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Prognostic role of time to positivity of blood culture in children with Pseudomonas aeruginosa bacteremia.

huiting xu
Chongqing Medical University Affiliated Children's Hospital https://orcid.org/0000-0001-5394-517X
Jie Cheng
Chongqing Medical University Affiliated Children's Hospital
Qinghong Yu
Chongqing Medical University Affiliated Children's Hospital
Qingyuan Li
Chongqing Medical University Affiliated Children's Hospital
Qian Yi
Chongqing Medical University Affiliated Children's Hospital
Siying Luo
Chongqing Medical University Affiliated Children's Hospital
Yuanyuan Li
Chongqing Medical University Affiliated Children's Hospital
Guangli Zhang
Chongqing Medical University Affiliated Children's Hospital
Xiaoyin Tian
Chongqing Medical University Affiliated Children's Hospital
Dapeng Cheng
Chongqing Medical University Affiliated Children's Hospital
Zhengxiu Luo (luozhengxiu816@163.com)
https://orcid.org/0000-0003-3029-9624

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Abstract

Background Pseudomonas aeruginosa (P. aeruginosa) is a major Gram-negative pathogen, which has been reported to result in high mortality. We aim to investigate the prognostic value and optimum cut-off point of time-to-positivity (TTP) of blood culture in children with P. aeruginosa bacteremia.Methods From August 2014 to November 2018, we enrolled the inpatients with P. aeruginosa bacteremia in a 1500-bed tertiary teaching hospital in Chongqing, China retrospectively. 52 case were analyzed. Receiver operating characteristic (ROC) analysis was used to determine the optimum cut-off point of TTP, and logistic regression were employed to explore the risk factors for in-hospital mortality and sepsis shock.Results Totally, 52 children with P. aeruginosa bacteremia were enrolled. The standard cut-off point of TTP was18 hours. Early TTP (≤18 hours) group patients had remarkably higher in-hospital mortality (42.9% vs 9.7%, P=0.014), higher incidence of sepsis shock (52.4% vs 12.9%, P=0.06), higher Pitt bacteremia scores [3.00 (1.00-5.00) vs 1.00 (1.00-4.00), P=0.046] and more intensive care unit admission (61.9% vs 22.6%, P=0.008) when compared with late TTP (>18 hours) groups. Multivariate analysis indicated TTP ≤18 h, Pitt bacteremia scores ≥4 were the independent risk factors for in-hospital mortality (OR 5.88, 95%CI 1.21-21.96, P=0.035; OR 4.95, 95%CI 1.26-27.50, P=0.024; respectively). The study also revealed that the independent risk factors for sepsis shock were as follows: TTP≤18h, Pitt bacteremia scores≥4 and hypoalbuminemia (OR 6.30, 95%CI 1.18-33.77, P=0.032; OR 8.15, 95%CI 1.15-42.43, P=0.014; OR 6.46, 95% CI 1.19-33.19 P=0.031; respectively).Conclusions Early TTP (≤18 hours) appeared to be associated with worse outcomes for P. aeruginosa bacteremia children.

Introduction

Pseudomonas aeruginosa (*P. aeruginosa*) is a major gram-negative and nosocomial pathogen, which is responsible for different sites of infection of the body, especially in critically ill and immunosuppressed patients [1,7]. Poor outcomes usually occurred in critically ill patients infected with *P. aeruginosa* [2]. Early assessment of the severity of *P. aeruginosa* bacteremia patients may contribute to assisting the therapy and monitor, so as to improve the outcomes of these patients [3,4]. Some studies have investigated tools to identify patients at high risk of mortality, such as APACHE score and PRISM score [30,31], however, theses prognostic scores can be complicated. Therefore, clinicians still need a simple and easy-to-measure tool.

Blood culture technique is crucial for bacteremia detection [5]. Previous studies have discovered that an early time to positivity (TTP) of blood culture can predict fatal outcomes among patients with different kinds of bacteremia [7-11]. However, few studies reported the correlation between TTP values and clinical outcomes in children with *P. aeruginosa* bacteremia, and the optimum TTP cut-off point also remained unclear. Therefore, the aim of our study is to evaluate the optimum TTP cut-off point, explore the correlation between TTP and clinical parameters, and to investigate the risk factors of clinical outcomes in *P. aeruginosa* bacteremia children.

Methods

Study designs and participants

Children's Hospital of Chongqing Medical University is a 1500-bed tertiary teaching hospital in Chongqing, China, ranked among the top three domestic children`s hospitals (rank list: http://top100.imicams.ac.cn/home). We conducted a retrospective study at this facility. Inpatients with *P. aeruginosa* bacteremia from August 2014 to November 2018 were identified retrospectively. The inclusive criteria were as follows: (i) inpatients; (ii) age≥18 years; (iii) with ≥ one positive *P. aeruginosa* blood culture; (iv) with systemic inflammatory manifestations. The exclusive criteria included any of the following: (i) patients who were lost to follow-up; (ii) patients with incomplete medical records; (iii) patients who missed their TTPs; (iv) patients with polymicrobial bacteremia.

Microbiological methods

An approximately 3 ml of venous blood was inoculated into aerobic each BACTEC PLUS bottle and transported to the microbiological laboratory in a timely manner. Blood cultures were processed employing the Becton-Dickinson diagnostic systems, which automated measured bacterial growth by continuously monitoring CO_2 production in every 5 minutes, through a fluorescent sensor technology. Those positive cultures were subsequently subcultured after Gram staining. The Vitek identification and susceptibility cards (bioMe´rieux Vitek) took charge of species identification and susceptibility detection.

Definition

P. aeruginosa bacteremia was defined as at least one blood culture positive for *P. aeruginosa* with systemic manifestation of infections [23]. Time to positivity (TTP) was measured as the length of time span between the beginning of blood incubation and the alert signal by an automated system [11]. We only recorded the shortest TTP if there were more than one positive sample. The immunosuppression was defined as primary immunodeficiency disease and/or receipt of high dose steroid therapy regularly more than half a month (≥prednisolone 10 mg/daily or equivalent dose), and/or receipt immunosuppressive chemotherapy within the last 2 months [7]. Neutropenia was defined as the number of neutrophils less than 500/ml [14]. Nosocomial infection was defined when manifestations and positive blood culture were obtained more than 48 hours after admission [14]. Pittsburgh bacteremia scoring system was used to evaluate the severity of bacteremia in children. We calculated the scores within 2 days prior or on the day of the first blood culture [8, 21, 22], The source of infection was determined only when there were both clinical and laboratory evidence of the site on the day of the first blood culture [8]. Otherwise it was defined as primary bacteremia [14]. Appropriate antimicrobial therapy referred to receipt of at least one active intravenous antimicrobial agent according to susceptibility result within 24 h after blood samples were collected and before susceptibility results were available [15], otherwise it was defined as inappropriate antimicrobial therapy. MDR (multiple resistant bacteria) was

considered when the strain was resistant to at least 3 antipseudomonal antibiotics [15]. Pseudomonas meningitis was diagnosed when patients fulfilled the following criteria: a positive *P. aeruginosa* culture of cerebrospinal fluid (CSF) and clinical evidence of *P. aeruginosa* meningitis [16]. *P. aeruginosa* peritonitis was diagnosed when patients had clinical evidence of an intra-abdominal source of infection and a positive ascitic fluid culture with *P. aeruginosa* [32]. Sepsis shock was diagnosed according the Guidelines for Management of Sepsis and Septic Shock: 2016 [17]. Pneumonia was defined according to the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America [18]. Hypoalbuminemia was defined as serum albumin concentration less than 2.5 g/dL [25].

Data collection

Date retrieved from the medical records included demographic characteristics (age, sex, weight), underlying conditions, place of bacteremia acquisition, the inappropriateness of empirical antibiotics use, TTP of blood culture, severity of bacteremia assessed by Pitt bacteremia scores and clinical outcomes.

Outcomes assessment

In-hospital mortality was considered as the primary outcome. The second outcome was sepsis shock.

Statistical analysis

Classification variables were presented as numbers (n) and percentages (%), and differences in proportions were compared by chi-squared test and Fisher's exact test if necessary. Continuous variables with abnormal distributions, presented as medians with inter-quartile ranges (IQRs), were analyzed by using the Mann–Whitney U test. Receiver-operating characteristic (ROC) analysis was conducted to determine the optimum cutoff point for TTP, with the maximum Youden's index was applied as the possible applicable predictive marker [18]. The predictive capability of TTP was assessed by the area under the ROC curve (AUC). $0.5<AUC\leq0.7$ implicated less predictive, $0.7<AUC\leq0.9$ indicated moderately predictive and $0.9<AUC<1$ referred to highly predictive [29]. Univariate and multivariate logistic regression was employed to find the association between risk factors and in-hospital mortality, septic shock. Variables with P-value <0.10 in univariate analysis further evaluated in multivariate models with forward LR selection. Meanwhile, the variables with P-value ≤0.05 were retained. Odds ratio (OR) and corresponding 95% confidence interval (CI) was calculated. Hazard curves were further assessed by Kaplan–Meier method. All analyses were performed by using SPSS software for Unix (Version 23.0; SPSS, Chicago, IL, USA). A P-value <0.05 (two-sided) was considered significant.

Results

Study population and patient characteristics

63 inpatients with ≥ one *P. aeruginosa* blood culture positive were enrolled retrospectively during this study period. Eleven of them were excluded (five cases had incomplete information, five cases infected with other bacteria, one case missed his TTPs). Therefore, 52 cases were analyzed in this study finally (Figure 1).

Median age of these patients was 1.79 (0.43-9.0) years. Median weight was 11 (7.00-27.00) kg, and the male account for 61.5% (32/52). The average of hospitalization stay was 22.52 (9.05-38.3) days. The most common underlying disease were immunosuppression (50.0%, 26/52), followed by neutropenia (46.2%, 24/52), and hypoalbuminemia (42.3%, 22/52). The common complications were pneumonia (50%, 26/52) and meningitis (9.6%, 5/52). The primary origins of infection were respiratory tract infection (42.3%, 22/52), skin and soft tissue infection (15.4%, 8/52), vascular-catheter related infection (15.4%, 8/52), and primary infection (13.5%, 7/52). 20 (38.5%) patients were admitted to intensive care unit. 22 (42.3%) patients were nosocomial. The median of Pitt bacteremia scores was 1.5 (1-4.00). 31 (59.5%) patients were given antibiotic prior to the blood culture, while 16 (30.8%, 16/31) patients had received inappropriate antimicrobial therapy within 24 hours after blood culture. There were 4 (7.7%, 4/52) patients infected with multiple resistant bacteria. The in-hospital mortality was 23.1% (12/52), and 28.8% (15/52) patients had sepsis shock. More details of clinical characteristics are shown in Table 1.

TTP of *P. aeruginosa* bacteremia in children

Median TTP was 18.74 h (IQR 16.14-20.77). The bar chart is shown in Figure 2. The optimal cut-off of TTP as a surrogate marker was evaluated by ROC analysis. The optimal point for TTP was 17.87 h with 75.0% sensitivity and 72.5% specificity (AUC 0.77, 95%CI 0.604-0.935), indicating a moderate predicting capability (Figure 3). Therefore 18 h was selected as the standard cut-off. The cases were divided into early TTP (TTP≤18 h) and late TTP group (TTP>18 h). The Kaplan–Meier survival curve of patients with the 2 TTP groups is shown in Figure 4 and Figure 5.

Comparison of clinical characteristics between early and late TTP groups

Table 2 shows the characteristics of early and late TTP groups. Early TTP group patients had significant higher in-hospital mortality (42.9% *vs* 9.7%, P=0.014), higher incidence of sepsis shock (52.4% *vs* 12.9%, P=0.006), higher Pitt bacteremia scores (3.00 *vs* 1.00, P=0.046) and more intensive care unit admission (61.9% *vs* 22.6%, P=0.008). There were more immunosuppression patients in late TTP group as compared to early TTP group (64.5% *vs* 28.6%, P=0.023). Four MDR were all detected in late TTP group patients. The demographic characteristics, other underling conditions, the complications, origins of infection, nosocomial infection, antibiotic given before blood culture, and length of hospitalization stay were with no remarkable differences (Table 2).

Comparison of clinical characteristics between the survival and the non-survival groups

The median TTP in fatal group was 15.19 (IQR 11.21-18.24) hours, obviously shorter than 19.42 (IQR 16.92-20.97) hours in survival group (P=0.005). Pitt scores in non-survival group were 4.50 (IQR 1.25-7.25), significantly higher than that in survival group [1.00 (IQR 1.00-3.75)]. The incidence of sepsis shock was remarkably higher in non-survival group when compared to survival group patients (58.3% vs 20.0%, P=0.025). More patients had hypoalbuminemia among survival group than fatal group (75.0% *vs* 32.5%, P=0.023). No significant differences were detected in other clinical characteristics (Table 3).

Risk factors of in-hospital mortality

Univariate analysis revealed that early TTP, Pitt bacteremia scores≥4 and hypoalbuminemia were associated with in-hospital mortality. Multivariate analysis showed early TTP (OR 5.88; 95%CI 1.21-21.96) and Pitt bacteremia scores≥4 (OR 4.95; 95%CI 1.26-27.50) were independently correlated with in-hospital mortality (Table 4).

Risk factors of septic shock

Univariate analysis also indicated that early TTP, Pitt bacteremia scores≥4, hypoalbuminemia and intensive care unit admission were correlated with sepsis shock. Multivariate analysis showed early TTP (OR 6.30; 95%CI 1.18-33.77), Pitt bacteremia scores ≥4 (OR 8.15; 95%CI 1.53-43.32), hypoalbuminemia (OR 6.46; 95% CI 1.19-33.19) were independently associated with sepsis shock (Table 5).

Discussion

Studies showed that early TTP can be a surrogate marker of a higher bacterial burden in the blood [7, 15, 21], which can be translated as more severe bacteremia. Moreover, one study showed that different bacterium has different median TTP [19]. Several factors can influence TTP of blood culture, such as bacterial burden, blood volume of the sample, source of infection, usage of antimicrobial agents, and patient's clinical characteristics [20], which might cause different length of TTP. In this study, we indicated TTP cut-off in *P. aeruginosa* bacteremia children was 18 h, which was significantly longer than that in adult *P. aeruginosa* bacteremia patients (13h) [8]. The possible explanation could be that lower volume of blood culture of children compared to adults (3mL in our study vs. 8-10 mL in adult study) led to lower bacterial burden [24]. Studies demonstrated that early TTP had significantly higher mortality in adult bacteremia patients caused by ram-positive bacteria such as *S. pneumoniae* [11], *S. aureus* [14], and gram-negative bacteria such as *E. coli* [9], *Klebsiella pneumoniae* [10] and *P. aeruginosa* [7,8]. Our previous studies indicated early TTP were associated with the worse outcomes in *S. aureus and S.*

pneumoniae bacteremia children [33, 34], Here, we found that TTP ≤ 18 h had moderate capability to predict in-hospital mortality in *P. aeruginosa* bacteremia children (AUC=0.770). Early TTP patients had approximately 5 folds higher risk of death and 6 folds higher risk of sepsis shock when compared to late TTP. Our study indicated the association between early TTP and fatal outcomes in children with *P. aeruginosa* bacteremia, which was in accord with previous studies.

It is commonly accepted that Pitt bacteremia scores can evaluate severity of bacteremia and provide prognostic information, Pitt bacteremia scores ≥4 can be assumed as critical bacteremia [21,22]. Our study is in line with previous study. It showed that Pitt bacteremia scores was statistically higher in early TTP and fatal group respectively compared with late TTP and surviving group. Moreover, multivariate analysis demonstrated that patients with Pitt bacteremia scores ≥ 4 had a higher risk of death and sepsis shock.

Even though there were studies showed that receiving correct empirical antimicrobial agents early was significantly important [7, 26]. Our data found no association between inappropriate empirical antimicrobial treatment and mortality, which was in accord with several studies [22, 27]. The plausible explanations for the differences are as follows: First, we included patients with community-required infection, therefore the initial treatment outside the hospital could be an interference factor. Second, we did not determine the precise delay time correlated with in-hospital mortality.

Our study also revealed that lower level of albuminemia is a possible independent risk factor of sepsis shock in children with *P. aeruginosa* bacteremia, which was not noted in previous studies of adults. Lokesh K. showed that hypoalbuminemic patients had higher incidence of poor outcomes in sick children, however, they excluded patients with poor basic state, which we didn't.[25]. Probably, critical illness and sepsis were the reasons for hypoalbuminemia, which could cause lower plasma colloid osmotic pressure and inadequate blood perfusion to vital organs [25, 28]. Nevertheless, the evidence of benefit of receiving albumin in patients with critical illness remains unclear, whether in adults or children [25, 28].

Recent studies reported that in adults patients, the origin of infection was correlated with TTP, especially catheter-related infection [7, 8, 14, 23]. Our study didn't detect the association between TTP and origins of infection was unclear. Primary infection and lack of bacterial culture might have resulted in bias.

This study had some limitations. Firstly, this is a retrospective study, therefore prospective study can be needed to strengthen our conclusion. Secondly, the small population size may lead to heterogeneous results. Thirdly, this is a single-center study. The relatively small sample and single-center study may lead to type II errors and decrease the ability to obtain solid proof, therefore, further study with multi-center and a larger sample size is needed to address this conclusion.

Conclusion

In conclusion, our study revealed that early TTP (TTP ≤18 h), along with Pitt bacteremia scores≥4 could predict poor outcomes for children with *P. aeruginosa* bacteremia. Therefore, TTP can be used as a need-to-measure prognostic tool by clinicians.

List Of Abbreviations

TTP: Time to positivity; *P. aeruginosa*: *Pseudomonas aeruginosa*; APACHE scores: acute physiology and chronic health evaluation scores; PRISM scores: pediatric risk of mortality scores; CI: Confidence interval; OR: Odds ratio; ROC: Receiver operating characteristic; IQR: Inter-quartile range; CSF: cerebrospinal fluid; MDR: multiple resistant bacteria.

Declarations

Ethics statement and consent to participate

The study was approved by the Ethics Committee of Children's Hospital of Chongqing Medical University. Informed consent was obtained from the parents when children were admitted to the hospital. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The data-sets analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no financial and non-financial competing interests.

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Authors' contributions

ZX L designed the experiments; HT X, J C and QH Y collected and checked the date. HT X carried out the experiments and wrote the manuscript; QY, QY L and XY T contributed to drawing figures and tables; SY L and YY L helped in the statistical analyses; all authors contributed to manuscript revisions and approved the final version for publication.

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Tables

Table 1. Clinical characteristics of 52 children with *P. aeruginosa* bacteremia.

Characteristics	n/median	%/IQR
Basic information		
Age（years）	1.79	0.43-9.0
Male	32	61.5
Weight（kilogram）	11	7-27.00
Underlying diseases		
Immunosuppression	26	50.0
Neutropenia	24	46.2
Hematologic malignancies	16	30.8
Congenital heart disease	6	11.6
Complications		
Pneumonia	26	50
Meningitis	5	9.6
Peritonitis	3	5.8
Origins of infection		
Respiratory tract infection	22	42.3
Skin and soft tissue infection	8	15.4
Vascular-catheter related infection	8	15.4
Primary bacteremia	7	13.5
Gastrointestinal infection	5	9.6
Post-surgery or-procedure bacteremia	2	3.8
Hypoalbuminemia	22	42.3
Intensive unit care	20	38.5
Nosocomial infection	22	42.3
Pitts bacteremia score	1.5	1-4.00
Antibiotic given prior to blood culture	31	59.5
Inappropriate empirical antimicrobial therapy	16	30.8
TTP	18.74	16.14-20.77
Length of hospitalization days	22.52	9.05-38.3
Multiple resistant bacteria	4	7.7
Outcomes		
Sepsis shock	15	28.8
In-hospital mortality	12	23.1

Table 2. Clinical characteristics and outcomes associated with TTP in 52 children with *P. aeruginosa* bacteremia.

Characteristics	Early TTP (TTP ≤ 18h, n=21)	Late TTP （TTP＞18h, n=31）	P values
Basic information			
Age(years) (median, IQR)	0.85(0.48-8.79)	2.66(0.30-9.01)	0.911
Male (n, %)	11(52.4%)	21(67.7%)	0.384
Weight（kilogram）(median, IQR)	8.5(7.5-24.75)	13.5(6.00-28.00)	0.668
Underlying diseases			
Immunosuppression (n, %)	6(28.6%)	20(64.5%)	**0.023***
Neutropenia (n, %)	10(47.6%)	14(45.2%)	1.000
Hematologic malignancies (n, %)	3(14.3%)	13(41.9%)	0.070
Congenital heart disease (n, %)	3(14.3%)	3(9.7%)	0.946
Complications			
Pneumonia (n, %)	12(57.1%)	14(45.2%)	0.572
Meningitis (n, %)	3(14.3%)	2(6.5%)	0.645
Peritonitis	2(9.5%)	1(3.2%)	0.727
Origins of infection			
Respiratory tract (n, %)	11(52.4%)	11(35.5%)	0.263
Primary bacteremia (n, %)	2(9.5%)	5(16.1%)	0.787
Vascular-catheter related infection (n, %)	3(14.3%)	5(16.7%)	1.000
Soft tissue infection (n, %)	2(9.5%)	6(19.4%)	0.567
Gastrointestinal infection (n, %)	3(14.3%)	2(6.5%)	0.645
Post-surgery or-procedure bacteremia (n, %)	0(0.0%)	2(6.5%)	0.240
Hypoalbuminemia (n, %)	12(57.1%)	10(32.3%)	0.093
Intensive unit care (n, %)	13(61.9%)	7(22.6%)	**0.008***
Nosocomial infection (n, %)	7(33.3%)	15(48.4%)	0.392
Pittsburgh bacteremia scores (median, IQR)	3.00(1.00-5.00)	1.00(1.00-4.00)	**0.046***
Antibiotic given prior to blood culture (n, %)	12(57.1%)	19(61.3%)	0.781
Length of hospitalization days (median, IQR)	21.04(2.82-41.29)	28.92(11.92-36.71)	0.176
Multiple resistant bacteria (n, %)	0(0.0%)	4(12.9%)	0.090
Outcomes			
Sepsis shock (n, %)	11(52.4%)	4(12.9%)	**0.006***
In-hospital mortality (n, %)	9(42.9%)	3(9.7%)	**0.014***

Table.3 Comparison of clinical characteristics in survival and non-survival groups in 52 children with *P. aeruginosa* bacteremia

Characteristics	Non-survival (n=12)	Survival (n=40)	P values
Basic information			
Age(years) (median, IQR)	1.55(0.21-9.80)	1.79(0.44-9.01	0.373
Male (n, %)	8(66.7%)	24(60.0%)	0.938
Weight (kilogram) (median, IQR)	10.00(4.85-29.88)	11.25(7.00-27.00	0.521
Underlying diseases			
Immunosuppression (n, %)	5(41.7%)	21(52.5%)	0.743
Neutropenia (n, %)	8(66.7%)	16(40.0%)	0.195
Hematologic malignancies (n, %)	2(16.7%)	14(35.0%)	0.395
Congenital heart disease (n, %)	1(8.3%)	6(12.5%)	1.000
Complications			
Pneumonia (n, %)	8(66.7%)	18(45.0%)	0.323
Meningitis (n, %)	2(16.7%)	3(7.5%)	0.699
Peritonitis (n, %)	0(0.0%)	3(7.5%)	0.333
Origins of infection			
Respiratory tract (n, %)	6(50.0%)	16(40.0%)	0.740
Primary bacteremia (n, %)	1(8.3%)	6(15.0%)	0.911
Vascular-catheter related infection (n, %)	1(8.3%)	7(17.5%)	0.752
Soft tissue infection (n, %)	3(25.3%)	5(12.5%)	0.551
Gastrointestinal infection (n, %)	1(8.3%)	4(10.0%)	1.000
Post-surgery or-procedure bacteremia (n, %)	0(0.0%)	2(5.0%)	0.434
Hypoalbuminemia (n, %)	9(75.0%)	13(32.5%)	**0.023***
Intensive unit care (n, %)	6(50.0%)	14(35.0%)	0.500
Nosocomial infection (n, %)	4(33.3%)	18(45.0%)	0.701
Pittsburgh bacteremia scores (median, IQR)	4.50(1.25-7.25)	1.00(1.00-3.75)	**0.043***
Antibiotic given prior to blood culture (n, %)	7(58.3%)	24(60.0%)	1.000
Inappropriate empirical antimicrobial therapy (n, %)	6(50.0%)	10(25.0%)	0.153
TTP (median, IQR)	15.19(11.21-18.24)	19.42(16.92-20.97)	**0.005***
Length of hospitalization days (median, IQR)	2.86(2.07-28.08	26.44(19.80-44.63	0.002*
Multiple resistant bacteria (n, %)	0(0.0%)	4(10.0%)	0.259
Sepsis shock (n, %)	7(58.3%)	8(20.0%)	**0.025***

Table 4. Logistic regression analysis of risk factors of in-hospital mortality among 52 children with P. *aeruginosa* bacteremia

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	P value	OR	95%CI	P value
TTP≤18h	7.43	1.92-28.79	0.004*	6.30	1.18-33.77	0.032*
Pittsburgh bacteremia scores≥4	11.79	2.88-48.25	0.001*	8.15	1.53-43.32	0.014*
Hypoalbuminemia	10.80	2.51-46.43	0.001*	6.46	1.19-33.19	0.031*
Inappropriate empirical antimicrobial therapy	0.69	0.10-3.00	0.623			
Intensive care unit admission	8.56	2.18-33.63	0.002*			

Table 5. Logistic regression analysis of risk factors of sepsis shock among 52 children with *P. aeruginosa* bacteremia

Variables	Univariate analysis			Multivariate analysis		
	OR	95%CI	P value	OR	95%CI	P value
TTP≤18h	7.00	1.61-30.48	0.001*	5.88	1.21-21.96	0.035*
Pittsburgh bacteremia scores≥4	6.00	1.48-24.27	0.012*	4.95	1.26-27.50	0.024*
Hypoalbuminemia	6.23	1.44-26.95	0.014*			
Inappropriate empirical antimicrobial therapy	3.00	0.79-11.45	0.108			
Intensive care unit admission	1.86	0.50-6.85	0.352			

Figures

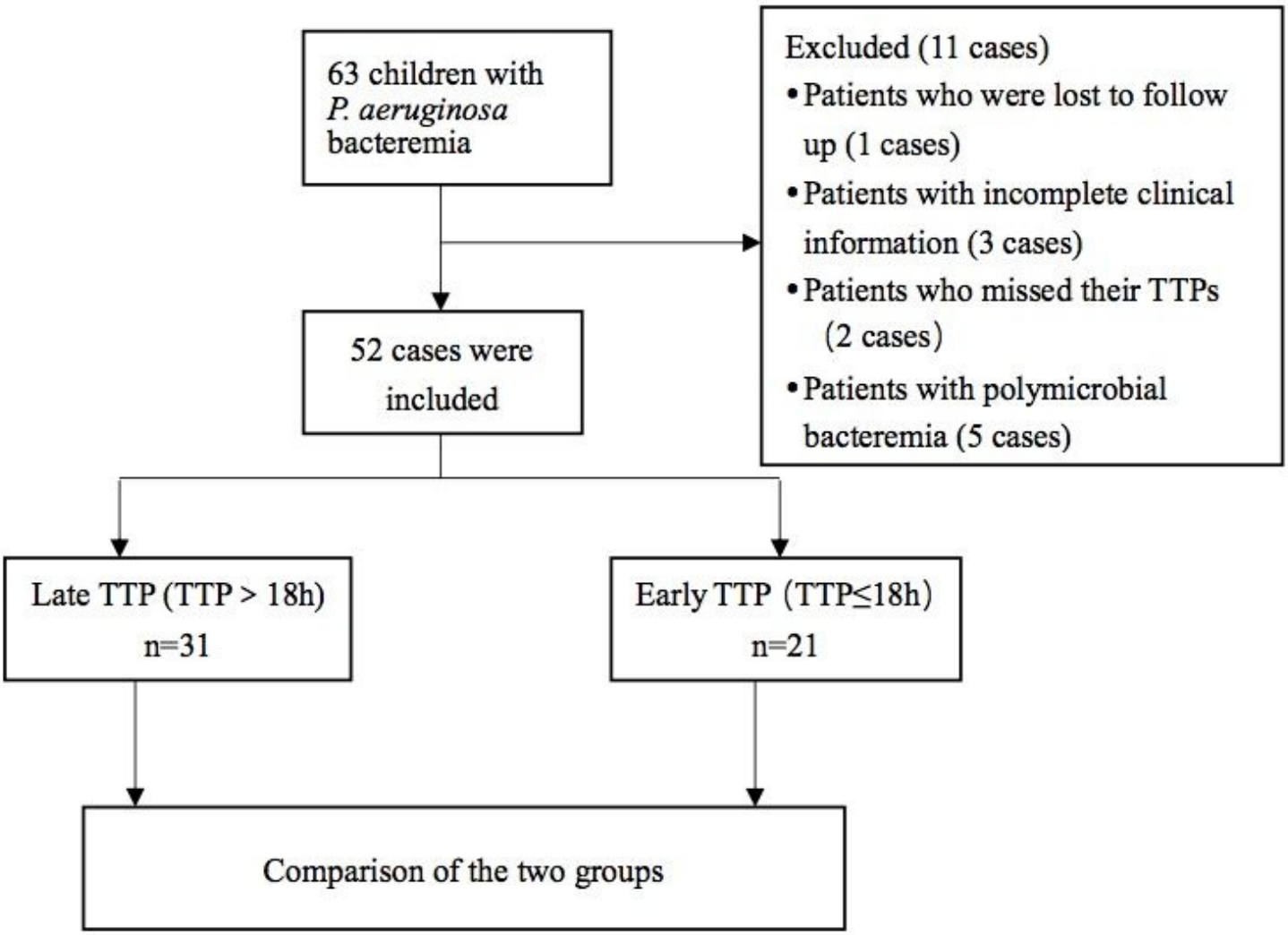

Figure 1

Flow diagram of the population.

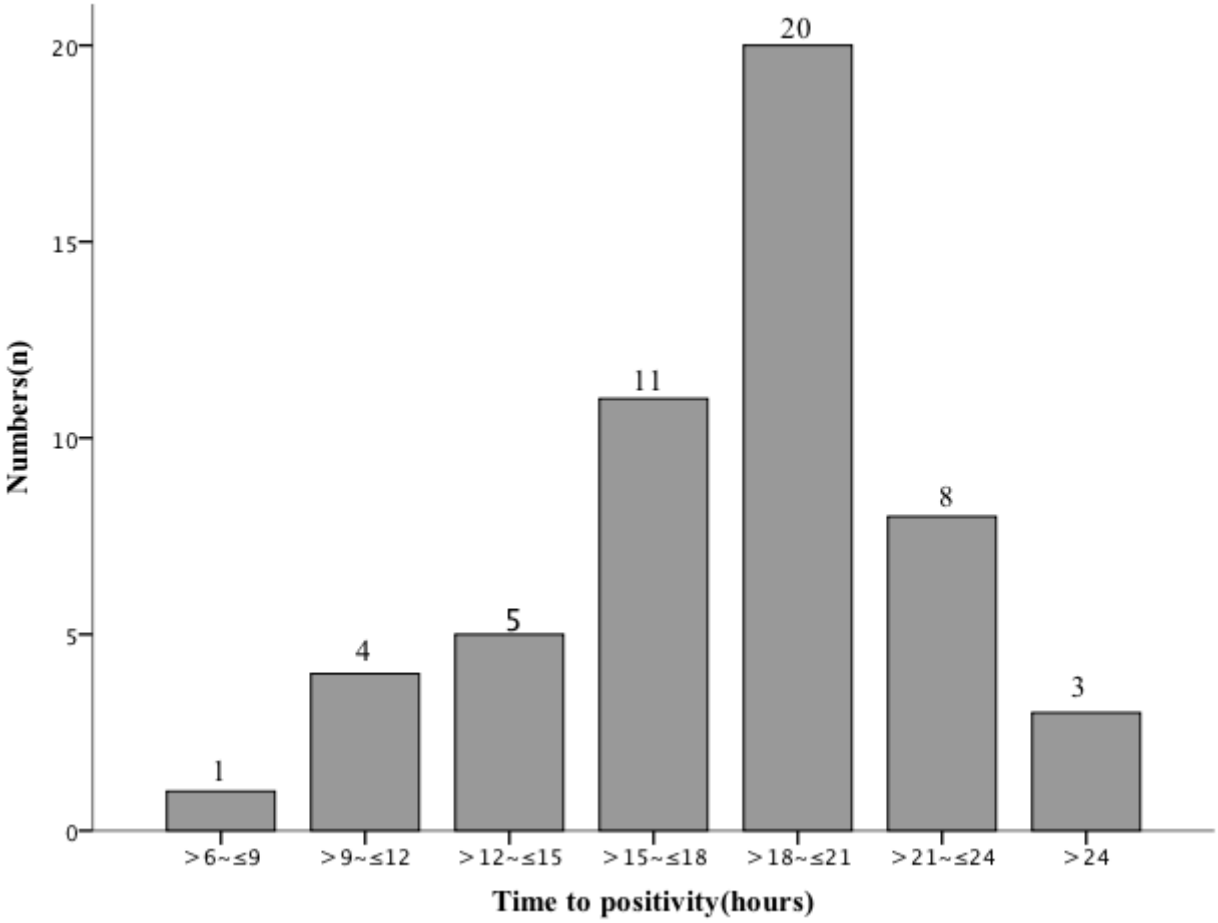

Figure 2

Bar chart of number of each period of TTP (Time-to-positivity) of children with P. aeruginosa.

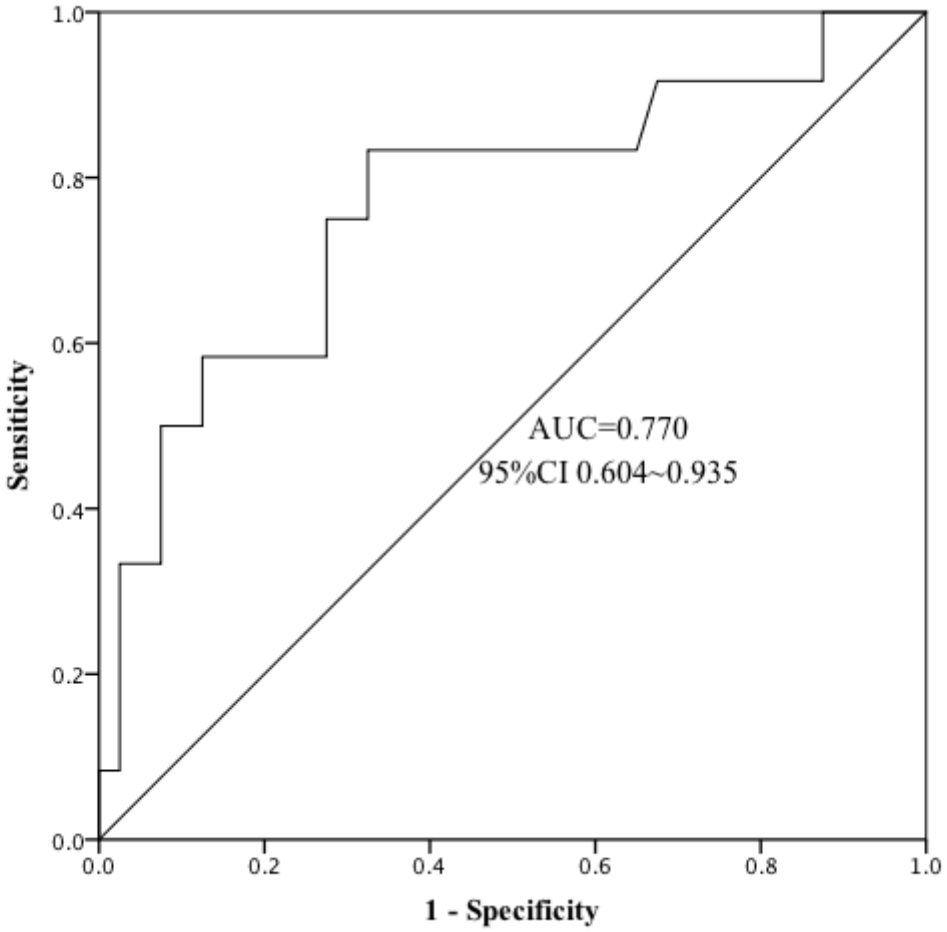

Figure 3

ROC (receiver operating characteristic) curves of TTP (Time-to-positivity). AUC stands for area under the curve.

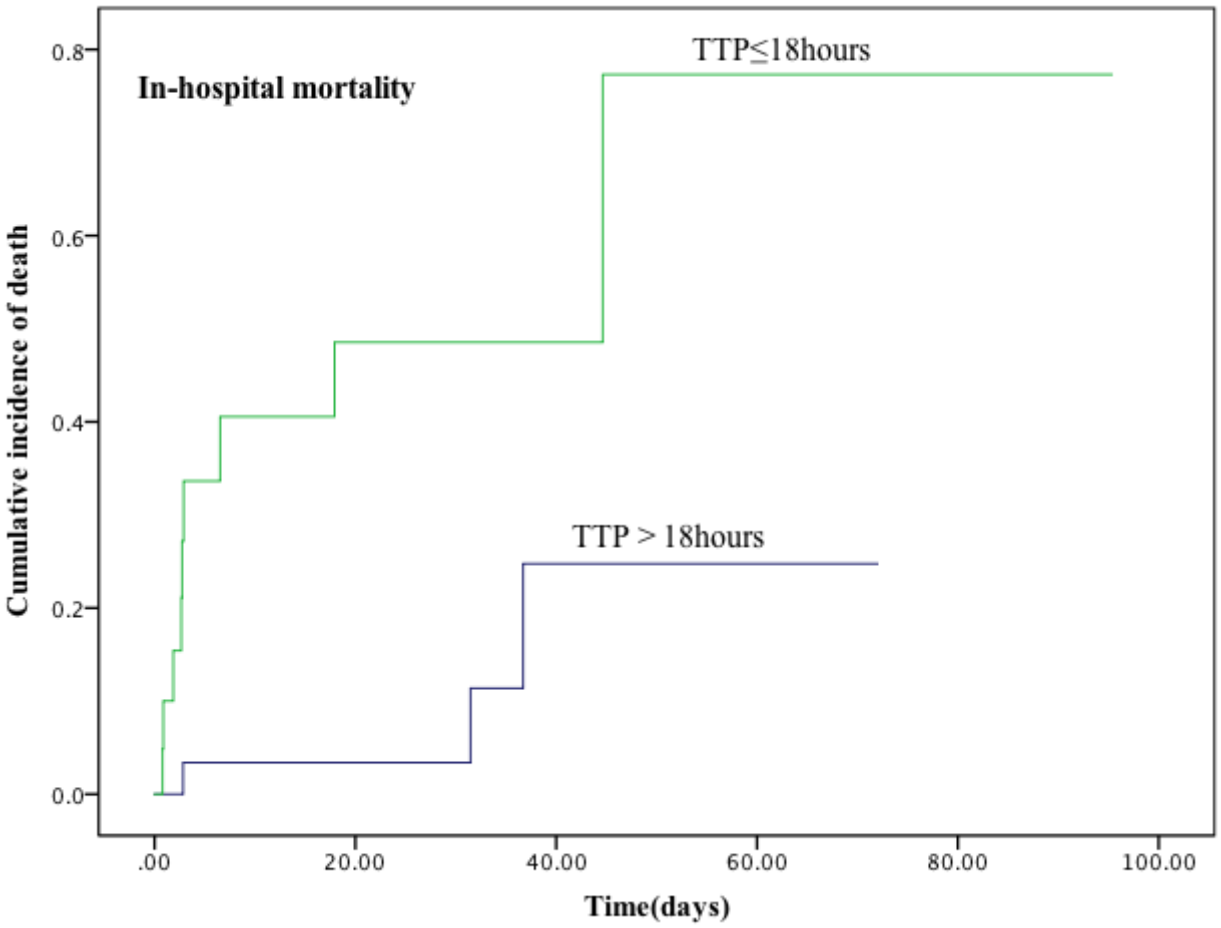

Figure 4

The Kaplan–Meier survival curve of 52 children with P. aeruginosa bacteremia according to in-hospital death. Patients were divided into 2 groups, according to 18 h, the optimal cut-off of TTP (Time-to-positivity).

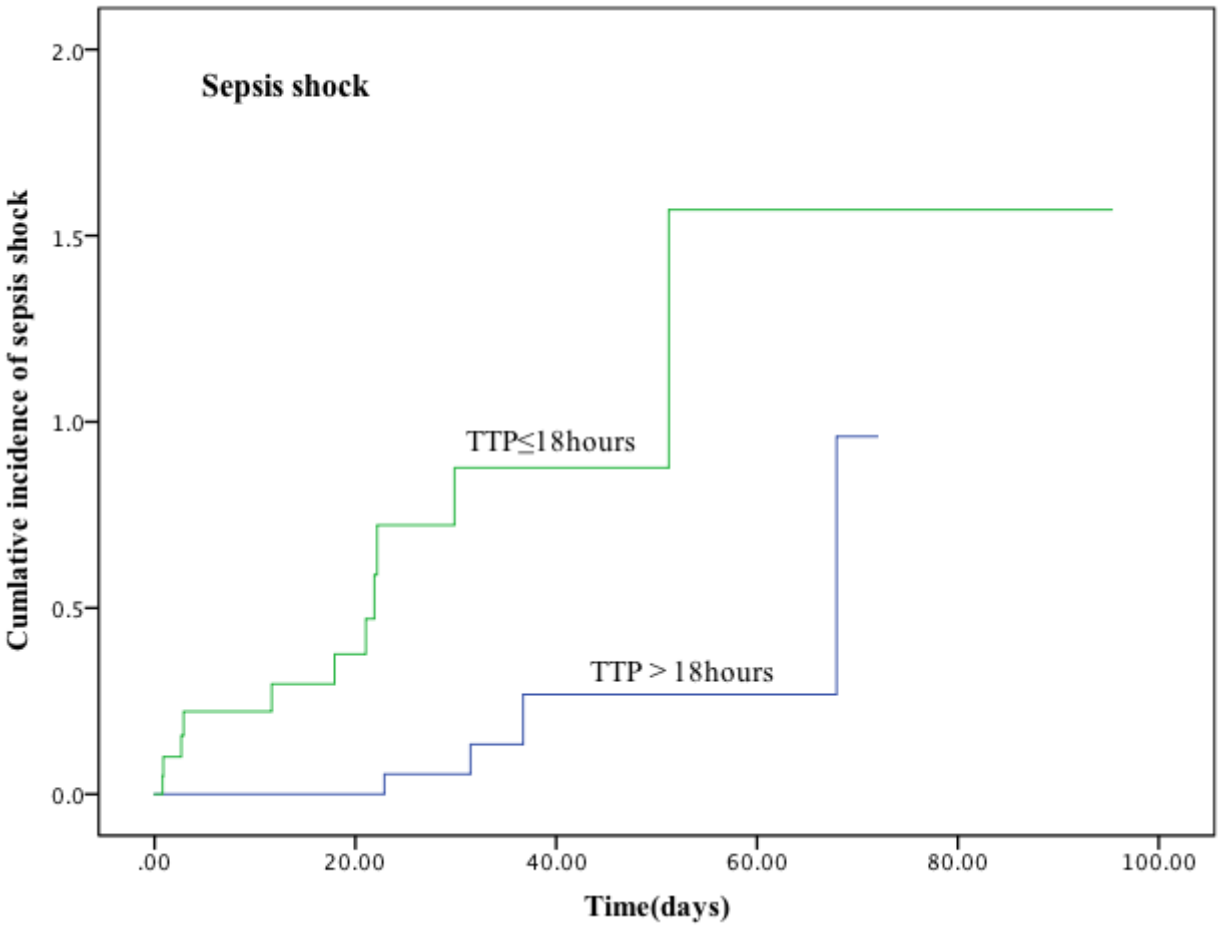

Figure 5

The Kaplan–Meier survival curve of 52 children with P. aeruginosa bacteremia according to sepsis shock. Patients were divided into 2 groups, according to 18 h, the optimal cut-off of TTP (Time-to-positivity)