Precision treatment for pneumonia care: Metagenomic sequencing takes the lead

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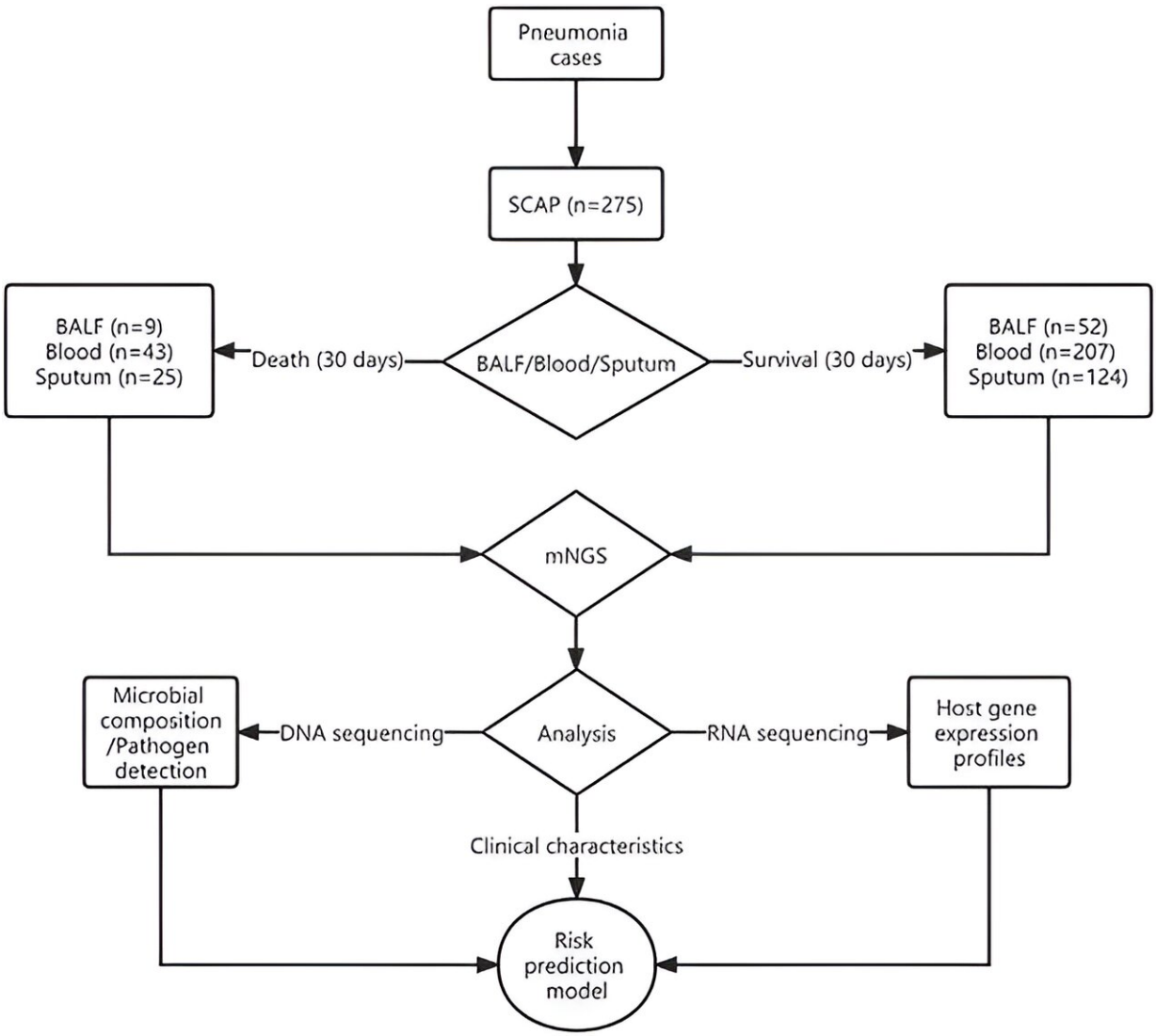


Study design. mNGS: metagenomic next-generation sequencing. BALF: bronchoalveolar lavage fluid. Pathogen detection is an integrated diagnosis

including routine bacterial/fungal cultures, polymerase chain reaction (PCR) for virus detection, urine—antigen test, pathogen—specific antibody titre, metagenomic next generation sequencing (mNGS) method, as well as features (laboratory tests and imaging findings). Credit: BGI Genomics

Community-acquired pneumonia (CAP) is a major infectious disease worldwide and contributes to high mortality and massive economic burden. Hospital mortality among the severe CAP (SCAP) remains high, ranging from 25% to more than 50%.

Early identification of patients at high risk of death is essential for improving patient outcomes. However, predicting outcomes in patients with SCAP is challenging, as the disease is complex and influenced by various factors, including the types of pathogen causing the infection, the host immune response, and underlying medical conditions.

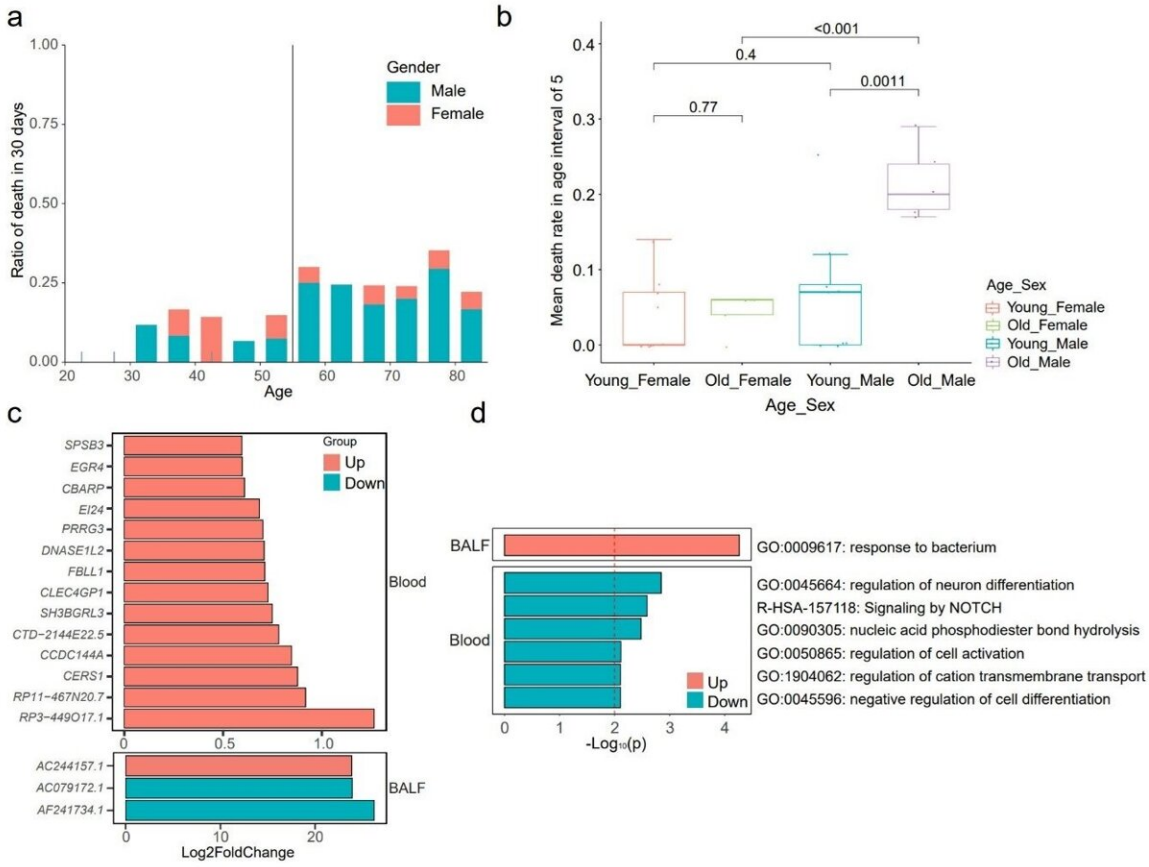
In this study published in *eBioMedicine*, a team led by BGI Genomics Chief Science Officer of Infection Department Dr. Jinmin Ma and team led by Ruijin Hospital Prof. Jieming Qu conducted research on SCAP patients to explore the pulmonary microbiota and host responses of different outcomes since the genetic differences could be detected more easily in the most severe patients as opposed to mildly severe ones.

Methods and findings

BGI Genomics researchers used metagenomic and transcriptomic analysis to identify a new set of biomarkers that can predict 30-day mortality in patients with SCAP.

The study included 275 patients with SCAP from 18 hospitals in China.

Researchers performed DNA and RNA-based metagenomic next-generation sequencing of bronchoalveolar lavage fluid (BALF), sputum, and blood samples from 275 SCAP patients with varied characteristics and outcomes to analyze the differences in the microbes and host responses between them.



Impact of age and gender on outcomes of SCAP patients and its potential mechanisms. (a) The column chart showing differential 30-day morality of SCAP patients at different ages. The vertical line shows the cut-off age for patients to be at higher risk of 30-day death. The males were indicated in blue. The females were marked in red. (b) The box plot shows the 30-day death rate of four groups, including the females aged 55 (red), the females >55 (light green), the males aged 55 (blue), and the males >55 (purple). (c) The column chart shows DEGs in BALF and blood in the elder (patients aged >55) group

compared to the young (patients aged 55) group. (d) The GO and KEGG pathway enrichment analysis of the outcomes-related DEGs between the elder male patients and the young male patients. Credit: BGI Genomics

The researchers identified nine sets of biomarkers, both metagenomic and transcriptomic, that were associated with 30-day mortality.

The biomarkers were validated in an independent cohort of patients with SCAP and were able to predict 30-day mortality with an accuracy of 85%. This is significantly higher than the accuracy of existing clinical prediction models, which typically have accuracies of around 70%.

Other key findings:

- The study revealed that 30-day mortality was independent of pathogen category, microbial diversity or specific microbial taxa, while significant differences in host gene expression patterns were suggested to be responsible for different outcomes.
- Clinical characteristics analysis showed that male sex with age over 55 years was a risk factor for poor prognosis, and specific enrichment of genes and signaling pathways were found in omics data.

Potential of biomarkers utilization

Improve the accuracy of predicting and reducing mortality, which could lead to better clinical decision-making.
Identify patients at high risk of death, who could then be targeted with more aggressive treatment.
Reduce the need for invasive procedures, such as lung biopsies, which are associated with risks.

Improve the allocation of health care resources by identifying patients who are most likely to benefit from intensive care.
Develop new therapeutic strategies by identifying biomarkers that are associated with poor outcomes.

More information: Jingya Zhao et al, A multicenter prospective study of comprehensive metagenomic and transcriptomic signatures for predicting outcomes of patients with severe community-acquired pneumonia, *eBioMedicine* (2023). DOI: 10.1016/j.ebiom.2023.104790

Provided by BGI Genomics