Title page

Hip fractures in South Africa: mortality outcomes over 12 months post fracture

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Mini abstract/Summary (word count 50)

With increased urbanisation and longevity in sub-Saharan Africa, the burden of osteoporosis and resultant hip fractures (HF) has increased. This study shows that 1 in 3 subjects die post HF, and that there are significant delays and barriers to surgery, reflecting the need to prioritise HF care in South Africa.

Mini abstract/Summary

With increased urbanisation and longevity in sub-Saharan Africa, the burden of osteoporosis and resultant hip fractures (HF) has increased. This study shows that 1 in 3 subjects die post HF, and that there are significant delays and barriers to surgery, reflecting the need to prioritise HF care in South Africa.

Abstract

Purpose: The outcomes following hip fractures are unknown in sub-Saharan Africa. This study aimed to quantify the mortality rate (MR) following hip fractures and to identify predictors of mortality over one year.

Methods: In this cohort study, demographic, clinical, and biochemical characteristics of consecutive patients with low trauma hip fractures, admitted to the five public sector hospitals in eThekwini (formerly Durban), were recorded. Cox regression analyses identified predictors of mortality at 30 days and one year.

Results: In the 200 hip fracture patients studied the mean age was 74.3 years (SD ± 8.8) and 72% were female. Hospital presentation was often delayed, only 15.5% presented on the day of fracture. At admission, 69.5% were anaemic, 42% had hyponatraemia, 34.5% raised creatinine, and 58.5% hypoalbuminaemia. All received skin traction before 173 (86.5%) underwent surgical fixation. Median time from admission to surgery was 19.0 days (IQR 12.3-25.0). Median hospital stay was 9.0 days (IQR 12.3–25.0). Mortality rates were 13% and 33.5% at 30 and 365 days, respectively. Over one-year, African patients were more likely to die than Indian patients (40.9% versus 30%, HR: 11.5 [95% CI 1.51, 2.57]; p=0.012); delays to surgery predicted death, HR: 1.02 [95% CI (1.00, 1.04)]; p=0.022. In multivariate analyses, death at one-year was most strongly predicted by an elevated serum creatinine (HR: 2.43, 95% CI (1.02, 5.76) p=0.044].

Conclusion: Hip fractures are associated with high MRs, in part explained by insufficient surgical capacity, highlighting the need for national efforts to improve hip fracture service provision.

Keywords: Hip fracture, mortality, osteoporosis, South Africa, survival

Introduction

Approximately 1.05 billion people currently live in sub-Saharan African (SSA) [1]. The SSA population is ageing more rapidly than in any other region globally with population projections of 161 million by 2050 for those aged over 60 years [2]. Rapid urbanisation is changing disease burdens across the region towards a greater prevalence of non-communicable diseases, including osteoporosis. Historically fractures were thought to be rare in the Black South African population [3]; however, recent data suggest similar patterns to those seen in White populations [4,5].

In high-income countries (HICs), of all fracture types, hip fractures (HFs) convey the poorest health-related outcomes with high health and social care costs. Although the last decade has seen substantial improvements in 30-day mortality, now 6.9% in the United Kingdom (UK) [6], one-year mortality remains relatively static at approximately 30% [7]. Furthermore, length of hospital stay is highly variable, as are levels of dependency with rates of discharge to nursing/residential institutional care homes of 12% in the UK and 53% in the United States (US). In the UK, four months after a HF only 10% are able to mobilise without walking aids [6,8]. Similarly, in the US, 35% remain unable to walk independently after one year [9].

Despite SSA having twice the number of adults than Northern Europe [10], there are limited studies describing outcomes after HF in the region [11,12]. Health care in SSA is further complicated by the high prevalence of human immunodeficiency virus infection, high trauma rates that compete for scarce orthopaedic resources, and limited social care infrastructure. Currently osteoporotic HFs are not considered as a healthcare priority, and investigation and treatment for osteoporosis is not universally available. The World Health Organisation (WHO) recently called for action to prevent and manage fragility fractures in SSA in the coming decade [13]. Hence, data quantifying patient outcomes post HF are urgently needed to inform clinicians, patients, families and policy makers, and to underpin clinical quality improvement programmes to improve future fracture services and thus patient outcomes.

In an ethnically diverse population in South Africa (SA), this study aimed to quantify mortality over the year following a fragility fracture of the hip and determine the principal predictors of mortality.

Methodology

Study design and setting

A prospective cohort study was conducted between August 2010 and October 2011, across the five public sector regional hospitals which offer orthopaedic services in the city of eThekwini (formerly Durban) on the east coast of SA. At the time, the population of eThekwini totalled 3 468 087 persons with 236 035 persons aged 60 years and over [14], of which Africans comprised 45.9%, followed by 26.3% Indians, 25.6% Whites and 2.2% Coloureds. Based on the ethnic distribution and differential access to medical insurance approximately 150 000 persons aged 60 years and over utilize these public sector hospitals.

Participant recruitment

Adults, aged 60 years and over, living permanently in the defined geographic area, admitted with a minimal trauma HF (defined as a fracture of the femur between the articular cartilage of the hip joint to 5 cm below the distal point of the lesser trochanter, following a fall from standing height or less), who consented, were enrolled in the study. Patient data were recorded at the hospital where the primary surgery occurred; all entries were cross-referenced within and between hospitals to prevent duplication. Individuals with pathological fractures, fractures distal to the lesser trochanter, traumatic fractures, and re-admissions for previous HF complications were excluded.

Data collection

A structured data collection tool captured demographic characteristics, employment and education level, and risk factors for osteoporosis and fractures. Comorbid diseases including prolonged immobilization (>3 months), history of malignancy, maternal history of HF, functional status and a detailed fall history (self-recollection and/or collateral from next-of-kin) were recorded. Calcium intake was calculated using the International Osteoporosis Foundation calcium calculator [15]. The internationally validated WHO Monitoring Trends and Determinants in Cardiovascular disease scale, was used to classify patients as present or past smokers [16]. Patients reported the number and type of alcoholic drinks consumed in the past week using a self-reported scale, validated in a Danish survey [17].

Functional level was assessed using the widely validated Physical Self-Maintenance Scale (PSMS) and the Lawton Instrumental Activities of Daily Living scale (IADL), which have good inter-rater reliability at 0.87 and 0.91, respectively [18.19]. The PSMS rates competence in basic ADLs (the ability to independently eat, dress, groom, walk, transfer to a bed, bath and use the toilet) from a minimum score of 0 (unable to do any activity) to a maximum achievable score of 17 (independent for all activities) [19]. The IADL, assesses an individual's ability to live independently, and scores range from 0 (fully independent) to 27 (fully dependent). The IADL assesses the individual's ability to use a telephone, walk a distance, shop, cook, complete household tasks, handiwork, laundry and manage medications and finances. Weight and height were recorded where physically able to be measured, and body mass index (BMI) calculated.

All patients had blood drawn for investigations for secondary causes of osteoporosis. Tests included: full blood count, serum urea, creatinine and electrolytes, liver function tests, corrected serum calcium, phosphate and magnesium, C- reactive protein 9CRP) considered elevated if ≥10.0 mg/L, parathyroid hormone (elevated if ≥ 7.1 pg/mL) and total 25-hydroxy vitamin D (25 OHD) levels which were categorised as sufficient ≥ 50.1 nmol/L or deficient/insufficient ≤ 49.9 mmol/L.

The dates of admission, surgery and discharge, type of orthopaedic prosthesis used, discharge destination and the results of radiological investigations performed on admission were recorded. Where surgery was not performed, details of conservative management were recorded. All in-hospital deaths were recorded, with dates and causes of death.

Participant follow-up

All patients were given appointment dates for follow-up at 30, 90, 180 days and at one-year post HF. For those unable to attend any appointment (usually due to impaired mobility or transport concerns), telephone interviews were conducted with the patient and/or their next-of-kin, to minimise loss to follow-up. Patients telephoned prior to each appointment. If a patient had died then the date and cause of death (if known), were recorded based on next-of-kin report. It was not possible to search death registry records for patients lost to follow-up.

Ethical approvals

The Biomedical Research Ethics Committee of the University of Kwa-Zulu-Natal (UKZN) granted ethical approval for this study (BF043/09). Approval was obtained from the KZN Provincial Department of Health and from all the hospitals and orthopaedic specialists involved in the patients' care. The study was conducted according to the ethical guidelines and principles of the International Declaration of Helsinki and Guidelines for Good Clinical Practice in the Conduct of Clinical Trials with Human Participants in SA [20].

Sample size calculation

The Epi Info 5 statistical software was used to calculate the required minimum sample size, based on the attainment of an 80% statistical power and 95% confidence interval, with 5% margin of error. The prevalence of established risk factors for osteoporotic HFs namely, age, gender, ethnicity, a prior diagnosis of osteoporosis, a previous fragility fracture and a maternal history of fracture, determined from international published literature, were used to estimate disease exposure as there are limited studies from African populations (Supplementary Table I).

Statistical analysis

Descriptive statistics are presented as mean (SD, standard deviation) for normally distributed continuous data, median (IQR, inter-quartile range) for skewed continuous data and count (percentages) for categorical data. We used the Student's t-test for comparison of two means, Mann-Whitney-U for comparison of two medians and the chi-squared (χ^2) or Fisher's exact test to assess associations between categorical variables.

The mortality rate (MR) was calculated as the numbers of deaths compared to survivors at 30 days and one year, excluding patients lost to follow-up. A Cox proportional hazards model was used to assess predictors of mortality over one year. All variables associated with mortality in the univariate analysis at 30 days and one year respectively, were assessed in the Cox proportional hazards model to identify variables which were independently associated with mortality.

The cohort was ordered by calendar-time. Contributions to risk were censored at the end of the 12 months or when lost to follow-up. Formal likelihood ratio tests for departure from the proportional hazard's assumption were used. No evidence of departure from proportionality was detected for any variable. Kaplan-Meier survival analyses and graphs were generated, and a Log Rank (Mantel Cox) test was performed to test for ethnic and/or gender differences in survival distributions.

Results

Hip fractures patient characteristics

Of 277 individuals with HFs consecutively admitted during the study period, 200 (72.2%) were willing and able to provide informed consent; 53 (19.1%) declined to participate and 24 (8.7%) were unable to provide informed consent due to cognitive impairment. These 77 patients were older than those who consented (80.0 ± 8.9 vs 74.3 ± 8.8; p <0.001). Compared to Indian (n=36; 24.7%) and African (n=21; 24.1%) patients a greater proportion of White patients (n=16; 43.2%) did not participate (p=0.03). Women (n=60) and men (n=17) participated equally (29.4 *vs.* 23.3%; p=0.32).

The baseline characteristics of the 200 patients enrolled are shown in Table I. Their mean (SD) age was 74.3 ±8.8 years; 72% were female; 21.3% were underweight (BMI<18.5kg/m^2). Indian patients comprised 55% (n=110), whilst 33% (n=66) were Africans. The majority of patients were receiving a government 'old-age pension' and had either no education or only primary-level education. Co-morbidities were common with 120 (60%) reporting hypertension, 57 (28.5%) diabetes mellitus, 55 (27.5%) osteoarthritis, 14 (7%) chronic back pain, and 10 (5%) a prior malignancy. Less commonly reported were a history of tuberculosis 8 (4%), rheumatoid arthritis 2 (1%), hyperthyroidism 3 (1.5%), and chronic renal failure 3 (1.5%). Despite 55 (27.5%) reporting a prior fragility fracture since the age of 40 years, only 7 (3.5%) had an established diagnosis of osteoporosis and only two patients were taking anti-osteoporosis treatment. Risk factors for osteoporosis and fragility fractures and details of diet and lifestyle factors are summarised in Table I.

The time between sustaining a HF and admission to hospital was highly variable with a median of 1.0 day (IQR 0.0-3.0 days) and a range of 0-122 days (Supplementary Table II). Only 31 (15.5%) presented to hospital on the same day that they sustained their HF. The longest delay reported was 122 days; this patient initially presented

the day after her fall to a local clinic, where the fracture was not diagnosed and she was sent home. She remained unable to walk and sought further health care four months later.

At admission 65.3% of women and 80.4% of men had an anaemia (female haemoglobin <12g/dL; male <13.5 g/dL), 42% of individuals had hyponatraemia, 41.5% elevated urea, and 34.5% elevated creatinine. The majority had raised CRP [62.5%] and hypoalbuminaemia (58.2%). The mean serum 25 OHD was 38.9 nmol/L ± 22.4 nmol/L with 66.5% patients being either 25 OHD deficient or insufficient (Table I); no ethnic differences were observed in 25 OHD levels. The mean serum PTH was 6.7 ± 3.7 pg/mL and 21% of patients had an elevated PTH level.

Hip fracture management

All patients received skin traction on admission, before 173 (86.5%) underwent surgical fixation. Twenty-seven patients (13.5%) were considered unfit for surgery based on the severity of comorbid medical conditions and were managed conservatively. The type of surgical fixation is shown in Supplementary Table II; the majority received either a sliding hip screw and plate or a bipolar hip replacement. The median time from admission to surgery was 19.0 days (IQR 12.3-25.0 days). A minority of patients, nine (4.5%), received their operation within 48 hours of admission. The longest delay was 75 days; this patient was initially considered too frail for surgery and was discharged, then underwent surgery on readmission. Only one intra-operative death was recorded.

Amongst those who survived their hospital admission, the median length of acute hospital stay was 9.0 days (IQR 12.3-25.0 days). The majority were discharged home (91%) and the remainder to a step-down hospital for rehabilitation.

Post-hip fracture mortality

Of the 200 patients, after 30 days 26 (13.0%) had died, rising to 35 (17.5%) by 90 days, 52 (26.0%) by 6 months and reaching 67 (33.5%). For 8% no further contact was possible after 30 days. Possible reasons included the contact numbers being no longer reachable, individuals relocating/moving, or unknown death.

Amongst the 26 patients who died before 30 days, the MR was similar between men and women (10 [17.9%] vs 16 [14.0%], HR: 0.58, p=0.18, [95% CI (0.27, 1.29)]; and African and Indian patients (13 [19.7%] vs 13 [11.8%], HR 0.78, p=0.20, [95% CI (0.53, 1.14)]. After one-year, MR remained similar between men and women (24 [41.1%] vs. 42 [30.6%], HR: 0.69, p=0.30, [95% CI (0.42, 1.15)]; (Figure IA). When stratified by ethnicity, the MR was greater in African patients, and lower amongst Indian patients (27 [40.9%] vs. 33 [30%], HR: 11.5, p=0.012, [95% CI (1.51, 2.57)]; (Figure IB).

Predictors of 30-day mortality: Unadjusted analysis

As expected, patients managed surgically were more likely to survive than those who were managed conservatively, with 30-day MRs 19 (11.1%) vs 7 (25.9%); (HR: 0.36, p=0.021 [95% CI (0.15, 0.86)]; respectively. Health care factors including time to admission, waiting time to surgery and length of hospital stay did not predict survival (Table II). Age was not associated with 30-day survival (HR: 1.01, p=0.58, [95% CI (0.97, 1.06)]. All those who died were of African or Indian ethnicity.

The clearest predictor of 30-day mortality was the PSMS score, such that for each point scored, a 14% reduction in the risk of death was observed (HR: 0.87, p=0.015, [95% CI (0.77, 0.98)]. All domains of the PSMS except for dressing and walking were associated with 30-day mortality (Supplementary Table III). Consistent with this, we found weak evidence that the IADL score predicted survival to 30-days (HR: 0.93, p=0.066, [95% CI (0.87, 1.01)]. Those who died were less able to cook and manage their own finances prior to their fracture. Whilst the majority of patient-level factors, including comorbidity profiles, did not predict 30-day mortality (Table II), the presence of an elevated urea (≥7.1 mmol/L), a low albumin (≤35 g/dL), and a raised CRP (≥ 10.10 mg/L) all predicted 30-day mortality (Table III). Vitamin D levels were either in the insufficient or in the deficient range in all patients who died and hence it was not possible to analyse its effect on mortality (Table III). While there was a positive correlation between an elevated PTH level and vitamin D deficiency (p=0.005), there was no correlation between an elevated PTH and mortality.

Predictors of one-year mortality: Unadjusted analysis

One-year survival did not appear associated with any lifestyle factor, co-morbidity, or risk factors for fragility fractures (Supplementary Table IV*).* However, time from admission to surgery did predict death, such that for each day of delay the risk of death increased by 2% (HR: 1.02, p=0.022, [95% CI (1.00, 1.04)].

Higher IADL scores were associated with survival, with survivors having a slightly higher IADL score at the time of fracture than those who died over the subsequent year (IADL scores: 23 vs. 21 respectively, HR: 0.96, p=0.078, [95% CI (0.91, 1.01)]; (Supplementary Table IV). Those who died were less able to self-groom, transfer to a bed independently, cook and manage their finances prior to their fracture (Supplementary Table V). At one year, PSMS no longer predicted mortality. The presence of an elevated urea, creatinine and CRP level and a low albumin and vitamin D levels all predicted one-year mortality (Supplementary Table VI).

Differences between African and Indian populations contributing to differences in mortality

Characteristics and risk factors were compared between African and Indian patients to assess potential ethnicity-specific predictors of mortality. No socio-demographic differences were seen between the two groups. Whilst, diabetes mellitus and osteoarthritis were more common in Indian compared to African patients, African patients had a higher frequency of hypertension. Apart from a higher calcium intake in Indians compared to Africans (458.6 ± 214.2 mg vs. 346.4 ± 209.3 mg/day; (HR: 0.97, p=0.009, [95% CI (0.94, 0.99)], no other differences were detected to account for the higher MR in African patients.

Predictors of mortality: Adjusted analyses

In multivariate analyses, no independent predictors of 30-day mortality were identified (Table IV). However, after one-year, elevated serum creatinine and elevated CRP level was identified as the strongest independent predictors of death (Table IV).

Discussion

To our knowledge, this is the first study to document MRs and clinical predictors of mortality in osteoporotic HFs in SA. We report high MRs, 13% and 33.5%, at 30 days and one year respectively. These rates are comparable to two more limited SA studies, the first of which retrospectively reported in-hospital and one-year MR of 14% and 32% respectively, which increased to 39% in the second year, in 57 patients aged 65 years and over, in a public sector hospital in Pretoria, Gauteng Province between 2006-2008. This study included only patients with an intertrochanteric fracture, of whom the majority were White, with only ~20% African [11]. In the second study (2001-2014), similar MRs, 12.5% and 34.3%, at 30 days and one year respectively were seen in patients who underwent cemented hemiarthroplasty for HF [12]. While our one-year mortality is comparable to international studies, the higher 30-day mortality seen in now three SA studies, is double that currently reported in HICs, where the MR has steadily decreased over time [6,21].

The significant association of conservative management, and objective measures of health status, namely, elevated serum creatinine and CRP levels, with death in the univariate and multivariate analysis supports the association of multiple comorbidities with death. Several studies report that an elevated serum creatinine predicts death at one year [22,23]. Hypoalbuminaemia, although not identified as an independent predictor in the multivariate analysis, has also been been reported to predict death [24,25]. Furthermore, the significant association between low vitamin D levels and death at one year in the univariate analysis, suggests that these patients were more likely to be house-bound with limited exposure to sunlight. While PTH levels have also been reported to be associated with increased mortality, independently of vitamin D levels in secondary hyperparathyroidism, in older patients with hip fractures (26), in this study there was no association between an elevated PTH levels and mortality. Possible reasons for the lack of association are a small sample size and just over 20% of patients did not have a PTH level.

Hip fractures typically occur in older persons with multiple comorbidities, both of which are predictors of mortality in other contexts [27-30]. The lower mean age in our study population (74.3±8.8 years) compared to that in HICs (e.g. 82±9.4 years in UK) [31], and our relatively small sample size, may explain the lack of association between age and mortality. Although some clinical information was available regarding comorbidities, these were likely under-reported or under-diagnosed prior to admission given that a relatively large proportion of patients (13.5%) were considered unfit for surgery for medical reasons. This despite both groups (surgical and conservatively managed) having similar prevalence of comorbidity.

Surgery is the definitive treatment for HF and time to surgery a significant predictor of mortality post-fracture [32]. The UK's National Institute for Health and Care Excellence (NICE) recommends surgery as soon as possible after admission [33] and the American and Canadian guidelines recommend surgery within 48 hours of HF [34,35]. Early surgery, within 24 hours, conveyed a significantly lower MR in a Canadian cohort study [36]. Resource availability, high demand, late patient transfer and delayed admission all influence time to surgery [32]. Our study was conducted in the resource-limited public sector with high demands on trauma services; although waiting time for surgery did not predict death in our study, time to admission and surgery were highly variable.

There are few data quantifying ethnic differences in post HF mortality. In the US, a study combining three cohorts reported a higher MR for non-White patients [37]. No studies are available from SSA for comparison, but in this study, the MR was significantly higher in African patients compared to Indian patients. Other than African patients being older than Indian patients, there were no clinical or laboratory explanations for this difference.

In a 2012 meta-analysis of 75 prospective studies poor functional status pre-fracture emerged as one of the 12 strong predictors of mortality post fracture [38]. Several studies report the association of poor walking ability and ADLs on the Katz and Barthel indices, with consequent higher mortality [39-41]. In our study, the PSMS and IADL was used as a measure of function; however, in the multivariate analysis they did not independently predict death. While a higher MR has been reported in men possibly related to a higher burden of chronic diseases [28, 42], this has not been consistently reported [43]. In contrast in our study, the MR in men was similar to women (41.1% vs 30.6%), perhaps due to the small numbers.

Limitations

This study has several limitations. Firstly, the study was undertaken in the public sector and may have led to certain high-risk groups being under-represented, especially White and Indian men and women; better access to theatre and intensive care units in private facilities may improve mortality. Furthermore, patients who refused or were unable to participate limit study generalisability. The relatively small number of patients, with 8% loss of follow up, will have influenced the ability to confirm known associations. It is unlikely that all those lost to follow up died, given that the MRs in this study, are broadly in keeping with studies from other LMICs. Co-morbidities were self-reported and are likely to have been understated. Finally, it is challenging to measure weight in the context of a HF and future studies should include alternative options for weight measurement.

Conclusions

This study of post HF mortality in urban SA reports that one in three patients dies over the course of a year; a substantial number did not receive surgery for their fracture, despite a strong evidence base for this procedure. In those who did, delays to surgery were common suggesting that although national guidelines endorsed by the National Osteoporosis Foundation of South Africa and Orthopaedic Society exist, these are not commonly followed [44]. This study therefore highlights the need to increase prioritisation of services for fragility HFs.

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BC: Study concept and design, analysis and interpretation of data, and preparation of manuscript.
CLG: analysis and interpretation of data, and preparation of manuscript

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