Poster Corner 6: Sepsis and Cardiovascular Dynamics

075 - MESENCHYMAL STEM CELLS ALTERED T LYMPHOCYTE DIFFERENTIATION UPON LPS OR HYPOXIA CHALLENGE VIA PARACRINE TRANSFORMING GROWTH FACTOR BETA-1 IN VITRO

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INTRODUCTION. Sepsis is characterized by the development of adaptive immune cell alterations under hypoxia or toxin condition induced by pathogens. Mesenchymal stem cell (MSC) s´ beneficial effects with immunosuppressive capacity in preclinical models of acute sepsis have been witnessed but meet difficulties to bedside treatments. MSCs could induce various effects on lymphocytes depending on environmental sensitivity. T helper 17(Th17) and regulatory T (Treg) cells in T cells differentiating play a vital role during inflammation process. However, T lymphocyte differentiation towards Th17 and Treg cells are not completely understood under different septic conditions.
OBJECTIVES. The aim of the current study was to evaluate whether lipopolysaccharide (LPS) or hypoxia could directly impact Treg and Th17 cells differentiation in vitro and the effects of MSCs.
METHODS. Purified CD4+ T cells isolated by positive CD4 selection from mice spleen were treated with LPS or at hypoxia condition. We investigated T cells differentiation towards Treg and Th17 with direct or indirect MSCs treatment respectively by adding MSCs into cell-culture inserts directly or into upper champers, followed by neutralization of TGF-β1 with anti-TGF-β1 antibody in the co-culture medium. Phenotypes of Treg and Th17 cells were identified by flowcytometry. T-cell proliferation was tested by cell-counting kit-8 assay. Supernatant was harvested from cell culture frozen at -80 C for cytokine analysis by enzyme-linked immunosorbent assay kits.
RESULTS. Treg/Th17 ratio significantly decreased after 48h LPS stimulation with dose above 100ng/ml or hypoxia. MSCs could significantly reversed reduced Treg/Th17 induced by LPS or hypoxia with no difference between direct and indirect co-culture groups. Moreover, TGF-β1 levels in MSCs treatment whether upon LPS or hypoxia were much higher than LPS or hypoxia group. Meanwhile, neutralizing TGF-β1 with anti-TGF-β1 antibody inhibited the role of MSCs improving reduced Treg/Th17 upon LPS stimulation. T cell proliferative capacity in MSCs treatment group upon LPS was higher than that in LPS group. The effects of MSCs were significantly blocked by anti-TGF-β1 antibody.
CONCLUSIONS. The data suggested that LPS priming and hypoxia directly impact T lymphocyte differentiation favoring Th17 rather than Treg phenotype resulting to reduced Treg/Th17 in vitro. MSCs treatment could reverse the reduced Treg/Th17. The main mechanisms was attributed mainly to TGF-β1 secreted by MSCs rather than cell-to-cell contact.
GRANT ACKNOWLEDGMENT. This work was supported by the National Natural Science Foundations of China (grants 81571874 and 81501705), the Natural Science Foundation of Jiangsu Province of China (grants BK2014134).

076 - INDUCED-PLURIPOTENT STEM CELLS-DERIVED CONDITIONED MEDIUM ATTENUATES THE INFLAMMATION IN *E. COLI*-INDUCED SEPSIS

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INTRODUCTION. Sepsis is the major challenge to intensive care unit, which is a disaster to an individual suffering bacterial infection. Severe systematic inflammation associates with multiple organ failure contributed to the high mortality in septic cases. Regenerative cell therapy, such as mesenchymal stem cells (MSCs) and hematopoietic stem cells (HSCs), have been reported to attenuate the inflammation in sepsis, also to have benefit on the improvement of survival rate. However, the therapeutic effect of induced pluripotent stem cells (iPSCs) on sepsis is still unknown

and needs to be investigated.
OBJECTIVE. In this study, we aim to examine the potentials of iPSC-derived conditioned medium (iPSC-CM) as a novel treatment on gram-negative bacteria triggered sepsis in immuocompromised rats.
METHODS. Male SD rats of weight ranged between 450-550 grams were immunocompromised by intraperitoneal injection of cyclophosphamide (150mg/kg). After then, each rat received intramuscular injection of *E. coli* (1×10^9 cfu/rat) for inducting sepsis. For the iPSC-CM therapy, either prophylaxis (intraperitoneal injection of 1 mL iPSC-CM right after the *E. coli* was injected) or treatment (intraperitoneal injection of 1 mL iPSC-CM four hours after the injection of *E. coli*) method was used. Eight hours later of *E. coli* injection, each group of rats was routinely cured with ceftriaxone (30mg/kg) in normal saline, in addition of another 1 mL iPSC-CM by intraperitoneal injection. The survival rate of rats was compared between different groups, and the inflammation of each treatment was evaluated by the expression level of inflammatory marker. Also, the expression of several inflammatory genes was examined by semi-quantitative PCR.
RESULTS. The survival rate of septic rats was calculated at 72th hour after the inoculation of *E. coli* following the iPSC-CM based therapy. Either prophylaxis or treatment of iPSC-CM based treatment slightly improved the survival rate of rats, but there was no significance observed. The iPSC-CM based therapy reduced the infiltration of immune cells presented in bronchoalveolar lavage fluid (BALF) of sepsis rats. The iPSC-CM base therapy suppressed not only the expression of inflammatory genes (*1L-1b,mip2,IL-6*) but also the inflammatory protein (COX-2,MMP9) expression in the lung tissue of septic rat
CONCLUSIONS. In this study, a model of Gram-negative bacteria induced sepsis of immunocompromised rats was established. The iPSC-CM based therapy might reduce the infiltration of inflammatory cells in the lung tissue of septic rat. In addition, the iPSC-CM based therapy also showed benefit on the extension of the life of modeled animals which might be considered as a potential therapy accompanying with antibiotics.

077 - TRANSCRANIAL DOPPLER AS AN EARLY PREDICTOR OF DELERIUM IN SEPTIC PATIENTS AND ITS CORRELATION WITH JAGULAR VENOUS OXYGEN SATURATION

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INTRODUCTION. Impairment of cerebrovascular autoregulation is considered one of the most important mechanisms leading to cerebral hypo- or hyperperfusion in haemodynamically unstable septic patients. That may lead to Sepsis-associated delirium (SAD) which increases morbidity and mortality.
OBJECTIVE. To investigate the ability of Trans cranial Doppler (TCD) for prediction of delirium in septic patient and its relationship with jagular venous oxygen saturation (JVo2) levels.
METHOD. A prospective, observational study was carried out in the medical intensive care unit during the period of January 2015 to January 2016. Patients were admitted as soon as they were diagnosed with sepsis. On the first day we used a 3-MHz Trans cranial Doppler probe to measure the Blood velocity and Pulsatility index in the middle cerebral artery (VMCA) TCD was then repeated daily for 3 consecutive days. Simultaneously we measured r jugular venous oxygen saturation (JVO2) on the same side of the highest VMCA. Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) was done for each patient once per day throughout ICU stay and after 6 hours after stoppage of sedation in sedated patient.
RESULTS. Out of 159 patients , 91 developed delirium . APACHE score was higher in the delirium group . Patients who developed delirium had significantly longer ICU LOS 13.9 day's vs7.8 Delirium group had lower mean MCA velocity and higher pulsatility index at all times .Positive correlation was observed between Jvo2 and VMCA on day 2 (r=0.8), and on day 3 (r=0.69). There was a negative correlation between PI and JVo2 on day 2(r= -0.5) and day 3(r=-o.57). Roc curve analyses the ability to detect delirium with a cut off value for Jvo2 measured at day 3(Jvo2 3) of 53.5 % (sensitivity 100%, specificity 100%, $P < 0.05$), and a cut off value for the PI at day 3 (PI3) of 1.2.(AUC= 0.88, CI 95%, 0.83-0.9 $P < 0.05$vsensitivity 70%, specificity 100%).
CONCLUSION. Changes in TCD findings together with JVo2 levels are associated with the development of delirium in septic patients.

079 - RESPIRATORY VARIATIONS IN ELECTROCARDIOGRAPHIC R-WAVE AMPLITUDE DURING HYPOVOLEMIA BY INFERIOR VENA CAVA CLAMPING IN PATIENTS UNDERGOING LIVER TRANSPLANTATION

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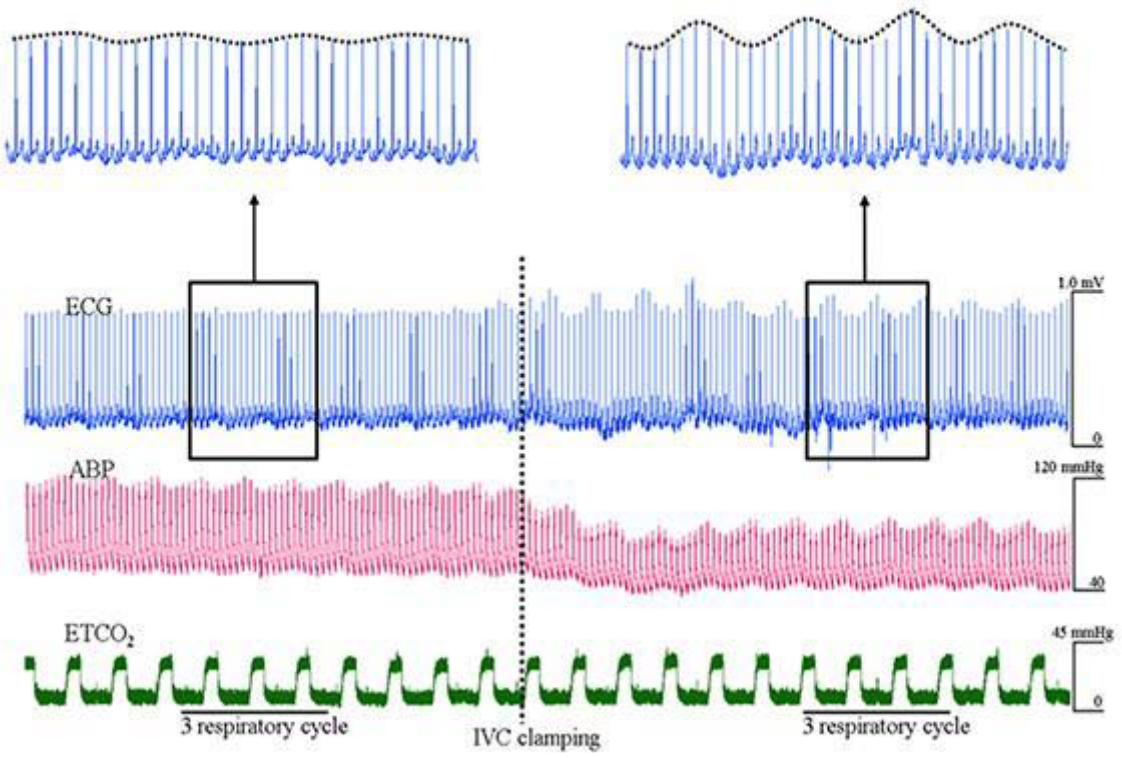
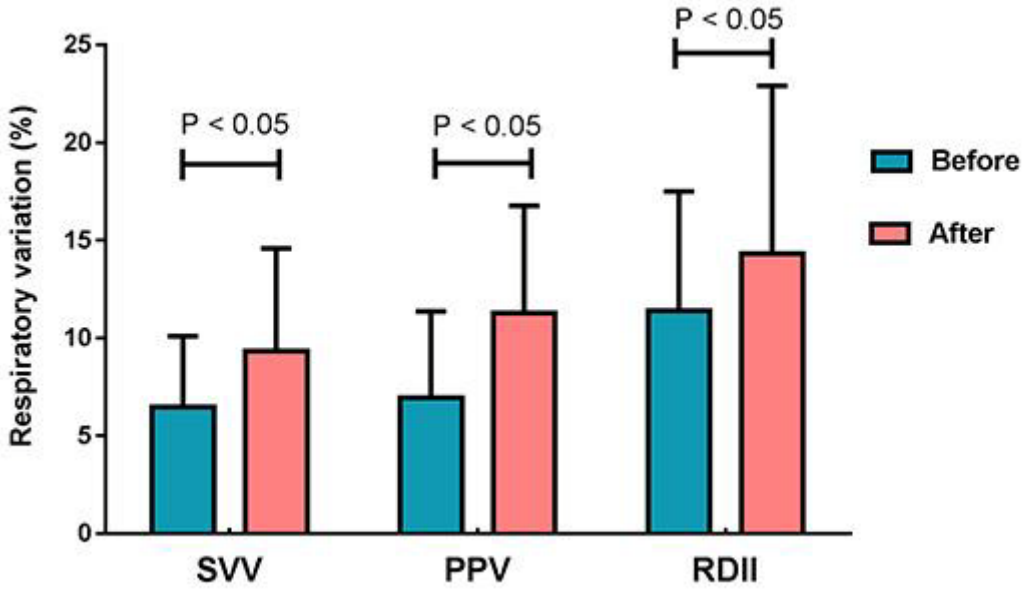
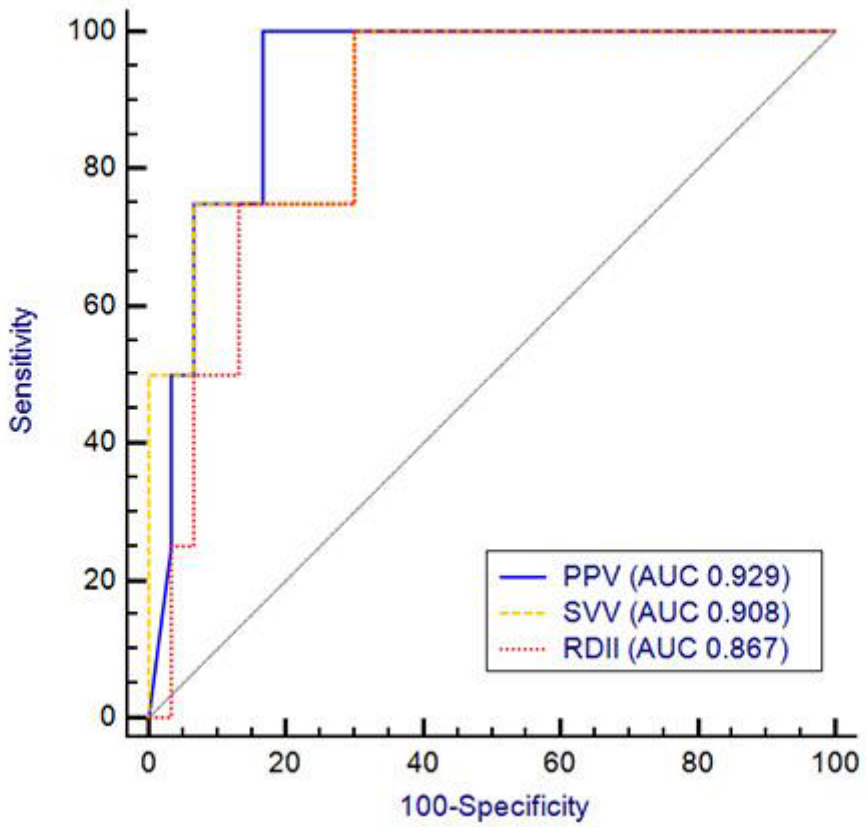
INTRODUCTION. The change of intraventricular volume could reflect electrocardiographic (ECG) R-wave amplitude and cardiopulmonary interaction induced by mechanical ventilation may generate respiratory variation in R-wave amplitude. The aim of this study was to examine whether the respiratory variation in ECG lead II R-wave amplitude(RDII) as dynamic index could predict intravascular volume status following inferior vena cava (IVC) clamping which induce to acute decrease in cardiac output and stroke volume undergoing liver transplantation (LT).
METHOD. We retrospectively investigated RDII before and after IVC clamping in 35 LT recipients. RDII was compared with other hemodynamic parameter from arterial waveform pressure analysis including cardiac output (CO_{FT}), cardiac index (CI_{FT}), stroke volume variation (SVV), pulse pressure variation (PPV), and stroke volume (SV_{FT}), and those from Swan-Ganz catheter including stat mode of continuous cardiac output and cardiac index (CCO_{stat}, CCI_{stat}), SV, stroke volume index before and after IVC clamping. We also compared RDII and other hemodynamic parameters in low (≤0.05μg/kg/min) and high (>0.05μg/kg/min) norepinephrine groups. A receiver operating characteristic (ROC) curve analyses with area under the curve (AUC) was used to assess the cutoff value of RDII for predicting cardiac output decrease >25%.
RESULTS. After IVC clamping, CO_{FT} and CCO_{stat} significantly decreased (P=0.005 and 0.004, respectively) while RDII significantly increased (P=0.005). The cutoff value and AUC of RDII predicting a decrease in CO_{FT} decrease > 25% were 38.9% and 0.867 with a specificity 70%, a sensitivity of 100% (95% confidence interval 0.706 - 0.958, P< 0.0001). RDII showed low sensitivity and specificity to predict CCO_{stat} decrease > 25% (AUC 0.532, 95% confidence interval 0.348 - 0.710, P=0.806). Furthermore, RDII changed significantly at low norepinephrine group, but not at high dose of norepinephrine (P=0.027 and 0.860 respectively).
CONCLUSION. We demonstrated that RDII could predict changes in cardiac output and have the possibility to be a noninvasive dynamic parameter measured in patients with hemodynamic fluctuation.



[Figure 1. After inferior vena cava (IVC) clamping, arterial blood pressure decreased sharply.]



[Figure 2. The change of variation of RDII, SVV or PPV during inferior vena cava (IVC) clamping]



[Figure 3. Ability of variation of RDII, SVV or PPV to predict a CO decrease > 25% (ROC curves)]

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080 - INITIAL VENOUS LACTATE LEVEL AT EMERGENCY DEPARTMENT AS A PREDICTOR OF MORTALITY IN SEVERE SEPSIS

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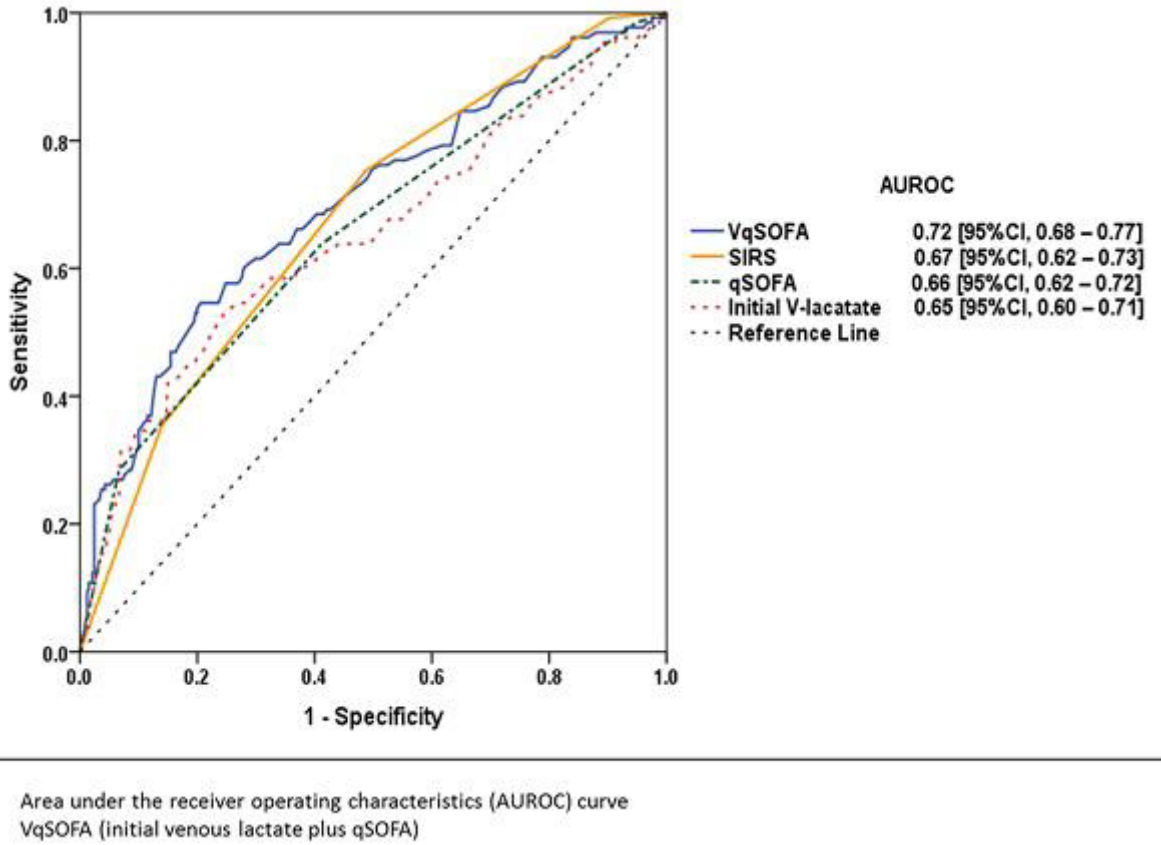
INTRODUCTION. Sepsis is the most common cause of death in critically ill patients. Most septic patients were detected and initially treated at emergency department. The effectiveness of early resuscitation was an important determinant of sepsis survival. Elevated serum lactate was an important marker of impaired tissue perfusion in septic patients. Venous lactate was easier and less painful than arterial samples, but there is limited data about venous lactate in determining outcome in septic patients.
OBJECTIVES. To determine the association between initial venous lactate and 28-day hospital mortality.
METHODS. This was a retrospective cohort study, single center study. We enrolled patients aged≥15 years who visited Ramathibodi emergency department with severe sepsis during August 2015 to March 2017. The predictive ability for mortality of initial venous lactate was compared with qSOFA score and SIRS criteria using area under the receiver operating characteristics (AUROC) curve. Multivariate analysis was performed to find independent predictors. Primary outcome was 28-day hospital mortality.
RESULTS. Of the 460 patients, 130 (28.3%) patients had 28-day hospital mortality. Independent predictors for 28-day hospital mortality were initial venous lactate (adjusted OR, 1.17 [1.09 - 1.24], P = 0.001) and qSOFA score (adjusted OR, 2.12 [1.58 - 2.83], P = 0.001). The initial venous lactate had a

modest ability to predict for 28-day hospital mortality (AUROC, 0.65 [95%CI, 0.60 - 0.71]). The different of ability to predict mortality was not statistically significant when compared between initial venous lactate, qSOFA score (p = 0.89) and SIRS criteria (p = 0.49). Combined initial venous lactate with qSOFA score was higher predictive ability (AUROC, 0.72 [95%CI, 0.68 - 0.77]).



[Receiver operating characteristic curves of predicted factors for 28-day hospital mortality.]

CONCLUSIONS. The initial venous lactate had ability to predict mortality. Use of combination initial venous lactate with qSOFA score was better than individual parameters.

KEYWORDS. Severe sepsis, Initial venous lactate, qSOFA, SIRS, Mortality

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Grants Acknowledgment:
The authors would like to thank all personnel and patients for helpful co-ordination.

081 - DIAGNOSTIC ACCURACY OF PROCALCITONIN COMPARED WITH SEPSIS-2 AND SEPSIS-3 CRITERIA IN EMERGENCY DEPARTMENT

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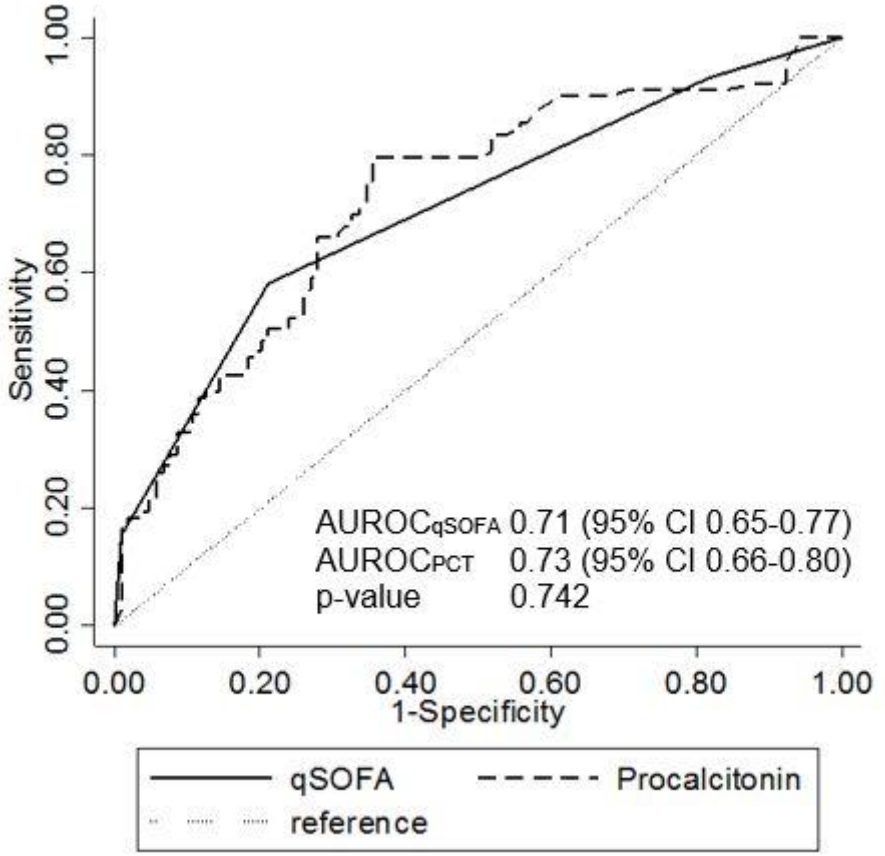
BACKGROUND. Procalcitonin (PCT) is a widely used sepsis biomarker due to its ability to early

predict septicemia. As PCT level is significantly correlated with SOFA in ICU setting, we postulate that PCT could be substituted for SOFA in assessing sepsis in an emergency department (ED). A limited study of tools for diagnosing sepsis using end organ failure has been conducted. Therefore, this study aims to compare the validity of PCT with Sepsis-3 and Sepsis-2 for diagnosing sepsis as an organ dysfunction.
OBJECTIVE. To evaluate the effectiveness of PCT, SIRS, qSOFA, SOFA in the diagnosis of sepsis, considering organ dysfunction.
METHOD. This prospective observational study was conducted in an ED, at one urban tertiary care hospital, Vajira Hospital, Thailand from June to September 2017. Eligibility criteria for inclusion were consecutive adults, age 18 and up, with presumed infection. Vital signs and the Glasgow Coma Scale (GCS) at nurse triage had been collected to access qSOFA, SOFA and SIRS, including blood test for PCT level. Sepsis was diagnosed by considering bacterial growth hemoculture result or end-organ dysfunction identified by one infectious disease specialist and one intensivist who were blinded to the objective of this study. The diagnostic efficiency of each tool has been analyzed in the context of the Area under the Receiver Operating Characteristic (AUROC), sensitivity and specificity.
RESULT. 207 ED participants were enrolled, 49.8% of which were diagnosed with sepsis. The diagnostic value of PCT was as effective as qSOFA. (AUROC 0.73 vs. AUROC 0.71, *p* 0.742). Compared to SIRS, the diagnostic efficiency was significantly higher for PCT (AUROC 0.58 vs 0.73, *p* 0.001). Sensitivity and specificity of qSOFA ≥ 1 was 93.2% and 18.27%. Sensitivity and specificity of qSOFA ≥ 2 was 58.2% and 78.85%. The diagnostic value of combining qSOFA ≥ 1 with PCT level ≥ 0.5 ng/mL performed better than qSOFA ≥ 2 (AUROC 0.72 vs. AUROC 0.69), with a higher sensitivity (69.9% vs. 58.3%).
CONCLUSION. To discriminate between sepsis and local infection, using PCT provided a more accurate diagnostic indication than SIRS. PCT performed effectively as qSOFA. However, the diagnostic efficacy of PCT combined with qSOFA was superior to solely using qSOFA.

[AUROC curve of SIRS and PCT for diagnosing sepsis]



[AUROC curve of qSOFA and PCT for diagnosing sepsis]

For Organ Failure	SIRS ≥ 2	qSOFA ≥ 2	SOFA ≥ 2	PCT ≥ 0.5 ng/mL	qSOFA ≥ 1 and PCT≥ 0.5 ng/mL
Sensitivity,%(95% CI)	96.1 (90.4-98.9)	58.3 (48.1-67.9)	83.5 (74.9-90.1)	75.7 (66.3-83.6)	69.9 (60.1-78.5)
Specificity,%(95% CI)	2.9 (0.6-8.2)	78.8 (69.7-89.2)	59.6 (49.5-69.1)	65.4 (55.4-74.4)	74.0 (64.5-82.1)
PPV,%(95% CI)	49.5 (42.4-56.6)	73.2 (62.2-82.4)	67.2 (58.3-75.2)	68.4 (59.1-76.8)	72.7 (62.9-81.2)
NPV,%(95% CI)	42.9 (9.9-81.6)	65.6 (56.6-73.9)	78.5 (67.8-86.9)	73.1 (62.9-81.8)	71.3 (61.8-79.6)
AUROC,%(95% CI)	0.50 (0.47-0.52)	0.69 (0.62-0.75)	0.72 (0.66-0.78)	0.71 (0.64-0.77)	0.72 (0.66-0.78)

[Diagnostic performance for Organ Failure]

082 - ASSESSMENT OF JUNIOR DOCTOR´S KNOWLEDGE OF THE NEW (SEPSIS-3) GUIDELINES IN A MAJOR UK TEACHING HOSPITAL

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INTRODUCTION. The original sepsis definitions based upon systemic inflammatory response syndrome criteria were updated in 2016 by an expert task force. The new (Sepsis-3) definitions reflect a better understanding of the pathobiology of the septic process [1]. In a major change, sepsis is now defined as "*organ dysfunction caused by a dysregulated host response to infection*". Organ dysfunction is represented by a change in the sequential organ failure assessment (SOFA) score. In addition a simple bedside variant using 3 parameters (quick or qSOFA) can be used to more promptly identify patients with suspected infection likely to have poor outcomes. As early identification of sepsis has the potential to improve outcome it is important, in our opinion, that first responder junior doctors are familiar with the new definitions.
OBJECTIVES. We aimed to assess the knowledge of the Sepsis-3 definitions in a cohort of junior doctors within the Queen Elizabeth University Hospital, Glasgow, UK.
METHODS. We conducted a survey in real time of foundation doctors who were in their first year of practice. As this was an assessment of their knowledge they were not allowed to consult external resources.

Can you define the SIRS criteria?
Can you define sepsis/severe sepsis/septic shock?
Were you aware that the definitions for sepsis have substantially changed this year?
Do you know what the updated version of these changes is called?
What is the new definition of sepsis?
How is organ dysfunction identified in the new definition?
How is septic shock now defined?
Under the new definitions, what should we use qSOFA for?
Can you define any of the 3 components of qSOFA?

[Survey Questions]

RESULTS. 33 Foundation doctors participated. Overall knowledge of the old and new sepsis definitions was poor. Only 36% of the doctors correctly defined the previous SIRS criteria with many incorrectly including blood pressure. 57% of doctors were aware that the sepsis definitions had changed. Nobody surveyed was able to state the name of the new definitions or correctly define them. 6% were aware of potential of q-SOFA and recall some or all of the variables.
CONCLUSIONS. The results of the survey are disappointing. Junior doctors are most likely to be involved in the early recognition, escalation and management of septic patients. These results have been the catalyst for an addition to the hospital´s education programme. A new online sepsis module education will be made available. This will highlight the sepsis definition changes and the use of the qSOFA at the bedside. We will undertake a further survey in a year's time to assess the impact of the education module and its effect on the referral rate of the septic patient to critical care.
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GRANT ACKNOWLEDGEMENT: This work was made possible thanks to an award from the Fiona Elizabeth Agnew Trust (FEAT).

083 - PREDICTION OF FLUID RESPONSIVENESS IN THE IMMEDIATE POST-OPERATIVE PERIOD OF CARDIAC SURGERY

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BACKGROUND. Fluid replacement is the cornerstone of management in the postoperative period of cardiac surgery. Yet only 50% of patients benefit from fluid loading while the rest may suffer from the danger of overhydration. Prediction of fluid responsiveness aims to identify those who are truly volume-deficient (responders) so they may be given adequate hydration. Several predictors were found to have variable degrees of accuracy and recommendations for use in different clinical settings. This study aimed to identify and compare the parameters that predict fluid responsiveness in post-cardiac surgery patients.
METHODOLOGY. A total of 101 patients were included in this prospective cohort study. Baseline hemodynamic parameters were recorded after surgery. An 8 mL/Kg IV fluid challenge was given and a repeat hemodynamic assessment was done. Patients with an increase in stroke volume of ≥15% were identified as fluid responders. Multivariate analysis was used to identify independent predictors of fluid responder status. Sensitivity and specificity analyses were done to determine the predictive accuracy of each parameter.
RESULTS. The rate of fluid responsiveness in this study was 54.5%. Independent predictors were: central venous pressure (CVP) ≤6 mmHg (p=0.001), pulmonary artery occlusion pressure (PAOP) ≤12 mmHg (p=0.016), PAOP increase by ≥7 mmHg (p=0.002), pulse pressure variability (PPV) >12% (p< 0.005), PPV decrease by >5% (p=0.049) and weight (p=0.04). PPV was the most sensitive (92%) and specific (74%); while PAOP was the least sensitive (70%) and CVP the least specific (51%). PPV had the highest ability to discriminate fluid responders (AUC 0.83) compared to PAOP (AUC 0.21) and CVP (AUC 0.40) (p< 0.0005).
CONCLUSION. PPV (a dynamic index) is superior to CVP and PAOP (static indices) in discriminating fluid responders in adult patients who underwent cardiac surgery. PPV is the favored tool to guide initiation of fluid therapy in this clinical setting.

084 - INTRAOPERATIVE CARDIAC ARREST & MAJOR NON-CARDIAC SURGERY ADMISSION TO THE TGENERAL SURGICAL ICU.

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INTRODUCTION. Intraoperative cardiac arrest is one of the worst unfavorable outcome associated with major non cardiac surgery. Knowing about predictors and outcome may help improve quality care of these patients.
OBJECTIVE. To study incidence, characteristics, predictors & outcome of intraoperative cardiac arrest during major non-cardiac surgery.
METHOD. This prospective observational study was done in all intraoperative cardiac arrest patients admitting to the 14 beds general SICU of the third referral university hospital during Jan 2013-Sep 2017. Information including: patient demographic data, comorbidities, preoperative medications, detail & complications associated with anesthesia & surgeries, type of cardiac arrest, epinephrine dose, time of ROSC, targeted temperature management (TTM), neurological outcome, 7 & 90 days mortality.
RESULT. There were 92 post cardiac arrest patients admitted to the ICU (3.6% of all ICU admission) with ROSC time 5 ± 27 mins) with 7 & 90 days mortality were 16.3% & 41 % respectively. Twenty nine patients (31.5%) had unfavorable neurological outcome. One third of the cardiac arrest were PEA and 48% were VT & VF. Thirty eight percent of the causes of cardiac arrest were associated with airway either during intubation, immediate after extubation or during airway surgery. Hypovolemic shock (28%) was the second most frequent cause either from severe bleeding or septic shock. Eleven patients were cardiac arrest from pulmonary embolism and 4 patients from anaphylaxis. Three fourth of the patient did not have TTM because of unfavorable condition such as severe bleeding. But there were not significant different of the neurological outcome between TTM of 33 °C & 36 °C (p< 0.05). One patient received ECPR & 2 patients had ECMO support with good outcome. Patients who survived with good neurological outcome were younger, significant less initiate time of chest compression, less ROSC time, less vasopressor in the first 24 hours, less underlying neurological

disease, higher Hb and received TTM.
CONCLUSION. Intraoperative cardiac arrest were significant associate with poor perioperative outcome in patient undergoing major non-cardiac surgery. Effort should be made to prevent this catastrophic event especially who underwent difficult airway management. Immediate effective chest compression and TTM may help improve neurological outcome in these patients.

085 - CLINICAL PROFILE AND OUTCOMES OF MDR GRAM NEGATIVE INFECTIONS ACQUIRED FROM COMMUNITY AND HOSPITALS - AN INDIAN PERSPECTIVE

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INTRODUCTION. MDR infections in the ICU are associated with increased mortality, morbidity and economic burden. There is a tremendous need for proper studying of MDR infections in community as well.[1]
OBJECTIVES. To describe site specific MDR infection rates and describe the microbiological and antibiotic resistance profiles of infecting pathogens, their impact on mortality.
METHODS. We conducted a six month retrospective study of MDR infections in ICU patients of a tertiary care centre from January to june 2017. . Data were obtained from the medical records department. Information like patient characteristics, microbiologic data, duration of ICU and hospital stay, antibiotic used, resistance pattern and mortality rates were collected.[1]
RESULTS.

MALE	36(81.81%)	15(60%)
SOURCE COMMUNITY ACQUIRED HOSPITAL ACQUIRED	4(9.09%) 40(90.9%)	3(12%) 22(88%)
INITIAL ANTIBIOTIC BL/BLI CARBAPENEMS COLISTIN	30(68.18%) 13(29.54%) 1(2.27%)	13(52%) 10(40%) 2(8%)
SITE VAP CAUTI CLBSI	32(72.72%) 9(20.45%) 3(6.81%)	20(80%) 3(12%) 2(8%)
ORGANISM K.Pneumoniae A.baumani P.aeruginosa E.coli	19(43.18%) 16(36.36%) 7(15.8%) 2(4.54%)	16(64%) 9(36%) 0 0
ICU LOS	12.93 DAYS	28.92 DAYS
HOSPITAL LOS	26.22 DAYS	30.30DAYS

[B.survivor vs C.non-survivor analysis]

MALE	46(74.19%)	5(71.4%)
AVERAGE AGE	60.1YEARS	58.86YEARS
VAP CAUTI CLBSI	49(79.03%) 8(12.9%) 5(8%)	3(42.85%) 4(57.14%) 0

K.PNEUONIAE A BAUMANII P. AERUGINOSA E.COLI	31(50%) 24(38.70%) 7(11.29%) 0	4(57.14%) 1(14.28%) 0 2(28.57%)
INITIAL ANTIBIOTIC BL/BLI CARBAPENEMS COLISTIN	37(59.67%) 22(38.70%) 3(4.83%) 0	6(85.71%) 1(14.28%) 0
ICU LOS	19.74DAYS	9.71DAYS
HOSPITAL LOS	29.58DAYS	12.14DAYS

[B.HOSPITAL ACQUIRED (62)VS C.COMMUNITY ACQUIRED(7)]

Out of 69 cases of MDR infections in the ICU, males constituted 81.81% of survivors and 60% among the non-survivors. Non-survivors were older than the survivors (64.36yrs vs 57.48yrs). DM and hypertension were equally distributed among the survivors and hypertension more in the non-survivors. Most of the infections were hospital acquired and there were a significant number of MDR cases from the community also. BL/BLI was the common initial antibiotic as per the local antibiogram. Pneumonia was the most common infection and K. pneumoniae was the most common MDR organism. Non-survivors had longer ICU and hospital length of stay. 10% from community, which is an alarming situation.

CONCLUSIONS. MDR bugs are associated with increased mortality, morbidity and prolonged ICU and mechanical ventilation days, thereby adding to increase in healthcare costs. Most alarming finding was the increasing and higher incidence of MDR infections acquired from the community.

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086 - MODULATION OF MMP1 AND MMP10 GENE BY PRO-INFLAMMATORY MACROPHAGE IN PULMONARY ARTERIAL HYPERTENSION VIA THE JNK, P38, AKT AND STAT3 SIGNAL PATHWAYS

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BACKGROUND. Pulmonary arterial hypertension (PAH) is characterized by vascular remodeling of pulmonary arteries, which is associated with abnormal proliferation of pulmonary arterial smooth muscle cells, deposition of extracellular matrix proteins and perivascular inflammation. Matrix metalloproteinases (MMPs), a family of over 30 members with highly conserved structural characteristics, are critical to the maintenance of the homeostasis of extracellular environment. Fewer studies have discussed the role of various MMPs in the pathogensis of PAH. Hence, the regulation of MMPs expression and underlying mechanism are unclear.

AIM. In this study, we explored the expression of MMP1 and MMP10 in PAH, and investigated the mechanisms involved in the regulation of MMP1 and MMP10.

METHODS. This study compared the MMP1 and MMP10 expression in the serum between healthy donors and PAH patients. The primary cultured human peripheral blood mononuclear cell(PBMC)-derived macrophages from PAH patients or healthy donors were subjected to the induction of MMP1 or MMP10 expression by LPS/IFN stimulation, and analyzed the expression of mRNA and protein. The

human PBMC-derived macrophages, in combined with chemical inhibitors (including ERK1/2, AKT, p38, JNK, STAT1 and STAT3) were used to investigate the signaling pathways involved in the regulation of MMP1 and MMP10. For *in vivo* study, the lung specimens from monocrotaline (MCT)-induced PAH rat were examined for the expression of MMP1 and MMP10.
RESULTS. The result showed that, in human serum, the level of MMP1 and MMP10 was significantly higher in PAH patients than the healthy donors. The elevated expression MMP1 and MMP10 was confirmed by *in vitro* cultured PBMC-derived macrophages. Under the stimulation of LPS/IFN, macrophages derived from PAH patients showed robust up-regulated expression of MMP1 and MMP10. Following the treatment of chemical inhibitors, the expressions of MMP1 and MMP10 were significantly suppressed by p38 or JNK or AKT or STAT3 inhibitors, while the inhibition of ERK or STAT1 signaling had no effects on MMP1 and the inhibition of ERK signaling had no effects on MMP10. For *in vivo* evidence, the expression level of MMP1 and MMP10 protein was critically elevated in the lung tissue of MCT-induced PAH rats compared to the control group. Immunohistochemical staining indicated the co-localization of MMP1 or MMP10 molecule with the COX-2-positive macrophages, which meant the expression of MMP1 and MMP10 was highly associated with the pro-inflammatory macrophage phenotype.
CONCLUSION. In this study, we provided that MMP1 and MMP10 were significantly up-regulated in pro-inflammatory macrophages in cultured human PBMC-derived macrophages and MCT-induced PAH rat model. The elevated MMP1 and MMP10 levels in the serum of PAH patients might be developed as useful biomarkers for PAH. We also indicated that blocking of JNK, p38, AKT and STAT3 signaling pathways may be a new strategy for PAH treatment.

087 - HEMOPHAGOCYTIC LYMPHOHISIOCYTOSIS: LIFE THREATENING COMPLICATION OF DENGUE. DIAGNOSIS, TREATMENT AND OUTCOME.

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INTRODUCTION. Hemophagocytic Lymphohistiocytosis (HLH) was first described in 1952 by Farquhar and Claireaux[1] HLH is caused by various malignancies,infections,autoimmune or hereditary diseases which cause dysreguated NK cells response leading to fatal clinical scenario. Dengue is caused by DENV 1-4 viruses which is transmitted by mosquito resulting in fever with myalgia,rash,bone pains with or without multiorgan failure[2] HLH is seldomly diagnosed in adults that too in dengue infections resulting in high mortality[3,4]
OBJECTIVE. 1.To study the clinical picture and treatment modalities among dengue associated Hemophagocytic Lymphohistiocytosis (HLH) in adults
2.Outcome
MATERIALS AND METHODS. Retrospective case series of six patients admitted in tertiary care ICU in Pune,Western India who were diagnosed as Dengue fever as per clinical findings and laboratory reports, with persistent systemic inflammatory response,drop in 2 or more cell lines with or without multi organ failure. Investigations like hemogram, Dengue IgM,IgG,NS1 antigen,ferritin, triglycerides,LDH,fibrinogen, liver function tests, abdominal sonography were done. Apart from supportive treatment of Dengue as per WHO guidelines, patients were treated with dexamethasone in all mild to moderate cases and severe cases needed IvIg. Additional etoposide was given in one case
RESULTS. Total 5 males and 1 female, average age 46.5 years. All patients satisfied HLH 2004 criteria as they were proven dengue fever with raised ferritin, triglycerides, splenomegaly, bicytopenia, deranged liver function tests, 2 patients had cerebral symptoms also. One patient required invasive ventilation,5 patients required platelet transfusionand nobody required renal replacement therapy.Out of six patients, 5 survived while one succumbed. Average APACHE II score was 13 and Predicted mortality rate as per APACHE II was 17%.
CONCLUSION. Dengue with persistent fever in toxic patient, with or without multi organ failure needs to be investigated for HLH as mortality is very high. High index of suspicion, early diagnosis and treatment is essential in dengue associated
Hemophagocytic Lymphohistiocytosis (HLH). Early diagnosis and treatment may improve survival.
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GRANT ACKNOWLEDGMENT. We did not received any grants.

088 - EMR BASED SEPSIS ALERT FOR EARLY DETECTION OF SEPSIS IS PEDIATRIC PATIENTS.

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INTRODUCTION. Early recognition of sepsis and treatment bundles improves outcomes such as decreased morbidityand mortality. EMR pediatric sepsis alerts triggered off of patient vital signs prompt nurses torecognize signs and symptoms of sepsis and escalate care as needed. We had an experience with amissed sepsis case with a bad outcome.
METHODS. We started initially with a paper based version of the sepsis alert. After one year it was changed to anEMR based sepsis alert that would fire based on abnormal vital signs based on age. The alert wouldfire up for the nurses to choose an appropriate action. The alert was active in PICU, genera; pediatric floor and Pedaitric ED. NICU and Cardiac units were excluded.
RESULTS AND DISCUSSION. We had a total of 59 cases with the diagnosis of severe sepsis/Septic shock from Oct 2014-July 2017.The total number of patients for the same time period was approximately 28316 patients (including ER encounters, PICU and general Pediatric floor admissions). We had total of 1877 unique sepsisalerts. The sensitivity and specificity of our alert were : 73.5 and 93.5% respectively. We are currently working on a two stage alert to improve the sensitivity os our existing alert. The alert will have more decision support tools to help the provider take the appropriate actions in a timely manner. This will be an interruptive alert, i.e. the provider has to take an action plan and can not dismiss the alert.

089 - EFFICACY OF EPINEPHRINE FOR NOREPINEPHRINE-REFRACTORY SEPTIC SHOCK

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INTRODUCTION. Septic shock refractory to norepinephrine is high mortality, and its appropriate management is unknown. Adding epinephrine to norepinephrine is effective in some cases. However, characteristics that predicts good response to additional epinephrine have not been reported.
OBJECTIVE. In this retrospective study, we investigate norepinephrine-refractory septic shock patients who were administered epinephrine. We compared patients who responded to administration of epinephrine and those who did not.
METHOD. This was a single-center retrospective observational study. Eligible subjects were septic shock patients who were admitted to our ICU l and administered continuous epinephrine between 1/1/2014 and 12/31/2017. Subjects were included if they had hypotension(mean arterial pressure ≦ 65 mmHg) at the time when epinephrine were started. We judged the responce to the administration of epinephrine as 7 day survival without mechanical circulatory support. Data from those who responded to epinephrine and poor did not were compared using non-parametric Mann-Whitney U test.
RESULT. Of the 35 eligible patients, 32 met the inclusion criteria. The age of patients was 61.8 ± 16.7 years(mean ± SD). The APACHE II score and SOFA score were 33.6 ± 7.88 and 13.3 ± 3.96 points. The dose of norepinephrine at baseline were 0.226 ± 0.08 μg/kg/min, and initiation dose of epinephrine were 0.08 ±0.067 μg/kg/min. The patients who responded to administration of epinephrine was 23 patients, while while those who did not was9 patients. Early hemodynamic response (3hours after administration of epinephrine) associated with good outcome (Odds ratio 84, 95% CI: 6.66-1059, p=0.0006). Low PaO_2-FiO_2 ratio(p= 0.006), low platelet(p=0.003), low arterial blood pH(p= 0.0112), and longer time after admission to the ICU before epinephrine administration(p= 0.004) were associated with poor outcome.
CONCLUSION. Early hemodynamic response associated with short-term prognosis. Epinephrine may effective for norepinephrine-refractory septic shock, especially administered in earlier phase of treatment, while acidemia, low platelet, low PaO_2-FiO_2 ratio may predict poor responce.

090 - SUPPLEMENTATION OF RECOMBINANT ANTITHROMBIN CONCENTRATES ON SEPTIC ANTITHROMBIN DEFICIENCY MIGHT HELP TO IMPROVE THE SOFA SCORE AND DIC SCORE IN COMPARISON WITH PLASMA-DERIVED ANTITHROMBIN CONCENTRATES.

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INTRODUCTION. In Japan, supplementation of recombinant antithrombin III concentrates (r-AT) has been approved for DIC-associated antithrombin III deficiency since 2015. Before then, 1500 IU/day of plasma-derived antithrombin concentrates (p-AT) was commonly administered for three consecutive days, regardless of patient body weight. However, the approved dose of r-AT 36 IU/kg is supposed to be equivalent to 30 IU/kg of p-AT, the dose can be increased with the patient´s body weight. Therefore, it is anticipated that r-AT group could provide a better treatment effect than a p-AT group.
OBJECTIVES. The aim of this study is to compare the treatment effect on plasma antithrombin III levels and the Japanese Association for Acute Medicine (JAAM) DIC score, and Sequential Organ Failure Assessment (SOFA) score between the r-AT group and p-AT group.
METHODS. This study was performed in a single university hospital in Japan. A total of 20 septic antithrombin deficiency patients who were administered either r-AT(n=11) or p-AT(n=9) for three consecutive days were retrospectively analyzed in terms of patient characteristics; the dose of supplemental antithrombin concentrates; plasma antithrombin activity; JAAM DIC score; and SOFA score on day 0, day 3, and day 6.
RESULTS.
1) The initial dose of r-AT was significantly higher than that of p-AT. On the other hand, whereas the converted dose of r-AT (equal to the initial dose/1.2) was higher than the initial dose of p-AT without significance.
2) The ICU survival rate in the r-AT group exhibited an improving tendency despite statistical significance compared to that of p-AT.
3) The serial changes of plasma antithrombin III levels rapidly increased in both groups.
4) JAAM DIC scores and SOFA scores in the r-AT group, in contrast to those in the p-AT group, revealed significant improvement.
CONCLUSION. The results of this study raised the possibility that the supplementation of r-AT might provide the advantage of improving DIC and multiple organ failures more than the supplementation of p-AT.