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Project Title:

Utility of a panel of acute lung injury biomarkers following lung resection – a pilot study.

Project Description

The common clinical syndromes of acute lung injury (ALI) and the more severe acute respiratory distress syndrome (ARDS) occur in response to a wide variety of insults and have high mortality. Diagnosis of ALI/ARDS relies on clinical criteria as outlined by the American–European Consensus Conference [1]. This definition has been criticised as not reflecting the underlying biological and pathological mechanisms. A new definition based on biochemical markers of inflammation rather than clinical consequences may facilitate earlier diagnosis or identification of patients at risk and/or serve as a predictor of clinical outcome or guide to therapeutic strategies [2, 3].

A wide range of potential biomarkers (each purportedly reflecting different parts of the complex pathological process that ALI/ARDS embodies) have been evaluated though none individually has been sufficiently strongly associated with outcomes to provide discriminating power for either diagnosis or prognosis. It has recently been suggested that combinations of several biomarkers or combinations of biomarkers and clinical indices may improve diagnostic / prognostic accuracy [2, 4]. Fremont et al recently evaluated 21 potential biomarkers. By the use of a backward elimination model these researchers identified a "top seven" panel of biomarkers (receptor for advanced glycation end products, procollagen peptide III, brain natriuretic peptide, angiopoietin-2, interleukin-10, tumor necrosis factor alpha, and interleukin-8) which in combination had a high diagnostic accuracy as reflected by the area under the receiver operating characteristic curve of 0.86 (95% CI, 0.82– 0.92) in differentiating ALI from controls [2].

One-lung ventilation, a necessary anaesthetic technique to facilitate surgical access during thoracic surgical procedures results in exposure of the ventilated lung to volutrauma, atelectotrauma and high inspired oxygen concentrations; conditions mimicking ventilator associated lung injury. Though the clinical syndrome of ALI occurs in only 5-10% of subjects undergoing thoracic surgery, biochemical evidence of pulmonary inflammation is detectable in all patients following lung resection. These observations have lead to one-lung ventilation being utilised as a model of lung injury [5, 6].

With research ethics committee approval and after obtaining informed consent we have collected plasma samples pre-, immediately post- and 24 hours post-operatively from 25 patients undergoing thoracic surgery for resection of primary lung cancer.

This study seeks to analyse the same "top 7" biomarkers identified by Fremont et al[2] in this population in order to:

1. Classify the response of this biomarker panel to the direct pulmonary and systemic inflammatory insult of one-lung ventilation and lung resection.
2. Determine the correlation between biomarker levels and PaO_2/FiO_2 ratio in the early post-operative period.

(Statistical analysis will be conducted in conjunction with the Robertson Centre for biostatistics at the University of Glasgow).

Measurement of biomarkers of ALI during the early post-operative period following lung resection may provide a useful monitor of patient wellbeing; rising / elevated biomarker levels may provide an early warning of impending lung injury facilitating triage to an appropriately monitored environment and allowing timely intervention. The purpose of this pilot study is to identify candidate markers for use in a larger prospective study.

**Stored samples referred to are from the "Endogenous Antioxidant Capacity and Oxidative Stress, Nitrosative Stress and Endothelial Dysfunction after Thoracic Surgery" study. REC reference 10/S0709/43. Funded by the National Institute of Academic Anaesthesia and the Intensive Care Society (BS). Informed consent has been obtained such that "unused samples may be stored and used for future research with permission of the regional ethics committee".*

References

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