Prevalence of pathological neck of femur fractures in patients undergoing arthroplasty at a tertiary referral hospital

by

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Declaration

I, the undersigned, hereby declare that the work contained in this assignment is my original work and that I have not previously submitted it, in its entirety or in part, at any university for a degree.

Signed:

Date: 26/01/2021

Contents

Publication-ready manuscript

The following MMed dissertation is prepared in accordance with a new format which requires the candidate to submit said dissertation to a scientific journal of choice.

The manuscript was written in preparation for submission to the **South African Orthopaedic Journal**. The candidate is required to fulfil all requirements, as requested by the South African Orthopaedic Journal, and outlined in the author's guidelines (Appendix A). These instructions prescribe, for example, the length of the abstract and the total manuscript as well as the referencing style to be used.

The manuscript was accepted for publication in this journal (Appendix E)

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Abstract

Background: This study aimed to determine the prevalence of pathological neck of femur (NOF) fractures at a tertiary referral hospital through histological examination of specimens in all NOF fracture patients undergoing hip arthroplasty. A secondary aim was to determine whether the current practice of sending all femoral heads for histological evaluation, to avoid missing unsuspected malignancies, is financially warranted.

Methods: A retrospective folder review of patients who underwent arthroplasty for NOF fractures was conducted. Patients with suspected pathological fractures were managed by the divisional Bone Tumour Unit whilst fragility traumatic fractures were managed by the Arthroplasty Unit. All femoral heads were sent for histological analysis regardless of suspicion of pathological fracture. Quotes from the public and private sector were sought to determine cost implications of sending femoral head specimens for histology

Results: A total of 311 patients were included. Of these, 11 patients (3,5%) had suspected pathological fractures, with fragility/traumatic fractures being diagnosed in the remaining 300 patients (96.5%). Histology results were available for 195 patients (62.7%) including all of the patients with suspected pathological fractures. No unexpected malignant histological results were observed whilst 9 of the suspected pathological fracture group had pathological fractures, confirmed with histology.

Conclusion: Pathological lesions were identified in 2.9% of patients undergoing arthroplasty for NOF fractures in our population, which is higher than other reports in the literature. Routine histological screening of femoral heads to exclude pathological fracture might not be necessary and cost effective, as pathological lesions can accurately be identified by clinical and radiographic evaluation.

Keywords: Femoral head histology; pathological fracture; neck of femur fracture; metastases; hip arthroplasty

Introduction

Femoral neck fractures pose a significant burden to the healthcare system in developed and developing countries, with the annual incidence expected to increase in the coming years.[1] The reason for this increase is suggested to be decreasing global mortality rates and the aging populations' subsequent risk for osteoporosis.[2] Over 84% of elderly patients with femoral neck fractures are reported to have underlying osteoporosis.[3] Osteoporotic or fragility femoral neck fractures result in significant morbidity and mortality. Most patients never achieve pre fracture functional status after surgical intervention [4] and up to 33% die within the first 12 months post operatively.[5]

A small minority of patients sustain femoral neck fractures because of underlying pathological lesions.[6] Pathological fractures may be caused by any bone lesion (benign, primary malignant or metastatic), but metastatic bone tumours and multiple myeloma are far more prevalent than other primary bony malignancies in the elderly population.[7] The American Cancer Association expects around 1,8 million new cancer cases to be diagnosed in 2020.[8] There is also a steady decrease in mortality rate of 1.5% per year in patients with cancer and as the populations' life expectancy increases there is an increased prevalence of bony metastases with subsequent risk of pathological fractures.[9]

Breast, thyroid, kidney, lung and prostate primary malignancies have a predilection for bony metastases, though any primary malignancy can metastasize to bone.[10] The vertebral column is most commonly affected by bony metastases while the proximal femur is the most common site for metastases to the appendicular skeleton.[11] This, along with the strong deforming forces across the hip joint disproportionately predispose the proximal femur to pathological fractures. 50% of pathological fractures occur at the femoral neck, 20% at the intertrochanteric area, and the remaining 30% in the rest of the femur.[11]

There are two studies in the English literature documenting the prevalence of pathological neck of femur fractures. Ramnisetty et al, in their review of 2223 consecutive neck of femur fractures, conducted in Birmingham, England, reported ten patients (0.004%) with pathological fractures.[6] This figure, however, does not represent true prevalence as only 90 of the 2223 patients in their cohort had histological evaluation. Davis et al. in their retrospective review at a Level 1 trauma centre in California, United States of America, evaluated 850 consecutive femoral neck fracture patients, and found no unexpected malignancy in any of the 466 (54.8%) specimens which were sent for histological evaluation.[12] Similarly, true prevalence of pathological fractures in this study cannot be deduced as 45.2% of femoral heads were not sent

for histological analysis, and hence missed pathological fractures cannot be definitively excluded.

True incidence of pathological femoral neck lesions in patients undergoing elective arthroplasty of the hip, in stark contrast, has been extensively researched.[13-16] However there is no clear consensus on whether it is necessary from an economic standpoint to send all resected specimens for histological examination in these patients.[15-16]

The aim of this study was to determine the prevalence of pathological neck of femur fractures at a tertiary referral hospital between 2014 and 2016 through histological specimens in all neck of femur fracture patients presenting for hip arthroplasty. The secondary aim was to determine if the current practice of sending all femoral heads for histological evaluation, to avoid missing unsuspected malignancies, is warranted and to explore the financial cost involved.

Methods

A retrospective, observational review of case notes, imaging studies and histological results of all patients who underwent arthroplasty for neck of femur fractures between January 2014 and December 2017 was conducted.

As per institutional protocol, all patients were divided into two groups depending on suspicion of pathological or fragility / traumatic neck of femur fractures according to clinical and radiographic findings, on admission. Patients with suspected pathological fractures were subsequently managed by the divisional Bone Tumour Unit whilst fragility and traumatic neck of femur fractures were managed by the Arthroplasty Unit (Figure 1). Clinical features raising concern of possible pathological fractures included i) antecedent hip pain, ii) atraumatic mechanism of injury and iii) a history of malignancy. Radiological features suggestive of pathological fractures included atypical fracture patterns (e.g. transverse fractures with minimal trauma) or any bony lesions (e.g. lytic, permeative, moth eaten lesions) at the fracture site or any other bone on the radiograph.

Patients were identified from records from both units. All patients that underwent a head-sacrificing procedure were included in the study whilst patients who received arthroplasty for reasons other than neck of femur fractures and patients treated with internal fixation were excluded. There was no exclusion for age.

All resected femoral heads were sent for histology regardless if malignancy was suspected or not (Figure 1) as per our current standard of care for these fractures. For the fragility / traumatic fracture group, the type of hip reconstruction following head resection was selected on an individualized approach but was based on the National Institute of Health and Care Excellence (NICE) guidelines. Cognitively sound community ambulators who are anesthetically medically fit are offered total hip arthroplasty over hemiarthroplasty.[17]

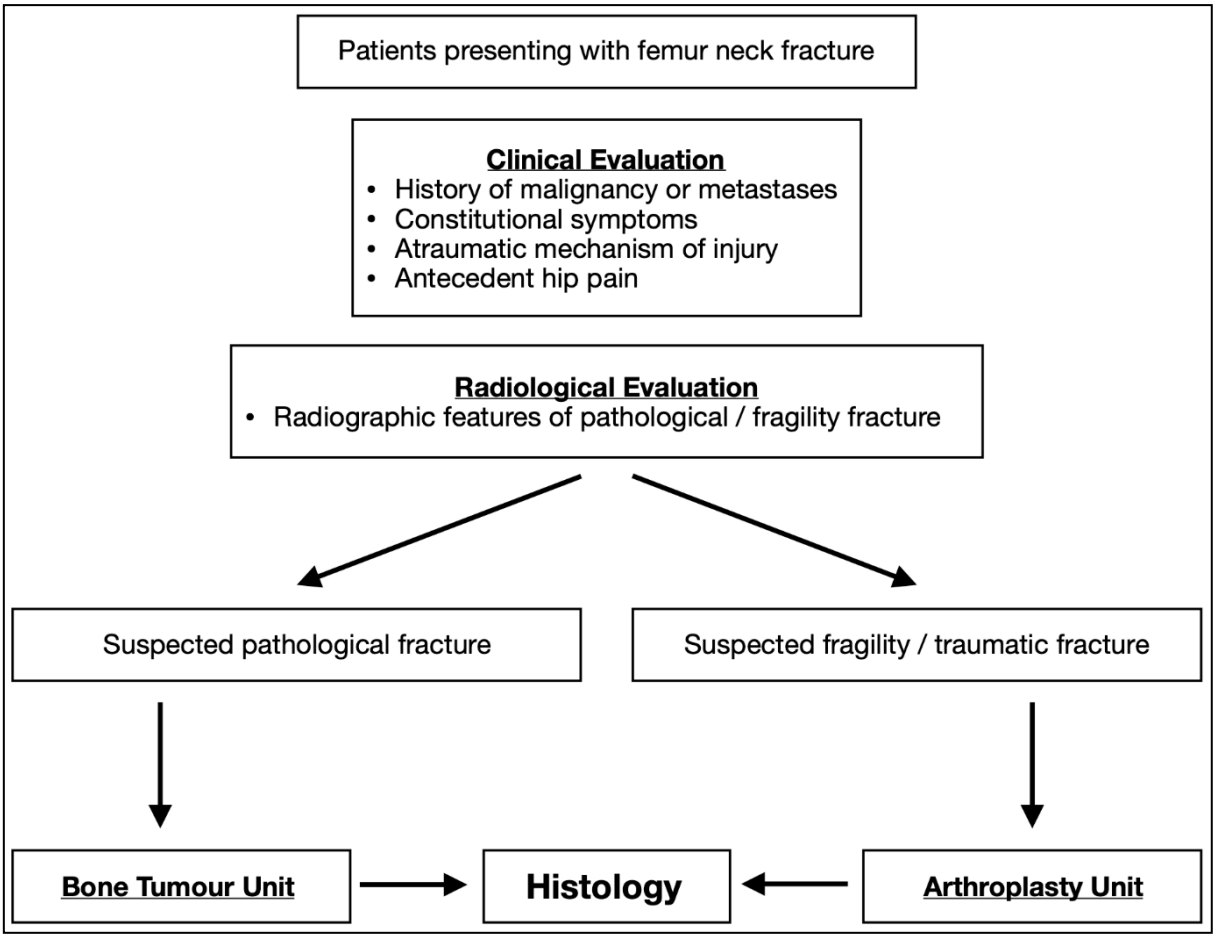

Figure 1. Flow diagram of patients presenting with neck of femur fractures.

Patients who presented with a suspicious fracture without a known primary malignant lesion were investigated in order to find the primary lesion and exclude a primary malignancy of bone and were then offered surgery. Patients with known metastasis (and those where the primary malignant lesion causing metastasis was found) were offered bipolar hemiarthroplasty with long cemented stems to prevent periprosthetic fracture. Primary implants used for fragility /

traumatic group fractures were DePuy Johnson & Johnson Corail Pinnacle system. Primary implants used for pathological fractures were Stryker Exeter V40 long femoral stems with bipolar hemi-arthroplasty heads.

To determine the financial implications of sending femoral heads for pathological examination, The National Laboratory Health Service, which provides histopathological examination for specimens in the state sector as well as Pathcare, which services the private sector, provided quotes in November 2019 of routine processing of these specimens.

Data was analysed using STATISTICA v13. Continuous demographic data (age) is reported as a mean and standard deviation together with 95% confidence intervals. Categorical data is described as frequencies and/or counts.

Results

A total of 311 patients who underwent arthroplasty for neck of femur fractures were included in this study. The cohort comprised 215 women (69%) and 96 men (31%) with a mean age of 73.4 years ± 12.6 (95% CI 72.0-74.).

A total of 11 of 311 patients (3.5%) were admitted with suspected pathological fractures, based on clinical and / or radiological suspicion with fragility / traumatic fractures being diagnosed in the remaining 300 patients (96.5%). Histology results were available for 195 patients (62.7%) including all of the patients with suspected pathological fractures, and 184 of the suspected traumatic / fragility fractures.

Nine of the suspected 11 patients were histologically confirmed to have a malignancy (Table 1) all of which were secondary to metastatic disease or multiple myeloma, with no primary sarcomas diagnosed. Of these, 4 out of 9 (44.4%) patients presented with an unknown primary malignancy and required a thorough clinical examination and basic haematological (tumour markers, myeloma workup) and radiological (CT chest / abdomen / pelvis) investigations to identify the primary malignancy prior to surgery. The histology from the resected femoral specimens for these patients confirmed the respective primary malignancy after initial workup.

Breast and lung carcinoma were the most common source of the primary malignancies accounting for six of the nine pathological fractures (3 each). Multiple myeloma, renal and prostate carcinoma accounted for the other three patients (Table 1, Figure 2).

Table 1. Patients with pathological findings on histology

Age	Gender	Known Primary	Known Metastases	X-ray Features of malignancy	Atraumatic Mechanism of Injury	Antecedent Hip Pain	Histology Results
65	Female	No	No	Lytic	No	No	Metastatic Lung Carcinoma
67	Female	No	No	Sclerotic	Yes	No	Metastatic Lung Carcinoma
75	Female	Yes	Yes	Permeative	No	No	Metastatic Breast Carcinoma
54	Female	Yes	Yes	Lytic	No	Yes	Metastatic Breast Carcinoma
51	Female	No	No	Permeative	No	Yes	Metastatic Lung Carcinoma
87	Male	Yes	No	Sclerotic	No	No	Metastatic Prostate Carcinoma
54	Female	No	No	Lytic	No	No	Multiple Myeloma
72	Female	Yes	Yes	Lytic	No	No	Metastatic Renal Carcinoma
54	Female	Yes	No	Lytic	Yes	Yes	Metastatic Breast Carcinoma

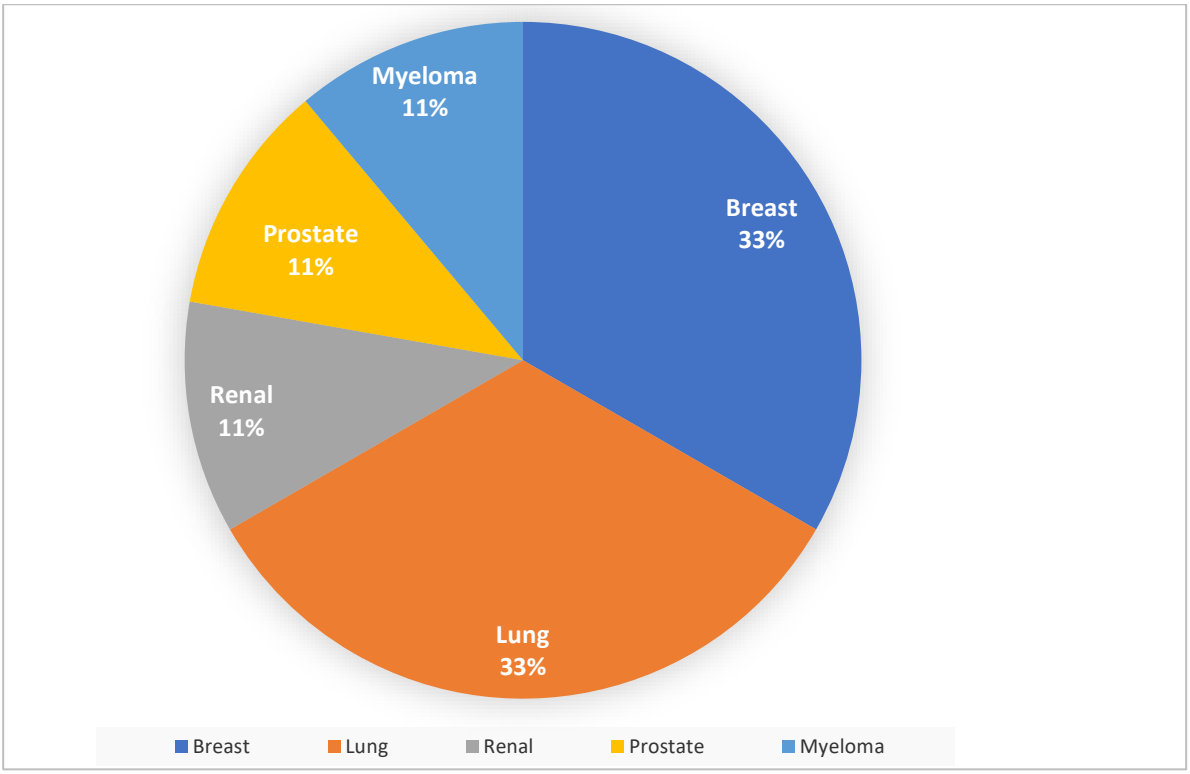

Figure 2. Percentage of primary malignancies responsible for metastatic lesions

The first of the two suspected pathological facture patients who did not have a pathological lesion on histology was a 68-year-old male known with prostate cancer and had a suspicious femoral neck lytic lesion on radiographs, not in keeping with the blastic metastasis usually associated with prostate cancer. After MRI (hip), CT (chest, abdomen and pelvis) and bone scan were noncontributory, the lytic lesion was biopsied to exclude a primary bony sarcoma or second primary malignancy. The biopsy showed no signs of pathological fracture and he subsequently received a total hip replacement. Histological evaluation of the resected femoral head confirmed the absence of any pathological lesions.

The second patient was a 47-year-old HIV positive female with a large breast mass with skin involvement. This was her index presentation to any healthcare facility for the breast mass. Radiographs revealed a subcapital neck of femur fracture and suspicious per trochanteric lytic lesion. She was assumed to have a pathological fracture secondary to metastasis from breast cancer and hence received a long-cemented stem bipolar hemiarthroplasty. Biopsy of the breast mass was done concurrently, and she was subsequently discharged to the care of the breast surgical oncology unit for further management. The breast biopsy confirmed malignancy (invasive carcinoma), however histology of the femoral head did not show any pathology.

Three of the nine (33.3%) patients with pathological fractures presented with antecedent hip pain, five (55.6%) with a known primary malignancy, three (33.3%) with known metastatic

disease, and two (22.2%) with an atraumatic mechanism of injury. All nine patients had radiographic features of pathological fractures (Figure 3).

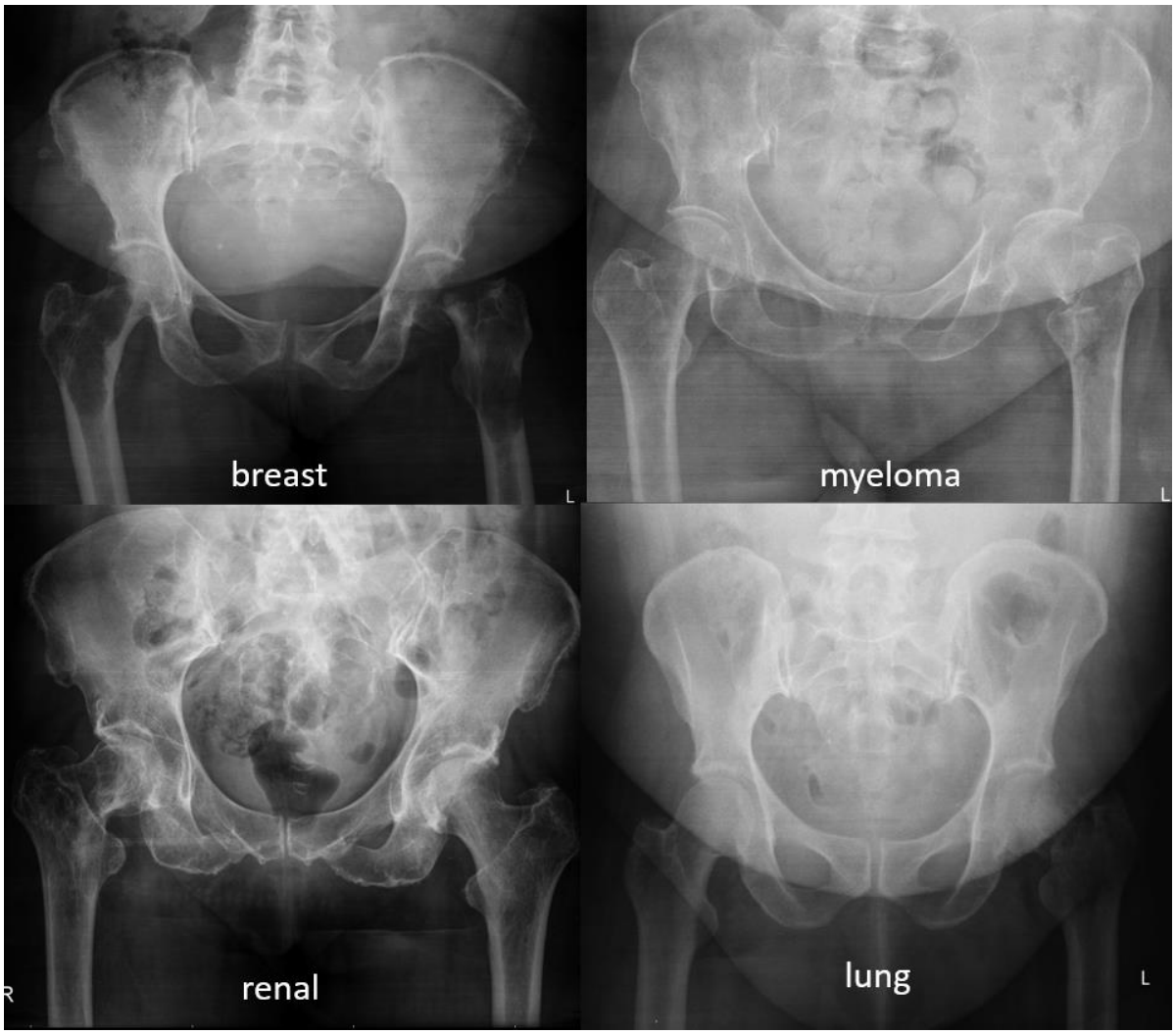

Figure 3. Anteroposterior Radiographs of patients from our study presenting with pathological fractures with the source of primary denoted below each image.

Histological results were available for 184 (of 300) patients in the fragility / trauma group. There were no unexpected malignant histological results found in this group. In 116 patients no histological results could be found. The reason these 116 excised femoral heads were not histologically analyzed as per institutional protocol was difficult to define retrospectively. Lost specimens, problems with transport of specimens from theatre to the pathology lab, human error, resulting in the specimens not being ordered are all considerations.

All but one of the patients with pathological fractures were treated with a long-cemented stem bipolar hemi arthroplasty. This patient returned two weeks post-surgery with a periprosthetic fracture below the implant, that required revision. There was no major intra-operative or

immediate post-operative morbidity or mortality related to cementation in patients who received long cemented stems for pathological fractures.

The approximate cost of a single femoral head histological examination in the private healthcare sector and the state healthcare system was ZAR 1956 (USD 134) and ZAR 540 (USD 37) respectively.

Discussion

The aim of the study was to establish the prevalence of pathological fractures at our institution and to determine the financial implications of sending all femoral heads for histological examination.

The first main finding of this study was that all pathological femoral neck fractures were secondary to metastatic disease and represented 2.9% of patients in the total cohort (9 of 311), or 4.6% (9 of 195) of those with confirmed histology findings. This is considerably higher than that reported by Davis et al (0.9%)[12] and Ramnisetty et al (0.45%)[6]. No conclusive reason can be given for this disparity in prevalence without further comparative studies. It could be explained by the lower number of femoral heads sent for histological examination (52% and 4% respectively) perhaps resulting in missed pathological fractures. More likely, it represents the delayed presentation due to health seeking behaviour[18] and lack of comprehensive screening programs for cancer[19], and hence delay in treatment, increasing prevalence of metastatic disease in the South African context. The patients with pathological fractures presented at a younger age (mean 63 years) than those with fragility fractures (mean 73 years), and this should be considered when treating these patients.

In view of the fact that there were no missed pathological fractures, and that 9 of 11 patients with pathological lesions were correctly identified on clinical features and radiographic findings in our series, sending all femoral heads routinely seems unnecessary. Almost half of the pathological fractures in the current series presented without a known primary malignancy, and in all these cases the primary was preliminarily identified using Rougraff et al[20] rudimentary diagnostic approach comprising basic blood tests and a computed tomography scan of the chest, abdomen and pelvis. Three of the four unknown primary tumours were of lung origin, in keeping with the nature of bronchogenic malignancies as they have few clinical symptoms initially and metastasize early, with metastatic lesions often the first manifestation of the disease[21].There were no pathological fractures due to bony sarcomas consistent with the rarity

of primary malignant bony lesions in elderly patients[22]. All four patients who presented with metastases of an "unknown primary" had a first histological diagnosis made on their femoral head specimens, as this preceded biopsy from the area of primary malignancy. This highlights the importance of pathological examination of the femoral heads from suspected lesions.

There is controversy in the literature regarding the use of short uncemented or longer cemented stems for patients with pathological fractures. Short uncemented stems weigh the risk of prosthetic loosening or periprosthetic fracture in the future , with the immediate risk of intraoperative haemodynamic instability or death with bone cement implantation syndrome associated with longer cemented stems[11,23]. In the current series we did not experience any cementation related complications in patients who received long cemented stems for pathological fractures.

A secondary aim was to determine the cost implications of sending all femoral heads for histological evaluation. In this study, femoral head histology (n=195) amounted to between ZAR 105 300 (USD 7274) and ZAR 381 420 (USD 26322) over the three-year period. As we were able to accurately exclude malignancy using clinical and radiographic criteria, sending only the suspicious femoral heads (n=11) for histological examination would have resulted in a reduced cost of between ZAR 99 360 (US$ 6864) and ZAR 359 904 (USD 24 838). As femoral neck fracture incidence is increasing globally[1], and considering financial constraints on the healthcare system, judicious use of resources is imperative. Subsequently, the findings of this study confirm the recommendation that clinicians should consider sending only the suspected pathological fractures for histological evaluation.

The limitations of this study include its retrospective nature and the fact that not all femoral heads were sent for pathological examination. We are therefore not able to definitively exclude pathological fractures for all patients, although we report a higher percentage than previous studies.

Conclusion

Pathological lesions were identified only in a small percentage of patients undergoing arthroplasty for neck of femur fractures in our population, albeit higher than other studies in the literature. Routine histological screening of femoral heads to exclude pathological fracture might not be necessary, as pathological lesions can accurately be identified by clinical and radiographic evaluation.

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Appendix A – Journal guidelines

South African Orthopaedic Journal

Scope and Policy

The scope of publication encompasses all orthopaedic surgery sub–disciplines including paediatric orthopaedics, hip, knee, tumour and sepsis, spine, shoulder and elbow, foot and ankle and hand surgery. In addition the journal addresses the subjects of orthopaedic service delivery, teaching, training and research. Publications should influence orthopaedic care on our continent.

The *South African Orthopaedic Journal* aims to advance the knowledge of all aspects of musculoskeletal medicine through publication of:

- Original research articles.
    - Clinical research
    - Basic science and theoretical research
- Review articles.
- Invited expert opinions.
    - A review of significant local or international publications journal article or cluster of articles dealing with a similar topic for the purpose of conveying a useful message.
- Editorials.
- Letters to the editor.
    - Forum to raise issues or debate aspects of previously published papers.

Criteria for publication

- The article falls within the scope of the journal.
- Methods, statistics, and other analyses are performed to a high technical standard and are described in sufficient detail.
- Results reported have not been published elsewhere.
- Conclusions are presented in an appropriate fashion and are supported by the data.
- The article is presented in an intelligible fashion and is written in standard English (British usage).
- The research meets all applicable ethical standards.
- The article adheres to guidelines provided in the instructions for authors section.

Guidelines for authorship

- Each author should participate and is responsible for the content and design of the study, the preparation of the manuscript and its revisions, and final approval.
- Other ‘contributors’ can be acknowledged at the end of the manuscript together with their contribution.
- Authors of manuscripts representing a multi–centre study may list members of the group in the footnote on the title page of the published article and their affiliations are listed in an appendix.
- The authors should clearly indicate the predominant surgeon or surgeons who have contributed patients to the study.

Registration of clinical trials

- A clinical trial is defined as any research study that prospectively assigns human participants or groups of humans to one or more health–related interventions to evaluate the effects of health outcomes. Interventions include drugs, surgical procedures, devices, behavioural treatments, dietary interventions, and process–of–care changes.
- Clinical trials should be registered in a public trials registry in accordance with International Committee of Medical Journal Editors recommendations.
- Trials must be registered and approved by the relevant authorities before the onset of patient enrolment.
- The Medicines Control Council (MCC) reference number and the SA National Clinical Trial Register (SANCTR) registration number should be included at the end of the abstract of the article.
- Purely observational studies (those in which the assignment of the medical intervention is not at the discretion of the investigator) do not require registration.

Reporting guidelines

- All articles should be prepared in accordance with the guidelines relevant to the study design that was used (listed below):

Randomised trials	CONSORT
Observational studies	STROBE
Systematic reviews	PRISMA
Case reports	CARE
Qualitative research	SRQR
Diagnostic / prognostic studies	STARD
Quality improvement studies	SQUIRE
Economic evaluations	CHEERS
Animal pre–clinical studies	ARRIVE
Study protocols	SPIRIT

- Randomised trials should be accompanied by a flow diagram that illustrates the progress of patients through the trial, including recruitment, enrolment, randomisation, withdrawal and completion, and a detailed description of the randomisation procedure.

Role of funding source

- Authors are requested to identify who provided financial support for the conduct of the research and/or preparation of the article and to briefly describe the role of the sponsor(s), if any, in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. If the funding source(s) had no such involvement, then this should be stated.

Formatting of Submissions

Text formatting

- Use Helvetica or Arial font, size 11.
- Use double line spacing throughout the document.
- Number the pages of the blinded manuscript consecutively.
- Use italics for emphasis.
- When referring to an article with multiple authors please use the following format: Rabinowitz *et al*. published their retrospective review.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Headings

- Use no more than three levels of displayed headings.

Abbreviations

- Define abbreviations and acronyms at first mention and use consistently thereafter.

Units

- Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

Figures

- Figures should be numbered consecutively with illustration Arabic numbers 1, 2, 3, etc.
- The figure should be listed in the text as follows: … wound irrigation and splinting (*Figure 1*).
- Figures should be clear and easily understandable with a full descriptive legend stating any areas of interest and explaining any markings, letterings or notations. All figures should be understandable without the main text.
- For radiographs please ensure you state the view used and the time point at which it was taken, as well as the demographic details of the patient if applicable.

- Figures should not be imbedded in the text file, but should be submitted as separate individual files. Each figure should be a separate file, entitled Figure 1, Figure 2, etc.
- Remove all markings, such as patient identification, from radiographs before photographing.
- All line or original drawings must be done by a professional medical illustrator.
- We accept a maximum of six figures.
- Do not submit any figures, photos, tables, or other works that have been previously copyrighted or that contain proprietary data unless you have obtained and can supply written permission from the copyright holder to use that content.

Tables

- Tables should carry uppercase Roman numerals, I, II, III, etc.
- Tables should always be cited in the text in consecutive numerical order.
- The table should be identified in the text as follows: Details of results are listed in *Table I*. Or, alternatively, … high–energy trauma that is often associated with these fractures (*Table II*).
- Tables should be used to present information in a clear and concise manner. All tables should be understandable without the main text.
- For each table, please supply a table heading explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table heading.
- Footnotes to tables should be indicated by superscript lower–case letters and included beneath the table body.
- Please submit tables as editable text and not as images. They should be created using the Table tool in Word.
- Do not embed tables in the text file, but submit them as separate individual files. Each table should be a separate file, entitled Table I, Table II, etc.
- We accept a maximum of eight tables.
- Do not duplicate information given already in the text.
- Do not submit any figures, photos, tables or other works that have been previously copyrighted or that contain proprietary data unless you have obtained and can supply written permission from the copyright holder to use that content.

References

- References should be numbered consecutively in the order that they are first mentioned in the text and listed at the end in numerical order of appearance.
- Identify references in the text by Arabic numerals in superscript after punctuation.
- References should not be a listing of a computerised literature search but should have been read by the authors and have pertinence to the manuscript.
- Authors should add DOIs to all references in articles.
- Accuracy of references is the author's responsibility and the author is to verify the references against the original documents.
- Manuscripts in preparation, unpublished data (including articles submitted but not in the press) and personal communications may not be included in the reference listing. They may be listed in the text in parentheses only if absolutely necessary to the contents and meaning of the article.
- The titles of journals should be abbreviated according to the style used in Index Medicus, obtainable through the website http://www.nlm.nih.govshould

- The following format should be used for references:

  Journal article:
  Sidhu GS, Ghag A, Prokuski V, Vaccaro AR, Radcliff KE. Civilian gunshot injuries of the spinal cord: a systematic review of the current literature. Clin Orthop Relat Res 2013;471:3945-55.

  Ideally, the names of all authors should be provided, but the usage of 'et al.' in long author lists (more than six authors) will also be accepted: Fong K, Truong V, Foote CJ, et al. Predictors of nonunion and reoperation in patients with fractures of the tibia: an observational study. BMC Musculoskelet Disord 2013;14:103.

  On–line journal article:
  Caetano–Lopes J, Lopes A, Rodrigues A, et al. Upregulation of inflammatory genes and downregulation of sclerostin gene expression are key elements in the early phase of fragility fracture healing. PLoS One 2011;6:e16947.

  Web reference (with authors):
  Cierny G, DiPasquale D. Adult osteomyelitis protocol. http://www.osteomyelitis.com/pdf/treatment_protocol.pdf. (date last accessed 05 March 2013).

  Web reference (no authors listed):
  No authors listed. International commission on radiological protection. http://www.icrp.org (date last accessed 20 September 2009).

  Chapter in a book:
  Young W. Neurophysiology of spinal cord injury. In: Errico TJ, Bauer RD, Waugh T (eds). Spinal Trauma. 3rd ed. Philadelphia: JB Lippincott; 1991: 377-94.

  Dissertation:
  Borkowski MM. Infant sleep and feeding: a telephone survey of Hispanic Americans [dissertation]. Mount Pleasant (MI): Central Michigan University; 2002.

  Abstract:
  Peterson L. Osteochondritis of the knee treated with autologous chondrocyte transplantation [abstract]. ISAKOS Congress, 2001.

Structure and content of submission

- We accept a maximum of 3500 words including the abstract and body of the text (excluding references).
- Exceptions to this rule may be made for systematic reviews and meta–analysis, at the discretion of the Editor–in–Chief.
- Please follow the following structure when preparing your submission.
  - Title page (Title, authors and affiliations, corresponding author and declarations)
  - Blinded manuscript (Abstract, key words, introduction, methods, results, discussion, funding sources, conflict of interest statement, ethical statement, acknowledgements and references)
  - Tables (with headings), each as a separate file.

- Figures (with legends), each as a separate file.

Title page

Title

- The title should be concise and informative.

Author names and affiliations

- Please provide the following information for each author:
  - Full names and surname, as well as title
  - Qualifications
  - Affiliation and address
  - ORCID ID (see Article Submission section)
- Please check that all names are accurately spelled.
- Indicate all affiliations with a lower–case superscript letter immediately after the author's name and in front of the appropriate affiliation details.
- Provide the full postal address of each affiliation, including the country name and, if available, the e–mail address of each author.

Corresponding author

- Clearly indicate who will handle correspondence at all stages of refereeing and publication, including post–publication.
- Ensure that the e–mail address and permanent address is given and that contact details are kept up to date by the corresponding author.
- Please note that the corresponding author's contact details will be provided in the final article.
- Provide the following information for the corresponding author:
  - Full names and title
  - Affiliation
  - Physical address
  - Postal address
  - Telephone Number
  - E–mail address

Declarations
Authors are to insert a section at the end of the title page entitled declarations. Following the declarations all authors need the to sign the document (please provide name of author, signature and date). The following statements are required under the declarations section:

a. Authorship
   The authors confirm that all authors have made substantial contributions to all of the following:
   - The conception and design of the study, or acquisition of data, or analysis and interpretation of data
   - The drafting the article or its critical revision for important intellectual content
   - Final approval of the version to be submitted.

b. Sound scientific research practice
The authors further confirm that:
- The manuscript, including related data, figures and tables has not been previously published and is not under consideration elsewhere
- No data have been fabricated or manipulated (including images) to support conclusions.
- This submission does not represent part of a single study that has been split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time (e.g. 'salami–publishing').

c. Plagiarism
The authors confirm that the work submitted is original and does not transgress the plagiarism policy of the journal.
- No data, text or theories by others are presented as if they were the authors' own.
- Proper acknowledgements of others' work has been given (this includes material that is closely copied, summarised and/or paraphrased); quotation marks are used for verbatim copying of material.
- Permissions have been secured for material that is copyrighted.

d. Conflict of interest statement
A conflicting interest exists when professional judgement concerning a primary interest (such as the patient's welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry). It represents a situation in which financial or other personal considerations from authors, reviewers or editors have the potential to compromise or bias professional judgment and objectivity. It may arise for the authors when they have a financial interest that may influence their interpretation of their results or those of others. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. All potential conflicts of interest need to be declared. The conflict of interest statement should list each author separately by name, i.e.,

'John Smith declares that he has no conflict of interest. Paula Taylor has received research grants from Drug Company A. Mike Schultz has received a speaker honorarium from Drug Company B and owns stock in Drug Company C.'

If multiple authors declare no conflict, this can be done in one sentence.

e. Funding sources
All sources of funding should be declared. Also define the involvement of study sponsors in the study design, collection, analysis and interpretation of data; the

writing of the manuscript; and the decision to submit the manuscript for publication. If the study sponsors had no such involvement, this should be stated.

f. Compliance with ethical guidelines
   - For all publications:

     'The author/s declare that this submission is in accordance with the principles laid down by the Responsible Research Publication Position Statements as developed at the 2nd World Conference on Research Integrity in Singapore, 2010.'

     Available from:
     http://publicationethics.org/resources/international-standards-for-editors-and-authors

     Institutional Review Board (IRB) ethical approval must have been given if the study involves human subjects or animals. Please provide the approval number. IRB documentation should be available upon request.

     'Prior to commencement of the study ethical approval was obtained from the following ethical review board: *Provide name and reference number'*

   - For studies with human subjects include the following:
     'All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.'

     'Informed written consent was or was not obtained from all patients for being included in the study.'
   - For studies with animals include the following sentence:
     'All institutional and national guidelines for the care and use of laboratory animals were followed.'
   - For articles that do not contain studies with human or animal subjects:
     'This article does not contain any studies with human or animal subjects.'
   - If doubt exists whether the research was conducted in accordance with the Helsinki Declaration, the authors must explain the rationale for their approach, and demonstrate that the institutional review body explicitly approved the doubtful aspects of the study. If any identifying information about patients is included in the article, the following sentence should also be included: Additional informed consent was obtained from all patients for which identifying information is included in this article.

     The Helsinki Declaration 2008 can be found
     at http://www.wma.net/en/30publications/10policies/b3/

Blinded manuscript

Abstract

- A structured abstract (maximum of 350 words), summarising the most important points in the article is required.
- The abstract consists of four paragraphs with the subheadings:
    - Aims (it is unnecessary to include an introductory section)
    - Patients and methods
    - Results
    - Conclusion
- References should be avoided. Avoid uncommon abbreviations. If essential they must be defined at their first mention in the abstract itself

Key words

- Immediately after the abstract, provide a maximum of six key words, using standard searchable terms. These key words will be used for indexing purposes.

Level of evidence

- Level 1 to 5.
- Please follow the level of evidence guidelines provided by the Oxford Centre for Evidence–Based Medicine (OCEBM); version 2.1.
- Available from: OCEBM Levels of Evidence Working Group. 'The Oxford Levels of Evidence 2'.Oxford Centre for Evidence–Based Medicine. http://www.cebm.net/index.aspx?o=5653

Introduction

- The introduction should contextualise the study by providing the background to the research; explain the problem that is to be addressed and provide the rationale for the study.
- Briefly outline the relevance of the study with respect to the current literature. Avoid a detailed literature survey or a summary of the results.
- The last sentence should outline the research question or hypothesis.

Patients (or Materials) and methods

- State the methods, outcome measures, and selection criteria. The following aspects need to be described:
    - The study design and research methodology
    - Whether randomisation (with methods) was applied
    - If case controlled, how the controls were selected
    - The time period under review
    - Number of patients/subjects under investigation and why this number was chosen
    - Inclusion and exclusion criteria
    - Case and outcome definitions
    - A description of the procedure or intervention, including post–operative protocol
    - The outcome measures or scores used
    - The minimum follow–up period
    - Statistical analysis paragraph. This should be included at the end of this section to detail statistical tests and package used, the reasons why these tests

were used, and what p–value was considered statistically significant. A power analysis is recommended for studies comparing two or more groups.

- Provide sufficient detail so that another researcher can replicate the study.
- The reader should understand from this description all potential sources of bias such as referral, diagnosis, exclusion, recall or treatment bias. This includes the manner in which investigators selected the patients. Consecutive inclusion implies all patients with a given diagnosis are included, while selective implies patients with a given diagnosis but selected according to certain explicit criteria (e.g., state of disease, choice of treatment).
- Do not describe standard procedure for common operations. Only include new procedures or adaptations to standard procedure.
- If you name any specific product, then it requires the name, city and state/country of the manufacturer.
- Present information in the narrative format and use the past tense.
- Where relevant, tables or figures may be included to provide information more clearly.
- Generally, no data should be presented in this section.

Results

- Describe the relevant results and analysis thereof.
- Provide details of the number of patients included and excluded, as well as the reason for exclusion.
- It is important to state the follow–up period (mean and range).
- The results can be broken down into separate sections, e.g. Treatment, Functional outcome, Complications, etc.
- Tables may be used but avoid repeating data reported in the text in the tables.
- All appropriate data should be presented as means with ranges, not with standard deviations (SDs). Medians should only be used when the data is skewed, accompanied by an interquartile range (IQR).
- Avoid using percentages in studies involving well under 100 subjects.
- All results must be backed up with p–values or survivorship analysis. All Kaplan–Meier data should be presented with the confidence intervals. Always present exact absolute p–values, whether significant or not, unless $p < 0.001$.
- However, p–values do not always convey the entire picture and where relevant the confidence interval will also be required (in addition to the power of the study reported in the methods section).

Discussion

- The question or hypothesis stated at the end of the introduction should be discussed and either supported or rejected.
- The results must be interpreted clearly and any deficiencies expressed. All possible confounding factors, sources of bias, or weaknesses in the study should be identified.
- Explore the significance of the results of the work, rather than repeating the results.
- The discussion must point out the relevance of the work described in the paper and its contribution to current knowledge.
- Explain what can be deduced from the results and how will it affect clinical practice.

- Include a review of the relevant literature, placing the results of the study in the context of previous work in this area.
- Discussion of relevant prior research and references must be concise. Avoid extensive citations and discussion of published literature but put emphasis on previous findings that agree (or disagree) with those of the present study.
- Do not repeat the introduction.
- Present the limitations of the study and suggest how the study could have been improved for a future study.
- Avoid making inferences from non–significant trends unless you believe your study is adequately powered to answer the question; in that case, provide a power analysis.

Conclusion

- Provide a summary statement which conveys the conclusions of the findings.
- Do not draw conclusions not supported by the data obtained from the specific study presented.

Conflict of interest

- 'Author A.B. (*use initials of relevant author, not full name in order for the document to remain blinded*) has received research grants from Company A. Author B.C. has received a speaker honorarium from Company X and owns stock in Company Y. Author C.D. is a member of committee Z.'
- If no conflicts of interest exist, state this as follows: 'The authors declare they have no conflicts of interest that are directly or indirectly related to the research.'

Ethical statement

- For studies involving human subjects please include an ethical statement as follows: 'All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.'
- For animal studies please include the following ethical statement: 'All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.'
- If the study did not involve human or animal subjects state that: 'This article does not contain any studies with human participants or animals performed by any of the authors.'
- Please also include an informed consent statement: 'Informed consent was obtained from all individual participants included in the study.'
- Or alternatively, for retrospective studies, please add the following sentence: 'For this study formal consent was not required.'
- If identifying information about participants is available in the article, the following statement should be included: 'Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.'

Funding sources

- List all funding sources as follows: 'This work was supported by the xxxx (grant numbers xxxx, yyyy).'

- When funding is from a block grant or other resources available to a university, college or other research institution, submit the name of the institute or organisation that provided the funding.
- If no funding was received, state as follows: 'No funding was received for this study.'

Acknowledgements

- Acknowledgements should be placed at the end of the discussion and before the references.
- In this section persons who were involved but did not earn authorship can be acknowledged.
- Statements should be brief. A person can be thanked for assistance or for comments.
- Should not include contributions by editors or referees.

References

- Please refer to the section on Formatting of submissions.

Tables and figures

- Table and figures should not be imbedded in the text file, but should be submitted as separate individual files. Each table should be a separate file, entitled Table I, Figure 2, etc.
- Each table and figure should be provided with a heading or legend.
- Please refer to the 'Formatting of submission' section for further guidelines.

Appendix B – Ethics Clearance

UNIVERSITEIT
STELLENBOSCH
UNIVERSITY

Health Research Ethics Committee (HREC)

Approval Notice

New Application

11/12/2018

Project ID :8744

HREC Reference #: S18/10/264

Title: Prevalence of pathological neck of femur fractures in patients undergoing arthroplasty at Tygerberg Hospital

Dear Dr SUHAYL KHAN,

The **New Application** received on 02/11/2018 17:45 was reviewed by members of **Health Research Ethics Committee 2 (HREC 2)** via **expedited** review procedures on 11/12/2018 and was approved.

Please note the following information about your approved research protocol:

Protocol Approval Period: This project has approval for 12 months from the date of this letter.

Please remember to use your **Project ID [8744]** on any documents or correspondence with the HREC concerning your research protocol.

Please note that the HREC has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.

After Ethical Review

Please note you can submit your progress report through the online ethics application process, available at: Links Application Form Direct Link and the application should be submitted to the HREC before the year has expired. Please see *Forms and Instructions* on our HREC website (www.sun.ac.za/healthresearchethics) for guidance on how to submit a progress report.

The HREC will then consider the continuation of the project for a further year (if necessary). Annually a number of projects may be selected randomly for an external audit.

Provincial and City of Cape Town Approval

Please note that for research at a primary or secondary healthcare facility, permission must still be obtained from the relevant authorities (Western Cape Departement of Health and/or City Health) to conduct the research as stated in the protocol. Please consult the Western Cape Government website for access to the online Health Research Approval Process, see: https://www.westerncape.gov.za/general-publication/health-research-approval-process. Research that will be conducted at any tertiary academic institution requires approval from the relevant hospital manager. Ethics approval is required BEFORE approval can be obtained from these health authorities.

We wish you the best as you conduct your research.

For standard HREC forms and instructions, please visit: Forms and Instructions on our HREC website https://applyethics.sun.ac.za/ProjectView/Index/8744

If you have any questions or need further assistance, please contact the HREC office at 021 938 9677.

Yours sincerely,

Mr. Francis Masiye,

HREC Coordinator,

Health Research Ethics Committee 2 (HREC 2).

National Health Research Ethics Council (NHREC) Registration Number:

REC-130408-012 (HREC1)·REC-230208-010 (HREC2)

Page 1 of 2

Federal Wide Assurance Number: 00001372
Office of Human Research Protections (OHRP) Institutional Review Board (IRB) Number:
IRB0005240 (HREC1)·IRB0005239 (HREC2)

*The Health Research Ethics Committee (HREC) complies with the SA National Health Act No. 61 of 2003 as it pertains to health research. The HREC abides by the ethical norms and principles for research, established by the*World Medical Association (2013). Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects;*the South African* Department of Health (2006). Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa (2nd edition); as well as the Department of Health (2015). Ethics in Health Research: Principles, Processes and Structures (2nd edition).

The Health Research Ethics Committee reviews research involving human subjects conducted or supported by the Department of Health and Human Services, or other federal departments or agencies that apply the Federal Policy for the Protection of Human Subjects to such research (United States Code of Federal Regulations Title 45 Part 46); and/or clinical investigations regulated by the Food and Drug Administration (FDA) of the Department of Health and Human Services.

Appendix C – Hospital Clearance

Western Cape Government
Health

TYGERBERG HOSPITAL
REFERENCE:
Research Projects
ENQUIRIES: **Dr GG Marinus**
TELEPHONE:**021 938 5752**

Project ID: 8744

Ethics Reference: S18/10/264

TITLE: **Prevalence of pathological neck of femur fractures in patients undergoing arthroplasty at Tygerberg Hospital.**

Dear Suhayl Khan

PERMISSION TO CONDUCT YOUR RESEARCH AT TYGERBERG HOSPITAL.

1. In accordance with the Provincial Research Policy and Tygerberg Hospital Notice No 40/2009, permission is hereby granted for you to conduct the above-mentioned research here at Tygerberg Hospital.

2. Researchers, in accessing Provincial health facilities, are expressing consent to provide the Department with an electronic copy of the final feedback within six months of completion of research. This can be submitted to the Provincial Research Co-Ordinator (Health.Research@westerncape.gov.za).

DR GG MARINUS
MANAGER: MEDICAL SERVICES

DR D ERASMUS
CHIEF EXECUTIVE OFFICER
Date: 26 March 2019

Administration Building, Francie van Zijl Avenue, Parow, 7500 Private Bag X3, Tygerberg, 7505
tel: +27 21 938-6267 fax: +27 21 938-4890 www.capegateway.go.v.za

Appendix D – Turnitin Report

Suhayl Khan

ORIGINALITY REPORT

%2	%2	%1	%0
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Mottolese, M.. "Use of selected combinations of monoclonal antibodies to tumor associated antigens in the diagnosis of neoplastic effusions of unknown origin", European Journal of Cancer and Clinical Oncology, 198808 Publication	%1
2	journals.sagepub.com Internet Source	<%1
3	www.bmj.com Internet Source	<%1
4	www.15-40.org Internet Source	<%1

EXCLUDE QUOTES	OFF	EXCLUDE MATCHES	OFF
EXCLUDE BIBLIOGRAPHY	OFF		

Appendix E - Acceptance Letter from the South African Orthopaedic Journal

Gmail

Suhayl Khan <suhaylahmedkhan@gmail.com>

[SAOJ] 438 Editor Decision

3 messages

Robyn Marais <robyn@jesser-point.co.za> Tue, Oct 13, 2020 at 4:11 PM
To: Suhayl Ahmed khan <suhaylahmedkhan@gmail.com>, Naweed Wadee <nwd295@gmail.com>, Marilize Burger <mcburger@sun.ac.za>, Koos Jordaan <kosjor@sun.ac.za>, Nando Ferreira <nferreira@sun.ac.za>

Suhayl Ahmed khan, Naweed Wadee, Marilize Burger, Koos Jordaan, Nando Ferreira:

Thank you for submitting your manuscript entitled " Prevalence of pathological neck of femur fractures in patients undergoing arthroplasty at a tertiary referral hospital" to the South African Orthopaedic Journal.

It is a pleasure to inform you that the above-mentioned manuscript has been accepted, as is, for publication in the *South African Orthopaedic Journal*. The comments of the reviewers are attached.

You will be contacted by our Managing Editor if any further information is required. Any queries concerning your manuscript should be addressed to the Managing Editor at: pat@saoj.co.za

Thank you for your contribution to the *South African Orthopaedic Journal* and we look forward to receiving further contributions in the future.

Yours sincerely
Prof LC Marais
Editor-in-Chief: *SA Orthopaedic Journal*

Email: robyn@jesser-point.co.za

South African Orthopaedic Journal