Time to blood culture positivity is an independent predictor of mortality, and endocarditis, in patients with Staphylococcus aureus bacteraemia

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Background: Staphylococcus aureus is the second most common pathogen isolated from blood cultures, and ranks first in terms of mortality. Time to blood culture positivity (TTP) is routinely available, but this information has attracted limited attention to date, although this variable may reflect inoculum, virulence, or a combination of both. We aimed to study the association between TTP, and clinical presentation, complications (including endocarditis), and outcome, in patients with S. aureus bacteraemia.
**Material/methods:** The VIRSTA study is a multicentric prospective cohort study that included all patients with *S. aureus* bacteremia from 2009 to 2011. We analyzed data from the four centers who prospectively collected data on TTP. The association between TTP and 30 day-mortality was analyzed using a Poisson regression. A logistic regression model was used for the association between TTP and definite endocarditis (Duke-Li criteria).

**Results:** We included 587 patients with *S. aureus* bacteraemia (71.6% male), with a mean age of 65.3 ± 16.3 years, and a 30 day-mortality of 20.6%. The median TTP was 13.7 h (interquartile range, 9.9-18). On multivariate analysis, 30-day mortality was associated with TTP ≤ 13.7 h (OR 1.69 [1.11-2.57]; p=0.02), as well as age, comorbidities (McCabe score), methicillin resistance, stroke, pneumonia, and C-Reactive Protein (table). TTP was also associated with endocarditis (n=42) in multivariate analysis, but the association was not linear, with an U-shape curve (figure): endocarditis was more common in the first (OR 2.32 [1.30-4.15]), and the last (OR 2.99 [1.05-8.53]) quartiles of TTP, p=0.002.

**Conclusions:** TTP may provide additional reliable information in patients with *S. aureus* bacteraemia on outcome (early growth as an independent predictor of death), and on the risk of endocarditis (higher in patients with short, or long TTP). For this latter risk, the non-linear association may reflect two unrelated phenomena: i) short TTP may reflect high inoculum and thus higher risk of endocarditis; ii) longer TTP may be related to increased doubling time of bacteria entered in a slow metabolic state in established endocarditis.

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR [95% CI]</th>
<th>P</th>
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<tbody>
<tr>
<td>TTP &gt; 13.7 h</td>
<td>1 (ref)</td>
<td></td>
</tr>
<tr>
<td>TTP ≤ 13.7 h</td>
<td>1.69 [1.11-2.57]</td>
<td>0.02</td>
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<tr>
<td>Age (per 1 year increment)</td>
<td>1.02 [1.01-1.03]</td>
<td>0.02</td>
</tr>
<tr>
<td>Meticillin-resistant <em>S. aureus</em></td>
<td>1.92 [1.20-3.07]</td>
<td>0.006</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.85 [1.36-5.96]</td>
<td>0.005</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1.69 [1.01-2.85]</td>
<td>0.04</td>
</tr>
</tbody>
</table>

TTP, Time to blood culture positivity

**Figure.** Association between time to blood culture positivity (TTP) and endocarditis in patients with *Staphylococcus aureus* bacteraemia
Fractional Polynomial (.5 .5),
adjusted for covariates