CLINICAL SCIENCE

Gender differences in ankylosing spondylitis-associated cumulative healthcare utilization: a population-based cohort study

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BACKGROUND: Ankylosing spondylitis (AS) is one of the most common rheumatic diseases with gender differences in prevalence and clinical presentation. This study aimed to examine whether such gender differences are correlated with cumulative healthcare utilization in Taiwan.

METHODS: The National Health Insurance Research Database supplied claim records of one million individuals from 1996 to 2007. Selected cases included patients aged ≥16 years. Certified rheumatologists diagnosed the patients in three or more visits and gave prescriptions for AS. Multivariate adjusted logistic regression analyses were used to calculate the influence of gender on cumulative healthcare utilization associated with AS.

RESULTS: The study included 228 women and 636 men. After adjustment for potential confounding factors, men had more cumulative outpatient visits associated with AS (odds ratio, 1.59; 95% confidence interval, 1.13 -2.23; $p = 0.008$). Men also exhibited a trend for higher frequency of AS-related hospitalization ($p = 0.054$).

CONCLUSION: Men are more likely to have high cumulative AS-associated healthcare utilization than women. Further investigation of the causal factors is warranted.

KEYWORDS: Administrative database; Ankylosing spondylitis; Gender difference; Health-care utilization; Population-based study.

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INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease characterized by pain and stiffness of the back and peripheral joints, with extra-articular manifestations.[1] It often develops in late adolescence but is usually diagnosed in young adults.[1] It is one of the most common rheumatic diseases with gender differences in prevalence and clinical presentation.[2] Although there is male predominance, the ratio of men to women has declined from 9-10:1 in earlier studies[3-4] to 2-3:1 in recent ones.[5-8]

Previous studies also show that women have a longer delay in diagnosis, more pain in the cervical spine and peripheral joints, less thoracic and lumbar spinal radiographic severity, lower Bath Ankylosing Spondylitis Radiology Index scores, and more functional limitations at the same level of radiographic damage.[2,7] However, whether there are gender differences in cumulative healthcare utilization is unknown.

The purpose of this study was to examine the influence of gender on healthcare utilization associated with AS, based on the Taiwanese National Health Insurance Research Database (NHIRD) from 1996 to 2007.

PATIENTS AND METHODS

Data source

The source of data was the NHIRD, covering in-patient and ambulatory care claims in the period 1996-2007. In Taiwan, the compulsory National Health Insurance Program was implemented in March 1995 and covered more than 95% of the population.[9] The Bureau of National Health Insurance (NHI) was the sole buyer of health services and regulated payments for medical care. Its computerized database was a good source for a population-based study.

This study used a representative database extracted randomly from the entire NHIRD dataset in 2005. The database had 1 000 000 persons, or approximately 5% of

Taiwan's population. Because the NHIRD consisted of de-identified secondary data released to the public for research purposes, this study was exempt from full review by the Internal Review Board. Self-treatment with over-the-counter (OTC) medications or alternative health services were not included in the database.

Although blood tests and radiographic data were not available in the database, the Bureau of NHI audited the accuracy of diagnoses by routinely sampling patient charts randomly to cross-check claims from all hospitals. Any hospital found to have discrepancies, malpractice, or over-charging faced heavy penalties. The audit of the Bureau of NHI promoted the accuracy of coding.[10]

Patients

This was a retrospective cohort study. Only those who had claims data in 2006 and 2007 were selected to exclude those who might be dead or lost to follow-up after 2005 (n = 893 859). The AS cases were defined as those with the diagnostic code of AS (code 720.0 in the International Classification of Diseases, Ninth Revision [ICD-9]) listed for an out-patient visit or hospitalization (i.e. provider-diagnosed AS). Those with three or more AS-associated out-patient visits, with prescription of AS-related drugs (i.e. non-steroid anti-inflammatory drugs [NSAIDs], methotrexate, sulfasalazine, steroids) were selected (n = 1608). To minimize the possibility of misdiagnosis, only those with at least three consensus AS diagnoses by certified rheumatologists were initially included (n = 976). Those aged <16 years in 1996 (n = 112) were also excluded. In the end, 228 women and 636 men with AS were included.

Variables of interest

Gender was the independent variable of interest. Outcome variables included cumulative out-patient visits, frequency of ophthalmic out-patient visit for uveitis, frequency of emergencies, AS-associated in-patient and rehabilitation visits, and frequencies of prescribed AS-related drugs. Healthcare utilization data was dichotomized, i.e. high vs. low, according to the 50^{th} percentile because these were not normally distributed.

Potential confounders included age, duration of follow-up (period between the date of first AS-associated visit and end of 2007), insured amount, and Charlson co-morbidity index (CCI). Insured amount was calculated from the patients' average monthly income and thus, also served as an economic index. Insured amount were transformed to ordinal variables according to the 25^{th}, 50^{th} and 75^{th} percentile. CCI, adapted by D'Hoore,[11] was calculated using diagnostic dose (ICD-9) listed for any out-patient and in-patient visits between the date of the first and the last AS-related visit. CCI was grouped into four ordinal categories: 0, 1, 2, and ≥3.

Statistical analysis

To examine the unadjusted male-female comparisons, t tests were used for normally distributed continuous variables, Mann-Whitney U tests for continuous variables that were not normally distributed, and χ^2 tests for categorical variables. Correlations between ordinal variables were studied using the Kendall Tau rank correlation coefficient, while correlations between dichotomous variables were studied using the Phi correlation efficient.

Multivariate adjusted logistic regression was used to examine the influence of gender on outcome variables. A two-tailed $p<0.05$ was considered statistically significant. All statistical calculations were performed using the Statistical Package for the Social Sciences (SPSS) for Windows Version 13.0 (SPSS, Inc., Chicago, Illinois).

RESULTS

The study cohort included 228 women and 636 men with AS. Their economic-demographic data and co-morbidity were compared in Table 1. Men showed an earlier age onset of healthcare utilization. Further analysis for ordinal variables showed a weak but positive correlation between age and Charlson co-morbidity index (Kendall's tau rank correlation coefficient = 0.189, $p<0.001$).

The cumulative AS-associated healthcare utilization between men and women were compared in Table 2. Men had higher risks of having higher cumulative healthcare visits associated with AS and showed a trend for higher frequency of hospitalization ($p = 0.076$). Frequencies of AS-related drug use between men and women were not different. There was a significant positive correlation between use of sulfasalazine and use of methotrexate (Phi correlation coefficient = 0.167, $p<0.001$).

After adjustment for gender, age, follow-up duration, insured amount, and CCI, men had increased risk of higher cumulative out-patient visits compared to women (odds ratio [OR] 1.59, 95% confidence interval [CI]: 1.13-2.23, $p = 0.008$) (Table 3). Men also showed a trend for higher frequency of hospitalization ($p = 0.054$). Other significant predictors of higher healthcare utilization included longer follow-up duration and higher CCI.

Table 1 - Comparison of economic, demographic and co-morbidity between men and women with ankylosing spondylitis patients*.

	Women (n = 228)	Men (n = 636)	p value
Age (yrs)	32 (25-41)	30 (23-39)	0.034
Age group (yrs)			0.204
16-30 (%)	43.0	50.5	
31-45 (%)	42.5	39.3	
46-60 (%)	13.2	8.8	
61-75 (%)	1.3	1.3	
>75 (%)	0.0	0.2	
Age at utilization onset** (yrs),	38 (30-46)	35 (28-44)	0.001
Insured amount group(NT$)			<0.001
< 12800 (%)	32.0	21.5	0.002
12800-20000 (%)	29.8	26.6	0.343
20000-31000 (%)	21.5	22.8	0.712
>31000 (%)	16.7	29.1	<0.001
Charlson comorbidity index group			<0.001
0 (%)	45.2	60.1	<0.001
1 (%)	24.1	12.7	<0.001
2 (%)	11.8	8.6	0.187
≥3 (%)	18.9	18.6	0.921

*Values are median (inter-quartile range).
**Age at utilization onset was defined as the age of initial out-patient or in-patient visit. P values were determined by chi-square tests.

Table 2 - Comparison of cumulative healthcare utilization associated with ankylosing spondylitis between men and women (1996-2007)*.

	Women (n = 228)	Men (n = 636)	p value
Follow-up duration (yrs)	5.8 (3.1-8.0)	7.1 (4.7-8.7)	<0.001
Number of outpatient visits	15.0 (9.0-31.8)	22.0 (12.0-47.0)	<0.001
≥ 21 outpatient visits (%)	39.0	53.9	<0.001
≥1 hospitalization (%)	7.0	10.5	0.076
≥1 emergent visit (%)	6.6	5.5	0.620
≥1 REHA visit (%)	16.7	20.9	0.176
≥1 OPH visit for uveitis (%)	18.4	17.3	0.686
NSAID use (%)	100	99.8	1.000
Methotrexate use (%)	21.5	16.7	0.108
Sulfasalazine use (%)	81.6	86.9	0.062
Oral steroid use (%)	86.8	83.6	0.287
Intra-articular steroid use (%)	2.6	2.8	1.000

*Values are median (inter-quartile range)
Abbreviations: REHA, rehabilitation; OPH, ophthalmic; NSAID, non-steroidal anti-inflammatory drugs

DISCUSSION

The main question addressed by this study is whether or not there is gender difference in healthcare utilization associated with ankylosing spondylitis. By current knowledge, this is the first study to demonstrate that men are more likely to have higher cumulative AS-associated outpatient visits compared to women. Singh et al., using a population based administrative database, report that gender does not influence healthcare utilization in AS patients.[12] However, in contrast to the current study, theirs investigated both AS and non-AS related healthcare utilization and for only one year.[12] Moreover, their study has been limited in examining the gender factor because of male predominance in the veteran population.[12]

There are several possible explanations to the findings here. First, men may have worse disease severity that drives higher healthcare utilization. Worse severity in men has been reported by Lee et al.[7] However, different from the current cohort, their cohort is composed of AS patients with >20 years duration and older age.[7] Second, the longer delay in diagnosis in women previously reported[2] may be a cause of later age of utilization onset found in this study and lead to an underestimation of healthcare utilization. Another possibility is the existence of gender difference in the general preference for healthcare utilization. However, the finding that men have lower healthcare utilization than women in a recent study from Taiwan provides supportive evidence to exclude this possibility.[13]

The present study reveals a male-to-female ratio of 2.79, consistent with recent reports.[5-8, 14] Unlike the PSOAS cohort,[7] women in this cohort do not have higher frequencies of sulfasalazine, methotrexate, and intra-articular steroid use. Furthermore, frequencies of sulfasalazine and steroid use in this cohort are higher than those in the PSOAS cohort. These differences may be due to a recall bias in the PSOAS cohort or ethnic differences.

This study has three advantages. First, use of an administrative database avoids the problem of under-reporting at higher numbers of visit.[15] Previous studies show that healthcare utilization in AS patients assessed in administrative databases [11,16-17] is higher than that assessed by patient report.[8,14,18-19] Second, a long observation period offers the opportunity to capture the real impact of AS. Third, this study has adjusted for confounding factors, including age, gender, follow-up duration, economic status, and Charlson co-morbidity index (CCI). The CCI, originally developed to predict mortality from medical records,[20] has been adapted for administrative databases that use the International Classification of Diseases, Ninth Revision (ICD-9).[11] CCI also reportedly influences healthcare utilization in osteoarthritis, a chronic rheumatic disease.[21] This study assumes that CCI may also influence healthcare utilization in AS and the data proves this. Although other possible confounding factors, including educational level, marital status, employment status, race, and current smoking status are unknown, none are significant predictors in the Singh's study.[12] Furthermore, over 98% of Taiwan's residents are of Chinese Han ethnicity, so the homogenous population is unlikely to be confounded by race. However, it also limits the generalization of the study result to other ethnicities.

This study has several limitations. First, although restrictive inclusion criteria have been used, bias due to miscoding and misclassification can still happen. Second, although this study uses a 12-year database, underestimation of healthcare utilization in patients with earlier or later disease onset cannot be discounted. Third, the NHIRD lacks the information for self-treatment with OTC medications, which may be

Table 3 - Significant predictors of utilization associated with ankylosing spondylitis, by multivariate analyses*.

Model characteristics	Outpatient visits (high)		Hospitalization (yes)	
Hosmer-Lemeshow test	11.326 (p = 0.184)		5.362 (p = 0.068)	
Nagelkerke R^2	0.173		0.250	
-2 log likelihood	1077.399		439.114	
Significant predictors	OR (95% CI)	P-value	OR (95% CI)	P-value
Male gender	1.59 (1.13-2.23)	0.008	1.83 (0.99-3.41)	0.054
Follow-up duration	1.26 (1.19-1.34)	<0.001	1.24 (1.10-1.39)	<0.001
CCI		<0.001		<0.001
1	1.64 (1.08-2.48)	0.020	11.34 (5.11-25.13)	<0.001
2	1.42 (0.86-2.34)	0.173	6.86 (2.71-17.38)	<0.001
≥3	2.43 (1.60-3.67)	<0.001	15.67 (7.43-33.07)	<0.001

*Multivariable regression models adjusted for the following variables: gender, age, follow-up duration, Charlson co-morbidity index, and insured amount.
Abbreviation: CCI, Charlson co-morbidity index

a confounding factor. However, a recent study from Taiwan does not reveal gender in preference for OTC medication use.[22] Lastly, other possible confounding factors like the duration of leaving, retirement status, and disease duration are unavailable in the NHIRD. However, if a Taiwanese resident migrates to other countries, the Bureau of NHI will abrogate his/her insurance.

This study excludes those without claims data in 2006 and 2007, which ensured that the enrolled patients did not have long-term leaving. As for short-term leaving, because the Bureau of NHI allows patients' families to visit doctors and take medicines for the patients, the influence of short-term leaving on the number of out-patient visits may be reduced. Because the insured amount is determined by average monthly income, the adjustment for insured amount in this study may also comprise adjustments for the status of retirement.

The true disease duration of AS is difficult to obtain via claims data because the duration between age at symptom onset and age at diagnosis usually lasts for several years and varies widely.[1] Ward's study also shows that cumulative five-year total costs of AS, which may be related to cumulative out-patient and in-patient visits, are not influenced by disease duration.[23]

In conclusion, this study demonstrates that men are more likely to have higher cumulated AS-associated out-patients visits compared to women. Further studies are required to examine whether higher AS-related cumulative healthcare utilization in men is caused by worse disease severity and/or shorter delay in diagnosis.

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