A robust clustering strategy for stratification unveils unique patient subgroups in acutely decompensated cirrhosis

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Abstract

Background

Patient heterogeneity poses significant challenges for managing individuals and designing clinical trials, especially in complex diseases. Existing classifications rely on outcome-predicting scores, potentially overlooking crucial elements contributing to heterogeneity without necessarily impacting prognosis.

Methods

To address patient heterogeneity, we developed ClustALL, a computational pipeline that simultaneously faces diverse clinical data challenges like mixed types, missing values, and collinearity. ClustALL enables the unsupervised identification of patient stratifications while filtering for stratifications that are robust against minor variations in the population (population-based) and against limited adjustments in the algorithm's parameters (parameter-based).

Results

Applied to a European cohort of patients with acutely decompensated cirrhosis (n = 766), ClustALL identified five robust stratifications, using only data at hospital admission. All stratifications included markers of impaired liver function and number of organ dysfunction or failure, and most included precipitating events. When focusing on one of these stratifications, patients were categorized into three clusters characterized by typical clinical features; notably, the 3-cluster stratification showed a prognostic value. Re-assessment of patient stratification during follow-up delineated patients' outcomes, with further improvement of the

prognostic value of the stratification. We validated these findings in an independent prospective multicentre cohort of patients from Latin America (n = 580).

Conclusions

By applying ClustALL to patients with acutely decompensated cirrhosis, we identified three patient clusters. Following these clusters over time offers insights that could guide future clinical trial design. ClustALL is a novel and robust stratification method capable of addressing the multiple challenges of patient stratification in most complex diseases.