

# Sepsis and infections 1

## 000005 - Retrospective study on the clinical utility of intravenous Fosfomycin in a tertiary care Indian Intensive Care Unit

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### Introduction

With increase in multi-drug resistant (MDR) organisms, many of the old antibiotics were reintroduced in to clinical area. Fosfomycin has gained attention as revisited antibiotic, because it has activity against both Gram-positive and Gram-negative MDR and extensively drug resistant (XDR) organisms. We have analysed retrospectively, the clinical utility of this drug in the current era of drug resistance.

### Methods

We included patients who received at least one dose of intravenous fosfomycin between October 2016 and March 2017 at tertiary care ICU, India. Data includes demographic details, SOFA score, diagnosis, outcome, organism isolated and its sensitivity. Details about fosfomycin administration (dose and adverse effects) were also noted.

### Results

A total of 50 patients were included. Mean  $\pm$  S.D. SOFA score at admission was  $7.72 \pm 3.6$ . Mean  $\pm$  S.D. stay in ICU was  $12.84 \pm 10.63$  days. 62.7% patients were diagnosed as having severe sepsis, out of which 27.9% were having ventilator associated pneumonia. At the time of fosfomycin initiation, organisms were isolated in 86% cases. Among these 77.3% were carbapenem resistant enterobacteriaceae (among them 64.7% were sensitive only to colistin). Fosfomycin was used as combination therapy in all cases. Median dose and duration of fosfomycin was 12g/day and 5 days respectively. On evaluation 30.2% patients experienced an improved clinical status by Day 7. Overall 28 day mortality was 51.2%. According to per day dose of fosfomycin clinical improvement was significantly higher (66.6%) in patients who received 18g, as compared to 14.2% with <8g dose ( $p=0.04$ ). Similarly clinical improvement was arithmetically higher (63%) in patients who received  $\geq 10$  days treatment ( $p=0.56$ ). No treatment emergent adverse events were observed.

## Conclusion

Higher intravenous fosfomycin dose (18g or more) for longer duration appears to positively impact the clinical outcome in critically ill patients, however further prospective studies, with more robust designs will be needed to back our results.

# 000018 - Dexmedetomidine improves microcirculatory alterations in initial resuscitated septic shock patients

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## Introduction

Dexmedetomidine were found to improve microcirculation in sepsis animal studies(15, 16) and non-sepsis patients. However, the effect of dexmedetomidine on microcirculation in septic shock patients is unknown.

## Objectives

Based on the hypothesis that dexmedetomidine might improve microcirculation in initial resuscitated septic shock patients, the study was to investigate the effects of dexmedetomidine on microcirculation in early septic shock patients despite initial resuscitation. Meanwhile, to elucidate the possible mechanisms of this effect, the correlation between dexmedetomidine dose and microcirculatory parameters as well as catecholamine level were studied.

## Methods

Early septic shock patients despite initial fluid resuscitation who still required norepinephrine to maintain target arterial pressure were enrolled. Hemodynamic and gas analysis variables, sublingual microcirculatory parameters were measured at baseline, and during the infusion of dexmedetomidine (0.7ug/kg/h). To investigate the possible mechanisms of the effect of dexmedetomidine on microcirculation, the dose-effect relationship of dexmedetomidine on microcirculation and catecholamine level were performed.

## Results

Forty-four septic shock patients were enrolled after initial resuscitation. Compared with baseline, total and perfused vascular density were statistically increased after infusion of dexmedetomidine, which was correlated with the dose of dexmedetomidine. During dexmedetomidine infusion, plasma norepinephrine and dopamine level were significantly decreased. Changes in plasma norepinephrine level contributed to dexmedetomidine infusion was well correlated with changes in total and perfused vascular density.

## **Conclusion**

In adult patients with resuscitated septic shock, dexmedetomidine improved microcirculation, which might be associated with plasma catecholamine level. However, double blinded large sample studies should be performed to verify the results.

# **000026 - Respiratory virus infections in pragmatically selected adult critically ill patients**

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## **Introduction**

Respiratory viruses become recognized causes of severe acute respiratory infections in adult critically ill patients as the advancement of modern diagnostics tools such as multiplexed respiratory viral panel testing. Since the cost of these multiplex assays remain high, intensivists may need to choose the most appropriate patients to test, in order to maximize the clinical benefit.

## **Objectives**

To assess the prevalence, characteristics, and outcomes of respiratory virus infections in pragmatically selected critically ill patients.

## **Methods**

We conducted a prospective cohort study in the medical intensive care units (ICUs) of a tertiary hospital. Adult critically ill adult patients with suspected respiratory virus infections were considered for inclusion. Patients with any known positive virology or microbiology test indicating a specific respiratory pathogen were excluded from this study. Respiratory tract specimens were collected according to clinical needs. The virology tests included viral culture and identification by immunofluorescent assay, influenza real-time polymerase chain reaction, and FilmArray respiratory panel (BioFire Diagnostics, Salt Lake City, Utah, USA). We performed multivariable logistic regression to identify factors associated with detection of respiratory viruses.

## Results

143 critically ill patients were enrolled during May 2017 and September 2018. All patients had respiratory distress and 81.8% of them received invasive mechanical ventilation. 57 (39.9%) patients have respiratory virus detected in their respiratory specimens. The most commonly detected virus are influenza virus (17), followed by respiratory syncytial virus (10), human rhinovirus / enterovirus (8), human metapneumovirus (8), parainfluenza virus (7), adenovirus (7), and coronavirus (2). Clinical factors associated with detection of respiratory virus include contact history with someone having upper respiratory tract infections (odds ratio (OR) 2.41, confidence interval (CI) 1.09 – 5.45,  $p = 0.030$ ), productive cough (OR 3.25, CI 1.19 – 9.67,  $p = 0.025$ ), and sore throat (OR 2.96, CI 1.02 – 8.93,  $p = 0.048$ ) in the multivariable analysis. On the causes of respiratory distress, 34 of 73 (47.9%) patients with pneumonia, 21 of 44 (47.7%) patients with acute decompensated heart failure, and 7 of 23 (30.4%) patients with acute exacerbation of chronic obstructive pulmonary disease have respiratory virus infections. The mechanical ventilation duration, length of ICU and hospital stay, ICU and 28-day mortality rate are not statistically different between patients with or without respiratory virus infections.

## Conclusion

Respiratory virus infections are prevalent in pragmatically selected ICU patients. Contact history and presence of respiratory tract symptoms may help the intensivist to determine if a patient needs advanced testing for respiratory viruses.

# 000055 - Plasma Midkine is Associated with 28-Day Mortality and Organ Function in Sepsis

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## Introduction

Midkine has been reported to play a crucial role in the process of inflammation, hypoxia and tissue injury. We aimed to investigate the plasma midkine levels in septic patients and its association with 28-day mortality and organ function.

## Methods

Septic patients were enrolled in the study. The baseline characteristics of the septic patients were recorded at admission. The peripheral blood sample was obtained at admission and plasma midkine level were evaluated by immunoassay. All patients were followed-up to 28 days with all-cause mortality recorded.

## Results

A total of 26 septic patients were enrolled with 18 survivors and 8 non-survivors on day 28. Plasma midkine was significantly elevated in survivor group compared with nonsurvivors [ng/L, 763.6 (404.7-1305) vs. 268.5 (147.8-511.4),  $P = 0.0387$ ]. Plasma midkine was increased in septic patients with moderate/severe acute respiratory distress syndrome (ARDS) compared with non/mild ARDS patients [ng/L, 522.3 (336.6-960.1) vs. 243.8 (110.3-478.9),  $P = 0.0135$ ], also in those with acute kidney injury compared with those without [ng/L, 489.8 (259.2-1058) vs. 427.9 (129.6-510.3),  $P = 0.0973$ ]. Plasma midkine level was associated with extravascular lung water index ( $P = 0.063$ ) and pulmonary vascular permeability index ( $P = 0.049$ ).

## Conclusion

Plasma midkine was associated with 28-day mortality, pulmonary and kidney injury in septic patients.

# 000056 - Epidemiology and risk factors for mortality in ICU patients with candidemia

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## Introduction

Candidemia is one of the most life-threatening infections in intensive care unit (ICU) patients. However, there are few studies about the epidemiology and risk factors for mortality in ICU patients with candidemia.

## Objectives

To describe the epidemiology and determine risk factors for mortality in ICU patients with candidemia.

## Methods

We performed a multicenter, retrospective cohort study. We identified adult patients ( $\geq 18$  years) who were admitted to ICUs in two university hospitals during January 2007 to December 2016. Patients diagnosed with candidemia during their ICU stay were included in the analysis. Patients' data were collected from their medical records. To identify factors associated with 30-day all-cause mortality, we performed univariate and multivariate logistic regression analysis. We entered a priori variables, as well as variables significant at  $P$  value  $< 0.05$  on univariate analysis, into the multivariate analysis. A priori variables were as follows: Acute Physiology and Chronic Health Evaluation (APACHE) II score within 24 hours of candidemia onset; therapeutic measures within 48 hours of candidemia onset (appropriate antifungal therapy alone, source control alone, or a combination of them [combined therapy]). All tests were 2-sided and  $P$  values  $< 0.05$  were considered statistically significant.

## Results

We identified 74 patients with candidemia during the study period. Of those, 52 (70.3%) patients were men and the median age was 68.0 years (interquartile range 63.0–76.0). The most common causative *Candida* species was *Candida albicans* (42 patients, 56.8%), followed by *Candida glabrata* (19 patients, 25.7%). Central venous catheter-related candidemia was the most frequent and accounted for 40.5% (30 patients). Within 48 hours of candidemia onset, 10 (13.5%) patients received appropriate antifungal therapy alone, 19 (25.7%) patients received source control alone, and 15 (20.3%) patients received combined therapy. Thirty-day all-cause mortality was 51.4%. On multivariate logistic regression analysis, APACHE II score (1-point increments) was a single factor independently associated with a higher 30-day all-cause mortality (odds ratio 1.10, 95% confidence interval 1.00–1.20,  $P = 0.042$ ). Other variables, including therapeutic measures within 48 hours of candidemia onset, had no significant association with mortality.

## Conclusion

Candidemia in ICU patients is still associated with high mortality. Early initiation of empiric antifungal treatment may be insufficient to improve survival in this population. Further investigations are required to elucidate the optimal timing of therapies and the roles of other strategies such as antifungal prophylaxis or preemptive antifungal therapy.

# 000060 - The Association between Clostridium Difficile Development and common Risk Factors in Acute Settings

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## Introduction

Clostridium difficile infection (CDI) is one of the most common causes of diarrhea related to the healthcare facility. (1) PPIs and broad-spectrum antibiotics use have led to increasing rates and severity of C. diff-associated disease (CDAD). (1,2) Previous studies have suggested that the overconsumption of PPIs is associated with the development of CDI in the community and hospital especially in the ICU. (3-7) There is limited data on CDI development and the related risk factors in our community.

## Objectives

The objective of this study is to estimate the prevalence of CDI in a tertiary academic medical center and to identify the risk factors associated with CDI development.

## Methods

This was a retrospective records review study conducted at tertiary academic medical center in Jeddah, Saudi Arabia, the study was approved by the Institutional Review Board (IRB). Eligible patients' records were adults ( $\geq 18$  years old) with confirmed C. diff diagnosis via lab results. The primary outcome was to estimate the CDI prevalence. Other secondary outcomes of interest include identification of the common risk factors associated with CDI development, relationship between the type and duration of the risk factor and CDI occurrence. Data were analyzed using descriptive statistics (number, percent, frequency). Qualitative variables compared by t-test and one-way ANOVA. A p value  $<0.05$  was considered statistically significant.

## Results

128 records had positive lab results and met the inclusion criteria. In our study we found that the prevalence of CDI in the last five years was 6.8%. More than half of the patients were exposed to PPI and broad-spectrum antibiotics (n=73) 56%. Piperacillin-tazobactam was the most common broad-spectrum antibiotic used in the study cohort (29.5%) and omeprazole accounted for higher PPI that is been used in our

study (53%). There was no statistically significant difference between the type of PPI and the duration from starting PPI to developing CDI ( $p = 0.242$ ). Also, there was no significant difference between the duration from starting or discontinuing the antibiotics to the onset of CDI ( $p = 0.745$ ,  $p = 0.241$ ) respectively.

## Conclusion

There was a low CDI prevalence in our community. The use of either PPIs and/or broad-spectrum antibiotics were strong predictable factors for CDI development regardless the duration of exposure.

# 000061 - Reduction of Vasopressor Dose and Outcomes in Patients with Severe Vasodilatory Shock in the ATHOS-3 Study

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## Introduction

Reduction in vasopressor dose may lead to improved outcomes by reducing toxicities. A randomized, placebo-controlled, double-blind study of patients with severe vasodilatory shock (VS) who remained hypotensive despite fluid and vasopressor therapy (ATHOS-3) demonstrated that the addition of angiotensin II (ang II) to standard vasopressors significantly increased mean arterial pressure (MAP) and decreased vasopressor burden. We analyzed norepinephrine equivalent dose (NED) reduction and outcomes in patients receiving ang II and placebo in a post-hoc analysis.

## Methods

Patients with persistent VS despite receiving adequate fluid therapy and  $>0.2$   $\mu\text{g}/\text{kg}/\text{min}$  of NED vasopressors were randomized to receive either IV ang II or placebo, titrated per study protocol, with other vasopressors held constant for hours 0-3. For hours 3-48, catecholamine sparing was assessed by reducing reliance on vasopressors while maintaining MAP. In this post-hoc analysis, we analyzed the



effect of ang II on NED reduction and outcomes in patients with  $\geq$  or  $<$  50% reduction in NED at 24 hours.

## Results

Patients were grouped by the NED at 24 hours relative to the Baseline NED. Within both treatment groups, earlier discontinuation of vasopressors and mechanical ventilation, and earlier discharge from the ICU and the hospital were statistically significant following Hour 24 NED reduction of  $\geq$  50% versus those with smaller or no decreases in NED. In the ang II group, 106/151 (70.2%) patients had  $\geq$  50% reduction in Hour 24 NED, compared to 69/139 (49.6%) patients in the placebo group ( $p = 0.0004$ ). Within the ang II treatment group, Day 28 mortality rates were 32% for patients with Hour 24 NED reduction  $\geq$  50% and 65% for patients with Hour 24 NED reduction  $<$  50% (RR = 0.330; 95% CI: 0.201-0.543;  $p = <0.0001$ ). Within the placebo group, there was also a statistically significant association of  $\geq$  50% reduction in NED with lower risk of death (RR = 0.497; 95% CI: 0.302-0.818;  $p = 0.0050$ ). Treatment-emergent adverse events (TEAEs), grade 3/4 TEAEs, serious adverse events (SAEs), and fatal AEs, occurred in fewer patients whose Hour 24 NED was reduced by  $\geq$  50% within each treatment group (Table 1).

Table 1	Ang II			Placebo		
	<50% Reduction	$\geq$ 50% Reduction	Total	<50% Reduction	$\geq$ 50% Reduction	Total
TEAEs	93%	83%	86%	93%	88%	91%
Grade 3/4 TEAEs	84%	54%	63%	74%	57%	66%
Serious AEs	82%	47%	58%	74%	51%	63%
Fatal AEs	64%	33%	42%	59%	36%	48%

## Conclusion

Among patients with VS, treatment with ang II resulted in a larger proportion of patients achieving a 50% or more reduction in NED at Hour 24 as compared with placebo. In this post-hoc analysis, a substantial reduction in NED was associated with statistically significant reduction in the risk of death and fewer TEAEs, and was associated with earlier discontinuation of vasopressors and mechanical ventilation, as well as earlier discharge from the ICU and the hospital in both groups.

# 000066 - Effect of Chlorhexidine bathing on the colonization or infection of drug-resistant Acinetobacter

# baumannii- a system review and meta-analysis

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## Introduction

There is limited evidence for chlorhexidine bathing to reduce nosocomial spreading of multidrug-resistant *Acinetobacter baumannii* (MDRAB) in the intensive care unit.

## Objectives

To perform a systematic review about whether chlorhexidine bathing can reduce the risk of multidrug-resistant *Acinetobacter baumannii* colonization and infection in the intensive care units.

## Methods

We searched PubMed, EMBASE, Web of Science and CINAHL from inception through June 2018 for randomized controlled trials, cohort, or interrupted-time series studies that applied chlorhexidine bathing as a mean to reduce MDRAB colonization or infection. Quality assessment for these studies was done.

## Results

One randomized controlled trial and 12 nonrandomized controlled trials reporting a total of 18,217 patients met the inclusion criteria; 251 patients in the chlorhexidine arm over 8,069 patients were colonized by *Acinetobacter baumannii*, compared with 360 patients in the control arm over 9,051 patients. Chlorhexidine bathing resulted in a reduced incidence of colonization of *Acinetobacter baumannii* in ICU patients: the pooled risk ratio using random effects model was 0.66 (95% confidence interval, 0.57-0.77;  $P < 0.001$ ). Statistical heterogeneity was high, with an  $I^2$  of 75.1%.

## Conclusion

Our meta-analysis has shown that chlorhexidine bathing decreases the risk of *Acinetobacter baumannii* colonization in ICU patients. The heterogeneity in study designs and settings highlights the need for well-designed randomized controlled study to confirmed these findings. Future investigations into the frequency of bathing needed to prevent *A. baumannii* colonizations and infections would be helpful, as a lower frequency of bathing could decrease not only the cost but the burden of nursing.

# 000070 - Comparative outcome between culture negative and culture positive sepsis

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## Introduction

Results of blood culture is crucial to guide definitive antibiotic treatment in sepsis patient. However, in approximately one third to two thirds of sepsis patients, no specific organism can be identified by blood culture test. Up to date, there is only few studies addressing the epidemiology and outcomes of culture-negative sepsis. Besides, contrary to previous belief, recent studies showed resource utilization and outcomes in culture negative and culture positive sepsis are generally comparable.

## Objectives

Since previous studies mainly focused on early mortality of severe sepsis or septic shock, we sought to investigate whether blood culture positivity may affect the early and mid-term outcome in whole spectrum of SIRS-defined sepsis patients.

## Methods

We conducted a retrospective multi-center cohort study. We evaluated the impact of blood culture positivity on the early(30-day) and late(90-day) mortality of sepsis. Univariate comparison was performed with Chi-square tests for categorical variables and Mann-Whitney U tests for continuous variables. Given known differences in patient characteristics between blood culture positive and blood culture negative patients, inverse probability of treatment weighting(IPTW) using the propensity score (PS) was employed to create weighted samples of individuals where measured baseline covariates were balanced between the two groups.

## Results

In the tri-center cohort, 1,405 patients with SIRS-defined sepsis were identified, comprising 655 (46.6%) patients with severe sepsis and 272 (19.4%) patients with septic shock. Of the total patients, 1189 (85.9%) were identified as blood culture negative sepsis (BCNS) and 216 (15.4%) as blood culture positive sepsis (BCPS).

The 90-day mortality was significantly higher in BCPS(21.3% vs. 12.9%,  $p=0.001$ ), but 30-day mortality was comparable in both groups (8.8% vs. 8.2%). Median hospital stay was longer in the BCPS group (15 days vs. 13 days,  $p=0.003$ ). Using IPTW adjusted analysis in full cohort, uncomplicated SIRS, and severe sepsis or septic shock, there was no significant difference for early mortality in three groups. For late mortality (30-90-day mortality), BCPS was associated with increased odds of late mortality as compared with BCNS in the full cohort (IPTW-OR, 1.95, 95%CI: 1.14-3.32), and in patients with severe sepsis or septic shock (IPTW-OR, 1.92, 95%CI: 1.10-3.33). Persistent Staphylococcal bacteremia may be an important contributing factor to worse late mortality in BCPS. After excluding Staphylococcal bacteremic patients, there were no significant difference in late mortality (IPTW-OR, 1.78, 95%CI: 0.87-3.62).

## Conclusion

Compared to blood culture positive sepsis(BCPS), the mid-term mortality was substantially lower among blood culture negative sepsis while short-term mortality was comparable in both groups.

# 000072 - Combining procalcitonin with the quick SOFA score improves sepsis mortality prediction

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## Introduction

Validation studies of qSOFA score showed suboptimal sensitivity in predicting sepsis mortality. We aimed to investigate whether procalcitonin can improve the sensitivity of qSOFA in predicting sepsis mortality.

## Methods

We conducted a retrospective multicenter cohort study with independent validation in a prospectively collected cohort. Derivation cohort included 1318 patients with presumed sepsis between June 1, 2015, and December 31, 2016 and the validation cohort included 493 prospectively collected patients in 2017. Serum procalcitonin levels were measured at admission with the commercial assay (VIDAS, bioMérieux, Marcy, France). Quick SOFA score and SIRS (Systemic Inflammatory Response Syndrome) criteria were calculated for each patient. PCT levels were assigned into 0, 1, 2 points for a serum level of <0.25, 0.25-2, and >2 ng/mL and added to the qSOFA score. The incremental value of PCT to qSOFA was then evaluated by logistic regression, ROC curve, and reclassification analysis. Lastly, we calculated the sensitivity, specificity, positive and negative predictive value of SIRS, qSOFA and qSOFA\_PCT in predicting in-hospital mortality.

## Results

A total of 1318 patients with presumed severe infection were enrolled with a 30-day mortality of 13.5%. Serum level of procalcitonin showed a high correlation with qSOFA score and 30-day in-hospital mortality. The area under the ROC curve in predicting mortality was 0.56 for SIRS criteria, 0.67 for qSOFA score, and 0.73 for qSOFA\_PCT. The risk prediction improvement was reflected by a net reclassification improvement of 35% (17%-52%,  $p=0.00011$ ). At a cutoff of 2 points, qSOFA has a sensitivity of 32.6% (95% CI: 25.8%-40.0%) and a specificity of 87.0% (87.3%-91.0%) to predict 30-day mortality. Incorporation of PCT into the qSOFA model could raise the sensitivity to 86.5% (95%CI: 80.6%-91.2%) with a specificity 47.5% (95%CI: 44.6%-50.5%). In the validation cohort, we confirmed qSOFA\_PCT greatly improve the sensitivity to 90.9%.

## Conclusion

A simple modification of qSOFA score by adding the ordinal scale of PCT value to qSOFA could greatly improve the suboptimal sensitivity problem of qSOFA and could be served as a quick screening tool for early identification of sepsis patients.

# 000076 - Survival impact and clinical predictors of acute gastrointestinal bleeding in patients with bloodstream infection

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## Introduction

Gastrointestinal bleeding (GIB) is a common complication of bloodstream infections (BSI). However, the impact of GIB on treatment outcomes among patients with BSI has not been clearly defined.

## Objectives

Our study aimed to determine the incidence of GIB in patients with BSI, to identify the independent risk factors of GIB, and to examine the independent impact of GIB on the outcome of patients with BSI.

## Methods

This was a propensity score-matched prospective cohort study. Patients 18 years of age and older who were admitted to the emergency department during the study period with bloodstream infection and followed for at least 90 days were included. Patients with history of liver cirrhosis and gastroesophageal varices were excluded. Independent risk factors of GIB were identified by logistic regression model with backward elimination. The survival impact of GIB on BSI was evaluated with the multivariate Cox proportional hazards model and propensity score matching with inverse probability treatment weight (IPTW) adjustment.

## Results

Of the 1034 patients with BSI and a complete 90-day follow up, 79 (7.64%) developed acute GIB. History of hemiparetic stroke (OR 3.12, 95% CI: 1.82, 5.36) and HIV infection (OR 8.90; 95% CI: 2.17, 36.46) were the two strongest independent predictors of GIB, followed by absence of fever on presentation, very old age, and male gender. GIB was associated with increased 90-day mortality (IPTW HR 1.74, 95% CI: 1.14, 2.65), independent of underlying comorbidities and sepsis severity. The Kaplan-Meier survival curve stratified by the presence of GI bleeding also confirmed the negative survival impact of GI bleeding.

## Conclusion

To the best of our knowledge, this is the first study to investigate the survival impact and clinical predictors of GIB in patients with BSI. Our study showed that patients with BSI and GIB had a significantly higher mortality than those without GIB. Active prevention and treatment of GIB are therefore recommended for patients with BSI and risk factors for GIB.

# 000101 - Galactomannan detection in bronchoalveolar lavage fluid corrected by urea dilution for the diagnosis of invasive pulmonary aspergillosis among nonneutropenic patients

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## Introduction

To investigate the diagnostic performance of galactomannan (GM) detection in bronchoalveolar lavage fluid (BALF) corrected by urea dilution and modification of the AspICU clinical algorithm among nonneutropenic patients.

## Methods

The multi-centre prospective study was performed from January 2016 to June 2018. GM detection in serum and BALF samples was performed in nonneutropenic patients on the day of clinically suspected invasive pulmonary aspergillosis (IPA) and urea was measured in the plasma and BALF. The corrected GM concentration in the BALF sample was calculated as:  $[\text{Corrected BALF GM}] = [\text{BALF GM}] \times [\text{Plasma Urea}] / [\text{BALF Urea}]$ . Receiver operating characteristic (ROC) curves were generated to determine the optimal cutoff value of corrected BALF GM and the AspICU clinical algorithm was modified based on it.

## Results

A total of 184 patients who were suspected IPA, were enrolled in this prospective study together with 30 patients with lung cancer as a control group. Seventy-eight patients were diagnosed with IPA, including 37 who were verified by pathology. The median uncorrected BALF GM value in the IPA proven cohort was 1.04 ODI (IQR 0.86-1.45), which was higher than the values in all non-IPA groups ( $p < 0.001$ ). The urea plasma-to-urea BALF ratio in the IPA group (4.18 [IQR 3.52-4.91]) was greater than that in the non-IPA group (3.42 [IQR 3.12-3.76],  $p < 0.001$ ). The corrected BALF GM values were not significantly different between the IPA proven diagnosis group and the IPA probable diagnosis group. However, the values in these two groups were

approximately two times higher than that in the non-IPA group ( $p < 0.001$ ). No significant correlation was identified between GM in the uncorrected BALF and serum samples ( $R^2 = 0.302$ ,  $p > 0.05$ ). However, when the GM values in the BALF sample were corrected by urea dilution, a significant correlation was detected ( $R^2 = 0.642$ ,  $Y = 1.89X + 2.486$ ,  $p < 0.01$ ). The ROC curve showed that defining the cutoff value as 2.94 optical density index (ODI) for the corrected BALF GM resulted in a sensitivity and specificity of 85.91% and 94.07%, respectively, and was more accurate than the use of the uncorrected values ( $p < 0.05$ ). When the AspICU clinical algorithm was modified based on corrected BALF GM, high sensitivity and specificity (both 100%) were revealed with a satisfactory AUC (1.00), which was verified in the 37 patients with a proven IPA diagnosis.

## Conclusion

The corrected BALF GM was valuable for diagnosing IPA in nonneutropenic patients. The modified AspICU clinical algorithm based on this measurement represents a reliable diagnostic instrument in clinical settings.

# 000112 - Recombinant thrombomodulin reduces histone H3 level in rats with sepsis

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## Introduction

Sepsis is the leading cause of death in critically ill patients. Recently, it has been reported that extracellular histones, which are known to act as damage-associated molecular patterns (DAMPs), can be released when cells undergo severe injury, resulting in immunostimulatory and cytotoxic responses [1, 2, 3]. Extracellular histones are known to be associated with immunothrombosis [4] and have also attracted attention as mediators of remote organ injury [1]. It is known that extracellular histones cause massive thromboembolism associated with consumptive coagulopathy, and it has been shown that administration of recombinant thrombomodulin (rTM) improved mortality in patients who had sepsis with severe coagulopathy [5]. However, it remains to be clarified whether rTM binds and neutralizes extracellular histones.

## Objectives



The aim of this study was to determine the plasma histone H3 levels in rats subjected to cecal ligation and puncture (CLP)-induced sepsis and assess the protective effects of rTM.

## Methods

We established a sepsis-induced model with CLP by using Wistar rats (male, weighing 250-300 g). Histone H3 levels were determined by ELISA at 0, 4, 8, 12, 16, 20 and 24 h after surgery. To determine the effect of rTM on the concentration of histone H3, rTM was administered intravenously after the CLP procedure. Rats were divided into 4 groups according to the dose of rTM given: control (only buffer), low-dose rTM (1 mg/kg), medium-dose rTM (3 mg/kg) and high-dose rTM (6 mg/kg) groups. Rat blood containing an anticoagulant was collected 12 h after rTM administration in each group, and plasma obtained after centrifugation was stored at -80 degrees Celsius until histone H3 determination.

## Results

Plasma histone H3 level was increased at 12 h and reached a maximum level at 24 h after the CLP procedure. Administration of rTM resulted in a decrease in histone H3 level in an rTM dose-dependent manner. Plasma levels of histone H3 in the medium (3 mg/kg) and high-dose (6 mg/kg) groups were significantly decreased compared with those in the control group and low-dose group (1 mg/kg) ( $p < 0.05$ ).

## Conclusion

The results of our study indicate that histone H3 level is increased over time following the onset of intra-abdominal sepsis and that administration of rTM reduces the level of histone H3. Further study is required to clarify the mechanism by which extracellular histone H3 level is decreased by rTM and the relationships of the rTM-induced decrease in histone H3 level with improvement of organ failure and survival rate.

# **000007 - Clinical outcome of hematologic and oncologic malignancy in patients with extracorporeal membrane oxygenation support**

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## Introduction

Clinical outcomes of hematologic and oncologic patients have improved, however, relevance of extracorporeal membrane oxygenation (ECMO) support in these patients remains still challenging and controversial.

## Objectives

We sought to compare the clinical outcomes of hematologic (HM) and oncologic malignancy (OM) in patients with extracorporeal membrane oxygenation (ECMO) support.

## Methods

We retrospectively reviewed consecutive adult patients with HM and OM, supported by an ECMO between January 2012 and December 2016 in a single-center registry. The primary outcome was survival to hospital discharge.

## Results

Of the 98 eligible patients, 30 (30.6%) were diagnosed with HM and 68 (69.4%) were diagnosed. 30 of 98 (30.6%) survived to hospital discharge and 46 (46.9%) patients were successfully weaned off ECMO. The survival to hospital discharge was significantly higher in OM patients compared to HM patients (13.3 vs 38.2 %,  $P = 0.026$ ). There was similar between two groups in 1-year survival after ECMO initiation (23.3 vs 29.4 %,  $P = 0.707$ ), however, follow-up 6 months survival after hospital discharge was significantly higher in OM patients (3.3 vs 26.5 %,  $P = 0.017$ ). Pre-ECMO pH was positively affected, while pre-ECMO VIS and respiratory failure, the reason for ECMO insertion, were negatively affected survival to hospital discharge in our study.

## Conclusion

Survival to hospital discharge was significantly higher oncologic malignancy patients compared to hematologic malignancy patients who received ECMO support. In addition, our findings suggest that the implantation of ECMO might be feasible in patients with HM and OM associated with reasonable expectation for survival to hospital discharge.

# 000037 - Correlation among Acinetobacter Baumannii and nursing, severity and outcome indexes in ICU patients

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## Introduction

Acinetobacter Baumannii strains are distinguished for their resistance to antibiotics and for long-term survival both in dry and in wet environments. Spreading of these strains may lead in developing severe infections in critically ill ICU patients.

## Objectives

The aim of our observation retrospective study was to test the hypothesis that a statistical significant correlation exists among nursing, severity and outcome indexes and percentage of Acinetobacter Baumannii positive cultures in severely ill patients in our both medical and surgical ICU served in community hospital.

## Methods

From January 2006 to December 2017, 1107 patients admitted to our ICU. From our database we looked for percent of total of Acinetobacter Baumannii positive cultures and nursing (number of patients, number of patients ventilated, length of stay, hospitalization days, ventilation days per patient ventilated, percentage of ventilated patients, plentitude, mechanical ventilation days), severity (age, APACHE II score, predicted mortality) and outcome (actual mortality, Standardized mortality ratio) indexes per year from 2006 to 2017 (mean values). Using linear correlation method, we looked for linear slope, correlation coefficient (r), and coefficient of determination (r<sup>2</sup>), and by linear regression method using ANOVA test we looked for p value, according Acinetobacter Baumannii % and ICU indexes.

## Results

	Slope	r	r <sup>2</sup>	St. error	P value
Noof patients	-1.4760	-0.3305	0.1092	1.3330	0.2941
Hosp days	-5.2510	-0.1283	0.0164	12.8310	0.6910
LOS	0.0834	0.2940	0.0864	0.0857	0.3536
Age	-0.2175	-0.4581	0.2098	0.1335	0.1343

% ventilated	-0.1868	-0.4118	0.1696	0.1307	0.1835
Plentitude	0.0247	0.0294	0.0008	0.2654	0.9275
Pts ventilated	-1.5430	-0.3731	0.1392	1.2130	0.2322
Days M V	-3.3450	-0.0951	0.0090	11.0690	0.7687
VD per pt	0.1676	0.6376	0.4065	0.0640	0.0257
APACHE	-0.1054	-0.3223	0.1039	0.0978	0.3069
Pred Mort.	-0.2852	-0.2967	0.0880	0.2903	0.3491
Actual mort	0.2147	0.2059	0.0423	0.3227	0.5209
SMR	0.0093	0.4840	0.2342	0.0053	0.1109

## Conclusion

According to our data, there was no statistical significant correlation detected among all severity, all outcome and most of the nursing indexes and Acinetobacter Baumannii positive cultures. On the other hand, there was a strong, positive, statistical significant correlation detected among Acinetobacter Baumannii positive cultures % and ventilation days per patient under mechanical ventilation. Our data suggest that when the number of ventilation days per ventilated patient goes up, the incidence of Acinetobacter Baumannii infection is elevating, but no impact in length of stay or mortality rate were detected.

## 000039 - Correlation among Klebsiella species and nursing, severity and outcome indexes in ICU patients

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## Introduction

Klebsiella species are distinguished for their resistance to antibiotics and capable of causing life threatening pneumonia in otherwise healthy people. Spreading of these strains may lead in developing severe infections in critically ill ICU patients.

## Objectives

The aim of our observation retrospective study was to test the hypothesis that a statistical significant correlation exists among nursing, severity and outcome indexes and percentage of Klebsiella species positive cultures in severely ill patients in our both medical and surgical ICU served in community hospital.

## Methods

From January 2006 to December 2017, 1107 patients admitted to our ICU. Mean age 66 years, mean length of stay (LOS) 12.2 days, mean APACHE II score on admission 21.5, predicted mortality 39.5 %, actual mortality 29.3 %, Standardized mortality ratio (SMR) 0.74. From our database we looked for percent of total of Klebsiella species positive cultures and nursing (number of patients, number of patients ventilated, length of stay, hospitalization days, ventilation days per patient ventilated, percentage of ventilated patients, plentitude, mechanical ventilation days), severity (age, APACHE II score, predicted mortality) and outcome (actual mortality, Standardized mortality ratio) indexes per year from 2006 to 2017 (mean values). Using linear correlation method, we looked for linear slope, correlation coefficient (r), and coefficient of determination (r<sup>2</sup>), and by linear regression method using ANOVA test we looked for p value, according Klebsiella species % and ICU indexes.

## Results

	Slope	r	r <sup>2</sup>	St. error	P value
N of patients	-2.0640	-0.2899	0.0840	2.1540	0.3607
Hosp days	2.3750	0.0364	0.0013	20.6030	0.9105
LOS	0.1921	0.4249	0.1805	0.1294	0.1686
Age	-0.1773	-0.2343	0.0549	0.2326	0.4635
% ventilated	-0.3068	-0.4244	0.1801	0.2070	0.1691
Plentitude	0.8340	0.2866	0.0821	0.4053	0.3665
Pts ventilated	-2.1480	-0.3260	0.1063	1.9690	0.3010
Days M V	-2.3700	-0.0422	0.0017	17.7030	0.8962
VD per pt	0.1188	0.2837	0.0804	0.1270	0.3716
APACHE	-0.0859	-0.1649	0.0271	0.1625	0.6086
Pred Mort.	-0.2627	-0.1715	0.0294	0.4772	0.5940
Actual mort	-0.1735	-0.1044	0.0109	0.5226	0.7468
SMR	0.0040	0.1306	0.0170	0.0096	0.6858

## Conclusion

According to our data, there was no statistical significant correlation detected among all severity, all outcome and all of the nursing indexes and the percentage of Klebsiella species positive cultures. Our data suggest that in our study, the impact of the incidence of Klebsiella species infection was not statistical significant or not strong enough to influence the length of stay or the outcome.

# 000089 - Minimise contamination of blood culture sampling in the Intensive Care Unit of a medical reform hospital in China

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## Introduction

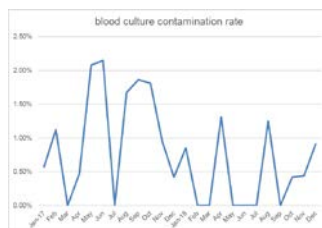
Blood culture is an important investigation for critically ill patients, when sepsis is suspected. Result of blood culture not only informs prognosis of individual patient, it also directly affects antimicrobial use. Contamination of blood culture result can cause inappropriate use and overuse of antimicrobial, which can directly and indirectly affect morbidity and mortality of patients. Blood culture sampling requires strict adherence to aseptic technique. It can be difficult for critically ill patients, as the vascular condition is frequently suboptimal.

## Methods

It was noticed that there was a rise in contamination of blood culture specimen in 1-2Q of year 2017. A multi-modular approach was adopted to manage the high contamination rate. The blood culture sampling technique was reviewed, including behind screen observation, viewing of CCTV. Face to face discussion with the involved staff in reviewing the process. Department guideline was revised, with incorporation of photos. Strengthening of sampling technique by training and coaching was also carried out.

## Results

The rate of blood culture contamination decreased from 2% to <1% in year 2018.



## Conclusion

Blood culture contamination can be further minimised with concerted efforts, although it maybe a challenging task in the ICU of developing country hospitals. It is definitely helpful to improve the safety and care of the critically ill patients.