*Corresponding authors. State Key Laboratory of Veterinary Etiological Biology, Key Laboratory of Veterinary Public Health of Ministry of Agriculture, Lanzhou Veterinary Research Institute, Chinese Academy of Agricultural Sciences, No. 1 Xujiaping, Chengguan District, Lanzhou 730046, People's Republic of China. Tel.: +86 931 8342359.
E-mail addresses: zhangyongguang@caas.cn (Y.-G. Zhang), changhuiyun@caas.cn (H.-Y. Chang)

Accepted 13 August 2015

http://dx.doi.org/10.1016/j.jinf.2015.08.006

Biomarkers in community-acquired pneumonia

Dear Editor,

We read with interest the article recently published by Watanabe and colleagues.[1] The authors evaluated the prognostic role of soluble suppression of tumorigenicity 2 on all-cause inhospital mortality in hospitalized patients with community-acquired pneumonia (CAP).

Despite the efficacy of modern treatment, CAP is the leading cause of death due to infection and also a frequent cause of medical consultations.[2] Prognostic scores, like the CURB-65 (confusion, urea, respiratory rate, arterial blood pressure and age) score and the pneumonia severity index have been developed and validated to estimate the risk of adverse outcome and to register a patient with CAP for hospital admission.[2,3] Biomarkers are also useful tools in the diagnosis, prognostics and follow-up treatment of CAP. Procalcitonin and C-reactive protein are commonly used biomarkers in CAP, as indicators of severity of disease and predictors of mortality.[4] Since CAP is an infectious disease, commonly-used laboratory parameters include the C-reactive protein, white blood cell count, and procalcitonin. However, recent studies showed that cardiac complications are common in patients with CAP, and cardiovascular biomarkers are found to be superior compared to inflammatory markers, especially for the determination of long-term prognosis in CAP.[5,6] Elevated levels of natriuretic peptides and troponins are reported to be common and are associated with a higher risk of adverse outcome in CAP. Chang et al. found that a raised levels of NT-proBNP is a strong predictor of early mortality independent of existing clinical risk prediction scores following admission to hospital for CAP.[5] Elevated Troponin T was also associated with increased risk of early mortality but was not a significant predictor once clinical risk scores or NT-proBNP levels were taken into account.[5] Mean platelet volume[7] and red blood cell distribution width levels[8] have also been shown to be valuable markers for predicting mortality and the severity of disease among patients with CAP at emergency department admission. We have very recently shown that CAP patients had significantly higher NT-proBNP, white blood count, and red blood cell distribution width values compared to those with control group and plasma concentration of NT-proBNP correlated with PSI and CURB-65 scores.[6] Our data demonstrated that B-type natriuretic peptide levels increased with rising disease severity as classified by the PSI in patients with CAP.

In the current article Watanabe et al. showed that serum levels of soluble suppression of tumorigenicity 2 (at day 3) are an early prognostic indicator of CAP, which adds to the predictive value of PSI. However, the authors did not provide the data on correlation between soluble suppression of tumorigenicity 2 levels with other biomarkers. Therefore, we would be grateful if the authors have and would provide the data regarding troponin, natriuretic peptide and procalcitonin levels on admission in patients with CAP.

DOI of original article: http://dx.doi.org/10.1016/j.jinf.2015.02.004

References

1. Watanabe M, Takizawa H, Tamura M, Nakajima A, Kurai D, Ishii H, et al. Soluble ST2 as a prognostic marker in community-acquired pneumonia. *J Infect* 2015 May;**70**(5):474–82. http://dx.doi.org/10.1016/j.jinf.2015.02.004 [Epub 2015 Feb 19].
2. Fine MJ, Smith MA, Carson CA, Mutha SS, Sankey SS, Weissfeld LA, et al. Prognosis and outcomes of patients with community-acquired pneumonia: a meta-analysis. *JAMA* 1996;**275**:134–41.
3. Fine MJ, Auble TE, Yealye DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community acquired pneumonia. *N Engl J Med* 1997;**23**:243–50.
4. Zhydkov A, Christ-Crain M, Thomann R, Hoess C, Henzen C, Werner Z, et al. ProHOSP Study Group. Utility of procalcitonin, C-reactive protein and white blood cells alone and in combination for the prediction of clinical outcomes in community-acquired pneumonia. *Clin Chem Lab Med* 2015 Mar;**53**(4):559–66.
5. Chang CL, Mills GD, Karalus NC, Jennings LC, Laing R, Murdoch DR, et al. Biomarkers of cardiac dysfunction and mortality from community-acquired pneumonia in adults. *PLoS One* 2013 May 7;**8**(5):e62612. http://dx.doi.org/10.1371/journal.pone.0062612.
6. Yıldırım B, Biteker FS, Başaran Ö, Alataş ÖD, Acar E, Sözen H, et al. Is there a potential role for echocardiography in adult patients with community acquired pneumonia ? A pilot study. *Am J Emerg Med* 2015. http://dx.doi.org/10.1016/j.ajem.2015.06.036.
7. Golcuk Y, Golcuk B, Bilge A, Irik M, Dikmen O. Combination of mean platelet volume and the CURB-65 score better predicts 28-day mortality in patients with community-acquired pneumonia. *Am J Emerg Med* 2015 May;**33**(5):648–52.
8. Braun E, Kheir J, Mashiach T, Naffaa M, Azzam ZS. Is elevated red cell distribution width a prognostic predictor in adult patients with community acquired pneumonia? *BMC Infect Dis* 2014 Mar 5;**14**:129.

Funda Sungur Biteker*
Muğla Sıtkı Koçman University, Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Turkey

Birdal Yıldırım
Muğla Sıtkı Koçman University, Faculty of Medicine, Department of Emergency Medicine, Turkey

*Corresponding author. Muğla Sıtkı Koçman Üniversitesi Tıp Fakültesi, Orhaniye Mah. Haluk Özsoy Cad, 48000 Muğla, Turkey. Tel.: +90 252 214 13 26.
E-mail address: fundam81@mynet.com (F.S. Biteker)

Accepted 9 August 2015

http://dx.doi.org/10.1016/j.jinf.2015.08.004

Serum IP-10 in the diagnosis of latent and active tuberculosis

KEYWORDS
Tuberculosis;
IP-10;
Latent TB;
Active TB;
Diagnostics

We read with interest the recent article by Wergeland et al., reporting that serum interferon-gamma inducible protein 10 (IP-10) may be a useful biomarker for differentiating between active tuberculosis (TB) and latent TB infection (LTBI), as well as for monitoring the effectiveness of anti-tuberculous therapy.[1] However, a key limitation of this study was the absence of a 'sick control' group of patients with respiratory tract infections. Prompted by this finding, we analysed data from our ongoing study investigating novel biomarkers of active and latent TB.

Our study included a total of 193 adults recruited at a tertiary hospital in Melbourne, Australia between 2012 and 2014. Participants were classified into four diagnostic groups based on stringent criteria: Group 1 — cases with culture-confirmed active TB prior to starting anti-tuberculous therapy (n = 38; n = 27 pulmonary TB, n = 11 extra-pulmonary TB); Group 2 — cases with untreated LTBI (defined as asymptomatic patients with positive tuberculin skin test (TST; cut-off 10 mm induration) and positive QuantiFERON-TB Gold In-Tube (QFT-GIT) assay) (n = 42); Group 3 — 'sick controls' comprising cases with lower respiratory tract infection caused by a pathogen other than *Mycobacterium tuberculosis* with negative TST and QFT-GIT results (n = 16); Group 4 — healthy controls comprising volunteers without risk factors for TB (ie no known TB contact and no travel to a high TB prevalence country) and with negative TST and QFT-GIT results (n = 33).

Similarly to Wergeland et al., we analysed unstimulated serum samples for a number of cytokines, including IP-10, by multiplex cytokine assays (Bio-Plex Human Cytokine Group I assays [Bio-Rad, Gladesville, Australia]) according to the manufacturer's instructions, using an xMAP *Luminex* 200 instrument, after incubation without stimulatory antigens in the presence of CD28/CD49d (Becton Dickinson) at 37 °C for 19 h. Non-parametric statistical tests were used to compare cytokine concentrations between participant groups (Kruskal—Wallis tests for multiple groups; Mann Whitney *U* tests for two-group comparisons). The study was approved by the Human Research Ethics Committee of the Royal Melbourne Hospital (approval no. 2011.128).

We found a statistically significant difference in the median serum IP-10 concentrations between patients with active TB and those with LTBI (Fig. 1). However, it is important to highlight that although median concentrations differed significantly between these two groups in both our study and the study by Wergeland et al., there was a significant overlap in the IP-10 concentrations observed in those groups (Fig. 1 below and Fig. 2 in Wergeland et al.'s paper), suggesting that establishing a sufficiently sensitive and specific cut-off to distinguish between active and

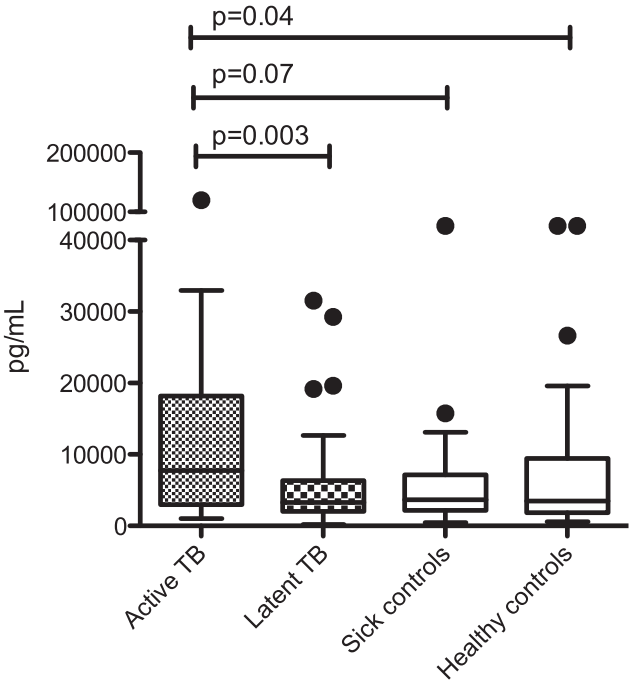

Figure 1 Box plot with Tukey whiskers showing serum IP-10 concentrations in patients with active TB, patients with LTBI, sick controls (lower respiratory tract infection) and healthy controls. The horizontal lines represent the medians and the lower and upper quartiles.

DOI of original article: http://dx.doi.org/10.1016/j.jinf.2015.02.004