Survey report on keratoplasty in China: A 5-year review from 2014 to 2018

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Abstract

To provide the general information on corneal transplantation (CT) in China, China Cornea Society designed a questionnaire on CT from 2014 to 2018 and entrusted it to 31 committee members for implementation of the survey nationwide. This article presents the results of the survey and compares the indicators used in the survey and those in the annual statistical report released by the Eye Bank Association of America (EBAA). The number of corneal transplantations completed by the 64 hospitals from 2014 to 2018 was respectively 5377, 6394, 7595, 8270 and 8980, totally 36,616 (22,959 male and 13,657 female). The five largest hospitals by the number of corneal transplantations completed by the 64 hospitals from 2014 to 2018 was respectively 5377, 6394, 7595, 8270 and 8980, respectively. The geographical distribution of keratoplasty performed in China is unbalanced. PK and ALK were the main techniques of CT and corneal leukoma, bacterial keratitis and corneal dystrophies were the main indications for CT in China.
Introduction

According to the World Health Organization, corneal diseases are one of the leading causes of blindness globally [1]. Approximately 180,000 cases of corneal transplantations are performed worldwide each year [2], of which 40,000 to 50,000 cases are in the United States, restoring vision for patients with corneal blindness [3,4]. China is the largest and most populous developing country in the world and corneal diseases are the second leading causes of blindness [5–7]. According to the multi-center study on infectious keratitis in China conducted by Song et al. in 2010, the number of people with corneal blindness in at least one eye in China was estimated to be about 3 million at that time [8].

Eye Bank Association of America (EBAA) is the only accredited organization in America that distributes donated eye tissues and collects information on the utilization of the tissues in all its member banks. Two articles based on the statistical reports of EBAA has been published, reporting the trends of penetrating keratoplasty (PK) from 1980 to 2004 and the condition of keratoplasty in the United States from 2005 through 2014 respectively [3,4]. All these data can provide information for ophthalmologists to understand the general situation of corneal transplantation (CT), and play a positive role in promoting the development of CT and the improvement in surgical techniques.

Although several single center based articles about keratoplasties have been published these years [9–14], currently, there is no national eye bank association or eye bank union in China, therefore, no exact data is available for the total number of corneal transplantations each year, the main indications for CT, surgical techniques of CT, etcetera, which limits the formulation and implementation of corneal blindness-related policies and then the process of restoring vision for the blind in China. To get an overview of keratoplasties in China, the Corneal Disease Group of Ophthalmological Society of Chinese Medical Association (China Cornea Society) designed a questionnaire on CT (S1 Table) and entrusted the questionnaire to its 31 committee members for the implementation of the survey in hospitals. 64 hospitals participated in the survey and returned the questionnaire. The results of the survey show that there are many differences in surgical techniques of CT, indications, and other aspects between China and America. The survey data are now available for reference.

Materials and methods

The China Cornea Society entrusted the questionnaire to its 31 committee members for the implementation of the survey in China. A total number of 64 hospitals were involved in the survey and asked to fill in the questionnaires. This study was approved by the Institutional Review Board of Shandong Eye Institute and adhered to the tenets of the Declaration of Helsinki.

Indicators of the survey included the number of keratoplasties performed between January 2014 to December 2018, general conditions of each patient, geographical distribution of surgeries, indications for surgeries, surgical techniques. Detailed data of each case was collected.

Indications for corneal transplantation

Indications for CT mainly include 1) fungal keratitis, 2) bacterial keratitis, 3) herpes simplex virus keratitis, 4) Acanthamoeba keratitis, 5) corneal dystrophies (granular dystrophy, lattice dystrophy, macular dystrophy, Fuchs’ dystrophy, and other dystrophies), 6) trauma (acid burns, alkali burns, thermal burns, and other burns), 7) immune-related keratitis (Mooren’s Ulcer, rheumatoid arthritis-associated peripheral ulcerative keratitis, and Stevens–Johnson syndrome), 8) corneal degeneration, 9) keratoconus, 10) pseudophakic bullous keratopathy (PBK), 11) corneal tumor, 12) corneal leukemia, 13) corneal perforation, 14) corneal staphyloma, 15) exposure keratitis, 16) pterygium-related corneal opacity, and 17) graft opacity.
Corneal transplantation techniques
Corneal transplantation techniques mainly include 1) PK, 2) lamellar keratoplasty (LK), in the form of anterior lamellar keratoplasty (ALK) and endothelial keratoplasty (EK), 3) keratoprosthesis, and 4) keratolimbal allograft.

Statistical method
The data were analyzed using SPSS Statistics version 25 (IBM, Armonk, NY). P values less than 0.05 were regarded as statistically significant.

Results
64 tertiary hospitals in China returned the questionnaires. According to the detailed information the hospitals provided, the number of CT performed in the five years was 5377, 6394, 7595, 8270, and 8980 respectively, totally 36,616.

Number of corneal transplantations in hospitals and geographical distribution
The five largest hospitals by number of corneal transplantations performed from 2014 through 2018 are Shandong Eye Institute (including Eye Hospital of Shandong First Medical University and Qingdao Eye Hospital of Shandong First Medical University) (4001), Zhongshan Ophthalmic Center (3837), Beijing Tongren Hospital (3079), No. 1 Hospital of Xi’an City (2569), Eye and Ear, Nose, Throat Hospital of Fudan University (2508) and totally conducted 15,994 keratoplasties, accounting for 43.68% of the totally reported keratoplasties (Fig 1).

According to the location of the hospitals reported, 30 provincial-level administrative units were included. The total number of CT performed in the five years in each administrative unit is as follows (Table 1).

The five largest provincial-level administrative units by number of CT have completed 19,911 cases (54.38%), while the five smallest units have only completed 67 cases (0.18%).

Age and gender distribution of cornea transplant recipients
Among the 36,616 patients who underwent CT, 22,959 (62.70%) were male and 13,657 (37.30%) were female. The distribution of age is as follows (Table 2).

Indications for corneal transplantation
The 5 leading indications for CT in China were corneal leukoma (7683, 20.98%), bacterial keratitis (4209, 11.49%), corneal dystrophies (4189, 11.44%), keratoconus (3578, 9.77%), and corneal perforation (2839, 7.75%) (Fig 2).

Surgical techniques
According to the data we collected, the number of PK accounts for 54.34% of all the keratoplasties performed in the five years, ALK 37.88%, EK 6.87%, keratoprosthesis 0.72%, and keratolimbal allograft 0.19% (Fig 3).

The most common surgical technique was PK, although decreasing from 57.97% in 2014 to 52.88% in 2018. ALK increased from 36.04% to 37.92% in the five years (P<0.001) and EK increased from 5.52% to 7.75% (P<0.001). The indications for ALK are shown in Table 3 and the indications for PK are shown in Table 4.
Discussion

Corneal diseases are a leading cause of blindness worldwide, second to cataract \[1,15\]. Due to the unbalanced global economy and ethnic differences, the causes of blindness, the proportion of the causes, the preferred surgical techniques of CT and the indications for surgery are not the same or even quite different in different countries and regions \[16–18\]. Currently, China does not have a national eye bank union, so it is not easy to collect exact information on CT from all the hospitals and eye banks. Therefore, the general data on CT in China is unavailable now. The Chinese Ophthalmological Society is the most authoritative academic association in ophthalmology in China and its Corneal Disease Group (China Cornea Society) is the most authoritative group in the cornea disease field in China, whose members are experts on cornea-related clinical work and academic research. The members are very familiar with the hospitals in their own administrative unit, so they were entrusted to collect information from the hospitals in their own administrative units. The survey has covered most of the qualified hospitals in performing keratoplasties in the recent five years and it is estimated that the cases...
included in the survey accounted for more than 90% of all the corneal transplantations, so the results can represent the condition of keratoplasties in China.

According to our survey, the four leading indications for CT in China from 2014 through 2018 were corneal leukoma, bacterial keratitis, corneal dystrophies, and keratoconus, while the four leading indications for CT in America from 2005 to 2014 were PBK, keratoconus, Fuchs’ dystrophy, and repeat CT [4]. Analyses of the results show that there are both similarity and difference on the indications for CT between China and America.

### Table 1. Total number of CT performed in the five years in each provincial-level administrative unit.

| Provincial-level administrative unit | Number | %  |
|-------------------------------------|--------|----|
| Beijing                             | 6077   | 16.60 |
| Shandong                            | 4427   | 12.09 |
| Guangdong                           | 3976   | 10.86 |
| Shanghai                            | 2791   | 7.62  |
| Zhejiang                            | 2640   | 7.21  |
| Shaanxi                             | 2569   | 7.02  |
| Fujian                              | 1671   | 4.56  |
| Jiangsu                             | 1650   | 4.51  |
| Sichuan                             | 1540   | 4.21  |
| Hunan                               | 1371   | 3.74  |
| Henan                               | 1043   | 2.85  |
| Hubei                               | 985    | 2.69  |
| Anhui                               | 917    | 2.50  |
| Liaoning                            | 825    | 2.25% |
| Heilongjiang                        | 787    | 2.15  |
| Jilin                               | 554    | 1.51  |
| Hainan                              | 505    | 1.38  |
| Guangxi                             | 392    | 1.07  |
| Chongqing                           | 384    | 1.05  |
| Shanxi                              | 379    | 1.04  |
| Jiangxi                             | 325    | 0.89  |
| Xinjiang                            | 313    | 0.85  |
| Tianjin                             | 241    | 0.66  |
| Yunnan                              | 134    | 0.37  |
| Ningxia                             | 53     | 0.14  |
| Guizhou                             | 34     | 0.09  |
| Gansu                               | 15     | 0.04  |
| Hebei                               | 8      | 0.02  |
| Inner Mongolia                      | 8      | 0.02  |
| Tibet                               | 2      | 0.01  |

* in descending order.

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### Table 2. Age distribution of cornea transplant recipients.

| Age (year) | Number (%) |
|------------|------------|
| <1         | 538 (1.47) |
| 1–10       | 3123 (8.53)|
| 11–20      | 2846 (7.77)|
| 21–30      | 3607 (9.85)|
| 31–40      | 3427 (9.36)|
| 41–50      | 6053 (16.53)|
| 51–60      | 7067 (19.30)|
| 61–70      | 6438 (17.58)|
| 71–80      | 2851 (7.79)|
| >80        | 666 (1.82) |

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Similarity: In both countries, keratoconus is among the top four indications of CT. Reason: Keratoconus occurs in all ethnic groups and it is related to heredity, therefore, the incidence rate of keratoconus in different countries is slightly different or comparable [19–22].

Difference: In America, endothelial dysfunction (including PBK and Fuchs’ dystrophy) is the main indication for CT, while in China, corneal leukoma, and infectious keratitis are the most common indications. Reasons: 1) The difference may be related to the economic development levels of the two countries. China is a developing country with an agricultural population of 800 million. The economic level and geographical conditions limit the promotion and application of agricultural machinery and the people still lack occupational safety awareness.

Fig 2. Indications for corneal transplantation. 
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Fig 3. Tendency of preferred surgical techniques. ALK = anterior lamellar keratoplasty; PK = penetrating keratoplasty; EK = endothelial keratoplasty. 
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and protection measures. As a result, the risk of infectious keratitis caused by trauma in farming is high [23], therefore, corneal leukoma and infectious keratitis become the most common indications for CT in China. 2) America has a relatively long history in performing cataract surgeries and the total number of surgeries is large. The wide application of anterior chamber intraocular lenses in the 1980's has accelerated the loss of endothelial cells after surgery, resulting in a large amount of PBK, which was one of the most common indications for CT from

| Indication                        | 2014  | 2015  | 2016  | 2017  | 2018  |
|----------------------------------|-------|-------|-------|-------|-------|
| Corneal leukoma                  | 280(14.45) | 338(15.23) | 387(12.86) | 591(17.93) | 455(13.36) |
| Keratoconus                      | 255(13.16) | 297(13.38) | 459(15.25) | 547(16.59) | 531(15.59) |
| Corneal tumor                    | 217(11.20) | 245(11.04) | 370(12.29) | 468(14.19) | 536(15.74) |
| Bacterial keratitis              | 223(11.51) | 232(10.46) | 406(13.49) | 391(11.86) | 458(13.45) |
| Corneal degeneration             | 164(8.46) | 151(6.80) | 245(8.14) | 323(9.80) | 296(8.69) |
| Corneal dystrophies              | 88(4.54) | 158(7.12) | 211(7.01) | 154(4.67) | 283(8.31) |
| Corneal perforation              | 126(6.50) | 144(6.49) | 199(6.61) | 176(5.34) | 167(4.90) |
| Immune-related keratitis         | 103(5.31) | 161(7.26) | 185(6.15) | 121(3.67) | 141(4.14) |
| Fungal keratitis                | 108(5.57) | 49(2.21) | 129(4.29) | 202(6.13) | 222(6.52) |
| Trauma                           | 107(5.52) | 129(5.81) | 157(5.22) | 104(3.15) | 98(2.88) |
| Herpes simplex virus keratitis   | 94(4.85) | 131(5.90) | 122(4.05) | 77(2.34) | 92(2.70) |
| Graft opacity                    | 32(1.65) | 47(2.12) | 56(1.86) | 84(2.55) | 85(2.50) |
| Pseudophakic bullous keratopathy | 93(4.80) | 74(3.33) | 43(1.43) | 9(0.27) | 10(0.27) |
| Pterygium-related corneal opacity | 16(0.83) | 25(1.13) | 20(0.66) | 26(0.79) | 19(0.66) |
| Acanthamoeba keratitis           | 23(1.19) | 27(1.22) | 10(0.33) | 11(0.33) | 10(0.29) |
| Corneal staphyloma               | 7(0.36) | 80(3.66) | 80(2.77) | 13(0.39) | 8(0.23) |
| Exposure keratitis              | 2(0.10) | 3(0.14) | 3(0.10) | 0(0) | 0(0) |

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| Indication                        | 2014  | 2015  | 2016  | 2017  | 2018  |
|----------------------------------|-------|-------|-------|-------|-------|
| Corneal leukoma                  | 942(20.22) | 1043(28.04) | 1064(26.30) | 1238(29.03) | 1194(25.14) |
| Bacterial keratitis              | 289(9.27) | 348(9.35) | 492(12.16) | 555(13.01) | 710(14.95) |
| Corneal perforation              | 214(6.87) | 315(8.47) | 360(8.90) | 518(12.15) | 600(12.63) |
| Corneal dystrophies              | 285(9.14) | 347(9.33) | 406(10.04) | 330(7.74) | 449(9.45) |
| Fungal keratitis                | 257(8.25) | 196(5.27) | 382(9.44) | 456(10.69) | 466(9.81) |
| Keratoconus                      | 296(9.50) | 387(10.40) | 342(8.45) | 247(5.79) | 213(4.49) |
| Graft opacity                    | 208(6.67) | 250(6.72) | 271(6.70) | 285(6.68) | 313(6.59) |
| Corneal degeneration             | 142(4.56) | 164(4.41) | 166(4.10) | 201(4.71) | 276(5.81) |
| Herpes simplex virus keratitis   | 117(3.75) | 107(2.88) | 141(3.49) | 177(4.15) | 230(4.84) |
| Pseudophakic bullous keratopathy | 145(4.65) | 111(2.98) | 136(3.36) | 105(2.46) | 136(2.86) |
| Trauma                           | 71(2.28) | 100(2.69) | 101(2.50) | 85(1.99) | 85(1.79) |
| Corneal tumor                    | 92(2.95) | 129(3.47) | 78(1.93) | 30(0.71) | 33(0.69) |
| Immune-related keratitis         | 39(1.25) | 65(1.75) | 65(1.68) | 24(0.56) | 28(0.59) |
| Pterygium-related corneal opacity | 1(0.03) | 144(3.87) | 8(0.20) | 0(0) | 2(0.04) |
| Corneal staphyloma               | 9(0.29) | 13(0.35) | 18(0.44) | 7(0.16) | 8(0.17) |
| Acanthamoeba keratitis           | 10(0.33) | 1(0.03) | 9(0.22) | 7(0.16) | 6(0.13) |
| Exposure keratitis              | 0(0) | 0(0) | 3(0.07) | 0(0) | 0(0) |

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2005 through 2014 [4]. Although the incidence rate of PBK has decreased worldwide these years with the development of facilities for cataract surgeries, the absolute number of people receiving cataract surgeries is still growing. According to the latest data, the cataract surgery rate in the United States was up to 10,000 in 2018, while in China, the rate was only 2000 to 3000 [24–26].

The main surgical technique in the United States from 1980 to 2004 was PK. However, in the following 10 years, PK dramatically decreased from 95% in 2005 to 42% in 2014 and has been surpassed by various LK techniques (in the form of EK and ALK) in 2011 [4]. Analyzing the results of our survey, we found that from 2014 to 2016 the proportion of PK decreased by 4.71% while LK increased by 4.71%, and then in 2017 and 2018, the proportion of the techniques were relatively stable. In addition, to find the long-term trend of preferred techniques, the authors analyzed a single center study conducted by Shandong Eye Institute, covering 5316 cases of CT from 1996 to 2007 and found that in the twelve years, PK decreased from 76.0% to 61.8% while LK increased from 24.0% to 38.2% [27]. Therefore, it can be seen that the trend of preferred techniques of CT in China and America was similar in the past twenty years, with a decrease in PK and an increase in LK. The change of preferred technique from full thickness PK to LK can reduce the risk of surgery and the risk of immune rejection after surgery. In addition, the application of the new LK technique, such as deep anterior lamellar keratoplasty (DALK) and Descemet’s membrane endothelial keratoplasty (DMEK), has made it possible for one or more people to share one donor cornea [28], which can reduce the burden of corneal blindness under the worldwide shortage of donor corneas.

Although in both China and America, the number of LK increased gradually, the respective proportion of ALK and EK and the indications were quite different. According to the statistical report of EBAA in 2014, ALK only accounted for 3.4% of various LK techniques while EK accounted for 96.6%. However, the results of our survey showed that ALK accounted for 83.03% while EK only accounted for 16.97% in China in 2018. The differences may be related to the establishment of eye bank association, the different indications in the two countries and the development of surgical techniques. 1) PK and EK require corneal tissue with high quality. In America, benefiting from the oversupply of donor corneas and the professional management by EBAA, the techniques can be performed with qualified corneas or even pre-cut grafts [29]. However, in China, there is a severe shortage of corneas nationwide [30,31]. No doubt that some eye banks may have corneas more than they need, but due to the lack of a unified management and distribution by a national eye bank association, the spare corneas in one eye bank can not be transferred to another bank for the maximum utilization in time. These corneas are usually dehydrated for a long period of preservation in the eye bank. After dehydration, the corneas can only be used for ALK. 2) In China, the indications for CT are mainly corneal leukemia and bacterial keratitis, which are not good indications for EK, while in America, the main indications for CT, PBK, and Fuchs’ dystrophy, are good indications for EK. 3) Due to the lamellar interface created during conventional LK, the postoperative visual acuity may be not as good as that after PK. The technical progresses have made it a reality for new techniques of LK to achieve a comparable visual acuity to PK [32]. In addition, for some diseases that were not typical indications for LK, such as chemical or thermal burns, herpes simplex keratitis scar, and bacterial keratitis scar, DALK is also applicable now, which contributes to the high proportion of LK [33,34].

Additionally, we noticed that the only common indication among the top four indications for CT in China and America was keratoconus, but the preferred techniques for it were quite different. Although there was an increase in ALK for keratoconus in America, PK remained the main surgical method, performed in 6224 patients while ALK only performed in 757 patients in 2014 [4]. In our survey, the proportion of ALK for keratoconus increased from
46.28% in 2014 to 71.37% in 2018 while PK decreased from 53.72% to 28.63%. The common practice of flattening the recipient bed in the process of ALK, which can affect the postoperative visual recovery due to the recipient bed wrinkles, may be a limiting factor for the application of ALK for patients with keratoconus in the past. With proper measures in surgery, the wrinkles can be avoided in the pupil area. Together with the application of DALK, the patients with keratoconus can obtain visual acuity comparable to PK [35]. Benefiting from improvements in techniques, even for cases with acute keratoconus, ALK can be performed before stroma scarring occurs. All these factors have contributed to the high proportion of ALK for keratoconus in China [36].

Due to immune rejection, chronic allograft dysfunction and late graft failure, the average survival time for graft after PK is only about 17 years. However, ALK can significantly lower the risk of chronic graft dysfunction and the graft can survive for about 49 years [37]. As most of the patients with keratoconus are teenagers, an early allograft dysfunction can affect their life. Therefore, ALK (including DALK), should be gradually popularized and applied worldwide for patients with keratoconus.

In our survey, information of CT from 2014 through 2018 in 64 hospitals were included. According to the data collected, the five largest hospital by number of CT surgeries completed 43.68% of the total number of CT surgeries in China and the five largest administrative units by number of CT surgeries performed 54.38% of the total number of CT surgeries in China. Except for No.1 Hospital of Xi’an City, the other 4 hospitals are in eastern China.

The geographical distributions of CT may correlate with the regional economy. The administrative units in eastern China have advantages over the units in central and western China. The rapid development of economy has opened people’s mind and increased their health needs. They are more willing to seek medical attention and more active in organ and tissue donation. In addition, the high economy level is the foundation of better transportation and medical level, which can benefit the patients and the cornea procurement.

Conclusions

In our survey, the data of CT in China from 2014 to 2018 were collected and analyzed to provide information for ophthalmologists at home and abroad to understand the condition of keratoplasty in China and then to conduct further studies. Although we have tried to contact as much hospitals as possible to collect information on CT, it is estimated that about 10% of the CT cases in China were not included. In addition, as this is the first time that a questionnaire has been designed to collect the general information of CT in China, limitations of the questionnaire exist inevitably. In the following five years, the questionnaire will be modified to collect more complete information (including the graft survival time) and use more standardized diagnoses and classification of indications to reflect the condition of CT in China comprehensively.

Overall, in China, the geographical distribution of keratoplasties and the number of keratoplasties performed in each hospital are quite unbalanced. To better serve the patients in central and western China, training for ophthalmologists, development of medical facility and popularization of donation knowledge at these regions are required. PK and ALK are the main surgical techniques for CT in China. Corneal leukoma, bacterial keratitis, and corneal dystrophies are the main indications for keratoplasties. These differences between China and America relate to the national conditions, economic development level, and ethnic characteristics.

Supporting information

S1 Table. Questionnaire of keratoplasty in China (Chinese and English version). (PDF)
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