Surgical site infection in hip arthroplasty in a 10-year follow-up prospective study: Risk and factors associated

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TITLE PAGE

Title: Surgical site infection in hip arthroplasty in a 10 year-follow-up prospective study: risk and factors associated

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ABSTRACT

Background: The increased demand for hip arthroplasty means a growing number of post-surgical complications. This study aims to assess the risk of surgical site infection (SSI) in a teaching hospital; develop regional, national and international external comparisons; and evaluate related SSI-risk factors, particularly according to the timing of surgery (urgent/unplanned or elective).

Methods: Prospective cohort study from January 2008 to December 2018. Patients were followed up to 90 days after surgery. Primary endpoint was SSI incidence according to the Centers for Disease Control and Prevention criteria. Multivariate analysis was conducted to find independently associated SSI-risk factors. The association between risk factors and SSI incidence was assessed by reference to odds ratio (OR). Analyses were also performed among urgent/unplanned and elective patients to identify whether SSI-risk factors differed between groups.

Results: The study population (n=1808) has an overall SSI rate of 3.0% (95%CI: 2.4-3.9). Timing of surgery caused an effect modification, so surgery duration>75th percentile (OR:3.8;95%CI:1.5-9.8) and inadequate preparation (OR:3.34;95%CI:1.1-10.0) were independent risk factors in the urgent/unplanned group; NHSN risk index≥2 (OR:6.3;95%CI:0.1-19.2) and transfusion (OR:3.6;95%CI:1.1-11.9) in the elective group.

Conclusions: Hospital infection surveillance systems allow identifying risk factors susceptible to change. Characterization of factors that caused an effect modification is key to identify areas of quality improvement, including reducing operating times, preventing perioperative blood transfusion, or improving patient preparation before surgery.

KEYWORDS

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HIGHLIGHTS

- The increased demand for hip arthroplasty means a growing number of post-surgical complications.
- Surgical site infection is the second most frequent complication after prosthetic loosening.
- Hospital-based infection surveillance is an important component for of surgical site infection control.
- Timing of surgery (elective or urgent/unplanned) influences the infection risk in orthopedic surgery.
- Operative times, blood transfusion or patient preparation before surgery, are key for infection prevention.

Background

Hip replacement is the most effective intervention to treat a deteriorated hip joint with persistent and disabling pain. Severe osteoarthritis is the most common indication for this procedure with an increasing demand as the population ages(1). Additionally, hip joint replacement may be conducted to treat severe joint damage following hip fracture(2,3), or other conditions, such as inflammatory arthritis, femoroacetabular compression syndrome, hip dysplasia, neoplasia and osteonecrosis(3). In the United States alone, over 370,000 total hip arthroplasties are performed each year, with growth projections ranging from 71.2% to 145% by 2030(4). In Spain, the number of hip replacement per 100,000 population increased by about 33% between 2004 and 2014, with an annual incidence of 112 cases per 100,000 inhabitants in 2014(1).

This increased demand of operative procedures implies an increasing number of patients at post-surgical complications risk. Surgical site infection (SSI) is the second most frequent complication after instability and prosthetic loosening(3,5) and remains among the most common healthcare-associated infections (HAI) among orthopedic inpatients(6). According to data from the US National Healthcare Safety Network (NHSN), SSI in hip replacement is reported at 1.3 per 100 interventions (range 0.7 to 2.4 according to NHSN risk index category)(6). In Spain, the HAI surveillance network Spanish Program for Clinical Indicators of Continuous Quality Improvement (*Indicadores Clínicos de Mejora Contínua de Calidad*/INCLIMECC) reported an infection incidence of 3.2 per 100 interventions between 1997 and 2012(7). Particularly, deep incisional and organ-space subtypes often lead to review of surgery, comorbidity, longer post-operative hospital stays, higher mortality and higher costs that impact on current scarce health-care resources(8). Hospital-based infection surveillance has proven to be an important component for of SSI prevention and control, allowing external comparison between centers, facilitating the characterization of risk factors, and providing indicators of improvement and feedback to surgeons(7,9-12). Different infection control

practices have had a variable impact on lower SSI rates and the lack of evidence in many areas raise awareness about the necessity of further research(5,13).

A particularity in hip arthroplasty is the encouragement to prioritize operative management in the case of hip fractures, which should be performed no later than 24-48 hours after admission(2, 14); in addition, revision hip arthroplasty may play an important role in unplanned hip surgery(15). Those patients treated urgently on an unplanned basis have shown worse clinical outcomes and higher costs related to care than patients treated electively(15). Other procedures out of orthopedic surgery have shown that certain risk factors are inherently different between elective and urgent/unplanned surgery(16). Therefore, more research is still needed on how the timing of surgery may influence the risk of SSI in orthopedic surgery.

The objectives of this study were: (i) to estimate SSI incidence in hip replacement surgery in our center, taking into account the NHSN risk index; (ii) to compare the incidence to rates in the United States, Spain, and Madrid Region where our center is located; and (iii) to identify any possible risk factor related to SSI, paying special attention if differences exist between patients treated electively or urgently on an unplanned basis.

Material and Methods

Patient sample

We conducted a prospective cohort study at a university teaching hospital to determine the incidence of SSI and identify any possible SSI-related risk factors among patients undergoing hip replacement surgery. All patients at least 18 years old who underwent hip surgical procedures with the code of the International Classification of Diseases, Ninth Revision, Clinical Modification categories (ICD-9-CM) associated with hip prosthesis procedure (00.70–00.73, 00.85–00.87, or 81.51– 81.53) were consecutively included. Surgical procedures were classified into total hip arthroplasty, partial hip arthroplasty or hip arthroplasty revision according to their ICD-9-CM definition. Patients with suspected or confirmed infection at date of surgery were excluded. All data were collected following the SSI's surveillance protocol

according to the NHSN surveillance procedure using the software developed by INCLIMECC(17). Briefly, all patients referred to hip replacement surgery were actively monitored from the time of admission until discharge, including any in-hospital readmission and outpatient's revision, within a follow-up period of 90 days after the operative procedure(7,9,17). An adequate sample size of 1177 subjects was estimated on the basis of an expected SSI incidence of 3%(7), a 95% CI, a precision of 1% and losses to follow up of 5%. To ensure the required sample size and the inclusion of complete annual periods, we studied patients intervened between 1 January 2008 and 31 December 2018. The Ethics Committee and Research commission of the hospital approved the study.

Outcome measures

Primary endpoint was SSI incidence according to the Centers for Disease Control and Prevention (CDC)/NHSN criteria, namely: (i) superficial incisional SSI, (ii) deep incisional SSI, and (iii) organ/space SSI(9). SSI rates and its 95% confidence intervals (95%CI), both overall and stratified according to the NHSN risk index, were calculated by dividing the number of SSIs by the number of specific operative procedures and multiplying the results by 100(9). Secondary endpoints examined included post-surgery in-hospital stay and mortality.

Covariate data collection

Detailed patients characteristics were collected: sex, age, comorbidity [kidney failure, coma, diabetes mellitus (DM), obesity (BMI > 30 kg/m2), malnutrition (BMI <18.5 kg/m^2), neoplasm, chronic obstructive pulmonary disease (COPD), immunosuppression, cirrhosis, injection drug abuse, neutropenia], American Society of Anesthesiologists (ASA) class, clinical diagnosis according to ICD-9-CM, pre-surgery in-hospital stay, wound class (clean, clean-contaminated, contaminated, and dirty), administration and appropriateness of antibiotic prophylaxis (choice, time of initiation, application method, dosage, and duration) according to the antibiotic guidelines issued by the infection prevention committee of the hospital (18) [Cefazolin 2g. iv. 30-60 mins prior induction of anesthesia and 24 hrs. postoperative; Vancomycin 1g. iv. 30-60

mins prior induction of anesthesia, in case of allergy and/or in methicillin-resistant *Staphylococcus aureus* (MRSA) positive patients], preoperative preparation adequacy [antiseptic showering with 2% chlorhexidine gluconate (CHG) soap, antiseptic skin preparation with 2% chlorhexidine-alcohol, and antiseptic mouth rinses with 0.12% CHG], hair removal, use of drains, blood transfusion, duration of operative procedure and identified microorganisms. Sample was categorized according to the NHSN risk index, estimated by the sum of three major risk factors: ASA score (1 point if >2); wound class (1 point if contaminated or dirty); and duration of surgery (1 point if higher than the 75th percentile), with values ranging from 0 to 3(10).

SSI rates comparison

We compare our SSI rates with those published for the Madrid Region, Spain and United States using the standardized infection ratio (SIR), a recommended reference tool for intra- and interhospital comparisons(17). SIR is calculated by dividing the number of observed infections by the number of expected infections given by the standard population (e.g. US NHSN aggregated data)(9). The SIR is interpreted as a relative risk; a SIR greater than 1.0 indicates that more SSIs were observed than expected and a SIR less than 1.0 indicates that fewer SSIs were observed than expected.

Statistical analysis

Patients' demographic and clinical characteristics were described. Univariate and multivariate analysis were conducted to find independently associated risk factors for SSI. Categorical variables were analyzed using Pearson's chi2 test or Fisher exact test. Student t test or one-way ANOVA, as appropriate, were used to compare continuous variables. Non-parametric U Mann-Whitney test or Kruskal-Wallis test, as appropriate, were used for non-normally distributed data. Shapiro-Wilk test was used to assess normality distribution. A multivariate logistic regression model was built through backward stepwise selection; this procedure allows the screening of a large number of associated risk factors quickly and efficiently(19). The cutoff points for adding

and removing variables were 0.05 and 0.10, respectively. The association between risk factors and SSI incidence was assessed by reference to odds ratio (OR). Both univariate and multivariate analysis were also performed between unplanned and elective patients to identify if SSI-risk factors differed between both groups. Immediate unscheduled admissions from consulting rooms, the emergency department, or transferred from other hospitals were considered for the urgent/unplanned group. Elective surgery was classified if it was planned and scheduled in advance.

Statistical analysis was performed using Stata v.25, with hypothesis testing based on a two-tailed test of significance $p<0.05$.

Results:

A total of 1808 patients met the inclusion criteria. The patient population was 57.2% (n=1034) female and had a mean age of 72.1 years (SD=13.5). DM (15.9%) was the most frequent preoperative comorbidity. The overall rate of interventions during the 10 year follow-up was 164 interventions (range 69-243). Mean duration of surgery was 118.6 minutes (SD=50.9); the 75th percentile (P75) for the duration of surgery was estimated at 135 minutes (Table 1). Half of the interventions (57.9%; n=1047) entailed total hip arthroplasty, 28.9% partial hip arthroplasty (n=523) and 13.2% hip arthroplasty revision (n=238).

Most patients underwent elective surgery (72.6%). Compared with the urgent/unplanned group, elective surgery patients most often had obesity, osteoarthrosis, underwent total hip replacement or revision arthroplasty, and more often had adequate antibiotic prophylaxis and preoperative preparation. Patients in the urgent/unplanned arthroplasty group were more often women, older, and had more frequent DM, COPD, kidney disease, neoplasia, and immunosuppression. The ASA score and the NHSN index were significantly higher among urgent/unplanned patients and they more often required blood transfusions and drains after surgery. Diagnosis of femoral fracture was observed at significantly greater rates in patients of the unplanned surgery cohort, with partial arthroplasty being the most frequently performed procedure (Table 1).

	Total (n=1808)	Urgent (n=496)	Elective (n=1312)	p-value
	n (%)	*n (%)*	*n (%)*	
Surgical Site Infection	55 (3.0)	24 (4.8)	31 (2.4)	**0.009**
Mean age (years) SD[1]	72.1 (13.5)	81.0 (10.5)	68.7 (12.9)	**0.000**
Gender (Female)	*n (%)*	*n (%)*	*n (%)*	
Female	1034 (57.2)	353 (71.2)	681 (51.9)	**0.000**
Male	774 (42.8)	143 (28.8)	631 (48.1)	
Clinical risk factors:	*n (%)*	*n (%)*	*n (%)*	
Obesity (BMI > 30 kg/m2)[2]	143 (8.6)	20 (4.3)	123 (10.3)	**0.000**
Diabetes Mellitus	265 (15.9)	88 (18.8)	177 (14.8)	**0.043**
COPD[3]	78 (4.7)	29 (6.2)	49 (4.1)	0.072
Renal disease	56 (3.4)	28 (6.0)	28 (2.4)	**0.000**
Cancer	116 (7.0)	44 (9.4)	72 (6.1)	**0.018**
Malnutrition (BMI <18 kg/m2)[2]	2 (0.1)	1 (0.2)	1 (0.1)	0.485
Cirrhosis	3 (0.2)	2 (0.4)	1 (0.1)	0.194
Immunosuppression	2 (0.1)	2 (0.4)	0 (0.0)	0.079
PWID[4]	1 (0.1)	0 (0.0)	1 (0.1)	1.000
Neutropenia	0 (0.0)	0 (0.0)	0 (0.0)	-
Coma	3 (0.2)	1 (0.2)	2 (0.2)	1.000
Most frequent clinical diagnosis (ICD-9-MC[3])	*n (%)*	*n (%)*	*n (%)*	
715.35 Osteoarthrosis, localized, not specified whether primary or secondary, pelvic region and thigh	696 (41.4)	112 (23.7)	584 (48.2)	**0.000**
820.09 Other closed transcervical fracture of neck of femur	242 (14.4)	140 (29.7)	102 (8.4)	

820.00 Closed fracture of intracapsular section of neck of femur, unspecified)	210 (12.5)	104 (22.0)	106 (8.8)	
996.46 Articular bearing surface wear of prosthetic joint	79 (4.7)	16 (3.4)	63 (5.2)	
715.36 Osteoarthrosis, localized, not specified whether primary or secondary, lower leg	66 (3.9)	2 (0.5)	64 (5.3)	
Mean preoperative hospital stay (days) (SD)	2.2 (3.3)	4.6 (4.1)	1.3 (2.4)	**0.000**
Operating room (emergency room)	105 (5.8)	68 (13.7)	37 (2.8)	**0.000**
Most frequent surgical procedures (ICD-9-MC)	*n (%)*	*n (%)*	*n (%)*	
81.51 Total hip replacement	1047 (57.9)	72 (14.5)	975 (74.3)	**0.000**
81.52 Partial hip replacement	523 (28.9)	381 (76.8)	142 (10.8)	
00.70 Revision of hip replacement, both acetabular and femoral components	178 (9.9)	37 (7.5)	141 (10.8)	
81.53 Revision of hip replacement, not otherwise specified	52 (2.9)	4 (0.8)	48 (3.7)	
00.71 Revision of hip replacement, acetabular component	5 (0.3)	0 (0.0)	5 (0.4)	
00.72 Revision of hip replacement, femoral component	3 (0.2)	2 (0.4)	1 (0.1)	
ASA score[2]	*n (%)*	*n (%)*	*n (%)*	
I	71 (3.9)	6 (1.2)	65 (5.0)	**0.000**
II	1149 (63.6)	200 (40.3)	949 (72.3)	
III	553 (30.6)	266 (53.6)	287 (21.9)	
IV	35 (1.9)	24 (4.8)	11 (0.8)	
Mean duration of surgery (min) (SD)	118.6 (50.9)	102.4 (40.6)	124.6 (53.0)	**0.000**
Degree of contamination	*n (%)*	*n (%)*	*n (%)*	

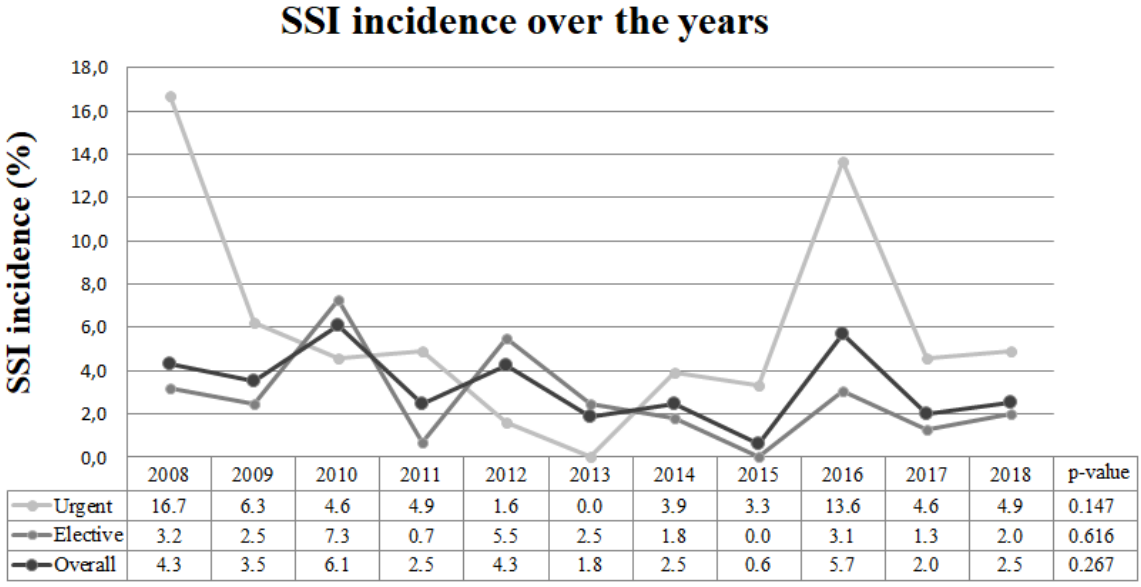
Clean	1752 (96.9)	478 (96.4)	1274 (97.1)	0.087
Clean-Contaminated	5 (0.3)	0 (0.0)	5 (0.4)	
Contaminated	6 (0.3)	4 (0.8)	2 (0.2)	
Dirty	45 (2.5)	14 (2.8)	31 (2.4)	
NHSN index[4]	*n (%)*	*n (%)*	*n (%)*	
0	898 (49.7)	149 (30.4)	759 (57.8)	**0.000**
1	753 (41.7)	277 (55.9)	452 (34.5)	
2	149 (8.2)	65 (13.1)	97 (7.4)	
3	8 (0.4)	5 (1.0)	4 (0.3)	
Preoperative preparation	*n (%)*	*n (%)*	*n (%)*	
Correct	1646 (91.0)	426 (86.1)	1220 (93.5)	**0.000**
Preparation not performed	13 (0.7)	4 (0.8)	9 (0.7)	
No oral antiseptic	112 (6.2)	49 (9.9)	63 (4.8)	
No surgical antiseptic	10 (0.6)	4 (0.8)	6 (0.5)	
Antibiotic prophylaxis	*n (%)*	*n (%)*	*n (%)*	
Appropriate prophylaxis	1441 (79.7)	367 (76.5)	1074 (83.2)	**0.002**
Inappropriate prophylaxis	330 (18.3)	113 (23.5)	217 (16.8)	
Duration	266 (14.7)	101 (21.0)	165 (12.7)	
Choice	45 (2.5)	8 (1.7)	37 (2.9)	
Time of start	19 (1.1)	4 (0.8)	15 (1.2)	
Indication	0 (0.0)	0 (0.0)	0 (0.0)	
Other risk factors	*n (%)*	*n (%)*	*n (%)*	
Hair removal	265 (16.2)	28 (6.1)	237 (20.1)	**0.000**
Transfusion	67 (4.3)	29 (6.3)	38 (3.5)	**0.013**
Drainage	1463 (86.4)	450 (93.8)	1013 (83.5)	**0.000**
Days until Infection (days) (SD)	8.4 (7.2)	7.2 (4.9)	9.2 (8.4)	0.320
Mean length of stay (days) (SD)	10.0 (8.3)	14.9 (10.5)	8.2 (6.5)	**0.000**

Mortality	20 (1.1)	18 (3.6)	2 (0.2)	**0.000**

[1]SD, Standard deviation. [2]ASA, American society of anesthesiologists. [3]ISD-9, International Classification of Diseases, 9th Revision. [4] NHSN, National Healthcare Safety Network. P-value: Comparison between type of surgical intervention (elective vs. urgent/unplanned)

Table 1: Characteristics of patients overall and between urgent/unplanned and elective groups

The overall SSI risk was 3.0% (n=55) and the SSI incidence density rate was 32.2 infections per 100.000 patients-day at the end of the follow-up. No significant SSIs incidence trend over the years was found (p=0.267) (Figure 1). The analysis of infections revealed that 72.7% (n= 40) patients had deep incisional SSIs, 16.4% (n=9) patients developed organ-space infection and 10.9% (n=6) had a superficial SSI. There was an upward trend in SSI incidence with the increase in the NHSN index: 2.0% among patients with an index of 0; 3.2% among patients with an index of 1; 8.3% among patients with an index ≥ 2 (p=0.003). The microorganisms most frequently isolated were *Staphylococcus epidermidis* (34.9%), *Staphylococcus aureus* (14.0%) and *Pseudomonas aeruginosa* (14.0%). The mean hospital stay was 20.2 days (SD=17.4) among patients with SSI compared to 9.7 days (SD=7.7) among patients without SSI (p<0.000). The overall mortality was 1.1% (n=20), mortality was higher among patients in the SSI group (5.6%) compared with non-SSI group (1.0%) (p=0.006). The urgent/unplanned group showed significantly higher SSI-risk (4.8% versus 2.4%, p=0.009), mean hospital stay [14.9 days (SD=10.5) versus 8.2 days (SD=6.5), p=0.000] and mortality (3.6% versus 0.2%, p=0.000) than elective surgery cases.



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	p-value
Urgent	16.7	6.3	4.6	4.9	1.6	0.0	3.9	3.3	13.6	4.6	4.9	0.147
Elective	3.2	2.5	7.3	0.7	5.5	2.5	1.8	0.0	3.1	1.3	2.0	0.616
Overall	4.3	3.5	6.1	2.5	4.3	1.8	2.5	0.6	5.7	2.0	2.5	0.267

SSI surgical site infection. P-value from the extended Mantel-Haenszel chi square for linear trend

Figure 1: SSIs incidence over the years (2008-2018).

We estimated an SIR of 2.40 with respect to the US NHSN/CDC (p=0.000)(6). When compared with the estimated incidence of SSI provided by INCLIMECC in 2018 for the Madrid Region (2.66%) and nationwide (1.97%), SIR was 1.14 (p=0.575) and 1.54 (p=0.015) respectively.

When potential risk factors were compared between SSI and non-SSI groups, univariate analysis showed that urgent/unplanned surgery, hip arthroplasty revision as surgical procedure, blood transfusion, ASA score >2, contaminated/dirty surgery and NHSN index ≥ 2 were significantly associated. Malnutrition, duration of surgery > P75, and inadequate preparation were at the limit of significance (p<0.10) (Table 2).

(n=1808)					
Risk Factors	SSI[1] patients n=55 (3.0%)	Non-SSI patients n=1753 (97.0%)	Odds Ratio	95 % CI	p-value
Mean age (years) (SD)[2]	71.6 (12.61)	72.1 (13.48)	1.00	0.98-1.02	0.804
Gender (male)	23 (41.8)	751 (42.8)	0.96	0.56-1.65	0.880
Obesity (BMI > 30 kg/m2)[3]	5 (10.4)	138 (8.6)	1.24	0.48-3.18	0.601

Diabetes Mellitus	10 (20.8)	255 (15.8)	1.40	0.69-2.85	0.347
COPD[4]	1 (2.1)	77 (4.8)	0.43	0.02-3.17	0.723
Renal disease	1 (2.1)	55 (3.4)	0.61	0.08-4.52	1.000
Cancer	3 (6.4)	113 (7.0)	0.90	0.28-2.95	1.000
Malnutrition	1 (2.1)	1 (0.1)	34.80	2.14-565.10	0.056
Cirrhosis	0 (0.0)	3 (0.2)	-	-	-
Immunosuppression	0 (0)	2 (0.1)	-	-	-
PWID[5]	0 (0.0)	1 (0.1)	-	-	-
Neutropenia	0 (0)	0 (0.0)	-	-	-
Coma	0 (0.0)	3 (0.2)	-	-	-
Mean preoperative hospital stay (days) (SD)[2]	2.7 (3.88)	2.2 (3.27)	1.04	0.97-1.10	0.277
Type of surgery (urgent/unplanned)	**24 (43.6)**	**472 (26.9)**	**2.10**	**1.22-3.62**	**0.006**
Emergency operating room	4 (7.3)	101 (5.8)	1.28	0.45-3.61	0.558
Surgical procedure					
Total hip arthroplasty	**23 (41.8)**	**1024 (58.4)**	**Ref.**		
Partial hip arthroplasty	**18 (32.7)**	**505 (28.8)**	**1.59**	**0.85-2.97**	**0.148**
Hip arthroplasty revision	**14 (25.5)**	**224 (12.8)**	**2.78**	**1.41-5.49**	**0.003**
NHSN index[8]					
0	**18 (32.7)**	**880 (50.2)**	**Ref.**		
1	**24 (43.6)**	**729 (41.6)**	**1.61**	**0.87-2.99**	**0.132**
2/3	**13 (23.6)**	**144 (8.2)**	**4.41**	**2.12-9.20**	**0.000**
ASA[6] score >2	**29 (52.7)**	**559 (31.9)**	**2.38**	**1.39-4.08**	**0.001**
Duration of surgery > P75[7]	19 (34.6)	417 (23.8)	1.69	0.96-2.98	0.066
Contaminated/Dirty surgery	**4 (7.3)**	**47 (2.7)**	**2.85**	**1.03-7.88**	**0.043**
Inadequate preparation	7 (13.7)	128 (7.4)	1.99	0.88-4.51	0.092
Inappropriate prophylaxis	10 (19.6)	320 (18.6)	1.07	0.53-2.15	0.856

Transfusion	**5 (11.4)**	**62 (4.1)**	**3.01**	**1.15-7.89**	**0.037**
Hair removal	6 (13.0)	259 (16.2)	0.77	0.32-1.84	0.562
Drains	45(91.8)	1418 (86.3)	1.79	0.64-5.03	0.261

[1]SSI, surgical site infection. [2]SD, Standard deviation. [3]BMI, body mass index. [4]COPD, chronic obstructive pulmonary disease. [5]PWID, people who inject drugs. [6]ASA, American society of anesthesiologists. [7]P75, 75th percentile. [8]NHSN, National Healthcare Safety Network.

Table 2: Univariate Analysis for SSI risk factors

The univariate analysis stratified by type of surgery identified risk factors that were common to both groups; for example, NHSN risk index ≥2 was significantly associated with SSI risk in both groups (Urgent: OR: 4.56, 95% CI: 1.11-18.81; p=0.036; Elective: OR: 4.64, 95% CI: 1.78-12.06; p=0.000). On the other hand, certain risk factors had higher OR in one group and nor the other. For example, hip arthroplasty revision, ASA score >2 and transfusion were significantly associated with SSI risk in the elective group but not in the urgent group. Conversely, duration of surgery > P75 was significantly associated with SSI risk in the urgent group (Urgent: OR: 3.03, 95% CI: 1.32-6.97; p=0.006; Elective: OR: 1.67; 95% CI: 0.80-3.54; p=0.169), and inadequate preparation was marginally significant (Urgent: OR: 2.63, 95% CI: 0.92-7.55; p=0.062; Elective: OR: 1.08, 95% CI:0.25-4.61; p=0.196) (Table 3).

(n=1808)					
Risk Factors	Urgent (n=496)		Elective (n=1312)		p-value for interaction
	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value	
Age (years)	0.97 (0.94-1.01)	0.105	0.99 (0.96-1.02)	0.418	0.493
Gender (male)	0.82 (0.32-2.10)	0.671	1.32 (0.64-2.70)	0.447	0.426
Obesity (BMI > 30 kg/m2)[1]	2.94 (0.53-11.52)	0.227	1.09 (0.32-3.66)	0.753	0.405
Diabetes Mellitus	1.37 (0.48-3.84)	0.552	1.32 (0.42-3.53)	0.582	0.960

COPD[2]	-	-	0.93 (0.12-6.98)	1.000	-
Renal disease	0.77 (0.10-5.97)	1.000	-	-	0.984
Cancer	0.47 (0.06-3.57)	0.709	1.30 (0.30-5.61)	0.668	0.424
Preoperative hospital stay (days)	0.99(0.89-1.10)	0.867	1.00 (0.86-1.16)	0.982	0.940
Emergency operating room	1.27 (0.42-3.84)	0.669	-	-	0.981
Surgical procedure					
Total hip arthroplasty	Ref.		**Ref.**		
Partial hip arthroplasty	0.75 (0.24-2.30)	0.609	**0.72 (0.17-3.12)**	**0.659**	0.970
Hip arthroplasty revision	1.74 (0.41-7.36)	0.449	**2.72 (1.24-5.94)**	**0.012**	0.595
ASA[4] score >2	1.45 (0.61-3.44)	0.403	**2.52 (1.22-5.21)**	**0.010**	0.334
Duration of surgery > P75[5]	**3.03 (1.32-6.97)**	**0.006**	1.67 (0.80-3.54)	0.169	0.362
Contaminated/Dirty surgery	2.59 (0.56-11.98)	0.206	2.78 (0.64-12.17)	0.157	0.948
NHSN index[6]					
0	**Ref.**		**Ref.**		
1	**2.78 (0.79-9.78)**	**0.110**	**1.70 (0.76-3.81)**	**0.200**	0.984
2/3	**4.56 (1.11-18.81)**	**0.036**	**4.64 (1.78-12.06)**	**0.000**	0.633
Inadequate preparation	**2.63 (0.92-7.55)**	**0.062**	1.08 (0.25-4.61)	0.916	0.333
Inappropriate prophylaxis	1.02 (0.36-2.84)	0.976	0.99 (0.37-2.61)	0.983	0.971
Transfusion	0.77 (0.10-5.97)	1.000	**6.14 (1.99-18.95)**	**0.000**	**0.082**
Hair removal	0.80 (0.10-6.22)	1.000	0.95 (0.35-2.54)	0.916	0.886
Drains	1.42 (0.18-10.93)	1.000	1.59 (0.48-5.34)	0.446	0.924

[1]BMI, body mass index. [2]COPD, chronic obstructive pulmonary disease. [3]PWID, people who inject drugs. [4]ASA, American society of anesthesiologists. [5]P75, 75th percentile. [6]NHSN, National Healthcare Safety Network

Table 3: Odds ratio estimations for SSI risk factors, stratified by type of surgery (urgent or elective)

The adjusted multivariate analysis showed NHSN risk index ≥2 (OR: 5.17, 95%CI: 2.15-12.43; p=0.000), unplanned urgent surgery (OR: 2.53, 95%CI: 1.27-5.06; p=0.008) and transfusion (OR: 2.59, 95%CI: 0.95-7.06; p=0.063) to be independently associated with SSI incidence. Regarding the analysis stratification by type of surgery, through the stepwise logistic regression both groups showed different independent risk factors. Patients undergoing unplanned hip arthroplasty had duration of surgery >75th percentile (OR: 3.84, 95%CI: 1.50-9.83; p=0.005) and inadequate preparation (OR: 3.34, 95%CI: 1.11-10.04; p=0.032) as independent SSI-risk factors, while NHSN risk index ≥2 (OR: 6.30, 95%CI: 2.07-9.22; p=0.001) and transfusion (OR: 3.65, 95%CI: 1.12-11.92; p=0.032) were predictive of SSI within the elective group (Table 4).

Overall (n=1808)			
Risk Factors	Odds Ratio	95 % CI	p-value
Age (years)	0.98	0.95-1.00	0.051
Type of surgery (urgent/unplanned)	**2.53**	**1.27-5.06**	**0.008**
Transfusion	2.59	0.95-7.06	0.063
NHSN[1] 1	1.87	0.88-3.99	0.103
NHSN[1] ≥ 2	**5.17**	**2.15-12.43**	**0.000**
Urgent/unplanned group (n=496)			
Risk Factors	Odds Ratio	95 % CI	p-value
Age (years)	0.98	0.97-1.02	0.365
Duration of surgery > P75[2]	**3.84**	**1.50-9.83**	**0.005**
Inadequate preparation	**3.34**	**1.11-10.04**	**0.032**

Elective group (n=1312)			
Risk Factors	Odds Ratio	95 % CI	p-value
Transfusion	**3.65**	**1.12-11.92**	**0.032**
NHSN[1] 1	2.06	0.77-5.55	0.152
NHSN[1] ≥ 2	**6.30**	**2.07-19.22**	**0.001**

[1]NHSN, National Healthcare Safety Network. [2]P75, 75[th] percentile

Table 4: Multivariate Analysis for SSI risk factors (backward stepwise method)

Discussion:

Surgical site infection is a hip arthroplasty complication that leads to increased morbidity and mortality(8). Achieving low SSI rates serves as a good measure for evaluating the surgical practice and the quality of the healthcare provided. In this study, we evaluated the SSI incidence in hip arthroplasty in a teaching hospital in Madrid, and an external comparison was made with the rates of the Madrid Region, Spain, and the United States. We found a SSI global rate of 3.0% within the study period of 10 years. These findings are at the upper limit to what existing literature reports on SSI rates ranging from 1.0% to 3.2% (6,7,20). Accordingly, results showed that the risk of SSI in our center was significantly higher than in both the United States and Spain. Given that SSI-risk has been related with several factors, including patient, intervention and post-operative dependent factors(13,21-23), those that may vary through facilities could lead to the observed differences.

Most notably, deep infection accounted as the most frequent type of infection in our study. Longer operative times had been identified as an independent risk factor for deep SSI (24). Larger studies reported on total joint replacement concluded that postoperative 30-day wound complications appeared to increase when the operative time exceeded above 120 min. Furthermore, operative time >120 minutes was an independent predictor after multivariate analysis (OR 1.44, 95% CI 1.21-1.71), with each 30-minute increase in operative time beyond

120 minutes increasing risk (25). Regarding total hip arthroplasty, a study with more than 89,000 patients, reported an increased risk of postoperative complications with operative times exceeded above 80 minutes (26). Mean operative time for our entire cohort was 118.5 (SD=50.9), which could contribute to the high incidence of infections found, showing even longer operative times among those with SSI (133.5 minutes versus 118.1 minutes). Operative time may be affected by a myriad of factors, both related with surgical environment, including the volume of hospital, the surgeon's experience or the type of implant, and patient characteristics, including patient age, BMI, ASA classification or preoperative blood transfusion(25). Careful following of those with longer procedure times may help identify cases at higher risk for complications and optimize their care.

This is consistent with the NHSN index that predicts surgical risk for infection based on three factors, being operative duration one of these(26). The NHSN index provides a reliable predictor of SSI risk, comprising variables that estimate the degree of contamination of the surgical site, measure the duration of an operation and serve as marker of host susceptibility(10). Periprosthetic joint infection after total joint arthroplasty (27) and SSI after knee replacement (28) had been independently associated with a NHSN index ≥2. We found not only an upward trend in SSI incidence with the increase in the NHSN index, but also NHSN index ≥2 remained as an independent risk factor for SSI (OR: 5.71, 95%CI: 2.15-12.43; p=0.000) after multivariate analysis. In the univariate analysis of the overall sample, the three components of the NHSN index were associated with the risk of SSI, in line with results disclosed by other authors(27,29). After adjustment, these associations disappeared, due to interdependence of these factors with the NHSN index.

Multivariate analysis also showed that unplanned urgent surgery was an independent SSI-risk factor. In this sense, Kukreja et al. (30) found in his study on complications in spine surgery that SSI incidence was higher in the urgent group, with significant differences remaining even after control for confounding variables. For his part, Kamath et al. (15) found that unplanned hip arthroplasty was associated with higher morbidity after surgery, as well as greater costs; no

assessment was made regarding SSI incidence. These results were similar to the findings of our study, where risk of infection was twice as high (4.8% versus 2.4%), postoperative hospitalization was almost twice as long (14.9 days versus 8.2 days) and mortality was significantly higher in unplanned than elective patients (3.6% versus 0.2%). In our case, unplanned patients represented 27.4% of the sample compared to 13% reported by Kamath; it also contrasts with records with lower incidences where the number of patients operated on unplanned basis were markedly lower than our cohort (27.4% versus 9.0%)(20). The high proportion of unplanned urgent procedures may also have contributed to the high incidence of infection found in our sample.

Urgent/unplanned surgery was not only independently associated with SSI-risk (OR:2.53, 95%CI:1.27-5.06), but timing of surgery also caused an effect modification, so magnitude of association between risk factors and SSI differed between elective and urgent/unplanned surgery groups. Out of orthopedic surgery, comparison between different timing procedures (emergent versus nonemergent) had found that most preoperative characteristics differed between groups with few exceptions, being key for consideration of patient risk stratification(16). This is important for identifying modifiable risk factors and outcomes that differ between non-emergency and urgent/unplanned operations, which helps to identify areas for quality improvement. The univariate analysis identified risk factors common to both groups, while certain risk factors had a higher OR in one group than in the other. After multivariate analysis, duration of surgery > 75th percentile and inadequate preparation were found to be independent SSI-risk factor in the unplanned group, while the NHSN index ≥2 and transfusion remained independent risk factors for the elective group.

Despite the differences, p-values for interaction between type of surgery and the rest of risk factors were not statistically significant and only the interaction term of timing of surgery with transfusion was marginally significant (p-value for interaction <0.10). It should be noted, however, that the modification of effects, although similar to the statistical interaction, implies a biological phenomenon related to the disease, so we believe that p-values alone do not

necessarily convey how meaningful our findings were. The distribution of risk factors suggests the need to focus on a subset of patients who would or would not benefit from an intervention, which would be an important issue of interest to epidemiologists and infection prevention specialists.

The NHSN index ≥2, as discussed above, is a known risk factor related to SSI, while duration of surgery >75 percentile may reflect complex procedures that entails longer exposure times and increasing risk of contamination and infection. Hip arthroplasty is one of the most common procedures requiring blood product transfusion; it may reflect the performance of complex procedures as well as the presence of comorbid conditions favoring the presence of anemia(31). In particular, allogeneic blood transfusion has been associated with an increased risk of SSI(5, 21). Our findings showed an increased risk of SSI among patients that received transfusions within the overall sample (7.5% versus 2.61%), as well as in the elective group (10.5% versus 1.88%). No differences were found in the unplanned group (3.5% versus 4.4%), although transfusions were more common among the urgent/unplanned group than the elective one (6.3% versus 3.5%). This is consistent with previous studies evaluating the influence of the type of admission (elective or emergent) on the pattern of perioperative complications(30). Unfortunately, the most appropriate blood management strategy for each patient had not yet been defined(5,21).

Skin asepsis has been suggested to substantially decrease skin number of bacterial colony counts(10,13), having chlorhexidine shows a superior efficacy to reduce SSI in total knee and hip arthroplasty(32). Inadequate preparation was greater at the unplanned group (11.8% versus 6.0%), the SSI group of the overall sample (13.7% versus 7.4%) and particularly among patients with SSI in the unplanned group (25.0% versus 11.2%). The unpredictability of unplanned surgeries requires the establishment of measures that allow to perform a preventive measure with an important role in the prevention of surgical wound such as preoperative skin cleansing. The use of chlorhexidine-impregnated cloths for advanced preparation instead of preoperative

chlorhexidine showers may be an alternative to avoiding absent or improper bathing techniques (33).

In addition, unplanned patients were older (81.0 years versus 68.7 years), had more comorbidities and fractures were the most frequent clinical diagnosis, and mean preoperative hospital stay was greater in the unplanned group than the elective one (4.6 days versus 1.3 days). These factors have been associated with prognosis after surgery, although there is still inconsistency regarding their contribution to an increased risk of SSI. On one hand, a systematic review regarding joint arthroplasty found no significant association with age, with no difference in risk between patients older and younger than 68 years (OR:0.99; 95%CI:0.55-1.17)(34). On the other hand, an increased risk of infection after primary total hip arthroplasty in patients older than 75 years was suggested(29). In our study, no significant association between risk of infection and age was found, although it was controlled in the multivariate analysis. Nevertheless, our sample showed an average age of 72 years, with 50% of patients being over 75 years old; and the urgent/unplanned group showed an even greater mean age, which could contribute to a greater tendency of our sample to infection. Longer preoperative hospitalization had also been associated with SSI risk according to the International Consensus on Orthopedic Infections in 2017, although there is still no consensus on the definition of prolonged hospitalization(35). Despite the differences between the unplanned and the elective group regarding this risk factor, the univariate and multivariate analysis were unable to find an association with SSI.

With respect to the rest of patient-dependent, intervention or post-operative factors, such as antibiotic prophylaxis, use of drains, removal of body hair, etc. (5,10,21-23,27), no consistent association was found. It could be attributed to an underpowered sample. In this regard, it is considered that because of low rate of SSI in joint surgery and the multifactorial nature of associated risk factors, to achieve the power necessary to provide statistical certainty of study conclusions, large numbers of patients are required(36). For instance, to demonstrate effectiveness of a decolonization protocol it would have required more than 72,000

patients to achieve 80% power(37). Underpowered sample could also explain the different distribution of some SSI-risk factors in the unplanned group, and the lack of significance in terms of interaction. This can be regarded as one of this study's limitations, difficult to solve if not with a multicenter study. In addition, we are aware that not all potential SSI-risk factors were assessed, such as MRSA carrier status or active infection by MRSA, nasal decolonization, rheumatoid arthritis, coagulopathy, Charlson Comorbidity Index, wound dehiscence, and so on. Despite these limitations, this study has some inherent strengths, since it is based on prospective data collection; an internationally accepted SSI definition was followed as well as a follow-up defined by the CDC (9), which allows for reliable comparability of our results; and as far as we know, this is the first study to consider how risk factors affect SSI differently depending on the timing of hip arthroplasty surgery.

Conclusions:

Hospital-based infection surveillance systems provide indicators of improvement and allow characterizing risk factors. In this prospective study, we identified independent risk factors susceptible to change, including the need to reduce operative times, establish measures to prevent perioperative blood transfusion or improve patient preparation prior to surgery. Timing of surgery caused an effect modification, so association between risk factors and SSI differed between groups, being key for consideration the risk stratification of patient to identify areas for quality improvement.

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