequency A (1.5 cycle/degree), B (3 cycle/degree), C (6 cycle/degree), D (12 cycle/degree), and E (18 cycle/degree) as measurement model regarding contrast sensitivity. The results were as follows: under normoxic conditions, the contrast sensitivity were 51.40 ± 5.39, 75.55 ± 6.24, 94.30 ± 9.89, 43.70 ± 7.40, and 11.55 ± 2.23 when tested in photopic environments; and the contrast sensitivity were 38.30 ± 4.76, 63.40 ± 7.67, 59.05 ± 9.96, 12.10 ± 3.39, and 3.80 ± 1.18 in mesopic environments, statistical significance existed at A (1.5 cpd), C (6 cpd), D (12 cpd), and E (18 cpd) ($p = 0.01$, 0.10, 0.01, 0.00, and 0.00), which were lowered 26%, 37%, 72%, and 67% respectively. Under hypoxic conditions, the contrast sensitivity were 36.35 ± 3.10, 75.20 ± 7.62, 70.05 ± 7.49, 28.35 ± 4.40, and 10.15 ± 1.70 when tested in photopic environments; and the contrast sensitivity were 40.95 ± 5.86, 57.25 ± 6.91, 44.70 ± 7.77, 10.20 ± 2.80, and 2.10 ± 0.55 in mesopic environments, there were statistical significance at B (3 cpd), C (6 cpd), D (12 cpd), and E (18 cpd) ($p = 0.36$, 0.02, 0.00, 0.00, and 0.001), which were lowered 24%, 36%, 64%, and 79% respectively. When both exposed in a photopic environments, under normoxic or hypoxic conditions, there were statistical significance regarding contrast sensitivity at A (1.5 cpd), C (6 cpd), and D (12 cpd), ($p = 0.001$, 0.96, 0.01, 0.02, and 0.22) and were lowered 29%, 26%, and 35% respectively. When both were exposed in a mesopic environments, under normoxic or hypoxic situations, no statistical significance regarding contrast sensitivity were noted at any spatial frequency ($p = 0.54$, 0.26, 0.06, 0.39, and 0.12). In spatial frequency C (6 cpd), the contrast sensitivity was lowered 26% when exposed under a 15% O2 hypoxic circumstances; lowered 37% when exposed in a mesopic environments; and lowered significantly about 53% when exposed under both hypoxia and mesopic circumstances simultaneously (Fig. 2).

3.4.3. Intergroup difference

Under a normoxic conditions and photopic environments, statistical significance were noted at B (3 cpd), C (6 cpd), and E (18 cpd) ($p = 0.65$, 0.001, 0.001, 0.21, and 0.001), and were lowered 5%, 30%, 31%, 21%, and 43% of each spatial frequency; when compared with the control group, notable decline of contrast sensitivity were noted among the LASIK group, with 35%, 30%, 36%, 46%, and 45% decline respectively in each spatial frequency, under mesopic circumstances. Under hypoxia and photopic circumstances, there were statistical significance noted at C (6 cpd), D (12 cpd), and E (18 cpd), ($p = 0.07$, 0.10, 0.00, 0.01, and 0.00), with 21%, 18%, 43%, 40%, and 56% decline respectively in each spatial frequency; when compared with the control group, there were statistical significance among the LASIK group regarding contrast sensitivity at B (3 cpd), C (6 cpd), D (12 cpd), and E (18 cpd), under mesopic circumstances (p = 0.10, 0.01, 0.01, 0.02, and 0.00), with 24%, 27%, 39%, 45%, and 61% decline respectively in each spatial frequency. As a whole, the contrast sensitivity of the LASIK group were lowered than that of the control group about 35%, under whether normoxic or hypoxic conditions; photopic or mesopic circumstances (Fig. 2).

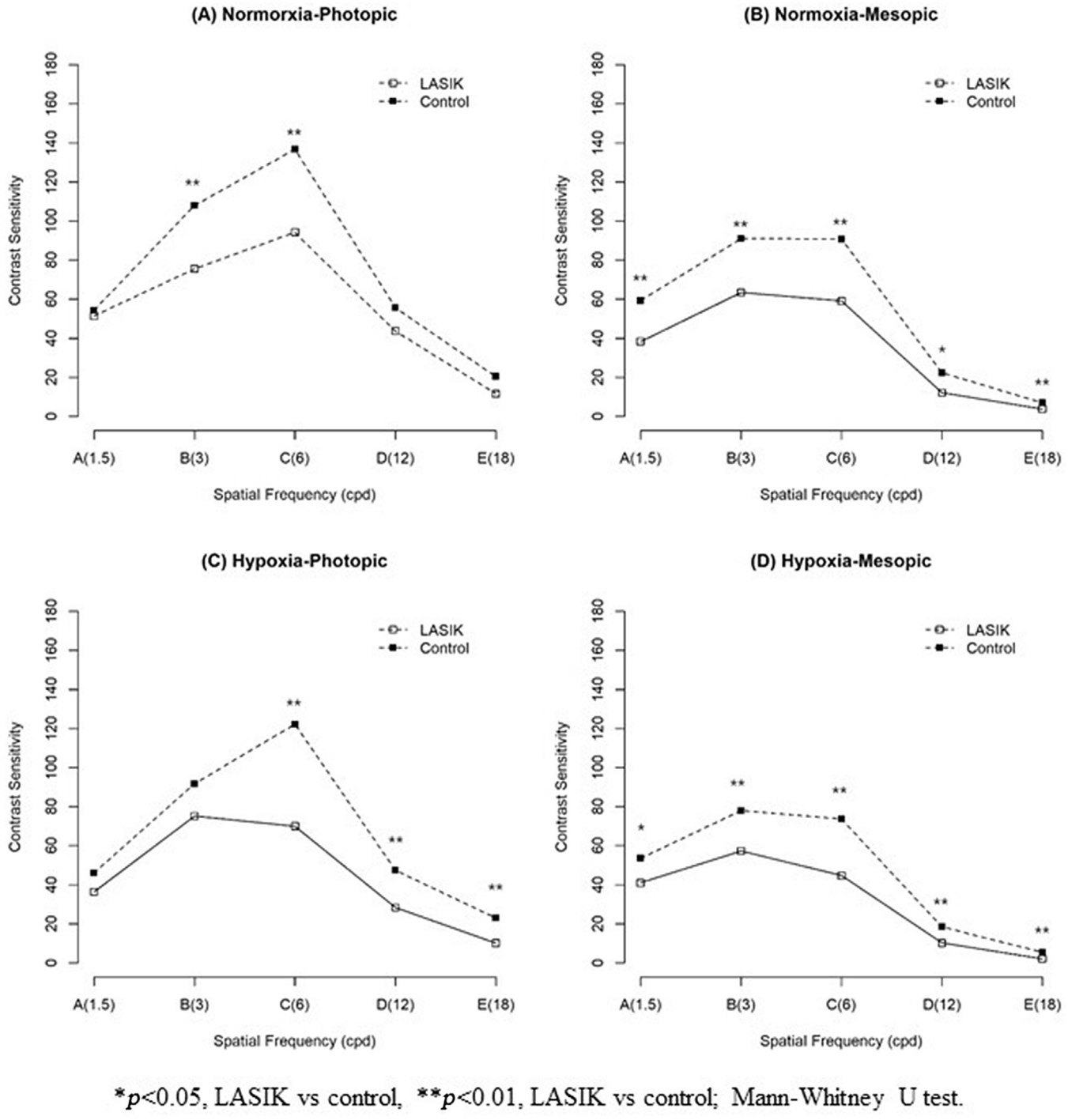


Fig. 2. (A) Comparisons of contrast sensitivity at 5 spatial frequency, A to E, under normoxia-photopic condition between LASIK and control groups. (B) Comparisons of contrast sensitivity at 5 spatial frequency, A to E, under normoxia-mesopic condition between LASIK and control groups. (C) Comparisons of contrast sensitivity at 5 spatial frequency, A to E, under hypoxia-photopic condition between LASIK and control groups. (D) Comparisons of contrast sensitivity at 5 spatial frequency, A to E, under hypoxia-mesopic condition between LASIK and control group.

3.5. Accommodation

3.5.1. Control group

According to the set distant sight marker, 2.75D was the baseline of accommodation. The measured accommodation were 3.45 ± 0.18 D in normoxic conditions; the measured accommodation were 3.31 ± 0.17 D in hypoxic conditions, there were no statistical significant difference ($p = 0.39$) between the both, and no matter under normoxic or hypoxic conditions, the measured accommodation both reached the set experimental baseline.

3.5.2. LASIK group

According to the set distant sight marker, 2.75D is the baseline of accommodation. The measured accommodation were 2.71 ± 0.21 D in normoxic conditions; the measured

accommodation were 2.29 ± 0.14 D in hypoxic conditions, there were a 16% decline of accommodation during hypoxia, and a statistical significant difference ($p = 0.03$) noted between the both, whether under normoxic or hypoxic conditions, the measured accommodation of both did not reach the set experimental baseline.

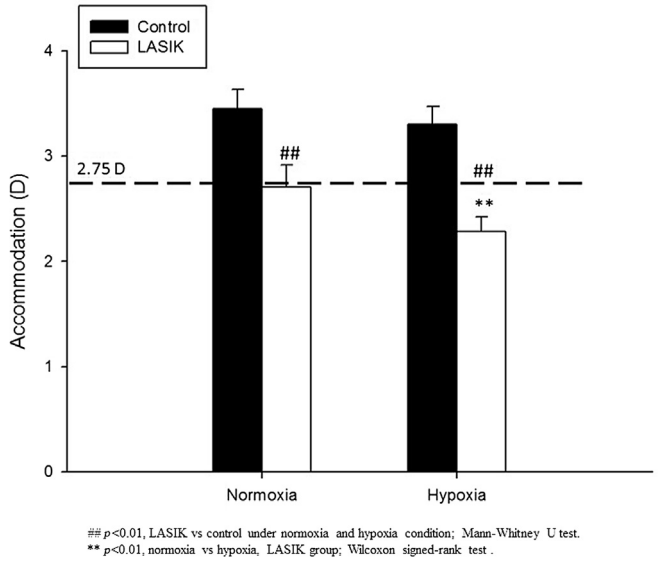
3.5.3. Intergroup difference

Under normoxic conditions, statistical significant difference ($p = 0.01$) was found between the groups, the measured accommodation of the LASIK group were lowered than that of the control group about 21%. Under hypoxic circumstances, statistical significance ($p = 0.00$) was also found between the groups, the measured accommodation of the LASIK group were lowered than that of the control group about 31%. (Fig. 3).

4. Discussion

This research was aimed at evaluation of the impact on visual performances post exposure to hypoxia and mesopic circumstances for whom had undertaken LASIK surgery. Collectively, mesopic circumstances contributed to the decrease of vision and contrast sensitivity, and the level of decrease were even more significant when a hypoxic condition was added. Both contrast sensitivity and accommodation decreased post LASIK surgery, and the range of decrease were more significant when exposed under hypoxic circumstances.

As early as 1939, McFarland et al. noted that the vision in dark environment would be deteriorated when were exposed under high altitude at 15,000 feet (11.7% O2), demonstrating that high value had already been placed on the impact on vision under hypoxic and mesopic environment.[13] In 1995, Johnson et al. proposed that vision would decline linearly along with the decline of brightness[14]; in 2009, a study by our institute also revealed that vision would decrease notably under mesopic environment in comparison with a brighter environment.[15]



$p<0.01$, LASIK vs control under normoxia and hypoxia condition; Mann-Whitney U test.
** $p<0.01$, normoxia vs hypoxia, LASIK group; Wilcoxon signed-rank test .

Fig. 3. Comparisons of accommodation under normoxia and hypoxia between LASIK and control groups.

Regarding the above studies, they were consistent with our result in respect of visual field, vision were notably decreased under mesopic environment, and were reduced to 1/3−1/6 of normoxic environment when exposed under hypoxic environment. In 1971, Kobrick et al. proposed that, night vision was decided by the rod cells of the retina, and that the function of rods were influenced by oxygen saturation before reaching the altitude of 10,000 feet.[16,17] In 1946, Hecht et al. indicated that the cone cells of retina played a dominant role in vision under photopic environment, and the function of cone cells would not be influenced by the decreasing of oxygen saturation below the altitude of 12,800 feet.[18] Hence, as the altitude inclined, the vision in dark environment wound be damaged earlier than that in brighter environment.

The pilots took a night navigation task in mesopic environment (0.034−3.4 cd/m2). Therefore, Connolly et al. emphasized his study on the impact on mesoptic vision under hypoxic environment. He suggested that contrast sensitivity would be lowered significantly when exposed to a hypoxic environment, and this decline of contrast sensitivity would be even more significant if under mesopic environment.[1−3]

There was an 11% decline of the contrast sensitivity of the control group under hypoxic environment during our experiment, a 34% decline under a mesopic condition, and a 46%, which is more notable, decline if under hypoxic and mesopic environment simultaneously, in accordance with the results from the past research. According to a study from Robert Montes-Mico et al., in 2003, there was a significant decline of contrast sensitivity of the subjects who underwent LASIK surgery and were exposed under hypoxic environment, the decline were even more notable if were under a mesopic environment.[7] There was a 26% decline regarding the contrast sensitivity of the LASIK group under hypoxic environment during our experiment, a 37% decline under mesopic environment, and a more notable, 53%, decline if were under hypoxic and mesopic environment simultaneously, also in accordance with the results from the past research. Hence, according to the results from the past research and our study, contrast sensitivity was likely to be affected by the oxygen saturation and brightness level of the environment.

During this study, the contrast sensitivity of the LASIK group is lower than that of the control group in any environment. According to a study by Wang et al., in 2004, flatness during laser cutting, severity of postoperative corneal swelling, and remnants of tissue fragments would cause tiny spaces between the corneal flap and stroma, further lowering the visual quality. Besides, due to the aspheric change of the morphology of cornea after LASIK, when pupils were dilated in a dark environment, peripheral light was not able to focus completely, which caused the increase of the spherical aberration in higher-order aberrations, further lowered the visual quality in dark environment, including contrast sensitivity.

In our experiment, there was statistical significance ($p < 0.05$) between the spherical equivalent refractive error (−4.23 ± 0.46 D) of the control group and preoperative

spherical equivalent refractive error (−5.28 ± 0.17 D) of the LASIK group, but the mean spherical equivalent of the both group were lower than −6.00 D, which belonged to moderate nearsightedness, with no significant impact on accommodation, and therefore with no effect on the results of accommodation during the experiment.

According to our experiment, the exposure to hypoxic environment would not affect the accommodation of the control group, but did cause the lowering of accommodation about 16% of the LASIK group. From the study of Nelson et al., in 2001, myopic shift phenomenon (increasing in degree of myopia) happened when the postoperative subjects from the LASIK group were exposed to 0% saturation of oxygen.[10] They also suggested that the LASIK surgery would alter the composition of corneal stroma, cause corneal swelling when exposed under hypoxic environment, and further result in the variation of degree of myopia.[10] This finding might explain the significant lowering of accommodation of the LASIK group under a hypoxic environment from our experiment.

During this experiment, the accommodation of the LASIK group was lower than that of the control group whether under normoxic or hypoxic environment, (lowered 21% and 31% in comparison with the control group, respectively), and both did not reached the set experimental baseline, 2.75D. There were a trend of decrease of the amplitude of monocular accommodation found among the postoperative 1 week, 1 month, and 7 year group of tested subjects. In this study, the accommodation postoperative 1 week showed statistical significant decrease ($p < 0.05$). This study suggested that the corneal curvature were flattened after cutting from the LASIK surgery which altered retinal imaging of optical imaging system, further causing the decline of accommodation postoperatively. This might explain that the result of decline of accommodation after LASIK surgery of our experiment.

In our experiment, there were 10 subjects from the LASIK group, distinguished from the methods of corneal flaps production, 8 underwent the traditional microkeratome and 2 underwent Intralase, but all were not using Wavefront-guided LASIK (W G LASIK) as method of keratectomy.

On the basis of previous studies about manufacturing methods of corneal flaps, the corneal flaps which produced from keratectomy, in comparison with those produced from the traditional microkeratome, would yield a more precise thickness of the corneal cuts and a more flattened edge, providing greater safety, biostability, reproducibility, elasticity, and reducing the postoperative complications.[19–22] Therefore, there might be slight error in the LASIK group in this experiment, although there was no statistically significant difference of visual performance among the 8 subjects whom underwent microkeratome and 2 subjects whom underwent Intralase from the LASIK group of our experiment.

Resulting from the limitation of the methods of surgery of the subjects in this study, the investigation of postoperative visual performances mainly aimed at the group who underwent traditional microkeratome; as the advance of medical technology, so were the LASIK surgery became more skilled, it was therefore fairly possible that there would be related research investigating about the postoperative visual performances targeting the group of Intralase and Wavefront-guided LASIK (W G LASIK) in the nearest future.

Among the 10 subjects from the LASIK group, postoperative period ranged from 1 to 7 years, with a mean of 3.6 years. Although all subjects reached at least a 20/20 standard vision, but the postoperative period were not consistent, and during the period, different habits in using the eyes or other living habits might possibly alter the visual quality further over- or under-estimate the influence post LASIK surgery. Further investigation including more subjects should be conducted in the future.

We have reviewed studies on the outcome of femtosecond laser-assisted LASIK compared to that of microkeratome-assisted LASIK. Previous ones showed no significant between the two groups or slight benefits in the femtosecond laser-assisted LASIK group. However, the most recent ones revealed significantly greater outcome in the femtosecond laser-assisted LASIK group regarding contrast sensitivity and accommodation.[23–25]

There was no strong evidence before our study started. But according to the recent studies, femtosecond laser-assisted LASIK may have some benefits over microkeratome-assisted LASIK. However, further studies are needed to evaluate visual outcomes, including contrast sensitivity and accommodation, between the two groups.

In conclusion, from the result of our experiment, vision was not affected by hypoxic exposure but were significantly lowered when exposed under mesopic environment, among either the control or LASIK group. The contrast sensitivity was significantly lowered under hypoxic environment in both groups, and the result was more notable if subjects were exposed under mesopic environment simultaneously. The amplitude of accommodation of the control group were not influenced by the hypoxic exposure, yet did caused significant lowering of the amplitude on the LASIK group even though there is no significant impact as compared to the control group. Issues such as whether different kinds of LASIK surgery would bring about different results is still awaiting for further investigation in the future, in order to provide a basis of study on vision correction by LASIK surgery, flight safety as a prerequisite, for pilots from particular aircrafts of our national army. It could also be utilized as the reference for the medical and aviation units of our national army during policy making regarding aircrew hiring, and for methods of correction regarding vision and visual quality.

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