Does Kashin-beck Disease Present Only Multisite Pain? A Cross-sectional Study of Pain Characteristics in Northwest China

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Abstract

Background

Kashin-Beck Disease (KBD) is an endemic, chronic joint disease. Multisite joint pain is the primary symptom of KBD, which have profound negative effects on individuals and society. However, studies on joint pain characteristics among the KBD population are still limited. The aims of this study were to explore characteristics of joint pain in patients with KBD and determine associated factors with joint pain.

Methods

This cross-sectional study included 167 patients with KBD and 169 patients from the general population with joint pain from Shaanxi Province in northwest China. Subjects were asked about joint pain characteristics and completed the numeric rating scale (NRS), the graded chronic pain scale (GCPS) and the EuroQol (EQ-5D) questionnaire. Differences between groups were determined using Chi-square, Student's t, Mann–Whitney U and 1-way ANOVA tests.

Results

Compared with the general group, patients with KBD reported a higher number of pain sites (7.2±3.8 vs 3.5± 1.8), a higher frequency of persistent pain (98.8% vs 50.9%), a higher percentage of analgesics usage (89.2% vs 30.7%), a higher pain intensity (73.8±15.2 vs 50.0±20.7) and pain –related disability (61.2±23.3 vs 41.6±23.2), and lower EQ-5D scores (0.34±0.27 vs 0.59±0.16). Among the 167 KBD patients, painful joints were symmetrically distributed between the bilateral limbs; the 5 most frequently reported painful joints for the bilateral sides were the knees (84.8%), ankles (79.2%), wrists (51.2%), shoulders (49.5%) and elbows (47.7%). The most severe pain joint was the knee (NRS:6.6), followed by the ankles (NRS:5.1), the fingers, shoulders and elbows had the similar NRS scores (NRS:4.0). Additionally, KBD patients experienced neuropathic pain to varying degrees. Compared to males, females reported a higher number of total pain sites, higher intensity and lower quality of life.

Conclusions

Besides multisite pain, the KBD patients suffered from symmetrical, persistent, and neuropathic pain. Weight-bearing joints (e.g., knee and ankle) were the most painful. These findings will provide scientific basis for establishing joint pain evaluation criteria and future pain intervention strategies for these KBD patients in China.

Background

Kashin-Beck disease (KBD) is a severe osteoarthropathy of unknown cause that is endemic, ranging from Russia, the north of Korea and the northeast to the southwest of China [1]. Three interacting causal mechanisms have been proposed, including a selenium deficiency, contamination of food by mycotoxins, and organic matter in contaminated drinking water [2]. Currently, it has been widely accepted that KBD is a result of environment-gene interaction [3]. KBD occurs most commonly in children aged 5-13 years and is characterized by the degeneration and necrosis of epiphyseal plate cartilage as well as articular cartilage at several other locations in the developing skeleton [4, 5]. It currently affects 22,567,600 inhabitants, and there were 574,925 patients in 2016 [6].

Clinically, the primary symptoms of KBD include multisite joint pain, morning stiffness, enlarged and shortened fingers, and deformed and enlarged joints with limited motion in the extremities [7]. Joint pain has been shown to have profound negative effects on individuals and society[8]. It is reported that the prevalence rates of joint pain varied from 58% to 97.5% in KBD patients[9, 10]. This value is extremely high but, unfortunately, data on the characteristics of KBD

joint pain is scarce. Previous studies on the KBD clinical symptoms mainly focused on the enlargement, deformation, and dysfunction of joints in limbs and radiological lesions of the right hand [11]. Although some studies have reported that KBD patients experienced multisite and bilateral joint pain[9, 12], while others have reported the pain intensity of specific joint in KBD patients (e.g., knees and elbows) [10], they did not provide more information on pain characteristics, such as the frequency and the number of painful joints. Although pain intensity is the most common pain domain assessed in research and clinical practice, pain intensity measures are suboptimal for distinguishing the effects of two active treatments[13].Knowledge of intensity, frequency, duration, site, quality and associated factors of joint pain gives a complete picture of the symptom. However, no study has addressed simultaneously these questions in KBD patients. Thus, the characteristics of KBD pain remain poorly understood. Our incomplete understanding of joint pain characteristics is a barrier to provide appropriate clinical treatment for KBD.

Currently, relieving the pain is an important target in the treatment of KBD [14]. However, pain treatment for KBD is mainly derived from experiences of osteoarthritis (OA) [15], including the administration of analgesic drugs [5], selenium supplementation [16], intra-articular injections of hyaluronic acid (IAHA) [14], surgical procedures[17, 18] and physical therapy [19]. Despite various treatment approaches, there is no specific disease pain measurement to assess joint pain after treatment. A sound pain assessment is an indispensable first step in the management of patients with pain. Thus, it is urgent to resolve this problem.

Our understanding of joint pain characteristics is a necessary prerequisite toward the development of a pain measurement tool and intervention strategies that can effectively address the joint pains of KBD patients. To our knowledge, there are very few studies focusing on KBD joint pain characteristics. Therefore, the purposes of this study were to detail the pain characteristics (e.g., pain intensity, pain frequency, pain location, pain interference, pain treatments) of KBD, and to determine which demographics were associated with pain characteristics. In so doing, it is anticipated that findings from this study will provide scientific basis for establishing joint pain evaluation criteria and future pain intervention strategies for KBD patients in China.

Methods

Setting

This study was conducted in Shaanxi Province in northwest China between May 2018 and October 2018. This is one of the regions with the most cases of KBD in China [20]. Two counties (Yongshou and Linyou) were randomly selected from total 62 endemic counties of Shaanxi Province. In the two counties, 6 villages of each county were selected randomly, and every available adult in these villages were invited to participate in this study.

Diagnostic criteria of KBD

In 2010, the National Health and Family Planning Commission of the People's Republic of China issued new Diagnostic Criteria for Kashin-Beck Disease (Diagnostic code: WS/T207-2010) [21]. The criteria of KBD include: a history of living in a KBD prevalent area, clinical manifestations (typically, short fingers, enlargement of finger joints, flexion of the distal finger and deformed fingers in hands) and radiography of the right hand (typically, irregular sclerosis and reappearance of a calcification zone in the metaphysis of the metacarpus and phalange). The diagnostic grade criteria for grading were as follows: Grade I, enlarged finger joints, limited motion and pain in the joints of the limbs; Grade II, shortened fingers and clinical symptoms of the first stage; and Grade III, dwarfism and clinical symptoms of the second stage.

Sample size calculation

The present study included a sample of patients with KBD and the general population. The KBD detected rate of 3.39% was expected based on a study conducted in Shaanxi Province in 2007 [22]. A sample size of 140 participants was estimated according to the following formula: $Z^2_{a/2}\ p(1-p)/d^2$ (where a =0.05, $Z_{a/2}$ = 1.96, p =0.0 339, d =0.03). This calculation is used to determine sample size in cross-sectional survey design [23], considering a sampling error of 3% and a confidence interval of 95%. To decrease the missing data, we recruited 167 KBD patients. Therefore, 169 general subjects with joint pain in same area were used as a comparison group in the present study.

KBD patients

Patients with KBD were recruited from Shaanxi Province in China. At the time of screening, patients underwent a medical history evaluation, complete physical examination, and examination of the right hand radiographs. The clinical diagnosis of KBD was determined by at least two senior orthopedic surgeons from the local hospital according to the Diagnostic Criteria for KBD (WS/T207-2010).

Inclusion and exclusion criteria

Patients were included if they were diagnosed with KBD, were able to understand Mandarin, and had no cognitive impairment. Patients with concurrent rheumatoid arthritis, any other type of inflammatory arthritis, fibromyalgia, another chronic pain disorder or communication difficulties (e.g., hearing or speech impairments) were excluded. Ultimately, a total of 167 patients with KBD were recruited in this study.

General population

During the course of sampling, the subjects who did not meet the diagnostic criteria for KBD were compared as a control group to better understand the pain characteristics of patients with KBD. Three hundred twenty-five local residents with similar age and sex were recruited. Patients with communication difficulties (e.g., hearing or speech impairments) were excluded. Out of these 325 subjects,169 answered yes to the question: “Are you generally bothered with joint pain?” Thus, 169 general participants were used as a comparison group in the present study.

Measurements

Patients with KBD and the general subjects completed a demographic questionnaire that obtained information on age, sex, ethnicity, marital status, occupation, and educational level.

Pain characteristic assessment

For both the KBD patients and the general subjects, pain was measured, including prevalence, duration, intensity, location, frequency, quality and method of treatment. The included subjects were asked to indicate whether they had pain. If they answered in the affirmative, we continued to ask about the sites, qualities (e.g., pins & needles, swelling, burning, could-freezing, throbbing and itching), the frequency of pain in the last month, and pain duration from initial onset until now. In addition, participants were asked which pain treatments they used (i.e., analgesics, physical therapy or surgery).

Pain sites

Participants marked the site of pain using a body pain drawing, which is the most common method for assessing the site and distribution of joint pain [24]. The subjects were asked to shade areas where they had a specific side of pain (left/right/both) over the prior 6 months. The sites included the following joints: 1) knee, 2) ankle, 3) hip, 4) shoulder, 5) elbow, 6) wrist, 7) interphalangeal joints, and 8) toe. The number of joint pain sites was summed. In this study, the

interphalangeal joint and toe joints were not easily counted; therefore, all painful interphalangeal joints were counted as one site of pain. In the analysis, we assessed a total of 16 joints. The number of joints affected in each patient ranged from 0 to 16.

Pain frequency

Pain frequency (i.e., how often one experiences pain within a certain time frame) is an important component of the chronic pain experience [25]. The one-month period was recommended as a reliable recall period [26] and has been applied in various studies [27, 28]. The frequency of joint pain in the last month was classified as “never,” “some of the days,” “about half of the days,” “most of the days,” or “every day”[29]. Persistent pain was defined as frequent (most days) or constant (every day) pain [30].

Pain intensity

Subjects were asked to provide separate intensity ratings for different pain sites. Pain intensity was measured on an 11-point numeric rating scale (NRS). The NRS is a one-dimensional pain assessment tool with scores ranging from 0 (no pain) to 10 (the worst pain imaginable), with higher scores indicating greater pain intensity. The NRS has been validated for use in the arthritis population [31].

The graded chronic pain scale (GCPS)

The GCPS is a multidimensional measure that assesses two dimensions of overall chronic pain severity during the past 6 months: pain intensity and pain-related disability. The GCPS consists of seven items. The pain intensity is calculated as the average of 3 questions concerning the present, worst, and average pain, as measured on a 0 to 10 scale, ranging from “no pain” to “pain as bad as could be”. “Disability days” refers to the number of days for which pain prevented usual activities. The pain-related disability is calculated as the average of three questions on pain interference with daily activities, social and working activities; the three items are rated on an 11-point scale (0 = no interference/change, 10 = unable to carry on activities/extreme change). Scores on these two subscales range from 0-100, where higher scores reflect greater pain intensity and disability. Pain severity was graded into 5 hierarchical categories: grades 0 to IV: Grade 0: no pain; Grade I, low disability-low intensity; Grade II, low disability-high intensity; Grade III, high disability-moderately limiting; and Grade IV, high disability-severely limiting. Because all the participants had pain in the current study, pain severity was graded into 4 hierarchical categories: grades I to IV. The GCPS is a valid and reliable instrument and suitable for use in all chronic pain conditions, including chronic musculoskeletal (MSK) pain [32]. The Chinese version of the GCPS possesses good psychometric properties, and the Cronbach α values for disability and characteristic intensity scales were 0.87 and 0.68, respectively [33].

The EuroQol (EQ-5D-3L) questionnaire

The impact of pain is a key aspect to consider along with assessing the severity of pain [34]. The EuroQol (EQ-5D-3L) is a standardized preference-based measure of health that provides a simple, generic measure for clinical and economic assessment [35]. The participants were asked to complete the EQ-5D questionnaire (Chinese version). The EQ-5D records the level of self-reported problems in five dimensions (i.e., mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each of the dimensions is divided into three levels of perceived problems: no problem (level 1), some problems (level 2) and extreme problems (level 3). China EQ-5D-3L value sets were used in this study [36]. The scores on the EQ-5D index range from −0.149 to 1, where 1 indicates no problem, zero indicates death and negative values indicate a health status worse than death. The EQ-5D-3L Chinese Version demonstrated fair to moderate levels of test–retest reliability and adequate construct validity in KBD individuals in China [37].

Quality control

Because nearly one-third of the subjects were illiterate, data were collected in face-to-face interviews by survey teams consisting of four Ph.D. students at the Department of Public Health at Xi'an Jiaotong University. All of the survey members had been trained in survey questionnaire procedures. Six staff members of the local Center for Disease Control and Prevention (CDC) helped us connect the included subjects, and our surveys were carried out at local community hospital. Completing the survey took approximately 20 to 25 minutes.

At the end of the survey, each participant received a thank you gift, such as a kitchen utensil. At the end of each day of interviews, all questionnaires were double-checked to check the quality of the questionnaires.

Statistical analysis

Continuous variables are presented as the mean ± standard deviation, and categorical variables are presented as frequencies and proportions. The differences were evaluated using Chi-square tests, independent samples t-tests (for continuous variables), and Mann–Whitney U tests (for ordinal data); paired samples t-tests were used to determine differences between the left and right sides (within subjects) in joint pain intensity and 1-way ANOVA tests, or Kruskal-Wallis tests were used for multiple group comparisons.

All data were analyzed using IBM SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp.). The level for significance in all analyses was defined as $P < 0.05$.

Ethics

All enrolled subjects were informed of the goal and design of this study and were assured of confidentiality before they provided written informed consent to participate in the study. The study was approved by the human ethics committee of the Health Science Center, Xi'an Jiaotong University.

Results

Sample characteristics

In all, 167 KBD patients and 169 general subjects were investigated in Shaanxi Province. All participants were Han Chinese. In the KBD group, nearly half of the patients were Grade I KBD (47.9%), followed by grade II KBD (43.1%), and Grade III KBD (9.0%). No significant differences were found between the KBD and general groups in sex, age, education, marital status, or occupation. The demographic characteristics of the groups are listed in Table 1.

Differences in pain site frequency and joint pain intensity in bilateral limbs of KBD patients

Of the 167 KBD patients recruited for this study, the most frequently reported painful joints for the bilateral sides were the knees (84.8%), followed by ankles (79.2%), wrists (51.2%), shoulders (49.5%) and elbows (47.7%), while the hip (11.3%) and toes (10.6%) were the least frequently reported painful joints. As shown in Fig. 1, painful joints were symmetrically distributed between the right and left limbs; Pain intensities varied between 2.0 and 6.6 on the NRS for these pain sites. The most severe pain joint was the knee (NRS:6.6), followed by the ankles (NRS:5.1). The least painful joints were the hips (NRS:3.2) and the toes (NRS:2.0) (Fig. 2). There were no significant differences in pain frequency and mean pain intensity scores between the bilateral limb joints (both p 0.05).

Differences in the pain characteristics between the KBD and general groups

In comparison to the general group, patients with KBD reported higher prevalence of joint pain (100%) than controls (52.0%, $p < 0.001$), longer pain duration (39.3±14.1) years for KBD patients (8.9±6.9) than for general subjects ($p < 0.001$), a significantly higher number of pain sites (7.2±3.8) for KBD patients than for general subjects (3.5±1.8, $p < 0.001$), higher pain frequency of persistent pain (98.8%) for KBD patients than for general subjects (50.9%, $p < 0.001$), and a higher percentage of analgesics usage (89.2%) than for general subjects (30.7%, $p < 0.001$). In the KBD group, the most commonly cited pain descriptors were pins & needles (56.3%), followed by aching, swelling, hot-burning and itching (53.9%, 41.9%, 36.5% and 27.5%, respectively). The most frequent sensation in the control group was “aching” (46.7%), followed by pins & needles (39.6%). Except for aching pain, dull pain and background pain, the two groups differed in pain quality with respect to pins & needles, swelling, burning, freezing and itching (all $p< 0.05$), as shown in Table 1.

Differences in GCPS pain intensity, pain disability, pain grade and EQ-5D scores between the KBD and general groups

As shown in Tables 2 and 3, significant differences were seen between KBD patients and the general subjects in pain intensity, pain disability, pain grade distribution and EQ-5D scores (all p□0.001). Patients with KBD reported higher average, worst, and current pain scores, had higher pain disability scores with daily activities, social activities, and working ability, had a higher proportion of Grade □ (high disability and severe limiting), and had worse health-related quality of life. Of note, Grade □ was the most frequent pain grade (45.5%), followed by Grade □ (26.9%), Grade □ (22.2%), and Grade □ (5.4%) in the KBD group. The distribution of pain grades in the general group was opposite to that of the KBD group, The two groups differed in the distribution of pain grade (p□0.001).

Factors associated with number of pain sites, pain frequency, GCPS pain intensity scores, pain disability scores, pain grade and EQ-5D scores in KBD subjects

The factors that were associated with joint pain characteristics are shown in Table 4. Females and those with lower education level reported a higher number of total pain sites (both p□0.05). Older participants reported a higher pain frequency and a longer pain duration (both p□0.05). Regarding pain intensity scores, females and those with higher KBD grade reported higher pain intensity scores (both p□0.05). Excepting age and marital status, participants who were female, had lower education levels, were farmers and had higher KBD grade reported lower EQ-5D scores (all p□0.05). Nonetheless, no pain characteristic differences were observed in terms of marital status, and there were no differences in pain grade distribution across the sociodemographic variables (all p□0.05).

Discussion

In this study, we observed firstly the KBD subjects mainly manifested the more joint pain locations, worse pain intensity, higher pain frequency, longer pain duration, higher frequency of analgesia use, higher percentage of pain-related disability and lower quality of life, compared with the non-KBD control group. These findings suggest that KBD joint pain is a serious problem and that we should pay more attention to these vulnerable populations contrast to that of general subjects with pain.

To our knowledge, the main findings of KBD pain characteristics are as following: (1) KBD patients suffered from multisite, symmetrical and persistent joint pain, (2) weight-bearing joints (e.g., knees and ankles) were the most painful, (3) patients with KBD may experience neuropathic pain to varying degrees, (4) females with KBD were more likely to report a higher number of pain sites, pain intensity and lower quality of life than males, and (5) a high proportion of analgesic use (89.2%) is the most important intervention to decrease the severity of pain. Taken together, these results indicate that joint pain of KBD is a significant and serious problem that requires more thorough understanding and treatment.

Compared with previous studies, there are some differences with respect to the pain characteristics. First, the mean number of pain sites is lower than in a prior study conducted in the Aba area by Huang et al, who reported that the average number of affected joints for KBD patients was 8.8 [10]. One reason is that the count methods differed from our study; in Huang's study, he counted joint pain or/and enlargement joints ranging from 0 to 14, while in our study, we counted only painful joints ranging from 0 to 16. Second, knees and ankles were the most severely and frequently affected joints in the current study. One explanation for this is that the knee and ankle move most frequently in daily life and are closely related to weight-bearing and/or working. However, this finding was somewhat different from a study conducted in Aba Tibetan area. In that study, the most severe site was the knee followed by the elbow[9]. The reasons for this discrepancy may be that the lifestyles are different in the two regions. Due to the high attitude environment, Tibetans often work in herding, while the people in Shaanxi Province often go into farming work (e.g., planting wheat and corn). Different working styles may mean that different body parts are used. The pain site may be different according to the body part used, degree of muscle activity, and working environment [38]. At present, many clinical trials of KBD pain interventions have focused on specific joint pain (e.g., knee pain) while routinely excluding individuals who report multiple pain issues[14, 39]. In the current study, other joints (e.g., fingers, elbows, shoulders) suffered mild pain, indicating that we should not pay attention to treatment of a specific joint pain. Future research should focus on the treatment of multiple cooccurring pain problems. Third, a higher proportion of analgesic use (89.2%) is the most important intervention to decrease the severity of pain, suggesting that joint pain was bothersome and did not receive appropriate treatment. The reasons might be the lack of knowledge concerning causal mechanisms of pain in KBD and, therefore, the lack of effective treatment. In addition, the proportions of physical therapy and surgical procedures were both significantly low, although previous studies reported that the two methods were effective. [17-19]. One explanation for this finding may be that the KBD patients may not have the stamina to engage in physical therapy due to long-term treatment; the other is that the subjects may not be able to afford the cost of surgery due to financial reasons [40]. Therefore, future research needs to develop various pharmacologic and nonpharmacologic interventions to manage pain in KBD patients.

Some researchers have viewed KBD as a special kind of osteoarthritis (OA) due to the similar characteristics [7]; however, there are differences between OA pain and KBD pain. for instance, 98% of the KBD subjects reported persistent pain, a finding that differed from that of OA. One study identified two distinct types of OA pain: one that was intermittent but generally severe or intense, and a more persistent 'background' pain or aching [41]. Therefore, we should consider the treatments of KBD pain based on its own pain characteristics.

Pain is currently categorized into nociceptive (often inflammatory) pain resulting from tissue damage; neuropathic pain, involving nerve damage; and idiopathic pain, which has no identified cause [42]. Because neuropathic pain is treated differently from other types of pain [43], recognizing neuropathic pain is important. Due to damage to joint cartilage[10], the joint pain reported in KBD patients is referred to as "nociceptive pain". However, many KBD participants in our study used pain descriptors that might typically be associated with a neuropathic pain process, such as pins & needles and burning. These findings suggest that patients with KBD may experience joint pain caused by both nociceptive and neuropathic mechanisms to varying degrees. Further research is warranted to examine the role of neuropathic pain in KBD and the relationship between nociceptive pain and neuropathic pain.

Literature regarding the associations between pain characteristics and demographics had not been investigated in detail. In the current study, women were more likely to report a higher number of pain sites, higher pain intensity and lower quality of life. These findings are consistent with prior studies on musculoskeletal pain [44, 45]. Additionally, the higher the grade of KBD is, the higher pain intensity and the lower quality of life are, suggesting that we could implement the Policy of Poverty Alleviation on KBD subjects according to KBD grade. A previous study found that age was related to KBD pain scores [9]. Nevertheless, in this study, we did not find an association between age and pain

intensity scores. A possible explanation for this observation is that the majority of samples in our study were older than 50 years of age, whereas the KBD patients in that study were younger than 50 years of age; older individuals may have learned to modify their work habits to avoid pain more than younger individuals [46].

Limitations

There were several limitations in this study. First, we may have overlooked the pain characteristics associated with the early stages of KBD due to a lack of new KBD cases. Second, many subjects were currently using analgesia or anti-inflammatory drugs, which may have resulted in conservative estimates of joint pain intensity. Third, we did not investigate the psychological dimension related to pain characteristics, as the majority of the participants were older than 50 years of age, and they became impatient due to the long time required for the survey. Future study is needed to survey the psychological factors related to pain characteristics.

Conclusion

In summary, this is the first study of joint pain characteristics of KBD patients. This study found that KBD patients reported more joint pain sites, worse pain intensity, higher pain frequency, longer pain duration, higher frequency of analgesia use, higher proportions of disability and lower quality of life than those in the control group. In the KBD group, the majority of the patients experienced multiple, symmetrical, persistent, and neuropathic pain; weight-bearing joints (e.g., knee and ankle) were the most painful. Furthermore, females were more likely report higher numbers of pain sites, higher pain intensity and lower quality of life. These findings will provide scientific basis for establishing joint pain evaluation criteria and subsequent pain intervention for KBD patients in China.

Abbreviations

KBD: Kashin-Beck disease; VAS: Visual Analog Scale; OA: Osteoarthritis; IAHA: Intra-articular injections of Hyaluronic Acid; NRS: Numeric Rating Scale; GCPS: The Graded Chronic Pain Scale; EQ-5D-3L: The EuroQol five-dimensional questionnaire three-level; CDC: Center for Disease Control

Declarations

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Authors’ contributors

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Wang Dimiao had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study design: Wang Dimiao, Mohammad Imran Younus, Hua Fang, Guo Xiong. Acquisition of data: Wang Dimiao, Chao Xu, Fang Hua, Liu Huan, Mohammad Imran Younus. Analysis and interpretation of the data: Wang Dimiao, Hua Fang. Writing: Wang Dimiao, Mohammad Imran Younus. Statistical analysis: Wang Dimiao, Mohammad Imran Younus.

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Ethics approval and consent to participate

The study was approved by the human ethics committee of the Health Science Center, Xi'an Jiaotong University, and all subjects provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Differences in demographics and pain characteristics between the KBD group and the general group

Characteristics	KBD group (n=167)	General group (n=169)	*p* value
Sex, n (%)			
Male	84 (50.3)	72 (42.6)	0.157
Female	83 (49.7)	97 (57.4)	
Age in years, mean ± SD (min-max)	58.4±10.2(40-83)	58.7±8.1 (40-81)	0.721
Education, n (%)			
Illiterate	49 (29.3)	46 (27.2)	0.272
Primary school	51 (30.5)	49 (28.9)	
Middle school	55 (32.9)	49 (28.9)	
≥High school	12 (7.2)	25 (14.8)	
Marital status, n (%)			
Single	18 (10.8)	11 (6.5)	0.163
Married	149 (89.2)	158 (93.5)	
Occupation, n (%)			
Farmer	158 (94.6)	165 (97.6)	0.151
Others	9 (5.4)	4 (2.4)	
Grade of disease, n (%)			
Grade I	80 (47.9)	/	
Grade □	72 (43.1)	/	
Grade □	15 (9.0)	/	
Pain prevalence, n (%)	167 (100.0)	169 (52.0)	**□0.001**
Pain duration (years), mean ±SD (min-max)	39.3±14.1 (25-59)	8.9±6.9 (1-30)	**□0.001**
Number of total pain sites, mean ±SD (min-max)	7.2±3.8 (1-16)	3.5±1.8 (0-4)	**□0.001**
Number of pain sites in the upper limbs, **mean ±SD (min-max)**	3.4±2.5 (0-8)	1.3±1.2 (0-4)	**□0.001**
Number of pain sites in the lower limbs, **mean ±SD (min-max)**	3.8±1.7 (1-8)	2.2±1.2 (0-4)	**□0.001**
Number of pain sites , n (%)			
1	5 (2.7)	21 (12.2)	**□0.001**
2-6	38 (23.0)	103 (61.0)	
7-11	54(32.4)	45 (26.8)	
12-16	70 (41.9)	0 (0)	

Frequency of pain in the last month, n (%)			
Never	0 (0.0)	0 (0.0)	**0.001**
Some of the days	0 (0.0)	24 (14.2)	
About half of the days	2 (1.2)	59 (34.9)	
Most of the days	53 (31.7)	41(24.3)	
Every day	112 (67.1)	45 (26.6)	
Pain quality, n (%)			
Pins & needles	94 (56.3)	67 (39.6)	**0.002**
Aching pain	90 (53.9)	79 (46.7)	0.190
Swelling pain	70 (41.9)	26 (15.4)	**0.001**
Hot-burning pain	61 (36.5)	12 (7.1)	**0.001**
Itching	46 (27.5)	2 (1.2)	**0.001**
Cold-freezing pain	30 (17.9)	12 (7.1)	**0.003**
Dull pain	17 (10.2)	8 (4.7)	0.057
Background pain	13 (7.8)	10 (5.9)	0.498
Pain treatment, n (%)			
Analgesics	149 (89.2)	52 (30.7)	**0.001**
Physical therapy	58 (34.7)	66 (39.1)	0.430
Surgical procedures	3 (1.8)	1 (0.6)	0.370

Table 2 Differences in GCPS between the KBD group and the general group

Items	KBD group (n=167)	General group (n=169)	*p* value
Pain intensity			
Current pain intensity, mean ±SD (min-max)	7.2±1.8 (2-10)	4.4±2.0 (0-9)	**0.001**
Worst pain intensity, mean ±SD (min-max)	8.1±1.9 (3-10)	6.0±2.7 (1-10)	**0.001**
Average pain intensity, mean ±SD (min-max)	6.8±1.6 (3-10)	4.6±2.0 (1-10)	**0.001**
Disability days, n (%)			
0-6	48 (28.7)	134 (79.3)	**0.001**
7-14	20 (12.0)	16 (9.5)	
15-30	33 (19.8)	19 (11.2)	
30	66 (39.5)	0 (0.0)	
Pain interference			
Daily activities, mean ±SD (min-max)	6.2±2.3 (0-10)	4.1±2.5 (0-10)	**0.001**
Social activities, mean ±SD (min-max)	5.6±2.6 (0-10)	3.8±2.5 (0-10)	**0.001**
Working ability, mean ±SD (min-max)	6.5±2.7 (0-10)	4.7±2.7 (0-10)	**0.001**
GCPS total pain intensity, mean ±SD (min-max)	73.8±15.2 (30.0-100.0)	50.0±20.7 (10.0-90.3)	**0.001**
GCPSpain-related disability, mean ±SD (min-max)	61.2±23.3 (0-100)	41.6±23.2 (0-100)	**0.001**
Pain grade, n (%)			
	9 (5.4)	75 (44.4)	**0.001**
	37 (22.2)	52 (30.8)	
	45 (26.9)	34 (20.1)	
	76 (45.5)	8 (4.7)	

Table 3 Differences in EQ-5D between the KBD group and the general group

EQ-5D items	KBD group (n=167)			General group (n=169)			*p* value
	No problem	Some problems	Extreme problems	No problem	Some problems	Extreme problems	
Mobility, n (%)	26 (15.6)	90 (53.9)	51 (30.5)	55 (32.5)	100 (59.2)	14 (8.3)	**0.001**
Self-care, n (%)	35 (21.0)	102 (61.1)	30 (17.9)	126 (74.6)	37 (21.9)	6 (3.5)	**0.001**
Usual activities, n (%)	11 (6.6)	123 (73.7)	33 (19.8)	61 (36.1)	106 (62.7)	2 (1.2)	**0.001**
Pain/discomfort, n (%)	0 (0)	95 (56.9)	72 (43.1)	0 (0)	153 (90.5)	16 (9.5)	**0.001**
Anxiety/depression, n (%)	32 (19.2)	103 (61.7)	32 (19.2)	59 (34.9)	110 (65.1)	0 (0)	**0.001**
EQ-5D index scores, (mean ±SD)	0.34±0.27			0.59±0.16			**0.001**

Table 4 Differences of pain characteristics and EQ-5D index scores among demographic characteristics in the KBD group

Items	Pain duration (years),(mean ± SD)	Number of pain sites,(mean ± SD)			Pain frequency in one month, (n)				
		Total	Upper limb	Lower limb	Never	Some of the days	About half of the days	Most of the days	Every day
Sex									
Male (n=84)	40.6±14.6	5.9±3.1*	2.7±2.2*	3.1±1.4*	0	0	1	27	56
Female (n=83)	38.0±13.8	7.9±3.2	4.0±2.6	4.1±1.8	0	0	1	26	56
Age range									
40-49 (n=10)	33.8±5.7*	8.0±3.5	3.3±2.3	4.7±1.1	0	0	0	4	6**
50-59 (n=71)	35.2±12.8	7.0±4.1	3.1±2.7	3.9±1.9	0	0	1	22	48
60-69 (n=74)	41.8±14.4	7.5±3.7	2.7±2.5	3.8±1.6	0	0	1	23	50
≥70 (n=12)	54.2±12.9	5.5±2.8	2.5±2.1	3.1±1.3	0	0	0	4	8
Education									
Illiterate (n=49)	38.9±14.1	7.6±3.3*	3.5±2.4	4.1±1.5*	0	0	0	16	33
Primary school (n=51)	38.4±14.3	6.7±4.0	3.1±2.5	3.7±1.8	0	0	1	13	37
Middle school (n=55)	39.9±14.9	6.4±3.4	2.9±2.4	3.5±1.5	0	0	1	19	35
≥High school (n=12)	42.0±12.5	4.3±3.6	1.5±2.3	2.8±1.6	0	0	0	5	7
Marital status									
Single (n=18)	39.1±15.9	6.0±3.1	3.2±2.6	3.0±1.1	0	0	0	7	11
Married (n=149)	39.3±14.2	7.3±3.8	3.4±2.5	3.8±1.6	0	0	2	46	101
Occupation									
Farmer (n=158)	39.1±14.4	7.6±3.7	3.5±2.4	3.9±1.7	0	0	2	50	106
Others (n=9)	42.8±10.7	6.9±4.2	3.0±2.5	3.9±1.3	0	0	0	3	6
Grade of KBD									

Grade I (n=80)	39.8±13.7	8.4±4.1	4.1±2.7	4.4±1.8	0	0	1	25	54
Grade Ⅱ (n=72)	37.3±15.1	6.3±3.0	3.0±2.1	3.4±1.4	0	0	1	23	48
Grade Ⅲ (n=15)	45.0±9.6	6.3±3.8	3.1±2.8	3.1±1.7	0	0	0	5	10

*p value<0.05, **p value<0.01

Table 4 Continued: Differences of pain characteristics and EQ-5D index scores among demographic characteristics in the KBD group

Items	GCPS pain intensity, (mean ± SD)	GCPS pain disability, (mean ± SD)	EQ-5D, (mean ± SD)	GCPS pain grade (n)			
				□	□	□	□
Sex							
Male (n=84)	71.3±14.7**	59. 6±22.6	0.39±0.27*	5	18	24	37
Female (n=83)	75.9±15.2	63.1±23.5	0.29±0.26	4	19	21	39
Age range							
40-49 (n=10)	69.3±13.8	59.0±26.2	0.43±0.15	0	2	1	7
50-59 (n=71)	73.2±15.6	59.3±23.5	0.38±0.26	5	19	19	28
60-69 (n=74)	75.1±15.1	62.5±23.1	0.31±0.29	4	13	21	36
≥70 (n=12)	71.9±14.3	63.7±23.2	0.28±0.26	0	3	4	5
Education							
Illiterate (n=49)	74.3±16.1	64.3±24.4	0.26±0.21**	5	6	16	22
Primary school (n=51)	76.0±14.3	63.5±22.4	0.35±0.25	1	16	11	23
Middle school (n=55)	71.5±15.2	57.6±23.0	0.39±0.27	1	13	16	25
≥High school (n=12)	72.8±15.2	56.6±20.0	0.44±0.24	2	2	2	6
Marital status							
Single (n=18)	74.9±15.3	67.8±25.7	0.30±0.29	0	4	6	8
Married (n=149)	73.7±15.3	60.4±22.5	0.35±0.27	9	33	39	68
Occupation							
Farmer (n=158)	74.2±15.3	62.8±23.1	0.32±0.27**	9	32	44	73
Others (n=9)	68.4±11.5	45.7±16.6**	0.54±0.18	0	5	1	3
Grade of KBD							
Grade I (n=80)	71.4±13.4*	60.9±22.7	0.45±0.24**	4	18	21	37
Grade □ (n=72)	74.7±16.5	62.6±24.2	0.29±0.27	4	16	19	33
Grade □ (n=15)	80.3±13.8	61.7±26.1	0.15±0.30	1	3	5	6

*p value<0.05, **p value<0.01

Figures

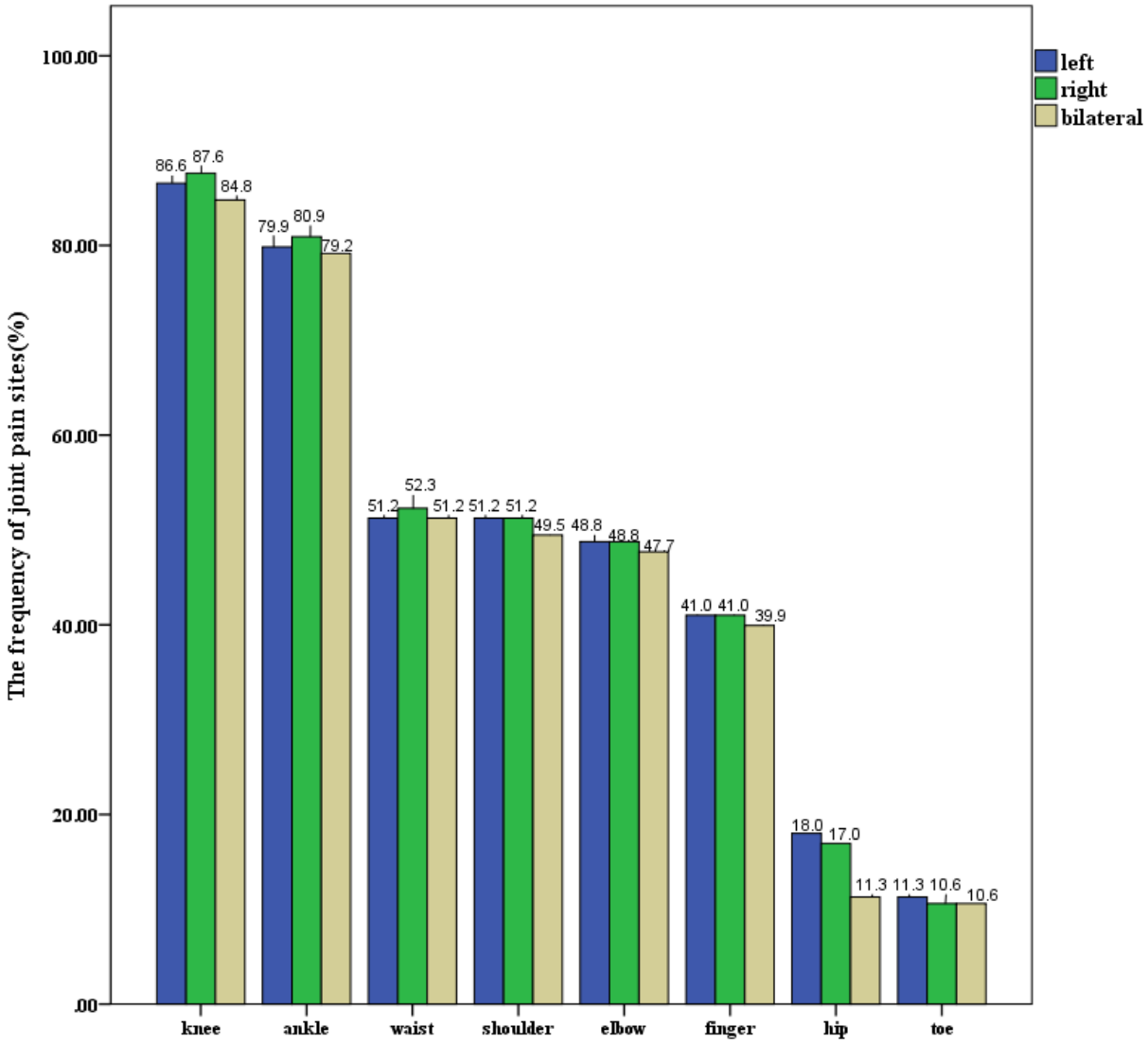

Fig. 1 The frequency of joint pain sites in the KBD group

Figure 1

The frequency of joint pain sites in the KBD group.

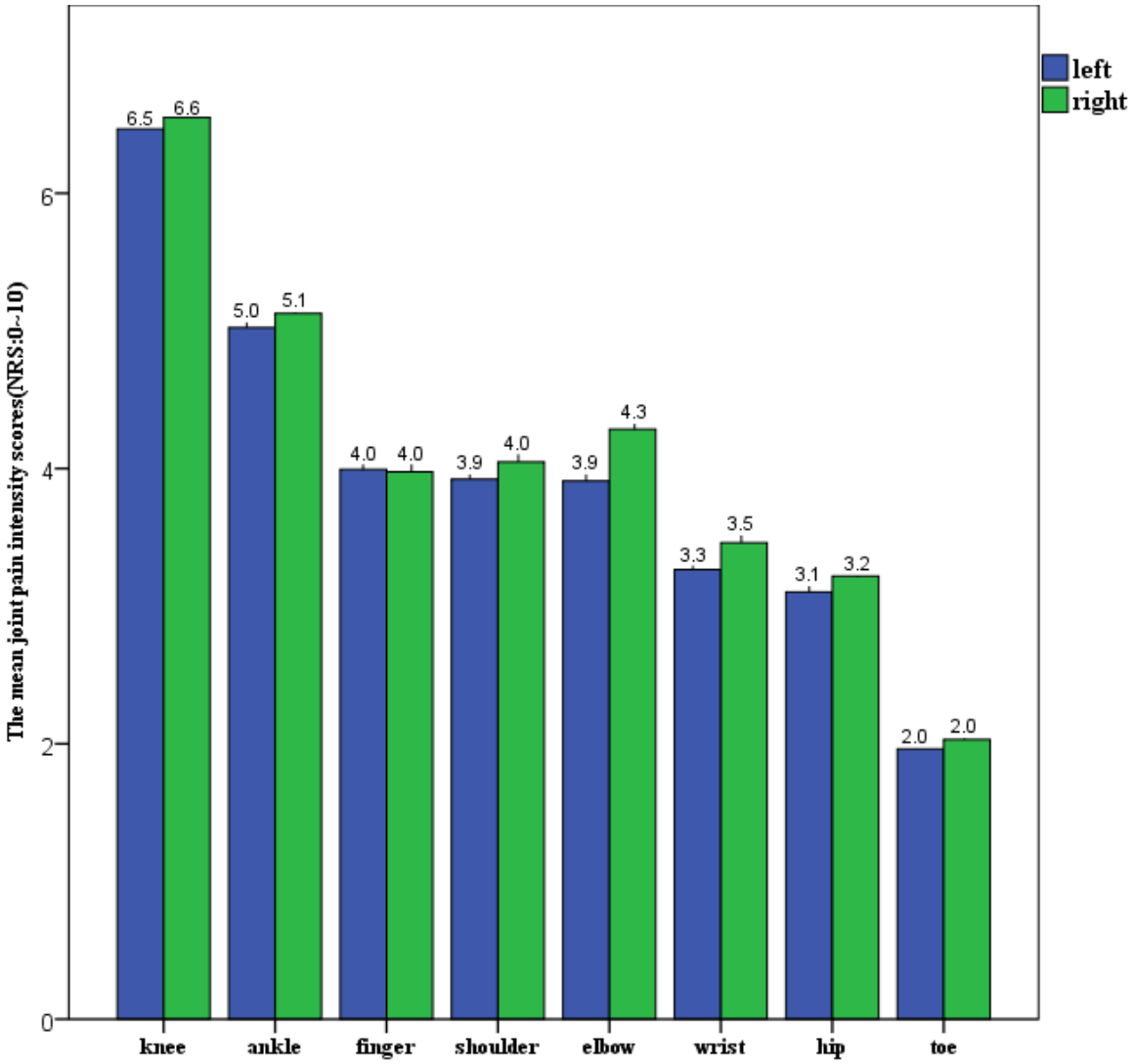

Fig.2 The mean joint pain inensity in the KBD group

Figure 2

The mean joint pain inensity in the KBD group.