SEROLOGIC PROFILING OF ANTIBODY RESPONSE FOR PREDICTION OF THE CLINICAL OUTCOME IN INVASIVE CANDIDIASIS

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Better prognostic predictors for invasive candidiasis (IC) are needed to tailor and individualize therapeutic decision-making and minimize its high morbidity and mortality. We investigated whether molecular profiling of IgG-antibody response to the whole soluble *Candida* proteome could reveal a prognostic signature that may serve to devise a clinical-outcome prediction model for IC and contribute to known IC prognostic factors. By serological proteome analysis and data-mining procedures, serum 31-IgG antibody-reactivity patterns were examined in 45 IC patients randomly split into training and test sets. Within the training cohort, unsupervised two-way hierarchical clustering and principal-component analyses segregated IC patients into two antibody-reactivity subgroups with distinct prognoses that were unbiased by traditional IC prognostic factors and other patients-related variables. Supervised discriminant analysis with leave-one-out cross-validation identified a 5-IgG antibody-reactivity signature as the most simplified and accurate IC clinical-outcome predictor, from which an IC prognostic score (ICPS) was derived. Its robustness was confirmed in the test set. Multivariate logistic regression and receiver-operating-characteristic curve analyses demonstrated that the ICPS was able to accurately discriminate IC patients at high-risk for death from those at low-risk and outperformed conventional IC prognostic factors. Further validation of the 5-IgG antibody-reactivity signature on a multiplexed immunoassay supported the serological proteome analysis results. We conclude that the ICPS, with additional refinement in future larger prospective cohorts, could be applicable to reliably predict patient clinical-outcome for individualized therapy of IC. Our data further provide insights into molecular mechanisms that may influence clinical outcome in IC and uncover potential targets for vaccine design and immunotherapy against IC.