# Broad-Range PCR in Selected Episodes of Prosthetic Joint Infection

The use of eubacterial PCR of the 16S rRNA (PCR) for diagnosing prosthetic-joint-associated infections (PJIs) is still a matter of debate. Several drawbacks need to be considered when using this technique, including the lack of susceptibility results (except for methicillin-resistant *Staphylococcus aureus*) and problems in identifying a mixture of bacterial species in a single specimen [1]. A number of studies have indicated that the routine use of PCR in PJIs does not offer a diagnostic advantage over bacterial culture [2–4]. However, this molecular method can detect bacterial DNA in samples when conventional cultures are negative due to previous antimicrobial exposure or unfavorable growth conditions. Taking these considerations into account, we use PCR only if the chance of bacterial growth is low because of previous surgical and antimicrobial treatment or previous negative culture results. In order to (re)assess the diagnostic value of PCR in those selected episodes of suspected PJI in which this method had been applied, we performed a retrospective study to define patient characteristics and to estimate the specificity and sensitivity of PCR versus bacterial culture. Our orthopedic surgery clinic is a 48-bed unit that acts as a primary care center for all types of orthopedic surgery of the extremities and as a tertiary care center for patients needing revision arthroplasty.

The study population consisted of patients with a joint prosthesis who were seen at our clinic from 2001 through 2005, and from whom specimens for bacterial culture and PCR were obtained because of possible PJI. The suspicion of PJI was based on clinical signs such as joint pain, effusion, erythema and warmth at the implant site, and/or implant loosening. Patient history prior to the diagnostic intervention was assessed for (1) antimicrobial treatment, (2) number of revisions performed on the affected joint, (3) confirmed and treated infection involving the affected joint within the last 24 months, and (4) implant loosening $\leq$ 12 months after implantation without other clinical signs of infection. Specimens (synovial fluid and/or biopsies from periprosthetic tissue) were obtained either during aspiration prior to surgery or during arthroscopy or open surgery. Bacterial culture and histopathologic diagnostics were performed as described previously [5]. The decision whether or not to use PCR was made by the physicians in charge following a review of the patient's history and prior to the intervention. However, the physicians were not involved in either analyzing or interpreting the data. Specimens were sent to a reference laboratory for analysis [6]. The technique is based on the amplification of bacterial 16S ribosomal DNA [6]. Criteria for definite PJI included the presence of a sinus tract communicating with the prosthesis or purulence surrounding the prosthesis at the time of surgery or acute or chronic inflammation consistent with infection on histopathologic examination [1, 7]. Infection was excluded when the above-mentioned criteria were not fulfilled, no antimicrobial treatment was administered after the episode, and no relapse occurred for at least 1 year.

Specimens for both PCR and bacterial culture were obtained in 29 episodes of possible PJI among 26 patients. This number accounted for 7.6% (23 episodes) of all revision arthroplasties ($n$ = 301) and 6.8% (6 episodes) of all joint punctures ($n$ = 88) during the study period. Patient characteristics are presented in table 1. Most episodes (48%) included a history of three or more surgical interventions (median 4, IQR 3–5) on the affected joint within a median time of 3.25 years (IQR 0.9–10.5) prior to the diagnostic intervention. The median number of obtained specimens per patient for bacterial culture was five (IQR 3–7) and for PCR, one (IQR 1–2).

No infection was present in 17 (59%) of the 29 episodes, although the duration of follow-up was $\leq$ 12 months in

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Table 1
**Demographic data and history of 26 patients with 29 episodes of suspected prosthetic-joint-associated infections (PJIs) from whom specimens for bacterial culture and broad-range PCR were obtained.**

| Characteristic | Number of episodes (%) |
|---|---|
| Median age (years) | 70.5 (range 53–80) |
| Sex | |
| Male | 13 |
| Female | 13 |
| Affected joint | |
| Hip | 13 (44.8%) |
| Knee | 16 (55.2%) |
| Patient history prior to presentation | |
| ≥ 3 revisions performed at the affected joint | 14 (48%) |
| Confirmed and treated infection at the affected joint within ≤ 24 months | 9 (31%) |
| Previous antimicrobial treatment | 8 (27.5%) |
| 0–2 Weeks prior to intervention | 3 |
| 2–4 Weeks prior to intervention | 1 |
| 4–8 weeks prior to intervention | 4 |
| Implant loosening ≤ 12 months after implantation without other clinical signs of infection | 6 (21%) |

two cases (4, 11 months) due to non-episode-related death and loss to follow-up, respectively. The PCR was negative in all 17 cases with clinically excluded infection. In contrast, there was bacterial growth in five episodes, but these were interpreted as contamination. In the infection episodes, one inaccurate PCR result was considered to be a false-positive. Based on these findings, the specificity for bacterial culture was 71% and for PCR 94%.

The criteria for PJI were fulfilled in 12 (41%) of the 29 episodes; this accounted for 8.5% of 142 confirmed PJI episodes (including 62% referred cases) during the study period. The results of bacterial culture and PCR are presented in table 2. In five episodes, both diagnostic approaches identified the same microorganism. However, in two of these, PCR revealed only one pathogen, while two distinct microorganisms grew in culture. In two further episodes, the pathogen was identified either only by bacterial culture or only by PCR. Hence, the sensitivity for bacterial culture was 58% and for PCR, 50%.

Little information is available for assisting clinical practitioners in selecting episodes in which PCR may be superior or complementary to bacterial culture for diagnosing PJI. The previous history of the patients included in this study (Table 1) highlights the importance of distinguishing PJI from other causes of joint failure. Based on this history, we decided it was reasonable to expand diagnostic means by an additional tool in these selected episodes.

Broad-range PCR and more advanced molecular methods show a high specificity (96%–100%) [3, 4, 8–12], but often a poor sensitivity (≤ 50%) in diagnosing PJI [3, 4, 8, 10, 12]. Similarly, the specificity was excellent in

Table 2
**Results of bacterial culture and broad-range PCR in 12 episodes of confirmed PJI.**

| Episode | Sample origin | Bacterial culture | | 16S rRNA-PCR | |
|---|---|---|---|---|---|
| | | Number of positive/ total number of specimens | Pathogen | Number of positive/ total number of specimens | Pathogen |
| 1 | Synovial fluid | 2/2 | *Streptococcus pyogenes* | 1/1 | *Streptococcus pyogenes* |
| 2[a] | Periprosthetic tissue | 2/13 | *Propionibacterium* sp. | 1/8 | *Streptococcus infantis* |
| 3 | Synovial fluid | 1/1 | *Staphylococcus aureus* | 1 | Negative |
| 4 | Periprosthetic tissue | 1 | No growth | 1 | Negative |
| 5 | Periprosthetic tissue | 1 | No growth | 1 | Negative |
| 6 | Synovial fluid | 1 | No growth | 1/1 | *Streptococcus bovis* |
| 7 | Periprosthetic tissue | 5/11 | *Staphylococcus aureus* | 1/1 | *Staphylococcus aureus* |
| | | 1/11 | *Enterococcus faecalis* | | |
| 8 | Periprosthetic tissue | 6 | No growth | 2 | Negative |
| 9 | Periprosthetic tissue | 6/9 | *Staphylococcus epidermidis* | 1/1 | *Staphylococcus epidermidis* |
| 10 | Periprosthetic tissue | 5/6 | *Pseudomonas aeruginosa* | 2/2 | *Pseudomonas aeruginosa* |
| | | 1/6 | *Enterococcus faecalis* | | |
| 11 | Periprosthetic tissue | 1/5[b] | *Staphylococcus epidermidis* | 1/1 | *Staphylococcus epidermidis* |
| 12 | Periprosthetic tissue | 5 | No growth | 1 | Negative |

[a] Identification of the pathogen in this episode was inconclusive, since in both diagnostic methods the ratio of number of positive: total number of specimens was low. However, based on the previous history (duration of symptoms 19 months) and the small fragment for amplification isolated from the biopsy, *Propionibacterium* sp. was interpreted as possible pathogen, and *Streptococcus infantis* as contamination; [b] Results from diagnostic arthroscopy. Four weeks later, one-stage exchange was performed and *Staphylococcus epidermidis* grew in 8 of 16 obtained biopsies

our selected episodes. In all episodes with a previous history of multiple revisions or previously treated PJI, PCR remained negative when no infection was present. Also, in only one out of six episodes with early implant loosening (≤ 12 months after implantation) but no other clinical signs of PJI was an infection present, and the PCR results matched accordingly. Importantly, in five episodes, PCR was useful in identifying false-positive results from bacterial culture.

The sensitivity of the PCR, however, was poor (50%). The overall sensitivity in diagnosing PJI increased to 67% when both PCR and bacterial culture were considered together (i.e. one or other or both positive). Since our study was performed retrospectively, and patients selected for PCR were not recruited according to strictly predefined criteria, the study could have been influenced by a selection bias. Therefore, no immediate recommendation about the use of PCR in PJI can be made.

However, the expense and diagnostic value of PCR in comparison to bacterial culture [2–4] warrant the use of this molecular method only selectively and not routinely, and in addition to bacterial culture. In our center, PCR has been performed in fewer than 10% of all revision arthroplasties (i.e. in patients with a complex history of joint disease) and found to have only a limited diagnostic value. In fewer than 20% of the episodes, PCR was helpful in recognizing false-positive culture results. In terms of the applicability of PCR in clinical practice, more studies are required to identify both a patient population and a diagnostic strategy in which the use of such a molecular tool is beneficial in diagnosing or excluding PJIs.

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