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Impact of Patient Characteristics and Surgery-Related Risk Factors on Endophthalmitis after Cataract surgery: A Meta-Analysis

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Keywords

Cataract surgery · Endophthalmitis · Phacoemulsification · Meta-analysis

Abstract

Introduction: Cataracts are the leading cause of blindness worldwide, with a notably high incidence rate. Endophthalmitis is the most severe complication following cataract surgery, often resulting in profound vision loss. This study evaluates the impact of risk factors such as age, sex, diabetes mellitus (DM), hypertension, posterior capsule rupture (PCR), type of surgery, and use of intraocular lens (IOL) material on the risk of endophthalmitis after cataract surgery. ***Methods:*** English and Chinese public databases were searched from inception to March 1, 2024. We included studies reporting the number of occurrences of endophthalmitis after cataract surgery on potential risk factors, including age, sex, DM status, hypertension status, intraoperative PCR, type of surgery and use of IOL material. The quality of the included studies was assessed using the Newcastle-Ottawa Scale. ***Results:*** A total of 57 studies were included and critically evaluated in the meta-analysis. The results showed that female sex was associated with a lower risk of endophthalmitis (odds ratio [OR]: 0.81; 95% CI: 0.75–0.87; $p < 0.001$). Individuals with diabetes who underwent cataract surgery were found to have a greater risk of endophthalmitis ($I^2 = 95\%$; OR: 4.90; 95% CI: 2.41, 9.95; $p < 0.001$), but the result may be influenced by publication bias. Individuals with hypertension (OR: 2.88; 95% CI: 1.53, 5.45; $p = 0.001$) and intraoperative PCR (OR: 9.18; 95% CI: 3.31, 25.43; $p < 0.001$) were found to have a greater risk of endophthalmitis. Phacoemulsification significantly reduced the risk of endophthalmitis compared with extracapsular cataract extraction (ECCE) (OR: 0.62; 95% CI: 0.45, 0.85) based on network meta-analysis. ***Conclusion:*** Male sex, hypertension, intraoperative PCR, and the use of the ECCE surgical approach are associated with a greater risk of postoperative endophthalmitis. Although an age-related trend in elevated risk was observed, this finding should be interpreted cautiously.

Introduction

The crystalline lens is a small, transparent ocular structure located in the anterior segment of the eye that focuses light on the retina. Opacification of the crystalline lens is known as cataract. Nearly one billion people are blind or visually impaired globally, with cataracts being the leading cause of blindness worldwide [1]. Despite

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being asymptomatic in the early stages, cataracts can progressively impair vision over time, significantly reducing an individual's quality of life and productivity [2]. Currently, the number of cataract cases is increasing due to the aging of the population. As cataract removal surgery and intraocular lens (IOL) implantation can effectively restore vision, blindness related to cataracts is largely preventable in most cases [3, 4].

Endophthalmitis refers to intraocular bacterial or fungal infections involving the vitreous and/or aqueous humor [5]. Endophthalmitis is one of the most serious complications of cataract surgery, often leading to severe visual impairment with devastating effects on vision [6]. Most cases of endophthalmitis present as acute, with symptoms lasting from hours to days. In various countries and regions, the etiological agents of infection may differ. In the USA and Europe, bacterial infections predominate, whereas in tropical areas such as India, fungal infections account for 10–20% of the cases. Many countries, societies, and institutions are monitoring the incidence of endophthalmitis related to cataract surgery. According to published reports in the ophthalmic literature, the current occurrence rates vary globally from 0.03% to 0.2% [7]. Despite its very low incidence, it can lead to profoundly serious consequences. Therefore, analyzing the factors influencing the risk of endophthalmitis will help identify high-risk populations for early prevention and intervention.

In a published meta-analysis, Shi et al. [8] examined the overall incidence rate and risk factors for endophthalmitis following phacoemulsification surgery. The results of the study indicated an overall incidence rate of 0.092% for post-cataract surgery endophthalmitis. They also suggested that the use of intracameral antibiotics could significantly reduce the occurrence of endophthalmitis [8]. Cao et al. [6] also analyzed the risk factors for acute endophthalmitis following cataract surgery. The results indicated that factors such as intracapsular or extracapsular cataract extraction (ECCE), clear corneal incisions, and intracameral injection of cephalosporin drugs were associated with acute endophthalmitis. However, this study was published in 2013, and a substantial amount of research was published between 2013 and 2023 [6]. Therefore, an update of this study is warranted. Additionally, in the analysis of risk factors, only the study-specific odds ratios (ORs) or relative risks (RRs) of the included studies were pooled, which is a one-sided or even erroneous approach. In studies analyzing risk factors, statistically significant results from logistic regression are often reported, and the outcomes are inclined toward positivity. Hence, this study intends to conduct a meta-analysis of results with original data.

This study will conduct a meta-analysis of research results reporting original data on the frequency of endophthalmitis after cataract surgery, further exploring the impact of factors such as age, sex, diabetes mellitus status, hypertension comorbidities, posterior capsule rupture (PCR), type of surgery, and use of IOL material on the risk of endophthalmitis after cataract surgery. Given that post-cataract surgery endophthalmitis is rare, this study imposed restrictions on the sample size and incidence rate of the included studies. Tomoyuki et al. suggested that a minimum of 10 events for each explanatory variable is necessary [9]. Abnormally high (above 1%) rates of endophthalmitis may indicate a nosocomial outbreak. Therefore, this study included a minimum sample size of 1,000 patients, a requirement of 10 events, and an incidence rate of lower than 1%.

Methods

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards.

Search Strategy

The two authors systematically searched the PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang, and Chinese Biomedical Literature Database (CBM) databases for eligible articles published up to March 1, 2024. The brief literature search strategies used were ("cataract surgery" or "phacoemulsification") and "endophthalmitis" and ("factor" or "predictor" or "risk"). Additionally, the reference lists of both original articles and relevant reviews were manually searched for potentially eligible studies.

The Eligibility Criteria

Studies meeting the following inclusion criteria were included in this systematic review and meta-analysis: (1) were prospective, retrospective, or cohort studies evaluating the incidence of endophthalmitis following cataract surgery; (2) reported the number of occurrences of endophthalmitis under different risk factors and the overall population size; and (3) reported the results of at least one established risk factor, including age, sex, presence of diabetes, hypertension, PCR occurrence, surgical type and specific IOL material. Studies were excluded if they met the following criteria: (1) lacked specific data on the number of occurrences and the data could not be extrapolated; (2) incomplete selection of the control group population, i.e., selecting only a subset of the control group for risk factor analysis using methods such as propensity score matching; (3) sample size less than 1,000; (4) fewer than 10 cases of endophthalmitis occurrence; (5) endophthalmitis risk exceeding 1%; and (6) reported data displaying significant errors or discrepancies.

Data Extraction and Quality Assessment

Two independent authors identified the following relevant data from each included study: first author name, year of publication, design type, sample source, study period, sample size, number of procedures/eyes, number of cases of endophthalmitis, and risk factors analyzed. For studies containing overlapping data, only the most recent or information-rich dataset was included. Any disagreements were resolved through mutual discussion. The Newcastle-Ottawa Quality Assessment Scale (NOS) was used to evaluate the quality of the included studies. The quality of RCTs is generally higher than that of observational studies; therefore, RCTs are additionally indicated in quality assessment. In this meta-analysis, studies with a score of ≥6 were defined as high-quality studies.

Statistical Analysis

Considering that the rarity of endophthalmitis, the OR with its 95% confidence interval (CI) was used to determine the occurrence risk using the Peto method. The heterogeneity of the included studies was assessed using Cochran's Q statistic and the I^2 index. An I^2 value greater than 50% indicated significant heterogeneity, and a random-effects model was used for analysis; otherwise, fixed-effects models were used. Since susceptible pathogens may differ in different regions, subgroup analysis between countries was performed. Publication bias was assessed by Egger's linear regression and Schwarzer's rank correlation test [10]. If publication bias existed, the trim-and-fill method was used to correct the results. All the statistical analyses were performed using the R programming language. Since surgical methods and IOL materials may be comparable across multiple arms, this study used a frequency method network meta-analysis to evaluate and merge the results of direct comparisons and indirect comparisons and used the surface under the cumulative ranking curve (SUCRA) to rank potential intervention methods. A comparison-adjusted funnel plot was used to assess potential publication bias. Statistical analyses were conducted using R software (version 4.3.2) with the "meta" and "netmeta" packages.

Results

After searching the English literature database, 2694 items were obtained, of which 977 were unique after deduplication. After the initial screening, 128 English studies were retrieved. The Chinese database was screened through a similar process, resulting in a total of 220 entries, 147 of which remained after deduplication. After the initial screening, the full-texts of the remaining 35 articles were evaluated. A total of 106 articles were excluded for the following reasons: (1) the study did not report original data (n = 64); (2) the case-control studies selected only a portion of the population without endophthalmitis as the control group (n = 19); (3) the incidence of endophthalmitis in the study was greater than 1% (n = 9); (4) the sample size was less than 1,000 cases or the number of endophthalmitis cases was less than 10 (n = 8); (5) the publication was repeated (n = 5); and (6) retracted research (n = 1). Overall, 57 articles were included in the final analysis (shown in Fig. 1) [9, 11–66].

Due to the use of large-sample size studies and the inclusion of exposed and control groups from the same cataract surgery population, the overall NOS scores were relatively high, with the majority of studies scoring 8 and 9 points. However, in most studies, the definition of endophthalmitis diagnostic criteria for the exposed group was inadequately described, leading to ambiguity. Nevertheless, the overall study design quality is highly desirable (Table 1).

Regarding the impact of sex on the risk of endophthalmitis after cataract surgery, it was suggested that male sex is associated with a greater risk of endophthalmitis (OR: 0.81; 95% CI: 0.75–0.87; $p < 0.001$). However, in some countries, such as Japan (OR: 1.65; 95% CI: 0.55, 4.96) and Singapore (OR: 0.70; 95% CI: 0.22, 2.18), the incidence was not significantly different between males and females (shown in Fig. 2). No potential publication bias was detected (Schwarzer: p = 0.722; Egger: p = 0.066) (online suppl. Fig. 1a; for all online suppl. material, see https://doi.org/10.1159/000543353).

Considering the effect of age on the risk of post-cataract surgery endophthalmitis, every 5 years was chosen as the cutoff value for patients aged 60–90 years in our study. The findings indicated that when 60 years was

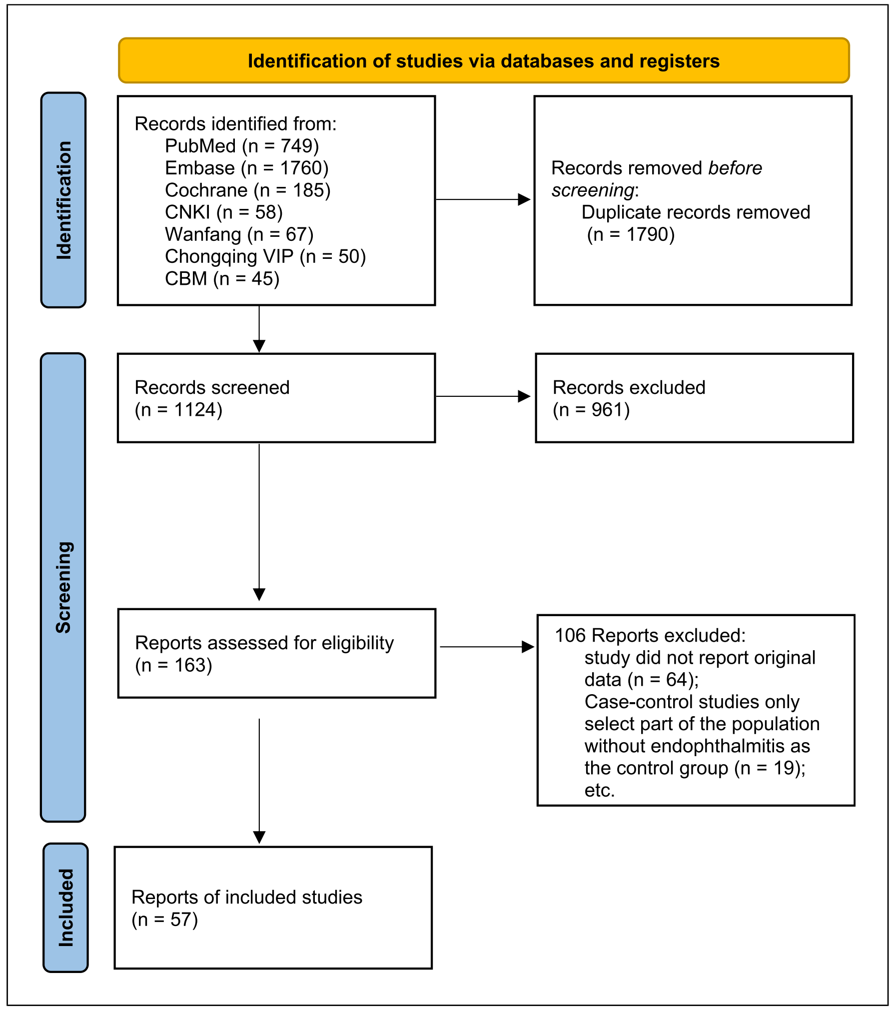


Fig. 1. Flowchart of the study selection process in this meta-analysis.

used as the cutoff point, the random-effects model did not significantly differ (OR: 1.03; 95% CI: 0.70, 1.51; p = 0.897). However, at 65, 70, 85, and 90 years, the incidence of endophthalmitis in the older age groups was significantly greater than that in the younger age groups at the respective cutoff points. Overall, the incidence of post-cataract surgery endophthalmitis significantly increased with increasing age (Table 2).

Notably, at the age of 80 years, there was no significant difference between the younger and older age groups (OR: 0.88; 95% CI: 0.76, 1.03; p = 0.110). When the cutoff point was set at 75 years, the incidence rate in the younger population was significantly greater than that in the older population (OR: 1.05; 95% CI: 1.00, 1.10; p = 0.046). Notably, 75 years is the average age at cataract surgery [67]. With 75 serving as the cutoff point, the total number of individuals in the age group younger than 75 years (n = 8,339,506) was closest to that in the age group older than 75 years (n = 6,498,028). As detailed cutoff values for every age were not provided in all included studies, the results of this study still need more research for confirmation. Therefore, caution should be exercised in interpreting the elevated risk of post-cataract surgery endophthalmitis with advancing age. The findings with a cutoff point of 75 warrant special consideration in future studies (Table 2).

Compared with individuals without diabetes, individuals with diabetes who underwent cataract surgery were found to have a greater risk of endophthalmitis (I^2 = 95%; OR: 4.90; 95% CI: 2.41, 9.95; p < 0.001). In populations from China, Malaysia, South Korea, the UK, and France, individuals with diabetes had significantly greater rates of postoperative endophthalmitis than those without diabetes. However, no significant differences were observed in the Japanese population, whereas in the Polish population, nondiabetic individuals had a

Table 1. Characteristics of included studies

Study	Type of design	Country/region	Data sources	Duration of data harvest	Surgery type	Sample size	Surgeries, *n*	Endophthalmitis cases	Risk factors	NOS
Junjie et al. [11] (2024)	Retrospective study	China	Xuanwu Hospital of Capital Medical University	2015–2023	Phacoemulsification/IOL implantation	12,308	NA	32	Age, sex, DM, HTN, PCR, IOL material	9
Low et al. [12] (2023)	Retrospective study	UK	The Royal College of Ophthalmologists' National Ophthalmology Database (RCOphth NOD)	2010–2021	Cataract surgery	920,286	1,351,415	308	Age, sex, IOL material, PCR, DM	8
Hou et al. [13] (2023)	Retrospective cohort study	China	Taiwan National Health Insurance Research Database	2000–2017	Cataract surgery	883,398	1,766,796	4,423	Age, sex, DM	9
Govinda Raj et al. [14] (2023)	Retrospective registry study	Malaysia	National Eye Database (NED)	2012–2020	Cataract surgery	231,281	267,966	185	Sex, age, DM, HTN	8
Dongling et al. [15] (2023)	Retrospective study	China	Ningxia Eye Hospital	2018–2021	Phacoemulsification	3,600	NA	12	Age, sex, DM	9
Friling et al. [16] (2021)	Retrospective cohort registry study	Sweden	Swedish National Cataract Register (NCR)	2002–2017	Cataract Surgery	NA	1,457,172	422	Age, sex, type of surgery	8
Sun et al. [17] (2021)	Retrospective study	China	Data from Qingdao Eye hospital	2008–2019	Cataract Surgery	55,612	55,612	42	Age, sex, DM, PCR	9
Jing et al. [18] (2021)	Retrospective study	China	Zhengzhou Second People's Hospita	2018–2020	Phacoemulsification	9,085	NA	41	Age, sex, HTN, DM	9
Aihua et al. [19] (2021)	Retrospective Study	China	Chuxiong People's Hospital	2017–2019	Cataract surgery	1,636	1,645	15	Age, sex, HTN, DM, type of surgery	9
YuMeng et al. 2020 [20]	Retrospective	China	The First Affiliated Hospital of Zhengzhou University	2014–2019	Phacoemulsification/IOL implantation	8,200	NA	23	Age, sex, DM, HTN	9
Pershing et al. [21] (2019)	Retrospective cohort study	USA	American Academy of Ophthalmology IRIS (Intelligent Research in Sight) Registry database	2013–2017	Cataract surgery	5,401,686	8,542,838	3,629	Age, sex	9

Table 1 (continued)

Study	Type of design	Country/region	Data sources	Duration of data harvest	Surgery type	Sample size	Surgeries, *n*	Endophthalmitis cases	Risk factors	NOS
Nowak et al. [22] (2019)	Retrospective cohort study	Poland	National Database of Hospitalizations	2010–2015	Cataract surgery	NA	1,218,777	1,331	Age, sex, DM	9
Kim et al. [23] (2019)	National sample cohort	Korea	Nationwide insurance claims data	2014–2017	Cataract surgery	982,203	1,505,103	953	Age, sex, HTN, DM, type of surgery	9
Baek-Lok et al. [24] (2018)	National sample cohort	Korea	National Health Insurance Service National Sample Cohort (NHIS-NSC)	2002–2013	Cataract surgery	45,235	70,719	49	Age, sex, DM	9
Wai e al. [25] (2018)	Retrospective cross-sectional study	Malaysia	The Malaysian Ministry of Health Cataract Surgery Registry (MOH CSR)	2008–2014	Cataract surgery	163,503	NA	131	Age, sex, DM, HTN, type of surgery, PCR	8
Ge and Cheng [26] (2018)	Retrospective study	China	The People's hospital of Pingdu	2012–2017	Phacoemulsification	4,500	6,180	12	Age, sex, DM, HTN, PCR	8
Rui et al. [27] (2018)	Retrospective study	China	Xiaogan Hospital Affiliated to Wuhan University of Science and Technology	2010–2016	Cataract surgery	12,676	NA	61	Age, sex, HTN, DM	9
Canming [28] (2018)	Retrospective Study	China	The Third People's Hospital of Baiyun District, Guangzhou	2015–2017	Cataract surgery	2,000	NA	15	Age, sex, HTN, DM	8
Wang et al. [29] (2018)	Retrospective Study	China	Zhongnan Hospital of Wuhan University	2011–2016	Cataract surgery	6,125	8,576	12	Age, sex, HTN, DM	8
Inoue [9] (2017)	Prospective study	Japan	The Japanese Prospective Multicenter Study Group for Postoperative Endophthalmitis after Cataract Surgery	2012–2013	Cataract surgery	52,983	NA	13	Sex, type of surgery, IOL material, PCR	8
Zhu [30] (2017)	Retrospective, consecutive case series study	China	30 small and medium-scale departments of ophthalmology	2011–2013	Cataract surgery	46,185	59,392	52	Age, sex, type of surgery, PCR	9

Table 1 (continued)

Study	Type of design	Country/ region	Data sources	Duration of data harvest	Surgery type	Sample size	Surgeries, *n*	Endophthalmitis cases	Risk factors	NOS
Haripriya et al. [31] (2017)	Retrospective, clinical registry-based study	USA	American Society of Cataract and Refractive Surgery (ASCRS) Hospitals	2014–2016	Cataract surgery	617,453	617,453	278	PCR	8
Luo et al. [32] (2017)	Retrospective Study	China	Zhongshan Ophthalmology Center, Sun Yat-sen University	2011–2016	Phacoemulsification	64,469	NA	15	Age, sex, HTN, DM	7
Jin [33] (2017)	Retrospective study	China	Guizhou Provincial People's Hospital	1996–2016	Cataract surgery	20,000	NA	11	Age, sex, DM	9
Daien et al. [34] (2016)	Population-based cohort study	France	1,546 French health care facilities	2010–2014	Cataract surgery	2,434,008	3,351,401	1,941	Age, sex, DM, type of surgery, PCR	9
Dong et al. [35] (2016)	Retrospective Study	China	Hebei Eye Hospital	2010–2015	Phacoemulsification	12,000	NA	30	Age, sex, HTN, DM	8
Wang et al. [36] (2016)	Retrospective Study	China	Xiaogan Central Hospital	2011–2015	Cataract surgery	5,600	NA	13	Age, sex, HTN, DM, type of surgery	8
Herrinton et al. [37] (2015)	Observational, longitudinal cohort study	USA	Kaiser Permanente, California	2005–2012	Phacoemulsification	204,515	315,246	215	Age, PCR	8
Li et al. [38] (2015)	Retrospective study	China	Affiliated Hospital of Luzhou Medical University	2012–2014	Cataract surgery	1,900	1,900	15	Age, sex, DM, HTN	7
Huang et al. [39] (2015)	Retrospective study	China	Qingdao Eye Hospital	2006–2013	Phacoemulsification	16,172		21	Sex, DM, PCR	9
Xuan et al. [40] (2015)	Case-control	China	Red Cross Hospital of Nanning city	2005–2013	Cataract surgery	11,105	13,326	16	Sex, type of surgery	9
Yao et al. [41] (2014)	Retrospective multicenter study	China	Eight eye centers of tertiary care hospitals	2006–2011	Cataract surgery	NA	201,757	66	Age, sex, type of surgery	9
Liu et al. [42] (2014)	Retrospective Study	China	Guangxi Yulin Second People's Hospital	2012–2014	Cataract surgery	1,572	NA	10	Age, sex; HTN, DM	8

Table 1 (continued)

Study	Type of design	Country/ region	Data sources	Duration of data harvest	Surgery type	Sample size	Surgeries, *n*	Endophthalmitis cases	Risk factors	NOS
Tingxia Yu, 2014 [43]	Retrospective Study	China	First Affiliated Hospital of Suzhou University	2007–2012	Cataract extraction	5,724	6,813	10	Age, sex, HTN, DM	7
Barreau et al. [44] (2012)	Prospective study	France	Dupuytren Hospital	2003–2008	Cataract surgery	5,115	NA	36	Age, sex	8
Tan et al. [45] (2011)	Cohort study	Singapore	Tan Tock Seng Hospital	1999–2010	Cataract surgery	NA	50,177	21	Sex, type of surgery	8
Ravindran et al. [46] (2009)	Retrospective study	India	Aravind Eye Hospital	2007–2008	Cataract surgery	NA	42,426	38	Type of surgery	9
Hatch et al. [47] (2009)	Retrospective study	Canada	Ministry of Health and Long-Term Care Ontario Health Insurance Plan physician claims database and the Canadian Institute for Health Information Discharge Abstract Database	2002–2006	Cataract surgery	NA	442,177	617	Age, sex, PCR	8
Mezaine et al. [48] (2009)	Retrospective observational case series	Saudi Arabia	King Khaled Eye Specialist Hospital	1997–2006	Cataract surgery	NA	29,509	20	Type of surgery	9
Luo et al. [49] (2009)	Retrospective Study	China	Zhongshan Ophthalmology Center, Sun Yat-sen University	2003–2009	Cataract extraction	9,660	10,898	27	Age, sex, HTN, DM	8
ESCRS Endophthalmitis Study Group [50] (2007)	prospective randomized	Multicenter	Twenty-four ophthalmology units	2003–2006	Phacoemulsification	16,603	NA	20	Sex, IOL material	9
Lundstrom et al. [51] (2007)	Nationwide prospective study	Sweden	The Swedish National Cataract Register	2002–2004	Cataract surgery	NA	225,471	109	Age, sex, type of surgery, IOL material	9

Table 1 (continued)

Study	Type of design	Country/region	Data sources	Duration of data harvest	Surgery type	Sample size	Surgeries, *n*	Endophthalmitis cases	Risk factors	NOS
Wu et al. [52] (2006)	Retrospective study	China	Chang Gung Memorial Hospital, Kaohsiung Medical Center	1991–2004	Cataract surgery	NA	21,562	46	Type of surgery	9
West et al. [53] (2005)	Population-based review	US	Medicare beneficiary claims files	1994–2001	Cataract surgery	381,756	477,627	1,026	Age, sex	9
Gisela Wejde, 2005 [54]	National prospective survey	Sweden	Swedish National Cataract Register	1999–2001	Cataract surgery	NA	188,151	112	Age, sex, type of surgery, IOL material	9
Lalitha et al. [55] (2005)	Retrospective, interventional, observational case series	India	Aravind Eye Hospital, Madurai	2002–2003	Cataract surgery	NA	36,072	19	Age, sex, type of surgery	9
Haapala et al. [56] (2005)	Retrospective study	Finland	hospital district of Southwest Finland	1987–2000	Cataract surgery	NA	29,350	47	Type of surgery	9
Li et al. [57] (2004)	Retrospective study	Australia	The Western Australian Data Linkage System	1980–2000	Cataract surgery	NA	117,083	210	Age, sex, type of surgery	9
Wong and Chee [58] (2003)	Prospective case series	Singapore	Singapore National Eye Center	1996–2001	Cataract surgery	NA	44,803	34	Age, sex, type of surgery, PCR	8
Nagaki [59] (2003)	RCT	Japan	Toyama Medical and Pharmaceutical University Hospital and affiliated hospitals	1998–2001	Small-incision cataract surgery	NA	7,622	15	Type of surgery, IOL material	RCT
Mayer et al. [60] (2003)	Retrospective study	UK	Department of Ophthalmology, Taunton and Somerset Hospital	1991–2001	Cataract surgery	NA	18,191	30	Type of surgery	9
Montan et al. [61] (2002)	Prospective study	Sweden	Swedish National Cataract Register	1998	Cataract surgery	NA	54,666	58	Age, sex, type of surgery, IOL material	9

Table 1 (continued)

Study	Type of design	Country/region	Data sources	Duration of data harvest	Surgery type	Sample size	Surgeries, *n*	Endophthalmitis cases	Risk factors	NOS
Kalpadakis et al. [62] (2002)	Retrospective	Greece	Eye Clinic of the Komotini General Hospital	1998–2001	Cataract surgery	2446	NA	20	Type of surgery	9
Montan et al. [63] (1997)	Retrospective	Sweden	St Eriks Hospital	1990–1993	Cataract surgery	NA	22,091	57	Type of surgery	8
Norregaar et al. [64] (1996)	Retrospective cohort study	Denmark	The Danish National Patient Register (DNPR)	1985–1987	cataract extraction	19,426	NA	61	Age, sex, type of surgery	8
Javitt et al. [65] (1994)	Retrospective	USA	The Medical Provider Analysis and Review (MEDRAR) file maintained by the Health Care Financing Administration	1986–1987	Cataract surgery	57,103	NA	44	Age, sex	9
Javitt et al. [66] (1991)	Retrospective	USA	The Medical Provider Analysis and Review (MEDRAR) file maintained by the Health Care Financing Administration	1984–1985	Cataract surgery	338,141	NA	440	Age, sex	9

DM, diabetes mellitus; HTN, hypertension; IOL, intraocular lens; NA, not available; NOS, Newcastle-Ottawa Scale; PCR, posterior capsule rupture; RCT, randomized controlled trial.

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (common)	Weight (random)	Odds Ratio Peto, Fixed + Random, 95% CI
Nation = China							
Junjie Bian 2024 [11]	14	5106	18	7202	0.2%	1.0%	1.10 [0.54; 2.22]
Chiun–Ho Hou 2023 [13]	2231	998520	2192	768276	27.0%	6.7%	0.78 [0.74; 0.83]
Dongling Feng 2023 [15]	6	1753	6	1847	0.1%	0.4%	1.05 [0.34; 3.27]
Jiajun Sun 2021 [17]	27	32933	15	22679	0.3%	1.3%	1.23 [0.67; 2.28]
Jing Gao 2021 [18]	19	4325	22	4760	0.3%	1.3%	0.95 [0.51; 1.76]
Aihua Chen 2021 [19]	6	942	9	694	0.1%	0.5%	0.48 [0.17; 1.35]
YuMeng Wu 2020 [20]	10	3873	13	4304	0.1%	0.8%	0.86 [0.38; 1.94]
Lei Ge 2018 [26]	5	2261	7	3919	0.1%	0.4%	1.25 [0.38; 4.04]
Rui Li 2018 [27]	25	5135	36	7541	0.4%	1.7%	1.02 [0.61; 1.70]
Canming Huo 2018 [28]	7	997	8	1003	0.1%	0.5%	0.88 [0.32; 2.43]
Shun Wang 2018 [29]	5	4019	7	4557	0.1%	0.4%	0.81 [0.26; 2.52]
Yanan Zhu 2017 [30]	32	21869	20	24316	0.3%	1.5%	1.77 [1.03; 3.05]
Yiwen Luo 2017 [32]	6	36429	9	28040	0.1%	0.5%	0.51 [0.18; 1.42]
Xin Jin 2017 [33]	5	8343	6	11657	0.1%	0.4%	1.17 [0.35; 3.87]
Wei Dong 2016 [35]	12	5822	18	6178	0.2%	1.0%	0.71 [0.35; 1.46]
Feng Wang 2016 [36]	6	2415	7	3185	0.1%	0.5%	1.13 [0.38; 3.40]
Youyi Li 2015 [38]	5	770	10	1130	0.1%	0.5%	0.74 [0.26; 2.08]
Yusen Huang 2015 [39]	18	9139	3	7033	0.1%	0.7%	3.29 [1.39; 7.79]
Zhongning Xuan 2015 [40]	9	6109	7	4996	0.1%	0.6%	1.05 [0.39; 2.82]
Ke Yao 2014 [41]	33	111590	33	90167	0.4%	1.8%	0.81 [0.50; 1.31]
Xuezhuang Liu 2014 [42]	4	700	6	872	0.1%	0.4%	0.83 [0.24; 2.90]
Tingxia Yu 2014 [43]	4	3225	6	3588	0.1%	0.4%	0.74 [0.22; 2.58]
Rongjiang Luo 2009 [49]	12	5157	15	5741	0.2%	0.9%	0.89 [0.42; 1.90]
Total (common effect, 95% CI)		**1271432**		**1013685**	**30.4%**	**.**	**0.80 [0.76; 0.85]**
Total (random effect, 95% CI)					**.**	**24.1%**	**0.95 [0.80; 1.12]**
Heterogeneity: Tau^2 = 0.0301; Chi^2 = 26.68, df = 22 (P = 0.2235); I^2 = 17.6%							
Nation = UK							
Liying Low 2023 [12]	171	786234	137	565181	1.9%	4.3%	0.90 [0.71; 1.12]
Nation = Malaysia							
Durgavashini Govinda Raj 2023 [14]	85	122215	100	109066	1.1%	3.5%	0.76 [0.57; 1.01]
Yong Zheng Wai 2018 [25]	45	85991	86	77512	0.8%	2.9%	0.48 [0.34; 0.68]
Total (common effect, 95% CI)		**208206**		**186578**	**2.0%**	**.**	**0.63 [0.50; 0.78]**
Total (random effect, 95% CI)					**.**	**6.4%**	**0.61 [0.39; 0.95]**
Heterogeneity: Tau^2 = 0.0774; Chi^2 = 3.96, df = 1 (P = 0.0466); I^2 = 74.7%							
Nation = Sweden							
Emma Friling 2021 [16]	238	890290	184	566882	2.5%	4.8%	0.82 [0.67; 1.00]
Mats Lundstrom 2007 [51]	67	146239	41	79214	0.6%	2.4%	0.88 [0.59; 1.31]
Gisela Wejde 2005 [54]	74	124381	38	63744	0.6%	2.5%	1.00 [0.67; 1.48]
Per Montan 2002 [61]	37	36309	21	18355	0.3%	1.5%	0.89 [0.52; 1.53]
Total (common effect, 95% CI)		**1197219**		**728195**	**4.1%**	**.**	**0.86 [0.74; 1.00]**
Total (random effect, 95% CI)					**.**	**11.2%**	**0.86 [0.74; 1.00]**
Heterogeneity: Tau^2 = 0; Chi^2 = 0.81, df = 3 (P = 0.8476); I^2 = 0%							
Nation = US							
Suzann Pershing 2019 [21]	1882	5022526	1746	3505684	21.9%	6.6%	0.75 [0.70; 0.80]
Emily S. West 2005 [53]	660	311317	366	166310	5.8%	5.8%	0.96 [0.85; 1.10]
Jonathan C. Javitt 1994 [65]	28	37560	15	19543	0.2%	1.2%	0.97 [0.52; 1.82]
Jonathan C. Javitt 1991 [66]	279	222183	161	103140	2.4%	4.7%	0.80 [0.65; 0.98]
Total (common effect, 95% CI)		**5593586**		**3794677**	**30.3%**	**.**	**0.79 [0.75; 0.84]**
Total (random effect, 95% CI)					**.**	**18.4%**	**0.83 [0.72; 0.97]**
Heterogeneity: Tau^2 = 0.0142; Chi^2 = 12.13, df = 3 (P = 0.0070); I^2 = 75.3%							
Nation = Poland							
Michal S. Nowak 2019 [22]	768	794209	563	424906	7.5%	6.1%	0.72 [0.64; 0.81]
Nation = Korea							
Soo Han Kim 2019 [23]	468	889531	483	616523	5.7%	5.8%	0.67 [0.58; 0.76]
Baek–Lok Oh 2018 [24]	24	43722	25	26997	0.3%	1.4%	0.58 [0.33; 1.03]
Total (common effect, 95% CI)		**933253**		**643520**	**6.0%**	**.**	**0.66 [0.58; 0.75]**
Total (random effect, 95% CI)					**.**	**7.2%**	**0.66 [0.58; 0.75]**
Heterogeneity: Tau^2 = 0; Chi^2 = 0.21, df = 1 (P = 0.6498); I^2 = 0%							
Nation = Japan							
Tomoyuki Inoue 2017 [9]	11	30863	2	21933	0.1%	0.4%	2.94 [0.97; 8.85]
Yasunori Nagaki 2003 [59]	9	4398	6	2794	0.1%	0.5%	0.95 [0.34; 2.69]
Total (common effect, 95% CI)		**35261**		**24727**	**0.2%**	**.**	**1.62 [0.76; 3.45]**
Total (random effect, 95% CI)					**.**	**1.0%**	**1.65 [0.55; 4.96]**
Heterogeneity: Tau^2 = 0.3349; Chi^2 = 2.12, df = 1 (P = 0.1454); I^2 = 52.8%							
Nation = France							
Vincent Daien 2016 [34]	960	1432826	981	1001182	11.7%	6.4%	0.68 [0.62; 0.74]
Germain Barreau 2012 [44]	15	2991	21	2124	0.2%	1.1%	0.50 [0.26; 0.97]
Total (common effect, 95% CI)		**1435817**		**1003306**	**11.9%**	**.**	**0.67 [0.62; 0.74]**
Total (random effect, 95% CI)					**.**	**7.5%**	**0.67 [0.62; 0.74]**
Heterogeneity: Tau^2 = 0; Chi^2 = 0.81, df = 1 (P = 0.3683); I^2 = 0%							
Nation = Singapore							
Colin S.H. Tan 2011 [45]	6	26472	15	23705	0.1%	0.7%	0.38 [0.16; 0.89]
Tien Yin Wong 2003 [58]	20	25036	13	19767	0.2%	1.1%	1.21 [0.61; 2.41]
Total (common effect, 95% CI)		**51508**		**43472**	**0.3%**	**.**	**0.77 [0.45; 1.31]**
Total (random effect, 95% CI)					**.**	**1.8%**	**0.70 [0.22; 2.18]**
Heterogeneity: Tau^2 = 0.5187; Chi^2 = 4.3, df = 1 (P = 0.0381); I^2 = 76.8%							
Nation = Canada							
Wendy V.Hatch 2009 [47]	315	264510	302	177667	3.7%	5.3%	0.69 [0.59; 0.82]
Nation = Multicenter							
ESCRS Endophthalmitis Study Group 2007 [50]	7	9459	13	6743	0.1%	0.7%	0.38 [0.16; 0.93]
Nation = India							
Prajna Lalitha 2005 [55]	9	16274	10	19798	0.1%	0.6%	1.10 [0.44; 2.70]
Nation = Australia							
Jianghong Li 2004 [57]	127	67844	83	49029	1.3%	3.7%	1.10 [0.84; 1.45]
Nation = Denmark							
Jens Christian Norregaard 1996 [64]	31	12592	30	6834	0.3%	1.6%	0.54 [0.32; 0.91]
Total (common effect, 95% CI)		**12677404**		**8688318**	**100.0%**	**.**	**0.77 [0.74; 0.79]**
Total (random effect, 95% CI)					**.**	**100.0%**	**0.81 [0.75; 0.87]**
Heterogeneity: Tau^2 = 0.0218; Chi^2 = 93.13, df = 47 (P < 0.0001); I^2 = 49.5%							
Test for subgroup differences (common effect): Chi^2 = 42.11, df = 14 (P = 0.0001)							
Test for subgroup differences (random effects): Chi^2 = 40.74, df = 14 (P = 0.0002)							

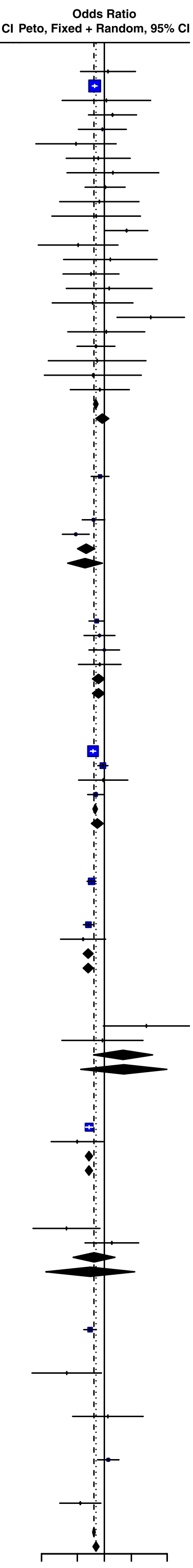


Fig. 2. Forest plot showing the difference in the risk of endophthalmitis after cataract surgery between males and females.

Table 2. Pooled results of risk of post-cataract surgery endophthalmitis among the different age cutoff points

Age, cutoff value	Studies, *n*	Younger people, *n*	Elder people, *n*	I^2	OR (95% CI)	*p* value
<60 vs ≥60	10	224,132	1,601,567	76%	1.03 (0.70, 1.51)	0.897
<65 vs ≥65	9	2,061,641	8,748,339	90%	0.59 (0.35, 0.97)	0.038
<70 vs ≥70	19	2,041,484	3,912,010	73%	0.84 (0.71, 0.99)	0.03
<75 vs ≥75	10	8,339,506	6,498,028	38%	1.05 (1.01, 1.09)	0.013
<80 vs ≥80	11	3,766,810	1,142,223	72%	0.88 (0.76, 1.03)	0.11
<85 vs ≥85	8	12,630,115	2,849,126	88%	0.69 (0.53, 0.90)	0.006
<90 vs ≥90	6	2,385,701	76,475	70%	0.42 (0.18, 0.96)	0.041

significantly greater incidence of endophthalmitis. This variation may be attributed to differences in populations and diagnostic criteria for diabetes mellitus. Significant heterogeneity was observed in the subgroup analyses across different countries ($p < 0.01$) (shown in Fig. 3). Additionally, potential publication bias may exist in the combined results (Schwarzer: $p = 0.105$; Egger: $p = 0.001$) (online suppl. Fig. 1b). Following the trim-and-fill method for pooling results, the significant differences between populations with and without diabetes changed (OR: 1.26; 95% CI: 0.51, 3.12; $p = 0.6169$). Therefore, the association between diabetes and endophthalmitis occurrence in individuals with diabetes may have been influenced by publication bias.

Compared with populations without hypertension, individuals with hypertension who underwent cataract surgery were found to have a greater risk of endophthalmitis (OR: 2.88; 95% CI: 1.53, 5.45; $p = 0.001$). Subgroup analyses revealed that hypertension was associated with a greater risk of endophthalmitis in the Chinese and South Korean populations, but the results for the Malaysian population did not significantly differ (shown in Fig. 4). Overall, no evidence of potential publication bias was found (Schwarzer: $p = 0.272$; Egger: $p = 0.405$) (online suppl. Fig. 1c).

Among patients who experienced PCR during surgery, those who experienced PCR were found to have a significantly greater risk of postoperative endophthalmitis (OR: 9.18; 95% CI: 3.31, 25.43; $p < 0.001$). This significant difference was consistent across all nationalities, with this disparity present in all subgroup analyses (shown in Fig. 5). Furthermore, no potential publication bias was detected (Schwarzer: $p = 0.337$; Egger: $p = 0.610$) (online suppl. Fig. 1d).

The impact of surgery type on outcomes was evaluated using network meta-analysis, and the results indicated that phacoemulsification significantly reduced the risk of endophthalmitis compared with ECCE (OR: 0.62; 95% CI: 0.45, 0.85), whereas small-incision cataract surgery (SICS) showed no significant difference compared to ECCE (OR: 0.95; 95% CI: 0.45, 1.98). There was also no significant difference between SICS and phacoemulsification (OR: 0.65; 95% CI: 0.32, 1.34) in the forest plot of the network meta-analysis (shown in Fig. 6a) or the league table (shown in Fig. 6b). No potential publication bias was found in the results (shown in Fig. 6c).

To analyze the impact of IOL materials on the risk of endophthalmitis, four types of materials were analyzed: acrylic, hydrogel, polymethyl methacrylate (PMMA), and silicone. The results indicated that when PMMA was used as the reference material, none of the other materials showed a significant difference in the risk of endophthalmitis (shown in Fig. 7a, b). Among the IOL materials analyzed, acrylic was relatively favored (SUCRA: 0.93) (shown in Fig. 7a). No potential publication bias was found (shown in Fig. 7c).

Discussion

Endophthalmitis is a serious complication following cataract surgery. This study conducted a comprehensive analysis of the reported frequencies of post-cataract surgery endophthalmitis considering various risk factors such as patient characteristics, intraoperative complications, surgery type, and IOL materials. The results suggest that male sex, hypertension, intraoperative PCR, and the use of the ECCE surgical approach are associated with a greater risk of postoperative endophthalmitis. Furthermore, although an increasing trend in the risk of endophthalmitis with age was observed, caution is advised in interpreting this finding since the elevated risk may be directly linked to age-related changes in immunity, complications, and surgical challenges.

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (common)	Weight (random)	Odds Ratio Peto, Fixed + Random, 95% CI
Nation = China							
Junjie Bian 2024 [11]	21	5033	11	7275	0.4%	3.8%	2.79 [1.38; 5.65]
Chiun−Ho Hou 2023 [13]	1987	760198	2436	1006598	62.4%	3.9%	1.08 [1.02; 1.15]
Dongling Feng 2023 [15]	7	1294	5	2306	0.2%	3.5%	2.65 [0.81; 8.64]
Jiajun Sun 2021 [17]	8	10306	34	45306	0.4%	3.7%	1.03 [0.47; 2.25]
Jing Gao 2021 [18]	19	984	22	8101	0.2%	3.6%	40.17 [14.97; 107.79]
Aihua Chen 2021 [19]	2	882	13	754	0.2%	3.6%	0.19 [0.07; 0.53]
YuMeng Wu 2020 [20]	5	355	18	7822	0.1%	3.0%	66.72 [8.96; 497.03]
Lei Ge 2018 [26]	6	1359	6	4821	0.1%	3.4%	5.13 [1.31; 20.15]
Rui Li 2018 [27]	32	1098	29	11578	0.3%	3.7%	260.35 [106.46; 636.71]
Canming Huo 2018 [28]	12	1047	3	953	0.2%	3.6%	3.05 [1.10; 8.44]
Shun Wang 2018 [29]	6	1711	6	6865	0.1%	3.4%	6.58 [1.60; 27.13]
Yiwen Luo 2017 [32]	5	6907	10	57562	0.1%	3.2%	10.65 [2.07; 54.68]
Xin Jin 2017 [33]	3	2037	8	17963	0.1%	3.0%	6.48 [0.92; 45.75]
Wei Dong 2016 [35]	18	1709	12	10291	0.2%	3.6%	42.76 [15.34; 119.20]
Feng Wang 2016 [36]	7	1280	6	4320	0.1%	3.5%	5.82 [1.59; 21.27]
Youyi Li 2015 [38]	9	506	6	1394	0.2%	3.5%	5.59 [1.77; 17.63]
Yusen Huang 2015 [39]	3	4664	18	11508	0.2%	3.7%	0.49 [0.19; 1.26]
Xuezhuang Liu 2014 [42]	8	251	2	1321	0.1%	3.2%	121.49 [22.26; 663.00]
Tingxia Yu 2014 [43]	7	984	2	5829	0.1%	3.1%	169.26 [26.36; 1086.89]
Rongjiang Luo 2009 [49]	20	1573	7	9325	0.2%	3.6%	126.54 [43.20; 370.60]
Total (common effect, 95% CI)		**804178**		**1221892**	**65.8%**	**.**	**1.19 [1.12; 1.26]**
Total (random effect, 95% CI)					**.**	**69.6%**	**8.58 [3.46; 21.27]**
Heterogeneity: $Tau^2 = 3.8837$; $Chi^2 = 447.84$, df = 19 ($P < 0.0001$); $I^2 = 95.8\%$							
Nation = UK							
Liying Low 2023 [12]	77	245640	231	1105775	2.6%	3.9%	1.58 [1.18; 2.11]
Nation = Malaysia							
Durgavashini Govinda Raj 2023 [14]	87	107454	98	123827	2.7%	3.9%	1.02 [0.77; 1.37]
Yong Zheng Wai 2018 [25]	53	69066	78	94437	1.8%	3.9%	0.93 [0.66; 1.31]
Total (common effect, 95% CI)		**176520**		**218264**	**4.5%**	**.**	**0.98 [0.79; 1.23]**
Total (random effect, 95% CI)					**.**	**7.8%**	**0.98 [0.79; 1.23]**
Heterogeneity: $Tau^2 = 0$; $Chi^2 = 0.17$, df = 1 ($P = 0.6770$); $I^2 = 0\%$							
Nation = Poland							
Michal S. Nowak 2019 [22]	309	344896	1022	874251	15.6%	3.9%	0.78 [0.69; 0.88]
Nation = Korea							
Soo Han Kim 2019 [23]	161	127337	792	1379673	4.2%	3.9%	2.98 [2.37; 3.75]
Baek−Lok Oh 2018 [24]	12	9394	35	58683	0.3%	3.7%	2.68 [1.17; 6.15]
Total (common effect, 95% CI)		**136731**		**1438356**	**4.6%**	**.**	**2.96 [2.37; 3.69]**
Total (random effect, 95% CI)					**.**	**7.6%**	**2.96 [2.37; 3.69]**
Heterogeneity: $Tau^2 = 0$; $Chi^2 = 0.06$, df = 1 ($P = 0.8104$); $I^2 = 0\%$							
Nation = France							
Vincent Daien 2016 [34]	1845	2273671	96	160337	6.9%	3.9%	1.31 [1.09; 1.56]
Nation = Japan							
Yasunori Nagaki 2003 [59]	2	910	13	6282	0.1%	3.3%	1.06 [0.23; 4.88]
Total (common effect, 95% CI)		**3982546**		**5025157**	**100.0%**	**.**	**1.17 [1.11; 1.22]**
Total (random effect, 95% CI)					**.**	**100.0%**	**4.90 [2.41; 9.95]**
Heterogeneity: $Tau^2 = 3.3471$; $Chi^2 = 569.37$, df = 27 ($P < 0.0001$); $I^2 = 95.3\%$							
Test for subgroup differences (common effect): $Chi^2 = 121.30$, df = 6 ($P < 0.0001$)							
Test for subgroup differences (random effects): $Chi^2 = 139.14$, df = 6 ($P < 0.0001$)							

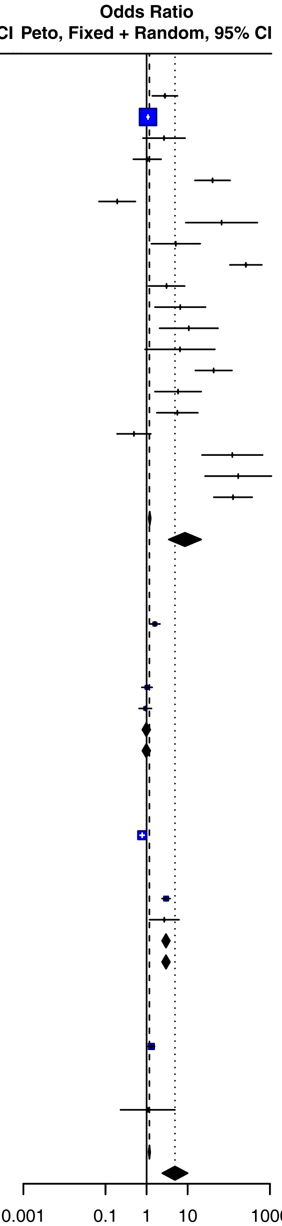


Fig. 3. Forest plot showing the difference in the risk of endophthalmitis after cataract surgery between populations with or without diabetes mellitus.

Male sex is a risk factor for endophthalmitis. A study has shown that in cataract patients, males exhibit significantly higher levels of testosterone compared with females [68]. Research on sex differences in COVID-19 patients suggests that females have stronger inflammatory, antiviral, and humoral immune responses [69, 70]. In addition, dry eye syndrome may have a more severe impact on females, with the activation of immune function potentially linked to the development of dry eye syndrome [71]. In males, testosterone can suppress cytokine responses. Therefore, the differential immune response between the sexes may influence the occurrence of postoperative endophthalmitis. Furthermore, androgens can affect the structure and function of the

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (common)	Weight (random)	Odds Ratio Peto, Fixed + Random, 95% CI
Nation = China							
Junjie Bian 2024 [11]	17	7110	15	5198	3.1%	6.2%	0.83 [0.41; 1.67]
Jing Gao 2021 [18]	12	1369	29	7716	2.1%	5.9%	3.05 [1.29; 7.18]
Aihua Chen 2021 [19]	7	629	8	1007	1.4%	5.6%	1.42 [0.50; 4.04]
YuMeng Wu 2020 [20]	2	476	21	7701	0.5%	4.4%	1.69 [0.29; 9.71]
Lei Ge 2018 [26]	4	1954	8	4214	1.0%	5.4%	1.08 [0.32; 3.65]
Rui Li 2018 [27]	26	1026	35	11650	1.8%	5.8%	106.03 [42.16; 266.67]
Canming Huo 2018 [28]	14	1016	1	984	1.5%	5.7%	5.55 [2.01; 15.33]
Shun Wang 2018 [29]	3	2169	9	6407	0.9%	5.2%	0.98 [0.27; 3.62]
Yiwen Luo 2017 [32]	5	25789	10	38680	1.4%	5.7%	0.76 [0.27; 2.13]
Wei Dong 2016 [35]	8	1562	22	10438	1.3%	5.6%	3.35 [1.15; 9.71]
Feng Wang 2016 [36]	8	1815	5	3785	1.1%	5.4%	3.79 [1.19; 12.12]
Youyi Li 2015 [38]	11	843	4	1057	1.5%	5.7%	3.26 [1.17; 9.07]
Xuezhuang Liu 2014 [42]	9	396	1	1176	0.7%	5.0%	31.78 [7.59; 133.05]
Tingxia Yu 2014 [43]	3	775	3	6038	0.2%	3.3%	46.25 [3.72; 575.43]
Rongjiang Luo 2009 [49]	6	1239	21	9659	1.1%	5.4%	2.94 [0.90; 9.67]
Total (common effect, 95% CI)		**48168**		**115710**	**19.6%**	**.**	**3.14 [2.38; 4.15]**
Total (random effect, 95% CI)					**.**	**80.3%**	**3.57 [1.69; 7.52]**
Heterogeneity: $Tau^2 = 1.7853$; $Chi^2 = 101.56$, df = 14 ($P < 0.0001$); $I^2 = 86.2\%$							
Nation = Malaysia							
Durgavashini Govinda Raj 2023 [14]	124	153518	61	77763	16.4%	6.6%	1.03 [0.76; 1.40]
Yong Zheng Wai 2018 [25]	71	94238	60	69265	12.7%	6.5%	0.87 [0.61; 1.23]
Total (common effect, 95% CI)		**247756**		**147028**	**29.0%**	**.**	**0.96 [0.76; 1.20]**
Total (random effect, 95% CI)					**.**	**13.1%**	**0.96 [0.76; 1.20]**
Heterogeneity: $Tau^2 = 0$; $Chi^2 = 0.52$, df = 1 ($P = 0.4705$); $I^2 = 0\%$							
Nation = Korea							
Soo Han Kim 2019 [23]	249	244684	704	1262326	51.3%	6.6%	2.07 [1.74; 2.46]
Total (common effect, 95% CI)		**540608**		**1525064**	**100.0%**	**.**	**1.80 [1.59; 2.03]**
Total (random effect, 95% CI)					**.**	**100.0%**	**2.88 [1.53; 5.45]**
Heterogeneity: $Tau^2 = 1.5822$; $Chi^2 = 149.36$, df = 17 ($P < 0.0001$); $I^2 = 88.6\%$							
Test for subgroup differences (common effect): $Chi^2 = 47.28$, df = 2 ($P < 0.0001$)							
Test for subgroup differences (random effects): $Chi^2 = 32.46$, df = 2 ($P < 0.0001$)							

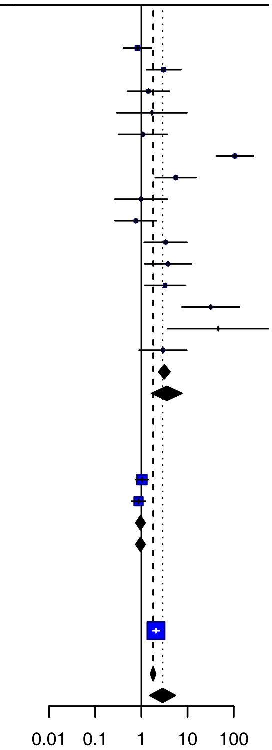


Fig. 4. Forest plot showing the difference in the risk of endophthalmitis after cataract surgery between populations with or without hypertension.

meibomian and lacrimal glands [72]. The structure and function of the lacrimal gland may affect the risk of postoperative endophthalmitis [73]. In summary, the higher testosterone levels in males may be associated with lower ocular immune responses and potentially impact the structure and function of the lacrimal gland. This may serve as a plausible explanation for the greater risk of postoperative endophthalmitis in males.

Age is an important risk factor for endophthalmitis following cataract surgery. Previous studies have often analyzed a single cutoff age; however, this study conducted a comprehensive analysis of several cutoff values. The results suggest that there may be a trend toward an increased risk of postoperative endophthalmitis with advancing age. However, in the analysis of individuals with the 75-year-old as the cutoff value for whom the population was relatively balanced, younger individuals were found to have a greater risk of endophthalmitis. Previous meta-analyses have shown a significant difference in the risk of endophthalmitis among people over 85 years old compared with younger people, which aligns with our research findings [6]. However, far fewer people over the age of 85 undergo cataract surgery than those under the age of 85. Nevertheless, the increased risk of endophthalmitis in the population aged 85 years and above can be explained by the natural aging process affecting physiological functions and the greater prevalence of accompanying medical conditions in this age group. The results from a large retrospective study indicated that being over 85 years old was a statistically significant risk factor for developing endophthalmitis [74]. In this study, the pooled analysis with a larger sample size did not perfectly show a gradual increase in the incidence of endophthalmitis in individuals aged 60 years and older as age increased. Although some trends were observed, age alone may not entirely explain the gradual increase in the risk of endophthalmitis. Factors such as age-related immune status, comorbidities, increased surgical risks, and longer

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (common)	Weight (random)	Odds Ratio MH, Fixed + Random, 95% CI
Nation = China							
Junjie Bian 2024 [11]	3	82	29	12226	0.9%	8.3%	15.97 [4.77; 53.51]
Jiajun Sun 2021 [17]	2	371	40	55241	1.3%	7.9%	7.48 [1.80; 31.06]
Lei Ge 2018 [26]	8	12	4	6168	0.0%	7.7%	3082.00 [654.35; 14516.23]
Yanan Zhu 2017 [30]	3	1625	49	44560	8.7%	8.3%	1.68 [0.52; 5.40]
Yusen Huang 2015 [39]	1	416	20	15756	2.6%	6.8%	1.90 [0.25; 14.16]
Total (common effect, 95% CI)		**2506**		**133951**	**13.6%**	**.**	**6.25 [3.78; 10.33]**
Total (random effect, 95% CI)					**.**	**39.0%**	**16.42 [1.12; 240.08]**
Heterogeneity: $Tau^2 = 8.7848$; $Chi^2 = 63.82$, df = 4 ($P < 0.0001$); $I^2 = 93.7\%$							
Nation = UK							
Liying Low 2023 [12]	32	20400	276	1330707	21.0%	9.2%	7.57 [5.25; 10.92]
Nation = Malaysia							
Yong Zheng Wai 2018 [25]	9	3142	122	160361	11.8%	9.0%	3.77 [1.92; 7.43]
Nation = Japan							
Tomoyuki Inoue 2017 [9]	1	547	12	52436	0.6%	6.8%	8.00 [1.04; 61.64]
Nation = US							
Aravind Haripriya 2017 [31]	29	7317	249	610136	14.8%	9.2%	9.75 [6.63; 14.33]
Lisa J.Herrinton 2015 [37]	9	3468	206	311778	11.4%	9.0%	3.94 [2.02; 7.68]
Total (common effect, 95% CI)		**10785**		**921914**	**26.2%**	**.**	**7.22 [5.18; 10.06]**
Total (random effect, 95% CI)					**.**	**18.2%**	**6.46 [2.67; 15.66]**
Heterogeneity: $Tau^2 = 0.3338$; $Chi^2 = 5.31$, df = 1 ($P = 0.0212$); $I^2 = 81.2\%$							
Nation = France							
Vincent Daien 2016 [34]	28	6015	1913	2427993	23.8%	9.2%	5.93 [4.08; 8.62]
Nation = Singapore							
Tien Yin Wong 2003 [58]	5	923	29	43880	3.0%	8.6%	8.24 [3.18; 21.32]
Total (common effect, 95% CI)		**44318**		**5071242**	**100.0%**	**.**	**6.49 [5.42; 7.76]**
Total (random effect, 95% CI)					**.**	**100.0%**	**9.18 [3.31; 25.43]**
Heterogeneity: $Tau^2 = 2.8967$; $Chi^2 = 78.26$, df = 11 ($P < 0.0001$); $I^2 = 85.9\%$							
Test for subgroup differences (common effect): $Chi^2 = 4.04$, df = 6 ($P = 0.6716$)							
Test for subgroup differences (random effects): $Chi^2 = 4.09$, df = 6 ($P = 0.6639$)							

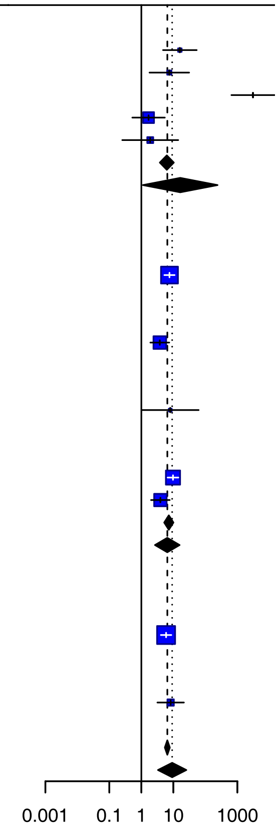
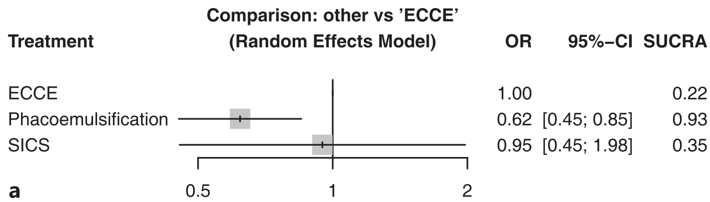


Fig. 5. Forest plot showing the difference in the risk of endophthalmitis after cataract surgery between populations stratified by whether intraoperative PCR occurred.

surgical durations may more directly account for the heightened risk of endophthalmitis.

Diabetes is generally thought to be associated with an increased rate of any infection, possibly due to reduced T-cell-mediated immune responses or impaired neutrophil function. Additionally, high blood glucose levels can lead to changes in vascular permeability and abnormal oxidative reactions, increasing the risk of infections [75]. Therefore, empirically, diabetic patients are considered to have a greater risk of endophthalmitis. However, large-scale retrospective analyses do not always consider detailed factors such as the duration of diabetes, blood sugar control, perioperative blood glucose levels, and their specific impacts. According to the results of this study, diabetic patients (with unclear blood glucose control status) were found to have a significantly greater risk of postoperative endophthalmitis than nondiabetic individuals, although this difference may be influenced by publication bias. Our meta-analysis suggested that individuals with hypertension have a greater risk of postoperative endophthalmitis. Hypertension can also lead to pathological changes in the eyes, such as increased intraocular pressure, hypertensive retinopathy, intraocular vascular thrombosis, and potential associations with immune system dysfunction, and prolonged surgical durations may increase the risk of postoperative endophthalmitis [76, 77].

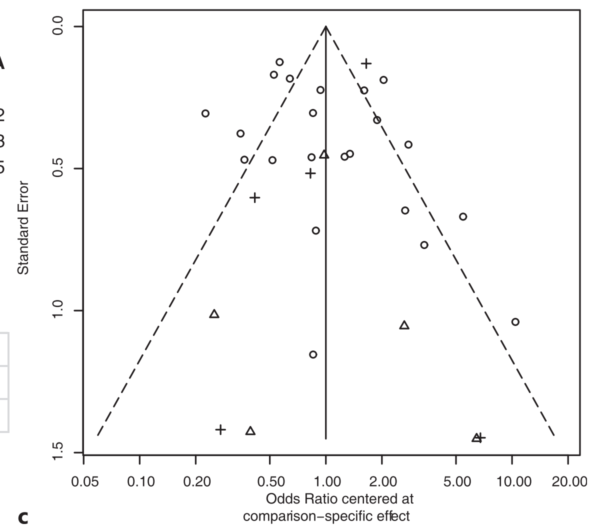
The occurrence of PCR during surgery can prolong the surgical time, thereby extending the exposure of the surgical wound during the procedure. This increases the risk of postoperative endophthalmitis. Furthermore, PCR also makes it easier for bacteria to enter the vitreous cavity. Methodologically, although the Peto method was the preferred method of meta-analysis in



a

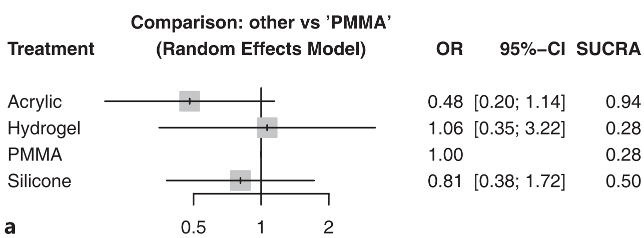
ECCE	**1.58 (1.15, 2.17)**	1.33 (0.49, 3.59)
1.61 (1.18, 2.21)	Phacoemulsification	0.60 (0.27, 1.31)
1.05 (0.51, 2.20)	0.65 (0.32, 1.34)	SICS

b



c

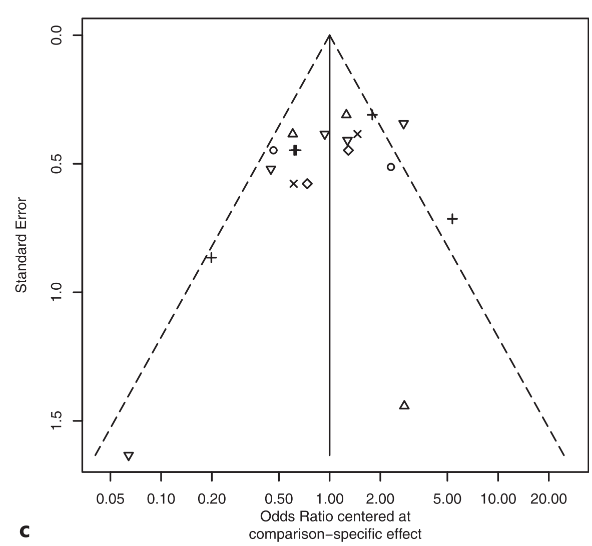
Fig. 6. Network meta-analysis showing the impact of different types of surgery on the risk of postoperative endophthalmitis. **a** Forest plot of network meta-analysis. **b** League table showing that the lower-left part is the network comparison result, and the upper-right part is the direct comparison result. The bold font indicates a significant difference. **c** The funnel plot of the network meta-analysis.



a

Acrylic	0.45 (0.14, 1.5)	0.52 (0.19, 1.4)	0.55 (0.25, 1.2)
0.45 (0.15, 1.4)	Hydrogel	1.02 (0.31, 3.3)	1.30 (0.39, 4.3)
0.48 (0.20, 1.1)	1.06 (0.35, 3.2)	PMMA	1.19 (0.55, 2.6)
0.59 (0.28, 1.2)	1.32 (0.44, 3.9)	1.24 (0.58, 2.6)	Silicone

b



c

Fig. 7. Network meta-analysis showing the impact of different IOL materials on the risk of endophthalmitis after cataract surgery. **a** Forest plot of network meta-analysis. **b** League table showing that the lower-left part is the network comparison result, and the upper-right part is the direct comparison result. **c** The funnel plot of the network meta-analysis.

this study, there was a significant imbalance in the number of individuals who experienced PCR, which resulted in abnormally large ORs; thus, this study presented the results of a meta-analysis using the Mantel-Haenszel method. However, the conclusions drawn from both methods are consistent, indicating that the occurrence of PCR significantly increases the risk of postoperative endophthalmitis.

In studies on surgical procedures, phacoemulsification is the most common type of cataract surgery. It utilizes ultrasonic energy to break down the lens nucleus and then aspirates it from the eye. SICS requires creating a larger scleral tunnel than phacoemulsification to allow access to the anterior chamber of the eye and manual removal of the entire nucleus. The results of this study revealed that there was no significant difference in the risk of postoperative endophthalmitis between phacoemulsification and SICS surgeries. Although the ECCE technique is still used clinically for cataract surgery; however, there is a clinical push toward the widespread adoption of phacoemulsification and SICS. Additionally, newer technologies, such as femtosecond laser-assisted cataract surgery, are being invented, applied, and promoted. With the advancement of higher level technologies, the risk of postoperative endophthalmitis is expected to further decrease. However, due to the limited number of current cases utilizing these advanced technologies, there is still a lack of analysis on the risk of postoperative endophthalmitis.

This study did not analyze the use of intracameral antibiotics for reducing the risk of endophthalmitis. This viewpoint has been corroborated in evidence-based studies. Currently, intracameral antibiotic therapy is the optimal choice for preventing post-cataract surgery endophthalmitis [78]. Compared with cataract surgery without antibiotics, intracameral cefuroxime injection significantly reduces postoperative endophthalmitis damage (OR: 0.14; 95% CI: 0.07–0.29, $p = 0.001$) [79]. A meta-analysis provided high-quality evidence indicating that the use of intracameral cefuroxime, with or without topical levofloxacin, can decrease the risk of postoperative endophthalmitis [80].

To our knowledge, this is the first large-sample study on the risk factors for postoperative endophthalmitis based on frequency data. Strict criteria were applied to the total sample size, number of endophthalmitis cases, and incidence rate in the included studies. This approach enhances the reliability of the results and conclusions.

However, there are still several limitations. Despite significant differences in sex and hypertensive populations, the clinical impact of the extremely low incidence rate of postoperative endophthalmitis has resulted in a minimal increase in the actual incidence rate. This study did not strictly limit the design types of the included studies, which included retrospective, prospective, and even RCT studies. For RCTs, the incidence of postoperative endophthalmitis may not be the primary purpose. This analysis did not distinguish between infectious and toxic endophthalmitis, focusing instead on all-cause endophthalmitis. The categories of risk factors considered in this study are still limited, with numerous potential risk factors remaining unexplored, such as chronic liver and kidney diseases that affect the body's immune system.

Conclusion

The results of this study suggest that male sex, hypertension, intraoperative PCR, and ECCE surgery are associated with a greater risk of postoperative endophthalmitis. There is a trend toward increasing risk of endophthalmitis with increasing age, but age may not directly contribute to the occurrence of endophthalmitis.

Statement of Ethics

A Statement of Ethics is not applicable because this study is based exclusively on published literature.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Study concept, design, and supervision: Shanshan Zhang and Jian Xu; data acquisition, statistical analyses, and drafting of the manuscript: Shanshan Zhang; and interpretation of data and critical revision of the manuscript for important intellectual content: Jian Xu. All authors agreed on final version of the manuscript for final submission.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary files. Further inquiries can be directed to the corresponding author.

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