The Impact of Delayed Primary Sjögren's Syndrome Diagnosis on Patient Outcomes: A Real-World Survey in the US

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BACKGROUND

- Primary Sjögren's Syndrome (pSS) patients frequently experience a prolonged period between symptomatic onset and diagnosis.

OBJECTIVE

- To describe the impact of delayed diagnosis on disease severity and patient outcomes in patients with pSS.

METHODS

Data Source

- Data were drawn from the Adelphi pSS Disease Specific Programme (DSP™); a point-in-time survey of rheumatologists and their consulting patients with pSS presenting in a real-world clinical setting in the US.

Eligibility Criteria

- Rheumatologists were eligible to complete the survey provided they had 3–30 years' experience and were treating patients with pSS.
- Patients were eligible if they visited a participating rheumatologist, had a diagnosis of pSS with some degree of systemic involvement, were aged ≥18 years, provided informed consent and not involved in a clinical trial.

Data Collection

- Rheumatologists completed patient record forms reporting on patient demographics and disease characteristics. EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) proxy scores were calculated by assigning scores to physician- and patient-perceived severity respectively in each of the associated domains.
- Patients self-completed patient-reported outcome (PRO) tools; including the EuroQol 5-dimension 3-level utility score (EQ-5D), EuroQol visual analogue scale (EQ-5D VAS), Work Productivity and Activity Impairment Index questionnaire (WPAI), and the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F).

Table 1. pSS patient demographics and clinical characteristics by time from onset of symptoms to diagnosis.

	Overall (n=276)	<3 months (n=81)	3-6 months (n=56)	6-12 months (n=49)	>12 months (n=90)
Patient age, mean years (SD)	52.3 (14.6)	51.7 (17.4)	51.3 (14.3)	51.3 (12.7)	53.9 (12.9)
Female, n (%)	246 (89.1)	73 (90.1)	60 (89.3)	43 (87.8)	80 (88.9)
BMI, mean (SD)	26.3 (5.0)	27.1 (6.5)	26.2 (4.0)	24.8 (3.0)	26.3 (4.8)
Ethnicity, n (%)					
White/Caucasian	233 (80.8)	62 (76.5)	47 (83.9)	41 (83.7)	73 (81.1)
African American	29 (10.5)	10 (12.3)	6 (10.7)	5 (10.2)	8 (8.9)
Other	24 (8.7)	9 (11.2)	3 (5.4)	3 (6.1)	9 (10.0)
Smoking status, n (%)					
Current smoker	16 (6.0)	4 (5.1)	2 (3.6)	2 (4.2)	8 (9.3)
Ex-smoker	62 (23.1)	18 (23.1)	13 (29.2)	14 (29.2)	17 (19.8)
Never smoked	190 (70.9)	56 (71.8)	32 (66.7)	32 (66.7)	61 (70.9)
Employment, n (%)					
Working full-time	144 (52.7)	40 (50.0)	34 (60.7)	25 (51.0)	45 (51.1)
Working part-time	28 (10.3)	8 (10.0)	4 (7.1)	7 (14.3)	9 (10.2)
Homemaker	33 (12.1)	6 (7.5)	7 (12.5)	5 (10.2)	15 (17.0)
Other	68 (24.9)	26 (32.5)	11 (19.7)	12 (24.5)	19 (21.7)
Months since diagnosis, mean (SD)	51.6 (62.2)	48.1 (55.2)	45.8 (43.6)	40.1 (50.2)	64.5 (80.1)

SD: Standard Deviation

METHODS (continued)

Data Analysis

- Patients were compared according to the time between onset of pSS symptoms and diagnosis (<3 months, 3-6 months, 6-12 months, and >12 months). Analysis of variance and Kruskall-Wallis tests were used to examine the impact of delayed diagnosis on ESSDAI, ESSPRI and PRO measures, and Mann-Whitney U-test for physician-perceived current severity using <3 months as the reference group.
- Multivariable linear and logistic regression analyses (controlled for duration of disease, patient age, sex, BMI, and ethnicity) examined the impact of delayed diagnosis on pSS severity (ESSDAI & ESSPRI) and PRO measures.

LIMITATIONS

- Sample is representative of the consulting patient population.
- Recall bias is a common limitation of surveys. Data collected at the time of consultation using patients record to limit recall bias.
- Geographically representative sample was obtained, information on physician location not provided.
- ESSDAI and ESSPRI scores are derived from proxy measures within the survey, rather than collected through direct use of the measures.
- Regression analyses could not be controlled for systemic activity at time of symptom onset or during the patient's journey to diagnosis.

RESULTS

- 71 rheumatologists provided information for 276 pSS patients.
- 29.3% of patients were diagnosed within 3 months of symptom onset, 20.3% 3-6 months, 17.8% 6-12 months and 32.6% >12 months. The mean and median time to diagnosis were 27.51 and 6.03 months respectively.
- In unadjusted comparative analyses, there were significant differences in EQ-5D-3L utility and VAS, FACIT-F, ESSPRI proxy scores, and physician-reported severity as time to diagnosis increased. Conversely, no significant differences were observed in work impairment and ESSDAI proxy scores (Figure 1).
- Furthermore, in adjusted regression models, further significant differences were observed in EQ-5D (<3 months vs. >12 months), ESSDAI proxy (<3 months vs. 6-12 months, and <3 months vs. >12 months), and ESSPRI proxy (<3 months vs. 3-6 months, and <3 months vs. 6-12 months). There was no significant difference between the ESSPRI proxy scores of patients diagnosed <3 months and >12 months following symptomatic onset. Physician-reported severity, in which physicians likely considered both systemic disease activity and symptom severity, also showed continued significant differences (<3 months vs. 6-12 months, and <3 months vs. >12 months) (Table 2).
- Adjusted logistic regression models indicate that the odds of a patient receiving ESSDAI and ESSPRI proxy scores >5 at time of diagnosis are 2.339 and 2.106 times greater respectively in patients who received a pSS diagnosis >12 months after symptomatic onset than those who were diagnosed in <3 months. Similarly, patients who received a diagnosis >12 months following symptomatic onset were 2.386 times more likely to be described as moderate or severe by their physician than those diagnosed in <3 months.
- Comparative analyses showed that there were significant differences in EQ-5D utility score, EQ-5D VAS, FACIT-F, proxy ESSPRI scores and physician reported severity between patients with differing time to diagnosis, assessed at the time of consultation. Relationships between diagnosis duration and WPAI scores were not statistically significant.

Figure 1. Unadjusted comparison of patient-reported outcomes, ESSDAI proxy and ESSPRI proxy scores by time from onset of symptoms to diagnosis. Error bars indicate 95% confidence intervals.

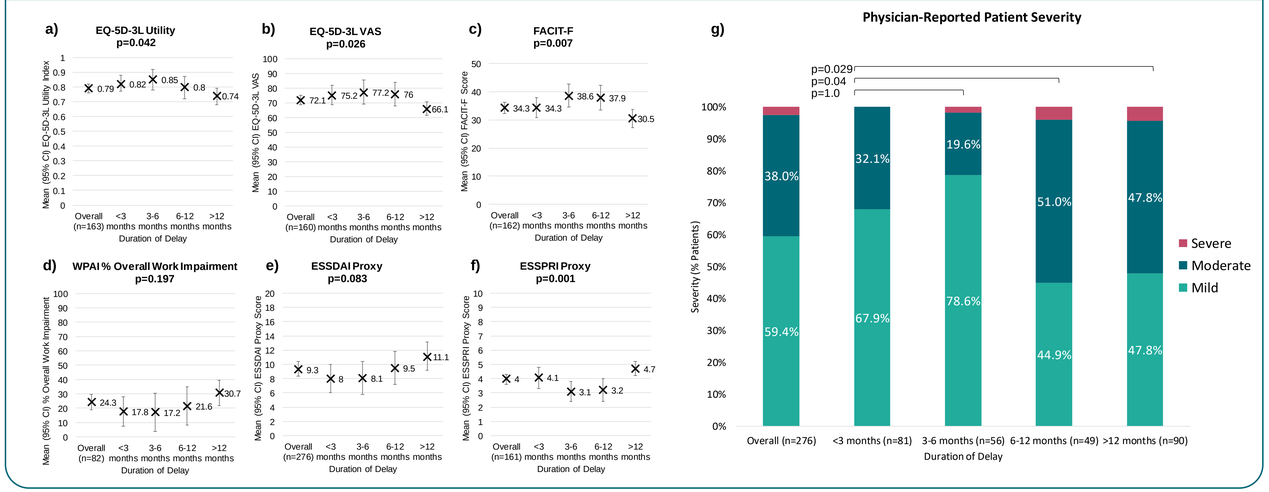

Table 2. Adjusted linear and logistic regression analyses of ESSDAI proxy and ESSPRI proxy scores by time from onset of symptoms to diagnosis.

	<3 months (n=81)	3-6 months (n=56)	6-12 months (n=49)	>12 months (n=90)	p-value
Linear Regressions	**Coefficient [95% Confidence Interval]**				
EQ-5D-3L Utility (n=163)	0 (ref)	5.09×10^{-3} [-0.082, 0.924]	-0.036 [-0.113, 0.042]	-0.102 [-0.181, -0.023]	<3months: ref 3-6 months: 0.907 6-12 months: 0.363 **>12 months: 0.013**
EQ-5D VAS (n=160)	0 (ref)	-0.048 [-9.207, 9.111]	-0.905 [-10.402, 8.591]	-9.819 [-16.325, -3.313]	<3months: ref 3-6 months: 0.992 6-12 months: 0.849 **>12 months: 0.004**
FACIT-F (n=162)	0 (ref)	2.487 [-2.748, 7.7121]	2.284 [-1.919, 6.487]	-4.409 [-9.827, 1.009]	<3months: ref 3-6 months: 0.345 6-12 months: 0.281 >12 months: 0.109
WPAI (% overall work impairment) (n=82)	0 (ref)	2.137 [-14.443, 18.718]	4.996 [-12.293, 22.286]	12.343 [-2.674, 27.359]	<3months: ref 3-6 months: 0.796 6-12 months: 0.563 >12 months: 0.105
Logistic Regressions	**Odds Ratio [95% Confidence Interval]**				
ESSDAI proxy (n=276) ≤5 >5	1 (ref)	1.115 [0.544, 2.286]	1.830 [0.849, 3.947]	2.339 [1.16, 4.72]	<3months: ref 3-6 months: 0.766 6-12 months: 0.123 **>12 months: 0.018**
ESSPRI proxy (n=161) ≤5 >5	1 (ref)	0.236 [0.056, 0.988]	0.346 [0.128, 0.925]	2.106 [0.877, 5.061]	<3months: ref **3-6 months: 0.048** **6-12 months: 0.035** >12 months: 0.096
Physician-reported patient severity (n=276) *Mild* *Moderate/Severe*	1 (ref)	0.583 [0.248, 1.373]	2.818 [1.362, 5.832]	2.386 [1.292, 4.406]	<3months: ref 3-6 months: 0.217 **6-12 months: 0.005** **>12 months: 0.005**

SD: Standard Deviation

CONCLUSIONS

- **Delayed diagnosis of pSS is associated with poorer patient outcomes, including worsening PRO scores, and ESSPRI scores.**
- **Patients who receive a delayed diagnosis are over twice as likely to experience ESSDAI and ESSPRI proxy scores >5, and experience moderate or severe disease as reported by their physician.**
- **pSS diagnosis periods could likely be attenuated by increasing disease awareness amongst physicians; thus, improving patient outcomes in pSS.**