



What is the time-to-positivity of blood cultures in infective endocarditis?

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Dear Editor,

We read with interest the recently work of Lindell et al. describing 51 cases of prosthetic valve endocarditis caused by *Propionibacterium* species and recommending prolonged incubation of blood cultures up to 14 days to minimize the risk of false-negative results [1].

Infective endocarditis (IE) is an endovascular infection, usually with continuous bacteremia [2]. Therefore, blood cultures are the cornerstone of IE diagnosis and provide live bacteria for both identification and susceptibility testing.

Bordeaux University Hospital is a French endocarditis referral center, where blood cultures are incubated for 14 days in cases of suspected IE [3]. To evaluate the clinical value of this practice, we conducted a retrospective study from January 2013 to December 2017 on the time-to-positivity (TTP) of blood cultures for possible or confirmed IEs. Blood cultures

were performed using the Becton Dickinson BD BACTEC FX™ platform. The TTP was defined as the time from the start of incubation to the alert signal [4–6]. For each patient,

Table 1 Characteristics of the 270 infective endocarditis cases

Characteristics	N = 270 (100%)
Patient demographics	
Male gender	204 (75.6%)
Age (years) (median, IQR)	69 (55.2–77.7)
Type of IE	
Native valve	147 (54.4%)
Prosthetic valve	123 (45.6%)
Acquisition mode of the IE	
Community-acquired	144 (53.3%)
Healthcare-associated	126 (46.7%)
Evolution ^a	
Embolism	155 (58.5%)
No embolism	110 (41.5%)
Microorganisms	
<i>Staphylococcus aureus</i>	78 (28.9%)
Coagulase-negative staphylococci	29 (10.7%)
Viridans group streptococci	46 (17%)
<i>Streptococcus gallolyticus</i>	26 (9.6%)
<i>Streptococcus pneumoniae</i>	2 (0.7%)
β-hemolytic streptococci	7 (2.6%)
<i>Enterococcus faecalis</i>	53 (19.6%)
<i>Enterococcus faecium</i>	4 (1.5%)
Other Gram-positive ^b	6 (2.2%)
HACEK	7 (2.6%)
Other Gram-negative ^b	7 (2.6%)
<i>Candida</i> sp.	5 (1.8%)

^a Information not available for 5 patients

^b The group “other Gram-positive” comprises *Lactococcus* sp., *Lactobacillus* sp., *Corynebacterium* sp., and *Aerococcus urinae*. The group “other Gram-negative” includes *Neisseria* sp., *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Stenotrophomonas maltophilia*. IE, infective endocarditis

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Fig. 1 Distribution of the time-to-positivity (TTP) of blood cultures in 270 cases of IEs

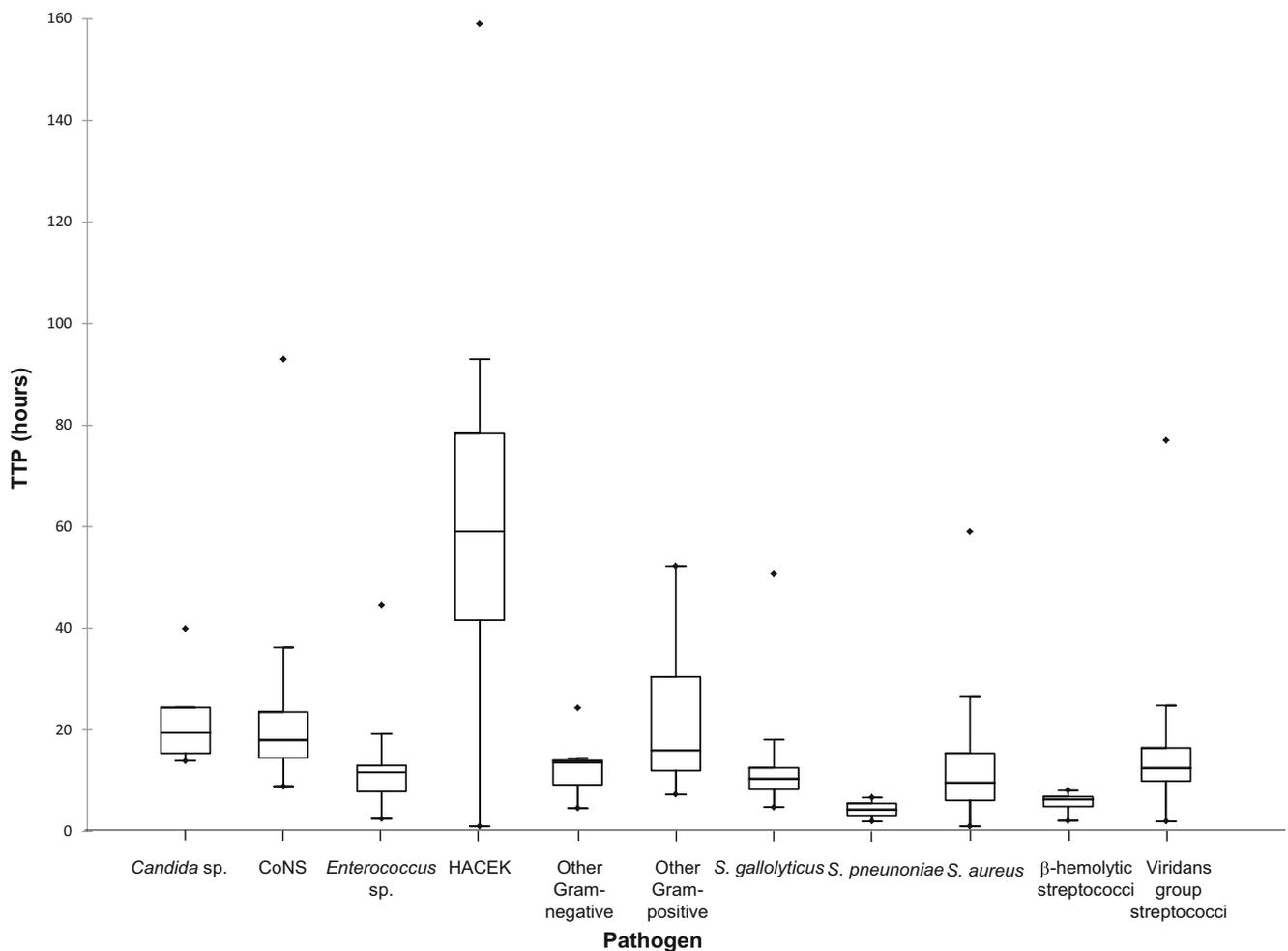
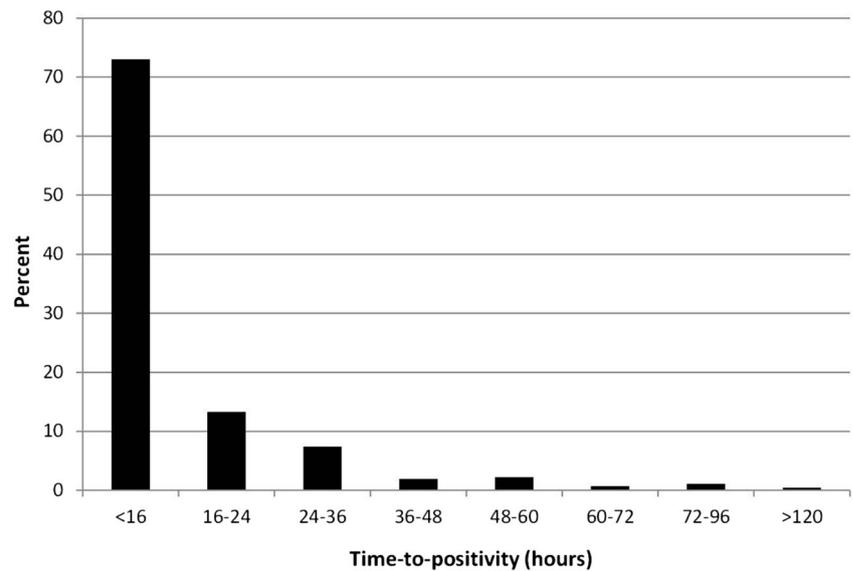


Fig. 2 Pathogens and time-to-positivity (TTP) distributions. The central rectangles span the first quartile to the third quartile of TTP, the segments inside the rectangle shows the medians. The ends of the whiskers represent one and a half times the interquartile range. Black points above and below the rectangles means the locations of the minimum and maximum

TTP values. The group “other Gram-positive” comprises *Lactococcus* sp., *Lactobacillus* sp., *Corynebacterium* sp., and *Aerococcus urinae*. The group “other Gram-negative” includes *Neisseria* sp., *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Stenotrophomonas maltophilia*. CoNS: coagulase-negative staphylococci

only the TTP of the first set of positive blood cultures was retained for analyses. When both aerobic and anaerobic bottles were positive, we used the shortest TTP. For statistical analyses, we used the Wilcoxon-Mann-Whitney, chi-square, or Fisher's exact test, as appropriate. Statistical significance was defined as a p value < 0.05 .

During the study period, 270 patients were enrolled. The characteristics of the patients are described in Table 1. Gram-positive bacteria, Gram-negative bacteria, and *Candida* sp. were identified in 251 (93%), 14 (5.2%), and 5 (1.8%) cases, respectively. The median TTP was 11.8 h (IQR, 7.5–16.6). The TTP was less than 24 h in 233 episodes (86.3%; Fig. 1). In eight (3%) and three (1.1%) episodes, the TTP was longer than 48 h and 72 h, respectively. The TTP was longer than 120 h in only one case. The TTP of the pathogens is illustrated in Fig. 2. The TTP of *Streptococcus pneumoniae* was the shortest (4.35; IQR, 3.2–5.5) and the TTP of HACEK was longest (59.1; IQR, 41.6–78.4). All blood cultures with *S. pneumoniae* or β -hemolytic streptococci were positive within 24 h (4.4; IQR, 3.2–5.5 and 6.3; IQR, 5–6.9, respectively). The TTP was significantly shorter in native valve (11; IQR, 6.8–15.7) than in prosthetic valve IEs (12.2; IQR, 8.7–19.3; $p = 0.041$). There was no difference between the TTPs of community-acquired (11.8; IQR, 7.5–16) compared with healthcare-associated IEs (11.9; IQR, 7.9–18), nor between patients with (12; IQR, 7.5–16.4) and without (11.4; IQR, 7.8–16.6) embolism.

In our study, despite extended incubation, blood cultures remained negative in the three cases of prosthetic valve IE caused by *Propionibacterium* sp., and diagnosis relied on culture of the excised valve.

The TTP of blood cultures is influenced by several factors, including blood volume in culture bottles, initial inoculums, or prior antimicrobial agents. These data were not recorded in our study. Overall, our results, added to previous data, support the premise that extended incubation of blood cultures beyond the standard 5-day protocol is rarely productive [7–9].

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