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CLINICAL ARTICLE

Epidemiological Characteristics of Major Joints Fracture-Dislocations

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Objective: To describe the epidemiological features of major joints fracture-dislocations between 2015 and 2019.

Methods: This retrospective study enrolled patients with majorintra-articular fracture-dislocations who were treated in the third hospital of Hebei Medical University from January 2015 to December 2019. A total of 582 patients (389 [66.84%] males and 193 [33.16%] females) were identified. The distribution characteristics of intra-articular fracture-dislocations involving shoulder, elbow, wrist, hip, knee, and ankle joints were included. The potential associations between fractures with concomitant dislocations and related factors, such as age, gender and sites were explored.

Results: There were 92 cases (15.81%) of shoulder joints, 67 cases (11.51%) of elbow joints, 45 cases (7.73%) of wrist joints, 181 cases (31.10%) of hip joints, 42 cases (7.22%) of knee joints, and 155 cases (26.63%) of ankle joints. The overall male-to-female ratio was 2.02:1.The highest proportion age group of the six types intraarticular fracture-dislocations included the ages 25-34 years. For males, the highest proportion age group was 25-34 years, for females, it was 45–54 years. For male patients, hip was the most common, accounted for 35.48%, but ankle fracture-dislocation was the most common for females, accounted for 30.57%. The highest proportion age group of shoulder fracture-dislocation included the ages 55-64 years(22.83%), with a male to female ratio of 1.24:1. While the age group with the highest risk of elbow, wrist, hip, knee and ankle fracture-dislocation was 25-34 years (28.36%) with a male to female ratio of 3.21:1, 15-24 years (31.11%) with a male to female ratio of 8:1, 45-54 years (27.07%) with a male to female ratio of 3.21:1, 15-24 years (45.24%) with a male to female ratio of 0.75:1, 25-44 years (43.87%) with a male to female ratio of 1.63:1, respectively. The most common site of joint fracture-dislocation in different age groups was corresponding as follows, 0-14 years (elbow), 15-24 years(knee), 25-34 years(hip), 35-44 years(hip), 45-54 years(ankle), 65-74 years (shoulder), \geq 75 years(shoulder).

Conclusion: Major joints fracture-dislocations were most common in the hip and the least common in the knee, and there were more men than women. Hip was the most common affected joint in men while ankle in women. Age and sex factors can significantly affect the location of intra articular fracture and dislocation. The current study could aid orthopaedic surgeons in a better understanding of this injury and help to implement targeted preventive measures.

Key words: Age distribution; Epidemiology; Fracture dislocation; Joints; Sex distribution

Address for correspondence Wei-guang Zhao, Department of Orthopedic Surgery, Handan Central Hospital, Handan 056002, Hebei, China; Tel : +86 18630006663; Fax : +86 0310 2112580; Email: zhaoweiguang361@163.com Disclosure: All the authors stated they had no conflict of interest. Received 27 December 2020; Revised 27 August 2021; accepted 16 September 2021

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Introduction

F racture-dislocation is a rare type of orthopaedic emergency and the prognosis is usually poor, so higher treatment techniques are needed. It remains one of the daunting challenges for orthopaedic surgeons. The standard of diagnosis and management of this type of injury is higher than that of simple intra-articular fractures or dislocations. The treatment principles and procedures of any kind of intra-articular fracture combined with dislocation should be as follows: first, the joint reduction should be attempted by manipulation within a short time after the injury, and the combined fracture can be treated by elective surgery if the preoperative examination is completed, if joint reduction is difficult, open reduction and intraoperative reduction of fractures are probably required. The ultimate goal is to ensure smooth articular surface without steps, firmly fix the fractures, and start joint functional exercise at an early stage. So compared with other fracture types of limbs, improper treatment of fracturedislocation often results in complications such as malformations, dysfunction and intractable pains. So their influence on the social and financial well-being of the patient is often more significant than that of other injuries. It is mostly caused by high-energy injuries or falling injuries. However, studies had shown that there were obvious differences in the causes of the injury among different gender and age. For example, children were more likely to be found in daily sports and games while young males were more likely to suffer traffic injuries such as cars and motorcycles crashes, and old females were susceptible to low energy injuries such as falls^{1,2}.

Age and gender can also obviously influence the type of fracture-dislocations^{3–5}. Illustrating the relationships between age, gender and fracture-dislocations can not only help orthopaedic surgeons to determine the key sites for examination, but also contribute to implementing targeted preventive measures to reduce the incidence of this serious injury.

However, most studies focus on clinical treatments at present, and there remains lack of large sample epidemiological investigation on the joints fracture-dislocations, furthermore, relevant research probably focused on one special joint (e.g. shoulder, elbow or hip joint), rather than multiple joints fracture-dislocations in the whole body. There has been many studies on intra-articular fractures or dislocations respectively, but reports specifically on intra-articular fractures with dislocations are sparse. What is more, up to now, there are few epidemiological studies on intra-articular fractures with dislocations all over the world, and in addition these outcomes of the research lack comparability due to the differences among study designs. Due to the relatively small sample size included in the existing studies, it is inevitable that there will be errors in the relevant statistical results or their scientific nature and accuracy will be reduced. Therefore, it is necessary to further implement associated investigation on these factors to identify the aggregation of large joints fracture-dislocations at different ages and genders. Primary prevention of this type of injury is particularly

important and may be the most critical factor in reducing the medical burden. While the epidemiological study on the injury is an important prerequisite and basis for the formulation of primary prevention measures, so we conducted this retrospective study on the clinical data's of 582 cases with major large joints fracture-dislocations aimed to clarify: (i) the distribution of different joints fracture-dislocations among the included patients; (ii) the influence of gender factor on each different fracture-dislocations of large joint; and (iii) the constitution of major joints fracture-dislocations in different age groups. Based on the results of this study, the ultimate goal is to provide effective targeted prevention strategies and guide the clinical key examination sites.

Patients and Methods

Patients Inclusion

Patients with large major joints fracture-dislocations of the limbs were identified in this study through the medical record inquiry systems and Picture Archiving and Communication Systems (PACS) of the Third Hospital of Hebei Medical University between 1 January 2015 and 1 December 2019.

Inclusion criteria: patients with complete medical data who diagnosed as joints dislocations according to the medical records and imaging examinations complicated with corresponding any kind of fractures as follows: (i) shoulder humeral head and anatomic neck, glenoid fossa of scapula; (ii) elbow—capitulum humeri, medial and lateral condyle of humerus, humeral intercondyle, coronal process, olecranon, capitulum radii; (iii) wrist—ulnar styloid, distal radial, scaphoid, lunate bone, triquetrum; (iv) hip—femur head, acetabulum; (v) knee—patella, femoral intercondylar, tibial plateau; and (vi) ankle—lateral, medial and posterior malleolus, or talus.

Exclusion criteria: (i) old fracture-dislocations; (ii) pathological and pseudo fracture-dislocations; and (iii) open or multiple traumas.

Data Collection and Fracture Classification

First, we screened out the list of eligible patients through the medical record system, then we reviewed medical records of enrolled patients and the age and gender of each patient with large major joint fracture-dislocations were well documented. Next, the preoperative X-rays, CT or MRI of the cases were collected by the use of picture archiving and communication system in our hospital. Finally, the images of each patient were reviewed by five orthopaedic surgeons with more than 10 years of experience. According to different fracture-dislocations site, these cases were divided into shoulder, elbow, wrist, hip, knee, and ankle joints. If there was any disagreement in the diagnosis, a final decision would be made through discussion with consensus achieved by at least three surgeons.

Age Groups and Gender

The patients were divided into eight groups by age: 0-14 years, 15-24 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years,

65–74 years and \geq 75 years. Gender divided into male and female.

Indicators Measures

A joint fracture-dislocation is defined as that fracture of a bone near an articulation with concomitant dislocation of that joint, so all the patients in this study met the definition by the aid of preoperative images such as X-ray, CT, or MRI. Fracture-dislocations in six large major sites of the human limbs were chosen to be analyzed and each joint fracturedislocation included the following types respectively:

Shoulder Joint Fracture-Dislocations

It is defined as a dislocation of the glenohumeral joint with a fracture such as: humeral head, anatomic neck, or glenoid fossa of scapula.

Elbow Joint Fracture-Dislocations

It is defined as a dislocation of the humeroradial joint or humeroulnar joint with a fracture such as: capitulum humeri, medial and lateral condyle of humerus, humeral intercondyle, coronal process, olecranon, capitulum radii.

Wrist Joint Fracture-Dislocations

It is defined as a dislocation of the radiocarpal joint with a fracture such as: ulnar styloid, distal radial, scaphoid, lunate bone, triquetrum.

Hip Joint Fracture-Dislocations

It is defined as a dislocation of the articulatio coxae with a fracture such as: femur head, acetabulum.

Knee Joint Fracture-Dislocations

It is defined as a dislocation of the patellofemoral joint or tibiofemoral joint with a fracture such as: patella, femoral intercondylar, tibial plateau.

Ankle Joint Fracture-Dislocations

It is defined as a dislocation of the tibiotalar joint with a fracture such as: lateral, medial and posterior malleolus, or talus.

Statistical Analysis

Descriptive datas were presented using the numerical values and composition ratios. The numbers of fracture-dislocations and composition ratios in each year were analyzed. The distribution of gender and distribution of joints fracture-dislocations in different age groups were all statistical analysed. The Kolmogorov–Smirnov test was used to check whether results were in accordance with the normal distribution. The different numbers of fracture-dislocations in each year were analyzed by ANOVA test, and the LSD or SNK-Q test was used to comparing two random years among five years. The compositions of fracture-dislocations between male and female for 5 years were analyzed by a Pearson chi-square test. All the analyses were

TABLE 1 Gend	ABLE 1 Gender distribution of 582 fracture-d	on of 582 frad	cture-dislo	cations f	tions from 2015 to 2019	:0 2019										
		2015			2016			2017			2018			2019		
Joint	Male	Female	Sum	Male	Female	Sum	Male	Female	Sum	Male	Female	Sum	Male	Female	Sum	Sum
Shoulder	9	80	14	9	6	15	10	ъ 2	15	18	13	31	11	9	17	92
Elbow	12	4	16	4	0	4	ю	2	ß	14	9	20	13	б	22	67
Wrist	18	ß	23	ß	0	Ŋ	9	0	9	10	0	10	Ч	0	Ч	45
Hip	27	4	31	16	D	21	25	7	32	32	12	44	38	15	53	181
Knee	ო	11	14	0	1	Ч	9	2	∞	7	0	0	7	10	17	42
Ankle	18	1	19	7	ო	10	16	4	20	9	2	∞	49	49	98	155
Sum	84	33	117	38	18	56	66	20	86	82	33	115	119	89	208	582

performed with the use of SPSS 22.0 (IBM, Chicago, IL, USA). A *P*-value of <0.05 was considered significant.

Results

Demographic Information and Fracture-Dislocations Classification

A total of 582 patients with appendicular large joints fracture-dislocations were identified during the 5-year period, accounting for 0.90% (582/64885) of the total fractures in the same period, including 389 males and 193 females. The overall male-to-female ratio was 2.02:1. From 2015 to 2019, the number of patients with fracture-dislocations was 117, 56, 86, 115 and 208 in turn.

There were 92 cases (15.81%) of shoulder joints, 67 cases (11.51%) of elbow joints, 45 cases (7.73%) of wrist joints, 181 cases (31.10%) of hip joints, 42 cases (7.22%) of knee joints, and 155 cases (26.63%) of ankle joints. There was no significant difference in the composition of fracture-dislocations among the five years (F = 2.096, P=0.119, Table 1, Fig. 1), but with a significant difference in the composition of fracture-dislocations between males and females ($\chi 2 = 35.171$, P = 0.000, Table 2, Fig. 2).

Age Group and Gender Distribution in Different Joint Fracture-Dislocations

For male patients, hip was the most common, accounted for 35.48%, but ankle fracture-dislocation was the most common for females, accounted for 30.57%. The proportion of knee fracture-dislocation was the smallest among male patients, accounting for 4.63%, while the patients with wrist fracture-dislocation making up to 2.59% were the rarest among the females (Fig. 2).

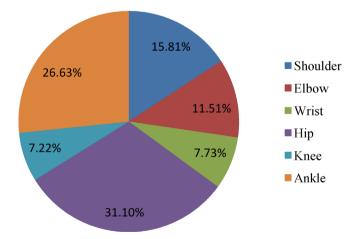
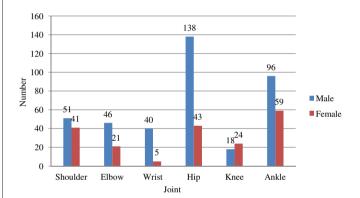


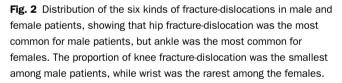
Fig. 1 Distribution of different joint fracture-dislocations in 582 patients, including 389 males and 193 females. There were 92 cases of shoulder joints, 67 cases of elbow joints, 45 cases of wrist joints, and 181 cases of hip joints, 42 cases of knee joints, and 155 cases of ankle joints.

EPIDEMIOLOGICAL CHARACTERISTICS OF MAJOR JOINTS

The highest proportion age group of the six types joints fracture-dislocations included the age 25-34 years (Fig. 3). For males, the highest proportion age group was

TABLE2Distrifemalepatients	bution of fracture-dislocatio	ons in male and
Joint	Male	Female
Shoulder	51 (13.11%)	41 (21.24%)
Elbow	46 (11.83%)	21 (10.88%)
Wrist	40 (10.28%)	5 (2.59%)
Hip	138 (35.48%)	43 (22.28%)
Knee	18 (4.63%)	24 (12.44%)
Ankle	96 (24.68%)	59 (30.57%)
Sum	389	193





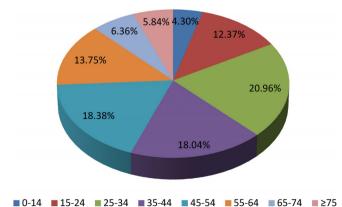


Fig. 3 The composition of fracture-dislocations in different age groups, showing that the highest proportion age group was 25–34 years. While 0–14 years was relatively infrequent.

25-34 years, for females, it was 45-54 years. The highest proportion age group of shoulder fracture-dislocation included the ages 55-64 years (22.83%), with a male to female ratio of 1.24:1. While the age group with the highest risk of elbow, wrist, hip, knee and ankle fracture-dislocation was 25-34 years (28.36%) with a male to female ratio of 2.19:1, 25-34 years (31.11%) with a male to female ratio of 8:1, 45-54 years (27.07%) with a male to female ratio of 3.21:1, 15-24 years (45.24%) with a male to female ratio of

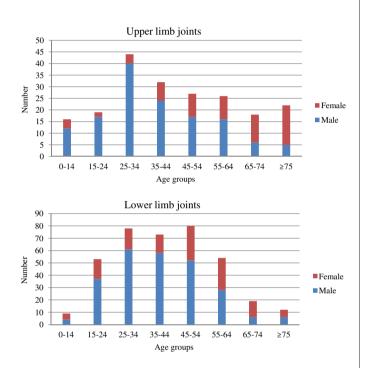


Fig. 4 (A) Age group and gender distribution in upper limb joints fracture-dislocations, showing that major joints fracture-dislocations of the upper extremity were most common in men between 25 and 34 years old while in women was \geq 75 years old. (B) Age group and gender distribution in lower limb joints fracture-dislocations, showing that the highest proportion age group was 25-34 years in males. While 45-54 years were most common in females.

EPIDEMIOLOGICAL CHARACTERISTICS OF MAJOR JOINTS

0.75:1, 25-44 years (43.87%) with a male to female ratio of 1.63:1, respectively. Age group and gender distribution in upper limb joints fracture-dislocations, showing that major joints fracture-dislocations of the upper extremity were most common in men between 25 and 34 years old while in women was ≥75 years old. While in lower limb joints fracture-dislocations, the highest proportion age group was 25-34 years in males, and 45-54 years were most common in females (Fig. 4A,B).

The Most Common Fracture-Dislocations in Different Age Group

The most common site of joint fracture-dislocation in different age groups was corresponding as follows, 0-14 years (elbow, 56.00%), 15-24 years (knee, 26.39%), 25-34 years (hip, 33.61%), 35-44 years (hip, 35.24%), 45-54 years (hip, 45.79%), 55-64 years (ankle, 35.00%), 65-74 years (shoulder, 43.24%), ≥75 years (shoulder, 58.82%) (Table 3).

Discussion

Fracture-dislocation is a fracture of bone near an articula-tion with concomitant disland tion with concomitant dislocation of that joint. While available literatures probably focused on one special joint (e.g. hip or shoulder) instead of multiple joint fracturedislocations in the whole body (Fig. 5). So it is necessary to carry out systematic large joint fracture-dislocation epidemiological studies aiming to provide effective targeted prevention strategies and guide the clinical key examination sites. Our study reports, for the first time, age- and gender- specific epidemiological characteristics of major appendicular fracture-dislocations from a level 1 trauma center during five years. Although this is not a national investigation study, but it includes a large number of cases in a long time span.

We had chosen age and sex factors because these two factors can significantly affect the site of fracture-dislocations. As early as 1882 Bruns⁴ first discussed the influence of age and gender on the incidence of various types of fractures. Alffram and Bauer⁶ studied the age and gender differences of 2672 cases of forearm fractures occurred in 5 years and found that: before the age of 40, the incidence of distal forearm fractures in males and females was approximately equal,

	Shou	lder	E	bow	V	Vrist		Hip	K	nee		Ankle	
Age	Male	Female	Sum										
0–14	0	0	10	4	2	0	1	0	3	5	0	0	25
15–24	7	0	3	0	7	2	13	3	10	9	14	4	72
25–34	10	1	16	3	14	0	34	7	0	3	27	7	122
35–44	6	2	12	3	6	3	31	6	1	1	26	8	105
15–54	5	4	4	6	8	0	37	12	1	4	14	12	10
55–64	14	7	0	3	2	0	16	7	3	0	9	19	80
65–74	5	11	1	1	0	0	4	6	0	1	2	6	37
≥75	4	16	0	1	1	0	2	2	0	1	4	3	34
Sum	51	41	46	21	40	5	138	43	18	24	96	59	582

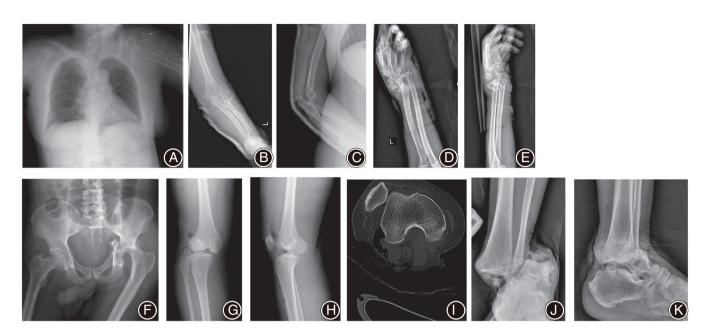


Fig. 5 Eleven representative images of intra-articular fracture-dislocations involving shoulder, elbow, wrist, hip, knee, and ankle joints. (A) This patient is an 81-year-old woman, with shoulder fracture-dislocations. (B, C) This patient is a 54-year-old man, with elbow fracture dislocations. (D, E) This patient is an 82-year-old man, with wrist fracture-dislocations. (F) This patient is a 67-year-old woman, with hip fracture-dislocations. (G, H, I) This patient is a 40-year-old woman, with knee fracture-dislocations. (J, K) This patient is an 81-year-old man, with ankle fracture-dislocations.

while after the age of 60, the number of female patients with fractures was more than seven times that of males. Singer⁴ conducted an epidemiological survey on 15,000 adult fracture patients in Edinburgh area, and found that between 15 and 49 years old, males were 2.9 times more likely to have fracture than females, while after 60 years old, the situation was reversed that females were 2.3 times more likely to have fracture than males. The influence of age and gender on the incidence and location of fractures also exists in the adolescent population. An epidemiological survey of 6% population of the Britain⁷ showed that the incidence of fractures in adolescent boys was higher than that in girls, and the peak time was 14 and 11 years old respectively, with significant differences between them. A recent study with demographics of fractures and dislocations across the entire United States had shown that the odds of sustaining a fracture and dislocation in males was both higher than females, with different incidence in different age groups. Based on previous studies, this research also confirmed that age and gender factors can also significantly influence the distribution of joint fracturedislocations.

Demographics on Age and Gender of Overall Joints Fracture-Dislocations

Male patients were about twice as likely as female, possibly because they often participate in sports or jobs that were vulnerable to injury. During five years, 181 cases were hip fracture-dislocations, accounting for 31.10%, which was highest proportion. The reason may be that although the

incidence of femur fractures was extremely low, approximately less than 0.5%, but acetabular fractures were not rare, with the incidence rates of 1.5%8. Hip fracture and dislocation were first reported by Cooper et al. in 17919 and Bigelow first described traumatic dislocation of the hip in detail in 1869¹⁰. An epidemiological study of acetabular fractures enrolled 32,614 patients over a 10-year period in France showed that incidence of acetabular fracture per 100,000 increased from 3.67 in 2006 to 4.95 in 2016⁸. Another study in Qatar included 103 cases with acetabular fractures discovered that posterior wall fractures were the most common (25.2%) and combined posterior dislocation of hip joint accounted for $21.3\%^{11}$. A retrospective analysis showed that posterior fracture-dislocations accounted for 57 of 107 traumatic dislocations of the hip¹². One Nigerian study found that 48 in the 50 cases of hip dislocation were posterior dislocation¹³.

Similar to previous research, the proportion of knee joint was the smallest among this investigation and it was the only type of fracture-dislocations in which women had more injury than men, with a female to ratio male of 1.33:1. This situation was associated with extreme morbidity, accounting for about 0.02% of orthopedic injuries¹⁴, and because of high incidence of patellar dislocation (42/100000), especially girls with 10 to 17 (108/100000)¹⁵.

The main causes of hip fracture-dislocations were high energy damage such as high-speed motor vehicle crashes or falls from a height. So that preventive measures should be taken to reduce this injury, such as legislating to use seat

EPIDEMIOLOGICAL CHARACTERISTICS OF MAJOR JOINTS

belts and building safety net to reduce injury when falling. Diagnosis of congenital patellar dysplasia and appropriate measures should be taken to strengthen knee protection for this type of adolescent girl in future activities can reduce the incidence of patellar fracture-dislocations of knee joints.

Age and Gender Distribution at Different Joints Fracture-Dislocations

The highest proportion age group of shoulder fracturedislocations included the ages 55-64 years (22.83%), with a male to female ratio of 1.24:1. The results were different from the previous epidemiological studies of simple shoulder fractures and shoulder dislocations. The 46.8% of 8940 shoulder dislocations were in patients between 15-29 years described by Zacchilli and Owens¹⁶ in the United States, with more male patients than females. What is more, they found only 28 fracture-dislocations in that large sample research, so shoulder fracture-dislocations were very rare at that age. Our previous epidemiological analysis of intraarticular fractures in 11084 patients showed that the highest proportion age group of shoulder fractures was ≥ 65 years (41.89%) and the male-to-female ratio was 0.76:1, which was the only age group the number of female patients exceeded that of male patients. The reason may be that osteoporosis of females was more severe or old women more than men^{17,18}. Our study, for the first time, showed that shoulder fracturedislocation having its own unique characteristics of age and gender distribution when comparing with simple fractures or dislocations.

While the age group with the highest risk of elbow and wrist was both at 25-34 years, with a male to female ratio of 2.19:1 and 8:1, respectively. A reliable study based on the National Electronic Injury Surveillance System involving elbow dislocations in the United States showed that the second highest age group was the 20 to 29-year-old group¹⁹. Males in this age group were more likely to have an elbow fracture-dislocations in traffic accidents or during strenuous exercises. The highest proportion age group of hip fracturedislocations were at 45-54 years, this might be due to the higher incidence of acetabular fractures associated with posterior femoral head dislocation or central dislocation in this age group²⁰. Since this injury could lead to severe complications such as necrosis of the femoral head, relevant measures should be taken to avoid its occurrence, such as speed limiting, enhancing safety configuration of motor vehicles, and enhancing construction safety, etc.

The highest proportion age group of knee fracturedislocations were at 15–24 years, with slightly more men than women. The reason may be that this age group of females have more patella fracture-dislocations. This result was similar to research by Thomas²¹ and Brian²², the former research showed mean age at dislocation was 21.4 \pm 9.9 years, and 331 patients (54.4%) were female and the latter indicated more than one half of injury involving athletic activity, such as basketball (18.2%), soccer (6.9%), and football (6.3%). Therefore, relevant sports protection measures should be formulated, such as wearing protective gears.

The ages 25–34 and 35–44 had the same high risk of ankle fracture-dislocations, so we combined these two age groups into one age group as 25–44. Ryan²³ conducted an epidemiological study of 673,214 ankle fractures showing that 20–49 years was risk age group, with mean age of 37 ± 22.86 (SD) years. Another study showed about 28% sustained a fracture-dislocation of all the ankle fractures and the most common risk factors were falls and various sports²⁴, suggesting that attentions should be paid to the protection of ankle joints in this age group males who engaged in more construction and exercise activities.

Distribution of Fracture-Dislocations by Age Groups

The most common site of joint fracture-dislocation at 0-14 years was elbow, considering high incidence of olecranon, humeral condyle²⁵ and more activity patterns in this age group. The result was similar to our former investigation²⁶ which included 8987 fractures showing that 7-11 years and the distal humerus were both the most common. The knee fracture-dislocation was the most common at 15-24 years because of patellar fracture-dislocations in this age group²⁷. In the age group of 25-34 years, 35-44 years and 45-54 years, hip joints were both the most frequently involved. These age groups belong to the backbone of the economy and main breadwinners of the family, so they were susceptible to high-energy damage such as high-speed motor vehicle accidents or falls from heights, resulting in hip fractures with dislocations. This study found the most common site of joint fracture-dislocation in different age groups was corresponding as follows, 55-64 years (ankle), 65-74 years (shoulder) and \geq 75 years (shoulder). Most of the two injuries were caused by osteoporosis due to the increase of age, so there were many injuries of low energy, such as the sprain feet caused by unstable walking, fall to ground hurting shoulders²⁸.

Divided by age groups, we identified the most common sites for fracture-dislocations in each age group, which would help to adopt safety measures to cut down this injuries and avoid related complications. Finally, the social cost and financial burden on their families would be reduced.

Limitations

Although the data in this study was from a level 1 trauma center and included a large sample, there were still some limitations. The sample came from one single hospital, it only represents the fracture-dislocation characteristics of some inpatients in one region. It was inevitable that there would be recall bias because of retrospective study. Finally, other factors such as occupation, residential category, mechanism of injury, season, fracture pattern and so on were not taken into account. Therefore, in the future, we will include more patients and analyze more relevant factors through multiple centers. Orthopaedic Surgery Volume 9999 • Number 9999 • 2021

Conclusion

The current study revealed the age and gender epidemiological characteristics of major joints fracture-dislocations, which could aid orthopaedic surgeons in a better understanding of this injury and help to implement targeted preventive measures.

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EPIDEMIOLOGICAL CHARACTERISTICS OF MAJOR JOINTS

Author Contributions

W.Z. conceived the idea for the study; Y.Z. designed the study. J.M., X.Y., Y.Z. collected the relevant data. Y.Z. and J.M. prepared the tables and figures. W.Z. performed the statistical analyses. All the authors interpreted the data and contributed to preparation of the manuscript.

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