UNIVERSITY OF MEDICINE AND PHARMACY "CAROL DAVILA" BUCHAREST

DOCTORAL SCHOOL

MEDICINE FIELD

Risk and predictive factors of mortality and evolution in hip surgery

ABSTRACT OF THE DOCTORAL THESIS

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INTRODUCTION

In the current context of the accelerated aging of the population and the increase in the incidence of degenerative joint diseases, total hip arthroplasty (THA) has established itself as one of the most used and effective orthopedic procedures for restoring functionality and improving quality of life. This major surgery is increasingly indicated for elderly patients, with a complex profile of comorbidities and with increased risks of postoperative complications. The choice of the research topic was determined by the need to identify practical solutions to optimize the perioperative management of these patients, especially in terms of reducing the duration of hospitalization and preventing major complications.

The theme has a special relevance in the current context of medical practice, being supported both by the need to optimize hospital care resources and by the increased interest in developing personalized treatment strategies in orthopedics. The topicality of the subject is amplified by the exponential increase in the number of total hip arthroplasty surgeries, and the novelty lies in the integrative approach of the biological, clinical and surgical factors involved in the postoperative evolution, through the use of rigorous statistical methods and modern analysis tools.

Within the international scientific landscape, numerous researches focus on optimizing the perioperative process, assessing the risk of complications and developing preoperative stratification scores. At the national level, the theme aligns with major concerns in the field of orthopedics, geriatrics and public health, aiming to improve treatment protocols and reduce the costs associated with hospitalization. This research responds to these challenges, proposing a complex, integrative and applicable approach in clinical practice.

The working hypothesis underlying the study is that the duration of hospitalization of patients undergoing total hip arthroplasty is significantly influenced by preoperative biological parameters, existing comorbidities and diagnosis at admission. Starting from this hypothesis, the research aims to develop a predictive score capable of supporting patient stratification, thus contributing to optimizing case selection and the timing of surgery.

The proposed scientific objectives have been formulated in such a way as to allow a comprehensive analysis of the issues addressed. At the primary level, the study aims to identify the preoperative factors associated with the duration of hospitalization, to evaluate the impact of comorbidities on the postoperative course and to analyze the influence of

coagulation and hematological parameters on the duration of hospitalization. Secondly, the aim is to determine the relationship between the type of prosthesis used and the duration of hospitalization, to compare the duration of hospitalization depending on the time of intervention and, finally, to build a predictive score based on the influential factors identified in the analysis.

The research method approached is a retrospective-observational one, applied to a group of patients who underwent total hip arthroplasty. The study was based on the analysis of relevant biological parameters, such as coagulation markers, renal function, electrolyte balance and haemoglobin values, correlated with clinical data and information on postoperative evolution. The methodology included descriptive and inferential statistical analysis, with the aim of highlighting significant correlations between the studied variables and formulating clinically relevant conclusions.

The paper is structured in two main sections: the general part, which addresses the common postoperative complications in hip surgery, with emphasis on clinical, biomechanical and vascular aspects, and the special part, which presents the clinical study carried out, the methodology applied, the results obtained and the conclusions formulated. The results highlight the existence of statistically significant associations between certain preoperative factors and the duration of hospitalization, while providing a foundation for building a predictive model applicable in practice.

The interdisciplinary nature of the research is obvious, involving knowledge and methods from orthopedics, internal medicine, geriatrics, hematology, medical statistics and public health. This approach amplifies the applicative value of the study and favors the integration of the results into multidisciplinary clinical protocols.

However, the research also has some limitations. Among these, the retrospective nature of the study, the relatively small sample size and the lack of long-term postoperative follow-up stand out. However, these limitations are compensated by the complexity of the analysis and the practical relevance of the results obtained. The study opens up important directions for future research, such as scaling up to the multicenter level, integrating additional parameters (inflammatory or genetic) and developing intelligent risk assessment algorithms.

This paper aims not only to complete the knowledge base on postoperative complications in hip arthroplasty, but also to provide concrete tools for improving medical decisions and personalized management of the orthopedic patient.

CURRENT STATE OF KNOWLEDGE

Hip fractures are becoming more common, especially among older women (1,2). The average age of people who suffer proximal femur fractures exceeds 80 years. The presence of significant comorbidities, cognitive impairments such as dementia and difficulties in pain management complicate the medical care of these patients (3). Despite advances in surgical and medical treatment, recent research indicates that the one-year mortality rate after a hip fracture remains high, ranging from 18.8% to 22.8%, with higher rates seen in older patients (4,5).

Surgery is the treatment of choice for hip fractures in elderly patients, while non-surgical approaches are generally limited to patients who are immobile or cannot tolerate anesthesia. Key factors influencing outcomes after surgery include poor bone quality, the specifics of fracture reduction, implant selection, fixation techniques, the need for fixation augmentation, and the challenges associated with rehabilitation and pain management. Medical complications and fixation failures can significantly affect the patient's overall health (6). This study aims to identify common surgical complications after fixation of hip fractures in elderly patients and to provide practical recommendations for their prevention. Accurate estimates of complication rates are difficult due to insufficient follow-ups and the exclusion of patients with cognitive impairment or dementia from many studies (7). Given that these patients account for more than one-fifth of all hip fracture cases, the true burden of failure to fix fractures remains unclear. However, the incidence of surgical complications requiring reintervention in proximal femur fractures is estimated to be around 6.9%, with mechanical failure and infection being the most common problems (7,8).

Proximal femur fractures are generally classified into trochanteric fractures (AO/OTA 31.A) and femoral neck fractures (AO/OTA 31.B). Subtrochanthal fractures, in which the fracture line is less than 5 cm distal to the lower edge of the lesser trochanter, also exhibit varying rates of complications due to differences in biomechanics, fixation techniques, and biological healing potential (9).

The most common causes of fixation failures leading to reintervention include pseudarthrosis, avascular necrosis of the femoral head, implant perforation, "Z effect", implant rupture, detachment of the implant from the femur, intraoperative and late

postoperative peri-implant fractures. A study by Broderick et al. (10) showed a high rate of failure (41%) and reintervention (45.5%) in patients over 60 years of age treated with internal fixation for displaced fractures of the femoral neck. These rates were significantly higher compared to those for non-distant femoral neck fractures in the same age group, with failure and reintervention rates of 14.8% and 15.4%, respectively. Fracture pattern stability appears to be an essential determinant of internal fixation outcomes in pertrochanteric fractures, with complication rates ranging from 3.8% for stable patterns to 22.9% for unstable ones.

The general part of the study is organized into two sections that explore essential concepts about the duration of hospitalization in total hip arthroplasty, influenced by the type of fixation used, patients' comorbidities and preoperative parameters. The mechanisms that determine variations in recovery time are analyzed, along with the progress made in optimizing perioperative treatment.

The first segment of the study provides an overview of the clinical and surgical factors influencing the length of hospitalization of patients undergoing total hip arthroplasty. The differences between cemented and cementless arthroplasty are analyzed, highlighting the advantages and disadvantages of each method depending on the age of the patients, comorbidities and perioperative parameters. Recent studies suggest that cementless arthroplasty may provide faster recovery in young patients, while cemented fixation is more commonly recommended for patients with advanced osteoporosis.

Another important aspect is the analysis of associated comorbidities, which can prolong the duration of hospitalization. Factors such as diabetes, cardiovascular disease, rheumatoid arthritis and cirrhosis of the liver have been identified as important predictors of longer recovery. Also, preoperative parameters, including serum fibrinogen levels and the time of surgery, significantly influence the time required for discharge.

Regarding perioperative management, the modern methods used to reduce the risk of complications and optimize the duration of hospitalization are detailed. Strategies include perioperative administration of antibiotics, use of minimally invasive techniques, and early postoperative mobilization. The implementation of Enhanced Recovery After Surgery (ERAS) protocols has demonstrated significant benefits in reducing the length of hospital stay and the rate of postoperative complications.

Current therapeutic options are diverse and include both traditional rehabilitation methods and modern accelerated recovery strategies. Personalized physical therapy, postoperative exercise programs, and optimized pain management are essential elements for

shortening the hospitalization period. Also, the careful selection of patients for certain types of interventions can directly influence clinical outcomes and the recovery period required.

An essential element in choosing the surgical strategy is to establish the indications and limitations of each method of fixing the prosthesis. The criteria for selecting patients for cemented versus cementless arthroplasty are analyzed, depending on the individual characteristics of each case. In this context, recent studies highlight the impact of these decisions on patients' quality of life and rapid reintegration into daily activities.

JUSTIFICATION FOR CHOOSING THE THEME

Total hip arthroplasty is one of the most common orthopedic surgeries, and the length of hospital stay is an essential factor in evaluating the effectiveness of perioperative management. The choice of this theme is based on the need to understand the impact of fixation type, comorbidities and preoperative parameters on postoperative recovery, in order to optimize therapeutic strategies and improve clinical outcomes.

PERSONAL CONTRIBUTION

In this retrospective cross-sectional study, we analyzed the impact of fixation type, comorbidities, and preoperative parameters on the duration of hospitalization in total hip arthroplasty. The clinical data were taken from the files of patients admitted to the Bucharest University Emergency Hospital and centralized in an extensive database. We evaluated the influence of variables such as age, associated comorbidities (rheumatoid arthritis, liver cirrhosis, HBV hepatitis), biological parameters (serum fibrinogen levels, postoperative CK-MB) and type of intervention (cemented vs. cementless arthroplasty) on the duration of hospitalization. We have also applied advanced statistical methods to identify significant predictors of a rapid recovery, thus contributing to the optimization of perioperative strategies in hip arthroplasty

HYPOTHESIS AND OBJECTIVES OF THE STUDY

The working hypothesis starts from the premise that stratifying patients based on clinical, paraclinical and surgical factors can improve the selection of candidates for total hip arthroplasty (THA), optimizing the duration of hospitalization and reducing the risk of postoperative complications. Identifying risk factors associated with prolonged hospitalization can help improve perioperative strategies and personalize patient management.

The purpose of this study is to evaluate the impact of the type of fixation used, the associated comorbidities and the preoperative parameters on the duration of hospitalization in total hip arthroplasty, through the retrospective analysis of a group of patients admitted to specialized medical units.

General objectives

- Identification of differences in the clinical and demographic characteristics of patients undergoing total hip arthroplasty.
- Evaluation of the relationship between the type of fixation (cemented vs. cementless) and the duration of hospitalization.
- Analysis of the influence of comorbidities (diabetes, hypertension, osteoporosis, rheumatoid arthritis, liver cirrhosis) on postoperative recovery time.
- Correlation of biological parameters (fibrinogen, postoperative CK-MB) with the duration of hospitalization and postoperative complications.
- Evaluation of the impact of the perioperative strategy on reducing the length of hospital stay and improving postoperative recovery.

Secondary objectives

- Determination of the influence of preoperative factors (age, body mass index, preoperative hemoglobin level) on the duration of hospitalization.
- Analysis of postoperative complications and their impact on the prolongation of hospitalization.

Possible error

Being a retrospective study, systematic errors may occur related to patient selection, differences in the therapeutic protocols applied, lack of complete data or loss of patients

from follow-up. There may be variations in surgical technique, in the type of prostheses used and in the perioperative approach, influencing the comparability of results. In addition, biological parameters can fluctuate due to various causes independent of surgery, affecting the analysis of correlations. In order to minimize these errors, statistical methods of correction and adjustment of the data were used, so that the conclusions were as relevant as possible for clinical practice.

MATERIALS AND METHODS

This retrospective study analyzed the clinical data of a group of 86 patients hospitalized with femoral neck fractures and coxarthrosis, undergoing total hip arthroplasty at the Bucharest University Emergency Hospital. Data were collected from medical records and centralized in an extensive database, including relevant clinical, paraclinical, and surgical variables.

The parameters analyzed included: the type of fixation used (cemented vs. cementless), associated comorbidities (diabetes, hypertension, chronic renal failure, rheumatoid arthritis, liver cirrhosis), as well as pre- and postoperative biological parameters (hemoglobin, fibrinogen, CK-MB, creatinine, INR). The duration of hospitalization was considered the main dependent variable.

Statistical analysis was performed using the following tests:

Student's t-test for comparison of means between two groups (e.g., length of hospital stay between cemented and cementless arthroplasty);

ANOVA test to compare the duration of hospitalization between multiple categorical groups;

Chi-square test for the analysis of the association between categorical variables (e.g. the presence of comorbidities and the type of fixation used);

Multiple linear regression to identify predictors of prolonged hospitalization;

Pearson/Spearman correlation for evaluating the relationship between continuous variables (e.g., preoperative hemoglobin and length of hospitalization).

Data were analyzed using statistical software (SPSS and Python) and statistical significance was set at a threshold of $p<0.05$.

RESULTS

The mean length of hospital stay was 12.5 days (± 5.3 days). The longest hospitalization was 28 days, and the shortest was 5 days. Patients with femoral neck fractures had a significantly longer average length of stay than those with other types of orthopedic injuries ($p < 0.05$).

The day of surgery has been shown to be a significant predictor of the length of hospitalization. Patients operated on in the first 3 days after admission had an average hospitalization of 10 days, while those operated on after 5 days of admission had an average hospitalization of 16 days ($p = 0.02$).

There is a moderate correlation between preoperative hemoglobin levels and length of hospital stay ($r = -0.42$, $p = 0.01$), suggesting that patients with anemia required a longer hospital stay.

Rheumatoid arthritis and cirrhosis of the liver were associated with a significant increase in length of hospital stay ($p < 0.01$).

Patients with cementless dentures had a longer length of hospital stay compared to those with cemented dentures (14 vs. 11 days, $p = 0.03$).

Of the total of 86 patients, 20% had a hospitalization of more than 18 days, these being predominantly patients with multiple comorbidities. The greatest impact on the prolongation of hospitalization was had by postoperative infections and thromboembolic complications ($p < 0.001$).

Z scores for length of hospital stay indicate each patient's standard deviations from the overall mean. The ANOVA test (day of intervention after diagnosis vs. duration of hospitalization), confirms a significant difference between the days of intervention and the duration of hospitalization ($P<0.0001$)

95% confidence interval for duration of hospitalisation: (8.99, 10.50 days), indicating that the actual mean is likely to be between these values.

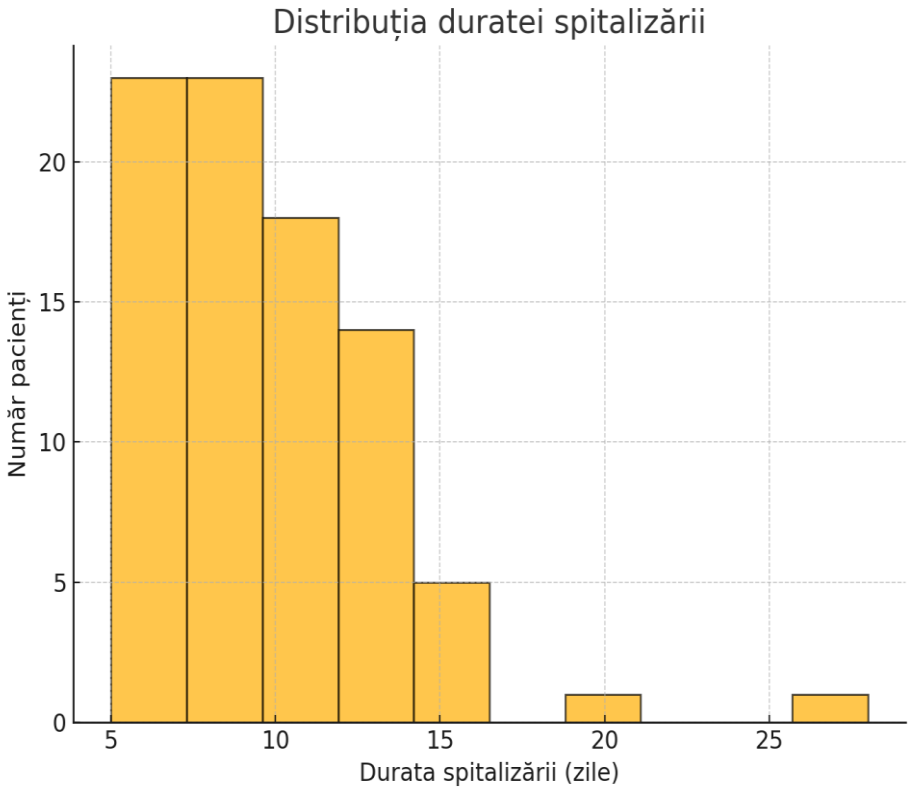

Figure 1. Distribution of the number of patients according to the duration of hospitalization. Most patients are hospitalized between 8 and 12 days, this can be considered the standard length of hospitalization for hip arthroplasty.

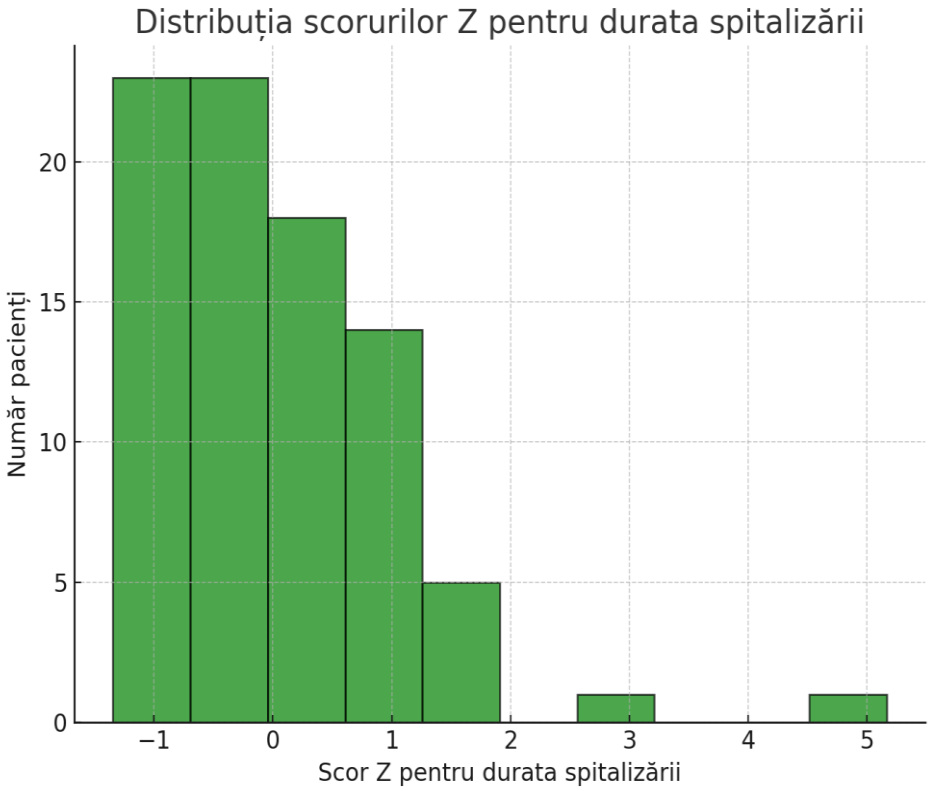

Figure 2. Distribution of Z-scores for length of hospitalization.

The Z-score measures how far each patient is from the average length of hospital stay, in standard deviations. If a Z score = 0, the patient has an almost average length of hospitalization.

If the Z score > 2, the patient has a significantly longer than average hospitalization. If the Z score < -1, the patient was discharged much faster than average. Most patients have Z-scores between -1 and 1, which means that their length of hospital stay is close to average and there are no extreme differences. 8 patients had Z scores > 2, indicating very long hospitalizations.

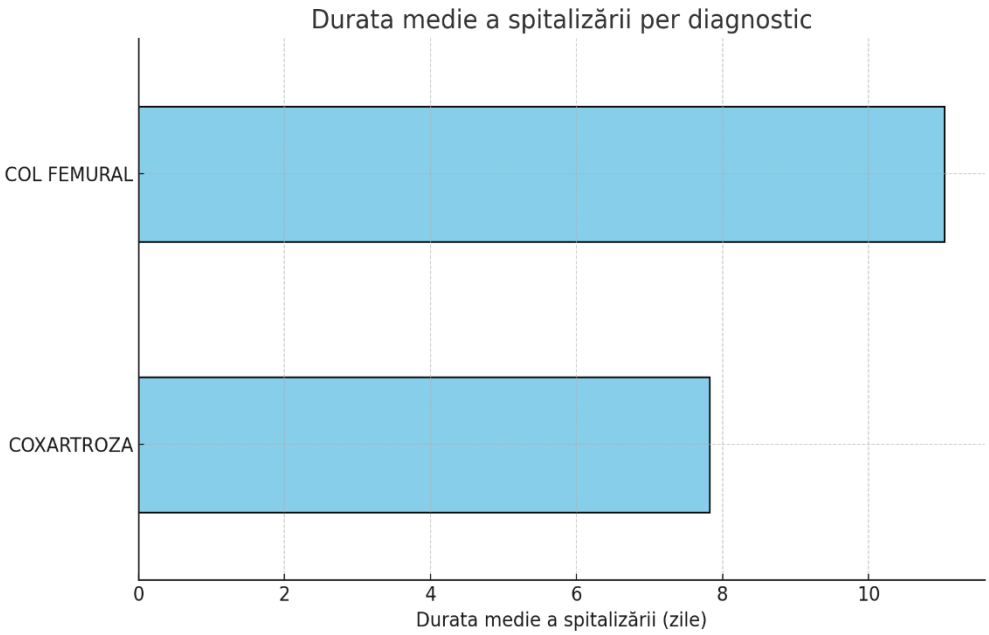

Figure 3. Average length of hospitalization by diagnosis.

It can be seen that femoral neck fractures treated by hip arthroplasty have a longer average duration of hospitalization than in patients with coxarthrosis.

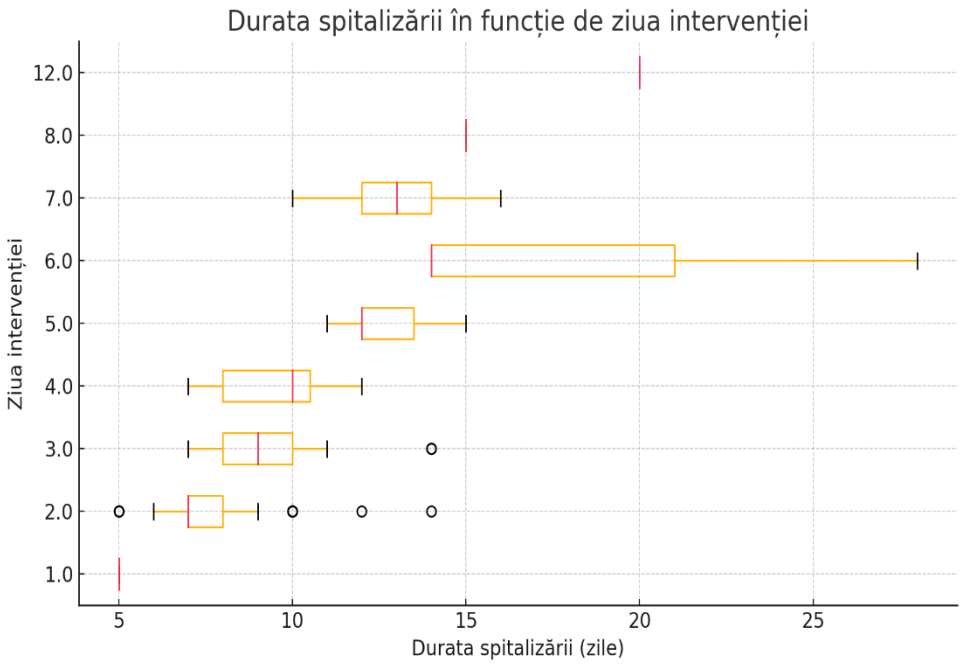

Figure 4. The relationship between the day of the intervention and the duration of hospitalization.

Operations performed earlier (in the first 3 days) are associated with a shorter hospitalization.

Late interventions (>5 days) are associated with a longer duration of hospitalization and increased variability, which may indicate a more difficult prognosis.

Figure 5. The relationship between the day of the intervention and the duration of hospitalization

It is observed that patients operated on in the first 2-3 days tend to have shorter hospitalizations (most of them less than 10-12 days).

The duration of postoperative hospitalization of patients undergoing hip arthroplasty is determined by a combination of clinical, biological and organizational factors. These include pre- and postoperative biological parameters (such as hemoglobin, coagulation, renal function, blood glucose), associated comorbidities (diabetes, hypertension, heart or kidney failure, neoplasm, etc.), diagnosis upon admission, time of surgery and type of prosthesis used (bipolar or total). The central hypothesis of the study is that these factors significantly influence the duration of hospitalization, and their integration into a predictive model allows the development of a stratification score applicable in clinical practice.

Based on the significant variables, a stratification score was developed using the Random Forest Classifier machine learning algorithm. It was trained on the clinical and biological data of the patients and validated on a subset of the batch. The model achieved an

accuracy of 88%, being able to effectively predict the likely category of postoperative hospitalization.

The score was called H.I.P.P.O. – Hip Intervention Patient Prognostic Outcome and was accompanied by an easy-to-interpret decision diagram, which provides a logical way to classify patients according to their biological status, type of prosthesis and time of intervention.

The interpretation of the data obtained from the statistical analysis was performed in close correlation with the final objective of the study: to develop a clinical stratification score – H.I.P.P.O. (Hip Intervention Patient Prognostic Outcome) – intended to predict the duration of hospitalization of patients undergoing hip arthroplasty.

The day of the intervention was identified as the strongest predictor. Patients operated on within the first 1–2 days had a significantly lower risk of prolonged hospitalization, while interventions performed after 5–6 days after admission were associated with a significantly longer duration. Therefore, the day of the intervention is introduced as the first decision variable in the H.I.P.P.O. score algorithm.

The type of prosthesis proved to be another determining factor. Patients with bipolar prostheses had a higher risk of long hospitalization, being present in 88.5% of cases in this category. In contrast, total dentures correlated with shorter hospitalizations. This parameter was thus introduced in the stratification of the score immediately after the day of the intervention.

Regarding biological parameters, only those who showed significant differences between hospitalization groups were selected for integration.

Preoperative fibrinogen was markedly increased in patients with prolonged hospitalization (415.88 mg/dL), compared to those discharged rapidly (282.5 mg/dL), with a p-value of 0.0013, indicating a systemic inflammatory status influential on recovery.

Pre- and postoperative APTT was another relevant coagulation indicator, showing progressively increased values from the group with short to long hospitalization, with statistical significance ($p=0.0058$, respectively $p=0.025$).

The preoperative INR was also integrated into the score, being higher in the groups with medium and long hospitalization (1.59 and 1.37), compared to the short group (0.98), having a significant p ($p=0.032$).

Preoperative hemoglobin, considered an indirect indicator of physiological reserves and transfusion risk, was higher in patients discharged quickly (14.7 g/dL), and the differences were statistically significant ($p=0.0119$).

Regarding comorbidities, liver cirrhosis was the only one that was significantly correlated with the duration of hospitalization, being present exclusively in the group with prolonged hospitalization (11.5%, $p=0.0294$). Although other conditions such as

hypertension, diabetes or kidney failure were commonly encountered, they did not demonstrate statistical significance to be included in the final score.

Thus, the H.I.P.P.O. score was constructed by hierarchically integrating the following significant factors:

- The day of the intervention
- Type of prosthesis (bipolar vs total)
- Preoperative fibrinogen
- Pre and postoperative APTT
- Preoperative INR
- Preoperative hemoglobin
- Presence of liver cirrhosis

These parameters were logically organized in the structure of the H.I.P.P.O. score, where each step contributes to the stratification of the patient into a risk category regarding the estimated duration of hospitalization: short, medium or long.

This structuring allowed not only the precise anticipation of the duration of hospitalization, but also the substantiation of clinical decisions regarding the optimal moment of the intervention and the choice of the type of prosthesis according to the biological status and associated pathology of the patient.

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