Myopia Project

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Myopia, also known as nearsightedness, is a refractive error, which is an urgent world-wide public health issue. Uncorrected refractive error (URE) causes a loss in global GDP estimated to be $202 billion per annum. [1]

The prevalence of myopia in United states is doubled in the last 50 years. It is predicted that 49.8% of world population will be affected by myopia by 2050.[2]

To address this myopia boom, the Prospective Evaluation of Radial Keratotomy (PERK) Study collected tremendous dataset. Researchers found the conflicting conclusion in the correlation between gender and the prevalence of myopia[3], which is one of the major topic of our discussion. Studies also have shown that the prevalence of myopia is associate with age,[4] which will be discussed in our analysis. Additionally, we also take the use of soft contact lens before surgeries and two common examinations, preoperative intraocular pressure (IOP) and diameter of the central clear zone (DCZ), into considerations. After that, we will evaluate whether these five characteristics are related to a good refractive outcome or not.

Method

Study Design

The PERK is a nine-center clinical trial of a standardized technique of radial keratotomy. Patients who had myopia with refraction in each eye between -2.00 and -8.00 diopters and above 21 years old were enrolled. The change in refraction before surgery and one year after surgery is measured to evaluate the effectiveness of the radial keratotomy. For safety considerations, patients were only allowed to have surgery for one eye in one-year period. A clinically important change refers to a change in refraction > 1

diopter after surgery. A clinically important effect refers to a mean difference in change between groups > 0.5 diopters.

The surgical technique consisted of eight incisions using a diamond micrometer knife with blade length determined by intraoperative ultrasonic pachymetry and the diameter of central clear zone determined by preoperative refraction (-2 to -3.12 = 4.0mm; - 3.25 to -4.37 = 3.5mm; -4.5 to -8.00 = 3.0 mm). With a smaller clear zone, the incisions would hopefully result in a greater change in refraction.

Data Analysis

Data for each patient presented both demographic and clinical characteristics, including age, gender, use of soft contact lens before surgery, intraocular pressure, and the diameter of the clear zone.

The overall performance of the radial keratotomy was analyzed with calculating the percentage of patients achieved good refractive outcome and the mean of change in refraction for patients before and one year after the surgery.

To analyze the association between each of the characteristics and the change in refraction before and one year after the surgery, we performed two sample t-test. Before that, we use F test to assess the equality of variance between groups. Two special cases are continuous variables age and intraocular pressure. Age was divided into four groups: 20- 30 years (20s), 30-40 years (30s), 40-50 years (40s), and 50-60 years (50s). We divided IOP (intraocular pressure) into two groups: IOP less than median, IOP more than median. The 95% confidence interval for the difference between groups within characteristics is calculated to so that if repeating this sampling method for many times,

95% of the time the true population mean would be in this range. T-test has assumptions including large sample size, random sampling, and normal distribution data.

To analyze the association between each of the characteristics and the refractive outcome, we performed Chi-Squared test and Fisher's Exact test. When evaluating age and IOP, we divided the data into groups as we did before. Chi-Squared test has assumptions including independence of groups within characteristic, the expected number of observations in each cell of the contingency table be greater than 5. Fisher's Exact test has assumption including random sampling, and small sample size.

All tests performed were 2-tailed in our study. Our chosen significance level is 0.05 throughout the whole study and a p-value less than 0.05 indicates statistical significance in our study.

RESULT

Demographics of the PERK study

The mean age of study population is 33.78 with a standard deviation(std) of 7.44. Patients' IOP has a mean of 14.43 with a std of 3.14. 205(53.11%) males and 181(46.89%) females participated in study. 261 patients (67.62%) have not used soft contact lens before surgery. 133, 129 and 124 patients have the diameter of the central clear zone in 3mm, 3.5mm, and 4mm, respectively**.**

After the surgery, the study obtained a mean refraction of -0.299 diopters with standard deviation of 1.22 diopters, and the minimum and maximum refraction are -4.25 and 3.25 diopters. About 65% of patients have a good outcome in -1 to +1 diopters inclusively with a 95% CI of (-0.42, 0.18). The change in refraction from baseline is statistically and clinically significant different from 0 in value 3.70 (95% CI: (3.56,3.83)).

Age

In age of 20s and 30s, 20s and 40s, 20s and 50s, 30s and 40s, 30s and 50s, 40s and 50s, each two age groups have statistically significant different change in refraction of -0.53(p=.0003, 95%CI: (-0.82,-0.25)), -1.01(p<.0001, 95%CI: (-1.46,-0.57), -2.25(p<.0001, 95%CI: (1.192, 1.511)), -0.48(p<.017, 95%CI: (-0.79,-0.09)), -1.72(p<.0001, 95%CI:(1.125, 1.367)), -1.24(p=.009, 95%CI: (1.268, 1.798)) (Table 2), and in Chi-squared tests (except for 30s to 50s applying Fisher's Exact test), each two age groups did not have a statistically significant association with good refraction outcome (p= 0.24, 0.77, 0.24, 0.23, 0.058, 0.35 respectively) (Table 3).

Preoperative intraocular pressure

Separated by the median of IOP (14.33), we got 195 patients whose IOPs are below median and 191 patients whose IOPs are above median. The difference of mean change in refraction between the two groups has a mean of -0.38 with a 95% CI (-0.65, -0.10). The p-value of F-test is 0.49, showing that the two group have equal variances. Thus, the statistic of t-test is -2.70 (p=0.01). The results show that the mean change in refraction is statistically significantly different between these two groups. However, the result would not suggest a clinically important effect (difference of mean change < 0.5). We choose to run a Chi-Square test to analyze the association between IOP and the outcome of the surgery (min(Eij)=66.8). The p-value of chi-square test (=0.18) is larger than 0.05. The result shows that the IOP of patients is not statistically significantly associated with whether or not the patients obtained a good refractive outcome.

Gender

205 (53.11%) are males and 181 (46.89%) are females. The p-value of F test is 0.0046. With unequal variances, the result of t test (p=0.0077) show that there is an effect of gender on the change in refraction after surgery. The mean for difference between gender groups is 0.3703 with a 95% CI (0.0987, 0.6518). The results show statistically significant association between gender and change of refraction after surgery. However, this difference is not clinically important (difference of mean change < 0.5). We choose to run Chi-Squared test to evaluate the association between gender and the outcome of the surgery (min(Eij)=63.3). We find that gender of patients has no statistically significant association (p=0.18) with whether or not the patients obtained a good refractive outcome.

Use of soft contact lens before surgery

125 patients (32.38%) have used soft contact lens before surgery and 261 (67.62%) have not used soft contact lens before surgery. The result of F test indicates that the variances of the two groups are equal. With equal variances, the results of t test (p=0.0003) show that there is an effect of use of soft contact lens before surgery on the change in refraction after surgery. The mean for difference between group is 0.5402 with a 95% CI (0.2493, 0.8312). The results show both statistically significant and clinically important association between gender and change of refraction after surgery. We choose to perform Chi-Squared test to evaluate the association between between the use of soft contact lens before surgery and the outcome of the surgery (min(Eij)=43.7). We find that the use of soft contact lens before surgery has a statistically significant association (p=0.0037) with whether or not the patients obtained a good refractive outcome.

Diameter of the central clear zone

We ran t-test in DCZ for 3 times with diameter of clear central zone of 3 and 3.5, 3 and 4, 3.5 and 4, and all of these tests had statistically and clinically significant difference of 1.17(p <.0001 95% CI: (0.86, 1.47)), 1.90(p <.0001 95% CI: (1.61, 2.18)), 0.73 (p <.0001 95% CI: (0.47, 0.97)), respectively. We use Chi-Squared test to show the association between the diameter of clear central zone and the good refractive outcome. With diameter of clear central zone of 3 and 3.5, 3 and 4, 3.5 and 4, and all of these tests had statistically significant association with good outcome, p=0.0001, p<.0001, p=0.037 respectively.

Discussion

Since the statistical methods we've learned is limited, we have to roughly separate the patients into two groups to evaluate whether Characteristic are related to the change in refraction and the outcome of surgery. The results are very brief and not persuasive enough. Such as IOP, as a continuous variable, being divided by median causes a massive information loss of IOP. We will achieve more believable results after we study more statistical methods.

In t-test, each pair of age group (except for age group 30s and 40s), and used soft contact lens before surgery and DCZ have statistically and clinically significant difference with change of refraction (e.g. the more difference in the DCZ group, the more difference the change will have). Age group 30s and 40s, gender groups and two preoperative intraocular pressure group and two IOP groups are statistically but not clinically different within each group.

Results from Chi-Squared test indicates that IOP, age, gender (female or male) has no statistically significant association with the refractive outcome of surgery (good or not)

while the use of soft contact lens before surgery and DCZ have statistically significant association with the refractive outcome of surgery (good or not).

Appendix

Table.1 Demographics of the PERK study

Characteristic	
Age, mean(SD), years	33.78(7.44)
Preoperative intraocular pressure, mean(SD), mmHg	14.43(3.14)
Gender	
Male, n(%)	205(53.11)
Female, n(%)	181(46.89)
Use of soft contact lens before surgery	
No, n(%)	261(67.62)
Yes, n(%)	125(32.38)
Diameter of the central clear zone	
3mm, n(%)	133(34.46)
3.5mm, n(%)	129(33.42)
4mm, n(%)	124(32.12)

Table.2 The relationship between patient characteristics and the change in refraction

Characteristic	Mean change in fraction(95% CI)	p-value (F-test)	t-statistic	p-value(t-test)
Age				
Age1(20-30)	3.21(2.98, 3.45)			
Age2(30-40)	3.74(3.57, 3.92)			
Age3(40-50)	4.23(3.81, 4.64)			
Age4(50-60)	5.26(4.62, 6.30)			
Difference (Age20s – Age30s)	-0.53(-0.82, -0.25)	0.314	-3.660	0.0003
Difference (Age20s –Age40s)	-1.01(-1.46, -0.57)	0.252	-4.470	<0.0001
Difference (Age20s – Age50s)	-2.25(-3.02, -1.48)	0.727	-5.790	<0.0001
Difference (Age30s – Age40s)	-0.48(-0.79, -0.09)	0.045	-2.410	0.017
Difference (Age30s – Age50s)	-1.72(-2.42, -1.02)	0.446	-4.860	<0.0001
Difference (Age40s – Age50s)	-1.24(-2.15, -0.32)	0.807	-2.680	0.009
Gender				
Male	3.87(3.66, 4.07)			
Female	3.49(3.32, 3.67)			
Difference	0.37(0.10, 0.65)	0.0046	2.68	0.0077
Use of soft contact lens before surgery				

No	3.87(3.70, 4.04)			
Yes	3.33(3.10, 3.55)			
Difference	0.54(0.25, 0.83)	0.17	3.65	0.0003
Diameter of the central clear zone				
3mm	4.69(4.45, 4.93)			
3.5mm	3.53(3.34, 3.71)			
4mm	2.80(2.64, 2.95)			
Difference (3mm - 3.5mm)	1.17(0.86, 1.47)	0.0032	7.56	<.0001
Difference (3mm - 4mm)	1.89(1.61, 2.18)	<.0001	13.15	<.0001
Difference (3.5mm - 4mm)	0.73(0.49, 0.97)	0.014	5.95	<.0001

[a)] The groups of age are based divided into four groups: 20- 30 years (20s), 30-40 years (30s), 40-50 years (40s), and 50-60 years (50s)

[b)] As to preoperative intraocular pressure, we split them into two groups by the median to make sure the number of patients in two groups is close.

Characteristic	Test	Statistics Value	p-value	Least Eij
Difference (Age20s – Age30s)	Chi-Squared	1.39	0.24	42.13
Difference (Age20s – Age40s)	Chi-Squared	0.085	0.77	20.13
Difference (Age20s – Age50s)	Chi-Squared	1.36	0.24	5.05
Difference (Age30s – Age40s)	Chi-Squared	1.43	0.23	17.38
Difference (Age30s – Age50s)	Fisher's Exact		0.058	4.21
Difference (Age40s – Age50s)	Chi-Squared	0.86	0.35	5.52
Preoperative intraocular pressure	Chi-Squared	2.77	0.096	66.8
Gender	Chi-Squared	1.82	0.18	63.3
Use of soft contact lens before surgery	Chi-Squared	8.41	0.0037	43.72
Diameter of the central clear zone (3mm-3.5mm)	Chi-Squared	15.13	0.0001	56.62
Diameter of the central clear zone (3mm-4mm)	Chi-Squared	43.18	<0.0001	45.35
Diameter of the central clear zone (3.5mm-4mm)	Chi-Squared	8.47	0.0036	29.9

Table.3 The relationship between patient characteristics and whether or not the patients obtained a good refractive outcome

[1] Fricke TR, Holden BA, Wilson DA, Schlenther G, Naidoo KS, Resnikoff S, Frick KD. Global cost of correcting vision impairment from uncorrected refractive error. Bulletin of the World Health Organization. 2012 Oct;90(10):728-38.

[2]. Holden, B. A., et al. "Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050." Ophthalmology123.5(2016):1036.

[3]. Holden, Brien A., et al. "Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050." Ophthalmology 123.5 (2016): 1036-1042.

[4]. Seang-Mei Saw, et al. "Epidemiology of Myopia." Epidemiologic reviews18.2(1996):175-87.