Risk factors for periprosthetic joint infection after total knee arthroplasty in Spanish population

Francisco Melchor
Hospital Nuestra Senora de Sonsoles
David Pescador (davidpescador@usal.es)
Hospital Universitario de Salamanca
Jose Mendoza
Hospital Universitario de Salamanca
Agustin Diaz
Hospital Universitario de Salamanca
Agustin Soler
Lister Hospital
Juan Blanco
Hospital Universitario de Salamanca

Research article

Keywords: Periprosthetic joint infection, risk factor, Spanish population

Posted Date: July 16th, 2019

DOI: https://doi.org/10.21203/rs.2.11413/v1

Abstract

Background: Periprosthetic joint infection (PJI) is the most serious and feared complication in total knee arthroplasty (TKA) and can have catastrophic consequences. The number of total knee arthroplasties has increased and will continue to increase so that the number of infections will also be greater in the future. The aim of this study is to identify the most relevant risk factors associated with infection after a total knee prosthesis in a Spanish population. Methods: This is a case-control study of patients who underwent total knee arthroplasty at the University Hospital of Salamanca during the period January 1 2010 until January 1, 2015. TKA PJI was detected in 66 patients. As controls, a similar number of patients from the same period who did not develop a periprosthetic infection were included. Demographic and clinical variables were collected. A descriptive and inferential analysis was performed. Results: Diabetes, ASA grade, obesity and the use or not of antibiotic loaded cement were statistically significant related to the appearance of the infection. For the variables of surgical time and ischemia time, this relationship disappeared when the logistic regression was made. Conclusions: Our study provides evidence that diabetes, cement type, ASA and BMI were independently associated with increased risk of PJI for TKA patients in a Spanish population. We think that modifiable risk factors were specifically relevant and for that reason we can reduce the infection rate.

Background

Total knee arthroplasty is a safe and effective procedure for the treatment of osteoarthritis and other knee diseases. Periprosthetic joint infection (PJI) is the most serious and feared complication in total knee arthroplasty (TKA) and can have catastrophic consequences. [1,2]. It causes a significant loss of quality of life and increases costs for the health care system [3]. The number of total knee arthroplasties has increased and will continue to increase so that the number of infections will also be greater in the future [4].

The incidence of PJI is variable, and in Spain it is approximately 2% [5]. There are several risk factors for PJI after TKA, including demographic factors such as age , sex , race , and comorbidities including diabetes, obesity, reumathoid arthritis [4,6–10] . Other risk factors that may be involved in the onset of infection are surgical factors, such as bone cement type (with or without antibiotics), surgical time, ischemia time [10–14]. The identification of the most important risk factor is a key element to implement measures that can reduce the rates of periprosthetic joint infection after TKA. Some risk factors can be modified, thus allowing a possible reduction in the incidence of infections.

The aim of this study is to identify the most relevant risk factors associated with infection after a total knee prosthesis in a Spanish population.

Methods

This is a case-control study of patients who underwent total knee arthroplasty at the University Hospital during the period January 1 2010 until January 1, 2015. During this period, TKA PJI was detected in 66 patients. As controls, a similar number of patients from the same period who did not develop a periprosthetic infection were included. Inclusion criteria included age over 18, no previous native knee infection, primary osteoarthritis and primary knee arthroplasty. Exclusion criteria included previous trauma, avascular necrosis, inflammatory arthroplasty, previous knee surgery and revision surgery cases.

Study population

All patients included were admitted to the University Hospital, a third level teaching hospital. Data was obtained from clinical records from the Clinical Documentation Unit of University Hospital for each patient (100% codification CIE 9). For the collection of the case group, a search of our database was performed using As keywords diagnosis of TKA infection, replacement of knee prosthesis, septic loosening of TKA was chosen. For the control group, the search term used was TKA arthroplasty. Demographic and clinical variables were collected. Also, variables were collected which could be related to the appearance of a possible periprosthetic infection. The characteristics of the sample are presented in Table 1.

Surgical procedures

All patients received antibiotic prophylaxis with cefazolin (2gr iv) or cefuroxime (1,5gr iv). vancomycin was used in patients allergic to penicillin. Following surgery, three further doses of cefazolin 1gr iv/8 hours/day or cefuroxime 750mg/iv/8 hours/day were administered. For skin preparation povidone iodine was used. A pneumatic tourniquet was used in all cases. All procedures were performed through a medial parapatellar approach. In all cases, all cemented impants were used, all patellae were resurfaced and a vacuum drainage was used.

Definition of periprosthetic infection

All cases that appeared in the clinical records with the diagnosis of periprosthetic knee infection were reviewed exhaustively to ensure the diagnosis was correct. The diagnosis of periprosthetic knee infection was made according to the criteria of the international consensus (Consensus international Parvizi): the following symptoms and signs were found: (1) a sinus tract communicating with the prosthesis; (2) positive culture results from tissue or fluid samples from the affected prosthesis; or (3) 4 of the following 6 criteria are present: (a) elevated serum C-reactive protein level and erythrocyte sedimentation rate, (b) elevated synovial white blood cell count, (c) high synovial polymorphonuclear (PMN) leukocyte percentage, (d) presence of purulence in the joint, (e) positive culture result from one sample from the affected joint, and (f) PMN leukocyte count of more than 5 per high-powered field in 5 high-powered fields on histologic analysis at 4006 magnification.

Statistical analysis

A descriptive analysis was performed. The distributions of demographic characteristics and risk factors between cases and controls were compared using t-student test for quantitative variables and chi-square tests for categorical variables. For the analysis of the effect of each risk factor on the appearance of the infection, a regression analysis was performed and the odds ratio was calculated. We have also calculated the association measures and the attributable fraction of risk for each factor, and the risk differences, selecting those factors that have shown greater impact. The attributable fraction of the risk means how much of the risk of occurrence of the infection is due to exposure to the risk factor. In other words, attributable fraction estimates the fraction of risk which could be avoided if the factor were eliminated. The calculation of this measure allows to know in a more exact way the effect of a risk factor in the appearance of an event.

Results

The average age and sex distribution are homogeneous in cases and controls. In the case group, 27% of patients received antibiotic loaded cement, compared to 57% of the patients who were in the control group and did not have an infection. Diabetes was more frequent, almost double, in patients who had an infection than the control group cases. Likewise, obesity was much more frequent in the case group. A higher American Society of Anesthesiologist (ASA) score of III and IV was seen in the infection group much more frequently than in the control group. It was also observed that those cases that presented the infection required more surgical time and longer tourniquet time. Of the variables studied, we found that diabetes, ASA grade, obesity and the use or not of antibiotic loaded cement were statistically significant related to the appearance of the infection. For the variables of surgical time and ischemia time, this relationship disappeared when the logistic regression was made. For the statistically significant variables we calculate the risk and association measures. The attributable risk and the association measures were calculated as shown in Table 2.

Discussion

Total knee arthroplasty is a surgical procedure that offers very good results with pain relief and restoration of function [15]. Infection is one of the most feared complications and is the most important cause of TKA revision. The proper management of the infected TKA usually requires new surgical procedures, prolonged hospital stays and prolonged antibiotic treatment and therefore, it is important to know what are the risk factors of the infection for its control [16,17].

In our country, the infection rate of knee arthroplasties is higher than those reported in other countries [4,17,18]. The data of infection rates in primary TKA presented in arthroplasty registers from some countries show infection rates less than 2% [19–21] , in our country it is around 2% [17]. The actual incidence of prosthetic knee infection may not be well analyzed. Several factors can introduce important biases [22] .Several risk factors have been linked to the onset of the knee prosthesis infection. Some factors are related to biodemographic characteristics. Many authors find that factors related to the patient are the most important risk factors in the onset of infection [23]. The most important

biodemographic factors related to TKA infection were ethnicity, obesity, diabetes, rheumatoid arthritis and comorbidities [23]. Other factors that may be involved in the onset of infection are surgical factors, such as type of cement used, surgical time, ischemia time, antibiotic prophylaxis, surgeon experience and operating room environment . Several authors have conducted studies about the risks factors for infection in TKA. There is no consensus for all the factors and there are even some contradictory data, but, it seems evident that there are some risk factors for prosthetic infection that should be corrected. Some of these factors are related to a greater susceptibility to infection such as steroid treatment or rheumatoid arthritis where we know that there may be some immunosuppression.

We have found significant differences between the two study groups for the risk factors indicated in table 1. These risk factors that are related to infection are: cement type, obesity, ASA grade and diabetes. In the case of surgical time and ischemia time, when a regression analysis was performed, the statistically significant association disappears.

Patient risks factors

In the case of patient risks factors, we find that diabetes, obesity an ASA score are statistically significant with TKA infection. Glycemic control was an important factor to preventing surgical site infection. Some studies have pointed out the relationship between diabetes and the increased risk of infection of arthroplasties [6,8,24,25] . For the obesity we find also a relationship with infection. Obesity is also a factor related to the development of periprosthetic infection of the knee, especially if it is associated with diabetes [24,26]. In a large study about risk factors for PJI in Knee arthroplasty Namba et al [10] finds a statistically significant relationship between obesity, diabetes, ASA grade and the risk of periprosthetic infection of the knee. Other risk factors identified in this study were the male gender and age. In our study, we did not find a relationship between gender and age with a higher risk of periprosthetic knee infection. But it must be borne in mind that the ASA grade is a reflection in part of the comorbidity suffered by the patient. On these three factors, it is possible to establish control measures, especially the glycemic normalization and weight loss. Among the patient factors, age and male gender have been indicated by some authors . In our study we have not found that these factors have an influence on the appearance of the infection. We did not find a relationship between urban or rural patient origin and PJI.

Surgical risks factors

For the surgical factors we find that only cement type have effect in the risk of PJI in knee arthroplasty. It would seem logical to think that the antibiotic-laden cement had a protective effect on infection appearance, but this fact has not been verified. The relationship between the use of cement with antibiotics and the risk of periprosthetic infection has been analyzed by several authors. Namba et al [10] in his large study does not find that the antibiotic-laden cement has a protective effect on the appearance of the periprosthetic infection, rather on the contrary. This author indicates that perhaps the patients with the highest risk of infection are those who receive cement with antibiotics. Tayton et al. [23] in a study from New Zealand Joint Registry find similar results. This author finds that the use of antibiotic loaded cement is a factor associated with the appearance of a periprosthetic infection a six month after knee

arthroplasty. Bhom et al [27] in a study with data from the Canadian registry finds that the use of cement with antibiotics has no effect on the revision rate after total knee replacement. Similarly, Hinarejos et al. [28] finds no difference between the use of cement with or without antibiotic and the risk of periprosthetic infection after total knee arthroplasty. Our results differ from those previously mentioned and it is difficult to find a cause that explains this disparity. In our study, the two groups presented similar basal characteristics and the use of cement with antibiotics or not depend on a decision of the main surgeon.

Other surgical risk factors studied were surgical time and ischemia time. In our study we have not found a relationship between both factors and the development of an periprosthetic infection when we conducted a logistic regression study. But,the duration of the surgical procedure has been linked to a higher risk of infection. Some authors have found a relationship between surgical time and PJI after knee arthroplasty [10,29]. These authors have even pointed out that times greater than 127 minutes may be associated with an increased risk of infection.

We think that modifiable risk factors were specifically relevant and for that reason we can reduce the infection rate.

This study presents some limitations. The size of the sample can be considered small, although this is a less important factor because it is a case-control study. Likewise, the type of statistical study can solve the smallest sample size. In the study of the risk factors related to infection, various statistical tools have been used. In some cases, some of the factors that were initially shown as relevant, lost their significance in another type of analysis. In this case we believe that the study of attributable risk fraction is interesting because it can offer us more evident data of the impact of a risk factor in the appearance or not of a clinical event, in this case the infection of the TKA. In our opinion, the findings of risk measures are interesting, especially the attributable risk that informs us of the impact of each risk factor in the incidence of infection, both for the study population and for the general population. To our knowledge, this is the first study that has presented this data. Our study provides evidence that diabetes, cement type, ASA and BMI were independently associated with increased risk of PJI for TKA patients in a Spanish population. These results allow us to establish some preventive measures of periprosthetic infection such as weight loss, glycemic control, comorbidity control, in addition to those already established in general terms such as antibiotic prophylaxis and skin preparation.

Conclusion

We think that modifiable risk factors were specifically relevant and for that reason we can reduce the infection rate.

Abbreviations

PJI: Periprosthetic joint infection ; **TKA**: total knee arthroplasty; **PMN:** polymorphonuclear ; **ASA:** American Society of Anesthesiologist

Declarations

Acknowledgements

The authors thank Agustin Diaz for is help in statistics.

Funding

This study did not have funds

Authors' contributions

FM and JM made contributed to acquisition of data, JB and DP interpretation of results and manuscript preparation. AD performed statistical analysis. FM, DP, JM, AD, AS and JF made contributions to the conception of this study. JB contributed to the study coordination and made revision of this manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This retrospective study was approved by the Ethic Committee of University Hospital of Salamanca and written informed consent was not required for retrospective studies.

Consent for publication

Consent for publication was not necessary

Competing interests

The authors declare that they have no competing interests.

References

1. Ritter MA, Farris A. Outcome of infected total joint replacement. *Orthopedics*. 2010;33(3). doi:10.3928/01477447-20100129-09
2. Lum ZC, Natsuhara KM, Shelton TJ, Giordani M, Pereira GC, Meehan JP. Mortality During Total Knee Periprosthetic Joint Infection. *J Arthroplasty*. 2018;33(12):3783-3788. doi:10.1016/j.arth.2018.08.021
3. Poultsides LA, Ma Y, Della Valle AG, Chiu Y-L, Sculco TP, Memtsoudis SG. In-Hospital Surgical Site Infections after Primary Hip and Knee Arthroplasty — Incidence and Risk Factors. *J Arthroplasty*. 2013;28(3):385-389. doi:10.1016/j.arth.2012.06.027
4. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of Primary and Revision Hip and Knee Arthroplasty in the United States from 2005 to 2030. *J Bone Jt Surg*. 2007;89(4):780. doi:10.2106/JBJS.F.00222

5. F. Jaéna, M.I. Sanz-Gallardoa, M.P. Arrazolaa, A. García de Codesa, A. de Juanesb, C. Resinesc G de TI de la C de M. Estudio multicéntrico sobre la incidencia de infección en prótesis de rodilla. *Rev Esp Cir Ortop Traumatol*. 2012;56. Núm. 1:1-96. doi:10.1016/j.recot.2011.08.001
6. Wu C, Qu X, Liu F, Li H, Mao Y, Zhu Z. Risk factors for periprosthetic joint infection after total hip arthroplasty and total knee arthroplasty in Chinese patients. Moldawer LL, ed. *PLoS One*. 2014;9(4):e95300. doi:10.1371/journal.pone.0095300
7. Malinzak RA, Ritter MA, Berend ME, Meding JB, Olberding EM, Davis KE. Morbidly obese, diabetic, younger, and unilateral joint arthroplasty patients have elevated total joint arthroplasty infection rates. *J Arthroplasty*. 2009;24(6 Suppl):84-88. doi:10.1016/j.arth.2009.05.016
8. Everhart JS, Altneu E, Calhoun JH. Medical comorbidities are independent preoperative risk factors for surgical infection after total joint arthroplasty. *Clin Orthop Relat Res*. 2013;471(10):3112-3119. doi:10.1007/s11999-013-2923-9
9. Bozic KJ, Lau E, Kurtz S, Ong K, Berry DJ. Patient-related risk factors for postoperative mortality and periprosthetic joint infection in medicare patients undergoing TKA. *Clin Orthop Relat Res*. 2012;470(1):130-137. doi:10.1007/s11999-011-2043-3
10. Namba RS, Inacio MCS, Paxton EW. Risk factors associated with surgical site infection in 30,491 primary total hip replacements. *J Bone Joint Surg Br*. 2012;94(10):1330-1338. doi:10.1302/0301-620X.94B10.29184
11. Wu C-T, Chen I-L, Wang J-W, Ko J-Y, Wang C-J, Lee C-H. Surgical Site Infection After Total Knee Arthroplasty: Risk Factors in Patients With Timely Administration of Systemic Prophylactic Antibiotics. *J Arthroplasty*. 2016;31(7):1568-1573. doi:10.1016/j.arth.2016.01.017
12. Wang H, Qiu G-X, Lin J, Jin J, Qian W-W, Weng X-S. Antibiotic Bone Cement Cannot Reduce Deep Infection After Primary Total Knee Arthroplasty. *Orthopedics*. 2015;38(6):e462-6. doi:10.3928/01477447-20150603-52
13. Naranje S, Lendway L, Mehle S, Gioe TJ. Does operative time affect infection rate in primary total knee arthroplasty? *Clin Orthop Relat Res*. 2015;473(1):64-69. doi:10.1007/s11999-014-3628-4
14. Yi S, Tan J, Chen C, Chen H, Huang W. The use of pneumatic tourniquet in total knee arthroplasty: a meta-analysis. *Arch Orthop Trauma Surg*. 2014;134(10):1469-1476. doi:10.1007/s00402-014-2056-y
15. Nilsdotter A-K, Toksvig-Larsen S, Roos EM. A 5 year prospective study of patient-relevant outcomes after total knee replacement. *Osteoarthr Cartil*. 2009;17(5):601-606. doi:10.1016/j.joca.2008.11.007
16. Daines BK, Dennis DA, Amann S. Infection prevention in total knee arthroplasty. *J Am Acad Orthop Surg*. 2015;23(6):356-364. doi:10.5435/JAAOS-D-12-00170
17. López-Contreras J, Limón E, Matas L, et al. Epidemiology of surgical site infections after total hip and knee joint replacement during 2007-2009: a report from the VINCat Program. *Enferm Infecc Microbiol Clin*. 2012;30 Suppl 3:26-32. doi:10.1016/S0213-005X(12)70093-9
18. Rodríguez-Baño J, del Toro MD, Lupión C, et al. [Arthroplasty-related infection: incidence, risk factors, clinical features, and outcome]. *Enferm Infecc Microbiol Clin*. 2008;26(10):614-620. http://www.ncbi.nlm.nih.gov/pubmed/19100191. Accessed November 24, 2018.

19. Springer BD, Cahue S, Etkin CD, Lewallen DG, McGrory BJ. Infection burden in total hip and knee arthroplasties: an international registry-based perspective. *Arthroplast today*. 2017;3(2):137-140. doi:10.1016/j.artd.2017.05.003
20. Koh CK, Zeng I, Ravi S, Zhu M, Vince KG, Young SW. Periprosthetic Joint Infection Is the Main Cause of Failure for Modern Knee Arthroplasty: An Analysis of 11,134 Knees. *Clin Orthop Relat Res*. 2017;475(9):2194-2201. doi:10.1007/s11999-017-5396-4
21. Meehan JP, Danielsen B, Kim SH, Jamali AA, White RH. Younger age is associated with a higher risk of early periprosthetic joint infection and aseptic mechanical failure after total knee arthroplasty. *J Bone Joint Surg Am*. 2014;96(7):529-535. doi:10.2106/JBJS.M.00545
22. Zhu M, Ravi S, Frampton C, Luey C, Young S. New Zealand Joint Registry data underestimates the rate of prosthetic joint infection. *Acta Orthop*. 2016;87(4):346-350. doi:10.3109/17453674.2016.1171639
23. Tayton ER, Frampton C, Hooper GJ, Young SW. The impact of patient and surgical factors on the rate of infection after primary total knee arthroplasty: an analysis of 64,566 joints from the New Zealand Joint Registry. *Bone Joint J*. 2016;98-B(3):334-340. doi:10.1302/0301-620X.98B3.36775
24. Jämsen E, Nevalainen P, Eskelinen A, Huotari K, Kalliovalkama J, Moilanen T. Obesity, diabetes, and preoperative hyperglycemia as predictors of periprosthetic joint infection: a single-center analysis of 7181 primary hip and knee replacements for osteoarthritis. *J Bone Joint Surg Am*. 2012;94(14):e101. doi:10.2106/JBJS.J.01935
25. Jämsen E, Nevalainen P, Kalliovalkama J, Moilanen T. Preoperative hyperglycemia predicts infected total knee replacement. *Eur J Intern Med*. 2010;21(3):196-201. doi:10.1016/j.ejim.2010.02.006
26. Dowsey MM, Choong PFM. Obese diabetic patients are at substantial risk for deep infection after primary TKA. *Clin Orthop Relat Res*. 2009;467(6):1577-1581. doi:10.1007/s11999-008-0551-6
27. Bohm E, Zhu N, Gu J, et al. Does adding antibiotics to cement reduce the need for early revision in total knee arthroplasty? *Clin Orthop Relat Res*. 2014;472(1):162-168. doi:10.1007/s11999-013-3186-1
28. Hinarejos P, Guirro P, Leal J, et al. The use of erythromycin and colistin-loaded cement in total knee arthroplasty does not reduce the incidence of infection: a prospective randomized study in 3000 knees. *J Bone Joint Surg Am*. 2013;95(9):769-774. doi:10.2106/JBJS.L.00901
29. Kurtz SM, Ong KL, Lau E, Bozic KJ, Berry D, Parvizi J. Prosthetic Joint Infection Risk after TKA in the Medicare Population. *Clin Orthop Relat Res*. 2010;468(1):52-56. doi:10.1007/s11999-009-1013-5

Tables

Table 1. The characteristics of the sample

–

	CONTROLS N=66	CASES N=66	*Significance*
Sex (Female/Male)	46/20	38/28	
Age (Median, IQR)	81.2 (8.8)	81.0 (13.7)	
Cement (with/without)	38/28	18/48	*p=0.000*
Pre-op Prophylaxis (Cefazolin/Curoxima)	23/43	27/39	
Diabetes (Yes/No)	13/53	24/42	*p=0.033*
Obesity (No/Overweight/Intermediate /Severe)	29/31/4/2	11/24/26/5	*p=0.000*
ASA (I/II/III/IV)	3/51/12/0	0/15/48/3	*p=0.000*
Origin (Urban/Rural/Institution)	27/28/0	23/37/6	
Surgical time (median, IQR). min.	70 (10)	112 (20)	*p=0.000*
Tourniquet time (median, IQR), min.	50 (10)	80 (14)	*p=0.000*

–

–

–

Table 2. Risk factors

	RD	GRD	AFE	AFP	OR
Cement	0.025	0.010	0.72 (CI :0.43-0.87)	0.51(CI :0.31-073)	3.62(CI: 1.06-5.12)
Diabetes	0.021	0.004	0.56 (CI :0.06-0.80)	0.20(CI :0.34-0.38)	2.33 (CI: 1.06-5.12)
Obesity IMC > 30	0.192	0.008	0.88(CI :0.70-0.96)	0.41(CI :0.27-0.55)	8.86 (CI: 3.36-23.33)
ASA (III-IV)	0.079	0.014	0.93 (CI :0.85-0.97)	0.72(CI:0.59-0.85)	15.30 (CI: 6.54-35.80)

RD: Risk Difference ; GRD: General population risk difference ; AFE: Attributable fraction in exposures; AFP: Attributable fraction in population ; OR :Odd ratio; CI : 95 % Confidence interval

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Statisticanalysis.docx