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Clinical Characteristics and Risk Factors for Mortality in Children with Carbapenem-Resistant *Klebsiella pneumoniae*-Induced Bloodstream Infections

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Abstract

Background: *Klebsiella pneumoniae* (KP) is commonly found in human intestinal and respiratory tracts.
Objectives: This study aimed to investigate the clinical characteristics and risk factors associated with mortality in children suffering from carbapenem-resistant *Klebsiella pneumoniae* (CRKP)-induced bloodstream infections.
Methods: We collected clinical data from 160 children diagnosed with CRKP-induced bloodstream infections. These children were divided into two groups based on their outcomes 30 days post-infection: A death group (n = 61) and a survival group (n = 99). Clinical symptoms and outcomes were meticulously documented.
Results: The death group experienced a significantly shorter hospital stay than the survival group. Additionally, higher incidence rates of sepsis, malignant tumors, renal diseases, infectious shock, surgical site infections, higher acute physiology and chronic health evaluation II (APACHE II) scores, and elevated procalcitonin levels were observed in the death group ($P < 0.05$). These factors were all identified as independent risk factors for mortality among children with CRKP-induced bloodstream infections ($P < 0.05$). The areas under the receiver operating characteristic (ROC) curves for the length of hospital stay, presence of malignant tumors, sepsis, renal diseases, APACHE II score, procalcitonin levels, infectious shock, and surgical site infections all exceeded 0.700, indicating their high predictive value for mortality.
Conclusions: The mortality rate among children with CRKP-induced bloodstream infections is high. Factors such as a brief hospital stay, presence of malignant tumors, sepsis, renal diseases, infectious shock, elevated APACHE II score, and high procalcitonin levels significantly contribute to the risk of death.

Keywords: Bloodstream, Carbapenem, Death, Infection, Risk Factor

1. Background

Klebsiella pneumoniae (KP), commonly found in the intestinal and respiratory tracts, is a prevalent gram-negative bacillus that can lead to urinary tract, respiratory tract, and bloodstream infections (1). Bloodstream infections are particularly concerning due to their high incidence and mortality rates, often exacerbated by invasive diagnostic and treatment methods used clinically (2). *Klebsiella pneumoniae*, a major causative agent of bloodstream infections, can lead to infectious shock if not promptly and effectively treated (3, 4). Although typically treated with potent antibiotics like carbapenems, KP has increasingly become resistant to many drugs due to the extensive use of broad-spectrum antibiotics (5). This resistance, especially to carbapenems carbapenem-resistant *Klebsiella pneumoniae* (CRKP), restricts treatment options and complicates management (6). Therefore, understanding the clinical features of CRKP-induced bloodstream infections is crucial for improving outcomes and treatment success rates. While research on CRKP-induced bloodstream infections

predominantly involves adults (7), there is a significant need to explore these aspects in children.

2. Objectives

This study aimed to analyze the risk factors for mortality in children with CRKP-induced bloodstream infections using a multivariate logistic regression model, and to discuss their clinical characteristics to aid in better control, early diagnosis, and treatment.

3. Methods

3.1. General Data

We collected clinical data from 160 children treated for CRKP-induced bloodstream infections in our hospital between January 2020 and January 2023. The cohort included 76 boys and 84 girls, averaging an age of 9.16 ± 6.13 years. The death group (n = 61) consisted of 29 boys and 32 girls, averaging 9.78 ± 8.45 years old, with a BMI of 16.18 ± 2.54 kg/m^2, and a hospital stay of 22.45 ± 4.89 days. The survival group included 47 boys and 52 girls, averaging 8.46 ± 8.33 years old, with a BMI of 16.45 ± 2.87 kg/m^2, and a hospital stay of 39.74 ± 6.84 days.

3.2. Inclusion and Exclusion Criteria

Inclusion criteria were: (1) children meeting the diagnostic criteria for bloodstream infections (8), (2) those identified with CRKP as defined by the CDC Guidelines for the Control of Carbapenem-Resistant *Enterobacteriaceae* (9, 10), and (3) those with at least one positive blood culture result after admission. Exclusion criteria included: (1) Children admitted for less than 24 hours, (2) those with poor compliance, or (3) those with incomplete clinical data.

Determination criteria for death in children with CRKP-induced bloodstream infections and grouping methods. All children with CRKP-induced bloodstream infections in our hospital received 20 mg/kg of meropenem intravenously, diluted in 10 mL of 0.9% sodium chloride injection (Sinopharm Pharmaceutical Co., Ltd., China), administered every 8 hours. Based on outcomes 30 days post-infection, patients were categorized into a death group or a survival group, with death serving as the endpoint event.

3.3. Clinical Data Collection

3.3.1. Baseline Data

We recorded gender, age, BMI, length of hospital stay, whether the child was an only child, place of residence, primary caregiver, and complications (such as sepsis, malignant tumors, renal, cardiovascular, and cerebrovascular diseases) using the hospital's medical record system.

3.3.2. Laboratory Indicators

We collected 5 mL of fasting venous blood from each child, which was then centrifuged to obtain serum. The levels of platelets, hemoglobin, white blood cells, red blood cells, and procalcitonin were measured using an automatic biochemical analyzer (Olympus, Japan).

3.3.3. Scale Evaluation

The severity of the children's conditions was assessed using the acute physiology and chronic health evaluation II (APACHE II) score, which totals 71 points, with higher scores indicating more severe conditions.

3.3.4. Bloodstream Infections

These were categorized into lower respiratory tract infection, urinary tract infection, surgical site infection, and abdominal infection based on the infection site.

3.4. Antimicrobial Susceptibility Testing

Blood cultures from 160 CRKP strains were conducted, followed by strain identification using a microbial identification time-of-flight mass spectrometer (Xiamen microTyper, China). Antimicrobial susceptibility results were obtained using the Phoenix-100 bacterial identifier (BD, USA) and interpreted according to the NCCLS Standards for Antimicrobial Susceptibility Testing (11).

3.5. Statistical Analysis

Data analysis was performed using SPSS version 26.0 (IBM Inc., USA). Measurement data normality was assessed. Normally distributed data were expressed as mean ± standard deviation ($\bar{x} \pm s$) and analyzed using the independent samples *t*-test. Categorical data were

Table 1. Antimicrobial Susceptibility Testing Results of 160 Carbapenem-Resistant *Klebsiella pneumoniae* Strains [a]

Antimicrobial Drug	Number of Strains	Sensitive	Intermediate	Resistant
Aztreonam	147	8 (5.44)	0 (0.00)	139 (94.56)
Ceftriaxone	160	0 (0.00)	0 (0.00)	160 (100.00)
Ampicillin-sulbactam	160	0 (0.00)	0 (0.00)	160 (100.00)
Ampicillin	160	0 (0.00)	0 (0.00)	160 (100.00)
Meropenem	119	7 (5.88)	0 (0.00)	112 (94.12)
Imipenem	160	10 (6.25)	0 (0.00)	150 (93.75)
Cefoperazone-sulbactam	138	6 (4.35)	2 (1.45)	130 (94.20)
Piperacillin-tazobactam	160	10 (6.25)	7 (4.38)	143 (89.38)
Amikacin	160	59 (36.88)	0 (0.00)	101 (63.12)
Gentamicin	160	29 (18.13)	5 (3.13)	126 (78.75)
Tobramycin	160	28 (17.50)	14 (8.75)	118 (73.75)
Ceftazidime-avibactam	35	35 (100.00)	0 (0.00)	0 (0.00)
Polymyxin B	53	50 (94.34)	1 (1.87)	2 (3.77)
Fosfomycin	98	9 (9.18)	12 (12.24)	77 (78.57)
Minocycline	120	102 (85.00)	10 (8.33)	8 (6.67)
Tigecycline	122	118 (96.72)	2 (1.64)	2 (1.64)
Compound sulfamethoxazole	160	86 (53.75)	0 (0.00)	74 (46.25)
Levofloxacin	160	12 (7.50)	10 (6.25)	138 (86.25)
Ciprofloxacin	160	8 (5.00)	9 (5.63)	143 (89.37)

[a] Values are expressed as No. (%).

expressed as percentages [n (%)] and analyzed using the chi-square test. Logistic regression analysis was used to explore independent risk factors for mortality in children with CRKP-induced bloodstream infections. Receiver operating characteristic (ROC) curves were plotted, and the areas under the ROC curves (AUCs) were calculated to evaluate the predictive value of these risk factors for mortality.

4. Results

4.1. Antimicrobial Susceptibility Testing Results of 160 Carbapenem-Resistant Klebsiella pneumoniae Strains

Antimicrobial susceptibility testing revealed that the strains were highly resistant to aztreonam, ceftriaxone, ampicillin-sulbactam, ampicillin, meropenem, imipenem, cefoperazone-sulbactam, piperacillin-tazobactam, levofloxacin, and ciprofloxacin. However, they showed high sensitivity to ceftazidime-avibactam and polymyxin B (Table 1).

4.2. Clinical Symptoms of Children with Carbapenem-Resistant Klebsiella pneumoniae-Induced Bloodstream Infections

The predominant clinical symptoms in children with CRKP-induced bloodstream infections included fever, chills, fatigue, dizziness, dyspnea, mental status changes, and cough. Fever and dizziness were the most common symptoms (Table 2).

Table 2. Clinical Symptoms of Children with Carbapenem-Resistant *Klebsiella pneumoniae*-Induced Bloodstream Infections [a]

Clinical Symptoms	Values
Fever	123 (76.88)
Chills	98 (61.25)
Fatigue	81 (50.63)
Dizziness	135 (84.38)
Dyspnea	64 (40.00)
Change in mental status	79 (49.38)
Cough	58 (36.25)

[a] Values are expressed as No. (%).

Table 4. Assignment of Variables

Variables	Meaning	Assignment
X1	Length of hospital stay	Continuous variable
X2	Malignant tumors	Yes = 1, No = 0
X3	Sepsis	Yes = 1, No = 0
X4	Renal diseases	Yes = 1, No = 0
X5	Acute physiology and chronic health evaluation II score	Continuous variable
X6	Procalcitonin	Continuous variable
X7	Infectious shock	Yes = 1, No = 0
X8	Surgical site infection	Yes = 1, No = 0
Y	Death of children with carbapenem-resistant *Klebsiella pneumoniae*-induced bloodstream infections	Death = 1, Survival = 0

4.3. Outcomes of Children with Carbapenem-Resistant Klebsiella pneumoniae-Induced Bloodstream Infections

Out of 160 children with CRKP-induced bloodstream infections treated at our hospital, 99 survived, representing 61.87% of the cases. The remaining 61 children died, accounting for 38.13%.

4.4. Clinical Data of Survival and Death Groups

The analysis of clinical data between the survival and death groups showed no significant differences in gender, age, BMI, only child status, usual residence, primary caregiver, cardiovascular diseases, cerebrovascular diseases, platelets, hemoglobin, white blood cells, red blood cells, lower respiratory tract infection, urinary tract infection, and abdominal infection ($P > 0.05$). However, the death group had a shorter hospital stay and higher incidence rates of sepsis, malignant tumors, renal diseases, infectious shock, surgical site infection, APACHE II scores, and procalcitonin levels compared to the survival group ($P < 0.05$) (Table 3).

4.5. Results of Multivariate Logistic Regression Analysis of Risk Factors for Death in Children with Carbapenem-Resistant Klebsiella pneumoniae-Induced Bloodstream Infections

Logistic regression analysis used the mortality of children with CRKP-induced bloodstream infections as the dependent variable (death group = 1, survival group = 0), with significant clinical indicators (hospital stay length, malignant tumors, sepsis, renal diseases, APACHE II score, procalcitonin, infectious shock, surgical site infection) as independent variables. These variables are detailed in Table 4. The analysis identified that hospital stay length, malignant tumors, sepsis, renal diseases, APACHE II score, procalcitonin, and infectious shock were independent risk factors for mortality ($P < 0.05$) (Table 5 and Figure 1).

4.6. Receiver Operating Characteristic Curves for Factors Affecting Mortality in Children with Carbapenem-Resistant Klebsiella pneumoniae-Induced Bloodstream Infections

Receiver operating characteristic curves were used to evaluate the predictive value of various clinical indicators for mortality in children with CRKP-induced bloodstream infections, with the death of children as the dependent variable (death group = 1, survival group = 0). The significant clinical indicators included the length of hospital stay, malignant tumors, sepsis, renal diseases, APACHE II score, procalcitonin, infectious shock, and surgical site infection. The areas under the ROC curves (AUC) for these indicators were all greater than 0.700, demonstrating their strong predictive value for mortality (Table 6 and Figure 2).

5. Discussion

Carbapenem-resistant *K. pneumoniae* is increasingly prevalent, with resistance rates to many effective antibiotics exceeding 40%, complicating treatment and increasing mortality rates from CRKP-induced bloodstream infections (12). In this study, 61 of the 160 children with CRKP-induced bloodstream infections admitted to our hospital died, representing 38.13% of cases, consistent with the noted high mortality rate.

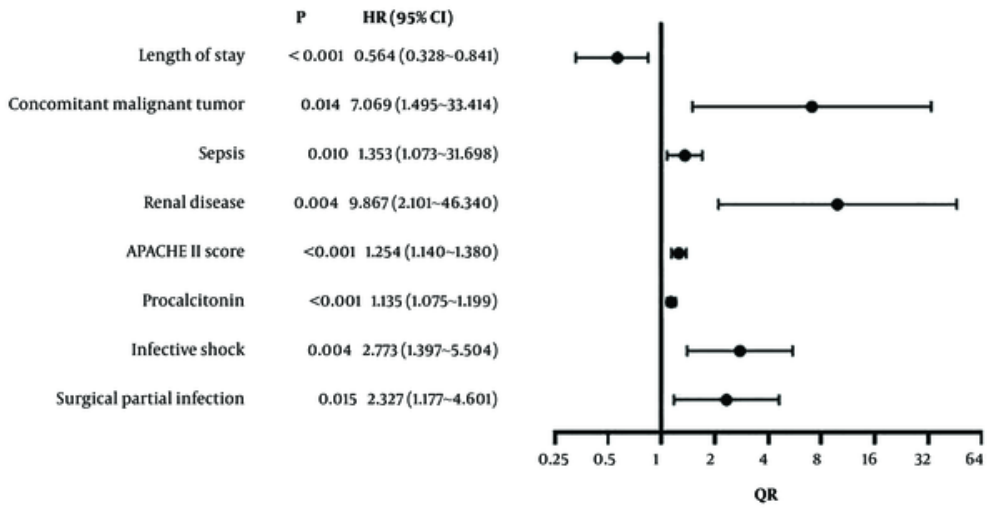

Figure 1. Forest plot of clinical symptoms based on multivariate logistic regression analysis

Table 5. Results of Multivariate Logistic Regression Analysis of Risk Factors for Death of Children with Carbapenem-Resistant *Klebsiella pneumoniae*-Induced Bloodstream Infections

Item	B	Standard Error	Wald	P-Value	OR	95% Confidence Interval
Length of hospital stay	-0.447	0.083	28.807	0.000	0.564	0.328 - 0.841
Malignant tumors	1.956	0.792	6.090	0.014	7.069	1.495 - 33.414
Sepsis	1.041	0.801	1.689	0.010	1.353	1.073 - 1.698
Renal diseases	2.289	0.789	8.413	0.004	9.867	2.101 - 46.340
Acute physiology and chronic health evaluationn II score	0.226	0.049	21.558	0.000	1.254	1.140 - 1.380
Procalcitonin	0.127	0.028	20.898	0.000	1.135	1.075 - 1.199
Infectious shock	1.020	0.350	8.502	0.004	2.773	1.397 - 5.504
Surgical site infection	0.845	0.348	5.892	0.015	2.327	1.177 - 4.601

Factors such as the length of hospital stay, malignant tumors, sepsis, renal diseases, APACHE II score, procalcitonin levels, infectious shock, and surgical site infections showed significant differences, indicating their relevance to mortality in these infections. Logistic regression analysis revealed that a longer hospital stay was a protective factor against death, while the presence of malignant tumors, sepsis, renal diseases, infectious shock, surgical site infections, a high APACHE II score, and high procalcitonin levels were independent risk factors for mortality.

Potential reasons include the following: Prolonged hospital stays allow for close monitoring of CRKP-induced bloodstream infections, timely adjustments in the face of antibiotic resistance, and early interventions that may reduce the risk of additional infections (13). Children with malignant tumors often undergo aggressive treatments like chemotherapy, radiotherapy, hormone therapy, and surgical resections that may compromise mitochondrial function and subsequently impair cell metabolism and immune responses, exacerbating their condition in the event of infections (14). Furthermore, tumors may locally infiltrate, destroying the natural defense barriers of tissues and increasing both the likelihood of infections and the risk of mortality (15).

Table 6. Results of Receiver Operating Characteristic Curve Analysis of Factors Influencing Death of Children with Carbapenem-Resistant *Klebsiella pneumoniae*-Induced Bloodstream Infections

Parameter	AUC	Cut-off Value	95% CI	P-Value	Specificity	Sensitivity	Youden Index
Length of hospital stay	0.957	29.500	0.927 - 0.988	0.000	0.839	0.915	0.754
Malignant tumors	0.760	1.500	0.681 - 0.840	0.000	0.839	0.681	0.520
Sepsis	0.712	1.500	0.627 - 0.797	0.000	0.786	0.638	0.424
Renal diseases	0.796	1.500	0.723 - 0.869	0.000	0.911	0.681	0.592
Acute physiology and chronic health evaluationn II score	0.811	19.375	0.737 - 0.884	0.000	0.660	0.786	0.446
Procalcitonin	0.796	22.345	0.722 - 0.869	0.000	0.479	0.768	0.247
Infectious shock	0.723	1.500	0.638 - 0.807	0.000	0.786	0.660	0.426
Surgical site infection	0.740	1.500	0.657 - 0.824	0.000	0.768	0.713	0.481

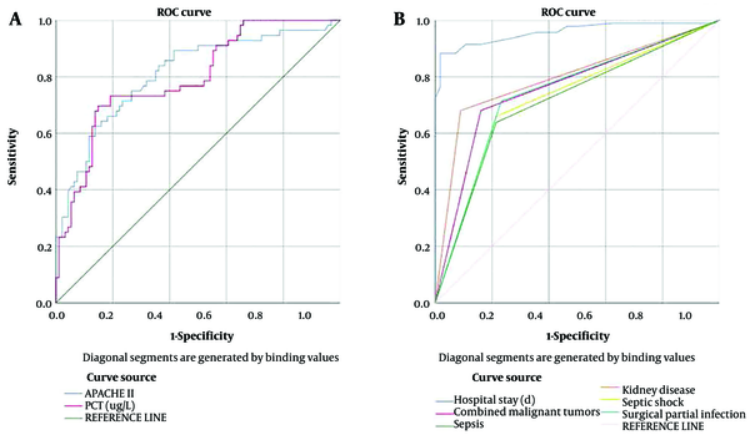

Figure 2. Receiver operating characteristic curves of factors influencing death of children with CRKP-induced bloodstream infections

In recent years, there has been a significant increase in the resistance of septic patients to antibacterial drugs, including carbapenems, which complicates the condition of children with CRKP (16). In cases of sepsis, various pathogenic bacteria enter the bloodstream, releasing toxins and metabolites that impair hemoglobin's oxygen-transport capacity, thereby damaging organ functions and exacerbating CRKP infections (17). Additionally, children with renal diseases experience more severe conditions during bloodstream infections due to compromised detoxification functions (18). In this study, the APACHE II scores were higher in the death group than in the survival group, aligning with findings from previous literature (19).

Furthermore, procalcitonin levels are directly proportional to the severity of bacterial infections (20). This study found that procalcitonin levels were significantly higher in the death group than in the survival group, consistent with previous research. Infectious shock, a critical systemic condition, is a major cause of mortality in patients with CRKP-induced bloodstream infections. It rapidly progresses, severely impairing vital organs and causing immune function abnormalities (21). Children with surgical site infections may experience systemic inflammatory responses triggered by bacteria or inflammatory factors entering the bloodstream, leading to complications such as sepsis and septicemia, which increase treatment difficulty and mortality (22).

The results of ROC curve analysis in this study showed that the AUC values for length of hospital stay, malignant tumors, sepsis, renal diseases, APACHE II score, procalcitonin, infectious shock, and surgical site infection were all greater than 0.700, indicating these

indicators' strong predictive value for mortality in children with CRKP-induced bloodstream infections.

5.1. Conclusions

The mortality rate is high among children with CRKP-induced bloodstream infections. Factors such as a short hospital stay, the presence of malignant tumors, sepsis, renal diseases, infectious shock, high APACHE II scores, and high procalcitonin levels are independent risk factors for death. These indicators can be utilized to improve prognosis as early as possible in clinical treatments.

Footnotes

Authors' Contribution: Xiaohua Shi designed this study and significantly revised the manuscript; Li Qian performed this study and wrote the manuscript.

Conflict of Interests Statement: The authors declared no conflicts of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Ethical Approval: All procedures performed in this study adhered to the ethical standards of the institutional research committee (approval No. CHNMU202001004) and were in accordance with the 1964 Helsinki Declaration and its later amendments.

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Informed Consent: All the patients signed informed consent.

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Table 3. Clinical Data of Survival and Death Groups [a]

Parameter	Death Group (n = 61)	Survival Group (n = 99)	Statistical Value	P-Value
Gender			0.003	0.959
Male	29 (47.54)	47 (47.47)		
Female	32 (52.46)	52 (52.53)		
Age ($\bar{x} \pm s$, y)	9.78 ± 8.45	8.46 ± 8.33	0.968	0.334
BMI ($\bar{x} \pm s$, kg/m ^{2})	16.18 ± 2.54	16.45 ± 2.87	0.603	0.547
Length of hospital stay	22.45 ± 4.89	39.74 ± 6.84	16.554	0.000
Only child			0.850	0.357
Yes	22 (36.07)	43 (43.43)		
No	39 (63.93)	56 (56.57)		
Place of usual residence			0.572	0.450
Rural	21 (34.43)	40 (40.40)		
Urban	40 (65.57)	59 (59.60)		
Primary caregiver			1.961	0.161
Relatives	47 (77.05)	66 (66.67)		
Others	14 (22.95)	33 (33.33)		
Sepsis			5.795	0.016
Yes	13 (21.31)	8 (8.08)		
No	48 (78.69)	91 (91.92)		
Malignant tumors			11.116	0.001
Yes	43 (70.49)	43 (43.43)		
No	18 (29.51)	56 (56.57)		
Renal diseases			16.860	0.000
Yes	40 (65.57)	32 (32.32)		
No	21 (34.43)	67 (67.68)		
Cardiovascular diseases			0.014	0.908
Yes	32 (52.46)	51 (51.52)		
No	29 (47.54)	48 (48.48)		
Cerebrovascular diseases			1.374	0.241
Yes	15 (24.59)	33 (33.33)		
No	46 (75.41)	66 (66.67)		
Platelets ($\bar{x} \pm s$, 109/L)	210.47 ± 31.86	220.49 ± 42.58	1.524	0.130
Hemoglobin ($\bar{x} \pm s$, g/L)	134.82 ± 12.71	139.12 ± 13.89	1.892	0.060
White blood cells ($\bar{x} \pm s$, 1012/L)	7.16 ± 3.14	7.30 ± 3.66	0.239	0.812
Red blood cells ($\bar{x} \pm s$, 109/L)	4.61 ± 1.50	4.48 ± 1.46	0.518	0.605
Procalcitonin ($\bar{x} \pm s$, μg/L)	29.87 ± 7.56	19.81 ± 9.03	7.000	0.000
Acute physiology and chronic health evaluation II score	23.19 ± 5.61	16.75 ± 5.13	7.180	0.000
Infectious shock			10.678	0.001
Yes	39 (63.93)	37 (37.37)		
No	22 (36.07)	62 (62.63)		
Lower respiratory tract infection			0.029	0.864
Yes	23 (37.70)	36 (36.36)		
No	38 (62.30)	63 (63.64)		
Urinary tract infection			0.163	0.686
Yes	26 (42.62)	39 (39.39)		
No	35 (57.38)	60 (60.61)		
Surgical site infection			6.349	0.012
Yes	39 (63.93)	43 (43.43)		
No	22 (36.07)	56 (56.57)		

Parameter	Death Group (n = 61)	Survival Group (n = 99)	Statistical Value	P-Value
Abdominal infection			0.014	0.905
Yes	21 (34.43)	35 (35.35)		
No	40 (65.57)	64 (64.65)		

[a] Values are expressed as mean ± SD or No. (%).