MR-proADM

Literature Review

The rapid risk assessment and early warning of developing complications in critically ill infectious patients
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Clinical studies

This literature review provides a brief overview of the use of MR-proADM in the risk assessment of critically ill infectious patients, and highlights some of the main benefits associated with the biomarker in this group of patients.

5 main findings are supported in the studies outlined in this booklet:

- Elevated or increasing MR-proADM levels in infectious patients admitted to the ED, may benefit most from an immediate transfer to the ICU
- MR-proADM provides a more accurate risk assessment than other biomarkers and current clinical scores, including PCT, CRP, Lactate, SOFA and APACHE II
- MR-proADM levels are significantly elevated in response to viral infections compared to other commonly used septic biomarkers
- MR-proADM concentrations significantly and uniquely rise in response to antimicrobial treatment failure, giving the treating physician an early indication concerning overall treatment response
- Increasing MR-proADM concentrations during hospitalization can indicate the development of additional adverse complications, such as nosocomial infections, organ failure and organ dysfunction, or indeed an increasing likelihood of mortality
Clinical actions

Accordingly, the following clinical actions can be deduced from the findings in the literature. These include:

An earlier transfer to the ICU from the ward or emergency department, based on MR-proADM measurements and clinical signs, may be made before the patient significantly deteriorates and increased treatment intensity becomes less effective, thus maximizing patient safety and potentially driving down in-hospital mortality.

A more accurate risk assessment on admission and over the course of a week can highlight changing patient risk and determine those patients which are in need of most urgent treatment. Furthermore, increasing MR-proADM concentrations during hospitalization can provide the earliest warning of any deterioration in the clinical status of the patient.

When used alone, diagnostic biomarkers may underestimate the severity of mixed septic infections, such as bacterial and viral, therefore the addition of MR-proADM ensures that the severity of all critically ill infectious patients is correctly determined at the earliest time point possible.

The combination of MR-proADM and PCT may be useful in helping physicians determine the earliest discontinuation of antimicrobial therapy if patients with initially low infectious levels respond well to antibiotic therapy. Furthermore, testing MR-proADM at baseline and during antimicrobial therapy may be useful in determining if a patient's clinical signs and symptoms are related to sepsis and a BSI, or to an additional non-infectious cause.

Knowledge that a patient will not develop additional adverse complications may result in an early transfer from the ICU onto a less acute ward, or conversely, elevated MR-proADM levels can indicate a developing adverse complication, which should result in further diagnostic investigations and treatment, thus ensuring maximal patient safety.
The predictive value of adrenomedullin for development of severe sepsis and septic shock in Emergency Department

Chen and Li
Biomed. Research International vol. 2013, Article ID 960101, 6 pages

Rationale
To evaluate the ability of adrenomedullin on ED admission as a predictor of organ dysfunction and shock in septic patients.

Patients/Methods
372 patients who fulfilled the sepsis criteria defined by the ACCP/SCCM were enrolled and followed for up to 3 days. Organ functions were reassessed at the end of the 3-day follow up or when clinical status deteriorated. APACHE II and SOFA scores, as well as venous blood samples, were obtained at the time of ED admission.

Results
- Adrenomedullin levels on admission to the ED were significantly different between patients who progressed to severe sepsis/septic shock, and those that did not (p < 0.0001)
- No other variable, including age, gender, comorbidity, infection site, APACHE II score or SOFA score, could predict the development to severe sepsis/septic shock
- The AUC for adrenomedullin to predict such a development was 0.847

Current clinical severity scores, such as APACHE II or SOFA, were not able to independently predict deterioration in septic patients on admission to the ED, as opposed to adrenomedullin concentrations, which were higher in patients that consequently deteriorated. Accordingly, patients who show increased levels of adrenomedullin in the ED may benefit from an earlier transfer to the ICU in order to initiate a higher treatment intensity, at the earliest possible time.
Adrenomedullin is a useful biomarker for the prognosis of critically ill septic children

Jordan et al.
Biomark. Med. 2014; 8(9): 1065-72

Rationale
Measurement of MR-proADM levels in critically ill septic PICU patients to determine its usefulness in predicting in-house mortality compared to other biomarkers commonly used, such as PCT and CRP. The degree of information provided by these biomarkers was also compared to other clinical scores of severity (PRISM III).

Patients/Methods
95 patients were admitted to a PICU over 12 months, and MR-proADM, PCT and CRP were measured from the same blood sample drawn immediately on admission. Clinical data such as age, sex, reason for hospitalization, PRISM III, the need for mechanical ventilation and/or the use of inotropes was also recorded.

Results
- Median concentration values of MR-proADM were significantly higher in patients requiring mechanical ventilation ($p = 0.035$), inotropes ($p = 0.001$) and in cases of in-hospital mortality ($p = 0.025$)
- MR-proADM levels showed a significant correlation with PRISM III scores
- PRISM III and MR-proADM levels had higher AUCs for survival prediction (0.78 and 0.77 respectively) than either PCT (0.67) or CRP (0.63)
- Only MR-proADM could significantly estimate PICU stay, where the mean length of PICU stay was significantly greater for patients with MR-proADM values above a cut-off of 2.2 nmol/L, than for those below this cut-off value

MR-proADM provided the most accurate risk assessment over the first 7 days of ICU admission compared to all other biomarkers, and exhibited the strongest correlation with organ failure, thus allowing any developing complications to be investigated and treated before any potential clinical deterioration.
Sustained value of proadrenomedullin as mortality predictor in severe sepsis

Andaluz-Ojeda et al.  

Rationale
To compare commonly used biomarkers and clinical severity scores, such as PCT, Lactate, CRP, MR-proADM, APACHE II and SOFA scores, to predict ICU mortality over the first 7 days, and to determine the association between biomarker levels and SOFA scores over the same period.

Patients/Methods
71 patients with severe sepsis or septic shock were admitted to the ICU from October 2013 to July 2014. Biomarker values were measured in the first 24 hours following ICU admission, and again on day 3 and day 7.

Results
MR-proADM was the only biomarker to:
- show significant differences between survivors and non-survivors over the three time points analyzed
- show the highest AUCs for mortality prediction, increasing from 0.75 on admission to 0.84 on day 7
- preserve the diagnostic accuracy for predicting mortality in the ICU over all time points
- show the strongest association with the extent of organ failure at all the time points evaluated

An MR-proADM cut-off of 0.94 nmol/L was determined on admission to help predict outcome. No patients with MR-proADM levels below this cut off died within the first 28 days following admission to the ICU.

MR-proADM provided the most accurate risk assessment over the first 7 days of ICU admission compared to all other biomarkers, and exhibited the strongest correlation with organ failure, thus allowing any developing complications to be investigated and treated before any potential clinical deterioration.
Usefulness of several biomarkers in the management of septic patients: C-reactive protein, procalcitonin, presepsin and mid-regional pro-adrenomedullin

Enguix-Armada et al.

Rationale
To compare the diagnostic and prognostic value of biomarkers and clinical severity scores such as CRP, PCT, Presepsin, MR-proADM, SOFA and APACHE II in the management of septic patients during the first 24 hours after ICU admission.

Patients/Methods
388 patients were admitted to the ICU, of which 246 met the criteria for severe sepsis or septic shock. Biomarker values were measured in the first 24 hours following ICU admission only, and survival analysis checked for proportional hazard (Cox) regression for independent continuous variables.

Results
- PCT exhibited the highest AUC for sepsis diagnosis (0.989) with MR-proADM showing the least diagnostic ability (0.815)
- However, MR-proADM was the only biomarker to show a significant prognostic probability value for mortality on admission ($p = 0.0003$), compared to all other biomarkers or clinical scores
- MR-proADM also showed a significant difference for stratifying the type of sepsis (severe sepsis versus septic shock; $p < 0.001$)
- A cut-off value of 1.2 nmol/L for survival and septic shock on admission was developed for MR-proADM, with a probability value of the log-rank test of $p = 0.0012$

Whilst PCT exhibited the highest accuracy for sepsis diagnosis, MR-proADM proved to be the only risk assessment score significantly associated with the risk of mortality upon ICU admission, thus allowing patients with a poorer prognosis to be identified earlier for a more intensive treatment strategy and investigation.
Diagnostic and prognostic role of procalcitonin (PCT) and MR-pro-Adrenomedullin (MR-proADM) in bacterial infections

Angeletti et al.
APMIS 2015 Jun; aop

Rationale
To evaluate the added benefits in the diagnosis, antibiotic therapeutic response and prognosis of bacterial infections when combining PCT and MR-proADM biomarker measurements.

Patients/Methods
182 patients with a suspected or defined diagnosis of bacterial infection were enrolled between October 2012 and March 2014. PCT and MR-proADM were measured in all patients on admission, at 12 - 24 hours and on the third or fifth day of antibiotic therapy.

Results
Average values of PCT and MR-proADM in severe sepsis and septic shock patients, calculated on the third to fifth day from the start of antibiotic therapy indicated that:
- PCT values did not show a statistically significant decrease in non-responding patients after antimicrobial therapy
- However, a statistically significant difference was found in MR-proADM measurements
- MR-proADM was unique in showing increasing concentrations amongst non-responders
- PCT values did not show a significant difference between septic survivors or non-survivors on admission or after 3-5 days
- MR-proADM values for survival were significantly different for sepsis patients on admission ($p = 0.0001$), and for sepsis ($p < 0.0001$) and severe sepsis/septic shock patients ($p < 0.0001$) after 3 - 5 days

The rational use of these two molecules in combination adds information concerning the effectiveness of the antibiotic therapy and timing, as well as on the prognosis of the infections, allowing the clinician to optimize the clinical management of the patient for both localized and systemic bacterial infections.
The utility of Proadrenomedullin and Procalcitonin in comparison to C-reactive protein as predictors of sepsis and bloodstream infections in critically ill patients with cancer

Debiane et al.

Rationale
Investigation of the role and utility of MR-proADM and PCT in comparison to CRP as biomarkers for the diagnosis, prognosis and therapeutic response in febrile, critically ill patients with cancer.

Patients/Methods
114 critically ill patients with cancer who were febrile on admission or became febrile during the course of their stay on the ICU. Biomarker levels were tested less than 24 hours from the onset of fever and repeated 4 - 7 days thereafter. Patients were microbiologically indentified as to whether they had a documented bacterial, fungal or viral infection. Patients were evaluated for clinical and microbiological response to antimicrobial therapy and the outcomes correlated with the biomarkers tested.

Results
In evaluating the patients’ response to antimicrobial therapy, it was found that:

- MR-proADM levels significantly decreased from baseline to follow-up in responders (p = 0.002), although concentrations significantly increased in non-responders (p = 0.0001)
- PCT levels significantly decreased in responders (p = 0.002) but did not significantly change in non-responders (p = 0.38)
- The AUC to predict a favorable response to antimicrobial therapy among all febrile patients was 0.79 for MR-proADM and 0.32 for PCT. In patients with documented infections, the AUC to predict response to therapy increased to 0.81 for MR-proADM and 0.73 for PCT

MR-proADM concentrations significantly and uniquely increased in patients who did not respond to antimicrobial therapy. Improvement in the management of these patients may therefore translate into improved outcomes, reduced mortality and the prevention of unnecessary diagnostic and therapeutic measures.
Persistent high level of circulating midregional-proadrenomedullin and increased risk of nosocomial infections after septic shock

Guignant et al.
J. Trauma Acute Care Surg. 2012 Jan; 72(1): 293-6

Rationale
Patients who develop septic shock are subsequently at risk of developing nosocomial infections (NIs), otherwise known as hospital-acquired infections (HAI). The current clinical challenge is to identify patients at risk of infection before the onset of microbial development, and accordingly, biomarker and clinical severity scores such as CT-proAVP, CT-proET-1, MR-proANP, MR-proADM, SOFA and SAPS II were tested to predict the development of NIs.

Patients/Methods
98 patients with septic shock were admitted to the ICU where the onset of septic shock was defined by the initiation of vasopressive therapy. Nosocomial infections were defined as infections (such as pulmonary, urinary tract, bloodstream and catheter-related) that occurred 48 hours after ICU admission and up to ICU discharge. SAPS II and SOFA scores were recorded on days 1 - 2 and 3 - 4, and biomarker measurements on days 1 - 2, 3 - 4 and 5 - 7.

Results
- No significant differences between patients with NIs and those without were observed for age, gender, number of comorbidities, SOFA, SAPS II, CT-proET-1, CT-proAVP or MR-proANP scores
- Significantly elevated MR-proADM concentrations were measured in patients who went on to develop NIs

Patients identified with the potential to develop nosocomial infections could benefit from focused strategies aimed at reducing infectious risk, such as the intensive screening of infections, the limitation of other risk factors, or therapeutic strategies aimed at boosting immune functions.
Performance of pro-adrenomedullin for identifying adverse outcomes in community-acquired pneumonia

España et al.  
J. Infect. 2015 May; 70(5): 457-66

Rationale

To evaluate the usefulness of PCT, CRP and MR-proADM for identifying adverse outcomes in patients with community-acquired pneumonia, as well as those patients who present with or are at risk of developing complications and are in need of intensified monitoring or treatment.

Patients/Methods

491 patients with a diagnosis of CAP were enrolled to the ED between July 2008 and July 2009. PSI, CURB-65 and SCAP scores were recorded within the first 4 hours after diagnosis, and blood samples for biomarker measurements were taken within 24 hours of arrival. Adverse outcomes were defined by the presence of one or more of the following: respiratory failure, acute renal failure, shock, ICU admission, mechanical ventilation, therapeutic failure, complicated pleural effusion and out-patient readmission.

Results

- PCT and MR-proADM values were significantly higher in patients that developed pneumonia related complications
- MR-proADM had the highest AUC (0.835) for predicting outcome, compared to PCT (0.677) and CRP (0.535)
- In combination with either SCAP, PSI and CURB-65 scores, MR-proADM gave the highest AUCs in predicting pneumonia related complications (0.879, 0.868 and 0.846 respectively) compared to either PCT or CRP
- MR-proADM values of above 2 nmol/L predicted pneumonia related complications in either 64 % or 98 % of patients, depending on their SCAP rating

Patients with MR-proADM values of less than 0.5 nmol/L did not suffer from any adverse complications, as opposed to the majority of those with values above 2 nmol/L. Thus, MR-proADM could be a complimentary tool with clinical scores for the identification of patients at risk of developing complications.
Prognostic power of proadrenomedullin in community-acquired pneumonia is independent of aetiology

Bello et al.

Rationale
To determine whether biomarkers, including CRP, PCT and MR-proADM, alone or in association with clinical severity scores (PSI and CURB-65) are accurate in their assessment of outcome in hospitalized patients, and the role of biomarkers in predicting the development of adverse complications.

Patients/Methods
228 patients were admitted to the ED and diagnosed with CAP. Data on CAP evolution and complications during hospitalization were assessed, as were antibiotics, days of hospitalization, ICU admission, oxygen and mechanical ventilation requirements and clinical stability. Complications included respiratory failure, need for MV, shock, left cardiac failure, renal failure, pleural effusion, and others. Venous blood samples were collected from all patients on admission to the ED, within 6 hours of arrival.

Results
- Levels of MR-proADM on admission increased significantly with increasing severity according to the PSI (p < 0.0001) and CURB-65 scores (p < 0.0001)
- MR-proADM was the only biomarker to distinguish between all different PSI score risk classes, with an AUC to distinguish between low and high risk CAP of 0.811, which was significantly higher than either PCT (0.620) or CRP (0.588)
- MR-proADM was significantly better at predicting adverse complications than all other biomarkers, with an AUC of 0.706, compared to PCT (0.635), CRP (0.618)
- When used alone, MR-proADM had the greatest accuracy in predicting 30 day mortality than any other biomarker or clinical severity score

Plasma levels of MR-proADM, obtained within 6 hours of ED arrival, can accurately predict short-, mid- and long-term mortality, as well as the development of adverse complications. Whilst measurements were only conducted on admission, it is likely that this predictive value would further increase upon serial measurements over 7 days in the ED.
Time-dependent Cox regression: Serial measurement of the cardiovascular biomarker proadrenomedullin improves survival prediction in patients with lower respiratory tract infection

Hartmann et al.
Int. J. Cardiol. 2012 Nov 29;161(3): 166-73

Rationale
To determine the prognostic utility of MR-proADM in patients presenting to the ED with presumed LRTIs, and to evaluate the biomarker’s potential for patient monitoring through serial measurements on top of the measurement obtained at the day of inclusion.

Patients/Methods
1359 patients were enrolled into 6 EDs, and biomarker measurements were taken on days 0 (day of admission), 3, 5 and 7.

Results
Significant added prognostic value is conferred by serial MR-proADM measurements over 7 days ($p = 0.0006$), with the largest added increase with regards to admission values coming from measurements taken on day 3 ($p = 0.0001$).

Using a cut-off of 1.5 nmol/L, MR-proADM values can be designated either as high (> 1.5 nmol/L) or low ($\leq 1.5$ nmol/L) and survival rates based on MR-proADM kinetics over 3 days can be grouped as the following:

- MR-proADM values on admission and day 3: High, High – survival rate = 83.3%
- MR-proADM values on admission and day 3: High, Low – survival rate = 96.2%
- MR-proADM values on admission and day 3: Low, Low – survival rate = 98.6%
- MR-proADM values on admission and day 3: Low, High – survival rate = 73.1%

Serial measurements of MR-proADM can accurately monitor a patient’s changing clinical risk, and increasing concentrations can serve as a “red flag” to highlight those who are developing adverse complications or deteriorating. On the other hand, patients with decreasing MR-proADM concentrations have a high survival rate, indicating an improvement in prognosis.
MR-proADM levels can provide a more accurate outcome prediction upon ICU admission for septic patients compared to other biomarker measurements and existing clinical severity scores, and can reflect the significant pathophysiological changes in sepsis.

Rationale
To evaluate the prognostic value of MR-proANP and MR-proADM in SIRS and septic patients, along with other biomarkers and clinical severity scores, such as IL-6, CRP, PCT and APACHE II.

Patients/Methods
51 critically ill patients were admitted from June to November 2007 to a medical ICU, and biomarker values and clinical severity scores recorded on the day of admission, the second day, and the day of either ICU discharge or death. Patients were divided into four groups: SIRS, sepsis, severe sepsis and septic shock.

Results
- MR-proADM levels significantly increased according to the clinical severity of infection, from SIRS to septic shock
- On ICU admission, MR-proANP and MR-proADM values in non-survivors were significantly higher than in survivors in each of the respective groups
- In contrast, the differences in PCT and IL-6 concentrations between survivors and non-survivors on the first day of admission were not significant
- Within the first 48 hours of ICU admission for sepsis, severe sepsis and septic shock patients, MR-proADM had an AUC of 0.87 for prediction of survival, compared to 0.81 for APACHE II, 0.81 for PCT, 0.71 for IL-6 and 0.53 for CRP
The ability of adrenomedullin to reduce endothelial permeability is of particular interest in DHF/DHS due to this condition being characterized by a transient dysfunction in the endothelial cell barrier resulting in plasma leakage. This may also have significant implications for organ failure and dysfunction in septic patients and the critically ill.

High plasma mid-regional pro-adrenomedullin levels in children with severe dengue virus infections

Michels et al.

Rationale
It is envisaged that Adrenomedullin may play a pathological role in dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS) due to its ability to maintain vascular tone and through the regulation of vascular endothelial integrity. MR-proADM plasma concentrations were subsequently measured and related to survival outcome and markers of protein and plasma leakage.

Patients/Methods
71 children aged below 15 years of age were admitted to the pediatric ward or ICU with a clinical diagnosis of suspected DHF or DHS. Blood was collected on admission, day 2 and the day of discharge.

Results
- Plasma MR-proADM concentrations were significantly higher in the DHF (p < 0.01) and DSS (p < 0.01) groups on admission compared with healthy controls
- No patients died of DHF, and MR-proADM concentrations in this group significantly decreased from admission to discharge
- MR-proADM concentrations remained elevated during the first 2 days in DSS patients, though were significantly lower at discharge in surviving patients
- In DHF and DSS groups, protein and plasma leakage was already present at enrollment, as well as the presence of pleural effusion (excess fluid that accumulates in the pleural cavity surrounding the lungs)
- MR-proADM was significantly correlated with protein and plasma leakage (p = 0.0001), as well as pleural effusion (p = 0.0001)
Pro-adrenomedullin, pro-endothelin-1, procalcitonin, C-reactive protein and mortality risk in critically ill children: a prospective study

Rey et al.
Crit. Care 2013 Oct 16; 17(5): R240

Rationale
Higher plasma biomarker concentrations of PICU patients may be associated with an increased prediction of mortality risk scores and a higher number of organ failures. Biomarker and clinical severity scores tested include MR-proADM, CT-proET-1, PCT, CRP, PRISM III and PIM 2.

Patients/Methods
254 patients were admitted onto two PICUs, and during the first 12 hours PIM 2 and PRISM III values were calculated and venous blood samples for biomarker measurements drawn. Patients were divided into high and low risk mortality groups, determined by PIM 2 and PRISM III scores, as well as groups according to the number of organ failures and overall infectious status during the first 24 hours after admission.

Results
- MR-proADM had the highest AUC of 0.866 for risk mortality score, with concentrations greater than 0.79 nmol/L having a sensitivity of 93 % and a specificity of 76 %
- MR-proADM had the highest AUC of 0.922 for the prediction of organ failure, with a concentration greater than 0.77 nmol/L having a sensitivity of 91 % and a specificity of 85 %
- A mortality risk score and organ failure prediction analysis in the infectious subgroup for MR-proADM gave the highest AUCs of 0.869 and 0.901, and concentrations greater than 0.80 and 0.81 nmol/L gave sensitivities of 100 % and 84 %, and specificities of 70 % and 79 % respectively

MR-proADM provided the highest predictive mortality and organ failure risk in the total study population as well as in all infectious patients. The early prediction of additional organ failure on admission has the potential to identify children at a higher risk of adverse complications, allowing treatment to be tailored on an individual basis at the earliest time point possible.
Prognostic value of plasma pro-adrenomedullin and antithrombin levels in neonatal sepsis

Hagag, Elmahdy and Ezzat
Indian Pediatrics 2011 Jun; 48(6): 471-3

Rationale
To elucidate the prognostic potential of MR-proADM, CRP and Antithrombin levels in neonatal sepsis.

Patients/Methods
40 term neonates with sepsis were admitted to the NICU, comprising of 20 cases with manifestations of mild sepsis, and 20 cases with severe sepsis. 20 neonates of matched gestational age and birth weight served as a control group. Blood samples were obtained before initiation of antibiotic therapy.

Results
- Serum MR-proADM levels were significantly higher in neonates with mild and severe sepsis than in the control group, as well as in neonates with severe sepsis versus mild sepsis
- Serum MR-proADM levels were significantly higher in non-surviving neonates compared to survivors

Both MR-proADM and Antithrombin levels can be useful markers in predicting clinical outcome in neonatal sepsis.
Proadrenomedullin as a prognostic marker in neonatal sepsis

Oncel et al.

Rationale
To investigate the presence of any correlation between proADM, IL-6 and CRP in neonatal sepsis of both preterm and term newborns, and to evaluate the value of proADM in the follow up of this disorder.

Patients/Methods
76 newborns were admitted to the NICU between May and September 2011. Patients with sepsis (Group 1) were further divided into two subgroups based on whether they had proven (positive blood cultures) or clinical (negative blood cultures) sepsis. Blood sampling was performed within the first 6 hours after initial presentation, and then repeated after 48 and 120 hours.

Results
- WBC, CRP, IL-6 and pro-ADM levels were significantly higher in newborns with sepsis compared to healthy controls. No significant differences were found between preterm newborns and term newborns.
- Pro-ADM levels were found to be significantly higher in the proven sepsis group compared to the clinical sepsis group (p < 0.001). No significant differences were found for the other biomarkers tested.
- Pro-ADM and IL-6 levels showed the fastest decline in concentrations, as opposed to CRP which exhibited a relatively slower decline.
- Using a cut-off of 3.9 nmol/L for septic patients compared to controls, pro-ADM exhibited the largest AUC (0.971) with a sensitivity of 100 % and a specificity of 87 %.

Pro-ADM is a novel biomarker that may especially be used for the early diagnosis of neonatal sepsis. The fact that pro-ADM levels showed more rapid decreases compared to CRP suggests that rather than being used alone, the use of pro-ADM in combination with conventional acute-phase reactants may be more useful in the diagnosis and follow up of neonatal sepsis.
Prognostic value of proadrenomedullin in severe sepsis and septic shock patients with community-acquired pneumonia

Suberviola et al.
Swiss Med. Wkly. 2012; 142:w13542

Rationale
To determine whether patients with CAP and a high risk of mortality can be detected using MR-proADM, and to compare any prognostic value with other biomarkers and scores commonly used in clinical practice.

Patients/Methods
49 patients with severe sepsis and/or septic shock were admitted to the ICU between January and September 2009 with a clinical and radiological diagnosis of pneumonia and fulfilling the criteria for severe sepsis or septic shock. APACHE II and SOFA scores, as well as the location before ICU admission, source of infection and organ dysfunction were all recorded at ICU admission. PSI and CURB-65 scores were also determined.

Results
- Patients with septic shock had higher levels of MR-proADM than those with severe sepsis
- MR-proADM consistently rose as PSI class advanced from II to V, whereas no differences could be found for PCT or CRP
- Median MR-proADM levels were higher in non-survivors than survivors, and differences were also significant with respect to ICU mortality, as opposed to PCT or CRP
- The receiver-operating curve for MR-proADM yielded an AUC of 0.72, which was higher than PCT (0.40) or CRP (0.44) and similar to PSI (0.74)
- Patients with MR-proADM values above a cut-off of 4.85 nmol/L had an in-hospital mortality significantly higher than those with values below this cut-off

MR-proADM levels correlate with increasing severity of illness and death, and high levels offer additional risk stratification in high risk CAP patients. Furthermore, the accuracy of MR-proADM levels on admission in predicting the severity and outcome of severe sepsis and septic shock CAP is higher than commonly measured laboratory parameters.
Initial levels of MR-proadrenomedullin: A predictor of severity in patients with Influenza A virus pneumonia

Valenzuela Sanchez et al. 2015. Abstract. 28th Annual congress of the European Society of Intensive Care Medicine

Rationale
To evaluate the usefulness of MR-proADM in comparison to CRP and PCT in the prognosis of patients with influenza A virus pneumonia.

Patients/Methods
66 patients were admitted to the ICU of five hospitals in Spain with the diagnosis of severe sepsis due to influenza A virus pneumonia. Biomarker levels were determined upon admission and compared to a control group of less severe influenza virus A pneumonia patients, who were not admitted to the ICU.

Results
- MR-proADM concentrations on admission were 1.4 nmol/L for the severe ICU influenza A virus pneumonia group, compared to 0.54 nmol/L for the control group (p < 0.001)
- There were no significant differences in PCT or CRP concentrations for those admitted to the ICU compared to those that were not
- The AUC for ICU admission/prognostic severity was 0.871 for MR-proADM, 0.677 for CRP and 0.577 for PCT
- The optimal cut-off for MR-proADM levels on admission was 1.09 nmol/L, with a sensitivity of 73.5 % and a specificity of 96 %
- Non-survivors showed significantly elevated MR-proADM levels compared to survivors (p = 0.0014), whilst neither PCT nor CRP showed any significant differences
- The AUC for prognostic mortality was 0.838 for MR-proADM, 0.640 for CRP and 0.599 for PCT

Initial MR-proADM levels on admission are effective in predicting an unfavorable outcome and the risk of ICU admission and mortality in patients with pneumonia due to the influenza A virus.
Glossary

ACCP/SCCM  American College of Chest Physicians/Society of Critical Care Medicine
APACHE II  Acute Physiology and Chronic Health Evaluation II
AUC  Area Under the Curve
BSI  Blood Stream Infection
CAP  Community-Acquired Pneumonia
CRP  C-Reactive Protein
CT-proAVP  C-Terminal pro-Arginine-Vasopressin
CT-proET-1  C-Terminal pro-Endothelin-1
DHF  Dengue Hemorrhagic Fever
DSS  Dengue Shock Syndrome
ED  Emergency Department
HAI  Hospital-Acquired Infection
ICU  Intensive Care Unit
IL-6  Interleukin-6
MR-proADM  Mid-regional pro-Adrenomedullin
MR-proANP  Mid-regional pro-Atrial Natriuretic Peptide
MV  Mechanical Ventilation
NI  Nosocomial Infection
NICU  Neonatal Intensive Care Unit
PCT  Procalcitonin
PIM 2  Pediatric Index of Mortality 2
PRISM III  Pediatric Risk of Mortality III
SAPS II  Simplified Acute Physiology Score II
SCAP  Severe Community-Acquired Pneumonia
SIRS  Systemic Inflammatory Response Syndrome
SOFA score  Sequential Organ Failure Assessment score
· Determine which patients should be admitted immediately to the ICU to ensure maximal patient safety

· The earliest indication of the development of adverse complications

· A more accurate risk assessment than other biomarkers or clinical severity scores

· The earliest recognition of non-responders to antimicrobial therapy

· Significantly increased concentrations in response to viral infections