Fatty acid binding proteins as biomarkers of disease severity and response to treatment in severe pneumonia required admission to intensive care unit

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In our previous article, we investigated the clinical usefulness of urinary levels of fatty acid binding proteins (FABPs) in assessing the severity of pneumonia and in predicting the treatment response of pneumonia in patients required admission to respiratory intensive care unit (ICU) (1). The results indicated that urinary levels of FABPs including intestine-FABP, adipocyte-FABP and heart-FABP measured on the day 1 after admission to respiratory ICU were significantly lower in pneumonia patients without septic shock than in those with septic shock. After stepwise regression analysis, adipocyte-FABP was the independent factor. The patients were divided into improved and non-improved subgroups. The urinary levels of four types of FABPs measured on the day 7 after admission to respiratory ICU were significantly lower in patients with improvement than in those without improvement. Adipocyte-FABP was shown to be the only independent factor after stepwise regression analysis. Taken together, the results of our previous study highly suggested that adipocyte-FABP in urine might serve as a new biomarker for assessing the severity of pneumonia and for predicting treatment response of pneumonia in patients required admission to respiratory ICU. To our knowledge, this is the first study to explore the clinical relevance of urinary FABPs in severe pneumonia patients in particular in those required admission to ICU.

In our previous study, we did not define the types of pneumonia in our studied subjects. The patients who had community acquired pneumonia (CAP), health care-associated pneumonia (HCAP) and hospital-acquired pneumonia (HAP) or nosocomial pneumonia (NP) were enrolled in our previous study, although the cases of HAP were quite few. We did not enroll the patients with ventilator-associated pneumonia (VAP) according to the patient selection criteria used in our previous study (1). In the case of pneumonia required admission to ICU, the impact of the types of pneumonia and pathogenic micro-organisms may have limited clinical relevance (2-4). In other words, the patient characteristics, co-morbidity and some other factors might be more important.

In our previous study we did not use the lung severity index (LSI) and CUBR-65 confusion, blood urea nitrogen (>7 mmol/L or >20 mg/dL), respiratory rate (>30 breaths/min), blood pressure (systolic pressure <90 mmHg or diastolic pressure <60 mmHg and with an age >65 years), because the scoring systems described as above were reported to be correlated with the mortality of patients with CAP, and were used to determine the patients with CAP might be treated at outpatient clinic, in general ward or in ICU (5-7). In addition, other severity scoring system including SMARR-COP and severe CAP (SCAP) developed for CAP were not used in our previous study because the pneumonia in patients studied were not limited to CAP (8,9).

The patients enrolled in our previous study were of clinical relevance because they were aged adults. The median and interquartile range of the ages of our studied subjects was 83.0 and 72.8–88.0 years. In addition, most patients had one or more co-morbidities. The patients with these demographic characteristics were reported to be with high risk factors for severe pneumonia requiring admission to ICU, and might have a higher mortality rate (10-13).

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Our previous study intended to evaluate the clinical usefulness of FABPs in assessing the severity of pneumonia and in predicting the treatment response of pneumonia in patients required admission to ICU. The severity of pneumonia was defined based on the presence or absence of septic shock. The outcome of the pneumonia patients was defined based on the improvement or non-improvement of pneumonia lesion(s) shown on the chest radiograms and improved oxygenation shown as the PaO_2/FiO_2 ratio (arterial oxygen tension/inspired fraction of oxygen ratio) with FiO2 < 40% on the day 7 after admission to respiratory ICU. In other words, we did not evaluate the in-ICU mortality rate and in-hospital mortality rate, and mortality rates at 28 day, 3 months and 6 months. In brief, we did not evaluate the clinical relevance of FABPs in predicting the outcome defined as immediate or short-term mortality of pneumonia patients required admission to ICU. However, our unpublished data indicated that intestine-FABP might be of value in predicting survival or non-survival of the pneumonia patients required admission to respiratory ICU (paper in revision).

The improvement of severe pneumonia in the patient required admission to ICU may be affected by many factors such as the pathogen(s) with or without multidrug resistance, the use of right antibiotics (empiric and/or therapeutic), the time to treatment with right antibiotics, the co-morbidity, the immune compromised status and general condition of the patients, the presence of complications and the experience of chest physicians and intensivists, etc. In addition, some medications including steroid, statins and anti-coagulant agents may affect the treatment response of pneumonia and outcome of the patients. We do agree that steroid may have impact on the treatment response and outcome of the patients with severe pneumonia (14). However, there is no consensus on the use of steroid such as the dose of steroid and treatment period in such patients. In our usual practice, the use of steroid and the dose of steroid used are at the discretion of in-charge physicians in respiratory ICU. The benefit of statins on severe pneumonia patients required admission to ICU deserves further prospective studies to verify. In general, any factor is difficult to be evaluated and identified its impact on the treatment response of pneumonia in the patients required admission to ICU.

In our previous study, we also studied the clinical usefulness of C-reactive protein (CRP) and procalcitonin (PCT) in blood of the patients with pneumonia required admission to respiratory ICU. The results showed limited benefit of these biomarkers measured on the day 1 after admission to respiratory ICU in assessing the severity of pneumonia and in predicting the treatment response of pneumonia in our studied subjects. We did not showed the blood data of both biomarkers measured on the day 7 after admission to respiratory ICU because the data were not available in all patients, and the data obtained from the selected patients showed limited value of these biomarkers in predicting the treatment response of pneumonia in the patients required admission to respiratory ICU. The blood data of CRP and PCT measured on the day 7 after admission to respiratory ICU failed to predict the treatment response of pneumonia because blood levels of these biomarkers obtained from the selected patients decreased 2–3 days after empiric antibiotic treatment irrespective of the treatment response.

It remains unknown why the data of urinary FABPs and inflammatory cytokines and blood levels of CRP and PCT on day 1 after admission to respiratory ICU showed no significant differences between pneumonia and non-infectious and non-inflammatory control groups (1). The demographic and laboratory data between the two groups were comparable. Only difference was the APACHE II score, and the APACHE II score was significantly higher in control group than in pneumonia group. Most patients in control group (n=12) were those with profoundly circulatory hypoxia (9 with heart failure and 1 with carbon monoxide intoxication). It is plausible that tissue hypoxia with subsequent tissue inflammation and injury may induce over-expression and production of FABPs in affected organs and/or tissues as shown in our previous study. Further studies with larger population are mandatory to verify the issues.

The results of our previous study might not answer the questions why FABPs could be of value in predicting the severity of pneumonia and/or in predicting the treatment response of pneumonia in the patients required admission to ICU. However, the results of our previous study may be the start to attract further studies to investigate the role of FABPs in pneumonia and other pulmonary diseases and/or disorders. Adipocyte-FABP was reported to be found in macrophages and involved in the inflammation, adipocytes could be detected in bronchial microvasculature of the patients with bronchopulmonary dysplasia and adipocyte could be found in bronchial epithelial cells in patients with allergic airway inflammation (15,16). As a consequence, adipocyte-FABP and other FABPs may be involved in pulmonary infectious and/or inflammatory diseases/

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disorders. Further studies with larger populations are needed to verify the role of FABPs in a variety of pulmonary diseases and/or disorders.

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Footnote

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