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ORIGINAL ARTICLE

Hip fracture predicts subsequent hip fracture: a retrospective observational study to support a call to early hip fracture prevention efforts in post-fracture patients

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Abstract

Summary In this real-world retrospective cohort, subsequent hip fracture occurred in one in four patients with any initial fracture, most often after hip fracture, on average within 1.5 years. These data support the need for early post-fracture interventions to help reduce imminent hip fracture risk and high societal and humanistic costs.

Purpose This large retrospective cohort study aimed to provide hip fracture data, in the context of other fractures, to help inform efforts related to hip fracture prevention focusing on post-fracture patients.

Methods A cohort of 115,776 patients (72.3% female) aged > 65 (median age 81) with an index fracture occurring at skeletal sites related to age-related bone loss between January 1, 2011, and March 31, 2015, was identified using health services data from Ontario, Canada, and followed until March 31, 2017.

Results Hip fracture was the most common second fracture (27.8%), occurring in ≥ 19% of cases after each index fracture site and most frequently (33.0%) after hip index fracture. Median time to a second fracture of the hip was ~ 1.5 years post-index event. Patients with index hip fracture contributed the most to fracture-related initial surgeries (64.1%) and post-surgery complications (71.9%) and had the second-highest total mean healthcare cost per patient in the first year after index fracture ($62,793 ± 44,438). One-year mortality (any cause) after index hip fracture was 26.2% vs. 15.9% in the entire cohort, and 25.9% after second hip fracture.

Conclusion A second fracture at the hip was observed in one in four patients after any index fracture and in one in three patients with an index hip fracture, on average within 1.5 years. Index hip fracture was associated with high mortality and post-surgery complication rates and healthcare costs relative to other fractures. These data support focusing on early hip fracture prevention efforts in post-fracture patients.

Keywords Osteoporosis · Hip fracture · Imminent risk · Real-world data · Mortality · Healthcare resource utilization

Introduction

Hip fractures pose high societal and humanistic costs. As common as acute myocardial infarction in adults aged ≥ 80 or in women aged ≥ 65, hip fracture prevalence is expected to increase due to an ageing population [1, 2]. They are associated with a median hospital length of stay of 13 days and high healthcare costs, predicted to increase to $2.4 billion by 2041 in Canada alone [1, 3, 4]. Within 1 year post-hip fracture, 25% of patients become institutionalized while 50% of long-term care patients become completely dependent or die [5, 6]. Mortality rate post-hip fracture is similar to that of acute myocardial infarction and partially related to complications of hip fracture surgery such as pneumonia, with

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in-hospital mortality having increased by two- to fourfold during the COVID-19 pandemic in various countries [7–11].

Hip fracture is a hallmark osteoporotic fracture with 70–90% of cases caused by this chronic disease [12]. Of patients with a hip fracture, 50% have a history of prior fracture at another skeletal site, yet these patients represent only 16% of the population targeted for fracture risk assessment [13]. In older adults, prior fracture is a significant predictor of a subsequent hip fracture, especially within the following 2 years [14–16]. Thus, recent clinical practice guidelines recommend considering patients with a recent fracture to be at very high risk for future fracture—known as imminent risk—and in need of a therapy efficacious enough to improve bone strength and reduce fracture risk within 2 years, followed by a maintenance therapy [17–20]. However, in Canada, only an estimated 10–20% and 28% receive fracture-risk assessment and/or management post-any fracture and post-hip fracture, respectively [21–24]. Thus, effective hip fracture prevention strategies are currently challenged by this large care gap.

Meanwhile, Canadian epidemiological studies to help inform efforts related to hip fracture prevention are lacking, with most studies conducted in the last decade focusing on pre- or postoperative management [25–30]. Thus, the primary objective of this large, real-world, retrospective cohort study of Ontarians aged > 65 was to characterize imminent risk of hip fracture by describing the frequency, distribution and median time to subsequent hip fracture, based on the site of initial fracture. The secondary objectives were to describe the frequency and distribution of fracture-related surgeries, surgery-related complications, healthcare costs and mortality 1 year following a hip fracture, relative to other fracture sites.

Methods

This was a population-based retrospective database study conducted in Ontario, Canada (population 14.7 million), using the ICES Data Repository [31]. The primary databases used are provided in Online Resource 1. The study protocol was approved by the Advarra Institutional Review Board.

Study participants

Adults aged > 65 years (i.e. 66 years and older) with an index fracture occurring at an osteoporotic fracture site between January 1, 2011, and March 31, 2015, were identified from hospital admissions, emergency and ambulatory care records using International Classification of Diseases (ICD)-10 diagnostic codes for fracture as a main diagnosis or admitting diagnosis (Online Resource 2). Patients were excluded if they presented with a fracture occurring at a non-osteoporotic site (i.e. skull, face, hands and feet) or associated with a trauma code (Online Resource 3), to minimize the inclusion of high-trauma fractures [32]. Patients were also excluded if they experienced a fracture during the 5-year lookback period prior to the index fracture date to minimize the influence of a pre-index fracture on examined outcomes. Adults aged < 66 were excluded in order to examine medication data in this cohort [4].

Variables of interest and outcome measures

Data were analysed up to March 31, 2017 (Online Resource 4); thus, depending on when the index fracture occurred, opportunity for follow-up was 2 (2015–2017) to 6 years (2011–2017). Index and second fractures occurring at each site were examined over the study follow-up. For second fractures, the same identification criteria were applied as for index fractures. Initial index fracture-related surgeries were assessed using Canadian Classification of Health Interventions codes over the study follow-up (Online Resource 5) and surgery-related complications (infections related to surgery, complications related to prosthetic devices, deep vein thrombosis and pulmonary embolism, pneumonia, myocardial infarction, stroke and cerebrovascular events, fracture resulting from surgery/periprosthetic fracture) were assessed using ICD-9 or 10 codes ≤ 30 days post-surgery (Online Resource 6). Death due to any cause and the following types of direct accrued healthcare utilization costs standardized to 2017 Canadian dollars (CAD) and 2017 US dollars (USD) (and recently described in more detail [4]) were assessed up to 1 year from the index date for all index fracture sites: hospitalizations (i.e. inpatient hospitalization and same-day surgery), inpatient rehabilitation, continuing care services (i.e. hospital-based continuing care, home care and long-term care), prescription drug benefit claims and other healthcare services (i.e. emergency department visits, hospital outpatient clinic visits, physician billings, physiotherapy billings and laboratory claims). One-year mortality and healthcare costs were also assessed post-second hip fracture only.

Data synthesis and analysis

Descriptive statistics were used to summarize clinical characteristics and outcomes. Outcomes are reported by each index fracture site unless otherwise indicated. Median time from index fracture of each site to second fracture of the hip was calculated. Direct 1-year healthcare utilization costs were calculated using a previously published algorithm, with the contribution of each healthcare cost type to the total cost reported [4, 33] The STROBE and RECORD statements were used to report the findings from this study.[34].

Results

Clinical characteristics

The cohort included 115,776 patients with an index fracture (Fig. 1), 72.3% ($n = 83{,}690$) of which were female (Table 1). The mean age (± standard deviation [SD]) at the date of index fracture was 80.4 (± 8.3) years with 48.8% ($n = 56{,}441$) of patients aged 66–80 years. The most common comorbidities in this cohort were osteoarthritis (76.2%, $n = 88{,}223$), diabetes (30.6%, $n = 35{,}434$) and stroke or cerebrovascular events (30.3%, $n = 35{,}030$). The proportion of patients on any osteoporosis treatment 1 year prior to index fracture was 28.3% ($n = 32{,}757$), as further described in a recent report on the same fracture cohort [35]. A hip fracture was the most common index fracture, occurring in 27.3% ($n = 31{,}613$) of patients (Table 1). The proportion of index hip fractures by age at index date was 66–70, 6.9%; 71–75, 9.8%; 76–80, 15.8%; 81–85, 23.8%; and 86 +, 43.8%.

Second fracture of the hip

Amongst patients experiencing a second fracture of any site over the study follow-up (17.8%, $n = 20{,}629$), hip fracture was the most common second fracture overall, occurring in 27.8% ($n = 5{,}745$) of patients (Table 1). Hip fracture was the most common second fracture after each index fracture site, except after a radius/ulna fracture where hip was the second most common (hip, 19.4%, $n = 189$ vs. wrist, 25.0%, $n = 243$) (Fig. 2A). Hip fracture occurred as the second fracture in ≥ 19% of patients for all index fracture sites, most often after hip index fracture (33.0%, $n = 1{,}660$; Fig. 2B). The proportion of second hip fractures by age at index date was 66–70, 6.2%; 71–75, 9.6%; 76–80, 16.7%; 81–85, 26.0%; and 86 +, 41.4%.

Median time from index fracture of any site to second fracture of the hip over the study follow-up was approximately 1.5 years (554 [interquartile range (IQR) 252–941] days) (Fig. 2B). When the index fracture occurred at the hip, the median time from index to second hip fracture was also approximately 1.5 years (566 [IQR 287–938] days). Median time to second fracture of the hip was the shortest after femur (397 [IQR 192–867] days), pelvis (484 [IQR 217–869] days) and vertebral (clinical; 493 [IQR 218–888] days) index fractures.

Contribution of index hip fractures to surgeries, complications and 1-year mortality

Amongst all patients requiring initial index fracture-related surgery (38.8%, $n = 44{,}949$) and those experiencing complications 30 days post-surgery (19.7%, $n = 8868$), the majority had an index hip fracture (64.1%, $n = 28{,}790$ and 71.9%, n = 6379, respectively) (Fig. 3). An index hip fracture was associated with the highest proportion of patients undergoing initial surgery (91.4%), followed by femur fracture (80.6%), and the second-highest experiencing complications (22.2%), preceded by femur fracture (35.8%). Mortality at 1 year (due to any cause) in the entire fracture cohort was 15.9% ($n = 18{,}392$). Index hip fracture was associated with the highest 1-year mortality rate (26.2%, $n = 8289$) and contributed to the most deaths (45.1%) of all index fracture sites

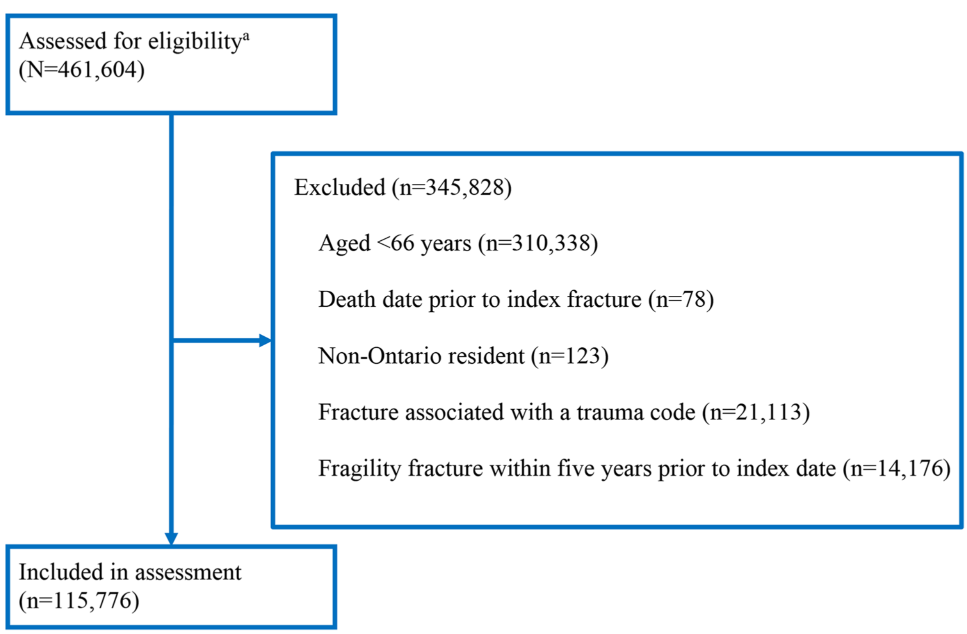

Fig. 1 Flow diagram of patients included in the cohort. [a]All patients with a valid IKN with a fracture occurring at an osteoporotic fracture site (hip, vertebral [clinical], wrist [distal radius, or both distal radius and ulna], clavicle/ribs/sternum, humerus, tibia/fibula/knee [including medial and lateral malleolus], pelvis, radius/ulna [proximal, midshaft or distal ulna only], multisite, femur) between January 1, 2011, and March 31, 2015. Fractures were identified using ICD-10-CA codes from hospital admissions, emergency room visits and ambulatory care. *ICD-10-CA* International Classification of Diseases, 10th revision, Canada, *IKN* ICES key number

Table 1 Clinical characteristics of the index fracture cohort

Characteristic	*n* (%)
Total number of patients	115,776
Sex	
Female	83,690 (72.3%)
Male	32,086 (27.7%)
Age	
Mean ± SD	80.4 ± 8.28
Median (IQR)	81 (74–87)
66–70 years	17,998 (15.5%)
71–75 years	17,847 (15.4%)
76–80 years	20,596 (17.8%)
81–85 years	24,119 (20.8%)
≥ 86 years	35,216 (30.4%)
Respiratory conditions[a]	
Asthma	17,538 (15.1%)
COPD	33,485 (28.9%)
Inflammatory conditions[a]	
Rheumatoid arthritis	4459 (3.9%)
Psoriasis	8076 (7.0%)
Spondyloarthritis	5084 (4.4%)
Osteoarthritis[a]	88,223 (76.2%)
Cancer[a]	8390 (7.2%)
Chronic kidney disease[a]	13,757 (11.9%)
Diabetes[a]	35,434 (30.6%)
Vascular events[a]	
Myocardial infarction	8175 (7.1%)
Stroke or cerebrovascular events	35,030 (30.3%)
Dementia[a]	24,092 (20.8%)
Osteoporosis treatment type[b]	
Any treatment	32,757 (28.3%)
Denosumab	1578 (1.4%)
Bisphosphonate	29,030 (25.1%)
Raloxifene	656 (0.6%)
HRT	3597 (3.1%)
Steroid use[a]	3340 (2.9%)
Opioid use[a]	34,834 (30.1%)
Fracture treatment location	
Urban	103,720 (89.6%)
Rural	10,626 (9.2%)
Missing	1430 (1.2%)
Index fracture by site[c]	
Hip	31,613 (27.3%)
Wrist (distal radius, or both distal radius and ulna)	17,859 (15.4%)
Clavicle/ribs/sternum	14,559 (12.6%)
Humerus	13,237 (11.4%)
Tibia/fibula/knee (including medial and lateral malleolus)	10,894 (9.4%)
Pelvis	8328 (7.2%)
Vertebral (clinical)	7721 (6.7%)
Radius/ulna (proximal, midshaft or distal ulna only)	4828 (4.2%)
Multisite	3735 (3.2%)
Femur	3002 (2.6%)
Any site	115,776 (100%)

Table 1 (continued)

Characteristic	*n* (%)
Second fracture by site[d]	
Hip	5745 (27.8%)
Clavicle/ribs/sternum	2460 (11.9%)
Wrist (distal radius, or both distal radius and ulna)	2249 (10.9%)
Humerus	2088 (10.1%)
Pelvis	1977 (9.6%)
Vertebral	1819 (8.8%)
Multisite	1518 (7.4%)
Tibia/fibula/knee (including medial and lateral malleolus)	1317 (6.4%)
Radius/ulna (proximal, midshaft or distal ulna only)	741 (3.6%)
Femur	715 (3.6%)
Any site	20,629 (100%)

Values reported as *n* (%) unless otherwise indicated

COPD chronic obstructive pulmonary disease, *HRT* hormone replacement therapy, *IQR* interquartile range, *SD* standard deviation

[a]Time frame for cancer was 5 years within index date and, for all other comorbidities and non-osteoporotic medications, was any time prior to index date

[b]Within 1 year of index date. Bisphosphonates include alendronate, cyclical etidronate, risedronate or zoledronic acid. Denosumab is not publicly covered in men and teriparatide in men or women in Ontario

[c]Percent of total number of index fracture cases ($N=115{,}776$) from January 1, 2011, to March 31, 2015. Reported from highest to lowest number. Patients with multisite fractures were analysed as their own group; they were not double-counted, and no site was prioritized. The ICD-10 codes used to identify fracture sites are listed in Online Resource 2

[d]Percent of total number of second fracture cases ($N=20{,}629$) from the date of index event to March 31, 2017. Reported from highest to lowest number. Fracture of the same site that was dated within 91 days of the index fracture was assumed to stem from the same fracture and was not counted as a second fracture. The anatomical location of multisite index fracture was used to exclude a second single-site fracture occurring in a similar location within 91 days. The ICD-10 codes used to identify fracture sites are listed in Online Resource 2

(Fig. 3). Second hip fracture was associated with a 25.9% ($n=1488$) 1-year mortality rate.

Contribution of hip fracture to healthcare utilization cost

Mean ± SD total healthcare cost across all index fracture sites was $39,089 ± 43,272 ($29,853 ± $33,048 in 2017 USD) per patient in the first year post-fracture. An index hip fracture had the second highest mean total healthcare cost of $62,793 ± 44,438 ($47,957 ± $33,939 in 2017 USD), closely after a femur index fracture ($65,489 ± 54,116 in 2017 CAD; $50,016 ± $41,330 in 2017 USD). The contribution of each type of healthcare cost after an index hip fracture was highest for hospitalizations (39%) and continuing care (32%), with less than one-third of total costs resulting from other healthcare services (14%), inpatient rehabilitation (11%) and prescription drug benefit claims (3%). The mean length of hospitalization stay decreased from 2011 (15.9 days) to 2015 (13.0 days). When the second fracture was a hip fracture, mean total first-year healthcare costs ranged $59,935–69,518 (±43,739–45,893; $45,774–$53,093 [±$33,405–$35,050] in 2017 USD) depending on index fracture site.

Interpretation

Hip fracture was the most common second fracture in this fracture cohort of patients aged > 65, occurring in one in four over 2 to 6 years of follow-up. An incident hip fracture was the most predictive of a second hip fracture, occurring in 33% of patients and within ~ 1.5 years in half of these cases. However, the risk of second hip fracture was consistently ≥ 19% over a median time of < 2 years across index fracture sites. Considering a 3% 10-year hip fracture risk is a high-risk threshold recommended by clinical practice guidelines [18], this is an important finding informing hip fracture prevention efforts to focus on all osteoporotic-related fracture sites as part of secondary hip fracture prevention [35]. Patients with an index hip fracture also accounted for the most deaths, surgeries and post-surgery complications within the first year post-fracture, and 1-year mortality rate after index hip fracture was the highest amongst all fracture

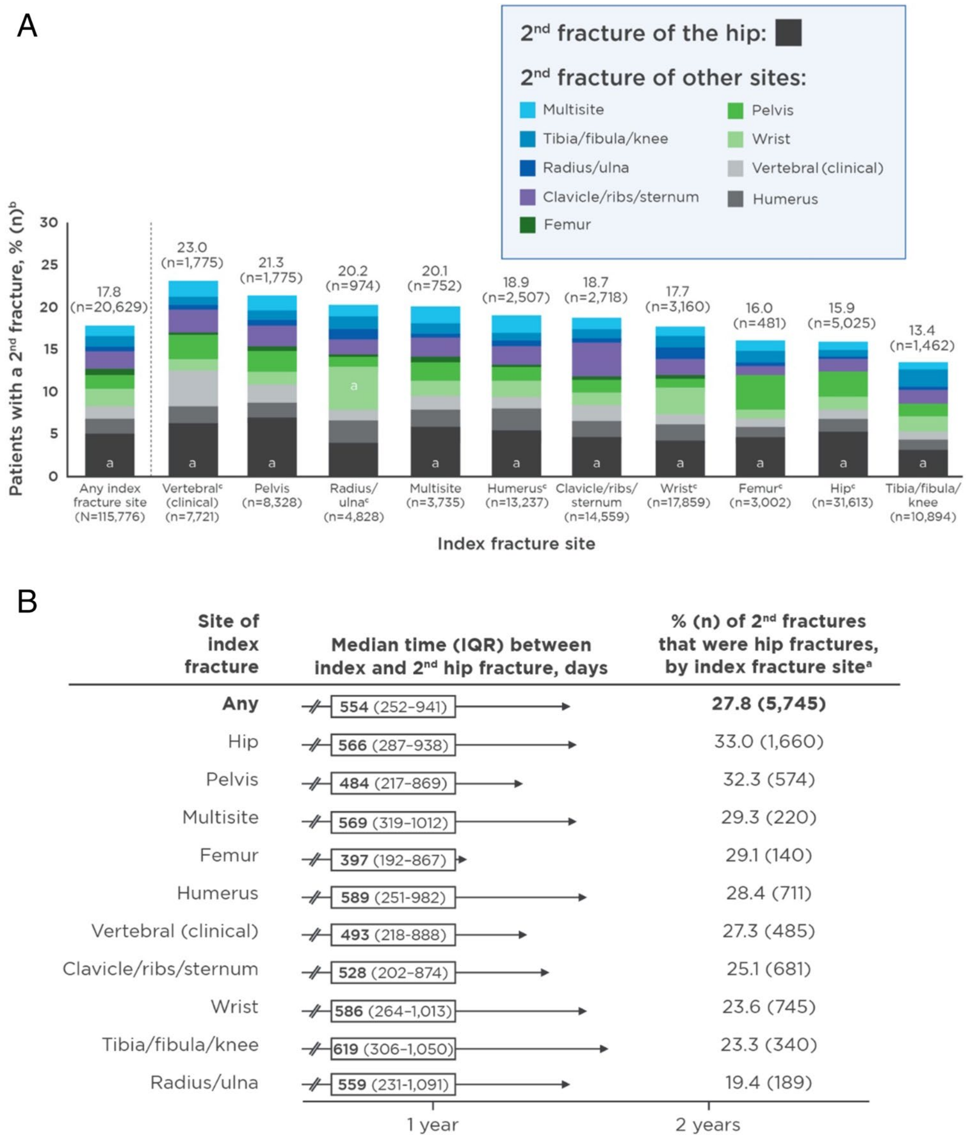

Fig. 2 Second fracture of the hip based on index fracture site. **A** Distribution of second fracture based on index fracture site. [a]The most common second fracture site for a given index fracture. [b]Percentages based on total number of patients with an index fracture occurring at a given site. Values at the top of each bar represent % (number) of second fracture of any site. [c]Index fracture occurring at major osteoporotic fracture site. **B** Median time to second hip fracture based on index fracture site. [a]Percentages based on the total number of second fractures in a given index fracture site. *IQR* interquartile range

sites examined. A hip fracture also accrued the second highest healthcare cost within the first year post-fracture, closely after femur fracture, in part due to high hospitalization and continuing care costs. Finally, although hip fractures are most common in geriatric patients, younger patients' risk cannot be overlooked considering one in three of index or second hip fracture cases were observed in patients aged 66–80.

Our observed 33% rate of a second hip fracture following an incident hip fracture over 2 to 6 years of follow-up was similar to that of 34% observed in another Canadian fracture cohort over 10 years of follow-up (aged ≥ 60, during 1990–2005) [36]. Observing a similar rate over a shorter follow-up is in line with prior studies of imminent fracture risk reporting subsequent fractures cluster in time after an incident fracture, wherein 61% of subsequent hip fractures followed over 10 years were reported to occur within the initial 2 years after an incident fracture [19, 37]. However, the imminent risk of *hip* fracture is currently not well-documented, as prior studies have primarily examined imminent risk of *any* fracture [38, 39]. A study of Canadians aged ≥ 66 observed a 1.6- to 6.5-fold higher risk of subsequent hip or femur fracture within 1 year after an incident fracture, with higher risks in men and younger age categories [16]. Studies reporting absolute imminent risks in US fracture cohorts aged ≥ 65 observed 4.8% of women and 1.4% of all adults experienced a subsequent hip fracture within 2 years after a prior fracture [15, 40]. Only one study reported imminent risk of hip fracture after an incident hip fracture in adults aged ≥ 65 and observed lower rates than those in our cohort, of 4% and 9% within 2 and 5 years, respectively [15]. This study also found spine, humerus or clavicle fracture was most predictive of a subsequent hip fracture, rather than incident hip fracture. This US fracture cohort had a similar age

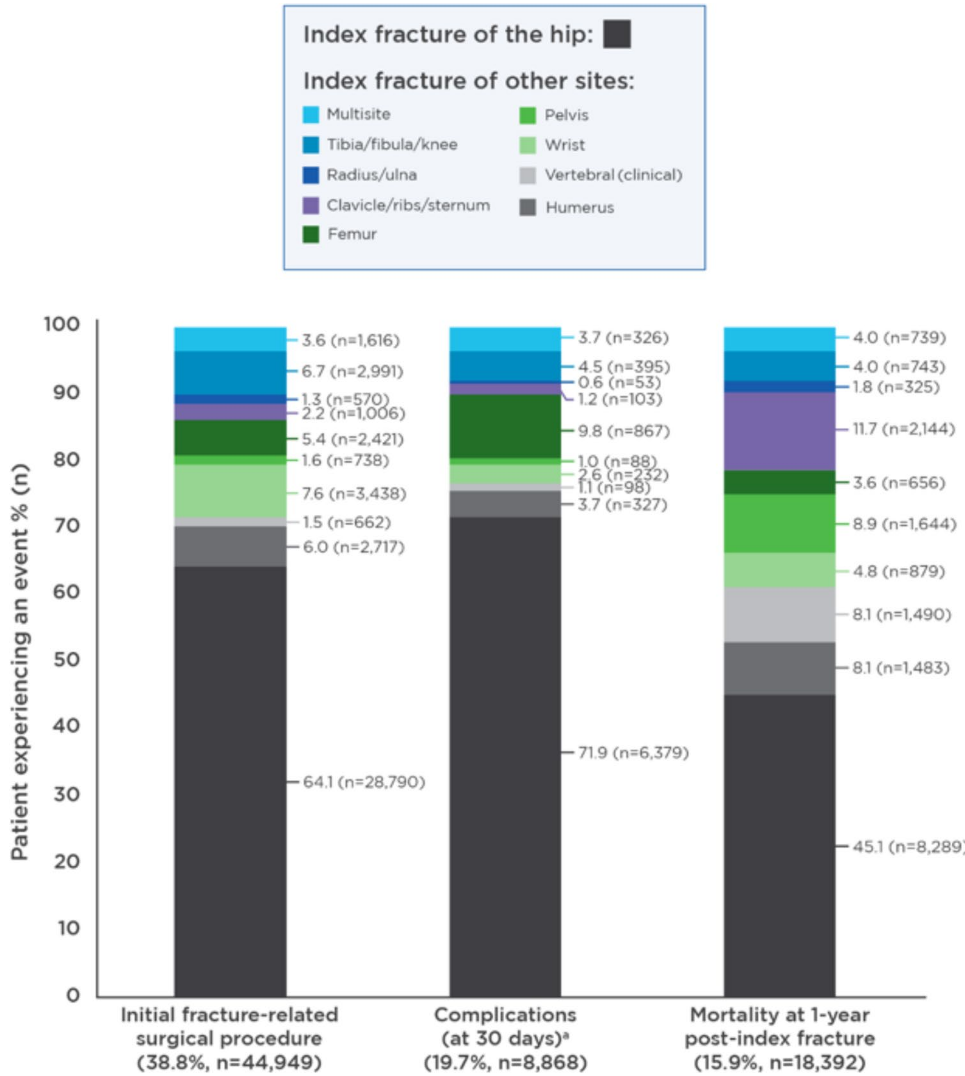

Fig. 3 Contribution of index hip fractures to the total number of patients undergoing initial surgery, experiencing complications or to 1-year mortality. [a]Percentages based on the number of patients who experienced ≥ 1 post-surgery complication within 30 days

distribution as our cohort but perhaps differed in hip fracture risk due to cultural differences, only examining women, and observing a much higher proportion of vertebral index fractures (28.9%). As such, country-specific studies of imminent risk of hip fracture after an incident hip fracture are needed.

Our data also contribute to evidence of high mortality and direct healthcare costs following hip fractures. Hip fracture was previously observed to have the highest mortality rate amongst other fracture sites in adults aged ≥ 50 [41]. Consistent with our observed 26% rate, 1-year mortality following a hip fracture was reported in 22% of women and 33% of men in a similar Canadian cohort [32]. We observed a similar 1-year mortality rate after second hip fracture, unlike another study of Canadians (aged ≥ 60) showing a higher monthly mortality rate after index vs. second hip fracture (16.2 vs. 21.1 per 1000) over longer follow-up (1990–2005) and with a smaller proportion of second hip fractures (7%) [32, 42]. The vulnerability of hip fracture patients was also recently highlighted in studies from Europe and the USA showing the short-term (< 12-week) mortality rate increased by two- to four-fold in *all* hip fracture patients during the COVID-19 pandemic, reaching 30–56% in COVID-19$^+$ hip fracture patients [8–11]. In light of these findings, future research is needed to assess mortality rate after second vs. index fracture and during the COVID-19 pandemic in Canada. Further, while we observed a hip fracture accrues the second highest healthcare costs, albeit closely after a femur fracture (as recently described in more detail [4]), prior studies observed it culminates in the greatest costs amongst other fracture sites [43, 44]. As in our study, a 2013 study of Ontarians aged ≥ 65 showed hospitalizations, and continuing care costs and rehabilitation were the primary drivers behind healthcare costs associated with hip fractures, with prescription drugs accounting for < 5% [32]. Meanwhile, to our knowledge, the contribution of hip fracture to surgeries and complications relative to other fractures sites has not been documented in other recent studies.

This Canadian epidemiological study can help inform current efforts related to hip fracture prevention, particularly those focusing on post-fracture patients. Hip fracture data was reported in the context of other fracture sites related to chronic bone loss due to ageing, and data was drawn from a province contributing to approximately one-third of fractures in Canada [45]. However, this study examined patients aged > 65 and almost one-third of patients were aged ≥ 86, which limits the generalizability of the results to the full population at risk of fracture (i.e. aged ≥ 50 [45]). By excluding patients who had another fracture 5 years prior to their index event, but not beyond, the cohort was potentially biased towards an older population, resulting in a mean age roughly 5 years higher than expected for adults aged > 65 [16]. Further, particularly vertebral fractures may be underestimated in this cohort considering only the 'Most Responsible Diagnosis' and 'Pre-Admit Comorbidity' were used to identify index fractures. Also, as in prior healthcare database research, the determination of fracture was based on the exclusion of high-trauma ICD codes and not independent adjudication of low-trauma fractures [32]. However, this may not be a limitation of the current study since recent research suggests both low- and high-trauma fractures are predictive of future fracture [46, 47]. Finally, future studies should assess surgeries and complications after second hip fracture too, as well as include other common post-surgery complications not included in the current study (e.g. urinary infection).

Conclusion

In this large, fracture cohort of adults aged > 65, a second fracture of the hip was observed in one in four patients with any index fracture and in one in three patients with an index hip fracture, on average within 1.5 years over 2 to 6 years of follow-up. Index hip fracture was associated with high mortality and post-surgery complication rates and healthcare costs relative to other fractures. These data further support early hip fracture prevention strategies focusing on adults aged ≥ 65 with a recent fracture to help reduce imminent hip fracture risk and high societal and humanistic costs.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00198-021-06080-5.

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Author contributions ES, JAD, JPB, JET, NB, TO and LS contributed to design of the study, review and interpretation of the data and drafting and review of the manuscript.

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Data availability The datasets generated during and/or analysed during the current study are available in the ICES repository upon request. The data that support the findings of this study are available from ICES. However, restrictions apply to the availability of these data, which were used under license for the current study and therefore are not publicly available [https://www.ices.on.ca/Data-and-Privacy/ICES-data]. Data are however available from the authors upon reasonable request and with permission from ICES.

Code availability Not applicable.

Declarations

Conflict of interest ES has received consulting fees from Acumed LLC, Amgen, Implants for Trauma Surgery, Pentopharm, Sanofi-Aventis, Smith & Nephew, Stryker, Swemac; received grant/research support from Amgen, Biocomposites, Smith & Nephew. JDA has received consulting fees from Amgen; received grant/research support from AbbVie, Amgen, Celgene, Eli Lilly, Pfizer, Radius. JPB has received consulting fees and honoraria from Amgen and Servier; received research funding from Mereo BioPharma, Radius Health, Servier; served on speakers' bureau for Amgen. JET has received consulting fees from Amgen, Analytica Laser International, AstraZeneca, Bayer, Edwards Lifesciences, Eli Lilly, The European Commission Initiative on Breast Cancer, Evidera, Flatiron, GSK, Merck, Novartis, PCDI Canada, Pfizer, Roche; received grant/research support from Amgen, Assurex/Myriad, AstraZeneca, CSL Behring, Edwards Lifesciences, Novo Nordisk, Sage; served on speakers' bureau for Allergan. TO, NB and LS are employees and own stock in Amgen.

Ethical approval The study protocol was approved by the Advarra Institutional Review Board.

Consent to participate Formal consent is not required for this type of study.

Consent for publication Not applicable.

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