

Session: EP190 Direct detection methods

**Category: 4b. Diagnostic bacteriology – non-culture based, including molecular and MALDI-TOF**

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## **Added diagnostic value and impact on antimicrobial therapy of 16S rRNA PCR and amplicon sequencing on resected heart valves in infective endocarditis**

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**Background:** For adequate management and therapy of infective endocarditis (IE), identification of the causative pathogen is crucial. Unfortunately blood cultures (BC) are negative in 2-30% of IE patients and heart valve culture (VC) is insensitive. 16S rRNA PCR and amplicon sequencing (16S rRNA PCR) performed on excised heart valves from IE patients proved to be accurate and more sensitive than VC but data on diagnostic performance and impact on antimicrobial therapy are scarce.

**Material/methods:** All patients undergoing valve surgery at the University Hospitals of Leuven for definite or possible IE, according to modified Duke Criteria, were prospectively included over a 3-year (2013-2016) period. Valves were analyzed with 16S rRNA PCR (UMD-Tissue; Molzym). BC, VC and serology results were collected. Criteria of Shrestha et al. (Ann Thorac Surg 2015) were used to define the microbial IE cause.

**Results:** 127 patients were included. Sensitivity of BC (87%) and 16S rRNA PCR (87%) was higher ( $p \leq 0.05$ ) than of VC (25%) in patients (n=120), post-operatively classified as definite IE. The remaining patients (n=7) were post-operatively classified as rejected IE. Valve origin, the causative pathogen or effective pre-operative antibiotics did not influence sensitivity of 16S rRNA PCR. Sensitivity of BC (53%), 16S rRNA PCR (82%) and VC (41%) in patients (n=17) with post-operative definite IE, not receiving antibiotics prior to valve surgery was not different ( $p > 0.05$ ). The added diagnostic value and clinical impact of valve 16S rRNA PCR is shown in Table 1.

**Conclusions:** Valve 16S rRNA PCR was significantly more sensitive than VC and confirmed positive BC results in 66% of cases. In 21% of cases, 16S rRNA PCR clarified culture results or was the only method detecting and identifying the causative pathogen. In 10% of cases, molecular testing results influenced antimicrobial therapy.

Table 1: Added diagnostic value and clinical impact of molecular results.

|  | Added diagnostic value<br>N=127 (%) | Impact on antimicrobial therapy<br>N=127 (%) |
|--|-------------------------------------|--|
| Causative pathogen detected only by 16S rRNA PCR   | 9 (7) <sup>a</sup>                  | 1 (1) <sup>b</sup>                           |
| Identification of the causative pathogen in cases with mixed or discordant BC/VC results   | 11 (9)                              | 6 (5) <sup>c</sup>                           |
| Negative result in culture-negative pre-operative definite/possible IE cases, all classified as rejected IE post-operatively   | 7 (5)                               | 5 (4) <sup>d</sup>                           |
| <b>No added diagnostic value:</b>  |                                     |  |
| - Confirmation positive BC results   | 84 (66)                             |  |
| - False negative result  | 14 (11)                             |  |
| - BC positive for <i>P. aeruginosa</i> , VC positive for <i>P. aeruginosa</i> / <i>S. sanguinis</i> and 16S rRNA PCR positive for <i>E. faecalis</i> / <i>Acinetobacter</i> spp. | 1 (1)                               |  |
| - BC/VC positive for <i>E. faecalis</i> with positive but unidentifiable molecular result  | 1 (1)                               |  |

<sup>a</sup>*Coxiella burnetii* (n=2), *P. acnes* (n=2), Coagulase-negative staphylococci (n=2), *S. gallolyticus* (n=1), *S. mitis* (n=1), *A. actinomycetemcomitans* (n=1); <sup>b</sup>Doxycyclin/rifampicin started after 16S rRNA PCR was positive for *C. burnetii*; <sup>c</sup>Narrowing antimicrobial spectrum; <sup>d</sup>Stop antibiotics.