European Review for Medical and Pharmacological Sciences 2022; 26: 84-91

Megaprosthesis in articular fractures of the lower limbs in fragile patients: a proposal for the therapeutic algorithm

R. VITIELLO[1,2], A. SMIMMO[1,2,3], A. DE FAZIO[1,2], M.B. BOCCHI[1,2], M.S. OLIVA[1,2], A. PERNA[1,2], G. MACCAURO[1,2], A. ZIRANU[1,2]

[1]Fondazione Policlinico Universitario A. Gemelli IRCSS, Rome, Italy
[2]Università Cattolica Del Sacro Cuore, Rome, Italy
[3]Mater Olbia Hospital, Università Cattolica del Sacro Cuore, Rome, Italy

Abstract. – OBJECTIVE: The use of megaprosthetic implants could provide substantial advantages in elderly population affected by complex fractures. The aim of the study was to identify the patients suitable to megaprosthetic implants in the treatment of lower limbs fractures, as well as periprosthetic fractures.

PATIENTS AND METHODS: From January 1st, 2015, to December 31st, 2021, all patients affected by femoral fractures with severe bone loss or previous surgery failure were retrospectively reviewed. ADL, IADL, SF-12 values pre- and post-operative were recorded. Hemoglobin value, NLR, PLR were recorded pre- and peri-operatively for all patients. Complications were recorded. All patients underwent a radiological follow-up. Significance was set at $p \leq 0.05$.

RESULTS: 23 patients were considered eligible, 10 males and 13 females; the mean age was 72.87 years old (± 12.33), while the mean BMI was 27.2 points (± 5.2). The mean follow-up was 2 years (± 1.4). The mean preoperative ADL and IADL scores were correlated with a positive independence of the patient, while the mean postoperative scores corresponded to a moderate-low independence. Also the mean Mental and Physical SF12 scores saw a decrease in values. NLR values were higher in the first group of patients with complications.

CONCLUSIONS: A careful multiparametric and multidisciplinary patient selection is required to identify the suitable patient to this treatment.

Key Words:
Megaprosthesis, Elderly, Fracture, Distal femoral replacement, Proximal femur replacement.

Abbreviations

Activity Daily Living: ADL; Instrumental Activity Daily Living: IADL; Open reduction and internal fixation: ORIF; Charlson Comorbidity Index: CCI; Short Form-12: SF-12; Platelet/lymphocyte ratio: PLR; Neutrophil/Lymphocyte ratio: NLR.

Introduction

The management of lower limb fractures can be challenging for orthopaedic surgeons. Due to the aging of the population, the number of lower limb fractures has been increasing worldwide. Moreover, the increase in the number of femur fractures represents a major public health concern since they are a main cause of decline in activities of daily living (ADL), disability, dependency and subsequent poor prognosis.

Distal femur fractures represent about 7% of all femur fractures in adults and often involve osteoporotic bone, thus further complicating the management and the surgery indications[1,2]. Incidence of this kind of fractures significantly increases in both genders in the over 60 years-old population, with a large female predominance[1]. Proximal femur fracture is one of the most common types of fracture in the elderly, occurring in 18% of women and in 6% of men worldwide[3].

The incidence of proximal femur fracture has raised worldwide in the last two decades along with the increase in the average age of the population. In fact, the global number of hip fractures is expected to increase from 1.26 million in 1990 to 4.5 million by the year 2050. Implant failure is a rare but catastrophic event extent that salvage procedures are invariably challenging and expose the patients to further complicated treatments. The encouraging outcomes of Proximal Femoral Replacement have broadened the indications to the treatment of severe bone loss also in non-oncological conditions[4].

Corresponding Author: Alessandro Smimmo, MD; e-mail: alessandro.smimmo@gmail.com

The management of the above-mentioned fractures largely depends on fracture type and patient characteristics[5-7]. Open reduction and internal fixation (ORIF) are theoretically the mainstay of surgical treatment. However, when it comes to elderly patients' factors related to the surgical technique itself, such as complexity and intraoperative timing, or even to the patients, such as bone quality, comorbidities and compliance, it shall be taken into account[8].

Studies[5] have agreed that an osteoporotic bone proximal to the fracture is unable to tolerate the forces of a rigid fixation construct. Furthermore, complex intraarticular fractures and periprosthetic fractures are difficult to manage both for the comminution close to the joint and for the poor postoperative compliance of these patients due to the cognitive decline and to the muscle weakness[9-14].

Frequently, the postoperative management of these fragile patients is complicated, requiring increasingly a period out of bearing, with a major risk of complications related to the lack of mobilization. Tumor megaprostheses are well known and much used for limb salvage in patients affected by primary or secondary bone or soft tissue tumours[15,16].

However, they have been recently proposed in traumatology for the management of comminute articular fractures and periprosthetic fractures of the knee and the hip as an alternative to ORIF[8,17]. Megaprostheses can probably find their better use in traumatology in the treatment of the fragile population; they can ensure indeed immediate weight bearing and fast recovery reducing the hospital stay, thus allowing a faster return to the normal activities daily living[18-20].

The aim of the present study was to evaluate the effectiveness of megaprosthetic implants in the treatment of lower limbs fractures, as well as periprosthetic fractures in the frail population.

We enrolled elderly patients undergone megaprosthetic implants surgery in our center in order to evaluate the prognostic factors that affect the clinical outcomes of these patients. Our aim was also to elaborate a diagnostic and therapeutic algorithm to adopt in these increasingly frequent and controversial cases.

Patients and Methods

All the patients admitted to the Orthopedic Department of the 'Fondazione Policlinico Universitario A. Gemelli IRCSS' from January 1st, 2015, to December 31st, 2021, affected by femoral fractures with severe bone loss or previous surgery failure, were retrospectively reviewed. A retrospective observational study according to the PROCESS guidelines was conducted on patients[21].

All the procedures performed were in accordance with the 1964 Helsinki declaration and its later amendments. Informed consent was collected from all the recruited patients. Inclusion criteria were: hip or knee periprosthetic fractures, previous arthroplasty infection (second stage of a two stage strategy), implant failure due to hardware breakage, proximal or distal articular femoral fracture with severe bone loss, aseptic nonunion. Exclusion criteria were: oncological patients, active bone infections, follow-up less than 1-year. Age was not considered as an exclusion criterion.

All patients underwent either hip or knee megaprosthesis according to the diagnosis. All the procedures were performed by two orthopedic surgeons fellowship-trained in traumatology and oncological surgery.

A general anesthesia was performed in all cases. All patients received Cephazolin 2 g i.v. as antibiotic prophylaxis before surgery, if not contraindicated[22]. A bladder catheter was placed in all the patients and removed within 72 hours after the surgery.

Patients who underwent proximal femoral replacement with hip megaprothesis were placed in lateral decubitus position. A lateral approach was used. Once exposed the bone, an end bloc resection was performed and a cementless silver coated megaprosthesis was implanted, according to the manufacturer technique[23]. The myodesis through the Trevira Tube© completed the surgery (Implantcast, GmbH, Buxtehude, Germany). One intra-articular closed-suction drainage was placed and then removed 48 hours after surgery.

Patients who underwent distal femur replacement with knee megaprothesis were instead placed supine. An anteromedial parapatellar approach was used in each case. After bone exposure, a block resection was performed, and a silver coated megaprosthesis was implanted, according to the manufacturer technique. Tibial components were cemented (Figure 1). One deep intra-articular suction drainage was placed and removed 48 hours after surgery.

Those enrolled in the study followed the same post-operative rehabilitation protocol: after 24 hours from the surgery, all the patients were seated with their feet out of the bed, whereas at 48

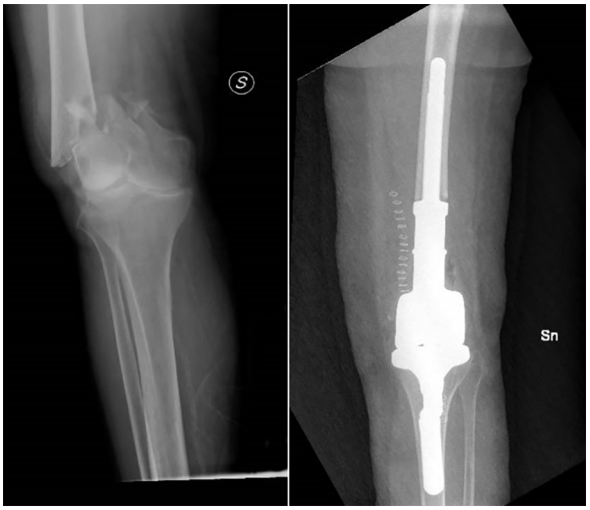

Figure 1. Ideal characteristic of the patient with complex fractures of the lower limbs eligible for Megaprosthesis.

hours were allowed to gradually weight bearing with the aid of a walker frame.

Patients were regularly followed-up at 2 and 4 weeks after surgery and then every 3 months for the first two years, then yearly. A control X-ray was performed at each clinical evaluation from the fourth week from surgery onwards.

Anthropometric and anamnestic data (e.g., smoking, etc.), routine blood exams results, and the length of stay were collected for each patient. Through the anamnestic data, the Charlson Comorbidity Index (CCI) and Clinical Frailty Scale were calculated[24,25].

A self-assessed questionnaire about the pre-fracture status was administered to all the patients upon hospital admission and at the last outpatient follow-up. ADL was the primary outcome, while the following were considered as secondary outcomes: Instrumental Activity Daily Living (IADL), Short Form-12 (SF-12)[26,27]. ADL is a 6 points scale that evaluate the essential activities for personal independence, while IADL is an 8-points scale that take into account the ability of the individual to interact with the society. SF-12 is a generic scale that assess the physical and mental status of the patients.

During hospitalization and the various outpatient appointments, all the complications were recorded (wound dehiscence, deep infection, pneumonia and urinary tract infection). Wound dehiscence or surgical site infection was defined as a delayed healing of the surgical wound with the presence of redness, edema and secretions in absence of deep tissue involvement[28].

Hemoglobin, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, creatinine and albumin values were recorded pre- and peri-operatively for all patients. Fractures were diagnosed through a standard X-rays series in each case. A computer tomography (CT) was always performed in case of articular fractures. Periprosthetic fractures were classified according to the Vancouver classification whereas articular fractures were described according to the AO classification.

Dislocation, mobilization, presence of radiolucency and aseptic loosening according to the Harris classification for the hip or the Anderson Orthopedic Research Institute (AORI) Classification for the knee were investigated postoperatively through X-rays evaluations[29,30].

GraphPad QuickCalcs (GraphPad Software, San Diego, CA, USA) was used for the data analysis. The data were reported as mean and standard deviation (± SD).

Statistical Analysis

A paired *t*-test was performed to compare the pre- and post-operative values of ADL, IADL and SF-12 score of each group. An un-paired *t*-test was used to compare anthropometric and anamnestic data, CCI, ADL, IADL, SF-12 score between groups. Significance was set for $p \leq 0.05$.

Results

Twenty-three patients were considered eligible. One patient was lost during the second year of follow-up. The primary outcome analyzed was the clinical outcome after the recovery of ADL and IADL scores. The secondary outcome was the incidence of complications.

There were 10 male and 13 females, the mean age was 72.87 years old (± 12.33); the mean BMI was 27.2 points (± 5.2). The mean follow-up was 2 years (± 1.4). Blood exams (such as preoperative and postoperative Hemoglobin, preoperative Albumin and Creatinine, preoperative Lymphocyte and Neutrophil counts, NLR and PLR), along with the length of stay, were also reported as a mean in Table I. The mean preoperative PLR (Platelet/lymphocyte ratio) and NLR (Neutrophil/Lymphocyte ratio) values correspond to a state of moderate systemic inflammation.

Almost all patients included in the study have undergone megaprosthesis implant surgery fol-

Table I. Patients clinical characteristics.

Mean Age (Years)	72.87 (± 12.33)
Mean Bmi (Kg/m^2)	27.19 (± 5.20)
Mean Hospitalization (Days)	11.61 (± 7.16)
Mean Follow-Up (Years)	2 (± 1.38)
Mean Preoperative Hemoglobin (Mg/Dl)	12.02 (± 2.13)
Mean Postoperative Hemoglobin (Mg/Dl)	9.68 (± 2.02)
Mean Preoperative Creatinine (Mg/Dl)	0.80 (± 0.26)
Mean Preoperative Albumin (G/L)	31.13 (± 10.34)
Mean Preoperative Neutrophil (×10^9/L)	6.34 (± 2.62)
Mean Preoperative Lymphocytes (×10^9/L)	1.28 (± 0.42)
NLR	6.58 (± 5.64)
PLR	227.60 (± 107.98)

BMI: Body Mass Index; NLR: Neutrophil-Lymphocyte Ratio; PLR: Platelet-Lymphocyte Ratio.

lowing periprosthetic fractures. 11 proximal femurs and 12 distal femurs were ultimately surgically implanted.

The mean Charlson Comorbidity Index was 4.3 points (± 1.7), which corresponds to a 53% survival rate at 10-year follow-up. The mean preoperative ADL and IADL scores, reported in Table II, correlate with a positive independence of the patient (so much so that he/she is able to manage his/her own needs), while the mean postoperative scores correspond to a moderate-low independence. The mean Mental and Physical SF12 scores have also seen a decrease in values. The mean results of preoperative and postoperative clinical and functional scores are reported in Table II.

A total of 6 patients who underwent megaprosthesis implantation had complications: wound dehiscence occurred in 5 patients, while only one had a periprosthetic joint infection. We therefore divided our population into two groups based on the occurrence or not of any complications after surgery. Examining the results collected, we noticed that the preoperative NLR values were higher in the first group of patients with complications (Group A). The mean NLR value in this group was 12.0 (± 7.27) in contrast with the second group (Group B) with a NLR value of 4.6 (± 3.53) (p=0.01). Despite that Group A also showed a clear decrease of the ADL score in the postoperative period compared to Group B (p=0.03), when compared with itself (paired value) in the pre- and post-operative period there were no differences. However, these results remain questionable because of the small sample size. Group B patients, in contrast, when compared with themselves, in the pre- and post-operative period showed a statistically significant decrease in SF12M (p=0.03) and IADL scores (0.04). We assessed our patients with the Clinical Frailty Scale in the preoperative period which, however, was not found to be a predictor of postoperative complications. Finally, we divided the population into those who had a worsening of the ADL score in the postoperative period (Group C) and those who kept this score stable (Group D). We noticed that Group C patients showed an MSF-12 (47.57±12.31) lower score in the pre-operative period compared to those in Group D (58.14±4.66) (p=0.05). In addition, Group C patients showed a worsening of both MSF-12 (34.6±9.2) and FSF-12 (34.4±9.9) scores in the post-operative period, compared with Group D (47.9±15.9 and 44±10.7, respectively p=0.01, p=0.02).

Table II. Patients clinical and functional outcomes.

Mean CFS	4.58 (± 0.77)
Mean CCI	4.30 (± 1.72)
Mean ADL:	
- Preoperative	5.42 (± 1.12)
- Postoperative	4.90 (± 1.58)
Mean IADL:	
- Preoperative	7.05 (± 1.35)
- Postoperative	5.24 (± 2.36)
Mean Mental SF-12:	
- Preoperative	53.85 (± 10.59)
- Postoperative	45.13 (± 15.05)
Mean Physical SF-12:	
- Pre-operative	42.49 (± 14.40)
- Post-operative	38.91 (± 10.82)

CFS: Clinical Frailty Scale; CCI: Charlson Comorbidity Index; ADL: Activities of daily living; IADL: Instrumental Activities of daily living; SF-12: Short Form health survey.

Discussion

In view of the increasing ageing of the society, the number of complex lower limbs fractures has been increasing all over the world. Orthopedic

surgeons should become more and more confident treating these fractures which are typical of the frail population, in order to be able to choose the most suitable surgical solution.

The main finding of the present study is that megaprostheses are a viable and safe option to treat non-oncological complex hip or knee primary or periprosthetic fractures in elderly patients. Our present results shows that megaprostheses can restore the pre-fracture functional status without worsening the general health situation with low rate of complications in a frail population.

Nevertheless, the current literature is still lacking on the use of megaprostheses in the fractures management and there are still no therapeutic algorithms neither specific guidelines on this matter[31,32]. Up to now, non-oncological megaprostheses have been mainly performed in elder and low-demand patients affected by articular distal femur fractures with severe bone loss, such as type 33.C1-2-3, according to the AO classification[31].

Several studies[31,33] have been published on the topic; however, their quality is mainly undermined by the small samples size and the wide heterogeneity of the populations, making difficult the outcomes comparisons across the literature.

Studies[34] comparing different treatment options for Vancouver type B3 fractures demonstrate a clear advantage of megaprosthesis in terms of both gained function and low postoperative complications rate. That is especially the advantageous postoperative management of these fragile patients. Joint replacement immediately allows indeed full weight bearing the day after surgery, thus encouraging an early mobilization crucial when it comes to advanced age[31]. On the opposite, ORIF techniques would require a longer intraoperative time and a slower postoperative approach[35]. Nevertheless, invasiveness and costs of prosthetic implants cannot be denied either.

There are two important points about the megaprotheses implant surgical technique that must be highlighted. Firstly, megaprostheses require the resection of various muscles tendon insertions with the subsequent loss of muscle strength. To overcome this, we used the Trevira Tube© (Implantcast, GmbH, Buxtehude, Germany) that seemed to improve the functional result by ensuring soft tissue adhesion to the prostheses, thus increasing the stability and the strength of the construct[15,36,37]. Secondly, all the megaprotheses implanted were silver-coated, thus the risk of infection has been proven to be reduced[38]; Donati et al[15], in their experience on oncological patients, reported that only 8% of the patients treated with silver-coated implants developed deep infections. Subsequent studies[16,39] confirmed that the use of silver-coated implants guarantees a decreased risk of infections compared to non-silver-coated implants.

Based on our results, we have tried to identify the patients suitable to this specific treatment (Figure 2). Firstly, according to our data, all the patients seemed to be fragile with low CFR and pre-operative ADL and IADL values.

In addition, a high pre-operative NLR value has been found to be a predictive factor of complications extent that in our opinion should be routinely evaluated before proceeding to surgery. We consider the mental health status another crucial aspect that can influence the therapeutic success; the SF12M evaluation may, in fact, give important information about the patient reaction to these invasive procedures. Due to the complexity of these frail geriatric patients, a multiparametric approach should be necessary to identify the suitable patient for this invasive but efficient treatment.

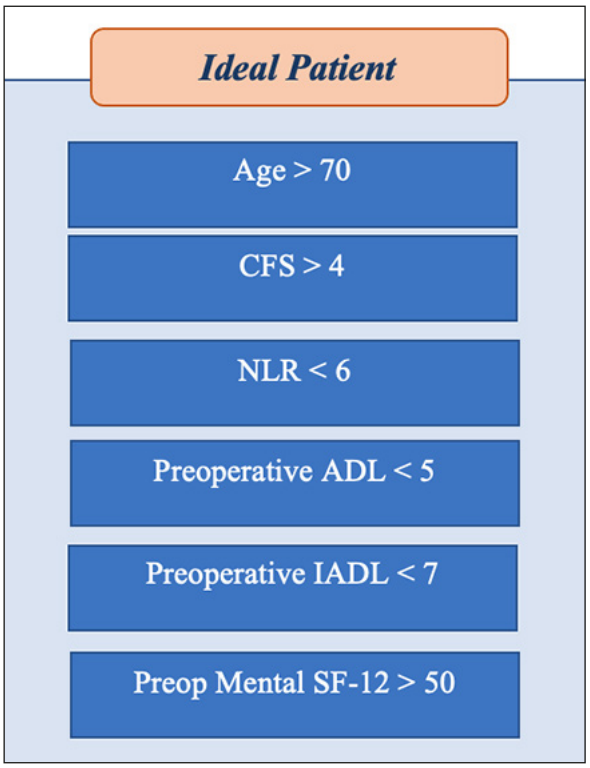

Figure 2. Ideal characteristic of the patient with complex fractures of the lower limbs eligible for Megaprosthesis.

Limitations

The present study has some limitations. First, it includes a very small sample size and a relative heterogeneous population. It must be considered that acute trauma with severe bone loss and poor bone quality, post-traumatic failures, aseptic nonunion, as well as periprosthetic fractures with component mobilization and poor bone stock, are not common conditions[18]. Moreover, no guidelines or therapeutic algorithms exist on this topic. Therefore, the results of the present study are of utmost importance, because they are supposed to encourage surgeons in considering both fracture and patient characteristics in order to tailor the surgical decision-making process on patient's needs.

Conclusions

The use of hip and knee megaprosthetic implants in traumatology is a safe and viable option in elderly patients. A careful patient selection through multiparametric and multidisciplinary approach is required to identify the suitable patient to this treatment.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of Orthopedic and Traumatology Institute.

Funding

Publication costs have been funded by the Orthopedic and Traumatology School of University "Cattolica del Sacro Cuore", Rome. The funders did not play any role in the design of the study, the collection, analysis, and interpretation of data, or in writing of the manuscript.

Authors' Contribution

All the authors approved the submitted version (and version substantially edited by journal staff that involves the author's contribution to the study) and agree to be personally accountable for the author's own contributions and for ensuring that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and documented in the literature. Conceptualization and Methodology: R.V.; Validation: G.M. and A.Z.; Formal Analysis: R.V. and A.P.; Investigation: A. d. F.; Writing – Original Draft Preparation: A.S. and M.S.O.; Writing – Review and Editing: M.B.B.; Supervision: G. M., A.Z.

ORCID ID

R. Vitiello: 0000-0003-2321-9665; A. Smimmo: 0000-0002-9390-0539; A. De Fazio: 0000-0001-8321-532X; M. B. Bocchi: 0000-0002-0363-4514; A. Ziranu: 0000-0002-6789-7495; G. Maccauro: 0000-0002-7359-268X.

Data Availability Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1) Batista BB, Salim R, Paccola CA, Kfuri Junior M. Internal Fixators: A Safe Option for Managing Distal Femur Fractures? Acta Ortop Bras 2014; 22: 159-162.
2) Gwathmey FW, Jones-Quaidoo SM, Kahler D, Hurwitz S, Cui Q. Distal Femoral Fractures: Current Concepts. J Am Acad Orthop Surg 2010; 18: 597-607.
3) Veronese N, Maggi S. Epidemiology and Social Costs of Hip Fracture. Injury 2018; 49: 1458-1460.
4) Mancino F, Di Matteo V, Mocini F, Cacciola G, Malerba G, Perisano C, De Martino I. Survivorship and Clinical Outcomes of Proximal Femoral Replacement in Non-Neoplastic Primary and Revision Total Hip Arthroplasty: A Systematic Review. BMC Musculoskelet. Disord 2021; 22: 933.
5) Rice OM, Springer BD, Karunakar MA. Acute Distal Femoral Replacement for Fractures About the Knee in the Elderly Orthop Clin North Am 2020; 51: 27-36.
6) Cauteruccio M, Vitiello R, Perisano C, Covino M, Sircana G, Piccirillo N, Pesare E, Ziranu A, Maccauro G. Euthyroid Sick Syndrome in Hip Fractures: Evaluation of Postoperative Anemia. Injury 2020; 51 Suppl 3: 9-12
7) Vitiello R, Perisano C, Covino M, Perna A, Bianchi A, Oliva MS, Greco T, Sirgiovanni M, Maccauro G. Euthyroid Sick Syndrome in Hip Fractures: Valuation of Vitamin D and Parathyroid Hormone Axis. Injury 2020; 51 Suppl 3: 13-16.
8) Vitiello R, Ziranu A, Oliva MS, Meluzio MC, Cauteruccio M, Maccauro G, Liuzza F, Saccomanno MF. The Value of Megaprostheses in Non-Oncological Fractures in Elderly Patients: A Short-Term Results. A short-term result. Injury 2022; 53: 1241-1246.
9) Hake ME, Davis ME, Perdue AM, Goulet JA. Modern Implant Options for the Treatment of Distal Femur Fractures. J Am Acad Orthop Surg 2019; 27: 867-875.

10) Conserva V, Vicenti G, Allegretti G, Filipponi M, Monno A, Picca G Moretti B. Retrospective Review of Tibial Plateau Fractures Treated by Two Methods without Staging. Injury 2015; 46: 1951-1956.

11) Atrey A, Hussain N, Gosling O, Giannoudis P, Shepherd A, Young S, Waite J. A 3 Year Minimum Follow up of Endoprosthetic Replacement for Distal Femoral Fractures - An Alternative Treatment Option. J Orthop 2017; 14: 216-222.

12) Farmer RP, Herbert B, Cuellar DO Hao J, Stahel PF, Yasui R, Hak DJ, Mauffrey C. Osteoporosis and the Orthopaedic Surgeon: Basic Concepts for Successful Co-Management of Patients' Bone Health. Int Orthop 2014; 38: 1731-1738.

13) Fischer H, Maleitzke T, Eder C, Ahmad S, Stöckle U, Braun KF. Management of Proximal Femur Fractures in the Elderly: Current Concepts and Treatment Options. Eur J Med Res 2021; 26: 86.

14) Cazzato G, Masci G, Liuzza F, Capasso L, Florio M, Perisano C, Vitiello R, Ciolli G, Maccauro G. Secondary Femur Fracture Following Treatment with Anterograde Nailing: The State of the Art. J Biol Regul Homeost Agents 2018; 32: 151-155.

15) Donati F, Di Giacomo G, D'Adamio S, Ziranu A, Careri S, Rosa M, Maccauro G. Silver-Coated Hip Megaprosthesis in Oncological Limb Savage Surgery. BioMed Res Int 2016, 2016: 9079041.

16) Piccioli A, Donati F, Giacomo GD, Ziranu A, Careri S, Spinelli MS, Giannini S, Giannicola G, Perisano C, Maccauro G. Infective Complications in Tumour Endoprostheses Implanted after Pathological Fracture of the Limbs. Injury 2016, 47 Suppl 4: S22-S28.

17) Rajasekaran RB, Palanisami DR, Natesan R, Jayaramaraju D, Rajasekaran S. Megaprosthesis in Distal Femur Nonunions in Elderly Patients—Experience from Twenty Four Cases. Int Orthop 2020, 44: 677-684.

18) Calori GM, Colombo M, Ripamonti C, Malagoli E, Mazza E, Fadigati P, Bucci M. Megaprosthesis in Large Bone Defects: Opportunity or Chimaera? Injury 2014; 45: 388-393.

19) Meluzio MC, Oliva MS, Minutillo F, Ziranu A, Saccomanno MF, Maccauro G. The Use of Knee Mega-Prosthesis for the Management of Distal Femoral Fractures: A Systematic Review. Injury 2020; 51 Suppl 3: S17-S22.

20) Covino M, Petruzziello C, Onder G, Migneco A, Simeoni B, Franceschi F, Ojetti V. A 12-Year Retrospective Analysis of Differences between Elderly and Oldest Old Patients Referred to the Emergency Department of a Large Tertiary Hospital. Maturitas 2019; 120: 7-11.

21) Agha RA, Sohrabi C, Mathew G, Franchi T, Kerwan A, O'Neill N. PROCESS Group The PROCESS 2020 Guideline: Updating Consensus Preferred Reporting Of CasESeries in Surgery (PROCESS) Guidelines. Int J Surg Lond Engl 2020; 84: 231-235.

22) Ziranu A, Lillo M, Fantoni M, Maffulli N, Maccauro G. Single Dose Cefazolin Is Safe and Effective for Pre-Operative Prophylaxis in Orthopaedic Oncology. J Biol Regul Homeost Agents 2018; 32: 45-49.

23) Oliva MS, Vitiello R, Cauteruccio M, Pesare E, Rovere G, Meschini C, Liuzza F, Maccauro G, Ziranu A. Cemented versus Cementless Megaprosthesis in Proximal Femur Metastatic Disease: A Systematic Review. Orthop Rev 2020; 12: 8689.

24) Charlson ME, Pompei P, Ales KL, MacKenzie CR. A New Method of Classifying Prognostic Comorbidity in Longitudinal Studies: Development and Validation. J Chronic Dis 1987; 40: 373-383.

25) Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A. A Global Clinical Measure of Fitness and Frailty in Elderly People. CMAJ Can. Med. Assoc. J. J Assoc Medicale Can 2005; 173: 489-495.

26) Noelker LS, Browdie R, Sidney Katz MD. A New Paradigm for Chronic Illness and Long-Term Care. The Gerontologist 2014; 54: 13-20.

27) Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, Bullinger M, Kaasa S, Leplege A, Prieto L, Sullivan M. Cross-Validation of Item Selection and Scoring for the SF-12 Health Survey in Nine Countries: Results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998; 51: 1171-1178.

28) Horan TC, Andrus M, Dudeck MA. CDC/NHSN Surveillance Definition of Health Care-Associated Infection and Criteria for Specific Types of Infections in the Acute Care Setting. Am J Infect Control 2008; 36: 309-332.

29) Harris WH, McCarthy JC, O'Neill DA. Femoral Component Loosening Using Contemporary Techniques of Femoral Cement Fixation. J Bone Joint Surg Am 1982; 64: 1063-1067.

30) Engh GA, Ammeen DJ. Classification and Preoperative Radiographic Evaluation: Knee. Orthop. Clin. North Am 1998; 29: 205-217.

31) Chen F, Li R, Lall A, Schwechter EM. Primary Total Knee Arthroplasty for Distal Femur Fractures: A Systematic Review of Indications, Implants, Techniques, and Results. Am J Orthop Belle Mead NJ 2017; 46: 163-171.

32) Parratte S, Ollivier M, Argenson JN. Primary Total Knee Arthroplasty for Acute Fracture around the Knee. Orthop Traumatol Surg Res OTSR 2018; 104: 71-80,

33) Windhager R, Schreiner M, Staats K, Apprich S. Megaprostheses in the Treatment of Periprosthetic Fractures of the Knee Joint: Indication, Technique, Results and Review of Literature. Int Orthop 2016; 40: 935-943.

34) Rayan F, Dodd M, Haddad FS. European Validation of the Vancouver Classification of Periprosthetic Proximal Femoral Fractures. J Bone Joint Surg Br 2008; 90: 1576-1579.

35) Jennison T, Yarlagadda R. A Case Series of Mortality and Morbidity in Distal Femoral Periprosthetic Fractures. J Orthop 2020; 18: 244-247.

36) D'Adamio S, Ziranu A, Cazzato G, Sanguinetti M, Manicone PF, Rosa MA, Maccauro G. Antifungal Properties of Silver Coating on Tumour Endoprostheses: An in Vitro Study. Eur Rev Med Pharmacol Sci 2019; 23: 252-257.

37) Oliva MS, Masci G, Vitiello R, De Santis V, Liuzza F, Grasso A, Minutillo F, Maccauro G Cazzato G. Hip Megaprosthesis in Oncological Surgery: Open Questions. J Biol Regul Homeost Agents 2019; 33: 45-49.

38) El Ezzo O, Oliva MS, Cauteruccio M, Saracco M, Vitiello R, Maccauro G, Perisano C. Innovations in Prevention of Infections in Oncological Megaprostheses: A Narrative Review. J Biol Regul Homeost Agents 2020; 34: 275-278.

39) Vitiello R, Bocchi MB, Gessi M, Greco T, Cianni L, De Maio F, Pesce V, Maccauro G, Perisano C. Induced Membrane by Silver-Coated Knee Megaprosthesis: Keep or Toss? J Biol Regul Homeost Agents 2020; 34: 101-106.