Mortality Rates of Patients with Proximal Femoral Fracture in a Worldwide Pandemic

Preliminary Results of the Spanish HIP-COVID Observational Study

Josep Maria Muñoz Vives, MD, Montsant Jornet-Gibert, PhD, J. Cámara-Cabrera, MD, MSc, Pedro L. Esteban, MD, Laia Brunet, MD, Luis Delgado-Flores, MD, P. Camacho-Carrasco, MD, PhD, P. Torner, MD, PhD, Francesc Marcano-Fernández, MD, PhD, and Spanish HIP-COVID Investigation Group*

Background: The outbreak of coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), in December 2019 in Wuhan, People's Republic of China, has developed into an unprecedented pandemic with enormous pressure on health-care providers around the world. A higher mortality rate has been described in older infected individuals. Patients with hip fracture are a particularly vulnerable population during this pandemic because older age is associated with a higher mortality rate. Our aim was to describe the early mortality rate and demographic variables in a hip fracture sample population in Spain during the coronavirus pandemic.

Methods: This is a multicenter, observational, retrospective, descriptive study. We collected data from 13 major hospitals in Spain from the beginning of the national state of alarm (declared on March 14, 2020, by the Spanish government) until the end of our study period on April 4, 2020. All patients who were ≥65 years of age, presented to the Emergency Department of the participating hospitals during this period with a diagnosis of proximal femoral fracture, and had a minimum follow-up of 10 days were included in the cohort. In addition to mortality, demographic and other potential prognostic variables were also collected.

Results: In this study, 136 patients with a hip fracture were included. Of these patients, 124 underwent a surgical procedure and 12 were managed nonoperatively. The total mortality rate was 9.6%. Sixty-two patients were tested for COVID-19, with 23 patients being positive. The mortality rate for these 23 patients was 30.4% (7 of 23 patients) at a mean follow-up of 14 days. The mortality rate was 10.3% (4 of 39) for patients who had been tested and had a negative result and 2.7% (2 of 74) for patients who had not been tested. Of the 12 patients who were managed nonoperatively, 8 (67%) died, whereas, of the 124 patients who were surgically treated, 5 (4%) died. Results differed among centers.

Conclusions: There is a higher mortality rate in patients with a hip fracture and an associated positive test for COVID-19.

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

The outbreak of a new coronavirus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing coronavirus disease 2019 (COVID-19), began in December 2019 with the first case appearing in the city of Wuhan, Province of Hubei, People's Republic of China[1]. On March 11, 2020, the World Health Organization (WHO) declared the disease a pandemic. By then, there were >118,000 infected individuals in 113 countries and territories[2]. At the time of this writing, the number of infected individuals had increased to >1.2 million worldwide[3].

COVID-19 has quickly become a global threat to public health, jeopardizing the well-being of all people around the world, but especially those most vulnerable[4]. Spain is one of the countries worst hit by the pandemic, with >145,000 individuals infected and a mortality rate of 9.9% (>14,500 deaths)[5]. In addition, the state of pandemic has social and economic consequences that threaten to collapse the health-care system. The control of COVID-19 propagation has become the main goal of several countries and there has been an unprecedented worldwide effort to collaborate and disseminate rapid scientific evidence to counteract its effects[6].

The surgical management of patients with this pathology represents a challenge for the surgeon and the staff in the operating room. Therefore, different guidelines and recommendations

*A list of the Spanish HIP-COVID Investigation Group members is included as a note at the end of the article.

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have been published for patients with COVID-19 who require surgical treatment[7-9]. These guidelines vary because the information about the virus changes continuously and they are adapted to the demographic characteristics in each region.

Elderly patients with a proximal femoral fracture are a vulnerable group during this pandemic. Proximal femoral fractures have an incidence of 620 cases per 100,000 individuals per year[10] and are common in those with comorbidities[11]. They are associated with a 20% to 40% mortality rate during the first year[12] and a 30-day mortality rate of 7% to 8%[13,14]. Nonoperative management or a delayed surgical procedure is associated with higher mortality[14,15].

It is not known how mortality rates can be affected in this select group of patients during this pandemic, because the only evidence available is a report analyzing 10 patients with fracture and COVID-19[16]. Elderly patients with a hip fracture are also at a higher risk of death in case of contagion by COVID-19 because of their age[17,18].

The overcrowding of health-care centers due to the alarming increase of patients with respiratory symptoms has prompted the staff of the hospitals to make certain changes to cope with this situation. Entire hospital areas dedicated to other specialties have been closed and have been adapted to patients with COVID-19, operating rooms for elective cases have been transformed into intensive care units, and all non-emergency surgical procedures have been cancelled in most Spanish hospitals.

The strain put on hospitals' surgical capacity to operate on patients with fracture, together with the unknown mortality rate associated with patients with a hip fracture and COVID-19 infection symptoms, has increased the necessity to understand the prognostic factors of this population to develop recommendations and guidelines. The objective of this observational study was to describe the early mortality rate in patients ≥65 years of age with an acute proximal femoral fracture during the global state of pandemic in Spanish hospitals and to describe the associated risk factors associated with mortality.

Materials and Methods

Study Design and Participants

This is a multicenter, observational, descriptive, retrospective, population-based study including a total of 13 hospitals within the Spanish territory. Eleven hospitals were level III (high-complexity trauma cases) and 2 hospitals were level II (medium-complexity trauma cases).

Included participants were patients ≥65 years of age presenting to the Emergency Department of the participating hospitals with the clinical and radiographic diagnosis of a proximal femoral fracture (31-A and 31-B according to the OTA/AO classification[19]) from a low-energy mechanism from March 14, 2020 (on the day that the Spanish government declared a state of national alarm due to COVID-19 and the pandemic surpassed 2,000 patients and 50 deaths from COVID-19 in Spain) until April 4, 2020, with a minimum of 10 days of follow-up. Exclusion criteria were patients with femoral shaft fractures, open fractures, pathological fractures, periprosthetic or peri-implant fractures, or polytrauma.

The study strictly followed the ethical principles of biomedical research. The approval of the Ethics Committee of Fundació Unió Catalana d'Hospitals (Catalan Hospitals Union Foundation) was obtained and documented (CEI 20/31), and the Ethics Committee's approval of all of the participating hospitals was procured. The requirement for informed consent was waived by the Ethics Committee.

Data Collection

Demographic, clinical, laboratory, treatment, and outcome data were extracted from electronic medical records by the site investigators of each hospital with use of a customized data collection form. Data were submitted to the methods center where missing, inconsistent, or implausible data were queried. The reported laboratory parameters were those obtained when the patients presented to the Emergency Department of the treating hospital. The reported clinical status and physical examination measurements were those observed on initial presentation. Because of confinement, the follow-up after discharge was done by telephone rather than in person when necessary.

Variables

The primary outcome of this study was early mortality. Demographic variables were sex, age, residence (nursing home or family home), and living in a risk area (defined as a hospital catchment area with >100 COVID-19 cases per 100,000 inhabitants). The reported clinical variables included the type of fracture, American Society of Anesthesiologists (ASA) classification, alterations in chest radiographs, and cough on presentation. The laboratory variables included white blood cell count and creatinine levels on presentation. The diagnosis of COVID-19 was determined by a polymerase chain reaction (PCR) test from throat swab samples. The variables related to treatment included the type of surgical procedure performed (fracture fixation or hip replacement) or nonoperative treatment and surgical procedure delay in days since presentation to the Emergency Department.

We collected hospital data including trauma center level according to the Spanish National Health System and a COVID-19 high-occupancy score evaluating the number of patients with COVID-19 in each hospital to define the strain on hospital resources. The degree to which a hospital has been strained during this pandemic is difficult to quantify, especially because the infection rate has been unevenly distributed across time and territory. The pandemic state has been a dynamic process, and, thus, it has been difficult to compare hospitals at 1 specific time point. The virus has put pressure not only on hospitals' infrastructures, but also on their staff, both physically and psychologically. To compare this strain across participating hospitals, we designed a score based on 3 indicators: (1) occupancy including >50% patients with COVID-19 at any point during the observation period, (2) decrease in the hospital's capability to operate on fracture cases during the observation period (e.g., lack of operating rooms, equipment, or personnel), and (3) institutional changes in the hospital's infrastructure to accommodate COVID-19

cases (e.g., closing operating rooms or closing outpatient clinics).

Any affirmative answer added 1 point, for a minimum of 0 points (low COVID-19 occupancy) to a maximum of 3 points (high COVID-19 occupancy).

Statistical Analysis

Statistical analysis was performed following the principles specified in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Topic E9 (CPMP/ICH/363/96).

Continuous variables were presented as the mean and the standard deviation, and categorical variables were presented as the number and percentage. We used the Mann-Whitney U test, chi-square test, or Fisher exact test to compare differences between survivors and non-survivors where appropriate. Only variables with <20% missing data were reported in this study.

A 2-sided α of <0.05 was considered significant. Statistical analyses were performed using SPSS Statistics, version 25 (IBM).

Results

A total of 136 patients were included: 123 patients (90.4%) had survived and 13 patients (9.6%) had died during our study period. Table I shows a summary of the main demographic variables collected. Variables are described for the total number of included patients and separately for the number of patients who survived and those who had died. The mean age of the patients included was 85 years of age, with a minimum age of 65 years and a maximum age of 101 years. There were 106 patients who lived in their family home and 30 patients who came from a nursing home. Seventy-one patients came from a catchment area with a known incidence of COVID-19 of >100 per 100,000 people (considered a high-risk area).

Eighty-four fractures were intertrochanteric, and 52 fractures were femoral neck fractures. There were 124 patients who underwent a surgical procedure and 12 patients who did not, either because they died before they underwent an operation or because they were deemed too unstable to undergo surgical treatment. The group of patients who

TABLE I Demographic Variables

Variable	Total (N = 136)	Survivor (N = 123)	Non-Survivor (N = 13)	P Value*
Sex†				0.310
Female	102 (75%)	94 (76.4%)	8 (61.5%)	
Male	34 (25%)	29 (23.6%)	5 (38.5%)	
Age‡ *(yr)*	85.3 ± 7.6	85.2 ± 7.7	87.0 ± 7.2	0.407
Residence†				0.009
Nursing home	30 (22.1%)	23 (18.7%)	7 (53.8%)	
Family home	106 (77.9%)	100 (81.3%)	6 (46.2%)	
Living in area of risk†§				0.081
Yes	71 (52.2%)	61 (49.6%)	10 (76.9%)	
No	65 (47.8%)	62 (50.4%)	3 (23.1%)	
Type of fracture†				0.396
Femoral neck fracture	52 (38.2%)	48 (39%)	4 (30.8%)	
Trochanteric fracture	84 (61.8%)	75 (61%)	9 (69.2%)	
ASA classification#	117	106	11	0.011
I†	2 (1.7%)	2 (1.9%)	0 (0%)	
II†	13 (11.1%)	13 (12.3%)	0 (0%)	
III†	88 (75.2%)	81 (76.4%)	7 (63.6%)	
IV†	12 (10.3%)	10 (9.4%)	2 (18.2%)	
V†	2 (1.7%)	0 (0%)	2 (18.2%)	
Surgery delay‡ *(days)*	2.4 ± 2.2	2.4 ± 2.2	2.2 ± 2.3	0.844
Treatment†				<0.001
Surgical	124 (91.2%)	119 (96.7%)	5 (38.5%)	
Nonoperative	12 (8.8%)	4 (3.3%)	8 (61.5%)	
Follow-up‡** *(days)*	14.3 ± 3.9	15.0 ± 3.02	7.5 ± 5.0	<0.001

*The p values were calculated by the Mann-Whitney U test, chi-square test, or Fisher exact test, as appropriate. †The values are given as the number of patients, with the percentage in parentheses. ‡The values are given as the mean and the standard deviation. §A risk area was defined as a hospital catchment area with >100 COVID-19 cases per 100,000 inhabitants. #Some data were missing for this category, so the values are given as the number of patients with available data. **The follow-up was from the day of presentation until death or the end of the study period.

TABLE II Description of Hospitals

Hospital No.	Hospital Trauma Center Level*	COVID-19 Occupancy Score†	No. of Patients with Hip Fractures Treated‡	No. of COVID-19-Positive Cases	No. of Deaths	Hip Fracture Mortality Rate per Hospital
1	II	3	19 (14.0%)	1	3	15.8%
2	II	2	9 (6.6%)	1	3	33.3%
3	III	3	7 (5.1%)	1	0	0%
4	III	3	7 (5.1%)	0	0	0%
5	III	3	7 (5.1%)	0	1	14.3%
6	III	3	4 (2.9%)	0	0	0%
7	III	3	5 (3.7%)	1	0	0%
8	III	3	13 (9.6%)	5	1	7.7%
9	III	3	8 (5.9%)	2	1	12.5%
10	III	3	18 (13.2%)	10	4	22.2%
11	III	1	22 (16.2%)	0	0	0%
12	III	3	7 (5.1%)	2	0	0%
13	III	3	10 (7.4%)	0	0	0%
Total			136	23	13	9.6%

*This is the level of complexity according to the Spanish National Health System: III indicated high complexity, II indicated medium complexity, and I indicated low complexity. †This is the measure of strain placed on a hospital's infrastructure because of the COVID-19 pandemic. ‡The values are given as the number of patients, with the percentage in parentheses.

were treated surgically had lower ASA scores. Only 8.1% of the patients who underwent a surgical procedure had ASA scores ≥4, whereas 50.0% of the patients managed nonoperatively had ASA scores of ≥4, showing a positive association between ASA score and the type of treatment selected (Fisher exact test, p = 0.002). The mean delay from

TABLE III Clinical Parameters on Presentation

Variable	Total	Survivor	Non-Survivor	P Value*	Mortality Rate per Variable
COVID-19 testing†	136	123	13	0.001	
Positive	23 (16.9%)	16 (13%)	7 (53.8%)		30.4%
Negative	39 (28.7%)	35 (28.5%)	4 (30.8%)		10.3%
Not tested	74 (54.4%)	72 (58.5%)	2 (15.4%)		2.7%
Cough on presentation†‡	123	113	10	0.008	
Yes	15 (12.2%)	11 (9.7%)	4 (40%)		26.7%
No	108 (87.8%)	102 (90.3%)	6 (60%)		5.6%
Lobar consolidation on chest radiograph†‡	135	122	13	0.016	
Yes	18 (13.3%)	13 (10.7%)	5 (38.5%)		27.8%
No	117 (86.7%)	109 (89.3%)	8 (61.5%)		6.8%
White blood cell count in 1 μL of blood					
No. of patients†	135	122	13		
Mean and standard deviation *(μL)*	2,713 ± 3,485	2,755 ± 3,591	2,314 ± 2,323	0.666	
Serum creatinine levels in blood					
No. of patients†	114	104	10		
Mean and standard deviation *(mg/dL)*	1.19 ± 0.73	1.19 ± 0.75	1.26 ± 0.57	0.794	

*The p values were calculated by the Mann-Whitney U test, chi-square test, or Fisher exact test, as appropriate. †The values are given as the number of patients, with or without the percentage in parentheses. ‡Data were missing for some patients.

TABLE IV Demographic and Clinical Data for Patients Who Tested Positive for COVID-19 and Died*

Variables	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Sex	Male	Male	Female	Male	Female	Female	Female
Age *(yr)*	89	93	85	100	89	95	88
Residence	Nursing home	Family home	Nursing home	Nursing home	Nursing home	Family home	Nursing home
Living in area of risk†	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Contact with COVID-19, confirmed positive, or suspected	Yes	No	Yes	Maybe	Yes	No	Maybe
Fracture type	Intertrochanteric	Intertrochanteric	Intertrochanteric	Intertrochanteric	Intertrochanteric	Intertrochanteric	Femoral neck
Dementia	No	No	No	Yes	Yes	No	Yes
Cough on presentation	No	Yes	No	Yes	No	Yes	No
Temperature on presentation *(°C)*	35.8	36.3	35.8	38.9	35.8	36.2	38.3
Oxygen saturation on presentation‡	95	99	95	88	96	97	93
Chest radiograph on presentation	Normal	Lobar consolidation	Normal	Lobar consolidation	Normal	Lobar consolidation	Normal
Confusion	No	No	Yes	Yes	No	No	No
Urea level in blood *(mg/dL)*	>45	<45	>45	NA	>45	<45	>45
Respiratory rate *(breaths per minute)*	<30	<30	NA	>30	<30	<30	<30
Blood pressure *(mm Hg)*	Systolic >90 and diastolic >60	Systolic >90 and diastolic >60	Systolic >90 and diastolic >60	Systolic <90 or diastolic <60	Systolic >90 and diastolic >60	Systolic >90 and diastolic >60	Systolic >90 and diastolic >60
CURB-65 score§	2	1	NA	NA	2	1	2
White blood cell count *(per μL)*	1,600	650	2,480	1,200	900	900	900
Creatinine serum level *(mg/dL)*	1.6	NA	1.09	1.43	1.32	0.63	0.90
Charlson Comorbidity Index score	7	5	9	6	10	4	5
ASA class	III	NA	IV	V	III	III	III
Time from presentation to COVID-19 confirmation *(days)*	6	3	3	1	1	1	On presentation
Time from presentation to death *(days)*	15	18	18	12	19	20	9
Time from presentation to surgery *(days)*	2	6	—	—	—	—	—
Treatment	Surgical (nail)	Surgical (nail)	Nonoperative	Nonoperative	Nonoperative	Nonoperative	Nonoperative
Comments	Pneumonia symptoms and COVID-19 diagnosis after surgery	Underwent surgery with diagnosis of pneumonia COVID-19	Patient unfit to undergo surgery	Patient unfit to undergo surgery	Patient unfit to undergo surgery	Patient unfit to undergo surgery	Patient unfit to undergo surgery

*NA = not available. †A risk area is defined as a hospital catchment area with >100 COVID-19 cases per 100,000 inhabitants. ‡This was tested with the patient breathing room air containing 21% oxygen. §This is the CURB-65 score for the severity of pneumonia, which takes into account the state of confusion (C), urea level in blood (U), respiratory rate (R), blood pressure (B), and age of ≥65 years as risk factors.

presentation to the surgical procedure was 2.4 days, with a minimum delay of 0 days and a maximum delay of 13 days.

Participating hospitals were mainly level III. A high COVID-19 occupancy score was reported in 11 centers. Table II shows the main characteristics of the participating hospitals including the number of hip fractures treated, the number of patients with hip fracture who tested positive for COVID-19, the number of deaths per hospital, and mortality rates. The number of patients included by each hospital ranged between 4 and 22 patients.

Table III shows clinical parameters on the presentation date to the Emergency Department except for the COVID-19 PCR test, which was not necessarily done on arrival. Variables are reported for the total number of included patients and also separately for the patients who survived and those who died. Twenty-three patients had a positive test result (COVID-19 PCR test), 39 patients had a negative test, and 74 patients were not tested because of low suspicion of infection. The presence of a cough was reported in 15 cases on presentation and lobar consolidation on initial chest radiographs (showing either unilateral or bilateral infiltrates) was observed in 18 cases. The mean white blood cell count was 2,713/μL, and the mean serum creatinine level was 1.19 mg/dL.

Of the 13 patients with hip fracture who died, 7 had tested positive for COVID-19. Details are shown in Table IV. Only 2 of the patients underwent surgical treatment; from presentation to surgical procedure, 1 patient waited 2 days and 1 patient waited 6 days.

Discussion

Our primary objective was to define the mortality rate of patients with hip fracture in Spain during the worldwide COVID-19 pandemic. The observed mortality rate at a mean follow-up of 14 days was higher than the 30-day mortality rate reported by the Spanish Registro Nacional de Fracturas de Cadera (National Hip Fracture Registry)[13] and other national registries in Europe[14]. Our cohort data were similar to the data reported by the Spanish National Hip Fracture Registry in terms of sex ratio, mean age, place of residence, type of fracture, ASA classification, surgical procedure delay, and surgical treatment[13].

During this study period, there was no consensus among hospitals on whom to test for COVID-19. Because of the sudden impact of the pandemic in Spain, there was an initial lack of tests for COVID-19 and protocols for testing patients differed among hospitals. In general, patients who presented in the Emergency Department with any respiratory symptoms (cough, fever, shortness of breath) were tested. However, patients who presented for any other cause and did not show symptoms on presentation were not systematically tested. From our data, for this 14-day follow-up period, the mortality rate was 30.4% for patients who tested positive for COVID-19 and 10.3% for patients who tested negative for COVID-19. Patients who were not tested had a mortality rate of 2.7%, similar to the mortality rates described during the same season in the previous year[13].

We observed that the hospitals with more COVID-19-positive cases also had higher mortality rates. The mortality rate for patients living in their family homes was significantly lower at 5.7% than that for patients living in nursing homes at 23.3%; nursing homes have been breeding grounds for the virus.

With regard to the clinical variables collected in the Emergency Department, both the presence of cough and a chest radiograph with lobar consolidation were associated with a higher mortality rate. The white blood cell count was similar in patients who survived and in those who died.

Twelve patients were managed nonoperatively; of these, 8 (67%) died. This rate is higher than previously reported mortality rates for patients treated nonoperatively[15]. The main reason for not treating patients surgically was that they were deemed unfit for a surgical procedure, as their higher ASA score suggests.

In contrast, of the 124 patients treated surgically, 5 (4.0%) died. Two patients tested positive for COVID-19, and 1 patient did not show signs of pneumonia before the surgical procedure and was diagnosed with COVID-19 at 4 days after the operation.

Our study had some limitations. First, because of the retrospective design, the measurement of laboratory parameters that have shown to be important prognostic factors in patients with COVID-19 (e.g., lactate dehydrogenase [LDH], ferritin levels, and D-dimer)[18] was uneven because hospitals implemented different protocols during this period. Only variables with a completeness of >80% were included in this study. Second, the short follow-up period may have led to an underestimation of the mortality rate for these patients. Finally, the interpretation of our findings may have been limited by the sample size.

Further research should be directed toward studying prognostic factors to understand the effect of a surgical procedure and its timing in the pro-inflammatory cascade (of importance in the clinical evolution of COVID-19 pneumonia) on the mortality rate.

To our knowledge, this is the first study describing mortality rates in patients with a proximal femoral fracture. According to these results, it seems that patients with COVID-19 infection, despite their higher mortality rates, could benefit from an early surgical procedure and, therefore, they should continue to undergo surgical treatment if they are clinically fit.

Whenever possible, treatment should be expedited as previously described in the orthopaedic literature[20]. Policies should be directed into restructuring hospitals to accommodate this vulnerable population even in the case of high COVID-19 hospital occupancy. ■

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García-Sánchez from the Hospital Universitario Vall d'Hebron–Barcelona; José María Pérez Sánchez, Miguel Ángel Giráldez-Sánchez, Pedro Cano Luís, Lourdes López Muñoz, Miguel Ángel González López, and Elena Pérez from the Hospital Universitario Virgen del Rocío–Sevilla; Pablo Castillón, Francesc Anglés, Jordi Salvador, Silvia Minguela, and Judith López Catena from the Hospital Universitario Mútua de Terrassa; Diana Noriego Muñoz, Mónica Galipienso Eri, and Jesús David García Montesinos from the Hospital Universitari Dr. Josep Trueta–Girona; M. Videla, Eudald Romero-Pijoan, Manel Lafuente Salinas, Ana Maria Lopez Louzao, and Joan Vilanova Laguna from the Hospital Sant Joan Despí Moisès Broggi; J. García-Coiradas, J.A. Valle-Cruz, and F. Marco from the Hospital Clínico San Carlos–Madrid; Santos Martínez Díaz, Fernando Marqués López, and María José Robles Raya from the Parc de Salut Mar–Barcelona; Santiago Gallardo, Raul Franco-Gómez, Raquel Samaniego Alonso, and Daniel Berlanga De Mingo from the Hospital Asepeyo–Sant Cugat; Enrique Guerado, Juan Ramón Cano Porras, Encarnación Cruz Ocaña, Alicia Ramírez Roldán, and Patricia Martinez Cuesta from the Hospital Costa del Sol–Málaga; and Alfredo Rodriguez and Javier García-Alba from the Hospital Sant Joan–Reus.

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Josep Maria Muñoz Vives, MD[1]
Montsant Jornet-Gibert, PhD[2]
J. Cámara-Cabrera, MD, MSc[3]
Pedro L. Esteban, MD[1]
Laia Brunet, MD[1]
Luis Delgado-Flores, MD[1]
P. Camacho-Carrasco, MD, PhD[2]
P. Torner, MD, PhD[2]
Francesc Marcano-Fernández, MD, PhD[3]

[1]Orthopaedic Department, Althaia, Xarxa Assistencial Universitària de Manresa, Manresa, Spain

[2]Orthopaedic Department, Hospital Clinic, Barcelona, Spain

[3]Orthopaedic Department, Parc Taulí Hospital Universitari, Universitat Autònoma de Barcelona, Sabadell, Spain

Email address for F. Marcano-Fernández: francescmarcano@gmail.com

ORCID iD for J.M. Muñoz Vives: 0000-0001-6239-180X
ORCID iD for M. Jornet-Gibert: 0000-0001-8915-2104
ORCID iD for J. Cámara-Cabrera: 0000-0002-8822-9082
ORCID iD for P.L. Esteban: 0000-0003-0575-3995
ORCID iD for L. Brunet: 0000-0003-3894-6996
ORCID iD for L. Delgado-Flores: 0000-0002-9191-1023
ORCID iD for P. Camacho-Carrasco: 0000-0003-4693-440X
ORCID iD for P. Torner: 0000-0002-0168-4091
ORCID iD for F. Marcano-Fernández: 0000-0001-5690-631X

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