·临床研究·

眼库供体角膜微生物培养结果及病原学分析

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摘　要:【目的】分析广东省眼库供体角膜微生物培养阳性率、病原谱、多重耐药菌(MDROs)检出情况及不同获取来源之间的差异,为眼库角膜植片质量控制及角膜移植术后感染防控提供参考。【方法】回顾性分析 2018-2025 年广东省眼库获取并于中山大学中山眼科中心进行角膜移植的 7 442 例供体角膜资料。术中剪取供体角巩膜缘组织进行细菌及真菌培养,对培养阳性样本进行微生物鉴定和药物敏感性试验。比较不同年份、不同病原体类型、不同获取来源的供体角膜微生物培养情况。【结果】7 442 例供体角膜中,微生物培养阳性样本共 251 例,培养阳性率为 3.37%,各年度阳性率为 1.50% ~ 5.31%。其中,细菌培养阳性 178 例(70.92%),真菌培养阳性 72 例(28.68%),细菌合并真菌培养阳性 1 例(0.40%)。真菌以念珠菌属、曲霉属为主。细菌检出中,革兰阴性菌多于革兰阳性菌,常见菌种为鲍曼不动杆菌、表皮葡萄球菌、嗜麦芽窄食单胞菌、粪肠球菌及荧光假单胞菌;MDROs 占比 75.47%,以鲍曼不动杆菌、表皮葡萄球菌及粪肠球菌为主,且近年来呈上升趋势。医院角膜获取项目(HCRP)来源供体角膜培养阳性率高于器官获取组织(OPO)来源($P<0.000\ 1$);HCRP 来源培养阳性供体角膜真菌检出率高于 OPO 来源 ($P=0.001\ 5$);OPO 来源细菌培养阳性供体角膜 MDROs 检出率高于 HCRP 来源($P=0.005\ 2$)。【结论】广东省眼库供体角膜培养阳性率总体较低,微生物污染风险整体可控。不同供体获取来源的病原学特征及耐药情况存在差异。持续开展微生物监测及耐药性监测,完善供体风险评估及培养结果反馈机制,有助于提高眼库质量管理水平,为角膜移植术后感染防控提供参考。

关键词:供体角膜;眼库;角膜移植;微生物培养;多重耐药菌
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Microbial Culture Results and Pathogen Profiles of Donor Corneas in Eye Bank

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Abstract:【Objective】To analyze the microbial culture positivity rate, pathogen spectrum, prevalence of multidrug-resistant organisms (MDROs), and differences among donor procurement sources in corneas from the Eye Bank of Guangdong Province, and to provide evidence for eye bank quality control and the prevention of post-keratoplasty infections.【Methods】This retrospective study included 7 442 donor corneas procured by the Eye Bank of Guangdong Province and used for keratoplasty at Zhongshan Ophthalmic Center, Sun Yat-sen University, between 2018 and 2025. During surgery, donor corneoscleral rim tissue was excised for bacterial and fungal culture. Culture-positive specimens underwent microbial identification and antimicrobial susceptibility testing (AST). Culture-positive corneas were compared

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across study years, pathogen categories, and donor procurement sources.【Results】Of the 7 442 donor corneas, 251 were culture-positive, corresponding to an overall culture positivity rate of 3.37%, with annual rates ranging from 1.50% to 5.31%. Among culture-positive corneas, 178 (70.92%) yielded bacteria alone, 72 (28.68%) yielded fungi alone, and 1 (0.40%) yielded both bacteria and fungi. *Candida spp.* and *Aspergillus spp.* were the predominant fungal isolates. Gram-negative bacteria were more frequently isolated than Gram-positive bacteria. The most common bacterial isolates were *Acinetobacter baumannii*, *Staphylococcus epidermidis*, *Stenotrophomonas maltophilia*, *Enterococcus faecium*, and *Pseudomonas fluorescens*. MDROs accounted for 75.47% of bacterial isolates, predominantly *Acinetobacter baumannii*, *Staphylococcus epidermidis*, and *Enterococcus faecium*, and demonstrated an increasing trend over the study period. Donor corneas procured through the Hospital Cornea Retrieval Program (HCRP) had a higher culture positivity rate than those obtained through Organ Procurement Organization (OPO) ($P<0.000\ 1$). Among culture-positive donor corneas, the proportion of fungal culture-positive corneas was significantly higher in the HCRP group than in the OPO group ($P=0.001\ 5$), whereas the proportion of MDROs among bacterial culture-positive corneas was significantly higher in the OPO group than that in the HCRP group ($P=0.005\ 2$).【Conclusions】The overall culture positivity rate of donor corneas from the Eye Bank of Guangdong Province is relatively low, indicating that the risk of microbial contamination is controlled. However, pathogen profiles and antimicrobial resistance patterns varies by procurement source. Ongoing microbiological and antimicrobial resistance surveillance, together with optimized donor risk assessment and timely reporting of culture results, may further improve eye bank quality management and help inform strategies for preventing post-keratoplasty infections.

Key words: donor cornea; eye bank; corneal transplantation; microbiological culture; multidrug-resistant organisms

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角膜移植术后继发感染是最严重的术后并发症之一[1-3]。为最大限度降低角膜植片微生物污染相关术后感染风险,眼库对角膜捐献供体筛选、角膜植片获取及保存过程等环节的质量控制至关重要。因此,对供体角膜进行微生物培养,并对培养阳性植片进行持续追踪和结果分析,对于保障角膜移植安全具有重要意义。目前供体角膜主要来源于器官获取组织(Organ Procurement Organization, OPO)和医院角膜获取项目(Hospital Cornea Recovery Program, HCRP)。角膜植片保存主要采用低温保存(hypothermic storage, HS)和器官培养(organ culture, OC)2种方式[4]。我国眼库目前多采用HS法保存角膜植片。与OC法通常在移植前对培养液进行微生物培养不同,HS法多在术中剪取植片边缘组织进行培养[5]。为保障术后安全,对HS法保存角膜植片的微生物培养结果进行追踪与统计显得尤为重要。目前国内尚缺乏供体角膜微生物培养的大样本监测数据,有关眼库供体角膜微生物污染及感染情况的报道亦较少。本研究对广东省眼库近8年获取并于中山大学中山眼科中心实施角膜移植的供体角膜微生物培养结果进行回顾性分析,比较不同供体获取模式下培养阳性率、病原体谱及多重耐药菌(multidrug-resistant organisms, MDROs)检出情况的差异,以期为完善眼库质量控制体系和提升角膜移植安全性提供参考。

1 材料与方法

1.1 供体角膜获取

本研究为回顾性观察性研究,遵循《赫尔辛基宣言》。所有供体角膜均由广东省眼库按照人体组织捐献及眼库管理相关规范获取,供体捐献程序均已获得捐献者生前或其近亲属(或授权代理人)的知情同意。本研究方案经中山大学中山眼科中心伦理委员会审批通过(批准号:2026KYPJ076)。

角膜获取严格遵循眼科手术无菌原则,获取过程如下。

消毒与铺巾:聚维酮碘(50 g/L)消毒眼周皮肤(范围上至发际,下至鼻翼高度,两侧至耳前),铺双

孔洞巾。双眼结膜囊内使用妥布霉素(4 g/L)充分冲洗。

角膜植片获取:开睑器开睑,沿角膜缘全周剪开球结膜,并分离至角膜缘后6~8 mm;手术刀片于角膜缘后3~4 mm做平行于角膜缘的巩膜切口,角膜剪沿巩膜切口环形剪开巩膜。轻柔分离睫状体及虹膜,游离带巩膜环的角膜植片。将获取的角膜放入角膜保存液(EUSOL-C, Alchimia, ITALY)中并及时低温存放。

恢复供体仪容:清除结膜囊血迹及眼内容物,植入义眼片,4-0丝线缝合眼睑,清理颜面部及眼睑污渍。

1.2 微生物培养及药物敏感性检测

本研究所分析的微生物培养标本来源于角膜移植术中常规剪取的剩余供体角巩膜缘组织,未额外增加供体组织获取范围或受体手术风险。

获取标本接种于血琼脂、巧克力琼脂和巯基乙酸肉汤中,在37 ℃的需氧和厌氧条件下孵育7 d,每天检查两次培养基以观察细菌生长情况。将部分样品涂在马铃薯葡萄糖琼脂上,在28 ℃、体积分数50%湿度的条件下孵育2周,如果发现真菌生长,则根据琼脂上的菌落特征和显微镜下的生长和形态特征鉴定菌种。

对于微生物培养阳性样本,使用VITEK-2 COMPACT系统(bioMerieux, St. Louis, MO, US)进行种类鉴定和抗生素敏感性试验。根据细菌种类测试的抗生素包括头孢菌素(如头孢唑林、头孢他啶和头孢呋辛钠)、氟喹诺酮类药物(如氧氟沙星和左氧氟沙星)、氨基糖苷类药物(如妥布霉素和新霉素)、万古霉素等。测试的抗真菌药物包括多烯类(制霉菌素、两性霉素B)、三唑类(氟康唑、伊曲康唑、伏立康唑、泊沙康唑)、棘白菌素类(卡泊芬净、米卡芬净、阿尼芬净)和氟胞嘧啶类(氟胞嘧啶)等。根据药敏检测结果,对3类或3类以上抗菌药物耐药的细菌归类为MDROs[6],其他细菌归类为非多重耐药菌(non-multidrug-resistant organisms, non-MDROs)。2025年受限于临床条件,未对所有菌株进行药敏检测。

1.3 统计方法

采用GraphPad Prism 10.1.2软件进行统计分析。计数资料以例数和百分比表示。各年度MDROs检出在细菌培养阳性供体角膜中占比的变化趋势采用简单线性回归分析。不同来源供体角膜培养阳性率、培养阳性角膜中病原体构成,以及细菌培养阳性角膜中MDROs检出比例的比较采用Fisher精确检验。双侧$P<0.05$为差异具有统计学意义。

2 结 果

2.1 供体角膜植片微生物培养阳性率

送检角膜植片边缘组织7 442例,其中微生物培养阳性样本251例,占总量的3.37%。年度供体角膜培养阳性率为1.50%~5.31%,其中2019年最低,2020年最高(图1)。

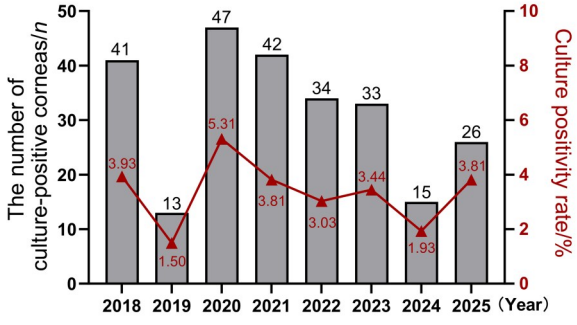


图1 2018—2025年度供体角膜植片微生物培养阳性数量及阳性率

Fig. 1 Annual numbers of culture-positive corneas and culture positivity rates from 2018 to 2025

2.2 供体角膜植片微生物培养结果

微生物培养阳性角膜植片中,检出真菌72例(28.68%),细菌178例(70.92%),细菌及真菌同时阳性1例(0.40%)。除2019年,细菌检出率均高于真菌检出率(图2A)。

73例真菌培养阳性角膜植片中,根据检出真菌形态学特征及属种类进行分类:念珠菌属34例(46.58%)、其他酵母样真菌2例(2.74%)、曲霉属15例(20.55%)、镰刀菌属5例(6.85%)、暗色丝状真菌5例(6.85%)、其他丝状真菌12例(16.44%)(图2B)。检出念珠菌属中11例为白色念珠菌,检出曲霉属中10例为黄曲霉(表1)。

179例细菌培养阳性供体角膜中,检出革兰阴性菌102例(56.98%),革兰阳性菌77例(43.02%)

（图2C）。革兰阴性菌中检出不动杆菌属42例、窄食单胞菌属21例、假单胞菌属16例、克雷伯菌属6例、埃希菌属4例、伊丽莎白菌属3例，肠杆菌属、类香味菌属、代夫特菌属及鞘氨醇单胞菌属各2例，气单胞菌属及变形杆菌属各1例（表2）。革兰阳性菌中检出葡萄球菌属45例、肠球菌属14例、微球菌属5例、棒杆菌属4例、芽孢杆菌属2例，库克菌属、类芽孢杆菌属、链球菌属、微杆菌属及丙酸杆菌属各1例，另有2例未能进一步鉴定（表3）。按细菌种类分类，所有细菌培养阳性供体角膜中检出最多的是鲍曼不动杆菌（42例，23.46%），其次为表皮葡萄球菌（25例，13.97%）、嗜麦芽窄食单胞菌（21例，11.73%）、粪肠球菌（14例，7.82%）、荧光假单胞菌（11例，6.15%）、金黄色葡萄球菌（7例，3.91%）、肺炎克雷伯菌（6例，3.35%）、藤黄微球菌（5例，2.79%；图2D）。

表1　真菌培养阳性供体角膜中检出真菌的分布

Table 1　Distribution of fungal isolates recovered from culture-positive donor corneas

Fungal isolate	No. of isolates/*n*	Among fungal isolates/%
Candida spp.	34	46.58
Candida albicans	11	15.07
Candida tropicalis	5	6.85
Candida parapsilosis	3	4.11
Candida glabrata	1	1.37
Candida orthopsilosis	1	1.37
Unidentified *Candida spp.*	13	17.81
Other yeast-like fungi	2	2.74
Aspergillus spp.	15	20.55
Aspergillus flavus	10	13.70
Aspergillus fumigatus	2	2.74
Aspergillus versicolor	1	1.37
Unidentified *Aspergillus spp.*	2	2.74
Fusarium spp.	5	6.85
Dematiaceous filamentous fungi	5	6.85
Other filamentous fungi	12	16.44

Percentages are calculated based on the total number of fungal isolates. *n*: number of isolates; %: percentage.

2.3　同一供体角膜植片培养结果一致性

培养阳性的角膜植片中，44例（22例供体）为同一供体双眼角膜均检出病原微生物，其中34例（17例供体）植片检出的微生物种类相同：3对为真菌，14对为细菌。其中12对为MDROs，鲍曼不动杆菌检出最多，共有5对（表4）。另外10例（5例供体）双眼角膜的微生物培养结果不一致。其余207例供体角膜（来源于207例供体）均为单侧培养阳性。

2.4　供体角膜植片多重耐药菌检出情况

2018—2024年细菌培养阳性的159例角膜中，药敏检测结果为MDROs的供体角膜共有120例（75.47%）。检出MDROs中，占比较多的是鲍曼不动杆菌（37例，30.83%）、表皮葡萄球菌（18例，15.00%）、粪肠球菌（13例，10.83%）、荧光假单胞菌（10例，8.33%）、嗜麦芽窄食单胞菌（9例，7.50%）、肺炎克雷伯菌（6例，5.00%）、大肠埃希菌（4例，3.33%）、溶血葡萄球菌（4例，3.33%；图3A）。

各年度MDROs在细菌培养阳性的供体角膜中占比为33.33%~91.30%，其中2019年最低，2023年最高。除2019年外，MDROs检出在细菌培养阳性中的占比均超过60%。整体上，近年来MDROs污染在细菌培养阳性中的占比较高，并呈上升趋势（图3B）。

表2 革兰阴性菌培养阳性供体角膜中检出菌的分布

Table 2 Distribution of Gram-negative isolates recovered from culture-positive donor corneas

Gram-negative bacterial isolate	No. of isolates/*n*	Among Gram-negative isolates/%	Among all bacterial isolates/%
Acinetobacter spp.	42	41.18	23.46
Acinetobacter baumannii	42	41.18	23.46
Stenotrophomonas spp.	21	20.59	11.73
Stenotrophomonas maltophilia	21	20.59	11.73
Pseudomonas spp.	16	15.69	8.94
Pseudomonas fluorescens	11	10.78	6.15
Pseudomonas putida	2	1.96	1.12
Pseudomonas aeruginosa	2*	1.96	1.12
Pseudomonas oleovorans	1*	0.98	0.56
Pseudomonas viridiflava	1	0.98	0.56
Klebsiella spp.	6	5.88	3.35
Klebsiella pneumoniae	6	5.88	3.35
Escherichia spp.	4	3.92	2.23
Escherichia coli	4	3.92	2.23
Elizabethkingia spp.	3	2.94	1.68
Elizabethkingia meningoseptica	3	2.94	1.68
Enterobacter spp.	2	1.96	1.12
Enterobacter amnigenus	2	1.96	1.12
Sphingomonas spp.	2	1.96	1.12
Sphingomonas paucimobilis	2	1.96	1.12
Myroides spp.	2	1.96	1.12
Delftia spp.	2	1.96	1.12
Aeromonas spp.	1	0.98	0.56
Aeromonas punctata	1	0.98	0.56
Proteus spp.	1	0.98	0.56
Proteus mirabilis	1	0.98	0.56

* One sample simultaneously yielded *Pseudomonas aeruginosa* and *Pseudomonas oleovorans*. Percentages are calculated based on the total number of Gram-negative bacterial isolates or the total number of bacterial isolates, respectively. *n*: number of isolates; %: percentage.

2.5 不同来源供体角膜植片培养阳性情况

2.5.1 不同来源供体角膜微生物培养阳性率 本研究用于角膜移植的7 442例供体角膜中，6 521例（87.62%）来自OPO，921例（12.38%）来自HCRP。微生物培养阳性的251例供体角膜中，193例（76.89%）来自OPO，58例（23.11%）来自HCRP。OPO来源角膜植片微生物培养总体阳性率为2.96%，HCRP来源角膜植片微生物培养总体阳性率为6.30%（图4A）。OPO来源角膜植片微生物培养年度阳性率为1.29%~4.62%，HCRP来源角膜植片微生物培养年度阳性率为2.86%~12.10%（图4B）。HCRP来源供体角膜微生物培养阳性率总体高于OPO来源（图4A、4B）。

2.5.2 不同来源供体角膜植片微生物培养结果 对两种来源培养阳性角膜植片的微生物培养结果进行统计。OPO来源中真菌培养阳性供体角膜45

表3　革兰阳性菌培养阳性供体角膜中检出菌的分布

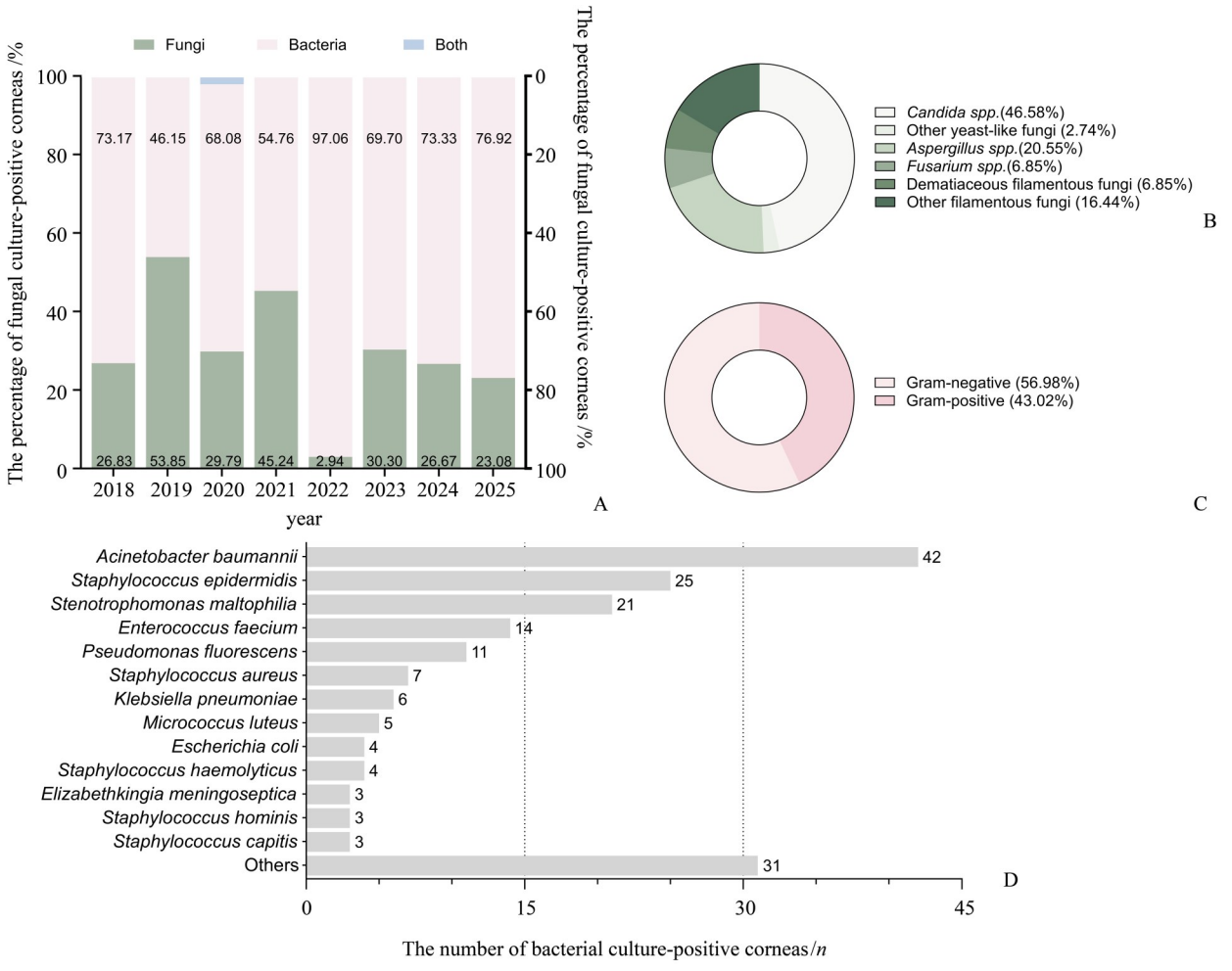
Table 3　Distribution of Gram- positive isolates recovered from culture-positive donor corneas

Gram-positive bacterial isolate	No. of isolates/*n*	Among Gram-positive isolates/%	Among all bacterial isolates/%
Staphylococcus spp.	45	58.44	25.14
Staphylococcus epidermidis	25	32.47	13.97
Staphylococcus aureus	7	9.09	3.91
Staphylococcus haemolyticus	4	5.19	2.23
Staphylococcus hominis	3	3.90	1.68
Staphylococcus capitis	3	3.90	1.68
Staphylococcus cohnii subsp. urealyticus	1	1.30	0.56
Staphylococcus warneri	1	1.30	0.56
Staphylococcus lugdunensis	1	1.30	0.56
Enterococcus spp.	14	18.18	7.82
Enterococcus faecium	14	18.18	7.82
Micrococcus spp.	5	6.49	2.79
Micrococcus luteus	5	6.49	2.79
Bacillus spp.	2	2.60	1.12
Bacillus subtilis	1	1.30	0.56
Bacillus cereus	1	1.30	0.56
Kocuria spp.	1	1.30	0.56
Kocuria varians	1	1.30	0.56
Paenibacillus spp.	1	1.30	0.56
Paenibacillus provencensis	1	1.30	0.56
Streptococcus spp.	1	1.30	0.56
Streptococcus sanguinis	1	1.30	0.56
Microbacterium spp.	1	1.30	0.56
Microbacterium aurum	1	1.30	0.56
Cutibacterium spp.	1	1.30	0.56
Cutibacterium avidum	1	1.30	0.56
Unidentified Gram-positive bacillus	1	1.30	0.56
Unidentified Gram-positive coccus	1	1.30	0.56

Percentages are calculated based on the total number of Gram-positive bacterial isolates or the total number of bacterial isolates, respectively. *n*: number of isolates; %: percentage.

例（23.44%），细菌培养阳性供体角膜147例（76.56%），细菌及真菌培养同时阳性1例（此处不纳入统计）；HCRP来源供体角膜中真菌培养阳性共27例（46.55%），细菌培养阳性共31例（53.45%），见图4C。总体上，HCRP来源培养阳性供体角膜真菌检出率高于OPO来源，OPO来源培养阳性角膜则以细菌检出为主（图4C、4D；表5）。

2.5.3　不同来源供体角膜植片多重耐药菌检出情况　对不同来源的供体角膜MDROs检出情况进行统计。2018—2024年微生物培养检出细菌的角膜植片中，128例来自OPO（包含1例细菌及真菌培养同时阳性，其药敏检测结果提示MDRO），31例来自HCRP。共检出MDROs阳性供体角膜120例，其中OPO来源为103例（103/128，80.47%），HCRP来源



A: Annual proportions of fungal and bacterial isolates among culture-positive donor corneas. B: Distribution of fungal isolates (n=73). C: Distribution of Gram-positive and Gram-negative bacterial isolates (n=179). D: Numbers of major bacterial species isolated.

图2 2018—2025年微生物培养阳性供体角膜病原体构成

Fig. 2 Pathogen composition of microbial culture-positive donor corneas from 2018 to 2025

为17例(17/31,54.84%;图4E)。总体上OPO来源供体角膜MDROs检出比例高于HCRP来源供体角膜(图4F)。

3 讨论

本研究回顾性分析了广东省眼库供体角膜的微生物培养结果。总体来看,供体角膜微生物培养阳性率处于较低水平,但由于眼库供体角膜获取量较大,受角膜供体疾病种类、死亡原因、获取场地、获取和保存操作技术等因素影响,每年仍有一定数量角膜植片受到污染,因此持续开展微生物监测和结果追踪具有重要的临床意义。

不同国家和地区报道的供体角膜培养阳性率差异较大,并与保存方式、取样部位、培养方法、检测时点、供体来源及眼库质控流程密切相关。欧洲及大洋洲多个眼库多采用OC方式(31 ℃~37 ℃,保存时间约1月)保存植片,通常可在移植前对保存液进行微生物检测,操作相对简便,可疑污染植片常被废弃,可以较好保证受体安全。法国区域眼库研究报道,OC方式培养阳性率约为5.5%;同一地区另一项14年回顾性研究显示,平均年度培养阳性率为6.8%(5.2%~8.9%)[7-8]。德国眼库的相关报道存在较大差异,平均年度培养阳性率为1.8%~7.8%,中位数为5.3%[9-11]。澳大利亚和新西兰眼库角膜培养阳性率为1.0%~2.5%[12-14]。亚洲和美国主要采用HS法(2 ℃~8 ℃,保存时间约7~14 d)保存角膜,通常在术中剪取植片边缘组织送检,操作

表4　同一供体双眼培养阳性角膜植片微生物检出情况

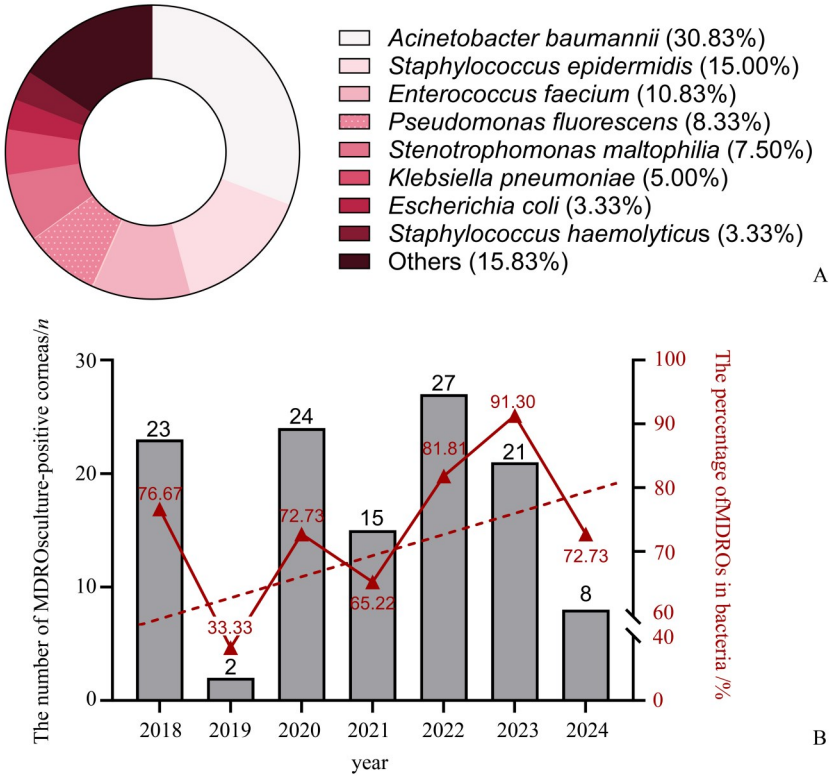
Table 4　Microbial isolates detected in paired culture-positive donor corneas from the same donors

Microorganism	Year								Total/*n*
	2018	2019	2020	2021	2022	2023	2024	2025	
Fungi									
Candida spp.	1	–	–	–	–	–	–	–	1
Aspergillus spp.	–	–	1	–	–	–	–	–	1
Unidentified filamentous fungi	–	–	–	1	–	–	–	–	1
non-MDROs									
Staphylococcus aureus	–	–	–	1	–	–	–	–	1
MDROs									
Acinetobacter baumannii	–	–	1	1	1	1	–	1	5
Pseudomonas fluorescens	3	–	–	–	–	–	–	–	3
Enterococcus faecium	1	–	–	–	–	–	–	–	1
Stenotrophomonas maltophilia	1	–	–	–	–	–	–	–	1
Enterobacter amnigenus	–	–	1	–	–	–	–	–	1
Klebsiella pneumoniae	–	–	–	1	–	–	–	–	1
Bacteria without AST									
Staphylococcus capitis	–	–	–	–	–	–	–	1	1
Discordant culture results	2	–	1	2	–	–	–	–	5
Total paired corneas/*n*	8	–	4	6	1	1	–	2	22

Each pair represents bilateral culture-positive donor corneas obtained from the same donor. Discordant culture results indicate paired corneas from the same donor with different microbial culture findings. MDROs：multidrug-resistant organisms；non-MDROs：non-multidrug-resistant organisms；AST：antimicrobial susceptibility testing；*n*：number of paired donor corneas.

相对复杂，且微生物培养结果通常在受体已接受角膜移植后才能获知。虽然目前尚无明确证据说明两种保存方式供体植片污染率存在差异，但是基于受体安全考虑，对HS方式保存供体植片的微生物检测结果进行追踪与统计是极有必要的。近5年，印度及土耳其报告其HS法角膜培养阳性率超过10%[15-16]。沙特阿拉伯曾报道培养阳性率为4.6%[17]。美国眼库早期的角膜培养阳性率为5.3%~19.4%[18-19]，2018年报道部分地区培养阳性率为1.91%[20]。中国部分眼库报道10年前角膜培养阳性率为8.2%~9.8%[21-22]。与上述研究相比，本研究中HS方式保存供体角膜培养阳性率处于较低水平（总培养阳性率3.37%），可能与近些年来眼库加强规范化管理和技术水平提高有关。

本研究中供体角膜检出的病原体以细菌为主，这一结果与多个国家眼库微生物培养监测结果一致[7-8,13]。国外眼库报道的细菌培养阳性中，葡萄球菌属、凝固酶阴性葡萄球菌、肠球菌属等革兰阳性菌较常见；真菌培养阳性以念珠菌属为主[7-12,16,23]。这可能与供体眼睑、皮肤、结膜囊菌群或获取及保存过程中的机会性污染有关。本研究中，革兰阴性菌略多于革兰阳性菌，较常见菌种为鲍曼不动杆菌、表皮葡萄球菌、嗜麦芽窄食单胞菌、粪肠球菌、荧光假单胞菌等，这些菌种可能与长期住院或昏迷患者的医院内感染有关。与多项眼库研究结果相同，念珠菌属是供体角膜真菌污染的重要病原体[7-8,11-12,24]。本研究还检出一定数量曲霉属、镰刀菌属、暗色丝状真菌及其他丝状真菌，这可能与华南地区温暖、潮湿的气候环境有关。既往研究认为，较高气温或夏秋季节获取的供体角膜污染率较高[11-12]。因此，在我国南方地区眼库质量控制中，除关注念珠菌外，也应重视曲霉菌、镰刀菌等丝状



A: Proportions of isolates among MDROs culture-positive corneas from 2018 to 2024 (n=120). B: Annual numbers of MDROs culture-positive corneas and their proportions among bacterial culture-positive corneas from 2018 to 2024 (y=4.043x − 8101, P=0.280 0, R^2=0.226 8). Simple linear regression was used. MDROs: multidrug-resistant organisms.

图3 2018—2024年多重耐药菌污染角膜植片检出情况

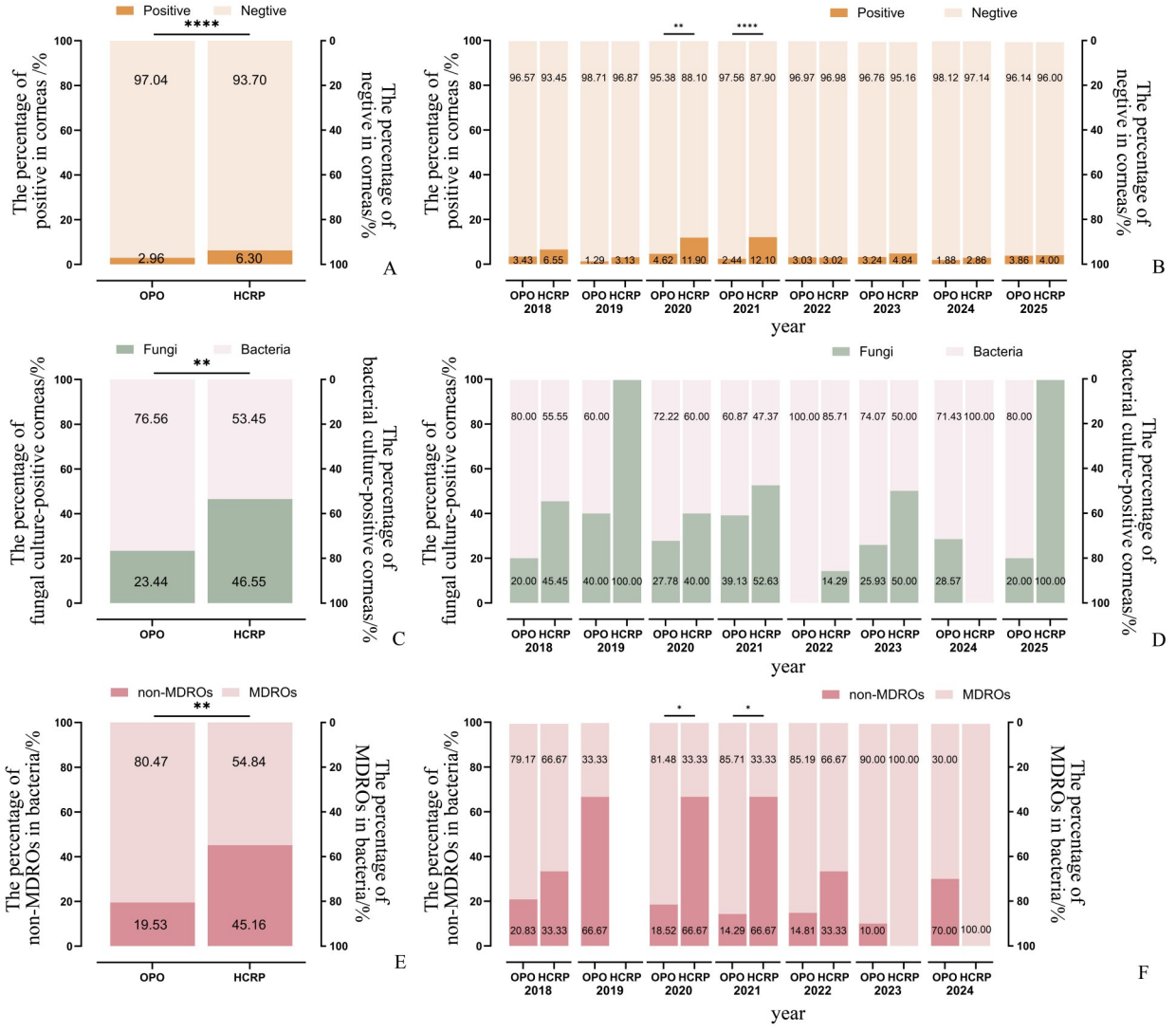
Fig. 3 Detection of multidrug-resistant organisms in donor corneas from 2018 to 2024

表5 不同来源供体角膜微生物培养结果分布

Table 5 Distribution of microbial isolates among donor corneas from different sources

Source	Culture result	Year								Total/n
		2018	2019	2020	2021	2022	2023	2024	2025	
OPO	Fungi	6	4	10	9	–	7	4	5	45
	Bacteria	24	6	26	14	27	20	10	20	147
	non-MDROs	5	4	5	2	4	2	3	NE	25
	MDROs	19	2	21	12	23	18	7	NE	102
	Fungi & Bacteria	–	–	1*	–	–	–	–	–	1
HCRP	Fungi	5	3	4	10	1	3	–	1	27
	Bacteria	6	–	6	9	6	3	1	–	31
	non-MDROs	2	–	4	6	2	–	–	NE	14
	MDROs	4	–	2	3	4	3	1	NE	17
	Fungi & Bacteria	–	–	–	–	–	–	–	–	0

* The antimicrobial susceptibility testing (AST) results indicated a MDRO in this sample. OPO: Organ Procurement Organization; HCRP: Hospital Cornea Recovery Program; MDROs: multidrug-resistant organisms; non-MDROs: non-multidrug-resistant organisms; NE: not evaluable; n: number of culture-positive donor corneas. NE indicates that the number of MDROs and non-MDROs could not be determined because AST was not performed for all relevant bacterial isolates.



A: Proportions of positive and negative corneas from OPO and HCRP, 2018 to 2025 ($P<0.000\ 1$). B: Annual proportions of positive and negative corneas from OPO and HCRP (Year=2020, P=0.009 5; Year=2021, $P<0.000\ 1$). C: Proportions of fungal culture-positive and bacterial culture-positive corneas from OPO and HCRP, 2018-2025 (P=0.001 5). D: Annual proportions of fungal culture-positive and bacterial culture-positive corneas from OPO and HCRP. E: Proportions of non-MDROs culture-positive and MDROs culture-positive corneas from OPO and HCRP, 2018-2024 (P=0.005 2). F: Annual proportions of non-MDROs culture-positive and MDROs culture-positive corneas from OPO and HCRP (Year=2020, P=0.034 2; Year=2021, P=0.022 8). Fisher's exact test was used. $^{*}P<0.05$; $^{**}P<0.01$; $^{****}P<0.000\ 1$. MDROs: multidrug-resistant organisms; non-MDROs: non-multidrug-resistant organisms.

图4　OPO与HCRP来源培养阳性供体角膜情况比较

Fig. 4　Comparison of microbial culture results among donor corneas from OPO and HCRP

真菌污染及其潜在的临床感染风险。

同一供体双侧角膜的培养结果有助于判断污染病原体的来源。本研究共有22对同源双侧角膜培养阳性，其中17对双侧培养结果一致，12对为MDROs。双眼检出相同病原体，提示更可能来源于供体自身眼表菌群或供体医院内感染，而非角膜取材及保存过程中的偶发污染，可结合供体生前疾病类型、血培养、痰培养或体液宏基因测序等结果进一步确认。同一供体双侧角膜培养结果不一致或单侧培养阳性者，则可能更多考虑为获取环境或获取保存过程中的机会性污染。双侧供体角膜培养阳性，或单侧阳性但微生物检出结果为真菌或MDROs的，应及时建立眼库与手术医生之间的反馈机制，加强对角膜移植受体的术后随访。

MDROs污染是角膜移植手术面临的严重感染风险。本研究中,检出的MDROs主要为鲍曼不动杆菌、表皮葡萄球菌、粪肠球菌、荧光假单胞菌、嗜麦芽窄食单胞菌和肺炎克雷伯菌。MDROs感染已成为全球公共卫生问题,重症监护病房(intensive care unit,ICU)的医院内感染是重要危险因素[25-28]。ICU住院时间是器官捐献者MDROs感染的明确独立危险因素[29],供体在ICU停留时间也会明显增加捐献角膜的污染风险[30]。本研究中的供体角膜全部都来自在医院内去世的捐献者,我们认为这可能是本研究MDROs检出较多且呈上升趋势的原因。安全性方面,有研究指出实体器官移植供体培养出MDROs会增加移植后早期感染的风险,但似乎不会影响移植物或受体的长期存活,在供体相对缺乏情况下,MDROs污染的供体应用仍需谨慎[31-32]。

临床实践中,角膜移植术后感染率远低于供体角膜培养阳性率,供体相关的角膜移植后严重感染较为少见[33]。供体角巩膜缘培养阳性与术后感染之间存在一定关联,但总体预测能力有限,尤其是细菌培养阳性对术后感染的预测价值相对较低[34]。但真菌培养阳性,尤其念珠菌属阳性,与术后真菌性角膜炎或眼内炎的相关性值得关注[24-35]。广东省眼库2015—2016年研究报告显示,与供体角膜相关的术后感染发生率极低(1.80%,2/111)[22]。本研究时间范围内(2018—2025年),广东省眼库仅收到2例角膜移植术后感染报告,但其供体与受体的培养结果并不一致,不能算作供体角膜污染所致的术后感染。因此,对于供体角膜培养阳性结果,应结合病原体类型、药敏结果、移植术式、受体眼表情况及术后临床表现综合判断,但培养病原体为真菌、MDROs或同源双侧阳性病例,应提高警惕,并加强术后早期随访。

不同来源的供体角膜培养结果存在差异,HCRP来源角膜培养阳性率总体高于OPO来源角膜,且其真菌污染占比更高。造成这种差异的原因可能是多方面的。HCRP供体死亡原因、死亡地点、遗体停放环境及取材环境较为复杂,供体年龄、基础疾病、死亡至取材时间、眼睑闭合情况等因素也可能影响供体角膜的污染风险,特别是外环境暴露、温暖潮湿地区真菌负荷以及死亡后眼表防御功能丧失等导致真菌的污染机会增加。相比之下,OPO来源角膜多来自器官捐献供体,获取环境和过程相对规范,这可能是其总体培养阳性率较低的原因。OPO来源角膜MDROs培养阳性比例高于HCRP,可能与OPO供体生前多为急危重症患者有关,ICU住院经历、机械通气、中心静脉置管、导尿、广谱抗菌药物使用及较长时间住院,均可能增加MDROs感染风险。因此,眼库角膜植片质控还应结合供体生前病史、ICU停留时间、抗菌药物暴露、全身感染情况及病原体耐药特征进行综合评估。

规范角膜获取与保存流程、加强消毒灭菌是减少供体角膜污染的有效方法,既往研究认为聚维酮碘浸泡时间及处理方式可能影响供体角膜缘培养阳性率[36]。不同取材部位也会影响病原体的检出率,供体角膜边缘取材培养的敏感性高于其他部位[37]。我们认为,对于HCRP来源角膜,应重点加强非手术室环境下的无菌操作和转运管理;而OPO来源角膜,则应关注供体生前ICU停留时间、侵入性操作、抗菌药物使用史、全身感染及MDROs感染情况,以便更准确评估角膜污染风险。

本研究为单中心回顾性研究,缺乏供体住院时间、ICU暴露、抗菌药物使用、全身感染及死亡至取材时间等资料,难以对角膜污染的危险因素进行深入分析。未来可开展多中心研究,结合供体临床资料、保存液培养、角巩膜缘培养及受体术后感染结局,进一步明确供体角膜污染的危险因素及其临床意义,为建立规范的眼库微生物监测和术后随访机制、提高角膜移植安全性提供依据。此外,广义的微生物培养除真菌、细菌外,还包括病毒、寄生虫等微生物,但本研究受限于临床实际条件暂未纳入,后续或可开展更全面的检测。

综上所述,广东省眼库供体角膜培养阳性率总体较低,培养阳性标本中细菌占比较高,且MDROs检出总体呈上升趋势。本研究革兰阴性菌及医院相关机会性病原体占比较高,提示医院环境可能对病原谱产生重要影响。HCRP来源角膜总体培养阳性率较高,而OPO来源细菌培养阳性角膜中MDROs占比较高,说明不同来源供体角膜具有不同风险特点。眼库质量控制应从单纯关注培养阳性率,进一步转向病原体类型、耐药特征、同源角膜追踪及供体临床背景的综合评估,完善培养阳性结果反馈及术后随访机制,以此进一步提高角膜移植安全性。

参考文献

[1] Davila JR, Mian SI. Infectious keratitis after keratoplasty[J]. Curr Opin Ophthalmol, 2016, 27(4): 358-366.

[2] Soleimani M, Tabatabaei SA, Bahadorifar S, et al. Unveiling the landscape of post-keratoplasty keratitis: a comprehensive epidemiological analysis in a tertiary center [J]. Int Ophthalmol, 2024, 44(1): 230.

[3] 江文慧,陈颖欣.角膜移植手术后眼表微环境与干眼的研究进展[J].眼科学报, 2026, 41(7): 586-599.
Jiang WH, Chen YX. Research progress on the eye surface microenvironment and dry eye after corneal transplantation[J]. Eye Sci, 2026, 41(7): 586-599.

[4] Cipolla J, Jo M, Sabater AL. A comprehensive review of donor corneal preservation strategies[J]. Cornea, 2024, 43(11): 1456-1465.

[5] Armitage WJ. Preservation of human cornea[J]. Transfus Med Hemother, 2011, 38(2): 143-147.

[6] Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance[J]. Clin Microbiol Infect, 2011, 18(3): 268-281.

[7] Khouani M, Debellemanière G, Malugani C, et al. Evaluation of microbial contamination of corneal transplants: one-year report from a French regional eye bank[J]. Cornea, 2014, 33(9): 899-904.

[8] Fabre L, Puyraveau M, Jeanvoine A, et al. Changes of contamination rate and microorganism evaluation in organ-cultured human corneas: a 14-year review from a French regional eye bank[J]. Cornea, 2021, 40(6): 696-703.

[9] Linke SJ, Fricke OH, Eddy M-T, et al. Risk factors for donor cornea contamination: retrospective analysis of 4546 procured corneas in a single eye bank [J]. Cornea, 2013, 32(2): 141-148.

[10] Gruenert AK, Rosenbaum K, Geerling G, et al. The influence of donor factors on corneal organ culture contamination[J]. Acta Ophthalmol, 2017, 95(7): 733-740.

[11] Röck D, Wude J, Bartz-Schmidt KU, et al. Factors influencing the contamination rate of human organ-cultured corneas[J]. Acta Ophthalmol, 2017, 95(8): e706-e712.

[12] Ling MLH, Wells M, Petsoglou C, et al. Factors affecting corneal organ culture contamination: a 6-year study at the New South Wales Tissue Bank[J]. Cornea, 2019, 38(7): 829-835.

[13] Kezic JM, Buckland L, Wiffen S. Microbiological screening of corneas stored in organ culture medium at Lions Eye Bank of Western Australia from 2011 to 2022[J]. Int Ophthalmol, 2024, 44(1): 280.

[14] Cunningham WJ, Moffatt SL, Brookes NH, et al. The New Zealand National Eye Bank study: trends in the acquisition and storage of corneal tissue over the decade 2000 to 2009 [J]. Cornea, 2012, 31(5): 538-545.

[15] Bolac R, Vural ET, Yildiz E, et al. The prevalence of positive donor corneoscleral rim culture and its association with ocular infection after transplantation[J]. Beyoglu Eye J, 2023, 8(1): 50-54.

[16] Jadeja JN, Rathore P, Patel PJ. Beyond the graft: microbial footprints of culture-positive corneoscleral rims in keratoplasty at a tertiary eye center[J]. J Cornea Ocul Surf, 2024, 2(1): 18-24.

[17] Meeraalam Z, Alreshidi SO, Albalawi HB, et al. Incidence and implications of culture-positive corneoscleral rims in corneal transplantation[J]. Infect Drug Resist, 2025, 18: 847-853.

[18] Wiffen SJ, Weston BC, Maguire LJ, et al. The value of routine donor corneal rim cultures in penetrating keratoplasty [J]. Arch Ophthalmol, 1997, 115(6): 719-724.

[19] Everts RJ, Fowler WC, Chang DH, et al. Corneoscleral rim cultures: lack of utility and implications for clinical decision-making and infection prevention in the care of patients undergoing corneal transplantation [J]. Cornea, 2001, 20(6): 586-589.

[20] Mian SI, Aldave AJ, Tu EY, et al. Incidence and outcomes of positive donor rim cultures and infections in the cornea preservation time study[J]. Cornea, 2018, 37(9): 1102-1109.

[21] Li G-G, Zhu H, Ji C-N, et al. Microbiological contamination in donor corneas preserved for medium-term[J]. Cell Tissue Bank, 2019, 20(3): 379-387.

[22] Li S, Zhong J, Tan Y, et al. Microbiological screening of hypothermic preserved donor corneas in keratoplasty[J]. Curr Eye Res, 2019, 44(10): 1067-1074.

[23] Patel HY, Brookes NH, Moffatt L, et al. The New Zealand National Eye Bank study 1991-2003: a review of the source and management of corneal tissue[J]. Cornea, 2005, 24(5): 576-582.

[24] Vislisel JM, Goins KM, Wagoner MD, et al. Incidence and outcomes of positive donor corneoscleral rim fungal cultures after keratoplasty[J]. Ophthalmology, 2016, 124(1): 36-42.

[25] Ma X, Wu Y, Li L, et al. First multicenter study on multidrug resistant bacteria carriage in Chinese ICUs [J]. BMC Infect Dis, 2015, 15: 358.

[26] De Waele JJ, Boelens J, Leroux-Roels I. Multidrug-resistant bacteria in ICU: fact or myth [J]. Curr Opin Anaesthesiol, 2020, 33(2): 156-161.

[27] Teng J, Imani S, Zhou A, et al. Combatting resistance: understanding multi-drug resistant pathogens in intensive care units[J]. Biomed Pharmacother, 2023, 167: 115564.

[28] Global burden of bacterial antimicrobial resistance 1990-2021: a systematic analysis with forecasts to 2050 [J]. Lancet, 2024, 404(10459): 1199-1226.

[29] Shen G, Zhang L, Fan W, et al. Establishment of a risk prediction model for multidrug-resistant bacteria in deceased organ donors: a retrospective cohort study in China[J]. Front Cell Infect Microbiol, 2023, 13: 1181630.

[30] Medina IFB, Oguido APMT, Urbano MR, et al. Intensive care unit time and prolonged enucleation to processing interval are associated with donor cornea contamination [J]. Graefes Arch Clin Exp Ophthalmol, 2020, 258(10): 2241-2249.

[31] Moradi F, Bahrami M, Nasrollahian S, et al. Global challenges of bacterial infections in organ transplantation: assessment of risk factors and predominant bacterial pathogen profiles threatening liver, kidney, heart, and lung transplant recipients[J]. BMC Infect Dis, 2025, 25(1): 1153.

[32] Zhou YM, Cui XQ, Zhao P, et al. The species, distribution, resistance of donor-derived pathogens and their impact on solid organ transplant recipients [J]. Front Immunol, 2026, 17: 1777244.

[33] Deogaonkar K, Roy A. Donor related corneal graft infection: a review of literature and preventive strategies [J]. Semin Ophthalmol, 2023, 38(3): 219-225.

[34] Wilhelmus KR, Hassan SS. The prognostic role of donor corneoscleral rim cultures in corneal transplantation [J]. Ophthalmology, 2007, 114(3): 440-445.

[35] Edelstein SL, Dematteo J, Stoeger CG, et al. Report of the Eye Bank Association of America medical review subcommittee on adverse reactions reported from 2007 to 2014 [J]. Cornea, 2016, 35(7): 917-926.

[36] Salisbury CD, Kirk CN, Lee WB, et al. Increasing povidone-iodine exposure in endothelial keratoplasty tissue processing and fungal infection impact[J]. Cornea. 2019, 38(9):1093-1096.

[37] Wang YJ, Sung KC, Lin WC, et al. Comparison of microbial sampling sites and donor-related factors on corneal graft contamination[J]. J Clin Med, 2022, 11(21):6236.

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