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The impact of second hip fracture on rehospitalization and mortality in older adults

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THE IMPACT OF SECOND HIP FRACTURE ON REHOSPITALIZATION AND MORTALITY IN OLDER ADULTS

Running head: second hip fracture in older people

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HIGHLIGHTS

- One out of six patients admitted for hip fracture were suffering for a second event
- >80% of patients admitted for second hip fracture were not on antiresorptive therapies
- Second hip fracture may increase risk of rehospitalization and mortality more than the first event

ABSTRACT

Purpose. Although a second hip fracture is not uncommon in the older population, the extent to which such an event may affect health-related outcomes has not been fully clarified. We aimed to evaluate the risk of new falls, functional decline, rehospitalization, institutionalization and mortality in older patients admitted for a second vs. a first hip fracture.

Methods. The sample consisted of 289 older patients admitted to the Orthogeriatric Unit of Bolzano Hospital (northern Italy) and surgically treated for a hip fracture from June 2016 to June 2017. Socio-demographic data and hospitalization-related information were collected and a multidimensional assessment was made upon admission and during the hospital stay. Fifteen months after discharge, data on mobility level, functional status, institutionalization, and new falls were obtained from personal or structured phone interviews. Information on rehospitalization and mortality was obtained from local hospital registers.

Results. One out of six patients (14.6%) admitted was suffering a second hip fracture, of which only 16.7% were on antiresorptive therapies. At the 15-month follow-up, individuals who had been treated for a second hip fracture were more likely than those treated for their first to have low mobility levels (OR=4.13, 95%CI:1.23-13.84), to be rehospitalized (OR=2.57, 95%CI:1.12-5.90), and to have a higher mortality (HR=1.81, 95%CI:1.05-3.12).

Conclusions. The occurrence of a second hip fracture may further affect the clinical vulnerability and mortality of older adults. These results highlight the need to implement preventive action to minimize the risk of re-fracture after the first event.

Keywords: second hip fracture; disability; hospitalization; institutionalization; mortality.

1. INTRODUCTION

Fractures are the most common and harmful consequences of accidental falls, especially in older people, who present a high prevalence of osteoporosis (Hernlund et al., 2013; Kanis JA on behalf of the World Health Organization Scientific Group, 2007). Hip fractures are the most feared of these events due to their substantial impact on health status and quality of life (Papadimitriou et al., 2017). Unfortunately incidence of hip fractures is on an upward trend (Chen et al., 2014). In the USA, more than 300,000 people suffer a hip fracture every year, and this number is expected to grow to 500,000 by 2040 (Hung & Morrison, 2011). Similar data have been reported in European countries, e.g. in Italy the annual cumulative incidence of hip fractures ranges between 40,000 and 90,000 (Piscitelli et al., 2012).

The impact of a hip fracture on an individual's health is extremely important. Indeed, hip fractures are associated with a 5- to 8-fold increase in all-cause mortality within the first 3 months (Haentjens et al., 2010). This increase in mortality persists also in the long-term suggesting that, in addition to the direct and indirect complications of hip fracture, other mechanisms may contribute to such excess risk (Haentjens et al., 2010; Katsoulis et al., 2017). Among these, the worsening of pre-existing chronic conditions and the accumulation of new comorbidities after the fracture are relevant but not the unique involved aspects. Another strong contributor can be the progressive limitation of mobility and self-sufficiency (Papadimitriou et al., 2017). Following a hip fracture, in fact, the cumulative incidence of dependency in daily activities ranges from 20 to 90%, and patients' recovery rates are slow and often incomplete (Magaziner et al., 1990, 2000), making hip fractures a significant problem for family and society (Hung & Morrison, 2011). Both the onset of mobility impairment and disability may be supported by the exacerbation of inflammatory status that

has been inversely associated to functional recovery (Miller et al., 2006). In addition, chronic inflammation can be linked to the worsening of health status and to the development of frailty (Van Epps et al., 2016), leading to a greater vulnerability to external stressors that increases the need of hospitalization and nursing home admission (Fried et al., 2001). The detrimental health and functional consequences of a hip fracture may further worsen if individuals experience a second event, making the picture even worse. Unfortunately, the occurrence of a second hip fracture is not uncommon scenario since most patients who suffer a hip fracture often present advanced age, frailty and severe osteoporosis that, overall, increase their risk of another fall-related fracture. As a matter of fact, after the first event, 19% of those who have had one fracture will suffer another in the following years (Galler et al., 2018; Guy et al., 2017). Of these, in more than half of cases, the second hip fracture is contralateral and occurs mostly within 4 years of the initial event (Galler et al., 2018).

Although the risk factors associated with hip fractures and the consequences of these events have been widely assessed (Berry et al., 2007; Pearse et al., 2003; Ryg et al., 2009; Sawalha & Parker, 2012), the factors more likely to be associated with a second fracture occurring and its impact on health-related outcomes are as yet less clear. More in-depth investigation of second hip fractures is needed to provide information for use in planning preventive strategies after the first event in order to promote the functional recovery of this particularly vulnerable group of older people.

In light of the above considerations, we aimed to assess the characteristics of older people who experienced a second hip fracture and the negative health-related outcomes of the event, i.e. mobility limitations, new falls, hospitalization, nursing home admission and mortality, compared with patients experiencing a first hip fracture. Our hypothesis was that a second hip fracture would have a greater impact on negative outcomes, such as mortality and mobility limitations, compared with the first event.

2. METHODS

2.1 Study design, setting and population

This is a prospective study that involved patients aged ≥65 years admitted to the Orthogeriatric Unit at the Bolzano Hospital (northern Italy) between June 2016 and June 2017 after a hip fracture. From an initial sample of 299 older patients, we excluded 6 individuals who died before undergoing surgery, and 5 who did not undergo hip fracture surgery, resulting in a final sample of 288 (73 males and 215 females). After a mean follow-up period of 15 months, 79 patients had deceased, and 35 had dropped out, leaving 174 patients who underwent a second evaluation through personal interviews (n=57) or, for those who had difficulties returning to the hospital for the follow-up assessment, structured phone interviews (n=117). Compared with patients who died or who underwent the follow-up assessment, those who dropped out were more likely to be younger (median [IQR] age 83 [80-87] vs. 88 [82-91], p=0.001), to live at home (97.1% vs. 81.8%, p=0.02), and to have a better functional status (median [IQR] pre-fracture Barthel Index [BI]: 100 [70-100] vs. 75 [50-100], p<0.001) and health status (median [IQR] Cumulative Illness Rating Scale [CIRS] - Comorbidity Index: 2 [1-3] vs. 3 [2-4], p<0.001). There were, however, no significant differences between these two groups in sex distribution and in the frequencies of second hip fracture, cognitive impairment and polypharmacy.

The study was carried out in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments, and the local ethical committee approved the protocol. All participants (or their next of kin) were fully informed about the nature, purpose and procedures of the study, and gave their written informed consent.

2.2 Data collection

Upon hospital admission, physicians assessed the patients and collected sociodemographic data (age, sex, living arrangements). They also carried out a multidimensional assessment of: functional status using the BI (Mahoney & Barthel, 1965); the use of a walking aid and level of mobility, measured with the Fracture Mobility Score (Voeten et al., 2019) and categorized as medium-high (mobile without aids, mobile outdoors with aids, or moving autonomously indoors) vs. low (mobile indoors with assistance or the use of a deambulator, or completely unable to walk); clinical complexity using the CIRS Comorbidity Index (CI) and Severity Index (SI) (Linn et al., 1968); polypharmacy, defined as the use of more than 5 drugs/day (Hajjar et al., 2007); the use of diuretics, benzodiazepines, opioids, antihypertensives, β-blockers, antidepressants, antipsychotics and steroids; and the presence of physician-diagnosed cognitive impairment. The following data were also collected during hospitalization: date of hip fracture, side and type; history and date of previous hip fractures (ipsilateral or contralateral); type of surgery, categorized as total/partial hip arthroplasty vs. internal fixation(Miyamoto et al., 2008); timing of operative repair (within ≤ vs.>48h of hospital admission); and beginning of rehabilitation during hospital stay.

After a mean follow-up period of 15 months, living arrangements (living at home vs. living in a nursing home), functional status (BI), mobility level, and the occurrence of new falls since hospital discharge, were assessed in the 174 patients with whom we carried out follow-up visits or structured phone interviews. Data on the number of hospitalizations and the vital status of all participants over the study period were obtained from the local hospital registers. For the purposes of our study, we considered the following health-related outcomes:

- functional change, defined as the difference between pre-fracture and post-fracture BI;
- mobility limitation, categorized as stable medium-high mobility level vs. stable low mobility level vs. worsened mobility level (i.e. from medium-high to low mobility level);
- new admission to nursing home (only for participants who were living at home at hospital admission);

- occurrence of at least one fall after hospital discharge, defined as any "event which results in a person coming to rest inadvertently on the ground or floor or other lower level", in accordance with the WHO definition (World Health Organization, 2007);

- occurrence of at least one hospitalization after hospital discharge;

- mortality.

2.3 Statistical analyses

Quantitative variables are expressed as means ± standard deviations, and discrete variables as frequency percentages. Characteristics of participants who were admitted for first vs. second hip fractures were compared using the Student's t-test for normally distributed continuous variables, the Mann-Whitney test for non-normally distributed variables, and the Chi-square test for discrete variables. Multinomial logistic regression analyses were run to investigate the association between having experienced a second hip fracture (*exposure*) and mobility limitation, new falls, rehospitalizations and nursing home admission (*outcomes*). The strength of these associations was expressed as odds ratios (ORs) with 95% confidence intervals (CIs). In these analyses, we excluded from the initial sample 12 patients (4.2%) who were admitted for a first hip fracture and who experienced a second during the follow-up period, since the latter events could have influenced the outcomes examined and may lead to misclassification bias. For each outcome, we performed multinomial models considering having experienced a second vs a first hip fracture, as main exposure, and taking death as an alternative outcome. Analyses were first adjusted by age and sex (Model 1), then also for potentially confounding factors for the associations tested based on the current literature and the biological plausibility of their effects (Model 2). The predictive strength of Model 1 and 2 were evaluated through pseudo R-squared, computed with the McFadden method. The association between having experienced a second hip fracture and all-cause mortality over the 15-month follow-up was tested by Cox regression and illustrated with Kaplan-Meier curves. To take into account the incidence of hip fractures during the follow-up period, we considered the second hip fracture

as a time-varying variable. The strength of this association was expressed as a hazard ratio (HR) with a 95%CI. Analyses were performed using SPSS 21.0 for Windows (Armonk, NY: IBM Corp) and R (*R Development Core Team (2008). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org.*, n.d.). Statistical tests were two-tailed and statistical significance was assumed for a p-value <0.05.

3. RESULTS

Of the 288 patients included in our study, 42 (14.5%) had been admitted for a second hip fracture, which had occurred after a median period of 2.7 years (IQR: 0.8-5.7 years) from the first event (31% within the first year); in 76.2% of these cases (n=32) the contralateral hip was affected. The characteristics of the sample as a whole and by occurrence of a second hip fracture are reported in **Table 1**. As can be seen, the median age of the patients was 87 (IQR: 82-91), and the median CIRS-CI was 3 (IQR: 2-4), with no significant differences between groups. Regarding functional status, the median pre-fracture BI of the sample was 75 (IQR: 50-100), but patients who had experienced previous hip fractures had significantly lower values than those at their first event (65 [IQR: 38.8-81.3] vs. 80 [IQR: 55-100], p=0.01). More than half the people with a second hip fracture had already had low mobility levels at admission, while around a third of those with a first hip fracture were found to have low mobility levels (p<0.001). Although no significant between-group differences were found with regard to the prevalence of polypharmacy, patients who experienced a second hip fracture were more likely than their counterparts to use antipsychotics (33.3% vs. 17.1%, p=0.01), diuretics (54.8% vs.40.7%, p=0.09) and antidepressants (42.9% vs. 28.9%, p=0.07), but less likely to use antihypertensive drugs (38.1% vs. 59.8%, p=0.01). Among the second hip fracture group, we found that 7 patients (16.7%) were taking antiresorptive therapies, while 15 (35.7%) were taking vitamin D, and 8 (19%) calcium supplements (data not shown).

Table 2 shows the results of the logistic regression for the association between the presence of a second hip fracture at hospital admission and health-related outcomes assessed after 15 months. After adjusting for potential confounders, patients who suffered a second hip fracture were more likely than those admitted for the first to maintain their low mobility levels (OR=4.13, 95%CI: 1.23-13.84) and to be rehospitalized at least once (OR=2.57, 95%CI: 1.12-5.90) during the follow-up period. With regards to both the risk of nursing home admission and the difference in BI loss we found no significant differences between the first (median [IQR] ΔBI: -20 [-40; -5]) and second hip fracture group (median [IQR] ΔBI: -15 [-27.5; -3.8]; p=0.24 from the Mann-Whitney test, data not shown).

During the study period, 18 patients who suffered a second (42.9%) and 61 patients a first hip fracture (24.8%) died (the survival curves for both groups are illustrated in **Figure 1**). The Cox regression, after adjusting for potential confounders, revealed that patients who experienced a second hip fracture had an 81% higher risk of mortality (HR=1.81, 95%CI: 1.05-3.12) than those admitted for a first hip fracture (**Supplementary Table 1**).

4. DISCUSSION

This study shows that, compared with a first hip fracture, the occurrence of a second hip fracture is associated with a worse prognosis in terms of mobility limitations, the need to be rehospitalized, and mortality.

Our findings confirm that a second hip fracture is not uncommon in older people. Indeed, almost one in six patients admitted to our Orthogeriatric Unit had experienced a second hip fracture. These findings are in line with previous reports, which found a cumulative incidence of second hip fracture of around 15% over a median 4.2-year follow-up period (Berry et al., 2007). Although some studies found that the second hip fracture was more likely to occur within one year of the prior event (Ryg et al., 2009; Yamanashi et al., 2005), we found, as did other studies (Berry et al., 2007; Chapurlat et al., 2003; Mitani et al., 2010; Sawalha & Parker,

2012; Schroder et al., 1993; Sheikh et al., 2019), a longer median time interval, i.e. 2.7 years, between the first and second fractures. These slight discrepancies may be due to the characteristics of the sample. Indeed, on the one hand, the older age and greater clinical complexity of our patients compared with those of previous studies (Ryg et al., 2009; Yamanashi et al., 2005) may have made them more vulnerable to new fractures. On the other hand, however, the first fracture in such frail older population may have resulted in substantial deficits in physical performance, which may either increase (Welmer et al., 2016) or, paradoxically, reduce the risk of new falls and fractures by limiting mobility.

Comparing the characteristics of patients who experienced a first vs. a second hip fracture at hospital admission, we found no significant differences between them either in the number and severity of comorbidities or in the prevalence of polypharmacy. However, among the medications used, we found that some fall-risk-increasing drugs (Woolcott et al., 2009), such as antipsychotics, diuretics, and antidepressants, were more likely to be used by those who experienced a second hip fracture. These data should alert physicians to the need to review the patient's therapy after repairing the fracture, in order to avoid the administration of drugs that could increase the risk of a new fall. A further interesting issue that emerged from our study, and in line with a previous work (Lönnroos et al., 2007), concerns the infrequency (<20%) of osteoporotic treatment in older adults who had already experienced a first fracture. This shows the need to raise awareness among physicians of the necessity for secondary prevention of hip fractures in older adults, which should, however, take into account the real potential benefit of antiresorptive drugs based on individual life expectancies and patients´ preferences (Scottish Government Polypharmacy Model of Care Group & Group, 2018). The intervention at the pharmacologic level, however, should be accompanied by the promotion of behavioral and environmental strategies that may help preventing falls in older adults (Rubenstein, 2006), especially in those who already present deficits in physical function due to a previous hip fracture.

With regard to self-sufficiency and physical performance, patients with a second hip fracture had significantly worse functional and mobility levels at ward admission than patients at their first event, the difference between the groups being almost 20 points on the BI. These findings may have affected our results regarding the association between re-fracture and functional decline and mobility limitation. We found that after the second fracture, patients who survived had a four-fold higher risk of their mobility level staying low and of remaining in a nursing home, but the results for worsening mobility or changes in BI over the follow-up period were not significant. Although some studies found that a second hip fracture seemed to have a greater impact on independent walking than a first event did (Fukushima et al., 2006; Pearse et al., 2003), others instead found significantly fewer patients with hip re-fracture experiencing worsening levels of mobility one year after the event (Sawalha & Parker, 2012). A possible explanation offered by the authors for these data, that could also be valid for our results, was that since patients admitted for the first hip fracture had significantly better self-sufficiency and mobility before the event, they had "more to lose" in terms of functional worsening compared with those admitted for the second hip fracture.

Our study suggests, however, that the greater burden of second hip fracture compared with the first event may also manifest as a higher risk of rehospitalization and mortality. Concerning the need for hospital care, evidence from the current literature largely shows that patients who experience a hip fracture have an increased risk of further hospital admissions (Boockvar et al., 2003; Kates et al., 2015; Lee et al., 2017). Interestingly, our study shows that this higher risk of rehospitalization might be further exacerbated by a second hip fracture, which seems, therefore, to have a greater impact on the clinical vulnerability of older patients. In keeping with this view and in line with previous studies (Berry et al., 2007; Ryg et al., 2009; Sawalha & Parker, 2012), we found that a second hip fracture significantly influenced mortality, the risk of which was more than twice that observed after the first event. We acknowledge that differences in the sociocultural contexts and healthcare systems between

our study and previous ones may have given rise to these different findings. However, overall our work suggests that the occurrence of a second hip fracture negatively impacts on health status not only by consolidating limitations in mobility, but also by increasing the individual's vulnerability to external stressors, which may result in hospital care being needed.

Among the limitations of our work, the small sample size and the relatively short follow-up period could have influenced our study results by reducing the statistical power and possibly underestimating the effect of second vs first hip fracture on negative health-related outcomes. A further issue concerns the evaluation of functional status only using the BI, which did not allow to investigate the impact of second vs first hip fracture on basic and instrumental daily activities. On the other hand, the prospective study design and the number of variables investigated may be considered some of the strengths of our work.

In conclusion, our study highlights the association between the occurrence of a second hip fracture in older adults and a higher risk of hospital admission and mortality. These findings draw attention to the importance of secondary prevention in older patients at their first hip fracture, acting both at the environmental/behavioral and pharmacologic level, in order to limit the risk of new fracture events and the related burden on their health.

CRediT author statement

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FIGURE LEGEND

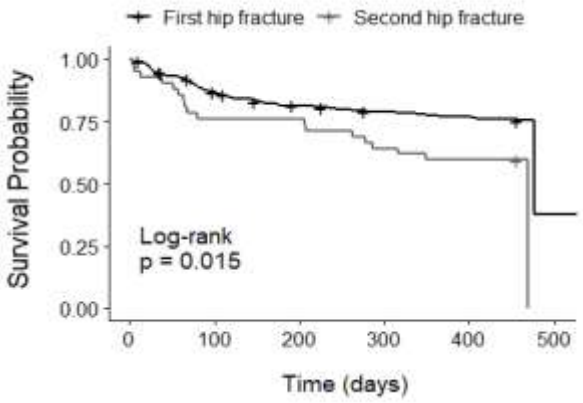

Figure 1. Survival curves of patients admitted for first vs. second hip fractures over a 15-month follow-up period

Table 1. Characteristics of the sample stratified by the presence of a second hip fracture

Baseline characteristics	All (n=288)	First hip fracture (n=246)	Second hip fracture (n=42)	p-value
Age (years)	87 (82-91)	87 (82-91)	87 (83.8-92)	0.89
Sex (women)	215 (74.7)	183 (74.4)	32 (76.2)	0.80
Living in nursing home	47 (16.3)	36 (14.6)	11 (26.2)	0.06
Cognitive impairment	105 (36.5)	86 (35.0)	19 (45.2)	0.20
CIRS-Severity Index	1.5 (1.4-1.7)	1.5 (1.4-1.7)	1.5 (1.5-1.7)	0.48
CIRS-Comorbidity Index	3 (2-4)	3 (2-4)	3 (2-4)	0.70
Use of >5 drugs/day	161 (55.9)	134 (54.5)	27 (64.3)	0.24
Use of medications				
Diuretics	123 (42.7)	100 (40.7)	23 (54.8)	0.09
Benzodiazepines	82 (28.5)	70 (28.5)	12 (28.6)	1.00
Opioids	31 (10.8)	24 (9.8)	7 (16.7)	0.19
Antihypertensives	163 (56.4)	147 (59.8)	16 (38.1)	0.01
β-blockers	72 (25.0)	61 (24.8)	11 (26.2)	0.86
Antidepressants	89 (30.9)	71 (28.9)	18 (42.9)	0.07
Antipsychotics	56 (19.4)	42 (17.1)	14 (33.3)	0.01
Steroids	19 (6.6)	17 (6.9)	2 (4.8)	0.60
Pre-fracture Barthel Index	75 (50-100)	80 (55-100)	65 (38.8-81.3)	0.01
Pre-fracture use of walking aid	150 (52.1)	120 (48.8)	30 (71.4)	0.01
Pre-fracture low mobility level	101 (35.1)	76 (30.9)	25 (59.5)	<0.001
Hip fracture type				
Intracapsular	138 (47.9)	123 (50.0)	15 (35.7)	0.09
Extracapsular	130 (45.1)	108 (43.9)	22 (52.4)	0.31
Other	20 (6.9)	15 (6.1)	5 (11.9)	0.17

Time to surgery (≤48h)	186 (64.6)	160 (65.0)	26 (61.9)	0.70
Type of surgery				0.51
Partial/total hip arthroplasty	123 (42.7)	107 (43.5)	16 (38.1)	
Internal fixation	165 (57.3)	139 (56.5)	26 (61.9)	
In-hospital rehabilitation	225 (78.1)	193 (79.4)	32 (71.1)	0.22

Variables are expressed as numbers (%) and mean±SD or median (25^{th}-75^{th} percentile), as appropriate. *Abbreviations:* CIRS, Cumulative Illness Rating Scale. P-values were obtained from the Student's t-test (quantitative variables) or the Chi-square test (qualitative variables) and refer to the differences between patients admitted for the first vs. the second hip fracture

Table 2. Associations between the occurrence of a second hip fracture (*exposure*) and mobility limitation, falls, hospitalizations and nursing home admission after 15 months (*outcomes*)

	Odds ratios (95% confidence intervals) *P values*	
Study outcomes	**Model 1**	**Model 2**
Mobility limitation[a]		
Stable medium-high mobility level	1 [ref]	1 [ref]
Stable low mobility level	4.11 (1.34-12.64) p=0.01	4.13 (1.23-13.84) p=0.02
Worsened mobility level	1.19 (0.33-4.26) p=0.79	1.32 (0.36-4.89) p=0.68
Falls (at least one vs. none)[b,c]	0.63 (0.25-1.62) p=0.34	0.74 (0.28-2.00) p=0.56
Hospitalizations (at least one vs. none)[d,e]	2.35 (1.05-5.28) p=0.04	2.57 (1.12-5.90) p=0.03
Nursing home admission[b,f]		
Stably living at home	1 [ref]	1 [ref]
Stably living in nursing home	3.32 (1.24-9.64) p=0.03	3.66 (0.95-14.15) p=0.06
New nursing home admission	2.23 (0.69-7.18) p=0.18	1.95 (0.55-6.86) p=0.30

Model 1 is adjusted for age and sex. *Model 2 is also adjusted for* pre-fracture living arrangements (at home vs. in a nursing home), use of antipsychotics, Cumulative Illness Rating Scale – Severity Index, and post-fracture rehabilitation. [a]Pseudo R-squared=0.07 (Model 1) and 0.18 (Model 2). [b]Additional covariates included in Model 2: pre-fracture Barthel Index and use of antihypertensive drugs. [c]Pseudo R-squared=0.05 (Model 1) and 0.16 (Model 2). [d]Additional covariates included in Model 2: Cumulative Illness Rating Scale – Comorbidity Index. [e]Pseudo R-squared=0.04 (Model 1) and 0.09 (Model 2). [f]Pseudo R-squared=0.05 (Model 1) and 0.26 (Model 2). *Note:* Each study outcome was tested separately in multinomial logistic regression analyses, considering second vs first hip fracture as exposure, and taking death as an alternative outcome.