Prevalence of Infective Endocarditis in Streptococcal Bloodstream Infections Is Dependent on Streptococcal Species

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STUDY DESIGN
RETROSPECTIVE DATA ANALYSIS

2008 – 2017

DENMARK
CAPITAL REGION (serving 1.5 Mio people)

DATASET
3 DANISH NATIONAL REGISTRIES
LOCAL DEPARTEMENTS OF CLINICAL MICROBIOLOGY
INCLUSION

PATIENTS / DATA
• BSI (-30d TO +14d)
• HOSPITALISATION >14d

BSI-CASE
• MIN. 1 POSITIVE BLOOD CULTURE BOTTLE (1 EPISODE = 14d)
• MONOINFECTION
• STREPTOCOCCUS SPECIES IDENTIFICATION AVAILABLE

INFECTIOUS ENDOCARDITIS
• ICD-10 CODES

BSI = bloodstream infection
IE = infectious endocarditis
1. STREPTOCOCCAL BSI
HOSPITALISED PATIENTS WITH STREPTOCOCCAL BSI

- 0.5% OF ALL BSI ANALYSED
- 6506 EPISODES
  (236 PATIENTS WITH >1 EPISODE)
<table>
<thead>
<tr>
<th></th>
<th>Demographics</th>
<th>Comorbidities*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age, mean (SD)</td>
<td>Male, n (%)</td>
</tr>
<tr>
<td><strong>All BSIs (N=6506)</strong></td>
<td>68.1 (16.2)</td>
<td>3437 (52.8)</td>
</tr>
<tr>
<td><em>S pneumoniae</em> (n=2598)</td>
<td>67.3 (16.2)</td>
<td>1237 (47.6)</td>
</tr>
<tr>
<td><em>S dysgalactiae</em> (n=901)</td>
<td>72.0 (14.1)</td>
<td>521 (57.8)</td>
</tr>
<tr>
<td><em>S pyogenes</em> (n=592)</td>
<td>64.4 (17.7)</td>
<td>283 (47.8)</td>
</tr>
<tr>
<td><em>S agalactiae</em> (n=441)</td>
<td>67.7 (16.9)</td>
<td>233 (52.8)</td>
</tr>
<tr>
<td><em>S anginosus</em> (n=437)</td>
<td>66.6 (15.7)</td>
<td>261 (59.7)</td>
</tr>
<tr>
<td><em>S mitisloralis</em> (n=408)</td>
<td>66.8 (17.6)</td>
<td>240 (58.8)</td>
</tr>
<tr>
<td><em>S galloyticus</em> (n=225)</td>
<td>73.9 (12.2)</td>
<td>140 (62.2)</td>
</tr>
<tr>
<td><em>S salivarius</em> (n=191)</td>
<td>68.4 (16.4)</td>
<td>106 (55.5)</td>
</tr>
<tr>
<td><em>S sanguinis</em> (n=133)</td>
<td>71.5 (14.2)</td>
<td>82 (61.7)</td>
</tr>
<tr>
<td><em>S parasanguinis</em> (n=107)</td>
<td>66.8 (15.8)</td>
<td>59 (55.1)</td>
</tr>
<tr>
<td><em>S gordonii</em> (n=95)</td>
<td>69.3 (15.8)</td>
<td>56 (59.0)</td>
</tr>
<tr>
<td><em>S constellatus</em> (n=91)</td>
<td>65.5 (16.6)</td>
<td>59 (64.8)</td>
</tr>
<tr>
<td><em>S mutans</em> (n=48)</td>
<td>71.9 (18.1)</td>
<td>23 (47.9)</td>
</tr>
<tr>
<td><em>S thermophilus</em> (n=45)</td>
<td>71.3 (14.7)</td>
<td>24 (53.3)</td>
</tr>
<tr>
<td>G adhereus (n=41)</td>
<td>69.6 (14.8)</td>
<td>26 (63.4)</td>
</tr>
<tr>
<td>S intermedius (n=40)</td>
<td>65.3 (16.3)</td>
<td>23 (57.5)</td>
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</tbody>
</table>

BSI indicates bloodstream infection; and IE, infective endocarditis.

*Medical history before IE.
†Native valve disease without prosthetic valve.
‡Cardiac implantable electronic device.
2. INFECTIVE ENDOCARDITIS IN STREPTOCOCCAL BSI
ICD-10 CODE + STREPTOCOCCAL BSI

7.1 % INFECTIVE ENDOCARDITIS

⇒ VARIATION: 0 – 48 %
⇒ HIGHLY SPECIES DEPENDENT
<table>
<thead>
<tr>
<th>Common BSIs</th>
<th>Low Risk (&lt;3%)</th>
<th>Moderate Risk (3% to 10%)</th>
<th>High Risk (10% to 30%)</th>
<th>Very High Risk (&gt;30%)</th>
<th>Number of BSIs (N=6506)</th>
</tr>
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<tbody>
<tr>
<td><em>S. pneumoniae</em>, n (% [95% CI])</td>
<td>30 (1.2 [0.8–1.6])</td>
<td></td>
<td></td>
<td></td>
<td>2598</td>
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<tr>
<td><em>S. dysgalactiae</em>, n (% [95% CI])</td>
<td>58 (6.4 [4.9–8.2])</td>
<td></td>
<td></td>
<td></td>
<td>901</td>
</tr>
<tr>
<td><em>S. pyogenes</em>, n (% [95% CI])</td>
<td>11 (1.9 [0.9–3.3])</td>
<td></td>
<td></td>
<td></td>
<td>592</td>
</tr>
<tr>
<td><em>S. agalactiae</em>, n (% [95% CI])</td>
<td>40 (9.1 [6.6–12.1])</td>
<td></td>
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<td></td>
<td>441</td>
</tr>
<tr>
<td><em>S. anginosus</em>, n (% [95% CI])</td>
<td>21 (4.8 [3.0–7.3])</td>
<td></td>
<td></td>
<td></td>
<td>437</td>
</tr>
<tr>
<td><em>S. mitis/salivarius</em>, n (% [95% CI])</td>
<td>79 (19.4 [15.6–23.5])</td>
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<td>408</td>
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**Moderately common BSIs**

| *S. gordonii*, n (% [95% CI]) | 115 (2.8 [2.3–3.4]) |                          |                        |                       | 291                     |
| *S. parasanguinis*, n (% [95% CI]) | 11 (2.6 [1.9–3.3]) |                          |                        |                       | 225                     |
| *S. constellatus*, n (% [95% CI]) | 5 (0.9 [0.6–1.3]) |                          |                        |                       | 53                      |

**Uncommon BSIs**

| *S. mutans*, n (% [95% CI]) | 23 (4.8 [3.3–6.8]) |                          |                        |                       | 48                      |
| *S. thermophilus*, n (% [95% CI]) | 5 (1.2 [0.8–1.6]) |                          |                        |                       | 41                      |
| *G. adiacens*, n (% [95% CI]) | 0 |                          |                        |                       | 40                      |
| *S. intermedius*, n (% [95% CI]) | 0 |                          |                        |                       | 26                      |
| *S. vestibularis*, n (% [95% CI]) | 0 |                          |                        |                       | 23                      |
| *S. infantarius*, n (% [95% CI]) | 0 |                          |                        |                       | 14                      |
| *S. equinus*, n (% [95% CI]) | 0 |                          |                        |                       | 12                      |
| *S. peroris*, n (% [95% CI]) | 0 |                          |                        |                       | 10                      |
| *S. crista/sirolis*, n (% [95% CI]) | 4 (0.9 [0.6–1.3]) |                          |                        |                       | 9                       |

**Rare BSIs**

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n>325 (>-5%)

n=65–325 (1% to 5%)

n=7–64 (0.1% to 1%)

n<7 (<0.1%)
RISK FOR IE
Figure 4. Risk of Infective endocarditis in streptococcal bloodstream infections according to risk factors and different streptococcal species. A multivariable logistic regression analysis of the risk of Infective endocarditis (IE) in streptococcal bloodstream infections (SBIs). A. The risk of IE according to age, sex, ≥3 positive blood culture (BC) bottles, native valve disease, previous IE, and cardiac device. B. The risk of IE in different streptococcal species adjusted for the factors in A and with S. pneumoniae SBIs as a reference. The results are presented as odds ratio (OR; 95% CI).
Figure 3. Prevalence of infective endocarditis in bloodstream infections with different streptococcal species.
The figure shows the prevalence of infective endocarditis (IE) in bloodstream infections (BSIs) with different streptococcal species. The horizontal axis (disproportionate) shows number of BSI cases and the vertical axis the prevalence of IE. The size of each circle represents the numeric number of IE cases according to the specific species. The area of each circle is proportional with number of IE cases with a range from 4 to 80 cases. The color scale from green to red highlights the increasing prevalence of IE.
STREPTOCOCCAL GROUP vs. SPECIES - RELEVANCE FOR IE?

- outdated?
- still relevant?
- more relevant than ever?
## Major criteria

### 1. Blood cultures positive for IE
a. Typical microorganisms consistent with IE from 2 separate blood cultures:
   - *Viridans streptococci*, *Streptococcus gallolyticus (Streptococcus bovis)*, *HACEK* group, *Staphylococcus aureus*; or
b. Community-acquired enterococci, in the absence of a primary focus; or
b. Microorganisms consistent with IE from persistently positive blood cultures:
   - ≥2 positive blood cultures of blood samples drawn >12 h apart; or
   - All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or
c. Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titre >1:800

### 2. Imaging positive for IE
a. Echocardiogram positive for IE:
The image shows a bar chart comparing the frequency of different species of bacteria found in various studies. The chart includes:

- S. mitis/oralis (n=79)
- S. galolyticus (n=68)
- S. dysgalactiae (n=58)
- S. sanguinis (n=46)
- S. gordonii (n=42)
- S. agalactiae (n=40)
- S. pneumoniae (n=30)
- S. anginosus (n=21)

The chart also indicates the frequency of surgery and one-year mortality rates for each species, with the following percentages:

- Surgery:
  - S. mitis/oralis: 17 (21.5)
  - S. galolyticus: 11 (16.2)
  - S. dysgalactiae: 7 (12.1)
  - S. sanguinis: 9 (19.6)
  - S. gordonii: 13 (31.0)
  - S. agalactiae: 10 (25.0)
  - S. pneumoniae: 8 (26.7)
  - S. anginosus: 6 (28.6)

- One-year mortality:
  - S. mitis/oralis: 22 (27.9)
  - S. galolyticus: 9 (13.2)
  - S. dysgalactiae: 17 (29.3)
  - S. sanguinis: 11 (23.9)
  - S. gordonii: 7 (16.7)
  - S. agalactiae: 10 (25.0)
  - S. pneumoniae: 6 (20.0)
  - S. anginosus: 5 (23.8)
Figure 4. Risk of infective endocarditis in streptococcal bloodstream infections according to risk factors and different streptococcal species. A multivariable logistic regression analysis of the risk of infective endocarditis (IE) in streptococcal bloodstream infections (BSIs). A, The risk of IE according to age, sex, ≥3 positive blood culture (BC) bottles, native valve disease, prosthetic valve, previous IE, and cardiac device. B, The risk of IE in different streptococcal species adjusted for the factors in A and with *S. pneumoniae* BSI as a reference. The results are presented as odds ratio (OR; 95% CI).
DISCUSSION
- ONLY PATIENTS WITH “IE-DIAGNOSIS” INCLUDED

- IMPORTANT DATA MISSING:
  - ECHOCARDIOGRAPHY
  - MICROBIOLOGY
  - CLINICAL DETAILS (TREATMENT, OUTCOME)
  - PATIENTS WITH BSI WITHOUT IE

- RELEVANCE STREPTOCOCCAL GROUP / SPECIES FOR IE?

- SIGNIFICANCE OF 1 SINGLE POSITIVE BLOOD-CULTURE?
Figure legend: The horizontal axis shows the different streptococcal groups and the vertical axis the prevalence of IE. The figure illustrates the IE prevalence within each streptococcal group, both in average (○) and in different species (●).

IE, infective endocarditis
Figure 4. Risk of infective endocarditis in streptococcal bloodstream infections according to risk factors and different streptococcal species.

A multivariable logistic regression analysis of the risk of infective endocarditis (IE) in streptococcal bloodstream infections (SBIs). A. The risk of IE according to age, sex, ≥3 positive blood culture (BC) bottles, native valve disease, prosthetic valve, previous IE, and cardiac device. B. The risk of IE in different streptococcal species adjusted for the factors in A and with S. pneumoniae SBI as a reference. The results are presented as odds ratio (OR; 95% CI).