



Original article

First multicenter survey on infectious keratitis following excimer laser surgery in Japan



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ABSTRACT

Purpose: To report the first multicenter survey in Japan on infectious keratitis after excimer laser surgery.

Methods: The laser *in situ* keratomileusis (LASIK) Safety Network (LSN) Committee sent questionnaires to 28 LSN member hospitals to assess the total number of laser corneal surgeries, the number of infection cases (including suspicious cases), and the postoperative follow-up rate during a 3-year period.

Results: Responses were obtained from 27 (96.4%) of 28 institutions. One phototherapeutic keratectomy infection case was reported among 22,415 excimer laser surgery cases, which equates to an incidence rate of 0.004%. The follow-up rate was 94.14% (67.2–100%), 80.11% (41.0–96.1%), 57.95% (11.5–93.0%), and 46.64% (4.7–93.0%) at 1 month, 3 months, 6 months, and 12 months of follow-up, respectively.

Conclusion: Infectious keratitis is a potentially devastating complication of excimer laser surgery. We did not see any infectious keratitis for refractive cases. This first multicenter survey in Japan on infectious keratitis provides important information on the safety of this therapy.

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1. Introduction

Excimer laser technology has evolved since it was first used in the early 1970s to etch silicone computer chips. Approximately 2 decades ago, the excimer laser began its evolution from a largely industrial cutting tool to the driving force behind precise, safe, and effective corneal refractive surgery. Excimer lasers are widely employed for laser *in situ* keratomileusis (LASIK), photorefractive keratectomy (PRK), and phototherapeutic keratectomy (PTK). This laser technology brought excimer laser surgery to the masses, and these laser surgeries are today the second most commonly performed ophthalmic procedure worldwide, after cataract surgery.

On February 25, 2009, the Japanese health authorities issued an alert that 70 (i.e., more than 10%) of 639 LASIK patients developed infectious keratitis—primarily nontuberculous mycobacterial

infections—after undergoing LASIK surgery between late September 2008 and mid-January 2009. Several outbreaks of post-LASIK mycobacterial infection have been reported.^{1–3} However, to our knowledge, this is the largest number of reported cases.⁴ This outbreak occurred surprisingly from a single private refractive surgery center in Tokyo, Japan. As of March 19, 2009, four of the 70 patients required hospitalization for intensive medical treatment; of these, two patients were believed likely to require corneal transplantation.

At the time, however, the precedent data on the incidence of infectious keratitis after excimer laser surgery had not been collected in Japan. Neither health authorities nor academic institutions in Japan conducted surveys on the subject. In fact, most academic university hospitals do not perform excimer laser surgeries on a regular basis. Because the number of patients undergoing these surgeries is increasing annually, the safety and efficacy of excimer laser surgery is a public health issue of considerable interest. We therefore established a network of physicians, the LASIK Safety Network (LSN), to collate these data. The prerequisites for joining this network were that the doctors should trust each

Conflicts of interest: The authors declare that they have no conflicts of interest.

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other and should be board certified. Furthermore, they should be trained in the cornea/refractive field and should follow their postoperative patients regularly.

The LSN Committee conducted a postexcimer laser surgery infectious keratitis survey to investigate the incidence of infectious keratitis after excimer laser surgeries among LSN institutions across Japan. This report presents the results of this survey.

2. Methods

In November 2010, the LSN Committee sent questionnaires to 28 LSN member hospitals to assess the previous 3-year-period (i.e., October 1, 2007 to September 30, 2010) concerning the total number of laser corneal surgeries, the number of infection cases

(including suspicious cases), and the postoperative follow-up rate at several time points (1 month, 3 months, 6 months, and 12 months) (Fig. 1). The definition of infectious keratitis in this report was the clinical appearance of a corneal ulcer and/or a positive culture result. The LSN members were asked to complete the questionnaire and send their responses back. No financial incentive was provided to the members for returning the questionnaire.

3. Results

We received responses from 27 (96.4%) of 28 institutions. One infection case was reported among 22,415 patients, which equates to an incidence rate of 0.004% (Table 1).

Questionnaire

TITLE: Survey on infectious keratitis following laser cornea surgeries

PURPOSE: The number of refractive surgeries has increased worldwide. However, in Japan there have been no multicenter surveys on the safety of laser corneal surgeries [e.g., laser *in situ* keratomileusis (LASIK), photorefractive keratectomy (PRK), epithelial LASIK (Epi-LASIK), laser epithelial keratomileusis (LASEK), and phototherapeutic keratectomy (PTK)]. We aim to report the manifestation of vision-threatening infectious keratitis after laser refractive surgeries.

METHOD: Each institution answered this questionnaire.

INCLUSION CRITERIA: All patients who underwent laser cornea surgery during the previous 3-year period (October 1, 2007 to September 30, 2010) and who were followed at least 1 month postoperatively.

EXCLUSION CRITERIA: Patients who received PTK for infectious keratitis (e.g., in some patients we performed PTK for cases of infectious keratitis such as *Acanthamoeba*).

Institution: _____

1. Total case number of laser cornea surgeries.

2. Total number of infectious keratitis (including suspicious cases).

3. Details on infectious keratitis (e.g., culture results, treatment, onset, slit lamp findings, visual acuity, etc.), if available.

(_____)

4. The follow-up rate at each time point:
 1 month cases (%)
 3 months cases (%)
 6 months cases (%)
 12 months cases (%)

Fig. 1. The questionnaire used for the survey. The questionnaire was originally written in Japanese. It has been translated into English for publication purposes.

Table 1

Case responses from LSN institutions for excimer laser surgery performed during a 3-year period from October 1, 2007 to September 30, 2010.

No.	Type of institution	Cases	Infection	Geographic area
1	Private	6182	0	Kanto
2	Private	4202	0	Chubu
3	Private	1788	0	Kanto
4	Private	1421	0	Shikoku
5	University	1324	0	Kansai
6	Private	1255	0	Kyusyu
7	Private	728	0	Kansai
8	Private	697	0	Kansai
9	Private	651	0	Chubu
10	Private	591	0	Tohoku
11	Private	560	0	Kyusyu
12	Private	551	0	Kanto
13	Private	364	0	Shikoku
14	Private	259	0	Tohoku
15	University	236	0	Kanto
16	Private	234	0	Hokkaido
17	Private	220	0	Hokkaido
18	Private	215	0	Kanto
19	Private	169	0	Chubu
20	Private	163	0	Chubu
21	University	147	0	Kanto
22	University	135	0	Hokkaido
23	University	118	1	Chugoku
24	Private	63	0	Kyusyu
25	Private	60	0	Chubu
26	University	48	0	Tohoku
27	University	34	0	Shikoku
TOTAL		22,415	1	

LSN = LASIK Safety Network.

This single infection case occurred after PTK for corneal dystrophy in the patient's left eye. The infection was evident 1 week after surgery, and intensive topical and oral antibiotic treatments were initiated. Treatment involved the administration of topical levofloxacin, topical cefmenoxime hydrochloride, ofloxacin eye ointment, and oral minocycline hydrochloride for 1 week. The organisms that were cultured were *Corynebacterium* spp. The preoperative uncorrected visual acuity (UCVA) and best spectacle-corrected visual acuity (BSCVA) were 0.05 and 0.08, respectively, whereas the postinfection UCVA and BSCVA were 0.1 and 0.2, respectively. We did not see any infectious cases in the refractive surgery group.

The follow-up rate at each time point was 94.14% (67.2–100%), 80.11% (41.0–96.1%), 57.95% (11.5–93.0%), and 46.64% (4.7–93.0%) at 1 month, 3 months, 6 months, and 12 months, respectively.

4. Discussion

Excimer laser-assisted cornea surgery is the mainstay in refractive surgery (e.g., LASIK, PRK) and in therapeutic treatment (e.g., PTK). As with other surgical procedures, case reports have described postoperative bacterial keratitis,^{5–11} fungal keratitis,^{12–14} or mycobacterial keratitis after refractive surgeries.^{15,16} Compared with other refractive procedures, LASIK preserves the integrity of Bowman's membrane and the overlying epithelium, thus decreasing the risk of microbial keratitis.¹⁷ However, infectious keratitis after LASIK or excimer surface ablation such as PRK has become an increasingly recognized sight-threatening complication of refractive surgery. The incidence of infectious keratitis is unknown and varies widely in studies. Based on a comprehensive review and analysis of the literature, Chang et al¹⁸ report that the incidence of infection after LASIK can vary widely from 0% to 1.5%. To our knowledge, the largest outbreak of infectious keratitis after LASIK surgery originated from a single center in Tokyo, Japan. The incidence of this infection outbreak was more than 10%.

Predisposing factors of infectious keratitis generally include a history of corneal surgery,^{8,19} breaks in the epithelial barrier,⁸ excessive surgical manipulation,⁵ intraoperative contamination,³ and delayed postoperative re-epithelialization of the cornea.^{8,16} The outbreak in Tokyo was from a nosocomial infection resulting from improper sterilization procedures for each patient and from a problem with the clinic's autoclave system, which had not undergone proper maintenance inspections.

Excimer laser surgery requires soft and hard resources such as space, lasers, clean rooms, and skilled technicians and nurses. This surgery is selective to healthy eyes, other than eyes with refractive errors (except PTK patients), and creates the hurdle for a government-covered insurance system, which is primarily concerned with diseased patients. A similar number of LASIK surgeries are performed *per capita* in the United States and in Japan, although a higher percentage of the total number of surgeries is executed mostly by private surgical centers in Japan. However, in the United States, LASIK surgeries are performed nationwide, including in many academic centers. In Japan, excimer laser surgeries are not widely accepted in resident and fellowship programs, and physicians are not exposed to the procedures on a regular basis. In addition, little collaboration has been established between academic and private institutions in Japan. Some claim the Japanese reticence is precipitated by its conservative culture and by media reports that “clouded the market with negativism for excimer laser surgery.”²⁰ These attitudes may partly explain why official or academic surveys have not been conducted in Japan, despite growing public interest.

Refractive surgeons in universities and private clinics in Japan therefore established a voluntary and collaborative group, called the LASIK Safety Network (Fig. 2). At the time of the survey, the institutions composing this group were 28 hospitals (8 universities and 20 private clinics) that performed excimer laser surgeries. As of February 2013, the number increased to 34 institutions (9 universities and 25 private clinics). There were no cases of infectious keratitis after LASIK or PRK in 22,415 patients during the 3-year survey period; however, a single case of infectious keratitis after

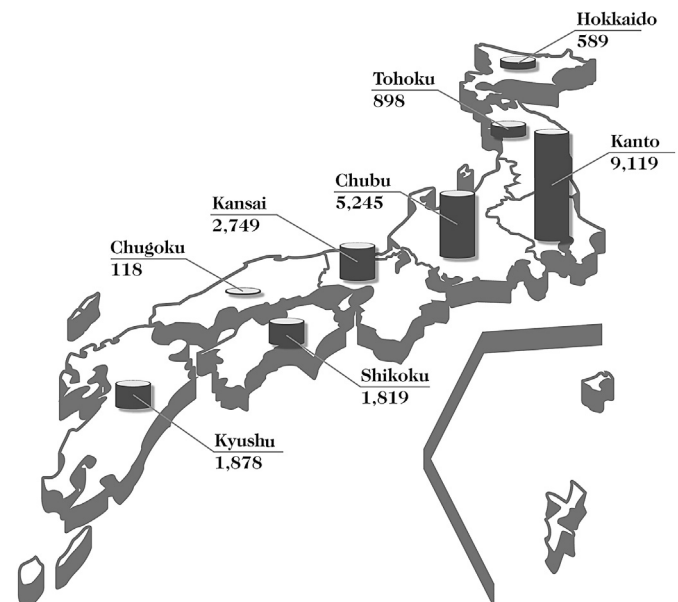


Fig. 2. The geographic area of each excimer laser clinic. The regions of Japan are not officially administrative units. However, Japan has been divided into eight regions: Hokkaido, Tohoku, Kanto, Chubu, Kansai, Chugoku, Shikoku, and Kyushu. We determined the number of cases in each area.

PTK has been reported. For the first time, this survey of LSN members provides useful information about infectious keratitis after excimer laser procedures in Japan. We believe that the responses from 27 institutions of the 28 institutions, which are based on 22,415 procedures, are representative of infectious keratitis after excimer laser procedures.

The low incidence of infection reported in this paper may be because of increased awareness and improved sterile techniques. A high degree of suspicion can result in good visual recovery from infectious keratitis, when coupled with a rapid diagnosis and appropriate therapy. Furthermore, preventative measures and great care are important before, during, and after surgery. Most laser surgeons in Japan use sterile drapes, gowns, gloves, and masks, just as they do for intraocular surgeries. Proper sterilization techniques can prevent the use of contaminated instruments. Several epidemics of atypical mycobacteria have been associated with the use of non-sterile water to clean instruments or the use of ice during laser surgery^{2,3,21}; therefore, all fluids applied to the eye before, during, and after refractive surgery should be sterile.²² To reduce the risk of developing infections after the operation, patients should be advised to avoid exposure to contaminated water, close contact with pets, and contaminated work environments until the epithelium heals.²³ However, with all efforts to avoid infection, doctors have to remember that some normal ocular bacterial flora is resistant to fluoroquinolone antibiotics (which are frequently used for laser refractive surgery) and that the infectious risk is not zero.²⁴

Major limitations of the survey include: (1) the retrospective noncontrolled nature of the study; (2) the responses of non-LSN members were not considered; (3) the period of the survey (2007–2010) was different from period of the infection outbreak (2008–2009); (4) the follow-up rate appeared widely variable among the members; and (5) the small percentage of infection cases relative to the number of reported total cases (400,000–500,000 cases in 2008).

It is possible that the infected patients may have gone to other institutions for help. However, in a small country such as Japan that has a small number of doctors performing laser vision correction, doctors usually hear rumors of postoperative infection cases, as we did, with an infection outbreak.

Despite these limitations, we believe this is a very important first step in the Japanese Excimer Laser Society, which academic societies and officials have not conducted to date. In conclusion, infectious keratitis is a potentially devastating complication of excimer laser surgery. This article reports the results of the first multicenter survey on infectious keratitis in Japan. We are moving towards conducting a nationwide survey of all institutions using excimer lasers for eye surgeries.

LASIK Safety Network

Minamiaoyama Eye Clinic, Minatomirai Eye Clinic, Eguchi Eye Hospital, Miyata Ophthalmic Hospital (Miyazaki Prefecture), Miyata Ophthalmic Hospital (Kagoshima Prefecture), Hayashi Eye Hospital, Tane Memorial Eye Hospital, Okamoto Eye Clinic, Hara Eye Hospital, Baptist Eye Clinic, Ogasawara Eye Clinic, Nagoya Eye Clinic, Tsuboi Eye Center, Kaiya Eyes Clinic, Sugita Eye Hospital, Fujita Eye Clinic, Miyake Eye Hospital, Tokai Eye Clinic, Seishin Eye Hospital, Satoh Yuya Eye Clinic, Ishida Eye Clinic, Kobayashi Eye Clinic, Obihiro Eye Clinic, Inouye Eye Hospital, Yoshino Eye Clinic, Keio University, Iwate Medical University, Asahikawa Medical

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