Cardiac complications as a major predictor of in-hospital death in infective endocarditis using machine-learning algorithm analysis

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Introduction: Despite advances in diagnostic and therapeutic strategies, infective endocarditis (IE) remains associated with devastating outcomes with substantial mortality rate. In patients who develop cardiac complications, an early aggressive therapeutic strategy regarding surgical intervention may be warrant. The epidemiologic profile of IE has been changed, which highlights the need for studies with risk stratification of patients hospitalized with IE.

Purpose: The study aim is to investigate variables strongly associated with in-hospital death and define groups of patients at different risk profile based on values of explanatory variables.

Methods: A prospective cohort including 349 consecutive patients with IE admitted to a quaternary hospital. The diagnosis was based on the modified Duke criteria and modified European Society of Cardiology criteria from 2015. Data regarding predisposing conditions, laboratory, imaging results, treatment, and outcomes were described. The primary endpoint was in-hospital mortality due to any complication related to IE. Cardiac complications were defined as development or worsening heart failure, prosthesis rupture or perivalvular extension of infection.

In-hospital death was analyzed through conditional inference trees and the composed nodes were discriminated in groups with different risks of death and by logistic regression model.

Results: The median age was 55 years, 59% of patients had native valve, 23.5% prosthetic valve and 35.5% intracardiac device-related IE. Rheumatic heart disease corresponded to 25%, 18% presented diabetes and 13.5% had chronic kidney disease as predisposing conditions. The main causative microorganism was Staphylococcus aureus (19%) and average C-reactive protein (CRP) at diagnosis was 72mg/L.

During treatment, 123 (35%) had cardiac complications, 73 (21%) neurological complications, and 45 (13%) suffered embolic events. A total of 105 (47%) patients underwent cardiac surgery. The overall in-hospital mortality was 35.5%. On multivariable analysis, the independent predictors of death were increasing age, high CRP, neurologic and cardiac complications (Figure 1), with C statistic of the model 0.76 (CI 95% 0.70-0.82).

According to the decision-tree analysis (Figure 2), patients with cardiac complications, CRP >71mg/L and age >43 years-old had 83.8% mortality rate, whereas those without cardiac or neurologic complications and CRP ≤51 had 7.1% in-hospital death. Among all predictors, cardiac complications showed the strongest association with the primary endpoint.

Conclusions: Cardiac and neurologic complications, elevated age and high CRP were independently associated with death. The machine-learning algorithm demonstrated that cardiac complications were the most important risk factor for in-hospital death. Early identification of patients who are at high risk of death can offer opportunity for more aggressive monitoring and approach to improve IE outcome.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>OR (CI 95%)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>1.016 (0.999-1.033)</td>
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<tr>
<td>CRP</td>
<td>1.005 (1.003-1.007)</td>
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<tr>
<td>Neurological events</td>
<td>3.960 (1.788-8.769)</td>
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<tr>
<td>Cardiac complications</td>
<td>4.364 (2.487-7.657)</td>
</tr>
</tbody>
</table>

Logistic regression model
Decision-tree analysis