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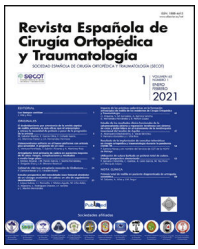

ORIGINAL ARTICLE

[Translated article] Risk factors associated with periprosthetic infection in patients with femoral neck fracture: A case–control study

J.M. Gómez-Palomo[a,b,*], A. Martínez-Crespo[c], C. Pérez-López[d], R. Víquez-da Silva[a], P. Zamora-Navas[a,e]

[a] *Unidad de Cirugía Ortopédica y Traumatología, Hospital Universitario Virgen de la Victoria, Campus Teatinos, Málaga, Spain*
[b] *Instituto de Investigación Biomédica de Málaga (IBIMA), Málaga, Spain*
[c] *Unidad de Cirugía Ortopédica y Traumatología, Hospital de Montilla, Montilla, Córdoba, Spain*
[d] *Unidad de Enfermedades Infecciosas, Microbiología y Medicina Preventiva, Hospital Universitario Virgen del Rocío, Sevilla, Spain*
[e] *Universidad de Málaga (UMA), Málaga, Spain*

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KEYWORDS
Femoral neck fractures;
Total hip arthroplasty;
Hip hemiarthroplasty;
Infection hip arthroplasty;
Infection hip prosthesis

Abstract
Background: Infection is one of the most important local complications in the patient with femoral neck fracture treated with arthroplasty. The aim of the present study is to describe and analyze possible risk factors that could be involved in periprosthetic infection in the patient with femoral neck fracture.
Methods: A retrospective case-control study was performed including patients with femoral neck fractures treated with arthroplasty in the period between January 2015 and December 2017. Cases were defined as patients with femoral neck fracture who after undergoing arthroplasty (hemiarthroplasty or total hip arthroplasty) had a periprosthetic infection, whose diagnosis was carried out according to the major and minor criteria described in the International Consensus on Musculoskeletal Infections (Philadelphia 2018). In order to mitigate the influence of variables that could be considered confounding variables, a multivariate analysis was carried out.
Outcomes: A statistically significant association was found between periprosthetic infection and certain variables present at the time of admission, including the presence of moderate or severe anaemia (OR: 10.91; 95% CI: 1.07-111.50; *P* = .007), thrombocytopenia (OR: 27.72;95% CI: 3.48-221.01; *P* = .002), history of thromboembolism event (OR: 8.80; 95% CI: 1.31-59.38; *P* = .026), anxious-depressive disorder in treatment with two or three drugs (OR: 21.36; 95% CI: 3.65-125.12; *P* = .001) and liver disease (OR: 32.04; 95% CI: 2.59-396.29; *P* = .007).

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* Corresponding author.
E-mail address: jmgomezpalomo@gmail.com (J.M. Gómez-Palomo).

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Conclusions: Periprosthetic infection in the patient with femoral neck fracture treated with arthroplasty could be related to the presence of certain variables at the time of hospital admission, including moderate or severe anaemia, thrombocytopenia, history of thromboembolic event, anxious-depressive disorder in treatment with two or three drugs or liver disease.

PALABRAS CLAVE
Fracturas del cuello femoral;
Artroplastia total de cadera;
Hemiartroplastia de cadera;
Infección de la artroplastia de cadera;
Infección periprotésica de cadera

Factores de riesgo asociados a infección periprotésica en el paciente con fractura del cuello femoral: estudio de casos y controles

Resumen
Antecedentes y objetivo: La infección es una de las complicaciones locales más importantes en el paciente con fractura del cuello femoral tratada con una artroplastia. El objetivo del presente estudio es describir y analizar posibles factores de riesgo que podrían estar implicados en la infección periprotésica del paciente con fractura del cuello femoral.
Material y métodos: Se realizó un estudio de casos y controles retrospectivo que incluye a pacientes con fractura del cuello femoral tratada con una artroplastia en el periodo comprendido entre enero de 2015 y diciembre de 2017. Se definieron como casos a los pacientes con fractura del cuello femoral que tras someterse a una artroplastia (hemiartroplastia o artroplastia total de cadera) tuvieron como desenlace una infección periprotésica, cuyo diagnóstico se llevó a cabo atendiendo a los criterios mayores y menores descritos en el Consenso Internacional de Infecciones Musculoesqueléticas (Philadelphia 2018). Con la intención de atenuar la influencia de variables que podrían considerarse confusoras, se realizó un análisis multivariante.
Resultados: Se apreció una asociación estadísticamente significativa entre infección periprotésica y determinadas variables presentes en el momento del ingreso, entre las que se encuentran la presencia de anaemia moderada o severa (OR: 10,91; IC 95%: 1,07-111,50; p = 0,007), trombocitopenia (OR: 27,72; IC 95%: 3,48-221,01; p = 0,002), el antecedente tromboembólico (OR: 8,80; IC 95%: 1,31-59,38; p = 0,026), el trastorno ansioso-depresivo en tratamiento con 2 o 3 fármacos (OR: 21,36; IC 95%: 3,65-125,12; p = 0,001) y la hepatopatía (OR: 32,04; IC 95%: 2,59-396,29; p = 0,007).
Conclusiones: La infección periprotésica en el paciente con fractura del cuello femoral tratado con una artroplastia podría relacionarse con la presencia de determinadas variables en el momento del ingreso hospitalario, entre las que se encuentran la anaemia moderada o severa, la trombocitopenia, el antecedente de evento tromboembólico, el trastorno ansioso-depresivo en tratamiento con 2 o 3 fármacos o la hepatopatía.

Introduction

Increase in life expectancy is accompanied by an increase in the incidence of hip fracture, which is considered one of the leading causes of mortality and disability in the elderly patient. Whereas in 1990, around 1.66 million hip fractures were diagnosed worldwide, it is estimated that this figure will reach 4.5 million by the year 2050.[1] The incidence of hip fractures is expected to rise to 4.5 million by 2050.

From an anatomical and physiological point of view, two main groups can be distinguished: intracapsular and extracapsular fractures. Intracapsular fractures include fractures of the femoral head and femoral neck, the latter being the most numerous group.[2] Thus, in this group, the majority correspond to displaced fractures of the femoral neck, which usually require a hemiarthroplasty (HA) or a total hip arthroplasty (THA).[3]

Hip arthroplasty is not free from complications,[4] notably from periprosthetic infection, which can be accompanied by readmissions and reoperations, long periods of antibiotic therapy and functional deterioration of the patient. The incidence of this complication is around 1.3% in elective hip arthroplasty; however, this figure could be as high as 4.7% in hip arthroplasty performed for fracture.[5] Given its importance, it is essential to identify which risk factors could be involved in its appearance, as the optimisation or elimination of these can contribute to reducing its incidence. In this regard, Breznicky et al.[6] suggest that key risk factors could include body mass index (BMI), diabetes and kidney or liver disease. The influence of variables such as the Charlson comorbidity index, length of hospital stay and perioperative transfusion rate have also been analysed.[7]

The aim of the present study is to describe and analyse risk factors that could be involved in periprosthetic infection in patients with femoral neck fractures.

Material and methods

We conducted a retrospective, case–control study including patients with femoral neck fractures treated with an arthroplasty, HA or THA, in the period from January 2015 to December 2017. Patients were excluded from the study if they had a bone metabolism disorder other than osteoporosis (osteomalacia, renal osteodystrophy or Paget's disease), patients under the age of 50 years, patients operated on in other hospitals, patients operated on in our hospital centre who lived in another health area (they underwent postoperative follow-up in their reference hospital) and those who did not give their consent to participate in the study.

In all cases, the procedure (HA or THA) was performed or supervised (when a resident operated) by an experienced surgeon. The decision to use HA or THA was made on the basis of the Charlson comorbidity index score (age and major comorbidities) and Barthel index score (degree of autonomy). However, although these scores are a very useful tool, no rigid criteria were established, as each case had to be individualised. When HA was chosen, a bipolar prosthesis was used in patients under 85 years of age and a monopolar prosthesis in older patients over 85 years of age. A cemented stem was used in HA. In contrast, in THA, a cemented stem was used in most cases, with the exception of a few patients in whom, after intraoperative assessment of bone density, cementless cementation was considered. When cementation was performed, cement was used without antibiotics. An uncemented acetabular component was also implanted in THA. All patients underwent a lateral Hardinge approach and the following perioperative measures were performed: preoperative antibiotic prophylaxis with 2 g cefazolin (except for penicillin allergy, in which case vancomycin was administered), thromboprophylaxis with low molecular weight heparin, spinal anaesthesia and rehabilitation protocol, which began in the immediate postoperative period.

Cases were defined as patients with femoral neck fracture who after undergoing arthroplasty (HA or THA) had a periprosthetic infection as an outcome, whose diagnosis was made according to the major and minor criteria described by Parvizi et al.[8] In contrast, all patients who after treatment with hip arthroplasty for femoral neck fracture did not develop a periprosthetic infection were considered controls. All controls were drawn from the same cohort as the cases. Inclusion and exclusion criteria were applied similarly in the selection of cases and controls.

All patients (or their authorised legal representatives) signed their informed consent. The ethical principles set out in the Declaration of Helsinki, as last revised in Fortaleza, Brazil, 2013, were followed throughout the project. Approval was obtained from the Malaga Provincial Research Ethics Committee at the session held on 30 July 2020.

At the time of hospital admission, demographic variables were collected (sex, age and BMI), various preoperative indices (Barthel, Charlson comorbidity, American Society of Anesthesiologists [ASA]), toxic habits (tobacco and alcohol consumption), comorbidities (obesity, AHT, dyslipidaemia, gout, peripheral venous insufficiency, diabetes, immunosuppression, thyroid, respiratory, cardiac, haematological, mental, renal, hepatic, oncological and neurological pathology), laterality, degree of displacement of the patient and the degree of neurological displacement, diabetes, immunosuppression, thyroid, respiratory, cardiac, haematological, mental, renal, hepatic, oncological and neurological pathology, laterality, degree of fracture displacement (Garden classification), type of procedure (HA or THA), operative time, profile of the surgeon performing the procedure (medical doctor vs. MIR and general traumatologist vs. traumatologist of the hip unit), preoperative (haemoglobin, platelets, urea, creatinine and glomerular filtration rate) and postoperative (haemoglobin) analytical parameters, need for transfusion (preoperative or postoperative), hospital stay (preoperative and postoperative). According to the World Health Organisation (WHO) classification, the diagnosis of mild anaemia was established in the presence of haemoglobin levels between 12 and 10 g/dl, and moderate or severe anaemia with values below 10 g/dl. Similarly, thrombocytopenia was diagnosed with platelet levels below 100,000 mm^{-3} which includes moderate and severe thrombocytopenia. Postoperative local complications were recorded, including periprosthetic infection (Tsukayama classification[9] and causative germ), dislocation, periprosthetic fracture, aseptic loosening, dysmetria, gluteal insufficiency and lameness. Systemic complications (moderate or severe anaemia, thromboembolic event, pneumonia, cardiac problem, delirium, urinary tract infection, gastrointestinal bleeding or multi-organ decompensation), readmissions and re-operations, mortality, pain (visual analogue scale [VAS]), function (Harris, Oxford and WOMAC scales), quality of life (EuroQol-5D) and patient satisfaction (dissatisfied, partially satisfied and satisfied) were also recorded.

Data were collected at admission, during the hospital stay and at outpatient check-ups, which were performed at 1, 3 and 12 months after the procedure. During follow-up, losses were identified and described.

Demographic variables (sex, age and BMI) were collected at the time of admission to hospital, and various possible biases were identified and addressed. Cases were precisely defined, with the intention of avoiding false cases (selection bias). Both cases and controls were classified comprehensively and homogeneously to avoid misclassification (classification bias). Data were extracted following a standardised protocol, similar in all participants, with the same sources of information in both groups (information bias). Also, in order to mitigate recall bias, the time between exposure and completion of the study was minimised.

The collected data were entered into an Excel database (Microsoft® Excel® 2016 MSO, version 2202 build 16.0.14931.20118) and analysed with the Statistical Package for Social Sciences (IBM SPSS® Statistics, version 25). From the point of view of descriptive statistics, quantitative variables were presented as measures of central tendency (arithmetic mean, median and mode) and measures of dispersion (standard deviations and ranges). Qualitative variables were described as frequencies and percentages. The qualitative analysis was carried out using Pearson's chi-square test. After confirming that the quantitative variables did not follow a normal distribution, the quantitative analysis was carried out with the Mann–Whitney U-test

Table 1 Socio-demographic variables and preoperative indexes.

Sex	
Men	140 (29.4%)
Women	336 (70.6%)
Age	84.93 ± 9.73 years (54–105)
BMI	26.42 ± 5.85 (15.57–49.95)
Barthel index	36.04 ± 25.67 (0–100)
Charlson comorbidity	5.5 ± 2.1 (0–15)
ASA	
Grade 1	15 (3.2%)
Grade 2	104 (21.8%)
Grade 3	263 (55.3%)
Grade 4	92 (19.3%)
Grade 5	2 (0.4%)

(independent samples). Differences were considered statistically significant when the *p*-value was less than .05.

A subgroup analysis was performed with the intention of identifying variables with a different distribution in cases and controls. In addition, after performing a bivariate statistical analysis, a multivariate analysis was performed.

In order to reflect the strength of association between the main outcome variable (periprosthetic infection) and the different independent variables, different odds ratios (OR) were calculated.

Results

This study included patients with femoral neck fractures treated with arthroplasty between January 2015 and December 2017. A mean follow-up of 4.48 ± .89 years (range: 2.97–5.98) was appreciated. The preliminary sample was 543 patients. However, 36 who were treated by osteosynthesis and 15 treated conservatively were excluded. Also excluded were 16 patients who moved to another health care area and therefore could not be followed up postoperatively. The final sample size was 476 patients.

The socio-demographic variables and preoperative indices are set out in Table 1.

A total of 226 fractures were identified with right laterality (47.5%), compared to 250 with left laterality (52.5%). There were 59 Garden 2 (12.4%), 183 Garden 3 (38.4%) and 234 Garden 4 (49.2%) fractures.

Regarding the type of procedure, 310 patients (65.1%) were treated with an HA and 166 (34.9%) with a THA. In terms of surgeon profile, 177 fractures (37.2%) were operated on by residents and 299 (62.9%) by area specialists. Likewise, 95 fractures (20%) were operated on by the hip unit, compared to 381 fractures (80%) that were operated on by the other units, including the trauma unit.

Periprosthetic infection, considered the main outcome variable, was the most frequent postoperative local complication. The case group, consisting of those patients who had a periprosthetic infection as an outcome, included a total of 15 patients (3.2%), compared to the control group of 461 patients (96.8%) who did not have a periprosthetic infection.

Table 2 Measurements of association between periprosthetic infection and comorbidity present on hospital admission. Calculation of odds ratio (OR), 95% confidence interval (95% CI) and *p* value.

Variable	OR	95% CI	*p*
Moderate or severe anaemia	10.91	1.07–111.50	.007
Thrombocytopenia	23.49	3.61–152.73	.001
Thromboembolic history	7.73	1.52–39.37	.002
Pulmonary thromboembolism	10.91	1.07–111.50	.007
Rheumatic valvulopathy	32.86	1.95–552.57	.001
History of haemorrhagic stroke	32.86	1.95–552.57	.001
Anxiety-depressive disorder	11.67	2.15–63.39	.001
Lung neoplasm	32.86	1.95–552.57	.001
Chronic liver disease	4.36	1.16–16.45	.010

Table 3 Multivariate analysis. Odds ratio (OR), 95% confidence interval (95% CI) and *p* value.

Variable	OR	95% CI	*p*
Thrombocytopenia	27.72	3.48–221.01	.002
Thromboembolic history	8.80	1.31–59.38	.026
Anxiety-depressive disorder	21.36	3.65–125.12	.001
Chronic liver disease	32.04	2.59–396.29	.007
Luxation	21.36	3.65–125.12	.001

Qualitative analysis using Pearson's chi-square test showed that periprosthetic infection was more frequent among patients with moderate or severe anaemia (25% vs. 2.9%, $p = .035$), thrombocytopenia (40% vs. 2.8%, $p = .001$), a history of thromboembolic disease (18.2% vs. 2.8%, $p = .043$), rheumatic valve disease (50% vs. 2.8%, $p = .043$), rheumatic valve disease (50% vs. 2.9%, $p < .001$), history of haemorrhagic stroke (50% vs. 2.7%, $p = .011$), anxiety-depressive disorder on treatment with 2 or 3 drugs (25% vs. 3.2%, $p = .044$), lung neoplasia (50% vs. 3%, $p = .001$) or chronic liver disease (20% vs. 2.7%, $p = .028$). As a measure of association, the OR was calculated and is shown in Table 2.

Periprosthetic infection was also more frequent among patients who postoperatively suffered a dislocation (25% vs. 2.8%, OR: 11.67, 95% CI: 2.15–63.39, $p = .023$). No statistically significant differences were seen for other local or systemic complications (37.5% vs. 33.3%, $p = .485$).

A multivariate analysis was performed, the results of which are presented in Table 3.

Table 4 shows a summary of the risk factors analysed, which did not show a statistically significant association with the infection variable.

The Mann–Whitney U test also showed no statistically significant differences with respect to the number of units transfused in the preoperative period (.12 ± .49 vs. .13 ± .52, $p = .973$) and postoperatively (.52 ± 1.02 vs. .40 ± .83, $p = .697$).

A multivariate analysis was performed, the results of which are presented in Table 3.

A summary of the risk factors analysed, which were not statistically significantly associated with the infection variable, is presented in Table 4.

Table 4 Variables of the exposure that were not statistically significantly associated with the infection variable.

Variable	No infection (controls)		Infection (cases)		*p*
Sex	Man	Woman	Man	Woman	.416
	137 (29–7%)	324 (70–3%)	3 (20%)	12 (80%)	
Age	<80 years	>80 years	<80 years	>80 years	.984
	124 (26–9%)	337 (73–1%)	4 (26–7%)	11 (73–3%)	
Charlson comorbidity	<4 points	>4 points	<4 points	>4 points	.368
	142 (30–9%)	318 (69–1%)	3 (20%)	12 (80%)	
Procedure	HA	THA	HA	THA	.075
	297 (64–4%)	164 (35–6%)	12 (80%)	3 (20%)	
THA cementation	Cementless	Cemented	Cementless	Cemented	.436
	48 (29–3%)	116 (70–7%)	1 (50%)	1 (50%)	
HA type	Monopolar	Bipolar	Monopolar	Bipolar	.402
	141 (49–6%)	143 (50.4%)	8 (61.5%)	5 (38.5%)	
Resident vs. specialist	Residents	Specialists	Residents	Specialists	.162
	174 (37.7%)	287 (62.3%)	3 (20%)	12 (80%)	
Hip unit vs. other units	Hip unit	Other units	Hip unit	Other units	.509
	91 (19.7%)	370 (80.3%)	4 (26.7%)	11 (73.3%)	
Peri-operative respiratory septic focus	29 (6.3%)		0 (0%)		.431
Peri-operative urological septic focus	13 (2.8%)		0 (0%)		.961
Ectopic admission	68 (14.8%)		3 (20%)		.574
Tobacco	95 (20.6%)		4 (26.7%)		.569
Alcoholism	26 (5.6%)		0 (0%)		.344
Morbid obesity	14 (3%)		0 (0%)		.493
Diabetes	148 (32.1%)		5 (33.3%)		.920
Immunosuppression	15 (3.3%)		0 (0%)		.478
Thyroid disease	54 (11.7%)		3 (20%)		.331
Respiratory disease	82 (17.8%)		3 (20%)		.826
Renal insufficiency	33 (7.2%)		2 (13.3%)		.367
Peripheral venous insufficiency	16 (3.5%)		0 (0%)		.463
Atrial fibrillation	73 (15.8%)		3 (20%)		.665
Ischaemic heart disease	43 (9.3%)		0 (0%)		.215
Heart failure	30 (6.5%)		1 (6.7%)		.980
Cardiac valve disease	24 (5.2%)		2 (13.3%)		.173
Neurological disease	47 (10.2%)		3 (20%)		.223
Dementia	85 (18.4%)		5 (33.3%)		.147
Pre- and post-operative analytical parameters					
Preoperative urea >50 mg/dl	167 (42.5%)		6 (46.2%)		.793
Postoperative creatinine >1.3 mg/dl	89 (19.4%)		3 (20%)		.953
Preoperative glomerular filtration rate <60 ml/min/1.73 m^2	201 (44.5%)		6 (40%)		.473
Preoperative transfusion	30 (6.5%)		1 (6.7%)		.980
Postoperative transfusion	111 (24.1%)		3 (20%)		.716

The Mann–Whitney U-test also showed no statistically significant differences in the number of units transfused preoperatively (.12 ± .49 vs. .13 ± .52, $p = .973$) and postoperatively (.52 ± 1.02 vs. .40 ± .83, $p = .697$).

Overall hospital stay was 12.0 ± 9.7 days (HA: 12.0 ± 5.9 days vs. THA: 11.0 ± 14.3 days). Also, hospital stay in cases was 13.0 ± 2.6 days vs. 12.0 ± 9.9 days in controls ($p = .053$).

With HA treatment (100% cemented) a mean surgical time of 39 ± 8 min was recorded, compared to 58 ± 11 min with THA (70.5% cemented vs. 29.5% uncemented), with no statistically significant differences between the surgical time variable and the periprosthetic infection variable ($p > .05$).

Table 5 shows the microorganisms identified according to the type of procedure (HA vs. THA) and the type of infection according to Tsukayama's classification, being considered significant when they were isolated in at least 3 intraoperative samples.

During the 12 months after the procedure, 52 patients (10.9%) died, which should be considered as loss to follow-up. Of the 52 patients, 32 (6.7%) died during hospital admission and 20 (4.2%) after hospital discharge. There were no statistically significant differences in in-hospital mortality (31 [6.7%] vs. 1 [6.7%], $p = .733$) or in the first year (51 [11.1%] vs. 1 [6.7%], $p = .498$) between cases and controls.

At 12 months post-fracture, functional and quality of life outcomes did not show statistically significant differences with respect to the periprosthetic infection variable; however, it was noted that patients with

Table 5 Distribution of causative microorganisms by type of procedure and Tsukayama classification.

Procedure	Tsukayama classification	Microorganism	Frequency and percentage
HA: 12 (80%)	Acute: 9 (75%)	*Staphylococcus aureus*	2 (22.2%)
		Polymicrobial (*S. aureus and S. epidermis*)	2 (22.2%)
		Escherichia coli	1 (11.1%)
		Pseudomonas aeruginosa	4 (44.4%)
	Chronic: 2 (16.7%)	*Staphylococcus aureus*	1 (50%)
		Enterobacter cloacae	1 (50%)
	Haematogenic: 1 (8.3%)	*Pseudomonas aeruginosa*	1 (100%)
THA: 3 (80%)	Acute: 1 (33.3%)	*Klebsiella pneumoniae*	1 (100%)
	Chronic: 2 (66.7%)	*Staphylococcus epidermidis*	2 (100%)

Table 6 Functional and quality of life outcomes at 12 months post fracture.

Variable	No infection Mean ± standard deviation	Infection Mean ± standard deviation	*p*
VAS pain	2.1 ± 1.4	1.7 ± 1.2	.533
Harris	77.4 ± 16.3	74.0 ± 12.5	.317
Oxford	15.2 ± 10.6	20.1 ± 11.0	.083
WOMAC	32.6 ± 22.4	42.8 ± 23.2	.070
EQ 5D index	.72 ± .28	.57 ± .45	.346
EQ 5D VAS	84.3 ± 15.0	77.7 ± 13.9	.066

infection had poorer functional and quality of life outcomes (Table 6).

Periprosthetic infection was associated with higher patient dissatisfaction (5.6% vs. 3.1%); however, this difference was not statistically significant ($p = .782$).

Discussion

Infection is one of the main complications in the patient with femoral neck fracture treated with arthroplasty. In our series it was the most frequent postoperative local complication. Given its importance, various authors have tried to identify which risk factors could be involved in its occurrence. Noailles et al.[10] presented a systematic review that related periprosthetic infection to the presence of comorbidity (obesity, liver disease or advanced age), to aspects related to the surgical procedure (performance by a junior surgeon, use of uncemented stems or delay in surgical scheduling) and to perioperative management (prolonged hospital stay, presence of haematoma, persistent drainage through the wound or urinary catheterisation). In this respect, the most relevant findings in the present study were the statistically significant association between periprosthetic infection and the presence of certain variables at the time of admission, including anaemia, thrombocytopenia, history of thromboembolic event, anxious-depressive disorder and chronic liver disease.

Moderate or severe anaemia is a risk factor for infection in hip fracture patients, which increases when the patient requires transfusion of allogeneic blood products. This appears to be related to immune changes following transfusion, including decreased levels of IL-2, inhibition of natural killer (NK) cells and decreased hypersensitivity response. Changes in immunomodulation have also been observed, leading to a reduced immune response to the presence of bacteria in the surgical site, which may favour the development of infection.[11]

The presence of moderate or severe thrombocytopenia in patients undergoing femoral neck fracture surgery increases the risk of bleeding during surgery, which can lead to the formation of haematomas, a ''breeding ground'' for bacterial proliferation and, in line with what was observed in our series, the development of infection. Along the same lines, patients with a history of thromboembolism treated with anticoagulant therapy also present an increased risk of infection, due to the formation of perioperative haematomas that may favour bacterial growth.[12]

In our analysis, a higher risk of infection was observed in patients with a history of anxiety-depressive disorder. Thus, alterations in angiogenesis and immunomodulation, as well as suppression of NK cells and antigen-presenting cells, which are essential for generating the immune response, have been described in these patients.[13,14]

Patients with advanced chronic liver disease have increased portal hypertension, hyperdynamic circulation and immunosuppression secondary to liver dysfunction, all of which increase the risk of infection. Likewise, in patients with chronic liver disease there is often intestinal bacterial translocation secondary to portal hypertension, polymorphonuclear (PMN) dysfunction, reduced complement and alterations in the reticuloendothelial system, all of which negatively affect the immune response.[15]

In relation to risk factors considered classic, such as diabetes mellitus, in contrast to that described by Park et al.,[16] in our series diabetic patients had a slightly higher incidence of periprosthetic infection (3.8% vs. 3.1%); however, this difference was not statistically significant ($p = .559$). There was

also no difference for other classical risk factors, including BMI ($p = .493$).[17]

Regarding the type of procedure, in line with the meta-analysis by Peng et al.,[18] our analysis did not identify statistically significant differences between patients treated with HA and THA ($p = .075$). However, a higher incidence of infection was observed in patients who underwent HA versus THA (13 [4.2%] vs. 2 [1.2%]).

Different authors, such as DeAngelis et al.[19] suggest that the incidence of periprosthetic infection could be reduced when the intervention is performed by surgeons with a fellowship in hip arthroplasty ($p = .01$). It has also been reported that infection is more frequent among surgeons who perform fewer hip arthroplasties/year ($p = .042$).[20] In this regard, in our series no statistically significant differences were observed between patients operated on by the hip unit and those operated on by other units, which tend to perform fewer hip arthroplasties/year.

Periprosthetic infection has also been associated with longer hospital stays.[10] In this regard, our analysis showed a modest increase in total length of stay in the group of patients who had an infection as an outcome. However, it was not statistically significant ($p > .05$).

In the present study, the most frequent causative microorganism was *Pseudomonas aeruginosa*, which differs from that described in the work of Guren et al.,[21] in which the most frequent microbiological findings were *Staphylococcus aureus* and polymicrobial infection. They also report that the presence of polymicrobial infection may be associated with a higher failure rate and higher mortality at one year after surgery.

With regard to function and quality of life in patients treated with arthroplasty for femoral neck fracture, it was observed that patients who had a periprosthetic infection as an outcome had poorer functional and quality of life outcomes. These findings are consistent with Wildeman et al.[22]

Among the limitations of the present study are those inherent to a case-control study: it is retrospective in nature, does not allow estimation of incidences and may present biases, which in our study were minimised by a precise definition of the cases (selection bias) and similar and standardised data extraction in both groups (information bias). Another limitation is that up to 177 procedures (37.2%) were performed by residents, as our centre is a teaching hospital.

Conclusions

Periprosthetic infection in the patient with femoral neck fracture treated with arthroplasty could be related to the presence of certain variables at the time of hospital admission, including moderate or severe anaemia, thrombocytopenia, history of thromboembolic event, anxiety-depressive disorder in treatment with 2 or 3 drugs or liver disease.

Level of evidence

Level of evidence 2.

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Authors' contribution

All signatories have contributed to the study design, the collection and analysis of data, the interpretation of the results, and the writing and revision of the final manuscript.

Transparency statement

The corresponding author, on behalf of the other signatories, guarantees the accuracy, transparency and honesty of the data and information contained in the study; that no relevant information has been omitted; and that all discrepancies between authors have been adequately resolved and described.

Conflict of interests

There are no conflicts of interest related directly or indirectly to the content of the study.

Right to privacy and informed consent

The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is held by the corresponding author.

Ethics Committee Approval

Approved by the Malaga Health Care Ethics Committee.

References

1. Veronese N, Maggi S. Epidemiology and social costs of hip fracture. Injury. 2018;49:1458–60, http://dx.doi.org/10.1016/j.injury.2018.04.015.
2. Shivji FS, Green VL, Forward DP. Anatomy, classification and treatment of intracapsular hip fractures. Br J Hosp Med (Lond). 2015;76:290–5, http://dx.doi.org/10.12968/hmed.2015.76.5.290.
3. Augat P, Bliven E, Hackl S. Biomechanics of femoral neck fractures and implications for fixation. J Orthop Trauma. 2019;33 Suppl 1:S27–32, http://dx.doi.org/10.1097/BOT.0000000000001365.
4. Slobogean GP, Sprague SA, Scott T, Bhandari M. Complications following young femoral neck fractures. Injury. 2015;46:484–91, http://dx.doi.org/10.1016/j.injury.2014.10.010.
5. Barbero JM, Montero E, Vallés A, Plasencia MA, Romanyk J, Gómez J. Infección de prótesis articular en el paciente con fractura de cadera. Diferencias frente a la infección de prótesis electiva [Prosthetic joint infection in patients with hip fracture. Differences from infection of elective prosthesis]. Rev Esp Quimioter. 2016;29:273–7.
6. Breznicky J, Hlavac M, Novak M, Hrncar M. Risk factors for periprosthetic joint infection of the hip and knee. Med Glas (Zenica). 2020;17:92–7, http://dx.doi.org/10.17392/1046-20.

7. Triantafyllopoulos GK, Soranoglou VG, Memtsoudis SG, Sculco TP, Poultsides LA. Rate and risk factors for periprosthetic joint infection among 36,494 primary total hip arthroplasties. J Arthroplasty. 2018;33:1166–70, http://dx.doi.org/10.1016/j.arth.2017.11.040.
8. Parvizi J, Tan TL, Goswami K, Higuera C, della Valle C, Chen AF, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. J Arthroplasty. 2018;33:1309–14.e2, http://dx.doi.org/10.1016/j.arth.2018.02.078.
9. Tsukayama DT, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. J Bone Joint Surg Am. 1996;78:512–23, http://dx.doi.org/10.2106/00004623-199604000-00005.
10. Noailles T, Brulefert K, Chalopin A, Longis PM, Gouin F. What are the risk factors for post-operative infection after hip hemiarthroplasty? Systematic review of literature. Int Orthop. 2016;40:1843–8, http://dx.doi.org/10.1007/s00264-015-3033-y.
11. Greenky M, Gandhi K, Pulido L, Restrepo C, Parvizi J. Preoperative anemia in total joint arthroplasty: is it associated with periprosthetic joint infection? Clin Orthop Relat Res. 2012;470:2695–701, http://dx.doi.org/10.1007/s11999-012-2435-z.
12. Bozic KJ, Lau E, Kurtz S, Ong K, Rubash H, Vail TP, et al. Patient-related risk factors for periprosthetic joint infection and postoperative mortality following total hip arthroplasty in medicare patients. J Bone Joint Surg Am. 2012;94:794–800, http://dx.doi.org/10.2106/JBJS.K.00072.
13. Ray A, Gulati K, Rai N. Stress, anxiety, and immunomodulation: a pharmacological analysis. Vitam Horm. 2017;103:1–25, http://dx.doi.org/10.1016/bs.vh.2016.09.007.
14. 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;470:130–7, http://dx.doi.org/10.1007/s11999-011-2043-3.
15. Deleuran T, Vilstrup H, Overgaard S, Jepsen P. Cirrhosis patients have increased risk of complications after hip or knee arthroplasty. Acta Orthop. 2015;86:108–13, http://dx.doi.org/10.3109/17453674.2014.961397.
16. Park BY, Lim KP, Shon WY, Shetty YN, Heo KS. Comparison of functional outcomes and associated complications in patients who underwent total hip arthroplasty for femoral neck fracture in relation to their underlying medical comorbidities. Hip Pelvis. 2019;31:232–7, http://dx.doi.org/10.5371/hp.2019.31.4.232.
17. Dobson PF, Reed MR. Prevention of infection in primary THA and TKA. EFORT Open Rev. 2020;5:604–13, http://dx.doi.org/10.1302/2058-5241.5.200004.
18. Peng W, Bi N, Zheng J, Xi N. Does total hip arthroplasty provide better outcomes than hemiarthroplasty for the femoral neck fracture? A systematic review and meta-analysis. Chin J Traumatol. 2020;23:356–62, http://dx.doi.org/10.1016/j.cjtee.2020.09.005.
19. DeAngelis RD, Minutillo GT, Stein MK, Schemitsch EH, Bzovsky S, Sprague S, et al., HEALTH Investigators. Who did the arthroplasty? Hip fracture surgery reoperation rates are not affected by type of training—an analysis of the HEALTH database. J Orthop Trauma. 2020;34 Suppl 3:S64–9, http://dx.doi.org/10.1097/BOT.0000000000001931.
20. De Jong L, Klem TMAL, Kuijper TM, Roukema GR. Factors affecting the rate of surgical site infection in patients after hemiarthroplasty of the hip following a fracture of the neck of the femur. Bone Joint J. 2017;99-B:1088–94, http://dx.doi.org/10.1302/0301-620X.99B8.BJJ-2016-1119.R1.
21. Guren E, Figved W, Frihagen F, Watne LO, Westberg M. Prosthetic joint infection—a devastating complication of hemiarthroplasty for hip fracture. Acta Orthop. 2017;88:383–9, http://dx.doi.org/10.1080/17453674.2017.1301009.
22. Wildeman P, Rolfson O, Söderquist B, Wretenberg P, Lindgren V. What are the long-term outcomes of mortality quality of life, and hip function after prosthetic joint infection of the hip? A 10-year follow-up from Sweden. Clin Orthop Relat Res. 2021;479:2203–13, http://dx.doi.org/10.1097/CORR.0000000000001838.