Medicine®

OPEN

Lower risk of musculoskeletal pain among patients with end-stage renal disease treated by hemodialysis

A frequency-matched retrospective cohort study

Jie-Sian Wang, MD[a,b], Jen-Huai Chiang, MD[a,c], Heng-Jung Hsu[d,*]

Abstract

Musculoskeletal pain is experienced by 5%–14% of the general adult population, and it is highly common among patients with chronic kidney disease (CKD). Therefore, the purpose of the study was to decide the prevalent rate of musculoskeletal pain in end-stage renal disease (ESRD) patients and to analyze this relationship between myalgia and ESRD using clinical features and determinants.

A total of 93,013 patients who received ESRD diagnoses during 2000 and 2010 and were followed up until December 31, 2011, were identified from the Longitudinal Health Insurance Database 2000 (LHID2000) of the National Health Research Institutes (NHRI); non-ESRD controls were also selected from the LHID2000.

The results indicated that the risk of chronic musculoskeletal pain is significantly lower in the hemodialysis treated ESRD cohort (subhazard ratio = 0.52, $P < .0001$), despite of sex, age, or comorbidities. Older patients were discovered to be at lower risk of chronic musculoskeletal pain (subhazard ratio = 0.94, $P = .0765$), with those aged 40 to 64 years having the highest hazard ratios (subhazard ratio = 1.21, $P < .0001$), and the prevalence of chronic musculoskeletal pain in women was higher than that in men (vs female sex; subhazard ratio = 0.69, $P < .0001$). Kaplan–Meier analysis revealed a higher cumulative incidence of myalgia development in the non-ESRD cohort compared with the ESRD cohort (log-rank test, $P < .001$).

Clinicians should assess the risk of chronic musculoskeletal pain in such patients and provide appropriate and timely support of hemodialysis.

Abbreviations: BMI = body mass index, CAD = coronary artery disease, CHF = congestive heart failure, CI = confidence intervals, CKD = chronic kidney disease, DM = diabetes mellitus, ESRD = end-stage renal disease, HD = hemodialysis, HR = hazard ratio, ICD = International Classification of Diseases, LHID2000 = Longitudinal Health Insurance Database 2000, LVH = left ventricular hypertrophy, NHI = National Health Insurance, NHIA = National Health Insurance Administration, NHIRD = National Health Insurance Research Database, NHRI = National Health Research Institutes, RA = rheumatoid arthritis, RLS = restless legs syndrome, SHR = subhazard ratio, SLE = systemic lupus erythematosus.

Keywords: bone, chronic, end-stage renal disease, frequency-match, musculoskeletal, pain

Editor: Muhammed Mubarak.

This study is partially supported by Ministry of Health and Welfare Clinical Trial Center of Taiwan (MOHW106-TDU-B-212-113004), China Medical University Hospital, Taichung, Taiwan, Project of Biobank Stroke Biosignature, Academia Sinica of Taiwan (BM10601010036), Clinical Trial Consortium for Stroke of Taiwan (MOST 106-2321-B-039-005), Tseng-Lien Lin Foundation, Taichung, Taiwan, Brain Disease Foundation, Taipei, Taiwan, Katsuzo and Kiyo Aoshima Memorial Funds, Japan.

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

Supplementary Table 1, http://links.lww.com/MD/C402

[a] *The Graduate Institute of Clinical Medicine Science, College of Medicine, China Medical University,* [b] *Division of Nephrology, Department of Internal Medicine,* [c] *Management Office for Health Data, China Medical University Hospital, Taichung,* [d] *Division of Nephrology, Department of Internal Medicine, Keelung Chang Gung Medical Hospital, Taiwan.*

[*] *Correspondence: Heng-Jung Hsu, Division of Nephrology, Department of Internal Medicine, Keelung Chang Gung Medical Hospital, No. 222, Maijin Road, Anle District, Keelung City 204, Taiwan (e-mail: hsuaaron@gmail.com).*

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

Medicine (2018) 97:33(e11935)

Received: 25 February 2018 / Accepted: 24 July 2018

http://dx.doi.org/10.1097/MD.0000000000011935

1. Introduction

Pain is prevalent in the general population. It is estimated that 10%–20% of adults experience some form of pain.[1] Moreover, 50%–70% of this pain is musculoskeletal, which means that 5% to 14% of the adult experience this type of pain.[2]

Musculoskeletal pain is highly prevalent among over 60% of patients with chronic kidney disease (CKD).[3,4] This finding can probably be attributed to end-stage renal disease (ESRD) patients[5] and even renal transplant patients.[6] The musculoskeletal pain has a significant impact on dialysis patients' health and lower quality of life.[7]

Most studies have not showed an association of musculoskeletal pain with the common derangements in patients with ESRD. The purpose of this study is to determine the prevalence of myalgia in ESRD patients and to analyze this relationship between myalgia and ESRD using clinical features and determinants.

2. Methods

2.1. Data sources

The National Health Insurance (NHI) program in Taiwan is a voluntary and single-payer medical program that was launched in 1995 and currently covers almost the entire population

(99.6%) of Taiwan. The National Health Insurance Administration (NHIA) performs an expert review of random samples for every 50 to 100 outpatient and inpatient claims in each hospital and every 3 months; a disease diagnosis without valid supporting clinical findings is considered medical fraud and carries a penalty of 100 times the amount claimed by the treating physician or hospital. Datasets in the National Health Insurance Research Database (NHIRD) for the 2000 to 2011 periods were used, including the Registry for Beneficiaries and Registry for Catastrophic illness, which contains data regarding beneficiaries with major disease whose treatment was approved by the NHIA. We used ambulatory and inpatient care records regarding care for catastrophic illnesses during 2000 to 2010, which were cross-referenced with the registry of catastrophic illness patients, to identify case cohort subjects. The comparison cohort was selected from the Longitudinal Health Insurance Database 2000 (LHID2000), which was created by the National Health Research Institutes (NHRI) by randomly sampling 1,000,000 beneficiaries from the Registry for Beneficiaries data files for the year 2000. The database includes all the longitudinal reimbursement information for this random sample from 1996 to 2011.

This study was approved by the Institutional Review Board of China Medical University (CMUH104-REC2-115).

2.2. Populations

Our cohort populations considered patients with ESRD (aged ≥18 years) whose condition was identified in 2000 to 2010 and who were followed-up until December 31, 2011, until the first diagnosis of myalgia, or until withdrawal from the NHI program. ESRD patients who received complete clinical and laboratory examinations followed by a careful and routine review conducted by a rheumatologist and the NHIA were granted catastrophic illness certificates. The accuracy of the diagnosis of ESRD for patients enrolled in the NHI program is highly reliable. Patients with ESRD should have accepted hemodialysis treatment. ESRD was denoted using an ICD-9-CM code of "585.x" from 2000 to 2010. After individuals who accepted peritoneal dialysis treatment were excluded, there were 93,013 patients with ESRD in the years 2000 to 2010. We excluded patients who were aged <18 years (n = 103) and those who received a diagnosis of myalgia before the date of the first ESRD diagnosis (n = 36,548), resulting in 56,362 patients with ESRD.

Non-ESRD controls were selected from the LHID2000. There were 872,630 patients without ESRD from 2000 to 2010. We excluded subjects aged <18 years (n = 167,558) and those who were diagnosed with myalgia before the index date (n = 213,079), which left 491,993 patients without ESRD (Fig. 1).

2.3. Baseline characteristics

Sociodemographic factors investigated included age and sex. The age of the patients was classified into the following 3 age groups: 18–39, 40–64, and≥65 years. Comorbidities were certified by using the ICD-9-CM codes in outpatient, inpatient, and catastrophic illness registry files. Comorbidities were diabetes mellitus (DM; ICD-9-CM: 250.x), hypertension (401–405), coronary artery disease (CAD; 410–414), congestive heart failure (CHF; 428), stroke (430–438), gout (274.9), systemic lupus erythematosus (SLE; 710.0), renal stone (592), rheumatoid arthritis (RA; 714.0), back pain (724.2) and cancer (140–208) (Table 1).

2.4. Primary outcome

The primary outcome is diagnosis of myalgia (ICD-9-CM: 729.x), as recorded in an outpatient or inpatient claim. Patients were defined as having myalgia if they had made at least 2 clinical claims every 3 months.

2.5. Statistical analysis

Differences in comorbidities and demographic characteristics between the ESRD and comparison populations were studied using the Chi-squared test for categorical variables and 2-sample t tests for continuous variables. The ESRD patients have a high risk of death, and there were confounding the estimated in risk of chronic musculoskeletal pain. The competing risk model was considered in this analysis of chronic musculoskeletal pain and death. Hazard ratios (HRs), subhazard ratios (SHRs), and 95% confidence intervals (95% CIs) were estimated for each variable by using Cox proportional hazard regression (Table 2). In order to further analyze the site of chronic muscloskeletal pain, we divided chronic muscloskeletal pain into myalgia and myositis (ICD-9-CM: 729.1), pain in limb (ICD-9-CM: 729.5) by using Cox proportional hazard regression (Table 3). Differences in the cumulative incident rate of myalgia between the ESRD and comparison cohorts were examined using Kaplan–Meier studies by conducting log-rank tests (Fig. 2). All statistical analyses were performed using SAS statistical software (v 9.4 for Windows; SAS Institute Inc., Cary, NC). Statistical significance was set at $P < .05$.

3. Results

We matched the ESRD patient at a frequency of 1:1 by sex, age (per 5 years), comorbidities (diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, stroke, gout, systemic lupus erythematosus, renal stone, rheumatoid arthritis, and back pain), and index year. Each cohort comprised a total of 34,157 patients. The demographic characteristics and comorbidities of the ESRD and non-ESRD cohorts are presented in Table 1. The mean (standard deviation) age was 61.51 (14.60) years for the ESRD cohort and 61.50 (14.57) years for the non-ESRD cohort. In addition, the mean (median) follow-up period was 3.61 (3.13) years for the ESRD cohort and 4.78 (3.24) years for the non-ESRD cohort. No significant differences were identified between the 2 cohorts for any variable.

Table 2 presents the uni- and multivariable Cox proportional subhazard models for the ESRD and non-ESRD cohorts. The significant adjusted subhazard ratios of myalgia in the Cox proportional subhazard model were 0.52 for ESRD (95% CI: 0.51–0.54), 0.69 for the male sex (vs female sex; 95% CI: 0.67–0.71), 1.21 for the 40–64-year age group (vs 18–39-year age group; 95% CI: 1.14–1.29), 0.87 for DM (95% CI: 0.84–0.9), 1.12 for hypertension (95% CI: 1.06–1.17), 1.17 for CAD (95% CI: 1.13–1.22), 0.84 for CHF (95% CI: 0.79–0.90), 0.82 for stroke (95% CI: 0.79–0.86), 1.09 for gout (95% CI: 1.03–1.15), 1.16 for renal stone (95% CI: 1.09–1.24), 1.38 for back pain (95% CI: 1.32–1.44) and 0.52 for cancer (95% CI: 0.49–0.56).

Table 3 presents the Cox proportional subhazard models for the ESRD and non-ESRD cohorts. The incidence rates of myalgia and myositis in the Cox proportional subhazard model were 43.94 per 1000 person-years for non-ESRD, 30.17 per 1000 person-years for ESRD; and incidence rates of pain in limb in the Cox proportional subhazard model were 7.27 per 1000 person-years for non-ESRD, 5.92 per 1000 person-years for ESRD.

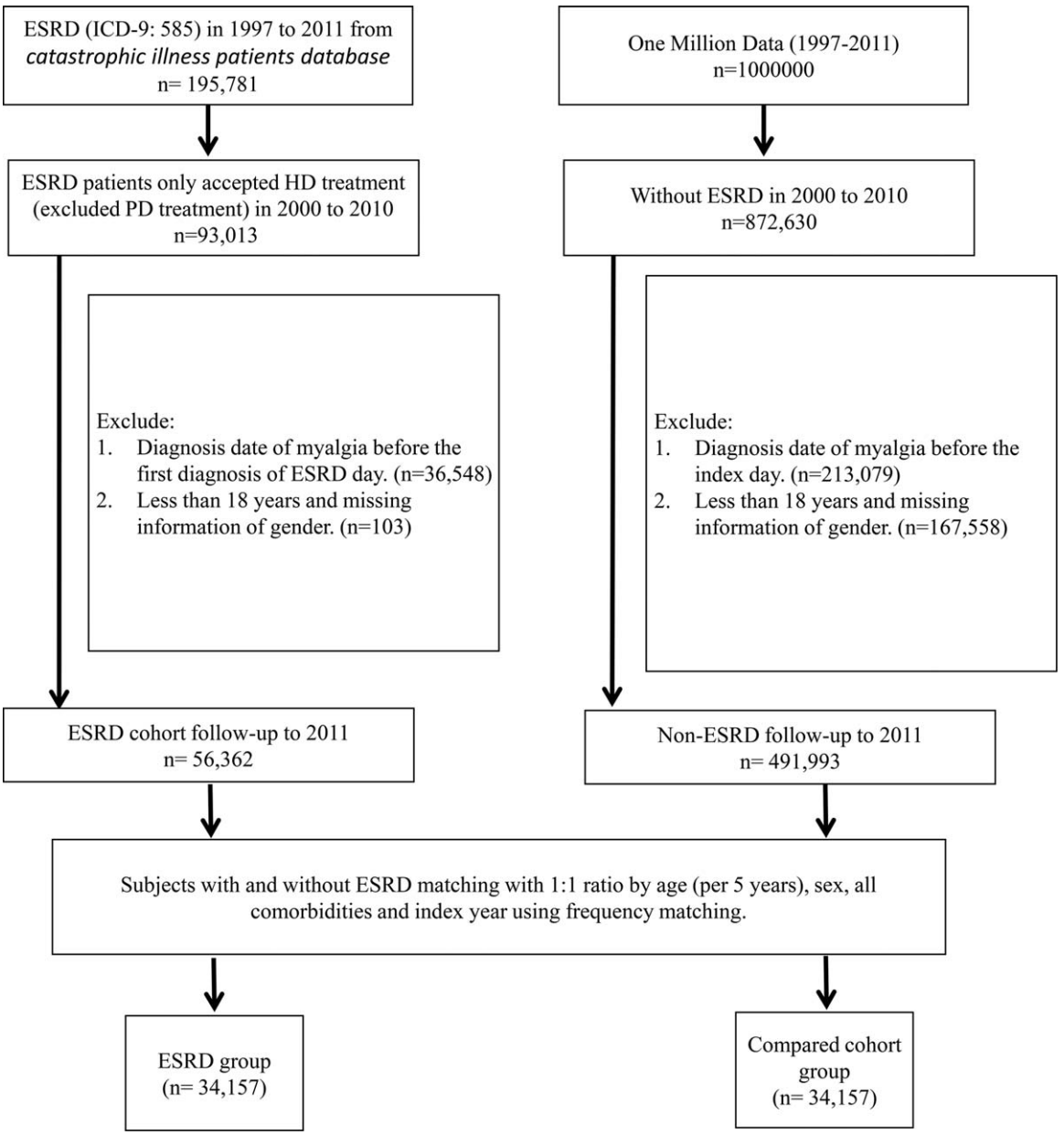

Figure 1. Selection of study patients.

The adjusted subhazard ratios in the Cox proportional subhazard model were 0.48 (95% CI: 0.46–0.50) for myalgia and myositis, and 0.58 (95% CI: 0.53–0.63) for pain in limb.

Kaplan–Meier analysis revealed a higher cumulative incidence of myalgia development in the non-ESRD cohort compared with the ESRD cohort (log-rank test, $P < .001$; Fig. 2).

4. Discussion

This is the first study using datasets in the National Health Insurance Research Database (NHIRD) to investigate musculoskeletal pain among the population with ESRD. The results of this study demonstrate that patients with ESRD significantly have lower risk of myalgia, even after adjusting potential confounding factors (SHR = 0.52, 95% CI: 0.51–0.54, $P < .0001$; Table 2).

Regardless of the location of the pain, the risk of pain is reduced in dialysis patients, which means that the pain of patients with dialysis is not related to the pain site (Table 3). The association of ESRD and lower myalgia may be multifactorial. The musculoskeletal pain in ESRD patients is linked to their primary kidney disease (e.g., polycystic kidney disease), comorbid conditions (e.g., renal osteodystrophy), or vascular calcification.[8,9] Altered vitamin D and abnormal calcium and phosphorus metabolism are common in ESRD patients, which will cause calcification of vessels, both in artery and arterioles, with subsequent arteriolar narrowing and increased vascular stiffness.[10] However, those patients received renal replacement therapy regularly to remove uremic toxins partially—such as phosphate, creatinine, para-cresol, also 4-methylphenol, indoxyl sulfate,[11] and parathyroid hormone. Those uremic toxins had been proved increasing the risk of musculoskeletal pain and

Table 1

Demographic characteristics and co-morbidity in patients with and without ESRD cohort groups after matching.

Variables	ESRD				*P*-value
	No (N = 34157, 50%)		Yes (N = 34157, 50%)		
	n	%	n	%	
Sex					.99*
Female	15,477	45.31	15,477	45.31	
Male	18,680	54.69	18,680	54.69	
Age, years					.99*
18–39 years	2708	7.93	2708	7.93	
40–64 years	16,156	47.3	16,156	47.3	
More than 65 years	15,293	44.77	15293	44.77	
Mean (SD)	61.51 (14.60)		61.50 (14.57)		.9249†
Baseline comorbidities					
Diabetes mellitus	15,920	46.61	15920	46.61	.99*
Hypertension	29,593	86.64	29,593	86.64	.99*
Coronary Artery Disease	10,998	32.2	10,998	32.2	.99*
Chronic Heart failure	3167	9.27	3167	9.27	.99*
Stroke	8103	23.72	8103	23.72	.99*
Gout	3578	10.48	3578	10.48	.99*
Systemic lupus erythematosus	49	0.14	49	0.14	.99*
Rheumatoid arthritis	13	0.04	13	0.04	.99*
Renal stone	2044	5.98	2044	5.98	.99*
Back pain	4882	14.29	4882	14.29	.99*
Cancer	2855	8.36	4402	12.89	<.0001

The mean (median) of follow-up duration was 3.61 (3.13) years and 4.78 (3.24) for ESRD cohort and compared cohort.
ESRD = end stage renal disease, SD = standard deviation.
* Chi-square test;
† Two sample *t*-test.

calcific uremic arteriolopathy (calciphylaxis).[12,13] So those patients who receiving regular dialysis may get some benefit as comparing with those advanced CKD patients without regular dialysis.

Compared to 18 to 39-year group, patients aged 40 to 64 years are at highest risk of musculoskeletal pain (SHR = 1.21, 95% CI = 1.14–1.29, $P < .0001$; Table 2), with those aged more than 65 years having lower risk of myalgia (SHR = 0.94, 95% CI =

Table 2

Cox model and competing risk regression analysis measured HR and SHR and 95% CIs of myalgia associated with and without ESRD and covariates after matching.

Characteristics	Event no. (n = 15200)	Crude			Adjusted-model			Adjusted-model		
		HR	(95% CI)	*P*-value	HR	(95% CI)	*P*-value	SHR	(95% CI)	*P*-value
ESRD										
No	9774	1.00	Reference		1.00	Reference		1.00	Reference	
Yes	5426	0.72	(0.7–0.74)	<.0001	0.73	(0.7–0.75)	<.0001	0.52	(0.51–0.54)	<.0001
Sex										
Female	8226	1.00	Reference		1.00	Reference		1.00	Reference	
Male	6974	0.71	(0.69–0.73)	<.0001	0.71	(0.69–0.74)	<.0001	0.69	(0.67–0.71)	<.0001
Age, years										
18–39 years	1253	1.00	Reference		1.00	Reference		1.00	Reference	
40–64 years	8304	1.33	(1.25–1.41)	<.0001	1.26	(1.19–1.34)	<.0001	1.21	(1.14–1.29)	<.0001
More than 65 years	5643	1.28	(1.2–1.36)	<.0001	1.15	(1.08–1.23)	<.0001	0.94	(0.88–1.01)	0.0765
Baseline comorbidities (ref = nosite comorbidities)										
Diabetes mellitus	6303	0.98	(0.95–1.01)	.2167	0.93	(0.9–0.96)	<.0001	0.87	(0.84–0.9)	<.0001
Hypertension	13,096	1.14	(1.09–1.19)	<.0001	1.09	(1.04–1.15)	.0002	1.12	(1.06–1.17)	<.0001
Coronary Artery Disease	4842	1.19	(1.15–1.23)	<.0001	1.18	(1.14–1.22)	<.0001	1.17	(1.13–1.22)	<.0001
Chronic Heart failure	1104	1.01	(0.95–1.08)	.6938	0.93	(0.87–0.99)	.0272	0.84	(0.79–0.9)	<.0001
Stroke	2836	0.97	(0.93–1.01)	.1112	0.92	(0.88–0.96)	<.0001	0.82	(0.79–0.86)	<.0001
Gout	1484	1.02	(0.97–1.08)	.4177	1.09	(1.03–1.15)	.0002	1.09	(1.03–1.15)	.0026
Systemic lupus erythematosus	27	1.01	(0.7–1.48)	.9417	1.01	(0.69–1.47)	.9675	0.97	(0.66–1.44)	.8815
Rheumatoid arthritis	4	0.59	(0.22–1.56)	.2867	0.57	(0.22–1.53)	.2682	0.58	(0.21–1.56)	.2781
Renal stone	974	1.14	(1.07–1.22)	<.0001	1.17	(1.09–1.25)	<.0001	1.16	(1.09–1.24)	<.0001
Back pain	2536	1.47	(1.41–1.54)	<.0001	1.40	(1.34–1.47)	<.0001	1.38	(1.32–1.44)	<.0001
Cancer	892	0.55	(0.51–0.59)	<.0001	0.56	(0.52–0.6)	<.0001	0.52	(0.49–0.56)	<.0001

Abbreviations: CI = confidence interval, ESRD = end stage renal disease, HR = hazard ratio, SHR = subhazard ratio.
Adjusted HR: adjusted for ESRD, age, sex and comorbidities in Cox proportional hazards regression.

Table 3

IRs, HR, SHR, and CIs of myalgia and myositis or pain in limb with and without ESRD patients.

	ESRD								
	No (n = 34157)			Yes (n = 34157)					
Outcome	Event	Person years	IR†	Event	Person years	IR†	Crude HR (95% CI)	Adjusted HR (95% CI)	Adjusted SHR (95% CI)
Myalgia and myositis (ICD-9-CM: 729.1)	7497	170,618	43.94	3790	125,638	30.17	0.65 (0.63–0.68)	0.66 (0.63–0.68)	0.48 (0.46–0.50)
Pain in limb (ICD-9-CM: 729.5)	1210	166,406	7.27	737	124,562	5.92	0.78 (0.71–0.86)	0.79 (0.72–0.87)	0.58 (0.53–0.63)

Adjusted HR: adjusted for age, sex and comorbidities in Cox proportional hazards regression.

CI = confidence interval, HR = hazard ratio, IR = incidence rates, per 1000 person-years, SHR = subhazard ratio.

0.88–1.01, $P = .0765$; Table 2). Older patients with aged ≥65 years have more complications and poor nutritional status. The poor nutrition may result in their reduced body weight, body mass index (BMI), and muscle atrophy, which induced musculoskeletal pain. Therefore, they might have deteriorated response of musculoskeletal pain. Additionally, in the United States (both with and without CKD), those patients with age between 60 to 69 prone to develop chronic musculoskeletal pain than those older patients (age more than 69 years old).[14] This is hypothesized to be due to blunting pain of peripheral and central nervous systems in older patients.

We found that the prevalence of musculoskeletal pain in women was higher than that in men (vs female sex; SHR = 0.69, 95% CI: 0.67–0.71, $P < .0001$; Table 2). The prevalence is affected by numerous factors, such as disease (complications), marriage (separated, divorced, widowed), emotional disorders (anxiety, depression), and society position (education, employment, income).[15] In Asian society, men are taught the concept of manhood when they grow up. Therefore, they also care about their "faces." We supposed that women tend to provide a clearer history of a specific condition than men do because they are highly sensitive.[16] This may explain the higher prevalence of musculoskeletal pain among women.

We found that diabetes mellitus (DM) was negatively associated with musculoskeletal pain in the ESRD cohort after adjustments (Table 2). Patients with ESRD and DM had a lower risk of 13% of musculoskeletal pain (SHR = 0.87, 95% CI: 0.84–0.9, $P < .0001$). This may be due to diabetic neuropathy (DN), a pain-inhibiting neuropathy caused by glucose metabolism dysfunction. In one diagnostic study, 75% of patients with DN had distal symmetrical neuropathy as a comorbidity.[17] Another study demonstrated that DN may hide diagnosis of osteoarthritis.[18] Moreover, hypertension and coronary artery disease have been reported to be more common in patients with

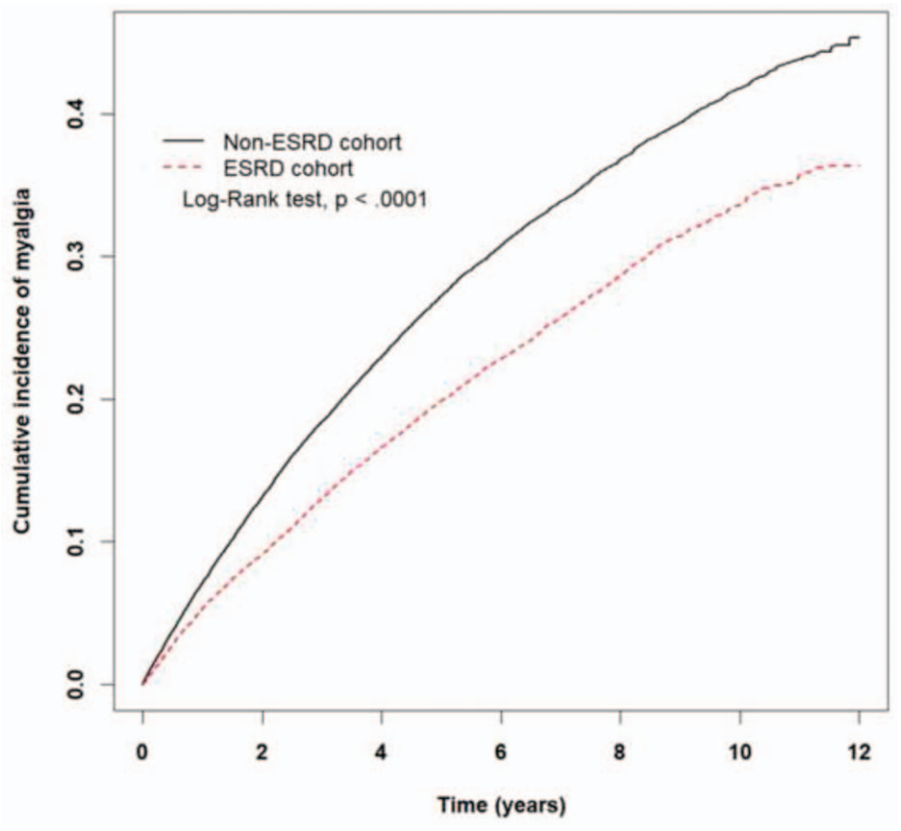

Figure 2. Kaplan–Meier studies by log-rank tests.

myalgia. Among many myalgia-associated systemic diseases, isolated hypertension was proposed as a major risk factor leading to vascular stiffness.

Chronic heart failure (CHF) appears to be a protective factor for musculoskeletal pain among patients with ESRD after adjustments (SHR = 0.84, 95% CI: 0.79–0.9, $P < .0001$; Table 2). Histologically, left ventricular hypertrophy (LVH) has been accompanied by myocardial stiffness and increased myocardial length.[19] Dialysis patients have extraordinarily high mortality rates. In one median follow-up, 1075-day study, all the patients with heart failure had musculoskeletal pain. However, the potential presence of competing risks was not accounted for in the statistical analyses.[20] We have taken the mortality of ERD cohort into consideration. Moreover, causes of 43% of all-cause mortality in dialysis patients include coronary artery disease, rapid electrolyte shifts, and arrhythmia.[21] Abnormalities in sympathovagal balance may explain less musculoskeletal pain in patients with ESRD.[22] Cardiovascular autonomic neuropathy prevalence rate will increase with the progress of renal disease.[23] Taking ESRD associated vascular stiffness and partial removal of uremic toxin into consideration, lower incidence of myalgia in patients with ESRD can be anticipated.

There is good evidence that stroke patients experience a lower incidence of musculoskeletal pain (SHR = 0.82, 95% CI: 0.79–0.86, $P < .0001$; Table 2). Consequently, in a review study, dysfunction of the central and peripheral nervous systems is common among patients with ESRD.[24] There are many neurological complications of uremia, including restless legs syndrome (RLS). In a case-control, in-hospital study, they concluded that RLS and acute stroke are significantly associated.[25] We supposed that patients with stroke and RLS may mask musculoskeletal pain due to ischemic neuropathy.

The results of our study revealed that patients with cancer significantly have lower risk of myalgia (SHR = 0.52, 95% CI: 0.49–0.56, $P < .0001$; Table 2). The patients with cancer may had some analgesics to relieve chronic musculoskeletal pain. They usually need combined oral with parenteral opioids for cancer pain. This may explain the lower prevalence of musculoskeletal pain among patients with cancer.

Conclusively, in this study, chronic musculoskeletal pain was negatively associated with the DM, CHF, stroke, and cancer. On the other hand, chronic musculoskeletal pain was positively associated with hypertension, CAD, gout, renal stone, and back pain. However, patients with SLE and RA had similar HRs as those patients without these conditions. This implies that autoimmune disease may not be the causality of chronic musculoskeletal pain in patients with ESRD (Table 2).

This study has several limitations. First, all diagnoses depended on the competence of clinical physicians. ICD-9-CM codes were used to define ESRD, myalgia, and comorbidities. The diagnosis of ESRD was the most accurate because it requires careful peer review before its confirmation; the insurance authority has a committee that evaluates claims data to prevent errors and violations. Second, this was a cross-sectional study that did not estimate or assess the intensity of musculoskeletal pain and its relationship with clinical biochemical data in the patients. Third, data regarding pain relief agents were lacking. Fourth, we did not collect information about the mental health status of the patients nor addressed socioeconomic and cultural factors, which may also have affected our interpretation of the results.

Despite these limitations, the results presented herein provide a confirm basis for studies that will further explain the relationship between ESRD and musculoskeletal pain. Further research is required to analyze what type of analgesic and what additional support measures are more effective for patients with ESRD.

4.1. Conclusion

The findings of the current study suggest that the prevalence of musculoskeletal pain is significantly lower in patients with ESRD than in those without ESRD. Clinicians should assess the risk of chronic musculoskeletal pain in such patients and provide appropriate and timely support of treatment.

Author contributions

Methodology: Jen-Huai Chiang.
Project administration: Jie-Sian Wang.
Resources: Jen-Huai Chiang.
Software: Jen-Huai Chiang.
Writing – original draft: Jie-Sian Wang.
Writing – review & editing: Heng-Jung Hsu.

References

[1] Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. Bull World Health Organ 2003;81:646–56.
[2] Malleson PN, Connell H, Bennett SM, et al. Chronic musculoskeletal and other idiopathic pain syndromes. Arch Dis Child 2001;84:189–92.
[3] Cohen SD, Patel SS, Khetpal P, et al. Pain, sleep disturbance, and quality of life in patients with chronic kidney disease. Clin J Am Soc Nephrol 2007;2:919–25.
[4] Hsu HJ, Yen CH, Hsu KH, et al. Factors associated with chronic musculoskeletal pain in patients with chronic kidney disease. BMC Nephrol 2014;15:6.
[5] Kelly A, Apostle K, Sanders S, et al. Musculoskeletal pain in dialysis-related amyloidosis. Can J Surg 2007;50:305–6.
[6] Sperschneider H, Stein G. Bone disease after renal transplantation. Nephrol Dial Transpl 2003;18:874–7.
[7] Fidan F, Alkan BM, Tosun A, et al. Quality of life and correlation with musculoskeletal problems, hand disability and depression in patients with hemodialysis. Int J Rheum Dis 2016;19:159–66.
[8] Murphey MD, Sartoris DA, Quale JL, et al. Musculoskeletal manifestations of chronic renal insufficiency. Radiographics 1993;13:357–79.
[9] Kurer MH, Baillod RA, Madgwick JC. Musculoskeletal manifestations of amyloidosis. A review of 83 patients on haemodialysis for at least 10 years. J Bone Joint Surg Br 1991;73:271–6.
[10] Shanahan CM, Crouthamel MH, Kapustin A, et al. Arterial calcification in chronic kidney disease: key roles for calcium and phosphate. Circ Res 2011;109:697–711.
[11] Adijiang A, Goto S, Uramoto S, et al. Indoxyl sulphate promotes aortic calcification with expression of osteoblast-specific proteins in hypertensive rats. Nephrol Dial Transpl 2008;23:1892–901.
[12] Lee JH, O'Keefe JH, Bell D, et al. Vitamin D deficiency. J Am Coll Cardiol 2008;52:1949–56.
[13] Meijers BKI, Claes K, Bammens B, et al. p-Cresol and cardiovascular risk in mild-to-moderate kidney disease. Clin J Am Soc Nephrol 2010;5:1182–9.
[14] Kennedy J, Roll JM, Schraudner T, et al. Prevalence of persistent pain in the U.S. adult population: new data from the 2010 National Health Interview Survey. J Pain 2014;15:979–84.
[15] Leveille SG, Zhang Y, McMullen W, et al. Sex differences in musculoskeletal pain in older adults. Pain 2005;116:332–8.
[16] Edwards RH. Hypotheses of peripheral and central mechanisms underlying occupational muscle pain and injury. Eur J Appl Physiol Occupat Physiol 1988;57:275–81.
[17] Bansal V, Kalita J, Misra UK. Diabetic neuropathy. Postgrad Med J 2006;82:95–100.
[18] Leaverton PE, Peregoy J, Fahlman L, et al. Does diabetes hide osteoarthritis pain? Med Hypotheses 2012;78:471–4.
[19] Foley RN, Parfrey PS, Harnett JD, et al. Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. Kidney Int 1995;47:186–92.

[20] Caravaca F, Gonzales B, Bayo MA, et al. Musculoskeletal pain in patients with chronic kidney disease. Nefrologia 2016;36:433–40.
[21] Herzog CA, Mangrum JM, Passman R. Sudden cardiac death and dialysis patients. Semin Dial 2008;21:300–7.
[22] Vinik AI, Erbas T, Casellini CM. Diabetic cardiac autonomic neuropathy, inflammation and cardiovascular disease. J Diabetes Investig 2013;4:4–18.
[23] Zander E, Schulz B, Heinke P, et al. Importance of cardiovascular autonomic dysfunction in IDDM subjects with diabetic nephropathy. Diabetes Care 1989;12:259–64.
[24] Brouns R, De Deyn PP. Neurological complications in renal failure: a review. Clin Neurol Neurosurg 2004;107:1–6.
[25] Schlesinger I, Erikh I, Nassar M, et al. Restless legs syndrome in stroke patients. Sleep Med 2015;16:1006–10.