Prevalence and Outcomes of Unexpected Positive Cultures in Presumed Aseptic Revision Total Hip Arthroplasty

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ABSTRACT

Introduction: Periprosthetic infection rates are sometimes underestimated, given that many cases of presumed aseptic failure may be due to unrecognized infection. The objectives of this study were: 1) to estimate the prevalence of unexpected positive intraoperative cultures; 2) to determine if any of the patient's comorbidities or risk factors were related to the presence of unexpected positive cultures; 3) to determine the implant survival during a follow-up of at least 12 months. **Materials and Methods:** A retrospective and observational study was carried out where, through electronic medical records, all revision total hip arthroplasties (THAs) from a single institution between 2014 and 2021 were identified. **Results:** Out of 49 single-stage revision THAs, 9 patients (18.4%) had an unexpected positive culture. The isolated microorganisms were *Staphylococcus aureus* (3), *Pseudomonas aeruginosa* (1), *Staphylococcus lugdunensis* (1), *Staphylococcus epidermidis* (2), *Staphylococcus haemolyticus* (1), *Streptococcus epidermidis* (1). In addition, when we evaluated the comorbidities of the patients, none had statistical significance in favoring unexpected positive cultures in aseptic revisions. We discovered that 2% of our sample with a follow-up period of 49 months developed reinfection. **Conclusion:** Our study showed a prevalence of unexpected positive cultures of 18.4%. None of the risk factors reported in the literature was associated with a higher risk of unexpected positive cultures, except for high ESR values. Our findings in the analyzed sample suggest that unexpected positive cultures in presumably aseptic revisions do not have significant consequences on implant survival, as found in the literature.

Keywords: hip arthroplasty; hip revision surgery; microorganism; periprosthetic infections.

Level of Evidence: III

Prevalencia y resultados de cultivos positivos inesperados en revisiones de reemplazo total de cadera presumiblemente asépticas

RESUMEN

Introducción: Las tasas de infección periprotésica, a veces, son subestimadas, ya que muchos casos de presunta falla aséptica pueden deberse a una infección no reconocida. Los objetivos de este estudio fueron: 1) estimar la prevalencia de cultivos positivos intraoperatorios inesperados, 2) determinar si las comorbilidades o los factores de riesgos de los pacientes tuvieron relación con la presencia de cultivos positivos inesperados, 3) determinar la supervivencia del implante en un seguimiento mínimo de 12 meses. **Materiales y Métodos:** Se realizó un estudio retrospectivo y observacional. En las historias clínicas electrónicas, se identificaron todas las revisiones de artroplastia total de cadera de una única institución entre 2014 y 2021. **Resultados:** De las 49 revisiones de artroplastia total de cadera en un tiempo, 9 pacientes (18,4%) tuvieron un resultado positivo inesperado. Los microorganismos aislados fueron: *Staphylococcus aureus* (3), *Pseudomonas aeruginosa* (1), *Staphylococcus lugdunensis* (1), *Staphylococcus epidermidis* (2), *Staphylococcus haemolyticus* (1), *Streptococcus epidermidis* (1). Ninguna comorbilidad tuvo significancia estadística para favorecer cultivos positivos inesperados en las revisiones asépticas. El 2% de la muestra, con un período de seguimiento de 49 meses, se reinfectó. **Conclusiones:** Nuestro estudio arrojó una prevalencia de cultivos positivos inesperados del 18,4%. Ninguno de los factores de riesgo reportados en la bibliografía se asoció con un mayor riesgo de cultivos positivos inesperados, excepto los niveles altos de velocidad de eritrosedimentación glomerular. Nuestros hallazgos son compatibles con los publicados y sugieren que los cultivos positivos inesperados en revisiones presumiblemente asépticas no tienen consecuencias significativas en la supervivencia del implante.

Palabras clave: Artroplastia de cadera; revisión de cadera; microorganismo; infecciones periprotésicas.

Nivel de Evidencia: III

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INTRODUCTION

The prevalence of primary and revision total hip arthroplasties (THA) increased substantially over time, it is higher in women than in men, and increases progressively with age.[1] The total number of revision hip arthroplasties performed in 2005 is expected to double by 2026.[2]

Revision THAs are carried out for multiple reasons. Registry data has indicated that 12% of hip and knee arthroplasty patients undergo revision surgery within 10 years of their initial surgery.[3]

It is imperative to rule out an infection as a possible etiology before a revision, because the treatment becomes completely different. There is still no perfect test to diagnose periprosthetic infection (PPI)[4] and it is important to note that PPI rates are sometimes underestimated, as many cases of presumed aseptic failure may be due to unrecognized infection.[5]

Unexpected positive intraoperative cultures of microorganisms obtained during a presumed aseptic THA review present a substantial challenge to the surgeon and his or her team.[4] Published prevalence varies considerably (4% to 38%, mean 10.5%)[5] and the infection-free implant survivorship rate and optimal treatment remain unclear.[6,7]

The objectives of this study were: 1) to estimate the prevalence of unexpected positive intraoperative cultures in presumably aseptic THA revisions, 2) to determine if there is a relationship between comorbidities or risk factors of patients with the presence of an unexpected positive culture, 3) to determine implant survivorship in these patients with at least 12 months of follow-up.

MATERIALS AND METHODS

We carried out a retrospective and observational study. We identified all revision THAs in the electronic medical records of a single institution that took place between 2014 and 2021.

Surgical records were reviewed to identify revision THAs performed for aseptic indications. Cleaning and debridement cases with implant retention and two-stage revisions were excluded from the analysis. We consider a revision to be initially aseptic based on the clinical symptoms (afebrile patient, no inflammatory signs of the wound, absence of fistula and secretion) and blood tests with normal values of white blood cells, glomerular filtration rate (GFR) and C-reactive protein (CRP), and analysis of joint puncture fluid with <3000 white blood cells and <80% polymorphonuclear cells.

Fifty-eight revisions for aseptic causes were identified in a total of 120 all-cause THA revisions (Figure 1). We excluded aseptic revisions with no available intraoperative cultures (n = 9) in order to establish a true cohort and estimate the prevalence of unexpected positive intraoperative findings, yielding 49 aseptic revisions with available culture data. In nine of the 49 aseptic revisions, at least one microorganism was isolated in solid culture media or culture broths.

All patients had at least one year of follow-up after the aseptic revision procedure.

Microorganisms were classified into three types: virulent, indolent, and miscellaneous/contaminants (Table 1). Management of unexpected positive intraoperative cultures was determined on the basis of the organism isolated. In accordance with the indication of the Infectious Disease Service of the institution, the patients were treated in the short term (8-12 weeks) if they met any of the following criteria: 1) one or more positive cultures for virulent organisms and fungi, and 2) two or more positive cultures for indolent organisms. In addition, the decrease in inflammatory parameters, GFR, and CRP was taken into account to define the end of antibiotic therapy.

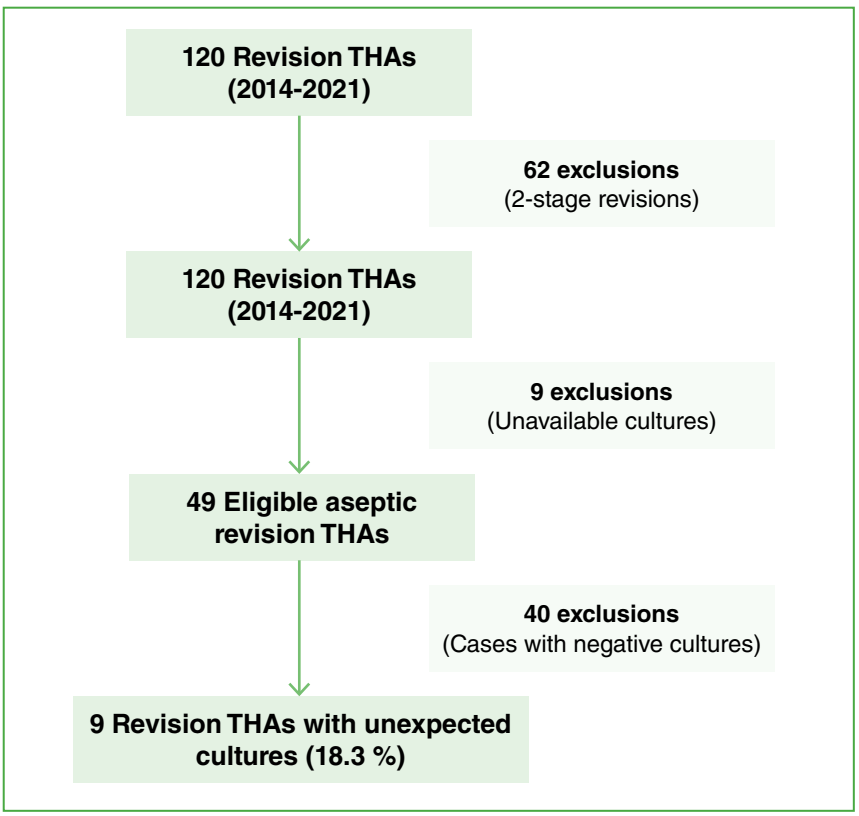

Figure 1. Flowchart showing selectable total hip arthroplasty revisions and the number of unexpected positive intraoperative cultures.

Table 1. Classification of microorganisms

Category	Group	Microorganism
Virulent	Gram-positive cocci	*Streptococcus viridans* (1) *Staphylococcus aureus* (3) *Enterococcus* (0)
	Gram negative	*Pseudomonas aeruginosa* (1) *Klebsiella pneumoniae* (0) *Escherichia coli* (0)
Indolent	Gram-positive cocci coagulase-negative *Staphylococcus aureus* *Propionibacterium acnes*	 *Staphylococcus epidermis* (2) *Staphylococcus haemolyticus* (1) *Staphylococcus lugdunensis* (1)
Miscellaneous/ Contaminant	Possible contaminant – Gram-positive cocci	Other coagulase-negative *Staphylococcus aureus*

RESULTS

The sample consisted of 49 patients, 61.2% of them were women, with a mean age of 66 years (range 30-86). Of the 49 single-stage total hip revisions, nine patients (18.4%) had an unexpected positive intraoperative culture. The reasons for revision were: presumed aseptic loosening (59.2%), periprosthetic fracture (24.5%), instability (12.2%) and polyethylene wear (4.1%) (Table 2).

Table 2. General characteristics of the patients

Variables	Categories	Number of patients	Percentage
Sex	Female	30	61.2
	Male	19	38.8
Age, mean (SD)		66.0 (14.4)	
ASA	1	2	4.1
	2	38	77.6
	3	9	18.4
Reason for revision	Aseptic loosening	29	59.2
	Periprosthetic fracture	12	24.5
	Instability	6	12.2
	Polyethylene wear	2	4.1

SD = standard deviation, ASA = American Society of Anesthesiologists.

The mean surgery time was 167 min (range 90-270). The mean time from primary THA to revision was 10 years (standard deviation [SD] = 6.3) and the mean follow-up time after revision was 30 months (range 12-80).

The isolated microorganisms are summarized in Table 1. Eight of the nine patients had two or more positive samples, one patient had only one positive sample. The decision on the specific antibiotic therapy for each patient and the duration of treatment was always made in conjunction with the Infectious Diseases Service. We did not carry out an analysis of the antibiotic therapy selected for each patient and its results because it exceeded the objectives of the study.

When CRP and GFR values were analyzed, the mean CRP was 1.1 (SD = 2.2) with values between 0.11 and 9.51. When comparing the CRP value between patients who had either positive or negative cultures, it was observed that the mean CRP was higher if germs had been isolated (2.39 vs. 0.80, respectively); however, the difference between these values did not have statistical significance (Table 3). Mean preoperative GFR levels were 21.8 (SD = 21.6) (range 1-103). When differentiating between patients with positive cultures and those without positive cultures, this parameter was higher in the former (mean 38.6 vs. 18.1, respectively), with a statistically significant difference (Table 3).

Table 3. Preoperative C-reactive protein and glomerular filtration rate values according to culture results.

	Culture	Mean	SD	Minimum	Maximum	p
C-reactive protein	Negative (n = 40)	0.80	1.98	0.11	9.51	0.053
	Positive (n = 9)	2.39	2.95	0.13	8.14	
Glomerular filtration rate	Negative (n = 40)	18.1	17.0	1	101	**0.044**
	Positive (n = 9)	38.6	31.6	3	103	

SD = standard deviation.

When evaluating patients' comorbidities and risk factors (rheumatoid arthritis, diabetes, obesity, smoking), none were associated with unexpectedly positive cultures. Neither were age and sex characteristics (Table 4).

Table 4. Distribution of the cultures according to the type of revision

Variables	Categories	Negative	Positive	p
Sex	Female	24	6	0.711
	Male	16	3	
Age		65.9 ± 15.1	66.3 ± 11.7	0.826
Diabetes	No	34	9	0.215
	Yes	6	0	
Rheumatoid arthritis	No	36	8	0.921
	Yes	4	1	
Body mass index >25 (obese/ overweight)	No	29	5	0.319
	Yes	11	4	

One patient (2.04%) of the sample, with a follow-up of 49 months, suffered a reinfection (Figure 2). An unexpected positive culture for coagulase-negative *Staphylococcus* was detected in two intraoperative samples. The patient is currently receiving suppressive antibiotic treatment due to his comorbidities and age. The rest of the patients with positive cultures (8 cases) have not had infection in the follow-up time.

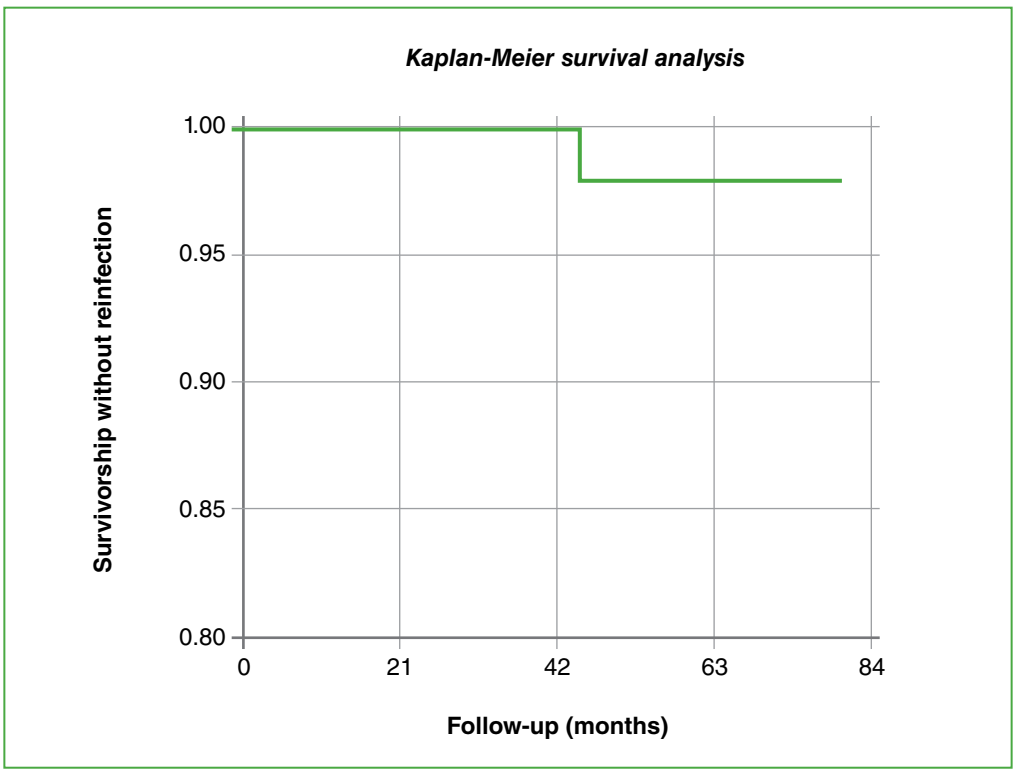

Figure 2. Kaplan-Meier curve showing implant survivorship without reinfection.

DISCUSSION

There is no consensus on the diagnostic criteria for PPIs; therefore, diagnosis and management of positive intraoperative cultures from presumably aseptic THA revisions are difficult.

Currently, PPI is diagnosed using the criteria of the Musculoskeletal Infection Society or the International Consensus Meeting.[8] The recommendation of the Infectious Disease Society of America on single positive cultures is to treat only highly virulent pathogens, such as *Staphylococcus aureus*.[5]

Current evidence suggests that a single positive culture in presumably aseptic revisions is associated with an increased risk of reinfections and re-screening. Milandt et al.[9] studied 54 hip arthroplasties and found that a single positive culture is a risk factor for re-revision. Our results indicated that 2.04% of the sample (n = 49) had a reinfection; however, when only patients with unexpectedly positive cultures (n = 9) were analyzed, that number increased to 11.11%.

The published prevalence of PPI is highly variable, this may be due to differences in pre-, intra- and postoperative management, and the lack of standardized criteria for the diagnosis of PPI and its treatment. Early aseptic loosening has been reported to be associated with unidentifiable PPIs.[8] Our analysis revealed that the main reason for THA revision was aseptic loosening (59.2%), eight of the nine patients with unexpectedly positive cultures underwent revision for this reason.

In this series, the infection-free implant survival time was 80 months, a considerably longer period than those published in other studies (from 26 to 66 months).[8]

Benign prostatic hyperplasia, male sex, obesity, elevated CRP, and adverse reaction to metal have been associated with an increased risk of prosthesis failure due to PPI.[8] In our results, none of these parameters had statistical significance in favoring unexpected positive cultures in these aseptic revisions, except for elevated GFR values. These differences may be due to the small sample size.

The results obtained suggest that unexpected positive cultures in presumably aseptic revisions are not significant in implant survivorship, data compatible with what has been published in other studies.[10,11] However, all the patients in the series received antibiotic treatment regardless of the criteria accepted by the Musculoskeletal Infection Society for the diagnosis of PPI.

As limitations of the study, we can highlight: 1) its retrospective nature and the size of the sample, 2) the fact that the technique used for the analysis of the cultures was direct examination of solid cultures or culture broths (at that moment, other methods that would have improved the infection detection technique, such as implant sonication, were not available), 3) that the number of samples sent varied considerably between patients, so there could be false negative results.

CONCLUSIONS

18.4% of the presumably aseptic THA revisions presented positive cultures and, in our series, there was no relationship with any comorbidity or risk factor of the patient. After the previous clinical and biochemical study, and the appropriate antibiotic treatment, we consider that unexpected positive cultures had no impact on implant survival. However, it is important to note that all patients with positive cultures were prescribed antibiotic treatment. For this reason, we affirm that an unexpected positive culture of low-virulence pathogens should not be disregarded as a simple contaminant and we recommend a minimum antibiotic treatment of two to three months with clinical and laboratory controls. On the other hand, based on the analysis of the results, we believe it is of fundamental importance to exhaust the pre-surgical diagnostic instances to define whether a revision surgery is aseptic or not, in order to obtain minimal or null percentages of unexpected positive cultures. A clinical analysis with exhaustive laboratory parameters and a pre-surgical joint puncture must be performed on all patients undergoing revisions. It is also very important to take a minimum of 3-5 intraoperative samples for the physical-chemical and bacteriological study.

More large-scale studies with diagnostic and treatment protocols are required to obtain more reliable results on the subject.

Conflict of interest: The authors declare no conflicts of interest.

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