

ORIGINAL ARTICLES

Mortality trends in a Cohort of Canadian Psoriatic Arthritis Patients

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ABSTRACT

Methods: We reviewed retrospectively the charts of psoriatic arthritis patients who died from 1995-2010. We included 13 deceased patients with a psoriatic arthritis diagnosis and compared them with 140 patients living with psoriatic arthritis that attend the same clinic. The population was derived from a single academic rheumatologist's practice in St. John's, Newfoundland, Canada. Patients are seen at six-month intervals with a history and physical exam performed at each visit. Laboratory data was collected at each visit. Diagnosis of psoriatic arthritis is based on the CASPAR Classification and Diagnostic Criteria for Psoriatic Arthritis.

Results: The mean age of the 13 deceased patients was 62.9 years. Of these, 38.5% were female and 85.7% had an erythrocyte sedimentation rate greater than 15 mm/hour vs. 36.4% of patients living with psoriatic arthritis. Of deceased patients, 16% had dystrophic nail changes vs. 59.6% of living patients. Health Assessment Questionnaire was found to show a significantly greater loss in function in deceased patients. (1.39 vs. 0.70, $p=0.002$). Almost half of the deceased patients had used Prednisone (46.2%) as opposed to 11.2% of living patients.

Conclusions: We realize that this study employs a small sample size. Increased ESR and Health Assessment Questionnaire score were found to be associated with mortality in psoriatic arthritis patients. Dystrophic nail changes were found to be protective for psoriatic arthritis patients.

Key Words: Psoriasis, Psoriatic Arthritis, Mortality, Arthritis Epidemiology

INTRODUCTION

Psoriatic arthritis (PsA) is often classified as a seronegative inflammatory spondylarthropathy and affects about 10% of individual affected with psoriasis. PsA occurs at a median of 10 years after the onset of psoriasis but 15-20% of PsA patients will develop joint lesions before skin lesions due to psoriasis appear (1).

Psoriatic arthritis was once thought to be a milder form of rheumatoid arthritis however many studies have subsequently established that PsA is often aggressive and is associated with various comorbidities and often takes a chronic, progressive course(2). The population of Newfoundland and Labrador, Canada lends itself to the study of PsA because of unique genetic characteristic in

this population. Geographic isolation, relative genetic homogeneity and the founder effect lend this population with unique genetic distribution that proves useful in investigation diseases such as PsA compare to admixed Caucasian populations in the world. A significant association between the presence of PsA and a gene named CARD15 has been discovered in a 2003 study by Rahman et al. (OR=2.97, $p=0.0005$) (3). There is a paucity of literature that investigates which factors affect mortality in psoriatic arthritis patients

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Table 1. Demographics and family history in deceased PSA vs early and established psa

	Deceased PsA Patients (n=13)	Early & Established PsA Patients (n=140)
Mean Age	55.5 Years	49.7 Years
Sex	61.5% Male 38.5% Female	47.2% Male 52.8% Female
Family History of Psoriasis	25%	27.8%
Family History of Arthritis	38%	55.3%
Family History of Psoriatic Arthritis	7.7%	18.6%

in a Newfoundland and Labrador rheumatology practice.

Incidence of psoriatic arthritis has been estimated to be six per 100,000 adults aged 16 and over in Finland by Kaipainen-Seppanen and Aho (4) with a mean age of diagnosis of 46.8 years of age. Shbeeb et al (5) conducted a study in Minnesota, USA and considered inflammatory

METHODS

We identified patients in a rheumatology practice in St. John's, Newfoundland & Labrador, Canada with a definite diagnosis of PsA that have died in the period from January 1st 1999 to December 31st 2009. Similarly to Gladman and colleagues, (11,13), the patients that compose both the deceased PsA patients and living patients in this study are treated in a single outpatient clinic.

Patients are seen at six-month intervals with a history and physical exam performed at each period. Further, laboratory data was collected at each visit. Diagnosis of psoriatic arthritis based on the CASPAR Classification and Diagnostic Criteria for Psoriatic Arthritis (14).

Similarly to a study by Khraishi and Murphy, (15) patient death will be ascertained by the following means: review of charts in the arthritis clinic, review of hospital records and death certificates. Further, local newspaper obituary section and contact with family members as well as family physicians will be employed to document patient death.

Basic demographic variables as well as clinical variables relevant to psoriatic arthritis such as nail involvement (pitting or onycholysis), family history of psoriasis, PsA or other arthropathy and presence and severity of psoriasis will be compared in the deceased psoriatic arthritis patients with patients living with psoriatic arthritis in that attended the same clinic. Health Assessment Questionnaire (HAQ) score gives a measure of how debilitating arthritis is in terms of reduced capacity to perform

daily activities and will also be assessed. This tool has been validated in use with psoriatic arthritis patients. (16) HAQ is a patient self-assessment scale that ranges from a low of zero to a high of three for high self-perceived disability. In this study, we will investigate the Standard Disability Index portion of the HAQ.

Clinical signs related to psoriatic arthritis that will be evaluated include distal interphalangeal joint (DIP) involvement, axial skeleton involvement, dystrophic nail changes (nail involvement), asymmetry of joint involvement, oligoarthritis, psoriasis and erythrocyte sedimentation rate. Asymmetry of joint involvement was defined as a difference of more than one in the number of affected joints between contralateral hands and feet. Oligoarthritis was defined as four or fewer joints displaying swelling or tenderness.

Medications that will be investigated include concomitant use of diabetes mellitus and hypertension medication as well as medication for depression or anxiety. The following disease-specific medications were investigated: methotrexate, sulfasalazine, prednisone, hydroxychloroquine, calcipotriol, (Dovonex), etanercept (Enbrel), infliximab (Remicade), and adalimumab (Humira). Disease-modifying anti-rheumatic drugs (DMARDs) included defined utilization of one or more of the following medications: methotrexate, sulfasalazine, hydroxychloroquin and plaquenil. The use of biologics includes the use of one or more of the following medications: etanercept, infliximab, and adalimumab.

STATISTICAL METHODS

Proportions for categorical variables will be reported as well as means and standard deviations for continuous variables analyzed and compared between deceased patients that were diagnosed with PsA and patients living with PsA. Further, an Independent samples T-test will be employed to test

Table 1. Demographics and family history in deceased PSA vs early and established psa

Clinical Sign	Deceased PsA Patients (n=8)	Early & Established PsA Patients (n=140)
DIP Involvement	25%	39.8%
Axial Involvement	13%	19.8%
Axial and Peripheral Involvement	13%	21.2%
Nail Involvement*	38%	59.6%
Asymmetry of Joints	57%	50.4
Oligoarthritis	43%	42.1%
Erythrocyte Sedimentation Rate > 15*	63%	36.4%

Asterisk (*) represents a statistically significant difference at $p = 0.05$.

Erythrocyte sedimentation rate over 15 was significantly more prevalent in deceased PsA patients (63%) than in early and established

for statistically significant differences in continuous variables between deceased patients with PsA and patients living with PsA.

The Chi-square statistic was used to detect associations between mortality and medication use, presence of comorbidities as well as clinical features of PsA. Fisher's exact test was employed in the case of low numbers. For all analyses, the minimum level of statistical significance, is 0.05, determined a priori. All statistical analyses were performed using SPSS version 15.0 for Windows (SPSS Inc.).

RESULTS

There were statistically significant differences between prevalence of hematological comorbidities between deceased patients and patients living with PsA. (38% vs. 8.3%, $p = 0.033$). Of these, the most common hematological comorbidity in both groups was anemia. In a review by Gabriel and Michaud, anemia was found to be a comorbid condition commonly found with Rheumatoid arthritis as well. Musculoskeletal comorbidities were very common in both deceased patients and patients living with PsA (50% and 57.6%).

Psoriasis is part of the criteria for diagnosing psoriatic arthritis (83% of deceased patients and 95.1% of patients living with PsA).

Not surprisingly, there was a greater proportion of deceased psoriatic arthritis patients with malignancy than those with early and established disease. Specifically, Bowel cancer (13% vs 0.7%), breast cancer (0% vs 1.4%), lymphoma (25% vs 0.7%), other cancers (13% vs 5.6%) and total proportion of patients with a malignancy (38% vs 7.6%). Of those, only the total number of malignancies was statistically significant at $a = 0.05$.

When comparing medications between patients with early and established disease, the only medications that were shown to be statistically significantly higher in use in early and established patients was Prednisone. ($p = 0.011$). Other medications investigated including methotrexate, Enbrel, Remicade, Sulfasalazine, Hydroxychloroquin, Humira, were not found to be used in a different amount between the early & established and mortality.

Neither a family history of psoriasis ($p = 0.864$), psoriatic arthritis ($p = 0.180$) or other type of arthritis ($p = 0.464$). In terms of clinical features characteristic for psoriatic arthritis, there was a statistically significant increase in the proportion of deceased patient with an ESR greater than 15 mm/hour in deceased patients and a statistically significant decreases proportion of nail involvement in deceased patients.

Other clinical signs of psoriatic arthritis were not found to have a statistically significant prevalence in the two groups investigated including axial involvement ($p = 0.611$), distal interphalangeal joint involvement ($p = 0.482$), asymmetrical joint distribution ($p = 0.699$), oligoarthritis ($p = 0.441$).

DISCUSSION

Though cardiovascular comorbidities have been specifically implicated in rheumatoid arthritis patients and indeed a major source of their increased mortality, prevalence of cardiovascular comorbidities is not significantly elevated in either group of PsA patients in this study.

When we compared the following continuous variables ages, age at diagnosis of PsA and diagnosis of psoriasis, most recent Health Assessment Questionnaire score (HAQ) , systolic

Table 3. Comorbidities in deceased versus early and established Psoriatic Arthritis

Comorbidity	Deceased PsA Patients (n=13)	Early & Established PsA Patients (n=140)
Hypertension	38%	32.6%
Psoriasis	83%	95.1%
Coronary Heart Disease	13%	4.2%
Musculoskeletal History	50%	57.6%
Gastrointestinal History	38%	45.8%
Angina	0%	0%
TIA	0%	0.7%
Respiratory System History	13%	20.8%
Obesity	38%	47.2%
Thyroid Disease	13%	4.2%
Peripheral Vascular Disease	0%	11.8%
Hepatobiliary System History	25%	16.0%
Peptic Ulcer	13%	4.9%
Hematological-Lymphatic History*	38%	8.3%
Cardiovascular System History No cardiovascular comorbidities	87%	91.5%
Cardiovascular System History One cardiovascular comorbidities	0%	6.4%
Cardiovascular System History Two or more cardiovascular comorbidities	13%	2.1%

Asterisk (*) represents a statistically significant difference at $p = 0.05$.

blood pressure, erythrocyte sedimentation rate (ESR) and total number of tender joints between deceased PsA patients to those defined with early or established PsA, we found HAQ score and ESR to have statistically significant associations with mortality. The deceased patients with PsA had a significantly higher HAQ score than patients still living with PsA: 1.47 vs. 0.70 ($p = 0.014$). The eight equally-weighted areas of the HAQ are difficulty in everyday activities, arising, dressing & grooming, eating, grip, performing activities related to hygiene, reach and walking.

Since ESR is a non-specific marker for inflammation, ESR may be related to severity of this seronegative inflammatory condition. The mean ESR of 84.6mm/hour for deceased PsA patients vs. 20.6mm/hour for patients living with PsA is significant. ($p = 0.021$) This is similar to a study by Gladman et al, (11) which found that ESR > 15mm/hour had value in predicting mortality of PsA patients. When ESR was categorized as such in this study, there was a significant association

between mortality and ESR status in PsA patients. ($p = 0.013$)

Beside erythrocyte sedimentation rate, presence of nail lesions (pitting or onycholysis) seems to be the only other statistically significant clinical variable. Similarly to Gladman et al (2), we discovered that a higher proportion of patients living with PsA that deceased patients that were diagnosed with PsA had nail involvement (59.6% vs. 38%, $p = 0.013$), this acts as a protective factor against mortality in PsA patients. This may be because the presence of nail involvement may cause patients to seek treatment earlier in the course of their disease.

There was no statistically significant difference in the proportions of prescribed non-PsA (concomitant) medication between deceased patients and those living with PsA. Methotrexate is the most commonly-prescribed DMARD in both groups and was prescribed to 38% of deceased PsA patients and 28% of patients with established PsA (Table 4). Prednisone was found to be

Table 4. Quantitative data in deceased PSA patients vs early & established PSA

Quantitative Variable	Deceased PsA Patients (n=13)	Early & Established PsA Patients (n=140)
Age as of December 31, 2009 or Age at Death	55.50 Years	49.67 Years
Age of Diagnosis Psoriasis	31.75 Years	35.70 Years
Age of Diagnosis Psoriatic Arthritis	47.00 Years	44.78 Years
Systolic Blood Pressure	134.14 mmHg	126.58 mmHg
Erythrocyte Sedimentation Rate *	84.60 mm/hour	20.62 mm/hour
Total Tender Joints	5.00	7.42
Health Assessment Questionnaire*	1.4725	.6968

Asterisk (*) represents a statistically significant difference at $p=0.05$.

statistically associated with mortality in PsA patients ($p=0.011$) as 50% of deceased patients had been prescribed Prednisone while only 11.2% of patients living with PsA enrolled at the same rheumatology clinic were using Prednisone. Further, use of any DMARDS was found to be significantly associated with mortality in PsA patients ($p=0.007$). When we removed patients that had been treated with prednisone from our analysis, we found that results were not significant $p=0.121$.

For each of the individual malignancies of breast cancer, bowel cancer and lymphoma, there was no statistically significant difference between the prevalence of these comorbidities in the two groups. However, when the proportion (Table 4) of patients with any type of malignancy was compared between patients with early and established PsA and deceased patients with PsA, we found that a significantly greater proportion of deceased patients suffer from at least one malignancy (38% vs. 7.6%, $p=0.027$) We found no statistically significant relationship between rheumatoid factor and positive history of cardiovascular events in PsA patients.

CONCLUSION

The presence of at least one malignancy was found to be related to increased likelihood of mortality in PsA patients though a relationship between particular cancers and mortality could not be ascertained. Moreover, use of DMARDS was also found to be statistically associated with mortality in PsA patients. Specifically, the use of Prednisone as found to be associated with mortality in PsA patients. Further, increased ESR and the absence of dystrophic nail changes are associated with

mortality in PsA patients.

LIMITATIONS

We understand that it may be difficult to apply conclusions for these results to all who suffer from psoriatic arthritis since the information is relevant to individuals that have been treated at a clinic; milder cases of psoriatic arthritis may be missed.

Further, the relatively small sample size of deceased psoriatic arthritis patients makes it difficult to properly interpret results from this group.

Since all patients from this study are seen in an outpatient clinic, we the results may show greater overall morbidity and mortality that in PsA in the general population that may be so mild as to go undetected or not require medical attention.

As a cross-sectional study, this study does not support inferences in causality. That is, though we can say that specific comorbidities and medications are associated with mortality in PsA patients, we cannot ascertain whether or not these characteristics cause an increased risk of death from PsA or whether these patients were sicker on the whole and therefore needed numerous disease-specific drugs.

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