Infection and Drug Resistance

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ORIGINAL RESEARCH

Postoperative Bloodstream Infections in Patients with Peritoneal Surface Malignancies Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: Risk Factors and Pathogen Resistance

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Objective: In this study we aimed to evaluate the postoperative safety of cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) for the treatment of peritoneal surface malignancies (PSM), and analyzed the risk factors and pathogen resistance associated with bloodstream infections.

Methods: We retrospectively analyzed the incidence of postoperative bloodstream infections in 1500 patients undergoing CRS and HIPEC for PSM. We utilized univariate and multivariate analyses to screen for independent risk factors associated with postoperative bloodstream infections in CRS combined with HIPEC.

Results: Among the 1500 cases of individuals undergoing CRS combined with HIPEC, 207 cases (13.8%) experienced bloodstream infections. A total of 233 strains of pathogens were isolated and cultured, consisting of 151 gram-positive cocci, 52 gram-negative bacilli, and 30 fungi. Coagulase-negative staphylococci (SCN) were the gram-positive cocci (54.94%), while *Klebsiella pneumoniae subsp. Pneumoniae* (7.30%) and *Escherichia coli* (5.58%) dominated the Gram-negative bacilli. *Candida albicans* was the predominant fungus. Staphylococci exhibited high sensitivity to tigecycline, linezolid, vancomycin, and quinupristin/dalfopristin. However, *K. pneumoniae* and *E. coli* were resistant to imipenem. Furthermore, five parameters were associated with the development of bloodstream infections: age ($P = 0.040$), surgical history ($P = 0.033$), prior tumor treatment ($P < 0.001$), tumor tissue type ($P = 0.034$), and completeness of cytoreduction (CC) score ($P = 0.004$). Among these, age ($P = 0.013$), prior tumor treatment ($P = 0.001$), tumor tissue type ($P = 0.032$), and CC score ($P = 0.002$) emerged as independent risk factors for postoperative bloodstream infections in patients undergoing CRS combined with HIPEC.

Conclusion: Postoperative bloodstream infections in patients with PSM undergoing CRS combined with HIPEC are predominantly attributed to SCN, *K. pneumoniae subsp. Pneumoniae*, and *C. albicans*. Notably, Enterobacteriaceae exhibited resistance to carbapenem. Independent risk factors for postoperative infections in PSM include age, prior tumor treatment, tumor tissue type, and completeness of cytoreduction score.

Keywords: bloodstream infections, cytoreductive surgery, hyperthermic intraperitoneal chemotherapy, pathogens drug resistance, pathogens

Introduction

Peritoneal surface malignancies (PSM) encompasses a spectrum of malignant tumors that emerge or progress on the surface of the peritoneum. This includes primary PSM, such as malignant peritoneal mesothelioma and peritoneal serous carcinoma, as well as secondary PSM resulting from the spread/metastasis of invading malignant tumor cells from other

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origins to the surface of the peritoneum.[1–4] The age-adjusted incidence rate of primary peritoneal surface malignancies is 6.78 per million. The rate is highest among white people and lowest among black.[5] Historically, PSM was viewed as an end-stage tumor and palliative care was the primary approach, yielding a median survival time of 6 to 12 months.[6] Advancements in peritoneal oncology have led to international exploration and development of an aggressive integrated treatment strategy, centered around cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC). Specifically, CRS involves excising visible tumor tissues in the abdominopelvic cavity, while HIPEC targets residual tumor tissues or micrometastases. The goal is to achieve complete tumor cytoreduction, leading to improvements in the quality of life and an extension of median survival. Importantly, this strategy is supported by robust evidence-based medical research.[7–9]

In order to optimize the survival benefits for patients with PSM the attainment of complete tumor cytoreduction often necessitates complex surgical procedures. These may include the combined resection and reconstruction of multiple abdominal and pelvic organs, extensive peritoneal debridement, and lymph node dissection followed by a regimen of hyperthermia and chemotherapy. However, it is crucial to acknowledge that this surgical approach entails an increased risk of postoperative bloodstream infections. This heightened risk is attributed to factors such as extensive tissue resection, blood loss, elevated physiological stress,[10] and the implementation of invasive procedures like arterial catheterization, venous catheterization, abdominal drainage catheterization, and urinary catheterization.

Presently, there is a scarcity of studies with small sample sizes that have examined the rate of postoperative bloodstream infections in patients with PSM undergoing CRS combined with HIPEC. In response to this gap, in the current study, we retrospectively analyzed the adverse events associated with postoperative bloodstream infections in a substantial number of patients with PSM treated with CRS combined with HIPEC. A large sample size was utilized to investigate the risk factors associated with bloodstream infections, providing guidance for the prevention of serious adverse events.

Materials and Methods

Clinical Data

Our hospital has implemented a comprehensive treatment approach for PSM from May 2015 centered around CRS combined with HIPEC. Over this period, we established an extensive database containing comprehensive information of 1500 patients with PSM up to December 2021. Inclusion criteria were formulated for patients meeting specific conditions: (1) Patients with Karnofsky Performance Scale score > 60; (2) Patients with peripheral white blood cells $\geq 3.5 \times 10^9$/L and platelets $\geq 80 \times 10^9$/L; (3) Patients with appropriate liver function with total bilirubin, alanine transaminase (ALT), and aspartate transaminase (AST) < 2 × the upper limit of normal (ULN); (4) Patients with appropriate renal function: indicated by blood creatinine < 133 μmol/L; (5) Patients with overall organ function, including heart, lungs, and other major organs allowing tolerance for major surgery.

Exclusion criteria were applied to patients meeting the following conditions: (1) Patients with multiple metastases in the lungs, brain, bone, and liver detected by preoperative examination; (2) Patients with total bilirubin, AST, ALT levels ≥ 2 × ULN; (3) Patients with blood creatinine ≥ 133 μmol/L; (4) Patients with evident mesenteric contracture diagnosed by imaging; (5) Patients with physical status and vital organ functions incompatible with tolerance of major surgery.[3,8] The study protocol received approval from the Ethics Committee of the hospital and all patients signed an informed consent form.

Methods

Basic Operation of CRS Combined with HIPEC

A specialized team dedicated to PSM treatment carried out CRS combined with HIPEC. After administering general anesthesia, patients were positioned horizontally (spread-eagled), and a mid-abdominal incision was made from the xiphoid process to the pubic symphysis. Upon laparotomy, a meticulous examination of tumor invasion spanning from the diaphragmatic peritoneum to the pelvic peritoneum was conducted. Comprehensive records were maintained regarding the nature and quantity of ascites as well as the location and size of the primary tumor and/or PSM. The PC index (PCI) was subsequently evaluated.[11] Following the standardized procedure for CRS,[12] systematic excision of the

primary tumor, peritoneal tumor, affected organs or tissues, and lymph nodes were performed in accordance with regional order. Patients with tumors amenable to complete reduction underwent radical resection, while those with tumors challenging complete reduction underwent maximal CRS, followed by an assessment of the CC.[13]

Post CRS, open HIPEC was administered using the following drug regimen: 120 mg cisplatin combined with 120 mg docetaxel for gastrointestinal malignancies, pseudomyxoma peritonei, malignant peritoneal mesothelioma, gynecological malignancies, and primary PSM; 3 g ifosfamide combined with 30 mg doxorubicin for retroperitoneal tumors.

Following HIPEC, reconstruction of digestive and urinary tracts or enterostomy was performed. Tension-reduced suturing and abdominal closure ensued after which patients were monitored and treated in the ward.

Diagnostic Criteria for Testing

The specimens were collected following the *National Operating Specifications for Experiments* and cultured with BACTEC9120 and FX200 automatic blood culture systems (BD Company, Sparks, MD, USA) along with their corresponding blood culture bottles. In response to instrument alarms, the blood agar plate, MacConkey plate, and chocolate plate were retrieved, and the isolated pathogens underwent strain identification and drug sensitivity tests using MicroScan Walkway 40 and VITEK2 compact systems. Breakpoints were determined based on the Clinical and Laboratory Standards Institute M100 standard (2015). For fungal identification, we utilized the VITEK2 compact system and drug sensitivity tests were conducted with ATB-FUNGUS3 (bioMérieux, Marcy l'Etoile, France) since 2015. The results were rigorously interpreted according to the identification criteria provided by bioMérieux.

Observation Indicators

The primary observation parameter focused on identifying the risk factors associated with postoperative bloodstream infections in CRS combined with HIPEC, while the secondary observational parameters encompassed the analysis of bacterial spectrum and resistance during postoperative bloodstream infections. The postoperative period was specifically defined as the duration from the day of surgery to 30 days postoperatively.

Statistical Analysis

Statistical analysis was performed using SPSS 21.0 software. Measurement data are presented as median values or mean ± standard deviation ($\bar{x} \pm s$) and analyzed using the *t*-test. Count data are expressed as rates and subjected to analysis using the chi-squared test. Multivariate analysis was conducted through logistic regression. A significant level of $P < 0.05$ was considered indicative of statistically significant differences. Pathogen distribution and drug resistance were statistically analyzed using WHONET 5.6 software.

Results

Basic Clinicopathologic Features

Table 1 outlines the main clinicopathological features of 1500 patients with PSM. The cohort comprised 572 males (38.1%) and 928 females (61.9%). Additionally, 989 patients (65.9%) had a surgical history and 921 patients (61.4%) had a history of tumor treatment. The distribution of peritoneal metastasis included 66 patients with gastric cancer (4.4%), 19 patients with small intestinal carcinoma (1.3%), and 278 patients with colorectal cancer (18.5%). Furthermore, 475 patients (31.7%) had pseudomyxoma peritonei, 278 patients (18.5%) had peritoneal metastasis of ovarian cancer plus primary PSM, 136 patients (9.1%) had malignant peritoneal mesothelioma, 161 patients (10.7%) had retroperitoneal tumors, and 87 patients (5.8%) had other type of cancers.

Relevant Information of CRS Combined with HIPEC

Table 2 provides details on the median surgical time for CRS combined with HIPEC. The included patients had median surgical time of 585 minutes (ranging from 90−1170 min), a median PCI of 20 scores (ranging from 1−39), a median intraoperative blood loss of 500 mL (ranging from 20−12,000), median intraoperative erythrocyte transfusion of 2 (0−28) U, median intraoperative plasma transfusion of 600 (0−2200) mL, median intraoperative fluid infusion of 6350 (570−20,960) mL, median intraoperative

Table 1 Basic Clinicopathologic Features of 1500 Patients with Peritoneal Surface Malignancies

Items	Value (%)
Gender	
Male	572 (38.1)
Female	928 (61.9)
Age (years)	
≤60	1027 (68.5)
>60	473 (31.5)
BMI (kg/m^2)	
≤18.5	145 (9.7)
18.5–25.0	956 (63.7)
>25.0	399 (26.6)
Surgical history	
Yes	989 (65.9)
No	511 (34.1)
Previous tumor treatment	
Yes	921 (61.4)
No	579 (38.6)
Tumor tissue type	
Peritoneal metastasis of gastric cancer	66 (4.4)
Peritoneal metastasis of small intestinal carcinoma	19 (1.3)
Peritoneal metastasis of colorectal cancer	278 (18.5)
Pseudomyxoma peritonei	475 (31.7)
Peritoneal metastasis of ovarian cancer plus primary Peritoneal Surface Malignancies	278 (18.5)
Malignant peritoneal mesothelioma	136 (9.1)
Retroperitoneal tumor	161 (10.7)
Other tumors	87 (5.8)

Table 2 Information of 1500 Patients with Peritoneal Surface Malignancies Undergoing CRS Combined with HIPEC

Items	Value
Surgical time (min), median (range)	585(90–1170)
PCI score, median (range)	20(1–39)
CC score, n (%)	
0	710(47.3)
1	272(18.1)
2	200(13.3)
3	318(21.2)
Intraoperative blood loss (mL), median (range)	500(20–12,000)
Intraoperative erythrocyte transfusion (U), median (range)	2(0–28)
Intraoperative plasma transfusion (mL), median (range)	600(0–2200)
Intraoperative fluid infusion (mL), median (range)	6350(570–20,960)
Intraoperative urine volume (mL), median (range)	1700(150–8000)
Ascitic volume (mL), median (range)	200(0–22,000)
Stoma, n (%)	
Yes	948(63.2)
No	552(36.8)
Number of organ resections, median (range)	2(0–10)
Number of peritoneal resections, median (range)	4(0–10)

urine volume of 1700 (150−8000) mL, median ascitic volume of 200 (0−22,000) mL, median organ resections of 2 (0−10), and median peritoneal resections of 4 (0−10). Furthermore, there were 948 patients with stoma (63.2%).

Incidence of Bloodstream Infections

Distribution of Pathogens in Blood Cultures

Out of the 1500 cases of individuals undergoing CRS combined with HIPEC bloodstream infections were observed in 207 cases (13.8%). Among these cases, 233 strains of pathogens were isolated and cultured, comprising 151 gram-positive cocci (64.81%), 52 gram-negative bacilli (22.32%), and 30 fungi (12.86%). The distribution of pathogens in postoperative hospital-acquired infections is described in Table 3.

Drug Resistance of Major Gram-Positive Cocci

The three most frequently isolated gram-positive cocci were coagulase-negative staphylococci (SCN, 128 strains), *Enterococcus faecalis* (11 strains), and *Staphylococcus aureus* (4 strains). Staphylococci exhibited high sensitivity to tigecycline, linezolid, vancomycin, and quinupristin/dalfopristin. *E. faecalis* demonstrated pronounced sensitivity to penicillin G, tigecycline, linezolid, and vancomycin. *S. aureus* exhibited high sensitivity to tigecycline, linezolid, vancomycin, and quinupristin/dalfopristin. The resistance patterns of major gram-positive cocci to antimicrobial drugs is summarized in Table 4.

Drug Resistance of Major Gram-Negative Bacilli

The top three gram-negative bacilli isolated were *Klebsiella pneumoniae subsp. Pneumoniae* (17 strains), *Escherichia coli* (13 strains), and *Acinetobacter baumannii* (7 strains). *K. pneumoniae subsp. Pneumoniae* exhibited relative sensitivity to amikacin and cefepime. *E. coli* demonstrated high sensitivity to piperacillin/tazobactam and amikacin, and imipenem-resistant *E. coli* strains were observed. *A. baumannii* showed sensitivity to Bactrim but presented a high overall resistance rate which was consistently above 50%. The resistance patterns of major gram-negative bacilli to antimicrobial drugs is displayed in Table 5.

Table 3 Distribution and Composition Ratio of Pathogens of Postoperative Hospital Infections

Pathogens	Strains	Composition Ratio (%)
Gram-negative bacilli	52	22.32
Klebsiella pneumoniae subsp. Pneumoniae	17	7.30
Escherichia coli	13	5.58
Acinetobacter baumannii	7	3.00
Enterobacter cloacae	7	3.00
Pseudomonas aeruginosa	5	2.15
Other	3	1.29
Gram-positive cocci	151	64.81
Coagulase-negative staphylococci	128	54.94
Enterococcus faecalis	11	4.72
Staphylococcus aureus	4	1.72
Enterococcus faecium	4	1.72
Other	4	1.72
Fungi	30	12.86
Candida albicans	13	5.58
Candida glabrata	7	3.00
Other	10	4.30

Table 4 Antimicrobial Drug Resistance Rate of Major Gram-Positive Cocci (%)

Antimicrobial Drugs	Coagulase-negative staphylococci (n=128)		*Enterococcus faecalis* (n=11)		*Staphylococcus aureus* (n=4)	
	Strains	Resistance rate	Strains	Resistance rate	Strains	Resistance rate
Penicillin G	128	97.7	11	0	4	100
Gentamicin	128	21.9	11	9.1	4	75
Rifampicin	128	5.5	—	—	4	25
Ciprofloxacin	117	59.8	11	45.5	4	75
Levofloxacin	128	62.5	11	45.5	4	75
Tigecycline	115	0	10	0	3	0
Erythromycin	128	82	11	72.7	4	100
Linezolid	128	0	11	0	4	0
Vancomycin	128	0	11	0	4	0
Quinupristin/dalfopristin	117	0	—	—	4	0
Tetracycline	117	15.4	11	81.8	4	75

Table 5 Antimicrobial Drug Resistance Rate of Major Gram-Negative Bacilli (%)

Antimicrobial drugs	(n=17)		(n=13)		(n=7)	
	Strains	Resistance rate	Strains	Resistance rate	Strains	Resistance rate
Ampicillin/sulbactam	17	70.6	12	75	7	57.1
Tazobactam/piperacillin	17	29.4	13	0	—	—
Ceftazidime	17	23.5	13	15.4	7	57.1
Ceftriaxone	17	41.2	13	53.8	7	57.1
Cefepime	17	17.6	13	23.1	7	57.1
Imipenem	17	23.5	13	7.7	7	57.1
Amikacin	17	17.6	13	0	—	—
Gentamicin	17	35.3	12	33.3	7	28.6
Tobramycin	17	23.5	12	8.3	7	28.6
Ciprofloxacin	17	35.3	12	91.7	7	57.1
Levofloxacin	17	35.3	13	92.3	7	28.6
Bactrim	16	43.8	13	61.5	7	0

Drug Resistance of Major Fungi

The primary fungus isolated from patients with bloodstream infections was *Candida albicans*, followed by *C. glabrata*. No strains resistant to fluconazole or voriconazole were identified. The resistance patterns of major fungi to antifungal drugs is depicted in Table 6.

Table 6 Antimicrobial Drug Resistance Rate of Major Fungi (%)

Antimicrobial Drugs	*Candida albicans* (n=13)		*Candida glabrata* (n=7)		*Candida parapsilosis* (n = 3)	
	Strains	Resistance rate	Strains	Resistance rate	Strains	Resistance rate
Fluconazole	13	0	7	0	3	0
Voriconazole	13	0	7	0	3	0

Univariate and Multivariate Analyses of Bloodstream Infections

Univariate Analyses of Bloodstream Infections

Univariate analysis was performed on the basic clinicopathologic features of patients and information of CRS combined with HIPEC. The results revealed that five parameters: age ($P = 0.040$), surgical history ($P = 0.033$), prior tumor treatment ($P < 0.001$), tumor tissue type ($P = 0.034$), and completeness of cytoreduction (CC) score ($P = 0.004$) were statistically significantly associated with the development of bloodstream infections (Table 7), indicating that these parameters may pose a high-risk for the development of bloodstream infections.

Multivariate Analyses of Bloodstream Infections

Factors with $P < 0.100$ in the univariate analysis were included in the logistic regression model for the multivariate analysis. The results demonstrated that age ($P = 0.013$), prior tumor treatment ($P = 0.001$), tumor tissue type ($P = 0.032$), and CC score ($P = 0.002$) were independent risk factors for postoperative bloodstream infections in patients undergoing CRS combined with HIPEC (Table 8).

Table 7 Analysis of Risk Factors Associated with Postoperative Bloodstream Infections in CRS Combined with HIPEC

Items	Bloodstream Infection Group	Non-Bloodstream Infection Group	*P*
Gender, n (%)			0.126
Male	69(33.3)	503(38.9)	
Female	138(66.7)	790(61.1)	
Age (years), n (%)			0.040
≤60	129(62.3)	898(69.5)	
>60	78(37.7)	395(30.5)	
BMI (kg/m^2), n (%)			0.947
≤18.5	21(10.1)	124(9.6)	
18.5–25.0	130(62.8)	826(63.9)	
>25.0	56(27.1)	343(26.5)	
Surgical history, n (%)			0.033
Yes	150(72.5)	839(64.9)	
No	57(27.5)	454(35.1)	
Previous tumor treatment, n (%)			<0.001
Yes	153(73.9)	768(59.4)	
No	54(26.1)	525(40.6)	
Tumor tissue type, n (%)			0.034
Peritoneal metastasis of gastric cancer	5(2.4)	61(4.7)	
Peritoneal metastasis of small intestinal carcinoma	1(0.5)	18(1.4)	
Peritoneal metastasis of colorectal cancer	44(21.3)	234(18.1)	
Pseudomyxoma peritonei	50(24.2)	425(32.9)	
Peritoneal metastasis of ovarian cancer plus primary Peritoneal Surface Malignancies	46(22.2)	232(17.9)	
Malignant peritoneal mesothelioma	20(9.7)	116(9.0)	
Retroperitoneal tumor	22(10.6)	139(10.8)	
Other tumors	19(9.2)	68(5.3)	
Surgical time (min), median (range)	595(108–1070)	585(90–1170)	0.491
PCI score, median (range)	22(1–39)	20(1–39)	0.139
CC score, n (%)			0.004
0	83(40.1)	627(48.5)	
1	38(18.4)	234(18.1)	
2	23(11.1)	177(13.7)	
3	63(30.4)	255(19.7)	

(*Continued*)

Table 7 (Continued).

Items	Bloodstream Infection Group	Non-Bloodstream Infection Group	*P*
Intraoperative blood loss (mL), median (range)	500(50–6000)	500(20–12,000)	0.883
Intraoperative erythrocyte transfusion (U), median (range)	2(0–20)	2(0–28)	0.429
Intraoperative plasma transfusion (mL), median (range)	600(0–1800)	600(0–2200)	0.991
Intraoperative fluid infusion (mL), median (range)	6560(2100 −14,780)	6300(570 −20,960)	0.075
Intraoperative urine volume (mL), median (range)	1500(300 −6400)	1700(150 −8000)	0.098
Ascitic volume (mL), median (range)			0.293
Stoma, n (%)			0.855
Yes	132(63.8)	816(63.1)	
No	75(36.2)	477(36.9)	
Number of organ resections, median (range)	2(0–9)	2(0–10)	0.524
Number of peritoneal resections, median (range)	5(0–10)	4(0–9)	0.890

Table 8 Logistic Regression Analysis of Risk Factors for Postoperative Bloodstream Infections in CRS Combined with HIPEC

Factors	Wald	OR	95% CI	*P*
Age (≤ 60 vs > 60)	6.231	0.666	0.484–0.916	0.013
Previous tumor treatment (No vs Yes)	10.134	0.565	0.397–0.803	0.001
Tumor tissue type	15.337			0.032
Peritoneal metastasis of gastric cancer vs other tumors	6.269	0.258	0.089–0.745	0.012
Peritoneal metastasis of small intestinal carcinoma vs other tumors	3.267	0.145	0.018–1.177	0.071
Peritoneal metastasis of colorectal cancer vs other tumors	1.568	0.672	0.360–1.252	0.211
Pseudomyxoma peritonei vs other tumors	8.169	0.406	0.219–0.753	0.004
Peritoneal metastasis of ovarian cancer plus primary PSM vs other tumors	1.790	0.652	0.349–1.220	0.181
Malignant peritoneal mesothelioma vs other tumors	2.072	0.589	0.286–1.211	0.150
Retroperitoneal tumor vs other tumors	1.002	0.696	0.343–1.415	0.317
CC score	15.101			0.002
0 vs.3	13.820	0.479	0.325–0.706	<0.001
1 vs 3	4.902	0.598	0.380–0.943	0.027
2 vs 3	0.952	0.729	–	0.329

Discussion

In the comprehensive treatment centered on CRS combined with HIPEC, CRS plays a crucial role in achieving complete resection of all visible tumors, thereby minimizing the tumor load. HIPEC, on the other hand, integrates hyperthermia and chemotherapy to enhance the effectiveness of chemotherapy in the presence of elevated temperatures. This approach aims to target micrometastases within the abdominopelvic cavity and eliminate free cancer cells. While CRS combined with HIPEC has demonstrated significant benefits in prolonging survival and improving prognosis for certain patients with PSM, it is characterized by high complexity, time-consuming procedures, extensive organ resection, large peritoneal surface area removal, and a high frequency of invasive procedures beyond surgery. Consequently, this complexity contributes to an elevated risk of postoperative bloodstream infections.

Postoperative bloodstream infections represent a severe systemic inflammatory response and patients with PSM experiencing severe bloodstream infections postoperatively may develop complications such as multiple organ failure, shock, and disseminated intravascular coagulation. These complications often lead to increased mortality rates and a poor prognosis. Blood culture results recognized as the gold standard for diagnosing bloodstream infections hold clinical significance in the early detection of this disease.[14]

In this present study, 207 patients with PSM developed bloodstream infections postoperatively, revealing 233 strains of pathogens, resulting in a blood culture positive rate of 13.8%. This rate was higher than that reported in previous studies in China.[15,16] The identified pathogens comprised 151 gram-positive cocci (64.81%), 52 gram-negative bacilli (22.32%), and 30 fungi (12.86%). The most frequently isolated strains were SCN (54.94%), followed by *K. pneumoniae subsp. Pneumoniae* (7.3%), *E. coli* (5.58%), *C. albicans* (5.58%), and *E. faecalis* (4.72%). The distribution, variance, and characteristics of these pathogens are influenced by factors such as disease type, disease severity, and treatment within the study population. Notably, the prevalence of gram-positive bacteria is associated with an increase in the number of invasive procedures in clinical practice presenting challenges in clinical treatment.[17]

Our drug sensitivity test revealed that *K. pneumoniae* exhibited relative sensitivity to amikacin and cefepime, while *E. coli* demonstrated high sensitivity to piperacillin/tazobactam and amikacin. Notably, these two pathogens, particularly *K. pneumoniae* (an imipenem-resistance rate of 23.5%), were found to be resistant to imipenem. *A. baumannii* displayed multidrug resistance, with a resistance rate greater than 50% for all drugs except Bactrim, gentamicin, tobramycin, and levofloxacin. This resistance pattern may be attributed to its complex resistance mechanisms.[18] Consequently, these pathogens warrant close attention from clinicians and hospital infection control departments.

Among staphylococci, SCN is a conditional pathogen widely distributed in nature, residing on the surface of the human body and in the cavities linked to the external environment. The prevalence of SCN as a causative agent in hospital infections has increased and is attributed to factors such as the use of immunosuppressants and antitumor drugs as well as invasive diagnostic and therapeutic procedures that can compromise the immune function of the organism. Additionally, inadequate sterilization during blood collection can contribute to contamination. A prior study highlighted that among patients with positive blood cultures for SCN, accurate diagnosis required the integration of clinical information and multiple sample tests to determine SCN as the pathogen. Ultimately, only 12% to 26% of patients with positive blood cultures for SCN were diagnosed with bloodstream infections.[19]

In our study, staphylococci displayed no resistance to vancomycin and linezolid, showcasing high sensitivity to tigecycline and quinupristin/dalfopristin. Among the Gram-positive cocci isolated through blood culture, *E. faecalis* ranked second only to staphylococci and exhibited sensitivity to penicillin, tigecycline, linezolid, and vancomycin, which is commonly employed in the treatment of enterococcus infections. The results of the present study showed that *E. faecalis* has a vancomycin resistance rate of 0%, aligning with data from the National Drug Resistance Monitoring Network.[20] Linezolid retained significant efficacy against enterococci positioning it as the preferred agent for the treatment of vancomycin-resistant enterococci.

Bloodstream infections caused by fungi is on the rise. Our study revealed that 12.86% of bloodstream infections were attributed to fungi, with *C. albicans* as the predominant fungus.[21] Notably, none of the identified fungi exhibited resistance to fluconazole and voriconazole. The morbidity and mortality rate associated with Candida-induced bloodstream infections ranges between 50% to 60%.[22] This greatly increases the economic burden and hospitalization duration for affected patients. Consequently, vigilant monitoring of fungi isolated through blood cultures is crucial. The mechanisms underlying drug resistance in pathogens are generally categorized into three types: modification of the drug target site, modification of drugs, and influence on the route of drug uptake. These mechanisms of drug resistance are complex and diverse with multiple factors interacting to form complex drug resistance.[23,24]

Furthermore, in our study, we compared the clinical data of 207 patients with PSM who developed postoperative bloodstream infections with that of 1293 patients who did not. The results revealed that five parameters, age, surgical history, prior tumor treatment, tumor tissue type, and CC score, were statistically significantly correlated with bloodstream infections ($P < 0.05$ or $P < 0.01$). Further binary logistic analysis demonstrated that age > 60 years, prior tumor treatment, tumor tissue type, and CC score were independent risk factors for postoperative bloodstream infections in patients with PSM. Patients aged over 60 years often experience a progressive decline in body function, frequently accompanied by underlying diseases, leading to a compromised immune function and an increased susceptibility to infections. In individuals with a history of prior tumor treatment, chemotherapy, although effective in inhibiting tumor growth, may concurrently induce adverse effects such as anemia, susceptibility to infections, and malnutrition. Additionally, immunotherapy, while targeting tumor cells, may inadvertently affect normally proliferating cells, reducing immune cell counts and impairing the body's ability to resist infections. This in turn raises the risk of bloodstream

infections. The four risk factors of age, prior tumor treatment, tumor tissue type, and CC score, are readily identifiable preoperatively. This information can serve as a basis for the grading and management of patients at a high risk of hospital bloodstream infections in clinical work. In cases of bloodstream infections, it is crucial to promptly select effective antimicrobial drugs within 24 hours of occurrence to mitigate the rate of postoperative infections.

Conclusion

In summary, our study revealed that postoperative bloodstream infections in patients with PSM treated with CRS combined with HIPEC were predominantly associated with pathogens such as SCN, *K. pneumoniae subsp. Pneumoniae*, and *C. albicans*. The analysis of pathogen drug resistance in our study contributes both theoretical and practical insights to the prevention and treatment of postoperative infections in PSM. Furthermore, we identified age, prior tumor treatment, tumor tissue type, and CC score as independent risk factors for postoperative infections in PSM. This information could serve as a foundation for the classification and management of patients at a high risk of hospital bloodstream infections in clinical practice.

Abbreviations

CRS, cytoreductive surgery; HIPEC, hyperthermic intraperitoneal chemotherapy; PCI, Peritoneal cancer index; CC, Completeness of cytoreduction; PSM, Peritoneal Surface Malignancies.

Data Sharing Statement

The datasets used or analysed during the current study available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethics Committee of Beijing Shijitan Hospital, Capital Medical University. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

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Disclosure

The authors declare that they have no conflict of interest regarding this work.

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