

A review of gender differences in proximal humerus fractures

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Summary. Proximal humerus fractures account for 4-5% of all fractures and are particularly frequent in the population of patients aged over 65 of both sexes. Moreover, their number is steadily increasing and, according to recent estimates, it might triple over the next 30 years. Despite the complexity of the problem, there is only limited evidence in literature of gender differences in proximal humerus fractures. According to existing data, these fractures are more common in the elderly female population, together with other fragility fractures such as wrist and proximal femur fractures. However, there is evidence that the mortality rate in patients with proximal humerus fractures is higher in the male population. The purpose of this study is to provide a review of the literature about gender differences in men and women with proximal humerus fractures in terms of incidence, anatomical and structural bone characteristics and mortality rate.

Key words: proximal humerus fractures, gender differences, incidence, anatomy, mortality rate.

Differenze di genere nelle fratture di omero prossimale: una review

Riassunto. Le fratture del terzo prossimale di omero rappresentano circa il 4-5% di tutte le fratture, essendo particolarmente frequenti nella popolazione di pazienti di età superiore ai 65 anni di entrambi sessi. Inoltre il loro numero è in costante aumento e, secondo stime recenti, potrebbe triplicare nei prossimi 30 anni. Nonostante la complessità del problema, evidenze circa differenze di genere nelle fratture di omero prossimale sono molto limitate. Dai dati esistenti in letteratura emerge come queste lesioni siano più frequenti nella popolazione femminile con età superiore ai 65 anni, al pari di altre fratture da fragilità come quelle di polso e del femore prossimale. Tuttavia il tasso di mortalità a seguito di queste lesioni sembra essere più elevato nel sesso maschile. Lo scopo di questo studio è di fornire una review della letteratura circa le differenze di genere tra uomini e donne con fratture del terzo prossimale di omero in termini di incidenza, caratteristiche ossee anatomiche e strutturali e tasso di mortalità.

Parole chiave: fratture di omero prossimale, differenze di genere, incidenza, anatomia, mortalità.

Introduction

Proximal humerus fractures (PHF) are the seventh most frequent fracture in adults, and the third in patients over 65, following wrist and femoral neck fractures. They represent 5.7% of diagnosed fractures¹. The incidence of proximal humerus fractures has been growing steadily, and it has been suggested that the rate might triple over the next 30 years. Kannus et al.² analysed PHF in patients 60 years of age and over, admitted to Finnish hospitals between 1970 and 1998. According to their research, the number and incidence (per 10⁵ persons) of fractures increased sharply from 208 (number) and 32 (incidence) in 1970 to 1,105 and 110 in 1998. Even after age-adjustment, the incidence of fractures showed a clear increase: in women from 50 in 1970 to 133 in 1998, and in men from 14 in 1970 to 49 in 1998. Lind T et al.³ noted that in 730 cases of PHF, 29% of the patients needed to be hospitalized; 75% of these were over 60 and only 21% underwent surgery, which represents 583 hospital days per year for a Danish city of 250,000 inhabitants.

Despite the magnitude of the problem, research on gender differences in fragility fractures has commonly focused on proximal femoral fractures because they represent the most dramatic consequence of the disease, and by their very nature demand urgent treatment^{4,5}. In contrast with this intensive research, little is known about gender differences in proximal humerus fractures. It may be argued that a fracture of the upper limb is less limiting because it does not prevent walking, but it can play a considerable role in depriving patients of their independence^{4,5}. This is usually temporary but in 6% of cases it may lead to permanent residence in a nursing home. Fractures of the upper limb also demand considerable allocation of resources. One-third of such fractures require surgical treatment and 37% in-patient rehabilitation. Furthermore, fractures of the proximal humerus are associated with longer in-patient rehabilitation than any other fracture of the upper limb^{4,5}.

In this review of the literature, gender-related differences in patients with proximal humerus fractures are analysed.

Incidence differences

As highlighted by Launonen et al.¹, the total incidence rate of PHF both in males and females is underestimated, since discharge registers include only hospitalized patients and thus exclude patients treated on an outpatient basis in emergency departments. In addition, a great number of proximal humerus fractures in Nordic countries are treated on an outpatient basis at local health care centers, and these patients are also not included in hospital discharge registers. However, population-based studies including both inpatient and outpatient data, reveal a higher incidence of fractures in the female group. In Rochester, Minnesota, USA, unadjusted incidences were observed to be 30 per 100,000 person-years for males and 71 per 100,000 person-years for females, as measured from 1965 to 1974⁶. In Copenhagen, Denmark, the incidence was 48 per 100,000 person-years for males and 142 per 100,000 person-years for females, as measured in 1983⁷. In a study conducted in South Korea over a period of 4 years, the incidence of proximal humerus fracture increased from 104.7/100,000 in 2008 to 124.7/100,000 in 2012 in women and from 45.3/100,000 in 2008 to 52.0/100,000 in 2012 in men, respectively. In terms of the gender-specific distribution of proximal humerus fracture from 2008 to 2012, the incidence of proximal humerus fracture in women (19.1%) was higher than in men (14.8%)⁸. Finally, a study conducted in Edinburgh, Scotland, from 1992 to 1996 did not determine the total incidence, but observed peak incidence rates among 80- to 89-year-old females of 260 per 100,000 person-years and 109 per 100,000 person-years among males⁹.

The greater involvement of the female gender in terms of PHF has been also reported by others studies¹⁰⁻¹², as summarized in Table 1.

While incidence of humerus fracture is said to be higher in women, men tend to be younger at the time of trauma. A recent study by Wilson et al.¹³ showed that proximal humeral fractures occur an average of 10 years

earlier in male patients compared to female patients. These male patients were also more likely to have sustained their proximal humeral fracture due to higher-energy mechanisms of injury than females (32.4% versus 7.9%; $p < 0.0001$). This suggested the trend of females presenting with proximal humeral fractures comprising individuals with fragility fractures sustained from low-energy falls, whereas males were more likely to present with high-energy injuries at a younger age. This distinction is important because the threshold for surgical treatment of fragility fractures where poor quality bone may hinder stable fixation is likely to be higher than in higher-energy fractures in younger patients.

Finally, in a 9-year study, Bahrs et al.¹⁴ showed that complex fractures tend to occur more often in younger male patients, which can be explained by the high ratio of high-energy traumas in this group. Secondly, in this study, the vast majority of patients consisted of female patients aged over 60 years who accounted for more than half of the patient population. Thus, authors demonstrated an association between high fracture complexity and female gender with an age over 60 years. In this group, complex fractures were observed more often than in age-matched males and were the result of a low-energy trauma in the majority of cases. In general, this may be associated with underlying osteoporosis.

Structural and anatomical differences

Traditionally, the increased risk of osteoporotic fracture in women compared to men has been attributed to their low bone mass as a consequence of reduced peak bone mass acquisition and increased rates of bone loss following menopause¹⁵. However, more recent studies indicate that several other factors influence fracture risk independently from BMD (bone mineral density), such as skeletal geometry and the material properties of bone¹⁶. In particular, in the proximal humerus, bone microarchitecture is of major importance, as reduced

Table 1. Summary of differences in humeral fractures incidence between genders.

| | Country | Period | Female incidence (100.000) | Male incidence (100.000) |
|---------------------------------------|-------------|-----------|----------------------------|--------------------------|
| Rose et al., 1982 ⁶ | USA | 1965-1974 | 71 | 30 |
| Kristiansen et al., 1987 ⁷ | Denmark | 1983 | 142 | 48 |
| Park et al., 2015 ⁸ | South Korea | 2008-2102 | 124 | 52 |
| Hagino et al., 1999 ¹⁰ | Japan | 1995 | 48 | 17 |
| Sakuma et al., 2008 ¹¹ | Japan | 2004 | 63 | 9 |
| Péntek et al., 2008 ¹² | Hungary | 1999-2003 | 84 | 47 |

bone quality complicates the surgical treatment of humeral fractures. In a histomorphometric analysis studying the distribution of bone volume per tissue volume (BV/TV) in proximal humerus, Barvencik et al.¹⁷ found that women over 60 years have a significant loss of bone mass in the medial and especially in lateral region of the proximal humerus compared to women younger than 40 years. This pronounced age-related decrease in BV/TV values was not present in men. The pronounced decrease of bone mass in the lateral region of the humeral head points to a structural weakness, which can explain the high incidence of avulsion fractures of the greater tuberosity in women and highlights this region as an osteoporotic fracture site.

Furthermore, there are gender differences in humerus skeletal geometry that may contribute to the greater risk of fracture in women compared to men. For example, long bone cross-sectional area is greater in men, which is thought to reflect higher rates of periosteal apposition from the time of puberty onwards¹⁵. One study of 68 girls and 59 boys aged 11.9 years, who underwent prospective peripheral quantitative computed tomography (pQCT) measurements, reported that periosteal growth was more rapid in pubertal boys compared to girls¹⁸.

Periosteal apposition plays an important role in establishing sex differences in bending strength in young adulthood and in maintaining or amplifying these sex differences in the face of bone loss during advancing age¹⁹. The reason for this is that the bending strength of a unit of bone mineral is proportional to the fourth power of the distance from the neutral axis, thus reflecting the lower risk of PHF in men.

In a study conducted on a sample of 1,317 children, Clark et al.¹⁵ found that humeral width and length were positively related to age and height in boys and girls combined, and to pubertal status in girls. In contrast, age, height and pubertal status did not influence the ratio between humeral width and length, presumably reflecting the action of mechanisms to ensure that skeletal shape remains constant as bones grow. In both pre- and early pubertal boys, humeral length was found to be shorter compared with girls, whereas humeral width was greater. Taken together, these findings suggest that gender, not puberty, affects the balance between periosteal and longitudinal growth. Hence, differences in overall skeletal shape between boys and girls, with humerus being wider in boys, appear to be established prior to puberty.

Mortality differences

In the literature, the mortality rate after humerus fractures is rarely discussed and, if mentioned, it is usually analyzed together with other fractures that do not affect the hips and vertebrae. This makes it difficult to evaluate

gender differences in patients with proximal humerus fractures. In most of the existing literature, the survival pattern in patients with PHF is similar to that reported in many studies of hip fracture, with an increase in the mortality rate 6–18 months after the fracture and a higher mortality rate in men than in women^{20–23}.

In a case-control study of 253 patients with a 12-year follow-up, Olsson et al.²⁴ reported that proximal humerus fractures were associated with excess mortality in men (HR: 5.4; 95% CI: 1.6–17.7), but not in women (HR: 1.0; 95% CI: 0.4–2.3). In this study, the mortality rate after proximal humerus fracture was higher than that of the general population even though the mortality rate decreased throughout the study period. Moreover, the most common causes of death in patients and controls were cardiovascular disease and malignancies. Similar results are reported by Piirtola et al.²⁵ In their population-based study with a 12-year follow-up, the authors reported that proximal humerus fractures were associated with excess mortality, but only in men (HR 5.4, 95% CI 1.6–17.7).

Shortt and Robinson²⁶ found that older age, male gender and the use of walking aids predicted mortality after proximal humerus fracture. They also identified factors associated with social independence to be predictive of mortality, finding patients no longer living in their own home to have an increased risk of mortality. Other reports confirmed that poor functional outcome after proximal humerus fractures was associated with social independence.

In contrast to previous studies, Wilson et al.¹³ found that female gender was associated with an increased risk of mortality. When combined with the demonstrated overall increased incidence of fracture in females and the trend toward females sustaining more low-energy fractures at older ages, this increased mortality in females appeared to be consistent. In particular, the 1-year mortality rate after proximal humeral fracture was found to be 9.8%. This is more than double the 4.25% background mortality calculated for this population.

Several studies have tried to analyze the reasons for higher mortality after proximal humerus fracture in both genders. According to recent literature, this aspect might be related with the associated fracture. In fact, proximal humerus fracture is associated with an increased risk of sustaining associated fractures⁸. Clinton et al.²⁷ reported that the humeral fractures are associated with a fivefold increased risk of subsequent hip fracture in the following year. Both hip and humerus fracture are shown to be associated with several factors indicating poor health²⁸. Clement et al.²⁹ reported that the standardized mortality ratio at one year was significantly greater after sustaining multiple fractures that included the proximal humerus fracture (2.06 SMR for single fracture and 4.95 SMR for multiple fractures, including proximal humer-

us fracture). They suggested that the combined fractures of the proximal humerus and femur were associated with the highest mortality risk at one year.

Conclusion

Studies on gender differences in proximal humerus fractures are limited in literature. However, this type of fracture is frequent and its prevalence is increasing. Ageing population is the cause, resulting in a population that is in poor general conditions with an increased risk of falling on increasingly fragile bone. According to existing data, the most patients suffering proximal humerus fracture are elderly women who sustain low-energy falls. On the contrary, males are more likely to present with high-energy injuries at a younger age. Osteoporosis, anatomical and bone structural characteristics play a role in determining these gender differences.

Key messages

- Proximal humerus fractures are particularly frequent in the population of patients aged over 65 of both sexes. The number of proximal humerus fractures is steadily increasing and it might triple over the next 30 years.
- According to existing data, most patients suffering proximal humerus fracture are elderly women who sustain low-energy falls.
- Males are more likely to present with high-energy injuries at a younger age.
- Osteoporosis, anatomical and bone structural characteristics play a role in determining these gender differences in fractures.
- There is evidence that the mortality rate in patients with proximal humerus fractures is higher in the male population.

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