Infection and Drug Resistance
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ORIGINAL RESEARCH

Nosocomial Infections After Pediatric Congenital Heart Disease Surgery: Data from National Center for Cardiovascular Diseases in China

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Purpose: Infection prevention and control (IPC) has a significant impact on the prognosis after pediatric cardiac surgery. This study aimed to provide surveillance data on the incidence and density of various infections during the COVID-19 epidemic and explore the influence of multi-drug resistant organisms (MDRO) on in-hospital prognosis after congenital heart disease surgery.

Methods: This single-center retrospective study included pediatric patients who underwent cardiac surgery between 2021 and 2022. The results of the postoperative bacterial and fungal cultures and antimicrobial stewardship were collected. The demographic characteristics (age and weight), operation-related parameters (RACHS-1 grade, duration of cardiopulmonary bypass, and aortic cross clamp), and surgical outcomes (extracorporeal membrane oxygenation, delayed sternal closure, mortality, duration of mechanical ventilation, length of intensive care unit stay and hospital stay, and hospitalization costs) of MDRO and non-MDRO patients were compared.

Results: A total of 4776 patients were included. There were 101 infectious culture results after the operation, with a nosocomial infection rate of 2.1%. There were 40 MDRO specimens from 36 patients, 50 non-MDRO specimens from 30 patients, and 11 fungal specimens from 10 patients. The incidence of pneumonia was 1.5%, with a ventilator-associated pneumonia incidence density of 7.2/ 1000 patient-days. The incidence of sepsis was 0.4%, with a catheter-related bloodstream infection incidence density of 0.24/ 1000 patient-days. The incidence density of catheter-associated tract infection was 0.45/ 1000 patient-days. The incidence of surgical site infection was 0.06%. The culture proportion before commencing antibiotics was 93% and the antibiotic consumption intensity was 30.7 DDD/100 bed-days. The length of intensive care unit stay in MDRO infection patients increased compared with that in non-MDRO infection patients, 30 (18,52) vs 17 (7,62) days, p=0.05).

Conclusion: The IPC performance of Fuwai Hospital achieved satisfactory results. MDRO infection can lead to prolonged intensive care unit stay.

Plain language summary: Developed countries have advanced infection prevention and control systems and comprehensive postoperative infection monitoring data for congenital heart disease. While developing countries have initiated efforts in infection prevention and control, global attention remains substantial. This study aimed to provide comprehensive infection surveillance data and identify possible implementation for further improvement in the National Center for Cardiovascular Diseases in China (Fuwai Hospital).

This was a retrospective single-center study. We included pediatric patients who underwent cardiac surgery at a pediatric surgical center between 2021 and 2022, with an age limit of 14 years. Exclusion criteria included patients undergoing medical therapy, interventional therapy, or surgical therapy in other centers in Fuwai Hospital.

Received: 4 January 2024
Accepted: 23 April 2024
Published: 26 April 2024

This study, for the first time, reports the incidence of comprehensive healthcare-associated infection surveillance and targeted surveillance (encompassing device-associated infection, surgical site infection, and multi-drug resistant organisms) after pediatric cardiac surgery at the National Center for Cardiovascular Diseases in China. In addition, we report the data on antimicrobial stewardship. We compared the surgical outcome and hospitalization costs between patients with multi-drug resistant organism infection and those without multi-drug resistant organism infection and found that multi-drug resistant organism infection can lead to prolonged intensive care unit length of stay.

The Fuwai Hospital achieved satisfactory infection prevention and control results. However, because China is a large developing country exhibiting notable variations in medical conditions across its diverse regions, prospective, multicenter, observational studies should be carried out for future research based on existing evidence.

Keywords: nosocomial infections, pediatric cardiac surgery, multidrug-resistant organism, surgical outcomes

Introduction

Congenital heart disease is the most common congenital malformation, with an overall incidence of 1%.[1] Approximately 70,000 patients with congenital heart disease undergo annual surgical treatment.[2] All patients require postoperative care in the intensive care unit (ICU). Many factors affect postoperative recovery, and the level of infection prevention and control (IPC) is very important.[3,4] To achieve the best IPC performance, it is necessary to build an IPC system, which is a complex systematic profession.

Developed countries have advanced IPC systems and comprehensive postoperative infection monitoring data for congenital heart disease. Pasquali SK and colleagues,[5] utilizing data from the STS Congenital Heart Surgery Database and Pediatric Health Information System for 32,856 patients across 28 centers from 2006 to 2010, reported a postoperative infection rate of 3.7%. Significant variations existed among hospitals, ranging from 0.9% to 9.8%. Kansy et al,[6] drawing data from the STS Congenital Heart Surgery Database from 1995 to 2010 including 6314 patients, identified 197 cases (3.1%) with significant infections (3% sepsis, 0.015% infective endocarditis, and 0.09% mediastinitis). Using data from the Vizient Clinical Database/Resource Manager from 2013 to 2015, Haughey et al[7] reported the incidence of catheter-related bloodstream infections after congenital heart disease surgery. This study included 1386 neonatal and 2913 infant patients, with an incidence of 1.5% in neonates and 0.8% in infants.

While developing countries have initiated efforts in IPC, global attention remains substantial. According to Chau NT and colleagues,[4] who analyzed data from the International Quality Improvement Collaborative Group spanning 2010 to 2012, involving 27 regions from 16 developing countries, a total of 14,545 patients were included. Among them, 793 cases (5.5%) experienced bacterial sepsis and 306 (2.1%) had surgical site infections. Murni IK and colleagues[8] conducted a literature review of infection data from high-income and middle-to-low-income countries. In high-income countries, the postoperative infection rate ranged from 1.2% (12/981) to 48% (22/46). Postoperative bacteremia rates varied from 1.5% (15/992) to 10.2% (12/127), and the incidence of fungal infections or invasive candidiasis ranged from 0.4% (6/1540) to 5.9% (10/169). Concerning pulmonary infections, the postoperative pneumonia rate in infants was 6.2% (8/127), with a ventilator-associated pneumonia incidence density of 17.1/1000 patient-days. In middle-to low-income countries, the incidence of postoperative infections varies widely. The incidence ranges from 7.8% to 40% for overall postoperative infections, 7% to 21% for postoperative sepsis in neonates, and 2.5% to 12.7% for surgical site infections. The incidence of candidemia was 0.07%. The postoperative pneumonia rates vary from 21% to 44%, and the incidence of ventilator-associated pneumonia ranges from 6.2% to 18.3%. The incidence of catheter-related urinary tract infections was 7%.

China also provides congenital heart disease postoperative IPC data for CHDs. In a single-center study conducted from 2012 to 2018, Yu et al[9] reported a nosocomial infection (NIs) rate of 10.8% among 11,651 pediatric patients. Another single-center study conducted by Ren C and colleagues[10] from 2012 to 2017 with 2171 patients revealed that 708 patients experienced pulmonary infections, resulting in an incidence of 32.6%.

Notably, these data suggest that IPC results in China lagged behind those in developed countries during that period. However, the past three years of the COVID-19 epidemic have witnessed tremendous developments in IPC management in China.[11] Because NIs surveillance serves as the cornerstone of IPC management, our study aimed to provide comprehensive surveillance data on the incidence and density of various infections and antimicrobial stewardship (AMS) during the COVID-19 epidemic to facilitate implementation of IPC measures and AMS bundles in the next step. Moreover, owing to the current lack of research on the effect of multi-drug resistant organisms (MDRO) on the in-hospital prognosis of pediatric cardiac surgery patients, our study compared the demographic characteristics, operation-related parameters, and surgical outcomes of MDRO and non-MDRO patients to determine the effect of MDRO infection on postoperative prognosis.

Methods and Materials

Inclusion and Exclusion Criteria

This retrospective, single-center study was conducted at the National Center for Cardiovascular Diseases in China (Fuwai Hospital).

The inclusion criteria were as follows: (1) pediatric patients with an age limit of 14 years. 2) Patients who underwent cardiac surgery at the pediatric surgical center between 2021 and 2022. The exclusion criteria were as follows: 1) patients undergoing medical therapy only, 2) patients undergoing interventional therapy only, and 3) patients undergoing surgical therapy at another center in the Fuwai hospital.

Diagnostic Criteria for Specific Infections

Postoperative pneumonia diagnostic criteria[12] include the presence of new or progressive pulmonary infiltration accompanied by infectious symptoms and signs (such as newly developed fever, purulent sputum, increased white blood cell count, decreased oxygenation, and changes in respiratory mechanics) with positive respiratory tract culture results.

Ventilator-associated pneumonia diagnostic criteria[12] include the presence of new or progressive pulmonary infiltration accompanied by infectious symptoms and signs (such as newly developed fever, purulent sputum, increased white blood cell count, decreased oxygenation, and changes in respiratory mechanics), and positive respiratory tract culture results in patients ventilated for ≥48 hours.

The sepsis diagnostic criteria:[13] positive blood culture results accompanied by low blood pressure, tachycardia, fever, increased white blood cell count, signs of shock (such as cold and cyanotic skin), and signs of organ dysfunction (such as oliguria, acute kidney injury, and altered mental status).

Catheter-related bloodstream infection diagnostic criteria:[14] patients with vascular catheters in place or those who had catheters removed within 48 h of bacteremia or fungemia, accompanied by fever (T > 38 °C), chills, hypotension, and at least one positive result from peripheral venous blood culture, with no other clear source of infection except the catheter.

Catheter-associated urinary tract infection diagnostic criteria:[15] patients with catheters in place or those who had catheters removed within 48 hours, exhibiting signs and symptoms consistent with urinary tract infection or systemic infection and not explainable by other causes, with positive urine culture.

Surgical site infection diagnostic criteria:[16] Within 30 days after the surgical procedure, the wound showed signs of redness, swelling, heat, and poor healing, with positive cultures.

Determination of contamination/colonization: Whether in sterile or non-sterile sites, if the culture result is positive without accompanying infection-related manifestations, contamination was considered and not included in the infection statistics. If common colonizing organisms are cultured in non-sterile sites without infection-related manifestations, colonization is considered and not included in the infection statistics.

Multi-drug resistant organisms (MDRO) mainly include methicillin-resistant staphylococcus aureus/staphylococcus epidermidis, carbapenem-resistant Enterobacteriaceae, carbapenem-resistant Acinetobacter baumannii, carbapenem-resistant pseudomonas aeruginosa, vancomycin-resistant enterococcus, and extended-spectrum beta-lactamases.

Data Collection

Postoperative bacterial and fungal culture results, along with drug resistance results, were collected from the medical records and infection control system. The infection rate was expressed as a percentage (%) and calculated as the number of positive cultures related to infection divided by the total number of patients. Device-associated infections were expressed as infection intensity (per 1000 patient-days), calculated as the number of related infection cultures divided by the number of days the patient used the device, multiplied by 1000%. The parameters related to antimicrobial stewardship included antibiotic consumption intensity (DDD/100 bed-days), rate of antibiotic prophylaxis withdrawal in patients receiving cardiac operations within 48 h, and the rate of culture before commencing antibiotics (%).

For all patients, the demographic characteristics (age and weight), surgery-related indicators (RACHS-1 grade, duration of cardiopulmonary bypass, and duration of aortic cross clamp), surgical outcomes (Extracorporeal Membrane Oxygenation assistance, delayed sternal closure, mortality, duration of mechanical ventilation, ICU length of stay (LOS), total LOS, and hospitalization costs) were collected from the medical records system and databases.

Statistical Analysis

All statistical analyses were performed using SPSS 25.0 (IBM Corp., Armonk, NY, USA). The expectation-maximization method was employed to estimate missing data. The Shapiro–Wilk test was used to assess the conformity of the continuous variables to the normal distribution. Normal distribution was expressed as the mean plus or minus the standard deviation, while non-normal distribution was expressed as the median accompanied by the interquartile range. Categorical variables are displayed in a numerical form, accompanied by their respective percentages. An independent *t*-test was used for normally distributed continuous variable analysis. Otherwise, the Wilcoxon rank-sum test was used for nonnormally distributed variables. Categorical variables were analyzed using the chi-squared test and Fisher's exact test. Statistical p-value ≤ 0.05.

Ethical Review

Approval was obtained from the Fuwai Hospital Ethics Committee in 2022 (ID: 2022–1859. The ethical principles followed the 1975 Declaration of Helsinki. This was a retrospective analysis based on anonymized data collected for routine clinical care and administrative purposes; therefore, the requirement for individual informed consent was waived.

Results

There are 5903 pediatric patients in the pediatric ICU between 2021–2022. After excluding patients undergoing medical therapy, interventional therapy, and surgical therapy in other center (1127 cases in total), 4776 pediatric patients were included in this study.

Following the exclusion of 131 community infection specimens and 29 colonization/contamination specimens, 101 positive postoperative culture results were obtained, indicating an NIs rate of 2.1%. Among these, 40 MDRO cultures were identified in 36 patients, 50 non-MDRO cultures in 30 patients, and 11 fungal cultures in 10 patients. The clinical data of the patients with MDRO and non-MDRO infections are shown in Table 1. The clinical data of patients with fungal infections are shown in Table 2. Details of the infection sites, microbial types, and drug resistance are shown in Table 3.

The postoperative nosocomial pneumonia, sepsis rate was 0.4% and surgical site infection rates were 1.5%, 0.4%, and 0.06%, respectively. The infection intensity was 7.2 /1000 patient-days for ventilator-associated pneumonia, 0.24/1000 patient-days for catheter-related bloodstream infections, and 0.45/1000 patient-days for catheter-associated urinary tract infections.

In terms of antimicrobial stewardship, the rate of culture before commencing antibiotics was 93% and the antibiotic consumption intensity was 30.7 DDD/ 100 bed-days. In China, the goal of antibiotic prophylaxis in patients undergoing cardiac operations is within 48 hours after the end of the operation; however, the actual compliance rate was only 8.5%.

The demographic characteristics, surgery-related indicators, postoperative mortality rates, mechanical ventilation hours, total LOS, and hospitalization costs between patients with postoperative MDRO infections (n=36) and those without MDRO infections (n=30) showed no statistically significant differences (p>0.05). However, there was an increase in pediatric ICU stay in patients with MDRO infections (30 (18,52) vs 17 (7,62) days, p=0.05). The details of the clinical data comparisons are shown in Table 2.

Table 1 The Clinical Data Between Patients with MDRO and Non-MDRO Infections

	Total (n=66)	MDRO (n=36)	Non-MDRO (n=30)	P value
Age (months)	11 (IQR: 3, 51)	13 (IQR: 3, 58)	8 (IQR: 2, 34)	0.50
Weight (kg)	8 (IQR: 4.7, 14.5)	8.1 (IQR: 4.9, 15.8)	7.9 (IQR: 3.9, 13.1)	0.3
RACHS-1[a]				0.74
2–3	49 (78)	27 (79)	22 (76)	
4–5	14 (22)	7 (21)	7 (24)	
Cardiopulmonary bypass surgery	62 (94)	33 (92)	29 (97)	0.74
Cardiopulmonary bypass minutes	176 (IQR: 127, 227)	187 (IQR: 124, 223)	170 (IQR: 129, 240)	0.62
Aortic cross clamp minutes	102±44	103±41	101±48	0.86
Postoperative ECMO	10 (15)	6 (17)	4 (13)	0.71
Delayed sternal closure	18 (27)	11 (31)	7 (23)	0.51
Death	2 (3)	2 (6)	0 (0)	0.50
90 days after surgery	0 (0)	0 (0)	0 (0)	NA
Mechanical ventilation hours	301 (IQR: 74, 1053	359 (IQR: 100, 1074)	276 (IQR: 30, 1053)	0.45
ICU LOS (days)	24 (IQR: 13, 59)	30 (IQR: 18, 52)	17 (IQR: 7, 62)	0.05
Total LOS (days)	48 (IQR: 33, 77)	49 (IQR: 33, 71)	44 (IQR: 27, 78)	0.47
Costs (10,000 yuan)	35.4 (IQR: 23.1, 55.5)	37.7 (IQR: 23.2, 58.6)	34.8 (IQR: 19, 52.9)	0.38

Note: [a]Three pediatric patients underwent cardiac surgery without corresponding RACHS-1 classification.
Abbreviations: MDRO, multi-drug resistant organism; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; LOS, length of stay.

Table 2 The Clinical Data of Patients with Fungus Infections

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Organism types										
Candida parapsilosis	+	+	-	-	+	-	+	-	+	-
Candida albicans	-	-	+	-	-	+	-	+	-	+a
Trichosporon asahii	-	-	-	+	-	-	-	-	-	-
Co-infection	+	+	-	-	+	-	+	+	+	+
Age (months)	42	10	19	82	84	0.1	37	4	1.9	0.8
Weight (kg)	12	5.4	11	26	27	3.8	14	5.5	3.9	2.6
RACHS-1	3	3	4	3	3	4	3	3	3	4
Cardiopulmonary bypass minutes	110	180	271	144	109	187	201	-	208	204
Aortic cross clamp minutes	-	131	141	96	54	129	81	-	129	143
Postoperative ECMO	-	-	+	-	-	-	-	-	-	-
Delayed sternal closure	-	-	+	-	-	+	-	-	-	+
Death	+	-	-	-	-	-	-	-	-	+
90 days after surgery	-	-	-	-	-	-	-	-	-	+
Mechanical ventilation hours	3443	2145	2338	791	1190	1275	1552	589	1183	1457
ICU LOS (days)	144	139	99	81	63	79	78	74	71	64
Total LOS (days)	181	159	109	124	84	84	171	77	115	76
Costs (10,000 yuan)	107.6	80.1	73.3	63.1	65.3	79.6	100	53.9	96.6	56.4

Note: [a]in blood and surgical site.
Abbreviations: ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; LOS, length of stay.

Discussion

During the COVID-19 pandemic, Fuwai Hospital strengthened the IPC system in comprehensive aspects, such as the performance of infection control departments, NIs surveillance, implementation of IPC measures, and antimicrobial stewardship. Among these, NIs surveillance is the cornerstone. Our pediatric ICU actively receives relative cultures from all patients with signs of infection. Based on the NIs surveillance data provided in this study, the overall rate of NIs was 2.1%, nosocomial pneumonia was 1.5%, sepsis rate was 0.4%, surgical site infection rate was 0.06%, infection intensity was 7.2 /1000 patient-days for ventilator-associated pneumonia, 0.24/1000 patient-days for catheter-related bloodstream

Table 3 The Details of NIs Sites, Microbial Types and Drug Resistance

Culture Sites	Organism Types		Name and Quantity of Organism
Sputum	MDRO	Cocci	*Staphylococcus aureus* 3 (3)
			Staphylococcus epidermidis 1 (1)
		Bacilli	*Stenotrophomonas maltophilia* 24 (24)
			Klebsiella pneumoniae 3 (3)
			Pseudomonas aeruginosa 3 (3)
			Elizabethkingia meningoseptica 1 (1)
			Acinetobacter baumannii 1 (1)
	Non-MDRO	Cocci	*Enterococcus faecalis* 1 (1)
		Bacilli	*Burkholderia cepacia* 9 (9)
			Klebsiella pneumoniae 7 (7)
			Acinetobacter baumannii 7 (7)
			Escherichia coli 5 (5)
			Pseudomonas aeruginosa 2 (2)
			Citrobacter freundii 1 (1)
			Enterobacter cloacae 1 (1)
	Fungus		*Candida parapsilosis* 2 (2)
			Candida albicans 2 (2)
			Trichosporon asahii 1 (1)
Blood	MDRO	Cocci	*Staphylococcus epidermidis* 2 (2)
		Bacilli	-
	Non-MDRO	Cocci	*Enterococcus Faecium* 2 (2)
		Bacilli	*Acinetobacter baumannii* 6 (6)
			Burkholderia cepacia 1 (1)
			Pseudomonas aeruginosa 1 (1)
			Serratia marcescens 1 (1)
			Bacillus subtilis 1 (1)
	Fungus		*Candida parapsilosis* 3 (3)
			Candida albicans 1 (1)
Urine	MDRO	Cocci	-
		Bacilli	*Klebsiella pneumoniae* 3 (3)
			Enterobacter cloacae 1 (1)
	Non-MDRO	Cocci	-
		Bacilli	*Klebsiella pneumoniae* 1 (1)
			Morganella morganii 1 (1)
			Escherichia coli 1 (1)
	Fungus		*Candida albicans* 1 (1)
Surgical site	MDRO	Cocci	-
		Bacilli	-
	Non-MDRO	Cocci	-
		Bacilli	*Enterobacter cloacae* 1 (1)
			Serratia marcescens 1 (1)
	Fungus		*Candida albicans* 1 (1)

Abbreviations: MDRO, multi-drug resistant organism; Nis, nosocomial infections.

infection, and 0.45/1000 patient-days for catheter-associated urinary tract infections, all of which suggest that, in our center, IPC performance has reached the standards of developed countries.[9]

However, through data analysis, we found some methods for further improvement. The intensity of ventilator-associated pneumonia in our center was relatively high. Although this is likely associated with delayed recovery in critically ill patients requiring prolonged mechanical ventilation for complex congenital heart disease, there is still room for improvement. In addition to the current bundle implementation, such as hand hygiene, early extubation, chlorhexidine oral care, head of the bed elevated about 30–45 degree, maintaining cuff pressure in endotracheal tubes, reducing sedation, preventing gastric distension, and preventing deep vein thrombosis, future efforts could explore the addition of nebulized inhalation of antimicrobial drugs to reduce the incidence of ventilator-associated pneumonia.[17]

Regarding MDRO, the proportion of gram-negative bacteria currently exceeds that of gram-positive cocci, aligning with the prevailing trend of MDRO in the ICU.[18] At our center, we have not yet identified vancomycin-resistant Enterococcus. This trend emphasizes the need for heightened attention when selecting antimicrobial drugs for congenital heart disease surgery. However, there is a relatively high proportion of Stenotrophomonas maltophilia, possibly because of the empirical use of broad-spectrum antibiotics in critically ill conditions after complex congenital heart disease surgery. To solve this problem, it is important to obtain relevant cultures before commencing antibiotics and de-escalate or discontinue antimicrobial drugs based on culture results.[19]

When comparing patients with and non-MDRO infection, there was no statistically significant difference in the demographic characteristics and surgery-related indicators between the two groups. However, differences were observed in terms of the surgical prognosis. Notably, patients with MDRO infection had an increased ICU-LOS compared to those without MDRO infection (30 (18, 52) vs 17 days (7, 62), p=0.05). Mortality, mechanical ventilation hours, total LOS, and hospitalization costs showed no statistically significant differences between the two groups. This result highlights the need to strengthen the IPC of MDRO (antimicrobial stewardship and IPC measures) after surgery[20] to improve surgical outcomes.

In the results of antimicrobial stewardship at our center, the culture proportion before commencing antibiotics was 93%, and the antibiotic consumption intensity was 30.7 DDD/100 bed-days. These results meet the national antimicrobial stewardship standards in China.[21] However, the actual compliance rate for antibiotic prophylaxis withdrawal in patients undergoing cardiac operations within 48 h was very poor (only 8.5%). In the future, it will be necessary to strengthen the AMS measures and standardize the application of antibacterial drugs.

In terms of bundled IPC measures, our pediatric ICU has implemented single-room isolation, hand hygiene, environmental hygiene, wearing gloves when caring for patients, and wearing protective clothing at risk of contamination. In the future, additional measures such as preoperative active screening[22] and postoperative daily chlorhexidine bathing[23] could be considered to further enhance IPC measures for MDRO infection.

In terms of fungal infections, statistical analysis was not performed due to the small number of cases, and 70% of them had a co-infection status. However, based on the current trend, due to the high mortality of patients with fungal infections (20%), the long LOS (112 days in median), and the high cost of hospitalization (764,500 CNY in median, approximately $113,500 at the exchange rate in 2022), early and proper antifungal prophylaxis and treatment with combined multidrug therapy are needed to reduce mortality and morbidity.[24]

Study limitations

Although this study provided detailed infection monitoring data, due to the limited sample size and the low positive rate of infection after surgery, the sample size was relatively insufficient when comparing the prognosis of infected patients. In the future, we will continue to expand the sample size and conduct research on the risk factors for postoperative infections.

Conclusion

The IPC performance of Fuwai Hospital achieved satisfactory results. In the future, it will be necessary to strengthen the AMS measures and standardize the application of antibacterial drugs. Gram-negative bacteria are the most common type of MDRO. Infection with MDRO can lead to prolonged ICU-LOS in pediatric cardiac surgery patients. Fungal infections may radically influence morbidity and mortality rates.

Data Sharing Statement

All the data collected for the study, including individual participant data (only deidentified individual participant data will be shared), a data dictionary defining each field in the set, and related documents such as study protocol and statistical analysis results, will be made available to others with publication by Email addresses with the consent of the corresponding author.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was supported by the Clinical Research Foundation of the National Health Commission of the People's Republic of China (grant number 2022-GSP-GG-32) and Research Foundation of Artificial Intelligence and Information Application (grant number: 2022-IT02).

Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

This paper has been uploaded to SSRN as a preprint (https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4657436). This paper is not currently under consideration with any other journal or publisher.

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