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Original Article

Global, regional, national trends of femur fracture and machine learning prediction: Comprehensive findings and questions from global burden of disease 1990–2019

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ABSTRACT

Background: Femur fracture is a type of fracture with high disability and mortality. There is no comprehensive analysis and prediction of the global distribution of femur fractures, so we conducted this study.
Methods: Age-standardized incidence rate (ASIR), age-standardized prevalence rate (ASPR), and years living with disability (YLDs) of femur fractures (excluding femoral neck) were downloaded from the Global burden of disease database. Trend analysis was performed, and 6 time-series machine learning algorithms were applied to predict the global ASIR, ASPR, and YLDs.
Results: ASPR for femur fracture had been increasing in most countries worldwide from 1990 to 2019, with the highest in East Asia (AAPC = 1.25 95%Confidence Interval (1.2, 1.3)) and lowest in Central Latin America (AAPC = −0.74 95%CI (−0.81, −0.67)). However, ASIR showed a significant downward trend worldwide, with East Saharan Africa decreasing the most (AAPC = −4.04 95%CI (−5.56, −2.47)), and East Asia elevating the most (AAPC = 1.11 95%CI (0.87, 1.42)). YLDs were increasing over the world, with East Asia still elevating the most AAPC= (3.9 95%CI (3.85, 3.95)), with the only region of decrease being Eastern Europe (AAPC = −0.28 95%CI (−0.3, −0.26)). Both ASPR and ASIR were higher in women than in men in the >75 year group, whereas YLDs was lower in women than in men in the >60 year group. Globally, the ARIMA model was optimal in the prediction of ASPR, the PROPHET model effected in the prediction of ASIR, and the PROPHET WITH XGBOOST model was the best in the prediction of YLDs. The projections showed increase in both ASPR and YLDs, except for ASIR decreasing by 2030.
Conclusions: Our study found a rise in femur fracture ASPR and ASIR from 1990 to 2019 in war conflict areas and East Asia, meanwhile, the YLDs of femur fracture increased in populous countries. In both 1990 and 2019, both ASPR and ASIR were higher in women over 75 years than that in men, but YLDs was higher in men over 60 years than that in women. In 2020–2030, while global femur fracture ASIR might decline, both ASPR and YLDs might rise.
The Translational Potential of this article: Femur fracture is a high-energy injury due to direct violence, and in war, conflicting and underdeveloped regions such as East Asia. Accidental injuries may occur due to the rapid development of industry and the frequent traffic accidents. This study suggests that we should focus on elderly women (≥75 years) in the above regions in the future. For older men (>60 years old), more attention should be paid to post-fracture functional rehabilitation and early reintegration into society to reduce the disability rate and lower the socio-economic burden.

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1. Introduction

Femur fracture is an important disease associated with poor outcomes, which is an emerging public health problem in an aging society with high morbidity and mortality [1,2]. According to the International Osteoporosis Foundation, the incidence of femur fractures is expected to increase due to global population aging [3–5]. The 1-year case fatality rate for patients with femur fractures was reported to be as high as 20–24%, and the risk of death might persist for more than 5 years [6]. As for functional outcomes, it was reported that 40% of patients with femur fractures were unable to walk independently. Over 60% femoral fracture patients required assistance, and 33% were totally dependent by nursing at 1 year after femur fracture [7–9]. Treatment and rehabilitation of femur fractures are expensive, especially for patients in low socioeconomic status. A typical femur fracture treatment in the first year might cost $40,000 in direct medical costs [10,11]. In addition to increased mortality and socioeconomic burden, patients with femur fractures were at increased risk for subsequent fragility fractures [12]. The global 1-year risk of re-fracture was approximately 2%–10%, and the estimated lifetime risk was 20%, but might be as high as 55% [13,14].

The Global burden of disease (GBD) Collaboration Group analyzed data on all fracture types and found that from 1990 to 2019, there was a slight decrease in global age-standardized incidence rate (ASIR), age-standardized prevalence rate (ASPR), and years living with disability (YLDs). However, the number of incidence, prevalence, and YLDs increased substantially, largely as a result of population growth and aging [15]. Central to understanding the global disease burden of femoral fractures is identifying inequality of injuries and healthcare resources. However, there are few studies comprehensively analyzing femoral fractures in depth. Therefore, we conducted this study to systematically analyze femoral fractures from three perspectives: incidence, prevalence, and disability, applying time-series machine learning (ML) models to forecast femoral fracture metrics for the future period 2020–2030. Based on the results of this trend analysis and prediction, we could point out the questions behind the results and try to answer them.

2. Methods

2.1. Materials

About GBD 2019 overview, Estimates of ASPR, ASIR, and YLDs for femur fractures were based on data from the 2019 GBD study (https://vizhub.healthdata.org/gbd-results/(accessed on October 20, 2023)). In this study, data sources for femur fractures included hospital records, emergency room records, insurance claims, surveys, and vital registration systems from different countries [16,17]. The GBD study used de-privatized data, and the data sources were aggregated by the Institute for Health Metrics and Evaluation at the University of Washington, where the University of Washington Institutional Review Board reviewed and approved the informed consent waiver [18].

Aoubt femur fracture data sources, GBD 2019 provided 369 diseases and injuries with 87 risk factors for 204 countries and territories. The GBD project team reported a detailed description of the methodology and published lethal and non-lethal estimates (https://vizhub.healthdata.org/gbd-compare/and https://ghdx.healthdata.org/gbd-results-tool). In GBD 2019, femur fracture cases were identified according to the International Classification of Diseases, 10th edition (ICD-10) [19,20].

Based on epidemiologic similarity and geographic proximity, the GBD categorized all countries and regions into 21 regions and into 5 categories based on sociodemographic indices (SDI; high SDI (>0.81), middle–high SDI (0.70–0.81), middle SDI (0.61–0.69), middle-low SDI (0.46–0.60), and low SDI (<0.46)). The SDI is a composite indicator of the social context and economic conditions that influence health in each country and region, which is a geometric mean on a scale of 0–1. SDI include per capita income, average educational attainment of the population aged 15 years and over, and the fertility rate of women under 25 years.

2.2. Statistical analysis

In descriptive analysis, Firstly, data on femur fractures (excluding femoral neck fractures) were screened and downloaded under the category of natural injuries in GBD. World maps covering 204 countries were created, visualizing the ASPR, ASIR, and YLDs of femur fractures in 1990 and 2019. Then, changes (annual average percentage change, AAPC) of ASPR, ASIR, and YLDs were calculated. AAPC is a summary measure of the trend over a pre-specified fixed interval. It allows us to use a single number to describe the annual average change over a period. Joinpoint software was used (version 4.9.1.0) from the National Cancer Institute's Surveillance Research Program for all AAPC calculations. Except for AAPC, all analyses in this study were conducted using R software (R Core Team, version 3.5.2, Vienna, Austria), and P value less than 0.05 was considered statistically significant.

In machine learning prediction for time-series, there are several types of models that can be used for time-series prediction, in which temporal information can be included by adding a set of delays to the inputs to represent the data at different points in time. In this study, modelize package was adpoted in R language for 6 machine learning algorithms to predict ASPR, ASIR and YLDs of femur fracture from 2020 to 2030, and 6 machine learning algorithms are as below: Autoregressive Integrated Moving Average (ARIMA), Prophet, Multivariate adaptive regression splines (MARS), Elastic Net, Random forest and extreme gradient boosting (XGBoost). ARIMA model is a statistical analysis model that employs time-series data to help researchers better understand a data collection or to forecast future trends. Prophet model is a Facebook open-source platform for forecasting time-series data that lets user better interpret and anticipate the demand. MARS is a non-parametric modelling method that extends the linear model, incorporating nonlinearities and interactions between variables. The elastic net is a particular case of the shrinkage method, which holds both ridge and least absolute shrinkage and selection operator regressions. Random Forest is an ensemble of decision trees algorithms that can be used for classification and regression predictive modeling. The XGBoost model is an ensemble system for tree boosting, which is based on the gradient direction of a loss function called gradient boosting machine [21,22].

3. Results

The worldwide ASPR in 1990 ranged from 170.77 (95% uncertainty interval 159.82, 181.88) to 1375.41 (95%UI 363.77, 5145.83). Fig. 1A showed that ASPR was at a high level in the high dimensional region and part of Central West Asia in 1990. The ASPR was low in the low latitude regions including part of Africa and Latin America. The ASPR ranged from 218.51 (95%UI 204.48, 233.79) to 1110.47 (95%UI 564.24, 2527.29) in Africa, and 241.85 (95%UI 224.49, 260.84) to 757.26 (95% UI 472.16, 1402.87) in Latin America (table S1). The 2019 worldwide ASPR was from 180.37 (95%UI 167.43, 193.22) to 1081.45 (95%UI 415.83, 3096.2). Fig. 1B showed that after 30 years, high latitudes still had high ASPR in 2019, while some new high ASPR countries such as Croatia (1015.05,95%UI 938.44, 1106.03) and Burundi (949.59, 95%UI 488.26, 2028.08) emerged.

In trends analysis, some countries were declining, while most countries were in an upward trend between 1990 and 2019. High latitude countries such as Russia (897.98 (95%UI 826.28, 980.98)) and Greenland (985.54 (95%UI 899.35, 1090.11)), and most of North Asia and Eastern Europe were still in high ASPR. ASPR in North Asia and Eastern Europe ranged from 236.56 (95%UI 218.9, 255.32) to 1081.45 (95%UI 415.83, 3096. 2) (table S1), with Afghanistan having the highest at 1081.45 (95%UI 415.83, 3096.2). Notably Syria's ASPR increased significantly from 272.17 (95%UI 226.49, 405.42) in 1990 to 903.19

(95%UI 409.09, 1982.78) in 2019.

The ASPR for femur fracture is on an increasing trend in most countries worldwide (AAPC >0) (Fig. S1). Of the 21 GBD regions, 10 had elevated ASPR, with East Asia having the highest (AAPC = 1.25, 95% confidence interval 1.2, 1.3) and Central Latin America reduced most (AAPC = −0.74, 95%CI -0.81, - 0.67). Of the 204 countries, 88 had an AAPC less than 0, ranging from −1.741 (95%CI -1.81, −1.67) to −0.005 (95%CI -0.04, 0.03). There were 116 countries with an AAPC greater than 0, ranging from 0.002 (95%CI -0.39, 0.39) to 4.341 (95%CI 3.01, 5.69). The seven countries with AAPC greater than 1 were Syria, Burundi, Haiti, Rwanda, China, Central African Republic, Yemen, and Pakistan with AAPCs of 4.34 (95%CI 3.01, 5.69), 3.16 (95%CI 2.49, 3.83), 1.74 (95%CI -1.68, 5.28), 1.39(95%CI 0.68, 2.11), 1.3(95%CI 1.2, 1.4), 1.22(95%CI -0.11, 2.57), 1.14(95%CI 0.92, 1.35) and 1.03(95%CI 0.86, 1.2), respectively.

In the distribution of ASIR (Fig. 2), the 1990 worldwide ASIR ranged from 44.05 (95%UI 35.09, 54.49) to 1104.33 (95%UI 342.54, 3071.57). Some countries in the African region were at high levels in 1990, with ASIR ranging from 47.37 (95%UI 37.89, 59.58) to 1104.33 (95%UI 342.54, 3071.57), North Asia and Oceania were at medium levels with ASIR ranging from 44.05 (95%UI 35.09, 54.49) to 594.56 (95%UI 450.36, 786.68) (table S1), and most of the region was at low ASIR levels. And by 2019, some countries with high ASIR were transformed into low ASIR countries, with the range of ASIR worldwide was from 49.97 (95%UI 40.37, 62.01) to 594.17 (95%UI 463.19, 769.42), which seemed to indicate that ASIR was decreasing worldwide.

Although worldwide, in 2019 the ASIR for femur fractures was significantly lower than in 1990. The ASIR was elevated in 8 of the 21 GBD regions, which was also highest in East Asia (AAPC = 1.11, 95%CI 0.87, 1.42). The most reduced region was Eastern Saharan Africa (AAPC = −4.04,95%CI -5.56, −2.47) (table S1). 114 of the 204 countries had an AAPC less than 0, ranging from −10.904 (95%CI -3.05, 22.97) to −0.002 (95%CI -0.11, 0.11) (Fig. S2). However, there were also 90 countries with an AAPC greater than 0, ranging from 0.015 (95%CI -0.05, 0.08) to 4.553 (95%CI 2.62, 6.52). Among them, 9 countries with AAPC greater than 1 include Yemen, Afghanistan, Syrian Arab Republic, South Sudan, Central African Republic, Libya, China, Burkina Faso, and Pakistan. Their AAPC values were 4.553 (95%CI 2.62, 6.52), 3.203 (95% CI 0.05, 6.46), 3.145 (95%CI -3.66, 10.43), 1.908 (95%CI 0.67, 3.16), 1.797 (95%CI 1, 2.61), 1.629 (95%CI 0.2, 3.08), 1.243 (95%CI 0.25, 2.25), 1.156 (95%CI 0.78, 1.54) and 1.023 (95%CI 0.79, 1.26), respectively.

In 1990, YLDs ranged from 0.12 (95%UI 0.08, 0.18) to 152656.98 (95%UI 99980.3, 218447.69) (Fig. 3). Countries with high YLDs were mainly located in India, China, USA and Russia with YLDs of 152656.98 (95%UI 99980.3, 218447.69), 110814.4 (95%UI 72335.41,

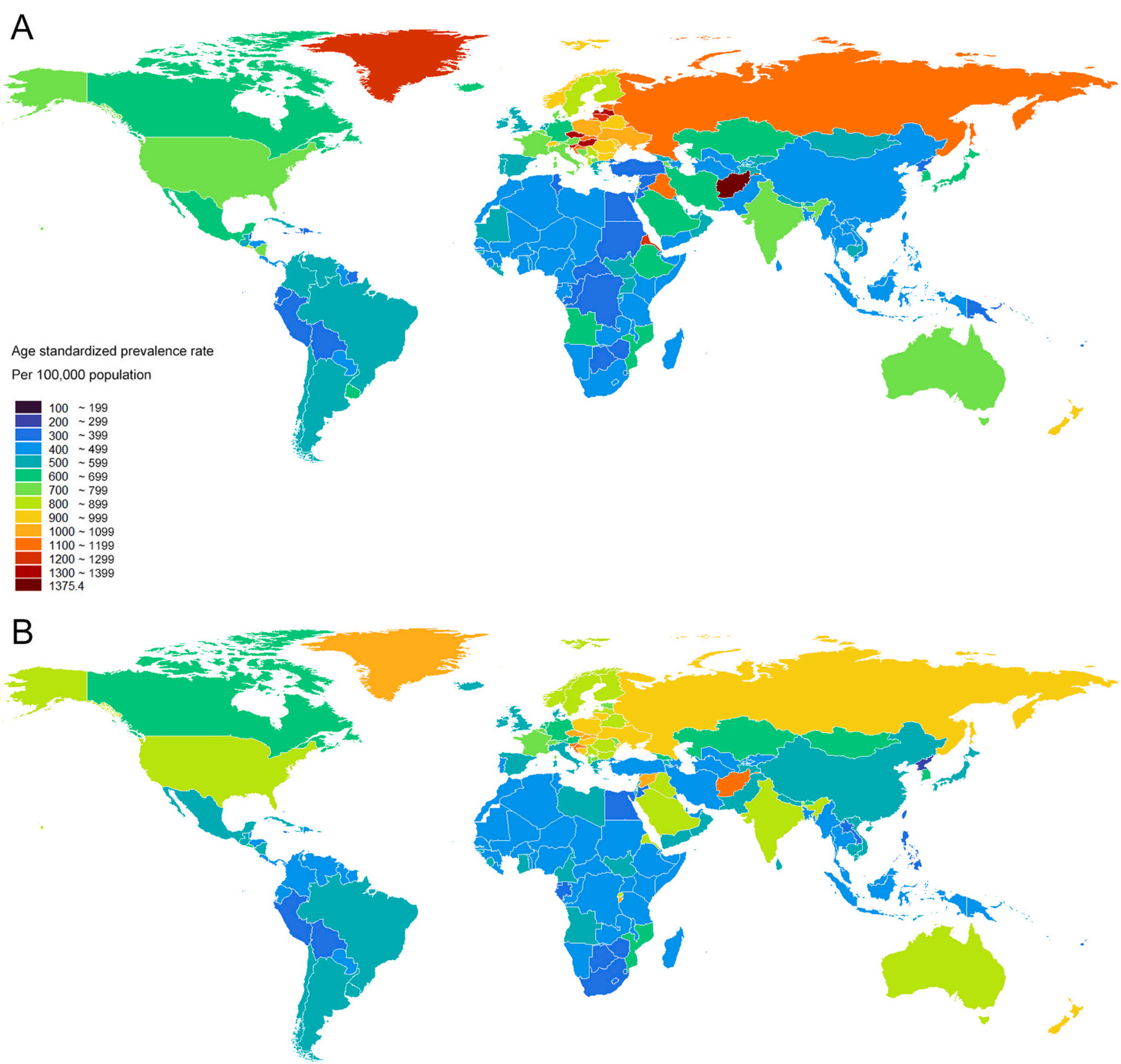

Figure 1. Femur fracture age standardized prevalence rate (ASPR) in 1990 (A); Femur fracture ASPR in 2019 (B).

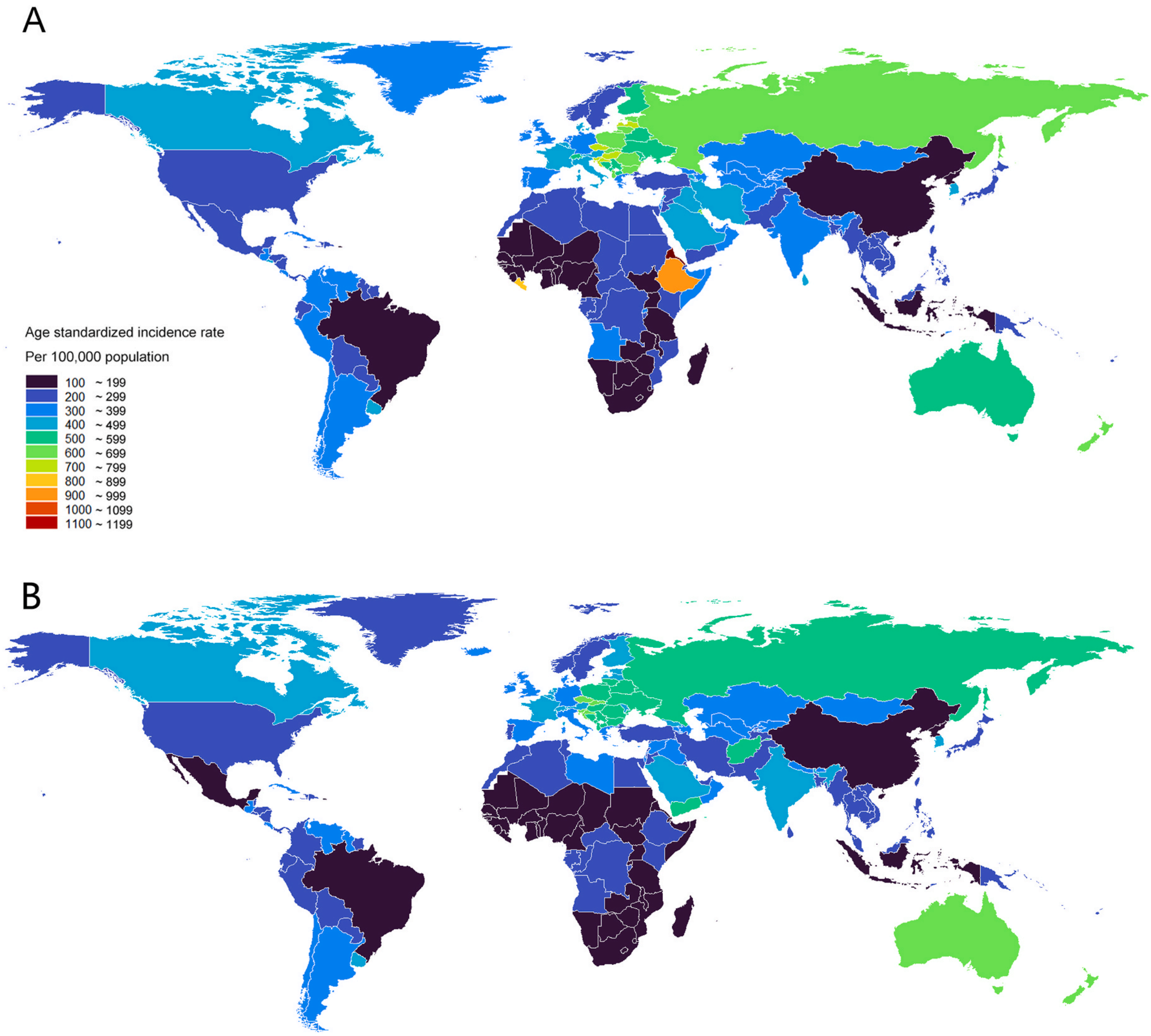

Figure 2. Age-standardized incidence rate (ASIR) in 1990 (A); Femur fracture ASIR in 2019 (B).

162670.08), 85030.43 (95%UI 55905.16, 122967.6) and 82481.05 (95%UI 54005.23, 118325.97), respectively. It could be seen that YLDs were higher in the populous countries. In 2019, YLDs ranged from 0.14 (95%UI 0.1, 0.21) to 387694.7 (95%UI 254599.36, 558267.12). It was mainly concentrated in India (387694.7, 95%UI 254599.36, 558267.12), China (342854.09, 95%UI 222602.94, 497940.1) and the United States (159576.01, 95%UI 105664.37, 230694.71), but Russia (80539.52, 95%UI 53098.74, 115523.87) had a decrease in YLDs.

The AAPC results showed that the YLDs increased in as many as 20 of the 21 GBD regions, with East Asia remaining the most elevated region (3.9, 95%CI 3.85, 3.95), and the only decreasing region was Eastern Europe (−0.28, 95%CI -0.3, −0.26) (table S1). The majority of countries in the world had an AAPC greater than 0, with 189 countries having an AAPC greater than 0, ranging from 0.04 (95%CI -0.06, 0.14) to 6.694 (95%CI 6.47, 6.92). Only 15 countries had an AAPC less than 0, ranging from −1.934 (95%CI -2.03, −1.84) to −0.095 (95%CI -0.17, −0.02). The five countries with an AAPC greater than 5 are the United Arab Emirates, Qatar, the Syrian Arab Republic, Burundi, and Yemen, with values of 6.694 (95%CI 6.47, 6.92), 6.466 (95%CI 6.17, 6.77), 5.959 (95%CI 3.38, 8.6), 5.853 (95%CI 1.94, 9.92) and 5.17 (95%CI 3.18, 7.2), respectively.

According to the different SDI regions, from 1990 to 2019, ASPR and ASIR of femoral fractures in high SDI and high-moderate SDI regions were reduced (AAPC<0), whereas ASPR and ASIR of femoral fractures in moderate SDI and moderate-low SDI regions appeared to be elevated (AAPC>0), and ASPR was elevated while ASIR was reduced in low SDI regions (table S1).

The analysis of the population pyramid showed that in 1990, females had a higher femur fracture ASPR than males in the 1–9 and 75+ age groups, while males had a higher femur fracture ASPR than females in the 10–74 age group. This male-female difference persisted in 2019 (Fig. S4).

Unlike the ASPR, the image of ASIR is not the typical trian gle (Fig. S5). In both 1990 and 2019, male ASIR was higher than female ASIR in the under-60 population. But in 2019, the difference between male and female ASIR was smaller than the difference in 1990 in the under-60 population. In contrast, in the over-60 population, for each 5-year increase in age, female ASIR was 1–2 times higher than male ASIR. It might indicate that the difference between male and female ASIR was small in 1990, but in 2019, the difference between females and males was gradually expanding.

In the population pyramid of YLDs, both 1990 and 2019 showed a spindle shape (Fig. S6). In 1990, females had higher YLDs than males in the below 60 years group. Males had a higher YLDs than females in the population aged 60 years and above. However, by 2019, the YLDs was low in younger and middle-aged males, while the YLDs was high in high-aged males.

The results of the time-series machine learning models showed that the optimal algorithms among the six algorithms were not the same for different metrics. The 6 models included EARTH (MARS), ARIMA,

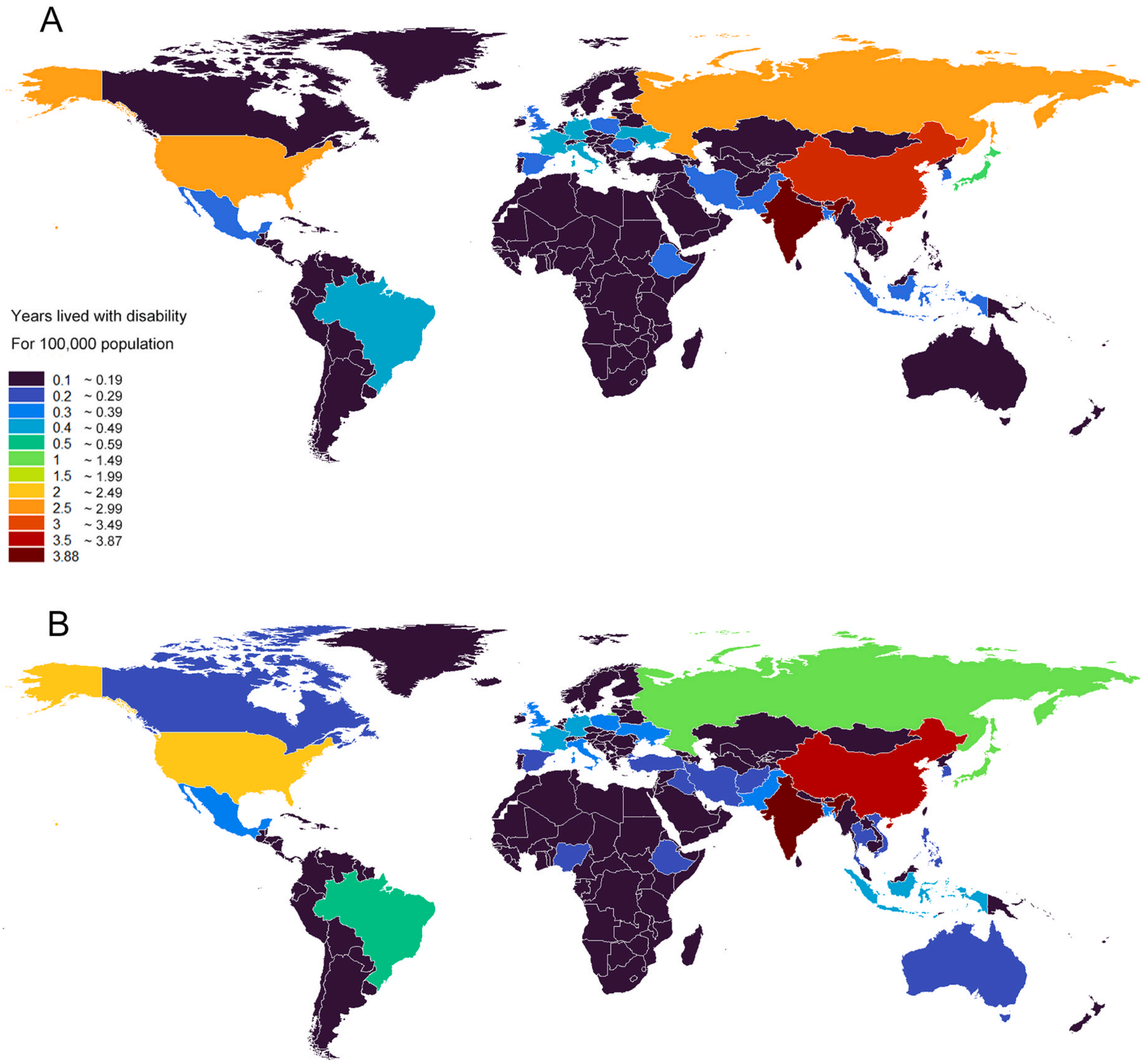

Figure 3. Femur fracture years lived with disability (YLDs) in 1990 (A); Femur fracture YLDs in 2019 (B).

PROPHET, GLMNET (Elastic Net), RANDOM FOREST, and PROPHET WITH XGBOOST. According to the 6 evaluation metrics (i.e., Mean Square Error, Mean Absolute Percentage Error, Mean absolute scaled error, Symmetric Mean Absolute Percentage Error, Root Mean Square Error and R^2), model was desired with a high R^2 along with a low Error.

ARIMA had the best effect among the predictive models of global femur fracture ASPR. The femur fracture ASPR was decreasing from 1990 to 2015, but this downward trend reversed between 2016 and 2019 (Fig. S7). The ARIMA model showed that the ASPR continue to rise from 2020 to 2030, suggesting that the ASPR for femur fracture would be likely to continue to rise in the next 10 years (Fig. S7).

In the prediction of global ASIR of femur fracture, PROPHET model work best and ASIR was in a fluctuating oscillating downward change over the last 30 years, and the prediction showed that it will be still in an oscillating downward trend over the next 10 years, from 2023 to 2030 (Fig. S8).

The PROPHET WITH XGBOOST model was the best predictor of global YLDs. Between 1990 and 2019, YLDs of femur fracture was on the rise, especially after 2015 the growth of YLDs became faster. The prediction results showed that YLDs will be still likely to continue to rise and maintain a high growth rate from 2020 to 2030 (Fig. S9).

4. Discussion

Our analysis showed there was a significant rise in ASPR for femur fractures in a number of countries, including Syria, Burundi, Haiti, Rwanda, China, Central African Republic, Yemen, and Pakistan. This was a phenomenon worth thinking about, and we proposed some preliminary explanations that the war in Syria might be an important risk factor for the apparent rise in femoral fracture ASPR. There might be a similar war-torn scenario for elevated ASPR in other countries, such as regional conflicts in Africa and the Palestinian-Israeli conflict. It was suggested that war might have a significant adverse impact on a country's health care system and impair the way to access and receive medical and surgical services. The victims of conflict- and terrorism-related fractures in North Africa and the Middle East might not be able to access appropriate surgical and medical care, which would help to mitigate the disability [23,24]. In addition, these injuries were more likely to be secondary to high-energy mechanism injuries. The Chinese explanation might not be attributable to war-torn conflict, and there were other reasons that should be explored and analyzed, such as the aging population in China as a populous country. This explanation was in line with previous studies that the risk of low bone mass and suffering osteoporotic fractures increased significantly with age, increasing fracture risk in Western countries and developing countries with progressively aging populations [20].

Against the backdrop of overall global ASIR reductions, there were still a number of countries experiencing rapid increases. These included Yemen, Afghanistan, the Syrian Arab Republic, South Sudan, the Central African Republic, Libya, China, Burkina Faso, and Pakistan. We speculated the regional environmental climate, public awareness of protection, and aging population in these countries were conducive to increase ASIR. Previous reports suggested that falls were the leading cause of femur fractures, and that the occurrence of falls might be caused by impaired vision, frailty, alcohol abuse, poor protective awareness, and environmental factors, and that these risk factors might be co-prevalent in countries with elevated ASIR [25,26].

YLDs had risen obviously globally, which might be due to the increased prevalence of femur fractures, especially in the older age groups, leading to disability. With population aging, YLDs increased significantly in all populous countries. Previous studies concluded that osteoporotic fragility fractures predisposed to severe disability in an already fragile patient population [27–29].

After analyzing the changes in the main indicators, it was also found that aging women were consistently more likely to suffer from femur fractures than men. This might be due to reduced bone density and osteoporosis in pregnancy, menopause and older women compared to men. Aging women had higher ASPR and ASIR than men. For people over 50 years of age living in developed countries, the lifetime risk of fracture was estimated to be approximately 50% for women and 20% for men. Both the World Health Organization (WHO) and the International Osteoporosis Foundation (IOF) recommend a 10-year timeframe as the basis for public health analyses and interventions [30,31].

About YLDs, aging men on the other hand were higher than women, suggesting that older men were more likely to experience disability than women. A fragility fracture demographic concluded that men without osteoporosis screening appeared to have a higher burden of subsequent fractures and disability than women in all age groups. This difference persisted after age adjustment and might reflect men's lower treatment awareness of osteoporosis after fracture compared with women [32].

In the YLDs indicators, the younger and middle-aged were decreasing, while the older age groups were increasing, possibly as a result of the global population aging along with a decrease in the birth rate. In terms of regional differences, East Asia showed a significant increase in all 3 indicators compared with other regions, possibly due to ethnic differences. A study concluded that East Asians did not consume much dairy products due to traditional dietary habits, which increase the risk of fractures [33].

Finally, the results of time-series machine learning model suggested that while the global femur ASIR would wave-line decline over the next 10 years, the ASPR would still rise, and the YLDs would rise substantially and rapidly. Considering the squeeze on healthcare resources by COVID-19, the treatment of femur fracture was bound to be affected, which might lead to the rise of YLDs. Therefore, regional and national intervention policies were needed to reduce the rapid rise of YLDs and improve the quality of life of femur fracture disabilities, including medical education, physician training and social insurance [25,34,35].

This study has several limitations. First, because the raw data were obtained from civil registration, vital statistics, and hospital records, the completeness of these systems affected the accuracy of the estimates. In some low-income countries or countries with frequent wars and lack of adequate health care systems, raw data were scarce. Second, our study was an ecological study, and we only could analyze the association between sex, age, and femur fracture. However, this study could not be used to make causal inferences between risk factors and femur fractures, and prospective studies were needed. The interpretations derived were correct at the population level but might not be appropriate for individuals. Third, since only 6 ML algorithms were compared in this study, other superior algorithms might exist in predicting femur fractures.

In conclusion, our study found that femur fracture ASPR and ASIR in war-conflict areas increased significantly from 1990 to 2019. The fastest increase in all three indicators of femur fracture was observed in East Asia, especially in populous countries, which should be highly emphasized. Both ASPR and ASIR were higher in aging females than in males, but YLDs was higher in aging males than in females. Finally, the prediction of time-series machine learning suggested that although ASIR of femur fracture would decrease globally, ASPR and YLDs would increase.

Data sharing

To download the data used in these analyses, please visit the Global Burden of Disease Results Tool (http://ghdx.healthdata.org/gbd-results-tool), made public by the Institute for Health Metrics and Evaluation.

Ethics approval

Since this research is based on global burden of disease study 2019 database. This study is approved by the ethics committee of GBD from Institute for Health Metrics and Evaluation.

author contributions

The conception and design: YBZ, QWJ and JWW, ; analysis and interpretation of the data: YZ, JJ and MC; the drafting of the paper: JYW and YJC; revising it critically for intellectual content: JYW and YJC; and the final approval of the version to be published: all authors; and that all authors agree to be accountable for all aspects of the work.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Abbreviations

ASIR	age-standardized incidence rate
ASPR	age-standardized prevalence rate
YLDs	years living with disability
ML	Machine learning
AAPC	annual average percentage change
GBD	Global burden of disease
ICD-10	International Classification of Diseases, 10th edition
SDI	Sociodemographic indices
MARS	Multivariate adaptive regression splines
ARIMA	Autoregressive Integrated Moving Average
XGBoost	extreme gradient boosting
95%UI	95%uncertainty interval
95%CI	95%confidence interval
WHO	World Health Organization
IOF	The International Osteoporosis Foundation

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jot.2024.03.002.

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