The Effect of Procedure Room Temperature and Humidity on LASIK Outcomes

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Objective: To determine whether procedure room temperature or humidity during LASIK affect refractive outcomes in a large patient sample.
Design: Retrospective cohort study.
Participants: A total of 202 394 eyes of 105 712 patients aged 18 to 75 years who underwent LASIK at an Optical Express, Inc., location in their United Kingdom and Ireland centers from January 1, 2008, to June 30, 2011, who met inclusion criteria.
Methods: Patient age, gender, flap creation technique, pre- and 1-month post-LASIK manifest refraction, and ambient temperature and humidity during LASIK were recorded. Effect size determination and univariate and multivariate analyses were performed to characterize the relationships between LASIK procedure room temperature and humidity and postoperative refractive outcome.
Main Outcome Measures: One month post-LASIK manifest refraction.
Results: No clinically significant effect of procedure room temperature or humidity was found on LASIK refractive outcomes. When considering all eyes in our population, an increase of 1°C during LASIK was associated with a 0.003 diopter (D) more hyperopic refraction 1 month postoperatively, and an increase in 1% humidity was associated with a 0.0004 more myopic refraction. These effect sizes were the same or similar when considering only myopic eyes, only hyperopic eyes, and subgroups of eyes stratified by age and preoperative refractive error.
Conclusions: Neither procedure room temperature nor humidity during LASIK were found to have a clinically significant relationship with postoperative manifest refraction in our population.
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It is unclear whether ambient temperature or humidity during the LASIK procedure affects refractive outcomes. In LASIK, the excimer laser is used to precisely remove a lenticule of tissue by ablating the corneal stomae, resulting in a change in refraction. Unlike the femtosecond laser that has an interface in direct contact with the cornea, the excimer applies laser energy which travels through room air to the cornea. It is therefore possible that changes in ambient temperature or humidity in the procedure room may affect the energy profile at the corneal surface, presumably by altering the absorption or light-scattering properties of the air between the laser source and the cornea. It has been observed that excimer ablation rates in hydrogel buttons,[1] ex vivo bovine corneas,[2] and human corneas[3] seem to be affected by their degree of hydration, suggesting that environmental factors that affect the level of corneal stromal hydration may change the response of corneal tissue to the excimer laser in clinical practice.

Limited in vitro experimental data have not demonstrated that the ablation properties of the excimer laser are affected by ambient temperature.[4] However, a few reports from moderately sized patient populations have suggested that ambient temperature or humidity may indeed have a clinically significant effect on refractive outcome after LASIK.[3,5]

The primary aim of this study was to determine in a large patient cohort whether procedure room temperature or humidity during LASIK has a clinically significant effect on the refractive outcome.

Materials and Methods

This study was deemed exempt from full review by the Committee on Human Research at the University of California, San Francisco, because it used only de-identified patient data. This work is compliant with the Health Insurance Portability and Accountability Act of 1996 and adhered to the tenets of the Declaration of Helsinki.

Our study group included all patients aged 18 to 75 years who underwent LASIK in their United Kingdom and Ireland centers from January 1, 2008, to June 30, 2011, who met inclusion criteria. All patients underwent a complete dilated ophthalmologic examination preoperatively when considering eligibility for LASIK. This examination included an assessment of the tear film, which must be considered normal to proceed, as well as a slit-lamp examination of the lids, lashes, and cornea, with and without fluorescein staining, and measurement of the tear break-up time. Eyes were included if their preoperative spherical equivalent manifest refraction was between −12.00 and +4.00 diopters (D) (inclusive), emmetropia was the goal of LASIK (eyes with a target of ametropia for monovision were excluded), data were recorded for ambient temperature and humidity during LASIK, and a manifest refraction was recorded 1 month after surgery. Manifest refraction was performed using a resolution-based technique in

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which the end point is the least amount of minus sphere that results in the best visual acuity ("push plus"). Cycloplegic refraction also was performed preoperatively (30 minutes after the instillation of 2 drops of 1% tropicamide) but was not performed postoperatively and therefore was not used for this study. The following data are also routinely recorded for all patients undergoing LASIK at Optical Express, Inc, and were gathered and analyzed for this study: patient gender and age, LASIK flap creation method (femtosecond vs. microkeratome), and preoperative manifest refraction. Temperature and relative humidity were recorded immediately preceding each LASIK procedure (Cable Free ThermoHygrometer, Model No. EMR963HG, Oregon Scientific, Portland, OR).

Operative Technique

No attempt was made to control humidity in the operating suite. The excimer laser nomograms used at Optical Express, Inc., were not based on ambient temperature or humidity; thus, no adjustments were made for these factors. LASIK surgery was performed by 1 of 23 surgeons working at Optical Express Inc., centers. The Moria ONE Use-Plus automated microkeratome (Moria S.A., Antony, France) was used with a 130-μm standard head (or a large-cut head for some hyperopic eyes) and a suction ring with adjustable stops chosen by the surgeon on the basis of the keratometry readings to create nasally hinged flaps. The IntraLase FS-60 laser (Abbott Medical Optics, Abbott Park, IL) created femtosecond flaps with a diameter ranging from 8.2 to 9.2 mm and programmed depth from 100 to 120 μm. All femtosecond flaps were created with the hinge placed superiorly. Patient and surgeon preference determined the choice of procedure. Excimer laser was performed on a VISX Star S4 IR platform (Abbott Medical Optics, Santa Ana, CA). For LASIK flaps created by the femtosecond laser, the flap was lifted in a dry technique with no sponge being applied to the stromal bed before excimer laser treatment. For flaps created by the mechanical keratome, the flap was lifted and a semi-moist sponge was wiped across the stromal bed to ensure a uniform hydration. The excimer laser treatment was then immediately applied. After excimer laser application, the stromal bed was irrigated and the flap was repositioned. Postoperatively, patients were prescribed a third-generation fluoroquinolone and 1% prednisolone acetate, each 4 times per day for 1 week, and instructed to use an artificial tear solution 4 times per day for 1 month.

Statistical Analysis

Univariate descriptive statistics were reported for pre- and postoperative spherical equivalent and for humidity and temperature. Kernel density smoothing was used to assess the distribution of each variable. We conducted linear mixed effects regression using 1-month postoperative spherical equivalent manifest refraction as the outcome and baseline spherical equivalent manifest refraction, temperature, and humidity as predictors. This analysis accounts for statistical dependence of the 2 eyes from within an individual patient. Additional analysis included Optical Express, Inc, store location as a crossed random effect. Analyses were stratified by age categories and preoperative refractive error; such stratification was feasible because of the large sample size. Continuous variables were compared using the Student *t* test. Because of the large sample size, application of classic frequentist approaches to the entire data set may yield statistical significance for effects of negligible quantitative importance. Before analysis, an effect size of 0.5 D was considered to be clinically significant.

Table 1. Patient Demographics

Age	Mean (SD) Yrs
All patients	39.1 (11.9)
Men	39.5 (12.1)
Women	38.9 (11.8)
Eye	**n (% of Total)**
Right	100 240 (49.5%)
Left	102 154 (50.5%)
Male	90 243 (44.9%)
Female	110 628 (55.1%)
Myopic	155 865 (77%)
Hyperopic	46 529 (23.2%)
Mixed astigmatism with spherical equivalent of zero	1527 (0.75%)
Preoperative Refraction	**Mean (SD) D**
Sphere	−1.92 (2.55)
Cylinder	+0.76 (0.76)
Spherical equivalent	−1.54 (2.58)

D = diopters; SD = standard deviation.

Results

The distribution of preoperative spherical equivalent was bimodal, with a larger peak for myopic individuals. Postoperative spherical equivalent, procedure room temperature, and relative humidity were evaluated and found to be unimodally and normally distributed.

In all, 202 394 eyes of 105 712 patients were included for analysis. The demographics of the included patients are listed in Table 1. There were more female than male patients. The mean procedure room temperature during LASIK was 21.0°C (69.8°F) (range, 15.0°C−30.0°C; standard deviation, 1.43°C). The mean humidity was 40.8% (range, 20.0%−80.0%; standard deviation, 6.30%). In all, 142 349 eyes (69.4%) and 60 045 eyes (29.7%) underwent flap creation by the femtosecond laser and the automated microkeratome, respectively.

When evaluating all eyes in the population together, procedure room temperature and humidity did not show a clinically significant relationship with postoperative manifest refraction, although as expected, the relationships were statistically significant ($P = 0.0094$ for temperature and $P < 0.0001$ for humidity). When considering all eyes, an increase of 1°C during LASIK was associated with a 0.003 D more hyperopic manifest refraction 1 month after the procedure, and an increase in 1% humidity was associated with a 0.0004 D more myopic manifest refraction 1 month after the procedure. For perspective regarding the lack of clinical relevance of these effects, the refractive change predicted to occur between the difference of the lowest and highest temperatures in our sample (15°C) would be 0.045 D, and the refractive change predicted to occur between the difference of the lowest and highest humidity in our sample (60%) would be 0.024 D.

When considering only eyes that underwent myopic LASIK, an increase of 1°C during LASIK was associated with a 0.003 D more hyperopic manifest refraction 1 month after the procedure, whereas an increase of 1% humidity was associated with a 0.0008 D more myopic manifest refraction. When considering only eyes that underwent hyperopic LASIK, an increase of 1°C during LASIK

Table 2. Number of Eyes in Age/Preoperative Refraction Subgroups

Preoperative Spherical Equivalent (D)	Age (Yrs)				
	18–29.9	30–39.9	40–49.9	50–59.9	60–74.9
−12≤×<−9	71	82	54	25	2
≤−9×<−6	2398	2376	1829	695	122
≤−6×<−3	14 612	14 485	10 634	4420	684
≤−3×<0	33 752	35 005	23 992	9124	1503
≤0×<+2	2355	3869	4851	6870	2300
≤+2×≤+4	760	1207	4866	9901	5835

was associated with a 0.006 D more myopic manifest refraction 1 month after the procedure, and an increase of 1% humidity was associated with a 0.0008 D more myopic manifest refraction. None of these effects was considered clinically significant. The effect of procedure room temperature and humidity on postoperative manifest refraction after LASIK remained clinically insignificant when flap creation technique, geographic location of surgery, and gender were included in a multivariate analysis.

Table 2 shows all subgroups of eyes stratified by age and preoperative refractive error, and the number of eyes in each group. It reveals that most patients were aged between 18 and 50 years with mild to moderate myopia. Only 2 patients were found to be both highly myopic and aged more than 60 years, and this small group was excluded from subgroup analysis.

Tables 3 and 4 list the effect sizes of changes in 1°C or 1% humidity on postoperative refractive error in each subgroup. In general, Table 3 reveals that the largest effect of temperature was seen in eyes that were more hyperopic preoperatively. This was most pronounced in the subgroup with a preoperative refractive error of +2.00 to +4.00 D and aged 18 to 30 years. In this subgroup, an increase in 1°C during LASIK was associated with a decrease in 1-month postoperative refractive error (more correction) of 0.048 D. This effect was considered not to be clinically significant, and all other age and refractive error groups experienced smaller effects from changes in procedure room temperature. These analyses were repeated with only male and only female eyes, and the same results were found.

The effect of procedure room humidity during LASIK on postoperative refractive error was exceedingly small in every subgroup. Table 4 reveals that the largest effect was seen again in hyperopes, specifically those with a preoperative refractive error between +2.00 and +4.00 D and aged 60 to 75 years. This effect of a 0.0086 D increase per percent relative humidity increase is extremely small and clinically insignificant. Indeed, procedure room relative humidity would need to change by an absolute value of 58.4 points (percent) to affect a 0.5 D change in postoperative refractive error in this subgroup. This analysis was repeated including only male and only female eyes, and the same results were found.

Discussion

Overall, our data showed no clinically significant effect of procedure room temperature or humidity on refractive outcomes in LASIK. These findings also were robust despite flap technique or location of surgery and within individual subgroups on the basis of age, refractive error, and gender. To our knowledge, this study represents the largest dataset used to evaluate these relationships.

No significant effect of temperature was found in most subgroups on the basis of age and preoperative refractive error (Table 3). A small effect of increased correction with increasing temperature was found in hyperopic eyes aged 18 to 40 years and 60 to 75 years (Table 3). The reason for this is unclear but may have to do with increased excimer treatment durations in hyperopic compared with myopic patients. Regardless, the effect is small with procedure room temperature needing to change by 10.4°C (18°F) to result in a 0.5 D predicted change in postoperative refractive error in this subgroup. Conversely, no clinically significant effect of humidity was found in all subgroups. Excimer laser treatment duration was not measured in this study but is presumed to be directly related to the magnitude of the preoperative refractive error, which showed no relationship with temperature or humidity.

Two smaller clinical studies have suggested that ambient temperature and humidity may affect LASIK outcomes more significantly than what is reflected by our data. On the basis of an analysis of retreatment rates rather than measured residual refractive error, Walter and Stevenson[3] found both procedure room humidity and temperature to correlate significantly with the amount of post-LASIK ametropia in the 368 eyes evaluated in their series. Of note, that study found outdoor temperature and humidity to correlate even more strongly with LASIK outcomes than the procedure room environment. These authors proposed that outdoor humidity might change corneal hydration status and thus the corneal stromal response to the excimer laser.[3] In another

Table 3. Effect of Procedure Room Temperature during LASIK on Refractive Outcome, Subgroup Analysis

Preoperative Spherical Equivalent (D)	Age (Yrs)				
	18–30	30–40	40–50	50–60	60–75
−12≤×<−9	0.00752 (0.00824)	0.00727 (0.00811)	0.0126 (0.0108)	0.0209 (0.0175)	Not applicable*
≤−9×<−6	0.00483 (0.00229)	0.00195 (0.00234)	0.00748 (0.00334)	0.00213 (0.00591)	0.0253 (0.0152)
≤−6×<−3	0.00303 (0.00114)	0.00207 (0.00116)	0.00403 (0.0015)	0.0113 (0.00299)	−0.00013 (0.00763)
≤−3×<0	0.00237 (0.00512)	−0.00354 (0.00381)	−0.00241 (0.00424)	−0.00169 (0.00416)	−0.00104 (0.0075)
≤0×<+2	−0.0135 (0.0123)	0.00712 (0.00992)	−0.00905 (0.00651)	−0.00385 (0.00452)	−0.00788 (0.00598)
≤+2×≤+4	−0.048 (0.0231)	−0.0375 (0.0214)	−0.00739 (0.0166)	0.000347 (0.0147)	−0.0406 (0.0224)

Each cell = effect of increase of 1°C on 1-month postoperative spherical equivalent (D), listed as mean (standard deviation).
*Too few patients in group for meaningful analysis.

Table 4. Effect of Procedure Room Humidity during LASIK on Refractive Outcome, Subgroup Analysis

Preoperative Spherical Equivalent (D)	Age (Yrs)				
	18–30	30–40	40–50	50–60	60–75
−12≤×<−9	−0.00328 (0.00189)	−0.000454 (0.0019)	−0.00437 (0.00244)	−0.00457 (0.00396)	Not applicable*
≤−9×<−6	−0.000938 (0.000517)	−0.000577 (0.000534)	−0.00101 (0.00076)	−0.000842 (0.00136)	−0.00487 (0.00381)
≤−6×<−3	−0.000655 (0.000259)	−0.000906 (0.000265)	−0.000815 (0.000347)	−0.0014 (0.000675)	0.000845 (0.00185)
≤−3×<0	−0.000968 (0.00117)	−0.00167 (0.000891)	0.000525 (0.00098)	−0.00225 (0.000961)	−0.00109 (0.00183)
≤0×<+2	0.00193 (0.00319)	0.00433 (0.00233)	−0.000688 (0.00148)	−0.000192 (0.00106)	−0.000113 (0.00143)
≤+2×≤+4	0.0047 (0.00571)	0.00416 (0.0051)	−0.00234 (0.0036)	−0.000262 (0.00357)	0.00856 (0.0056)

Each cell = effect of increase of 1% relative humidity on 1-month postoperative spherical equivalent (D), listed as mean (standard deviation).
*Too few patients in group for meaningful analysis.

report, de Souza et al[5] evaluated 237 eyes that underwent LASIK and suggested that the temperature and relative humidity of air in their LASIK procedure room may have affected their refractive outcomes.

The results of the present study differ from those aforementioned. An extremely small effect of ambient temperature and virtually no effect of ambient humidity were found on LASIK outcomes in our large population. These differences in study findings may not be surprising. Indeed, smaller samples of data are inherently more susceptible to findings that are a result of chance. Our study sample includes approximately 500 times more eyes than those in the previous reports. Indeed, most of the individual subgroups analyzed in this study include a number of eyes that exceeds that included in the aforementioned studies combined.

The VISX Star S4 IR excimer laser was used for all eyes in this series. The manufacturer recommends it be operated with an ambient temperature between 15°C and 27°C (60−80°F) and with 35% to 65% relative humidity.[6] In our population, no eyes were treated at ambient temperatures of 15°C or less, although 414 eyes were treated at 27°C or more. In addition, 42 657 eyes were treated at 35% or less relative humidity, and 320 eyes were treated with 65% or more relative humidity. We independently evaluated the groups of eyes that were treated outside the manufacturer's recommendations and found no clinically significant effect of temperature or humidity on postoperative refractive error in those groups.

Study Limitations

One limitation of the present study was that only 1-month postoperative refractive error was measured. It is possible that different results regarding the effects of temperature and humidity on LASIK outcomes might be seen in our population if more follow-up data were available. However, an explanation for procedure room temperature or humidity affecting postoperative LASIK outcomes beyond only 1 month postoperatively would have to invoke some process involving a differential healing pattern as opposed to a difference in laser ablation efficiency at the time of treatment.

In our study, procedures were performed within a temperature range of 15°C to 30°C and 20% to 80% relative humidity, confirming the predictability of laser ablation rates within this range. Our data do not allow us to comment on a possible effect of ambient temperature and humidity on LASIK outcomes outside of these ranges.

In conclusion, our series of more than 200 000 eyes reveals that there is likely no clinically significant effect of procedure room ambient temperature nor humidity (within the ranges we evaluated) on refractive outcomes in LASIK. Small effects of temperature on refractive outcome were found in a few subgroups of patients, but these effects were not clinically significant. Procedure room humidity was found to have no effect on refractive outcome.

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Footnotes and Financial Disclosures

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