# Extended Oral Antibiotic Prophylaxis in Primary Hip Arthroplasty: Does it Decrease Periprosthetic Joint Infections?

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## ABSTRACT

The prevalence of periprosthetic infections (PPIs) after primary total hip arthroplasty (THA) is approximately 2%. The objective of this study is to determine if there are statistically significant differences between the proportion of acute PPIs with extended oral antibiotic prophylaxis (7 days) vs standard oral antibiotic prophylaxis (24 hours).

A prospective clinical trial was conducted between July 2021 and May 2022. A total of 28 adult patients with hip fracture underwent a primary arthroplasty and received extended oral antibiotic (EOA) prophylaxis for 7 days with first-generation cephalosporins. They were compared to a secondary database of the hospital registry, which included a total of 95 adult patients with hip fractures who underwent primary arthroplasty and received a standard oral antibiotic (SOA) prophylaxis for 24 hs. In the EOA group, the rate of acute PPI was 10.71%, while in the SOA group it was 17.89%. When comparing the rate in both groups, no statistically significant differences were found (p=0.36). Although the available literature suggests that extended antibiotic prophylaxis can be a simple, safe, and cost-effective measure to counteract the patient's non-modifiable factors and thus reduce periprosthetic infections, our study found no evidence that it reduces the proportion of acute PPI at 30 days in primary hip arthroplasties.

**Keywords:** Periprosthetic joint infections; primary hip arthroplasty; extended oral antibiotic prophylaxis; standard oral antibiotic prophylaxis.

**Level of Evidence:** II

## Profilaxis antibiótica extendida para pacientes sometidos a una artroplastia de cadera primaria: ¿disminuye el riesgo de infecciones periprotésicas?

## RESUMEN

**Introducción:** La prevalencia de infecciones periprotésicas luego de una artroplastia total de cadera primaria es aproximadamente del 2%. El objetivo de este estudio fue determinar si existen diferencias estadísticamente significativas entre la tasa de infecciones periprotésicas agudas ante una profilaxis antibiótica extendida (7 días) y una profilaxis antibiótica estándar (24 h). **Materiales y Métodos:** Se realizó un estudio clínico prospectivo, entre julio de 2021 y mayo de 2022, que incluyó a 28 adultos con fractura de cadera sometidos a una artroplastia primaria que recibieron profilaxis antibiótica con cefalosporinas de primera generación durante 7 días a quienes se comparó con 95 adultos con fracturas de cadera con una artroplastia primaria y profilaxis antibiótica de 24 h, extraídos de una base de datos secundaria del registro del hospital. **Resultados:** La tasa de infecciones periprotésicas agudas fue del 10,71% en el grupo con profilaxis extendida y del 17,89% en quienes recibieron profilaxis estándar, sin diferencias estadísticamente significativas (p = 0,36). **Conclusiones:** Si bien, según la bibliografía disponible, la prolongación de la profilaxis antibiótica puede ser una medida simple, segura y rentable para contrarrestar los factores no modificables del paciente y así reducir las infecciones periprotésicas; en este estudio, no se demostró que la profilaxis antibiótica extendida disminuya la tasa de infecciones periprotésicas agudas a los 30 días en pacientes con artroplastias de cadera primarias.

**Palabras clave:** Infecciones periprotésicas; artroplastia de cadera primaria; profilaxis antibiótica extendida; profilaxis antibiótica estándar.

**Nivel de Evidencia:** II

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**How to cite this article:** Zalba J, Donnari E, Poza Román DD, Paschetta Arrue AM, Pirola JM, Alvez EC, Di Fazio Sale JP, Tellarini B, Pesci JP. Extended Oral Antibiotic Prophylaxis in Primary Hip Arthroplasty: Does it Decrease Periprosthetic Joint Infections? *Rev Asoc Argent Ortop Traumatol* 2023;88(5):527-538. https://doi.org/10.15417/issn.1852-7434.2023.88.5.1756

## INTRODUCTION

Periprosthetic joint infections (PJI) are often devastating and represent a major public health problem. Its prevalence following primary total hip arthroplasty (THA) is estimated to be approximately 2%.[1]

There is no consensus definition of PJI in the world, as there is no single reference diagnostic test. It is a developing concept that will evolve as scientific evidence is updated.[2] In 2018, major and minor criteria for diagnosis were established at the Second International Consensus on Periprosthetic Joint Infection held in Philadelphia (Table 1).[3]

**Table 1.** Major and minor criteria for the diagnosis of periprosthetic joint infection

| | |
|---|---|
| **Major criteria (any of the following)** | Fistula communicating with the prosthesis |
| | Isolation of the same microorganism in at least 2 samples of periprosthetic tissue or synovial fluid. |
| **Minor criteria (6 or more)** | Elevated C-reactive protein or D-dimer values >100 mg/l |
| | Leukocyte count in joint fluid >10,000 |
| | Leukocyte esterase: ++ |
| | Alpha-defensin: 1.0 |
| | Elevated polymorphonuclear leukocytes in synovial fluid (%): 90% |
| | Pus inside the affected joint |
| | Isolation of a microorganism from a single intraoperative tissue or joint fluid sample. |
| | ≥5 polymorphonuclear leukocytes per high-power field observed at ≥5 high-power fields (400x magnification)[6] |

Postoperative antibiotics and duration of treatment have been identified as critical factors when discussing PJI. During the first 2 h after surgery, host defense mechanisms decrease the overall bacterial load and, in the following 4 h, it remains constant, as host defenses eliminate bacteria at the same rate as they replicate. The first 6 h are known as the "golden period", after which bacteria multiply exponentially. Postoperative antibiotics effectively decrease the bacterial load and extend this "golden period".[1]

The hypothesis of this prospective study was that administration of antibiotics for 7 days after surgery further prolongs this golden period and that differences in the rate of acute PJI are statistically significant when compared to administration of antibiotics for 24 h postoperatively.

The objective of the study was to determine whether there are statistically significant differences in the rate of acute PJI between extended antibiotic prophylaxis (EAP) and standard antibiotic prophylaxis (SAP).

## MATERIALS AND METHODS

A prospective clinical study was conducted between July 2021 and May 2022. Inclusion criteria were: adult patients with a total or partial hip arthroplasty secondary to a lateral or medial fracture, antibiotic prophylaxis with first-generation cephalosporins intravenously. Exclusion criteria were: patients with arthroplasty secondary to hip osteoarthritis, revision arthroplasty, resection arthroplasty, osteosynthesis in hip fractures, prophylaxis with an antibiotic other than a first-generation cephalosporin, subacute or chronic PJI, infection of another concomitant site (urinary tract, respiratory tract, skin or soft tissues), preoperative antibiotic therapy, lack of postoperative follow-up, and deaths before surgery.

Twenty-eight adult patients with hip fracture who had undergone a primary THA and had received prophylaxis with a first-generation cephalosporin for 7 days (EAP group) were included. This EAP consisted of 1 g of a first-generation cephalosporin administered intravenously, every 8 h, for 7 days to patients weighing <80 kg and 2 g for those >80 kg. Five fractures (17.86%) were caused by lateral hip fractures, while 23 (82.14%) were caused by medial hip fractures (Figure 1).

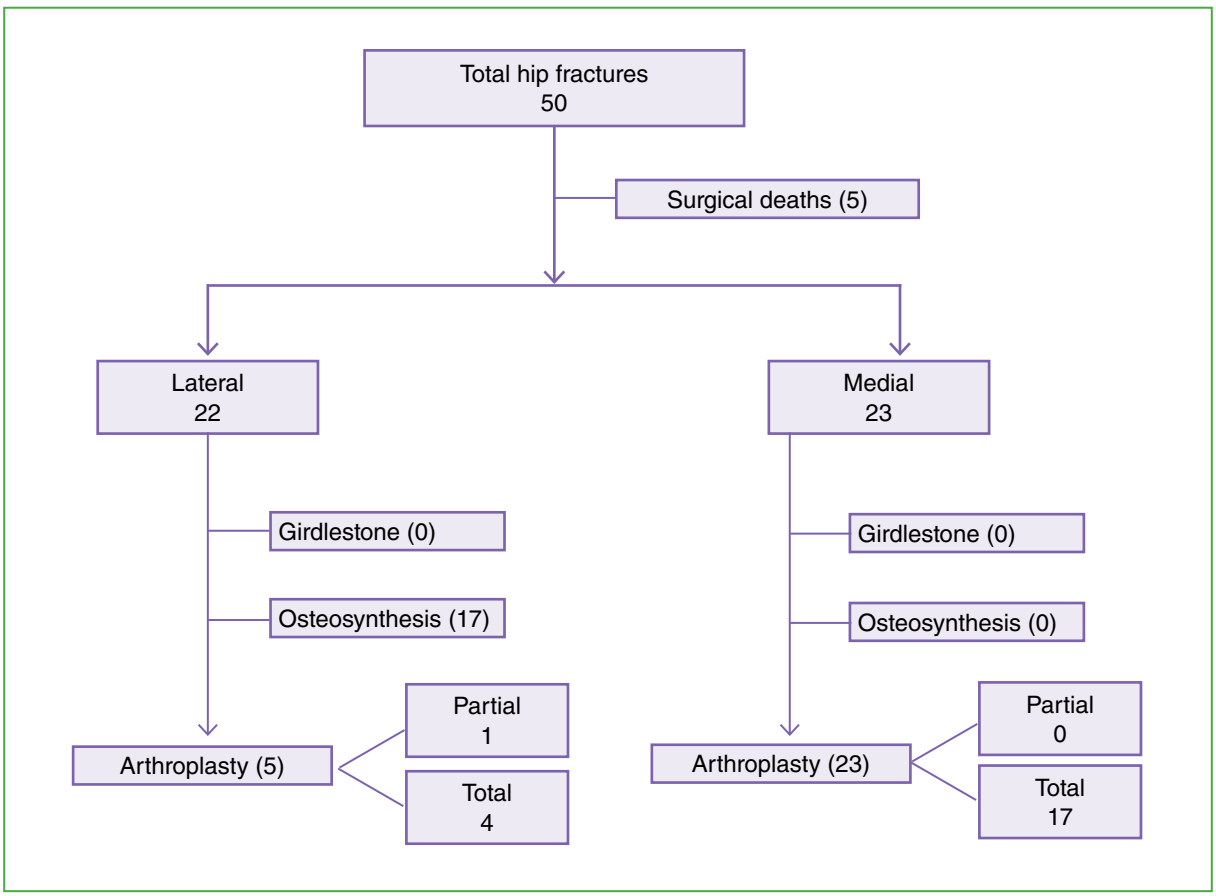


**Figure 1.** Extended antibiotic prophylaxis (7 days).

For comparison, we used the Department's own secondary database, which contains information on all patients operated on since 2011. The period analyzed was from June 2017 to June 2021. The registry contains patient information, date of surgery, hospital stay, comorbidities, implant survival, postoperative clinical outcomes and complications, including PJI. All data were corroborated by the electronic medical records of the institution's operating system.

The second group (SAP) consisted of 95 adults with hip fracture undergoing primary THA, who had been administered prophylaxis with a first-generation cephalosporin intravenously, for 24 h. This SAP consisted of 1 g of a first-generation cephalosporin administered intravenously every 8 h for 24 h to patients weighing <80 kg and 2 g for those >80 kg. Eighteen fractures (18.95%) were caused by lateral hip fractures, while 77 (81.05%) were caused by medial hip fractures (Figure 2).

In both groups, first-generation cephalosporins were used because they are the antibiotic of choice in Argentina for antibiotic prophylaxis in all trauma surgery.[4]

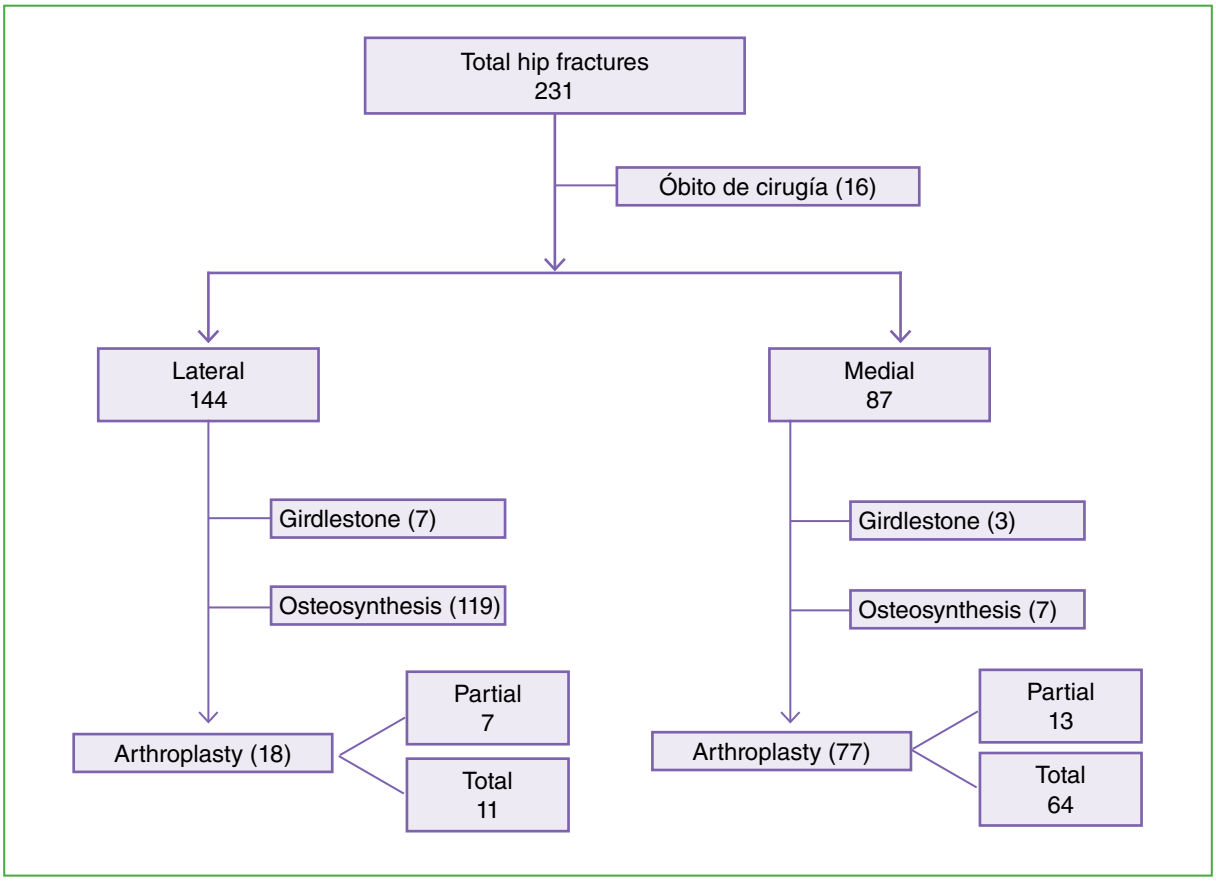


**Figure 2.** Standard antibiotic prophylaxis (24 h).

The criteria listed in the Second International Consensus on Periprosthetic Joint Infection of 2018 were used to establish the concept of PJI.[3] These criteria were adjusted to the hospital resource of the Orthopedics and Traumatology Service of the Hospital Municipal de Agudos "Dr. Leónidas Lucero", and acute PJI was defined as the presence and combination of one or more of the following signs or symptoms: seropurulent, haemopurulent, or purulent discharge through the wound, wound dehiscence, signs of phlogosis in the wound, persistent pain, wound fistulas, increased serum inflammatory parameters (white blood cells >12000/µl, erythrocyte sedimentation rate >10 mm, C-reactive protein >10 mg/l), temperature ≥37.5 ºC.

Two-thirds of acute PJIs occur during the inoculation of microorganisms in the course of the surgical procedure. Depending on their virulence, they can be acute (within the first 4 weeks), subacute (within 2 to 3 months) or chronic (between 3 months and 3 years).[1] In our series, only acute PJIs, those occurring within the first 30 days postoperatively, were analyzed.

Most surgeons and institutions have implemented key prevention initiatives aimed at reducing PJI risk factors, including non-modifiable factors such as ASA >3, obesity, smoking, diabetes, glucocorticoid exposure, chronic kidney disease, cancer, and rheumatoid arthritis; and modifiable factors such as a duration of surgery >3 h and failure to be prescribed systemic antibiotic prophylaxis.[1,2] Taking these factors into account, in both groups, the following variables were considered: age, sex, days of hospitalization, type of fracture (medial or lateral), type of primary arthroplasty (partial or total), duration of antibiotic prophylaxis (24 h or 7 days), acute PJI (yes or no), comorbidities (yes or no) and type of comorbidities (arterial hypertension, diabetes, smoking, cardiovascular events, psychiatric disease, neurological disease, rheumatic disease, oncological disease and hematological disease).

We analyzed whether there were statistically significant differences in the rate of patients suffering acute PJI according to whether they had received an EAP or an SAP. In turn, we evaluated whether there is an association between the patient's comorbidity variables (yes or no) and the presence of PJI (yes or no) in primary THA.

In all cases, a p-value <0.05 was considered significant. SPSS version 19 and Epidat 4.2 were used for data processing.

## RESULTS

The study sample consisted of 28 patients in the EAP group (7 days) and 95 patients in the SAP group (24 h) who had undergone primary THA.

The average age of the EAP group was 79.11 years (Figure 3), 10.71% were male and 89.29% were female. The average hospital stay lasted 10.14 days (Figure 4).

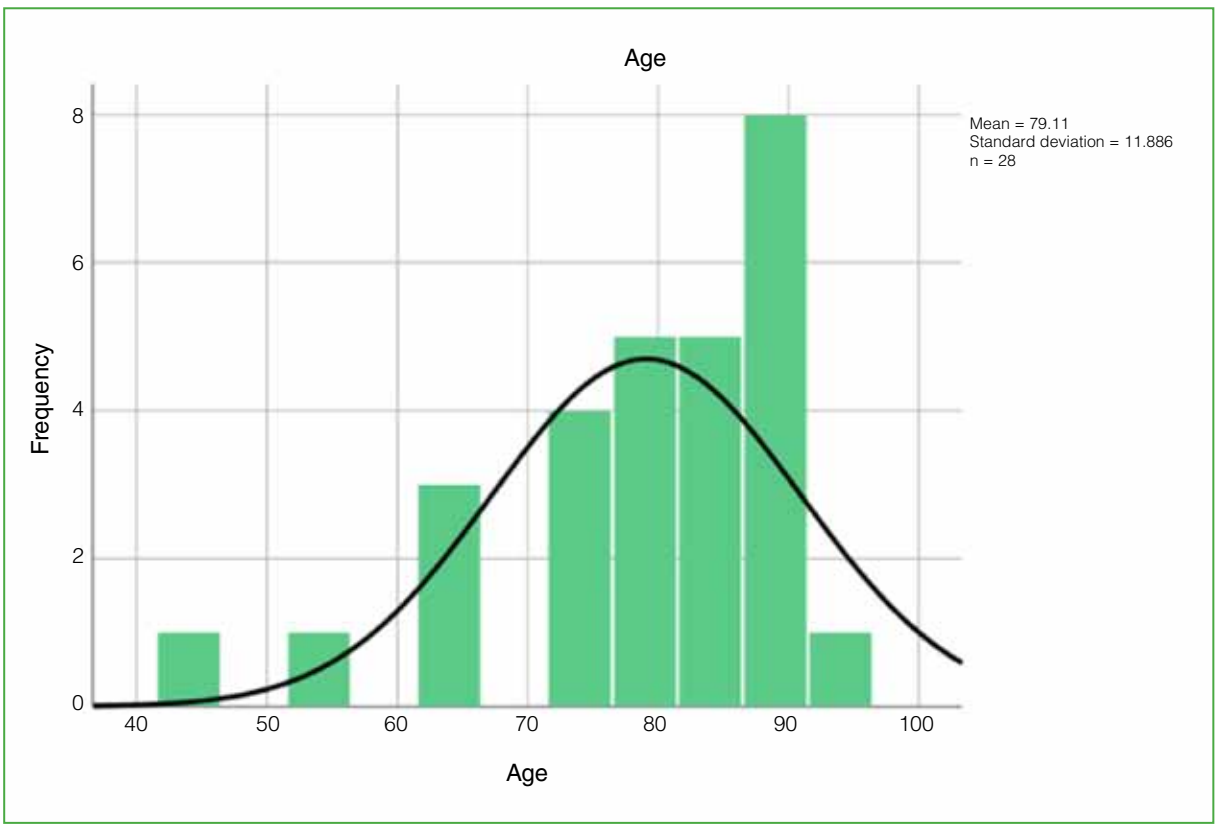


**Figure 3.** Age distribution in the group with extended antibiotic prophylaxis.

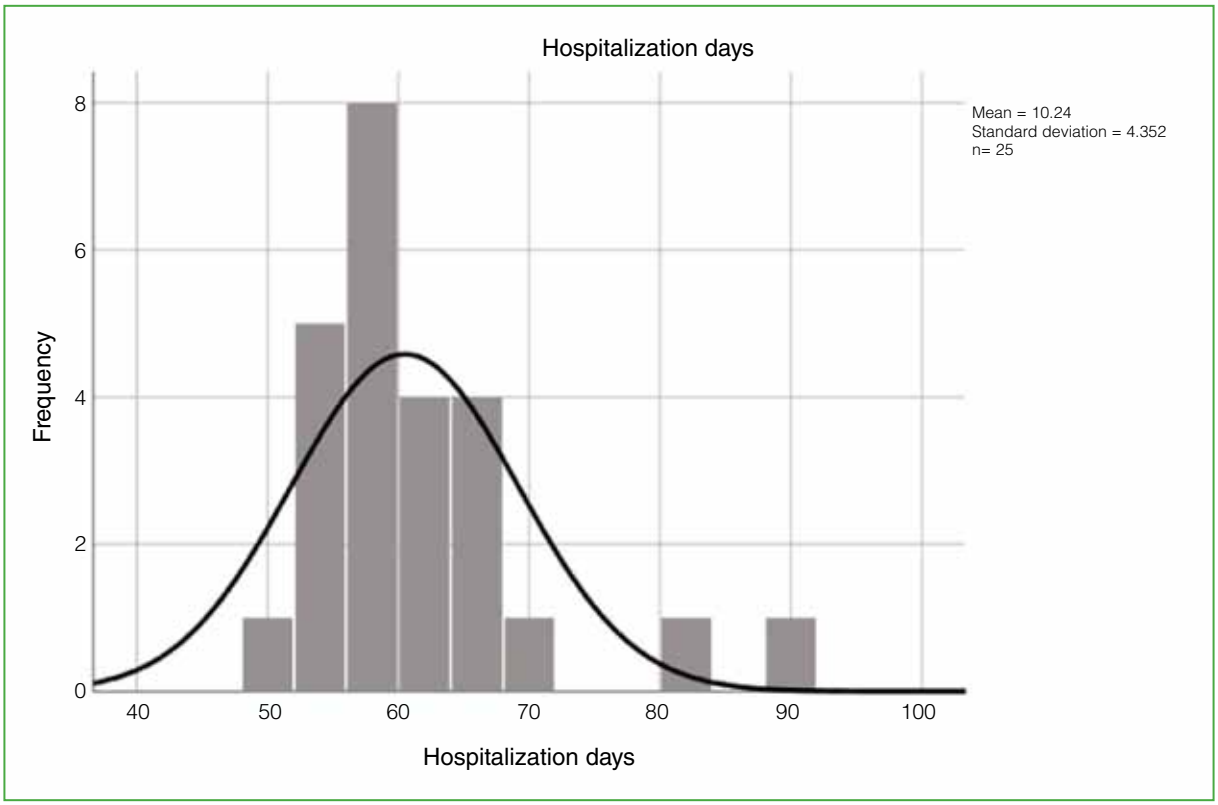


**Figure 4.** Distribution of days of hospitalization in the group with extended antibiotic prophylaxis.

In this group, 82.14% of the fractures were medial and 75% of the patients had undergone hip arthroplasty. 89.29% had comorbidities and the most prevalent were arterial hypertension (64.29%), cardiovascular events (28.57%), and diabetes and neurological diseases (14.29%). The average number of infected patients in this group was 10.71% (Tables 2 and 3).

**Table 2.** Variables of patients hospitalized for hip fracture.

| | Standard antibiotic prophylaxis (n = 95) | Extended antibiotic prophylaxis (n = 28) |
|---|---|---|
| **Age** | | |
| Average | 79.22 | 79.11 |
| Average, men | 79.63 | 67.67 |
| Average, women | 79.14 | 80.48 |
| **Sex** | | |
| Male | 16 (16.84%) | 3 (10.71%) |
| Female | 79 (83.16%) | 25 (89.29%) |
| **Days of hospitalization** | | |
| Average | 13.21 | 10.14 |
| Average, men | 15.63 | 9.33 |
| Average, women | 13 | 10.24 |
| **Type of fracture** | | |
| Medial | 77 (81.05%) | 23 (82.14%) |
| Lateral | 18 (18.95%) | 5 (17.86%) |
| **Type of arthroplasty** | | |
| Total | 75 (78.95%) | 21 (75%) |
| Partial | 20 (21.05%) | 7 (25%) |
| **Periprosthetic infection** | | |
| Yes | 17 (17.89%) | 3 (10.71%) |
| No | 78 (82.11%) | 25 (89.29%) |

**Table 3.** Comorbidities of patients hospitalized for hip fracture.

| | Standard antibiotic prophylaxis (n = 95) | Extended antibiotic prophylaxis (n = 28) |
|---|---|---|
| **Comorbidities** | | |
| Yes | 79 (83.16%) | 25 (89.29%) |
| No | 16 (16.84%) | 3 (10.71%) |
| **Type of comorbidities** | | |
| Arterial hypertension | 48 (50.53%) | 18 (64.29%) |
| Diabetes | 12 (12.63%) | 4 (14.29%) |
| Smoking | 10 (10.53%) | 2 (7.14%) |
| Cardiovascular events | 21 (22.11%) | 8 (28.57%) |
| Psychiatric disease | 14 (14.74%) | 7 (25%) |
| Neurological disease | 21 (22.11%) | 4 (14.29%) |
| Rheumatic disease | 3 (3.16%) | 3 (10.71%) |
| Oncologic disease | 11 (11.58%) | 1 (3.57%) |
| Hematologic disease | 7 (7.37%) | 2 (7.14%) |

The average age of the SAP group was 79.22 years (Figure 5), 16.8% were male and 83.16% were female. The average length of hospitalization was 13.21 days (Figure 6). Of the fractures, 81.05% were medial and 78.95% of the patients had undergone hip arthroplasty. A total of 83.16% had comorbidities and the most prevalent were arterial hypertension (50.53%), cardiovascular events (21%), and neurological diseases (21%). The average number of infected patients in this group was 17.89% (Tables 2 and 3).

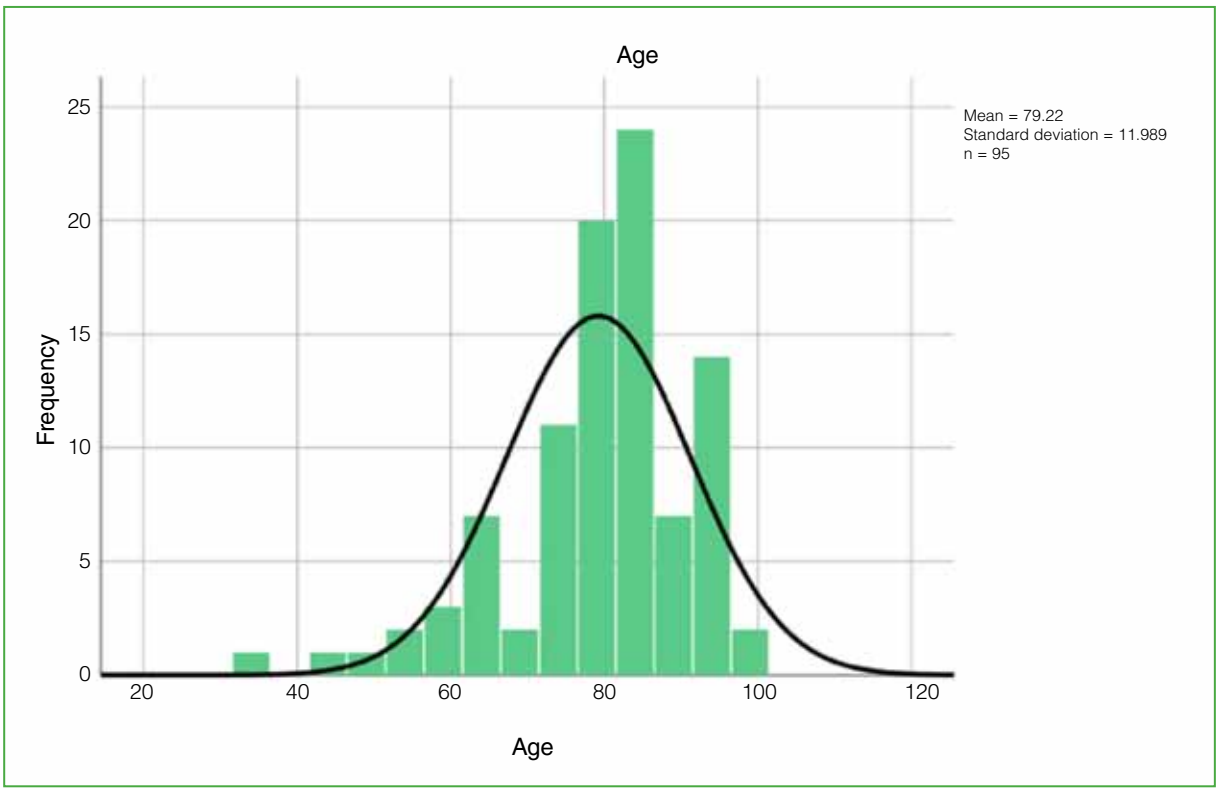


**Figure 5.** Age distribution in the group with standard antibiotic prophylaxis.

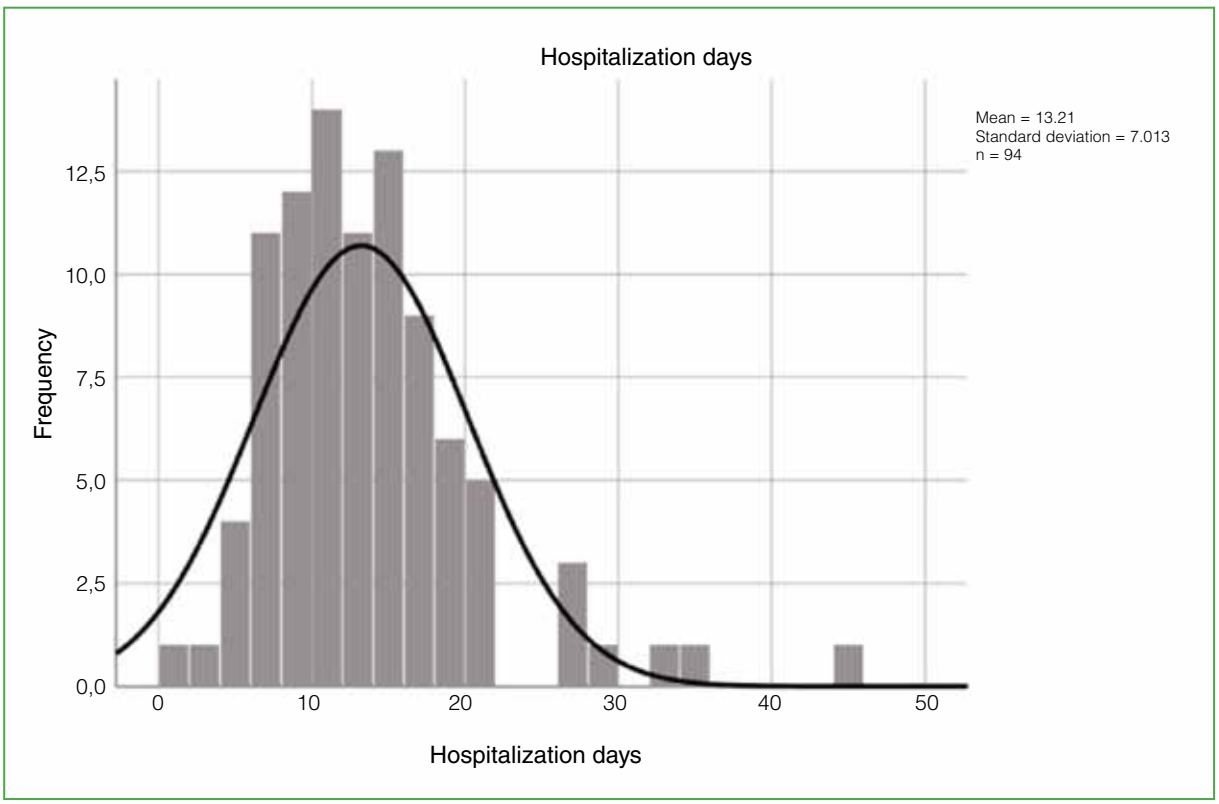


**Figure 6.** Distribution of days of hospitalization in the group with standard antibiotic prophylaxis.

The age and sex of patients in both groups were comparable (mean age, p = 0.96 and sex p = 0.43). When analyzing the PJI rate between both groups, no statistically significant differences were obtained (p = 0.36) (Table 4).

When the results were adjusted for patients with comorbidities, a total of 22 cases were obtained in the EAP group and 79 cases in the SAP group, the PJI rate was three (13.6%) and 16 (20.2%) cases, respectively, without statistical significance (p = 0.4) (Table 4).

With respect to hospital stay, statistically significant differences were obtained. Patients in the EAP group were hospitalized fewer days than those in the other group (p = 0.005) (Table 4).

**Table 4.** Analysis of variables of patients hospitalized for hip fracture.

| | Standard antibiotic prophylaxis | Extended antibiotic prophylaxis | |
|---|---|---|---|
| **Age** | | | |
| Average | 79.22 | 79.11 | 0.966 / (-4.985; 5.205) |
| Average, men | 79.63 | 67.67 | |
| Average, women | 79.14 | 80.48 | |
| **Sex** | | | |
| Male | 16 (16.84%) | 3 (10.71%) | 0.43/(-0.076; 0.198) |
| Female | 79 (83.16%) | 25 (89.29%) | 0.43/(-0.198; 0.076) |
| **Days of hospitalization** | | | |
| Average | 13.21 | 10.14 | 0.005/(0.939; 5.201) |
| Average, men | 15.63 | 9.33 | |
| Average, women | 13 | 10.24 | |
| **Periprosthetic infections** | | | |
| Yes | 17 (17.89%) | 3 (10.71%) | 0.366/(-0.066;0.210) |
| No | 78 (82.11%) | 25 (89.29%) | |
| **Type of fractures** | | | |
| Medial | 77 (81.05%) | 23 (82.14%) | |
| Lateral | 18 (18.95%) | 5 (17.86%) | |
| **Type of arthroplasty** | | | |
| Total | 75 (78.95%) | 21 (75%) | |
| Partial | 20 (21.05%) | 7 (25%) | |

## DISCUSSION

The currently accepted SAP consists of administering the antibiotic within one hour prior to surgery. The World Health Organization and the Centers for Disease Control and Prevention recommend not administering a prophylactic antibiotic after wound closure. However, in 2018, the Second International Consensus on Periprosthetic Joint Infection and the American Association of Orthopedic Surgery disagreed with this behavior. They advised continuing intravenous antibiotic prophylaxis for 24 h after arthroplasty, as in the SAP group in this series.[3-5]

In recent times, there has been increasing research on the use of EAP after hip arthroplasty, especially in those patients at risk of developing PJI, as in our study.[1,3,5-8]

In this series, no statistically significant differences were found when antibiotic prophylaxis was administered for 7 days compared to SAP (p = 0.36). Branch-Elliman et al. obtained similar results, and concluded that prolonging its duration was not associated with a reduction in surgical site infections.[9] Likewise, Kheir et al. found no statistically significant difference in the decrease in the rate of PJI in the SAP group compared to the EAP and risk factor groups.[1] Bukowski et al. evaluated whether EAP in patients undergoing aseptic hip revision decreased the risk of PJI, and also found no statistically significant differences.[10]

A study by Garabano et al. reported a PJI rate of 7.27% in primary THA. The rates were slightly higher in both groups for both EAP and SAP (17.89% and 10.71%, respectively).[4]

According to Inabathula et al., postoperative EAP results in a statistically and clinically significant reduction in the infection rate in selected patients at high risk of infection 90 days after primary THA. On this basis, it is possible that the outcomes would have been comparable if the patients in our study had been followed for a longer period of time. In addition, the study compared the impact of antibiotic prophylaxis in patients undergoing primary THA and multiple risk factors, and it was observed that patients who had not received EAP for 7 days were four times more predisposed to PJI. In contrast, in our series, when adjusting for comorbidities, there were no statistically significant differences.[11]

Regarding hospital stay, patients remained hospitalized for an average of 13 days in the SAP group and 10 days in the EAP group, figures similar to those published by Garabano et al. (mean of 10 days), but significantly shorter in the EAP group.[4]

One limitation of our study is the difficulty in including some variables considered risk factors for PJI, such as nutritional status, alcoholism, chronic consumption of corticosteroids, and colonization by methicillin-resistant *S. aureus*, since secondary data sources were used.[1] Regarding the sample size, it could be considered that if the number of patients in the EAP group increased, statistically significant differences could be obtained with respect to PJI, when compared to the SAP group.

According to published studies, prolongation of antibiotic prophylaxis may be a simple, safe and cost-effective measure to counteract non-modifiable patient factors and thus reduce PJI, but, in this study, no statistically significant differences were found 30 days after surgery. This highlights the need for further research to support the hypothesis.

In summary, the definition of PJI continues to be a point of discussion, subject to the hospital resources and protocols of each institution, coinciding with the diagnostic dynamism proposed by the literature.

In this study, EAP has not been shown to decrease the rate of acute PJI after 30 days in patients with primary THA for fractures of the proximal third of the femur. Considering that antibiotic prophylaxis is a fundamental factor in the prevention of these infections, this measure should be further studied, since it has been shown to be effective in selected patients in reducing PJI at 90 days and one year after surgery.

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

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