Getting ahead in lung infection

S123 PROCALCITONIN IDENTIFIES ACUTE HEART FAILURE BIOMARKERS IN PATIENTS WITH ACUTE HEART FAILURE IN NEED OF ANTIBIOTIC THERAPY: OBSERVATIONAL RESULTS FROM THE BACH (BIOMARKERS IN ACUTE HEART FAILURE) TRIAL

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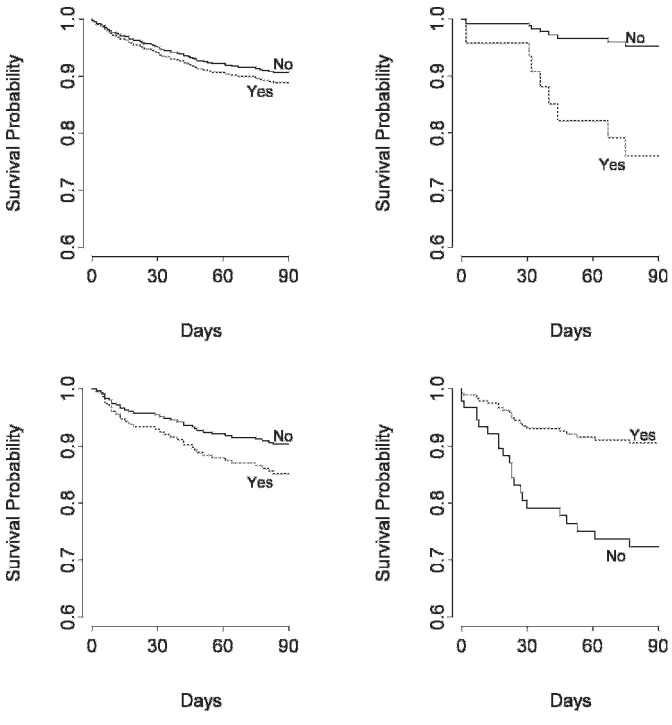
Background Procalcitonin (PCT) levels have been used to diagnose bacterial infection and sepsis. PCT has also been suggested as a surrogate marker reflecting the response to a clinically relevant bacterial infection and requirement for antibiotic treatment. However, they have never been used to identify bacterial infection co-morbidity in patients with acute heart failure (AHF).

Methods The BACH (Biomarkers in Acute Heart failure) trial was a prospective, 15-centre diagnostic and prognostic study of 1641 patients presenting with dyspnoea, 568 of which have been diagnosed with AHF. Patients were included if they had a diagnosis of heart failure, defined by two cardiologists blinded to marker results and reviewing all available data 30 days after enrolment. Here, we evaluate the association between PCT, received antibiotic therapy and all-cause mortality within 90 days, the primary outcome of the trial. Missing covariate data were imputed using the mean.

Results PCT was significantly associated with all-cause mortality within 90 days for patients diagnosed with AHF ($p = 0.025$, Cox regression). The proportion of antibiotic treatment during follow-up was significantly higher in patients with elevated PCT levels ($p = 0.0008$, twofold increase). Finally, after adjusting for covariates such as site, wheezing, history of stroke, creatinine, and neutrophil count to level out group differences, patients with a PCT level >0.205 ng/ml (fifth quintile of PCT in all patients with AHF) have a significantly worse outcome if not treated with antibiotics ($p = 0.046$, fig 1 bottom right). On the other hand, patients with very low PCT values (<0.051 ng/ml, first quintile, fig 1 top right) have a significantly better outcome if not treated with antibiotics ($p = 0.049$). In all patients, as well as in patients with PCT levels between 0.051 and 0.205 ng/ml, the antibiotic treatment effect was not significant ($p = 0.58$ and $p = 0.36$, fig 1 top and bottom left, respectively).

Conclusion Our results suggest that in patients with AHF, PCT may act as a surrogate marker reflecting the response to a clinically relevant bacterial infection and requirement for antibiotic treatment. Moreover, results for patients with low PCT levels suggest that patients may be affected by adverse events from the antibiotic therapy. As antibiotic therapy was not a randomised treatment in the BACH trial, results need to be confirmed in a prospective RCT.



Abstract S123 Figure 1.

S124 A META-ANALYSIS OF SEVERITY SCORES FOR PREDICTING ITU ADMISSION IN PATIENTS ADMITTED WITH COMMUNITY-ACQUIRED PNEUMONIA

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Introduction Existing international guidelines recommend using pneumonia severity scores to predict intensive treatment unit (ITU) admissions in patients hospitalised with community-acquired pneumonia (CAP). The most commonly used severity scores are the CURB-65, Pneumonia Severity Index (PSI) and modified American Thoracic Society (mATS) criteria. The aim of our study was to explore the utility of these scores in predicting ITU admissions.

Methods We performed a systematic review and meta-analyses according to MOOSE guidelines. A sensitive search strategy of PUBMED and EMBASE from 1980 to 2009 identified 25 studies reporting prognostic information for CURB-65, PSI, mATS and alternative scores. Three reviewers independently collected data and

Abstract S124 Table 1 Comparisons of the different scores in predicting intensive treatment unit admission

	PSI	CURB-65
No. of studies	11	6
No. of patients	8907	6462
Sensitivity	0.76 (0.73–0.78)	0.42 (0.38–0.48)
Specificity	0.49 (0.48–0.50)	0.77 (0.76–0.78)
PLR	1.47 (1.38–1.57)	1.72 (1.39–2.13)
NLR	0.52 (0.45–0.59)	0.79 (0.71–0.87)
Diagnostic OR	2.90 (2.41–3.50)	2.25 (1.64–3.07)
AUC	0.61 (0.56–0.65)	0.64 (0.57–0.71)
Cochran Q statistic	14.02 df = 10, p = 0.2	7.50 df = 5, p = 0.2

AUC, area under the receiver operator curve; NLR, negative likelihood ratio; PLR, positive likelihood ratio.

assessed study quality; 11 studies met the criteria for inclusion in the meta-analysis. Odds ratios across studies were pooled using a DerSimonian–Laird (DSL) random-effects model approach. Statistical heterogeneity was assessed using the Cochran Q statistic. Relationships between sensitivity and specificity were plotted using summary receiver operator characteristic (ROC) curves.

Results The Kappa statistic showed substantial agreement in rating study quality ($\kappa = 0.7$). 11 studies were included for analysis of PSI and 6 studies for CURB-65. No significant heterogeneity was identified. Table 1 represents the comparisons of the different scores in predicting ITU admission. There were insufficient studies for alternative scoring systems (CRB-65, modified ATS criteria, SMART-COP, ESPANA score, BTS criteria) to perform a meta-analysis.

Conclusion None of the currently available scoring systems is sufficiently sensitive or specific to predict ITU admissions. Further prospective studies are needed to modify these scores.

S125 LONG-TERM NEBULISED GENTAMICIN IN NON-CYSTIC FIBROSIS BRONCHIECTASIS IMPROVES MICROBIAL LOAD, EXERCISE TOLERANCE, EXACERBATION FREQUENCY AND HEALTH-RELATED QUALITY OF LIFE

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Aim To establish the efficacy of long-term nebulised gentamicin in patients with non-cystic fibrosis bronchiectasis.

Methods A randomised controlled study of 57 patients with non-cystic fibrosis bronchiectasis and a history of chronic colonisation with potentially pathogenic organisms in their sputum when clinically stable. Treatment was for 12 months, with 27 patients receiving twice-daily nebulised gentamicin (80 mg) (group G) and 30 receiving twice-daily 0.9% saline (group S). Patients were reviewed 3 monthly until 15 months. End points included: qualitative and quantitative sputum bacteriology; forced expiratory volume in 1 s (FEV_1); forced vital capacity (FVC); incremental shuttle walk test (ISWT); and the Leicester Cough Questionnaire (LCQ). Data are presented as median (interquartile range) and groups compared using the Wilcoxon and Mann–Whitney U test.

Results 57 patients (24 male, 33 female, ($p = 0.1$)) completed the study and all were chronically colonised. The median age in group G was 58 (53–67) years and in group S 64 (55.7–69) years, $p = 0.2$. Table 1 details the start of treatment, end of treatment and follow-up results for each group.

Conclusion Long-term nebulised gentamicin significantly reduces sputum bacterial density, improves exercise tolerance, reduces exacerbations and improves health-related quality of life in patients with non-cystic fibrosis bronchiectasis.

S126 MOLECULAR DETECTION OF COMPLEX MICROBIAL COMMUNITIES IN SPUTA OF PATIENTS WITH CYSTIC FIBROSIS AND NON-CF BRONCHIECTASIS

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Background Introduction of molecular techniques to the study of cystic fibrosis (CF) airway infections has established that conventional microbiological culture underestimates the complex microbial communities present. To date no studies have addressed whether patients with non-CF bronchiectasis (BX) display the same phenomenon.

Methods Sputa from 9 patients with CF (mean age (±SD) 30.8 (±5.3)) and 11 with BX (mean age (±SD) 59.6 (±11.6)) were examined. The bacterial communities in each sample were assessed using two methods: standard culture techniques and molecular recognition by amplification and sequencing of the *16S rRNA* gene.

Results From the CF samples, routine cultures yielded *Pseudomonas aeruginosa* (PsA) in 5 patients, 2 as the sole bacterial species and 3 mixed with other organisms. (*Achromobacter xylosoxidans* (AX), *Stenotrophomonas maltophilia* (SM) and *Staphylococcus aureus* (SA)). One patient had *Burkholderia cepacia* alone, one SA alone, one AX alone and one no bacterial growth, but *Candida* species. In the BX samples, five patients cultured PsA with one also having AX. One patient had SM and in the remaining five no bacterial species were cultured. The 16S rRNA method resulted in a total of 863 high quality sequences being generated from all subjects. Bacterial genomes were identified in all samples, including the 5 patients with BX who were negative to culture. The results identified a predominance of Proteobacteria (>70%), most often *Pseudomonas* sp. and *Achromobacter* sp. in both groups. Firmicutes (*Staphylococcus* sp. and *Streptococcus* sp.) were also commonly present: CF (23%) and BX (12%). Bacteroidetes (2%), Fusobacteria (8%) and Actinobacteria (2%) phyla were detected in the BX samples but were only present in 0.2% of sequences from the CF samples, suggesting greater microbial diversity in the patients with BX. This difference between the two sample groups was confirmed statistically by community comparisons with the LIBSHUFF program ($p<0.001$).

Conclusion Our results indicate that molecular methods can identify the presence of significant numbers of bacterial genomes in sputum samples from patients with CF and BX, even when standard cultures have failed. Additionally, the BX bacterial communities appeared more complex than those in patients with CF.

Abstract S125 Table 1 Treatment end points

	G 0 months	G 12 months	G 15 months	S 0 months	S 12 months	S 15 months
Bacterial density Log_{10} (CFU/ml)	8.0 (7.6–8.3)	3.0 (1.0–5.9)*‡	7.3 (5.9–7.8)†	7.9 (7.3–8.2)	7.7 (7.2–8.1)	7.5 (6.5–8.2)
FEV_1 (litres)	1.9 (1.6–2.3)	1.6 (1.5–2.1)*	1.7 (1.3–2.1)	1.6 (1.2–2.3)	1.6 (1.2–2.1)	1.7 (1.3–2.1)
FVC (litres)	2.8 (2.3–3.4)	2.5 (2.1–2.9)*	2.7 (2.2–3.1)	2.9 (2.1–3.3)	2.7 (2.2–3.2)	2.7 (2.2–3.2)
ISWT (m)	350 (270–530)	510 (360–690)*‡	420 (340–580)†	345 (258–450)	415 (267–530)	385 (232–490)
Exacerbations		0 (0–1)‡	0 (0–1)		1.5 (1–2)	0 (0–1)
LCQ	14.1 (11.8–16.2)‡	17.7 (14.9–18.3)*	14.9‡ (11.1–18.1)†	17.5 (14.9–19.4)	16.4 (14.0–19.5)	17.1 (15.5–19.5)

*$p<0.05$ when compared with 0 months in group G.
†$p<0.05$ when compared with month 12 in group G.
‡$p<0.05$ when comparing group G with group S for all time points.
CFU, colony-formning units; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; ISWT, incremental shuttle walk test; LCQ, Leicester Cough Questionnaire.

S127 RANDOMISED CONTROLLED TRIAL OF HIGH CONCENTRATION VS TITRATED OXYGEN THERAPY IN COMMUNITY-ACQUIRED PNEUMONIA

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Introduction and Objectives Guidelines recommend the routine administration of high concentration oxygen therapy in the treatment of community-acquired pneumonia. The objective of the study was to investigate the effect of high concentration oxygen therapy on $PaCO_2$ in patients with suspected community-acquired pneumonia.

Methods 150 patients with suspected community-acquired pneumonia presenting to three hospital Emergency Departments were randomised to high concentration oxygen (8 l/min via medium concentration mask) or titrated oxygen (to achieve oxygen saturations between 93 and 95%) for 60 min. Transcutaneous CO_2 ($PtCO_2$) was measured at 0, 20, 40 and 60 min. The primary outcome variable was the proportion of patients with a rise in $PtCO_2$ ≥4 mm Hg (0.53 kPa) at 60 min.

Results Table 1 shows the proportion of patients with a predetermined rise in $PtCO_2$ from baseline at 60 min

Abstract S127 Table 1

<>	High concentration, n (%)	Titrated, n (%)	Relative risk (95% CI)	p Value
Change in $PtCO_2$ ≥4 mm Hg (0.53 kPa)	36 (50%)	11 (14.7%)	3.4 (1.9 to 6.2)	<0.001
Change in $PtCO_2$ ≥4 mm Hg and PtCO ≥38 mm Hg (5.05 kPa)	19 (26.4%)	5 (6.7%)	2.7 (1.2 to 6.0)	0.01
Change in $PtCO_2$ ≥8 mm Hg (1.06 kPa)	11 (15.3%)	2 (2.7%)	5.7 (1.3 to 25.0)	0.007

$PtCO_2$, transcutaneous CO_2.

Conclusions High concentration oxygen therapy results in an increase in $PtCO_2$ when delivered to patients presenting with suspected community-acquired pneumonia. We recommend that in community-acquired pneumonia, oxygen therapy is titrated as required to relieve arterial hypoxemia.

S128 ACUTE KIDNEY INJURY ON ADMISSION INDEPENDENTLY PREDICTS NEED FOR DIALYSIS AND 30-DAY MORTALITY IN PATIENTS WITH PNEUMONIA

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Introduction Existing pneumonia severity scores focus on admission blood urea to assess kidney injury. A consensus definition of acute kidney injury (AKI) based on creatinine values, the RIFLE criteria, allows patients to be classified into three AKI categories and has been shown to predict mortality in intensive care unit (ICU) populations with sepsis. We aimed to assess its value with regards to predicting dialysis and 30-day mortality on admission in patients with pneumonia.

Methods A prospective observational study of consecutive patients (January 2005 to January 2008) admitted with pneumonia was carried out. We classified each patient according to their maximum RIFLE class using admission creatinine (risk ≥1.5× baseline creatinine, injury ≥2× baseline, failure ≥3× baseline or no AKI <1.5× baseline). Outcome variables of interest were predictors for dialysis, requirement for mechanical ventilation/inotropic support and 30-day mortality.

Results RIFLE categories and outcome variables for 1241 patients are shown in table 1. Patients were evenly matched with regards to age and sex. On univariate analysis patients with AKI were more likely to have pre-existing renal disease, severe pneumonia (CURB-65 ≥3 and Pneumonia Severity Index (PSI) ≥4), confusion, hypotension, tachycardia, raised white cell count (WCC) and raised C-reactive protein (CRP), and were more likely to be prescribed angiotensin-converting enzyme inhibitor (ACE-I)/angiotensin II receptor blocker (AIIRB) treatment (all $p<0.05$). On multivariate analysis, factors predicting development of AKI include severity of pneumonia (PSI) (adjusted odds ratio (AOR) 1.74 (1.46 to 2.08), $p<0.0001$), elevated CRP (AOR 1.04 (1.03 to 1.06), $p<0.0001$) and prior use of ACE-I/AIIRB (AOR 1.77 (1.19 to 2.58), $p = 0.005$). On multivariate analysis adjusting for severity of pneumonia (PSI), RIFLE criteria independently predicted requirement for dialysis (AOR 3.20 (2.01 to 5.11), $p<0.0001$). RIFLE criteria were more specific, with a higher area under the receiver operating characteristic curve (AUROC) (0.84 (0.79 to 0.88)) than either PSI (0.78 (0.73 to 0.83)), CURB-65 (0.77 (0.71 to 0.82)) or urea >7 alone (0.69 (0.63 to 0.74)) for predicting dialysis. Adjusting for severity of pneumonia (PSI), RIFLE class independently predicted 30-day mortality (AOR 1.48 (1.15 to 1.91), $p = 0.002$) and requirement for mechanical ventilation/inotropic support (AOR 2.22 (1.74 to 2.83), $p<0.0001$).

Abstract S128 Table 1 Age, sex and outcome variables in patients with no acute kidney injury (AKI) vs kidney injury (risk, injury or failure)

	No AKI	Risk	Injury	Failure	p Value
n (1241)	1018	130	63	30	
Age (years)	67 (50–78)	67 (55–77)	65 (53–75)	66 (61–70)	NS
Gender (% male)	49.3%	49.2%	49.2%	46.7%	NS
30-day mortality	6.0%	15.4%	22.2%	43.3%	<0.05
CURB-65 ≥3 (%)	18.8%	57.7%	66.7%	69.6%	<0.05
PSI ≥4 (%)	32.8%	60%	66.7%	95.7%	<0.05
MV and/or IS	5.0%	18.5%	36.5%	43.3%	<0.05
Dialysis	0.7%	2.3%	14.3%	36.7%	<0.05
Duration of admission (days)	5 (2–11)	8 (4–15)	12 (5–24)	8 (2–17)	<0.05

IS, inotropic support; MV, mechanical ventilation; PSI, Pneumonia Severity Index.

Conclusion The RIFLE classification is a simple tool to assess and classify AKI on admission and independently predicts need for dialysis, requirement for mechanical ventilation and/or inotropic support and 30-day mortality in patients with community-acquired pneumonia.

COPD: counting the costs

S129 LENGTH OF STAY AS AN INDICATOR OF THE EFFICIENCY OF HOSPITAL CARE FOR COPD

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Chronic obstructive pulmonary disease (COPD) is the second most common reason for emergency medical admission. The National COPD Resources and Outcomes Project (NCROP) audit in 2003 and 2008 showed that length of stay (LOS) varies widely, and National Institute for Health and Clinical Excellence (NICE) guidelines suggest that early discharge schemes offer opportunities to reduce the burden.