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Multiple deep tissue cultures in primary total hip arthroplasty: prognostic value for periprosthetic infection

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Fernando P Ferro, Felipe S Bessa, Hélder Miyahara, Leandro Ejnisman, Jose RN Vicente and Alberto T Croci

Abstract

Background: The risk of infection after total hip replacement (THR) is significant, with negative impact on quality of life and high costs. Bacteria can contaminate the surgical site despite aseptic techniques; however, there is debate regarding the benefit of identifying bacteria during the primary procedure. Although taking multiple samples for culture is a well-established practice in revision arthroplasty, doing so in primary cases remains controversial. We aimed to investigate whether there is a prognostic value in the culture of samples taken during primary THR, seeking a correlation between the positivity of the cultures and subsequent prosthetic joint infection (PJI).

Methods: Deep samples (capsule, femoral and acetabular bone) were collected from 426 patients undergoing elective primary THR. Follow-up was at least 3 years. Microbiological profiles of cultures were analysed. Patient data were reviewed for the identification of risk factors presumably associated with a higher risk of PJI.

Results: 54 surgeries (12.6%) had positive cultures. 16 cases (3.8%) developed infection, of which 5 had a positive culture in the primary surgery. Infection rate was 9.3% in patients with positive culture and 3% in those with negative culture ($p < 0.05$), with an odds ratio of 3.34 (95% CI, 1.09–10.24). Patients with previous hip surgery had an infection rate of 8.5%, compared to 2.9% in patients with no previous surgery ($p < 0.05$).

Conclusions: Routinely harvesting microbiologic samples in primary THR is not justified, as it has no consequence in clinical decision for most patients. It might be recommended in selected cases that are suspected to be at high risk for infection, especially previously operated patients (conversion arthroplasty).

Keywords

Culture, infection, microbiology, primary total hip arthroplasty, risk factors

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Introduction

Among all possible complications after total hip replacement (THR), infection is 1 of the most challenging, due to the high levels of morbidity and costs involved.[1–3] Treatment often requires additional surgical procedures, long hospital stays, extended antibiotic therapy and implant exchange/removal.[3]

Most prosthetic joint infections (PJIs) are assumed to be acquired in the operating room; some infections occur exogenous in the early postoperative days by wound contamination and some occur due to haematogenous spreading.[4,5] 1 possible way of identifying the source of infection might be to identify micro-organisms during the primary surgery. Al-Maiyah et al.[4] studied the contamination of surgical gloves during operation and found a contamination rate of 9% in primary THR. Several studies investigated the utility of culturing samples obtained from suction drain tips and swabs.[6–11] The results of routine intraoperative swabs in primary THR are not conclusive, as no

Institute of Orthopedics and Traumatology, Hospital das Clínicas, Faculty of Medicine, University of São Paulo, Brazil

Corresponding author:
Fernando P Ferro, Rua Dr. Ovidio Pires de Campos, 333 Cerqueira César, São Paulo, SP 05403-010, Brazil.
Email: fpferro@gmail.com

correlation between the microbiological findings and the outcome concerning PJI could be proven yet. The usefulness of swabs to diagnose PJI has to be questioned at all. Nowadays, microbiological examination of intraoperative samples are the state of the art to diagnose PJI,[12] but there is a lack of data whether they are reliable to predict and prevent PJI when taken in primary THR.

We wanted to investigate whether microbiological analysis of intraoperative samples can predict later PJI in a large cohort of primary THR. This might be useful in the prevention or early treatment of PJI. Our hypothesis was that patients with positive cultures during primary THR would be at a higher risk for developing infection. The second hypothesis was that the germs in the positive cultures were the causative bacteria in later PJI.

Methods

In a retrospective study, all patients undergoing primary elective THR were included consecutively between 2009 and 2011. The study was IRB approved. The operations were performed by 6 senior staff surgeons from a single university teaching hospital and a resident or fellow in training. All operations were made through a lateral approach (Hardinge[13]). If any hardware was present due to previous surgery and interfered with proper implant positioning, it was removed in the same procedure. Porous titanium-aluminum noncemented femoral components and noncemented acetabular cups were inserted.

Prophylactic cefuroxime (1.5 g) was administered 30 minutes before incision and then repeated twice daily (total dose 3 g/day) for 48 hours. It was not weight adjusted and was not repeated during surgery. Patients underwent skin disinfection with chlorhexidine gluconate 2% approximately 30 minutes before incision. All surgery rooms had laminar airflow. Skin was prepped with alcoholic chlorhexidine 0.5% immediately before draping and incision. A vacuum suction drain was used for 48 hours after surgery.

3 culture samples were collected from all patients from the joint capsule, acetabular bone and femoral bone. About 4 cm^3 of tissue was obtained for each sample. The most distal portion of the joint capsule at its femoral insertion was resected. Acetabular bone samples were obtained from the inside of the reamers. Femoral bone samples were obtained from the surface of the rasps. All involved senior surgeons adhered to the same sample collection routine, which was determined by the senior author and explained to all surgeons.

After collection, samples were stored directly in a sterile container with thioglycollate and then taken directly to the laboratory. Time from harvesting to incubation should be less than 2 hours according to our institutional guidelines. Incubation time was 10 days.

If a patient had a positive culture but no clinical signs of infection, antibiotics were not prescribed and follow-up routine was the same. Patients who developed PJI during follow-up were treated according to the clinical situation independent of the results of the tissue cultures.

Patients were seen at 2, 6, and 12 weeks post-op, then 6 months, and then annually. Patients were free to request an earlier visit if they had complaints. The minimum follow-up time was 36 months.

Postoperative infection was defined according to established guidelines: a purulent fistula communicating with the joint or two positive culture samples with identical bacteria. Infection was also confirmed if 4 of the following 6 criteria existed: (1) elevated ESR or CRP; (2) elevated synovial leukocyte count; (3) elevated synovial neutrophil percentage; (4) presence of purulence in the affected joint; (5) isolation of 1 micro-organism in 1 culture of periprosthetic tissue or fluid; (6) positive histology.[14]

The following patient-related data were evaluated and retrieved from medical records: age, sex, length of hospital stay, diagnosis, previous hip surgery, alcohol abuse, smoking, diabetes, neoplasm, human immunodeficiency virus (HIV), injected drug use, immunosuppressant drugs used to treat autoimmune conditions, urinary tract infection (within 6 months of surgery), peripheral vascular disease, skin infection, and American Society of Anesthesiologists (ASA) classification.

Data were stored in an Excel for MAC (Redmond, USA) worksheet. For statistical analysis, SPSS 23 for MAC (Armonk, USA) was used. The descriptive statistics of categorical data are explicitly expressed by their absolute numbers and their respective proportions; the continuous data are expressed by means and standard deviations.

2 outcomes were analysed: "Infection" and "Positive culture". To build the prediction model, we performed an analysis of association between the outcomes and risk factors, using the Pearson's chi-square test. Odds ratios (ORs) were generated with their respective 95% confidence intervals (95% CIs). Significance was established at $p < 0.05$.

Results

446 hips were eligible, 20 hips were excluded because of missing data, leaving 426 for analysis. 230 patients were male (53.9%), the mean age was 50.2 years (SD 13.4, range 17–83). 71 patients (16.6%) had previous hip surgery. The most common diagnosis was primary osteoarthritis (37.7%), followed by femoral head osteonecrosis (ON, 29.8%) (Table 1).

215 patients (50.4%) were ASA 1, 203 (47.6%) were ASA 2, and only 8 (1.9%) were ASA 3. This was not statistically correlated to culture positivity or PJI.

In 54 (12.7%) hips at least 1 culture was positive. Cultures were positive at the hip capsule in 23 cases (5.4%), at the femoral bone in 29 cases (6.8%) and at the acetabular bone in 13 cases (3.1%). There was a wide range of isolated species (Table 2).

Table 1. Correlation between diagnosis, positive culture and PJI.

Diagnosis	*n* = (%)	Positive culture *n* = (%)	PJI *n* = (%)
All	426	54 (12.7%)	16 (3.8%)
Primary osteoarthritis	159 (37.3%)	21 (13.3%)	1 (0.6%)
Inflammatory disease	39 (9.1%)	4 (10%)	1 (3%)
Childhood disease	62 (14.6%)	8 (12.9%)	3 (4.8%)
Infection sequelae	13 (3.1%)	2 (15.4%)	1 (7.7%)
ON	127 (29.8%)	14 (11.1%)	5 (4.0%)
Post-traumatic	26 (6.1%)	5 (19.2%)	5 (19.2%)

PJI, prosthetic joint infection; ON, osteonecrosis.

Table 2. Microbiological findings in the 3 regions at index operation.

	Capsule	Femur	Acetabulum
Total	23	29	13
Acinetobacter sp	2	2	1
Bacillus sp	0	1	1
Corynebacterium sp	4	1	4
Enterobacter cloacae	0	0	1
Enterecoccus durans	0	1	0
Micrococcus sp	3	1	0
Pantoea spp	1	0	0
Prevotella sp	0	1	0
Propionibacterium acnes	1	0	1
Pseudomonas sp	2	3	0
coagulase-negative *staphylococcus* (CNS)	4	10	1
Staphylococcus aureus	0	1	0
Staphylococcus capitis	0	1	1
Staphylococcus cohnii	0	1	0
Staphylococcus epidermidis	3	4	1
Staphylococcus haemolyticus	2	2	0
Staphylococcus saprophiticus	1	0	0
Staphylococcus warneri	0	0	2

10 patients had 2 positive cultures (2.3%) and no hip had 3 positive cultures. There was no hip with 2 positive cultures with the same micro-organism. Smoking was the only significant risk factor for at least one positive culture ($p = 0.002$) (Table 3).

16 hips (3.8%) developed PJI during follow-up. The mean time between primary surgery and diagnosis of PJI was 78 days (range 15–504). The most frequent detected germ was *Staphylococcus aureus* (10 hips), 4 patients developed a multibacterial infection (Table 4). The only significant risk factor for PJI was previous surgery ($p = 0.037$).

Treatment options were: non-operative with antibiotics alone (4 hips, all with no bacteria identified), debridement, antibiotics and implant retention (DAIR, 5 hips) or implant exchange (7 hips) (Table 4). 4 infected patients refused further surgery and received antibiotic treatment alone; in these patients, joint aspiration culture was negative and the diagnosis of infection was based on minor criteria.[15] Antibiotic therapy was empirically selected.

Of all 54 patients with positive cultures, 5 (9.3%) developed PJI. In 2 of these 5 hips no germ was identified, in the remaining 3 hips the causative bacteria of the PJI differed from the positive biopsy at primary operation (Table 5).

Hips with a positive culture at primary operation had a PJI more frequently ($p = 0.023$). The absolute risk of developing a PJI in case of positive culture was 9.3%, the odds ratio of developing PJI was 3.34 (95% CI, 1.09–10.24).

Discussion

It is believed that most PJIs are acquired in the operating room with micro-organisms from the patient's skin and suspended particles. Davis et al.[16] reported that a contamination of the surgical field occurred in up to 63% of arthroplasties, and some of these contaminations lead to PJI. Thus, typical skin microbes like coagulase-negative staphylococci (CNS) are frequently isolated in PJIs.[17]

Obtaining intraoperative cultures to identify high-risk patients for PJI has been attempted in several studies. In 1973, Fitzgerald et al.[18] suggested that there would be a positive correlation between culture positivity and subsequent infection. More recent data showed that the culture of the drain tip has no predictive value of PJI.[6–8] Similar findings were described for swabs.[9] In 2008, Picado et al.[10] described their experience after a protocol of collection of 4–6 deep swaps before wound closure after primary THR. They found that an isolated culture had no predictive value, but that 2 or more positive cultures with the same germ were associated with a higher risk of infection. They concluded that taking several swabs would be a reasonable strategy to detect patients with increased risk for PJI.

We observed a wide diversity of bacteria at the index operation not representing the typical spectrum for PJI and no patient had two positive samples with the same germ. We found 12.7% hips with at least one positive culture. This number may seem high at first glance, but is

Table 3. Incidence of positive cultures and of PJI in relation to risk factors.

Demographic data	*n* (%)	Positive culture *n* (%)	*p*	PJI *n* (%)	*p*
All	426	54 (12.7)		16 (3.8)	
Male	230 (53.9%)	34 (14.8%)	0.158	10 (4.4%)	0.692
Previous hip surgery	71 (16.6%)	11 (15.5%)	0.445	6 (8.5%)	**0.037**
Alcohol abuse	32 (7.5%)	5 (15.6%)	0.614	2 (6.3%)	0.506
Smoking	72 (16.9%)	17 (23.6%)	**0.002**	3 (4.2%)	0.556
Diabetes mellitus 1/2	34 (8%)	2 (5.9%)	0.211	1 (2.9%)	0.739
Neoplasm	5 (1.2%)	1 (20%)	0.624	0%	0.645
HIV infection	4 (0.9%)	1 (25%)	0.46	0%	0.681
Immunosuppressant drug	55 (12.9%)	6 (10.9%)	0.663	0%	0.104
Urinary tract infection	35 (8.2%)	3 (8.6%)	0.44	1 (2.9%)	0.715
Peripheral vascular disease	2 (0.5%)	0%	0.558	0%	0.772
Cutaneous infection	5 (1.2%)	1 (20%)	0.624	0%	0.645

PJI, prosthetic joint infection; HIV, human immunodeficiency virus.

Table 4. Microbiologic findings of the intraoperative samples and during treatment of the 16 patients with PJI.

	Capsule	Femur	Acetabulum	Treatment	Culture at debridement	Culture at exchange
1	*0*	*0*	*0*	DAIR	*S. aureus*	–
2	*0*	*0*	*S. epidermidis*	IV antibiotics without surgery	–	–
3	*0*	*0*	*0*	DAIR	*S. epidermidis*	–
4	*0*	*0*	*0*	exchange	–	*S. aureus*
5	*0*	*Corynebacterium sp*	*0*	exchange	*S. aureus*	*S. aureus*
6	*0*	*Bacillus sp*	*0*	DAIR	*S. aureus*	–
7	*0*	*0*	*0*	PO antibiotics without surgery	–	–
8	*0*	*0*	*0*	PO antibiotics without surgery	–	–
9	*0*	*0*	*0*	exchange	*S. aureus*	*S. aureus*
10	*0*	*0*	*0*	exchange	*S. aureus*	*S. aureus*
11	*0*	*0*	*0*	DAIR	*E. cloacae* + *S. aureus* + CNS	–
12	*0*	*0*	*0*	exchange	*S. aureus* + *E. cloacae*	negative
13	*0*	*0*	*0*	exchange	*S. aureus*	*S. aureus* + *S. marcecens*
14	*0*	*0*	*0*	exchange	*S. aureus*	negative
15	*CNS*	*0*	*0*	PO antibiotics without surgery	–	–
16	*CNS*	*0*	*0*	DAIR	*P. mirabilis* + *E. cloacae*	–

CNS, coagulase-negative *staphylococcus*; DAIR, debridement and implant retention.

Table 5. Microbiologic findings of the 5 hips with positive cultures and PJI.

	Index surgery	Treatment	Culture at debridement	Culture at removal
1	*S. epidermidis*	IV antibiotics without surgery	–	
2	*Corynebacterium spp.*	exchange	*S. aureus*	*S. aureus*
3	*Bacillus spp.*	DAIR	*S. aureus*	
4	CNS	PO antibiotics without surgery	–	
5	CNS	DAIR	*P. mirabilis* + *E. cloacae*	

CNS, coagulase-negative *staphylococcus*; DAIR, debridement and implant retention.

in line with some previous published data.[6,10,19,20] Jonsson et al.[21] reported 38% positive cultures (collecting swabs) in primary THRs and 53% in primary TKRs. When compared to the high number of positive cultures, their incidence of clinical infection was low, as we found for our population too. They concluded that a high number of culture samples seem to be contaminated after collection. Sample contamination can occur at any time including all

steps from harvesting, storage, transportation, and processing and can lead to false positive cultures. Many of our isolated species are present in the normal human skin microbiota, although they may occasionally be associated with opportunistic infections in immunocompromised patients (*Pantoea spp., Corynebacterium spp*.). The broad spectrum of grown micro-organisms, many of them atypical for PJI, suggest that many of our positive cultures were contaminations too.

On the other hand, there could be a variability in time between collection and incubation, due to transit and lab time prior to incubation.[22] In the present study, we tried to get the probes in the laboratory within 2 hours but we were unable to confirm that all probes were correctly stored or processed in this timeframe. Delicate micro-organisms (e.g. anaerobics) might have been missed, leading to false negative results.

We observed a low diversity of bacteria in patients who had infection. The predominant organisms were notorious for causing PJI, including *S. aureus*, as well as gram-negative pathogenic species (*Enterobacter cloacae, S. marcescens and Proteus mirabilis*),[23] representing a more typical spectrum for PJI as compared to the micro-organisms detected during the index operations.

Previous surgery was the only risk factor we found for PJI and the reason might be multifactorial. The number of included patients was too low to detect other associated risk factors for PJI and this was not aim of the study. Our study group has a relatively young when compared to typical populations of THR. Our hospital is unable to handle many patients with several comorbidities requiring intensive care after surgery, but we tend to operate on younger patients with more complex sequelae, which is reflected by only 37.7% patients with primary OA as diagnosis. This could contribute to our relatively high rate of PJI (3.8%).

It is remarkable that patients with positive cultures had a 3.34-fold increased risk to develop PJI. However, none of the detected germs at primary THR was causative for later PJI. Thus, we found no concluding evidence that persisting infections from previous surgery could cause later PJI or that new contaminants during operation can be detected as the causative bacteria for later PJI. Many of the positive cultures might have been caused by some kind of contamination during the whole process of analysis. Complex cases might have had an increased risk both for contamination of the samples and for later PJI by other micro-organisms. The probable contamination of the surgical site that led to PJI might have occurred after taking the samples, might have occurred in other anatomic localisation (e.g. subcutaneously) or the initial bacterial load was too low for positive samples but high enough to cause symptoms of PJI later.

Many risk factors are the same for positive cultures and for PJI. Only a few risk factors could be detected, and the risk might be multifactorial, but for such an analysis, the number of patients was too low. This can explain the correlation between positive samples and PJI but do not prove that positive samples cause later PJI. None of our patients would have had a benefit from antibiotic treatment based on the germs detected at index operation. In case of PJI an adequate therapy should be based on microbiologic findings after aspiration and biopsies, as is already done according to most recent consensuses.

Our study has several limitations. Operating time and body mass index (BMI) were not systematically recorded. Both are established risk factors for PJI, and it can be assumed that they might affect the rate of positive samples too. This might explain the correlation between positive samples and later PJI too.

There was no sonication of the removed hardware, which could have yielded even more positive cultures, and possibly increased the probability to predict the germ of later PJI. On the other hand, sonication has a rather high rate of contamination too, thus the use of sonication would probably not have affected our conclusions.

The included patients were rather young with few comorbidities; nevertheless, the overall infection rate was high. There was a low percentage of primary OA and many patients with ON or previous surgery, implying a high proportion of high-complexity cases, which can be an explanation. For these reasons, our risk analysis for PJI may not be generalisable to other hospitals.

Tranexamic acid was not routinely used, there was no specific regimen for blood management and many cases were rather complex. This might have led to higher blood loss and transfusion rates. These parameters were not recorded systematically but could be an explanation for the high rate of PJI too, as they are well-known risk factors for PJI.

The strength of the study is the high number of included cases and a complete follow-up of 3 years. Another strength is the prospective sample collection in a consecutive series of primary THR. It is the first study of this size using tissue samples instead of swabs, which is proven to be more sensitive and specific.[12]

We could confirm our hypothesis that patients with positive cultures during primary THR have a higher risk for developing PJI. However, the germs in the positive cultures never were the same bacteria in later PJI and thus we had to reject our second hypothesis that the germs found in the cultures were causative for consecutive PJI.

Conclusion

Routinely harvesting microbiologic samples in primary THR is not justified, as it has no consequence in clinical decision for most patients. It might be recommended in selected cases that are suspected to be at high risk for infection, especially previously operated patients (conversion arthroplasty).

Declaration of conflicting interests

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