

Delayed Referral of Female Patients with Rheumatoid Arthritis

LEROY R. LARD, THOMAS W.J. HUIZINGA, JOHANNA M.W. HAZES, and THEODORA P.M. VLIET VLIELAND

ABSTRACT. *Objective.* To analyze whether sex differences in referral exist in patients with rheumatoid arthritis (RA).

Methods. At the Department of Rheumatology of the Leiden University Medical Center, a special early arthritis clinic (EAC) was established. General practitioners (GPs) were encouraged to refer patients with joint complaints to the EAC. Subsequently, the diagnosis RA was made by a rheumatologist.

Results. In this report, 142 women and 82 men were included. The delays in patient's first encounter with a GP for both sexes were comparable. However, a significant difference in the GP's delay in referring female patients with RA to the EAC in comparison with male patients was observed (median of 93 days vs 58 days; $p = 0.008$).

Conclusion. This report determined GP referral delay of female patients to a rheumatologist. GPs should be made aware that early detection and early referral of patients with RA are crucial for early treatment. (J Rheumatol 2001;28:2190-2)

Key Indexing Terms:
RHEUMATOID ARTHRITIS

FEMALE PATIENTS

Rheumatoid arthritis (RA) is a chronic autoimmune disease that predominantly affects women. Several studies reported that therapy with second-line antirheumatic drugs must be started early if a beneficial effect on joint destruction is to be expected^{1,2}. Delay in diagnosis by the physician may hamper early treatment^{3,4}. Several studies have described differences between sexes in the use of medical services⁴⁻⁸. At the Department of Rheumatology of Leiden University Medical Center, a special clinic for patients with arthritis of recent onset was established, the early arthritis clinic (EAC). Concerning the relevance of early treatment of patients with RA, we investigated if sex differences in referral also exist in RA patients in our EAC.

MATERIALS AND METHODS

Patients. The EAC was the only center for rheumatic patients in a semi-rural area with 300,000 inhabitants. The general practitioners (GPs) were motivated to refer patients if at least 2 of the following features were present: joint pain, joint swelling, and reduction of joint mobility. All patients referred to the special EAC by GP were seen within 2 weeks. Patients were accepted in the EAC if (1) arthritis was confirmed by a rheumatologist; (2) the history of symptoms lasted < 2 years; and (3) the patient had not seen a rheumatologist elsewhere for the same problem⁹.

From the Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands.

L.R. Lard, MD; T.W.J. Huizinga, MD, PhD; T.P.M. Vliet Vlieland, MD, PhD, Department of Rheumatology, Leiden University Medical Center; J.M.W. Hazes, MD, PhD, Department of Rheumatology, Academic Hospital Rotterdam.

Address reprint requests to Dr. L.R. Lard, Department of Rheumatology, Leiden University Medical Center, PO Box 9600, 2300 RC, Leiden, The Netherlands. E-mail: l.r.lard@lumc.nl

Submitted October 10, 2000; revision accepted April 30, 2001.

Subsequently, the diagnosis of definite RA was made according to the 1987 American College of Rheumatology (ACR) criteria¹⁰, but without the requirement of a 6 week observation period of arthritis by a rheumatologist⁹.

A standard diagnostic investigation was performed at the first visit at the EAC, consisting of patient history (age, sex, patient's medical encounter delay, family physician's referral delay), physical examination [a joint tenderness score (Ritchie)¹¹ and swollen joint score], laboratory examination [erythrocyte sedimentation rate (ESR) and rheumatoid factor (RF)], and radiological examination. The patient's medical encounter delay was the time between onset of complaints and first medical encounter. The family physician's referral delay was the time between the first medical encounter of the patient and the first visit to the EAC referred by the GP.

A total of 54 joints were assessed for soft tissue swelling, with a maximal swollen joint count of 22, since the metacarpophalangeal and proximal and distal interphalangeal joints at each side were counted as one joint. Also a disease activity score (DAS) was measured at the first visit¹². The DAS is a composite index of disease activity that includes the number of painful joints, number of swollen joints, and ESR. It is used to monitor disease activity in RA patients in clinical trials. The formula of the DAS was as follows: $DAS = 0.54 \times (\sqrt{\text{Ritchie score}}) + 0.065 \times (\text{number of swollen joints}) + 0.33 \times \ln \text{ESR} + 0.224$.

Statistical analysis. Differences between referral of men and women were tested with the Mann-Whitney U test. The test was 2 tailed and $p < 0.05$ was considered significant.

RESULTS

Between 1993 and 1999, 142 female and 82 male consecutive patients who entered the EAC and fulfilled the ACR classification criteria for RA 2 weeks after EAC entry were included in this report. Table 1 shows that both sexes were comparable for medical encounter delay and demographic and clinical data. However, we observed a significant difference in family physician's delay in referring female patients with RA to the EAC compared to male patients — a median

Table 1. Characteristics of 22 patients with RA.

	Men, n = 82	Women, n = 142
Age (yrs)*	59 (19–85)	57 (17–87)
Patient's medical encounter delay (days)*	17 (0–396)	20 (0–482)
Family physician's delay (days)*	58 (3–369)	93** (1–697)
RF positivity, %	58	59
DAS*	3.34 (1.62–5.77)	3.60 (1.61–6.07)

* Median (range). Differences were tested with the nonparametric Mann-Whitney U test. ** $p = 0.008$.

of 93 days (1–697) vs 58 days (3–369) ($p = 0.008$). At 6 months, 89% of the men and 73% of the women had been referred to a rheumatologist, with the median physician's delay being 55 (3–170) days in men and 73 (1–162) days in women ($p = 0.11$).

DISCUSSION

This report shows a significantly delayed referral of female patients with RA by general practitioners to a rheumatologist, although the disease activity on the first visit to the EAC was similar for both sexes. Thus, the difference in referral to a rheumatologist seems more likely to be sex-specific than due to a difference in disease severity. Möttönen, *et al*¹³ also observed no significant differences in clinical activity in either sex at baseline.

Sex differences in the use of medical services has been observed in other studies. Hawker, *et al*⁴ described a significant underuse of hip and knee arthroplasty in women with severe arthritis compared to men. An explanation for this difference suggested by the authors was that women were less likely to be referred to orthopedic surgeons for consideration of arthroplasty or perhaps were referred after a longer interval. Other studies also show that women are less likely to undergo orthopedic surgery for degenerative arthritis, cardiac catheterization and revascularization, or renal transplantation than are age matched men with similar disease extent^{5–8}.

Several possibilities could account for a delayed referral of female patients to a rheumatologist. A possibility could be that more women, more often, consult their GP for musculoskeletal symptoms, which might make it difficult for GPs to diagnose RA early in women. Another possibility could be that male patients might be more demanding in medical aid for socioeconomic reasons. It could also be hypothesized that the referrals could happen at a certain level of severity irrespective of duration, which might suggest that the disease has a milder course in women. However, a milder course in women in comparison with men has not been observed in other studies.

Our study was limited because only one district has been analyzed and because we were not able to know which patients were not referred to the EAC. Whether this differ-

ence in referral is also observed in other districts or countries has not yet been reported.

For some men and women, the GP's referral delay was 6 months or longer. As several studies^{1,2} have shown that early antirheumatic drug treatment of RA is more beneficial than delayed treatment, the lack of early referral of these patients is worrisome.

Drossaers-Bakker, *et al*¹⁴ found in their cohort of patients with RA a nearly linear joint damage progression in the radiographs of hands and feet (measured according to the Sharp method¹⁵) of Sharp score 9 per year. We observed a statistically significant difference of 35 days in GP's referral delay between men and women. Thus a 5 week difference in initiation of treatment means a possible difference of 0.9 Sharp score, which may not be judged as relevant. However, because of the pain and discomfort of the disease and untreated disability that may interfere with work or function at home, it may be desirable to refer patients earlier.

We observed that there is a significant delay in referral of female patients to rheumatologists compared to male patients with RA. Special educational programs to instruct family physicians on the importance of early detection and early referral of RA patients may be beneficial.

REFERENCES

- Boers M, Verhoeven AC, Markusse HM, *et al*. Randomised comparison of combined step-down prednisolone, methotrexate and sulphasalazine with sulphasalazine alone in early rheumatoid arthritis. [published erratum: Lancet 1998;351:220] Lancet 1997;350:309–18.
- Stenger AA, van Leeuwen MA, Houtman PM, *et al*. Early effective suppression of inflammation in rheumatoid arthritis reduces radiographic progression. Br J Rheumatol 1998;37:1157–63.
- Chan KW, Felson DT, Yood RA, Walker AM. The lag time between onset of symptoms and diagnosis of rheumatoid arthritis. Arthritis Rheum 1994;37:814–20.
- Hawker GA, Wright JG, Coyte PC, *et al*. Differences between men and women in the rate of use of hip and knee arthroplasty. N Engl J Med 2000;342:1016–22.
- Katz JN, Wright EA, Guadagnoli E, Liang MH, Karlson EW, Cleary PD. Differences between men and women undergoing major orthopedic surgery for degenerative arthritis. Arthritis Rheum 1994;37:687–94.
- Tobin JN, Wassertheil-Smoller S, Wexler JP, *et al*. Sex bias in considering coronary bypass surgery. Ann Intern Med 1987; 107:19–25.
- Steingart RM, Packer M, Hamm P, *et al*. Sex differences in the management of coronary artery disease. N Engl J Med 1991;325:226–30.
- Bickell NA, Pieper KS, Lee KL, *et al*. Referral patterns for coronary artery disease treatment: gender bias or good clinical judgment? Ann Intern Med 1992;116:791–7.
- van der Horst-Bruinsma IE, Speyer I, Visser H, Breedveld FC, Hazes JM. Diagnosis and course of early-onset arthritis: results of a special early arthritis clinic compared to routine patient care. Br J Rheumatol 1998;37:1084–8.
- Arnett FC, Edworthy SM, Bloch DA, *et al*. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315–24.
- Ritchie DM, Boyle JA, McInnes JM, *et al*. Clinical studies with an

articular index for the assessment of joint tenderness in patients with rheumatoid arthritis. *Q J Med* 1968;37:393-406.

12. van der Heijde DM, van't Hof MA, van Riel PL, et al. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. *Ann Rheum Dis* 1990;49:916-20.
13. Mottonen T, Paimela L, Leirisalo-Repo M, Kautiainen H, Ilonen J, Hannonen P. Only high disease activity and positive rheumatoid factor indicate poor prognosis in patients with early rheumatoid arthritis treated with "sawtooth" strategy. *Ann Rheum Dis* 1998;57:533-9.
14. Drossaers-Bakker KW, de Buck M, van Zeben D, Zwinderman AH, Breedveld FC, Hazes JM. Long-term course and outcome of functional capacity in rheumatoid arthritis: the effect of disease activity and radiologic damage over time. *Arthritis Rheum* 1999;42:1854-60.
15. van der Heijde DM, van Riel PL, Nuver-Zwart IH, van de Putte LB. Sulphasalazine versus hydroxychloroquine in rheumatoid arthritis: 3-year follow-up [letter]. *Lancet* 1990;335:539.