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Original article

Has the median nerve involvement in rheumatoid arthritis been overemphasized?

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ABSTRACT

Rheumatoid arthritis (RA) is a well and widely recognized cause of carpal tunnel syndrome (CTS). In the rheumatoid wrist, synovial expansion, joint erosions and ligamentous laxity result in compression of the median nerve due to increased intracarpal pressure. We evaluated the published studies to determine the prevalence of CTS and the characteristics of the median nerve in RA and its association with clinical parameters such as disease activity, disease duration and seropositivity. A total of 13 studies met the eligibility criteria. Pooled data from 8 studies with random selection of RA patients revealed that 86 out of 1561 (5.5%) subjects had CTS. Subclinical CTS, on the other hand, had a pooled prevalence of 14.0% (30/215). The cross sectional area of the median nerve of the RA patients without CTS were similar to the healthy controls. The vast majority of the studies (8/13) disclosed no significant relationship between the median nerve findings and the clinical or laboratory parameters in RA. The link between RA and the median nerve abnormalities has been overemphasized throughout the literature. The prevalence of CTS in RA is similar to the general population without any correlation between the median nerve characteristics and the clinical parameters of RA.

O envolvimento do nervo mediano na artrite reumatoide tem sido excessivamente valorizado?

Palavras-chave:
Nervo mediano
Artrite reumatoide
Síndrome do túnel do carpo

RESUMO

A artrite reumatoide (AR) é uma causa bem e amplamente reconhecida de síndrome do túnel do carpo (STC). No punho acometido pela artrite reumatoide, a expansão sinovial, as erosões articulares e a frouxidão ligamentar resultam em compressão do nervo mediano decorrente do aumento da pressão intracarpal. Avaliaram-se os estudos publicados para determinar a prevalência de STC e as características do nervo mediano na AR e sua associação com parâmetros clínicos, como a atividade e duração da doença e a soropositividade.

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Preencheram os critérios de elegibilidade 13 estudos. Os dados agrupados dos oito estudos com seleção aleatória de pacientes com AR revelaram que 86 de 1.561 (5,5%) indivíduos tinham STC. Por outro lado, a STC subclínica teve uma prevalência combinada de 14% (30/215). A área de seção transversa do nervo mediano dos pacientes com AR sem STC foi semelhante à de controles saudáveis. A grande maioria dos estudos (8/13) não apresentou relação significativa entre os achados no nervo mediano e os parâmetros clínicos ou laboratoriais na AR. A ligação entre a AR e as anormalidades do nervo mediano foi excessivamente valorizada em toda a literatura. A prevalência de STC na AR é semelhante à da população em geral, sem qualquer correlação entre as características do nervo mediano e os parâmetros clínicos da AR.

Introduction

Beyond the joints, rheumatoid arthritis (RA) may present with extra-articular manifestations such as pulmonary fibrosis, subcutaneous nodules and peripheral neuropathy in up to 10–20% of patients.[1] The wrist is the most frequently affected joint in RA with carpal tunnel syndrome (CTS) as a potential sequelae. In the rheumatoid wrist, synovial expansion, joint erosions and ligamentous laxity result in loss of carpal tunnel height and increased carpal tunnel pressure. This contributes to impaired axonal transport, compression of the median nerve and vessels in the perineurium causing median nerve ischemia.[2,3] The other plausible culprit mechanisms that have been implicated in rheumatoid neuropathy are drug toxicity, vasculitis and amyloidosis.[4]

Carpal tunnel syndrome (CTS) is by and large a clinical diagnosis, although electrophysiological tests (nerve conduction studies [NCS], electromyography [EMG]) and sonographic assessment of the median nerve may be useful to support the diagnosis, detect subclinical CTS and rule out other abnormalities.[5] Unfortunately, the neuropathic pain in RA is often overlooked and mistaken for arthritic pain.[6]

Hart et al. was the first to describe neuropathy in RA in year 1957.[7] Since then, several electrophysiological and sonographic studies have examined the median nerve in RA with variable findings. The purpose of this systematic review, is therefore, to summarize the results of these studies and to determine in RA the prevalence of CTS, characteristics of the median nerve and its association with the clinical parameters such as disease activity, disease duration and seropositivity.

Methods

Search strategy

We searched the literature for clinical studies on median nerve in RA using the following databases: Science Direct, Pubmed/Medline, Ovid, ISI Web of Knowledge, EBSCO and Scopus. These search terms used were “rheumatoid arthritis”, “median nerve,” “carpal tunnel syndrome” and “neuropathy”. To ensure completeness, we went through papers not only on CTS explicitly but also on less specific conditions that might encompass the median nerve/CTS like peripheral neuropathy.

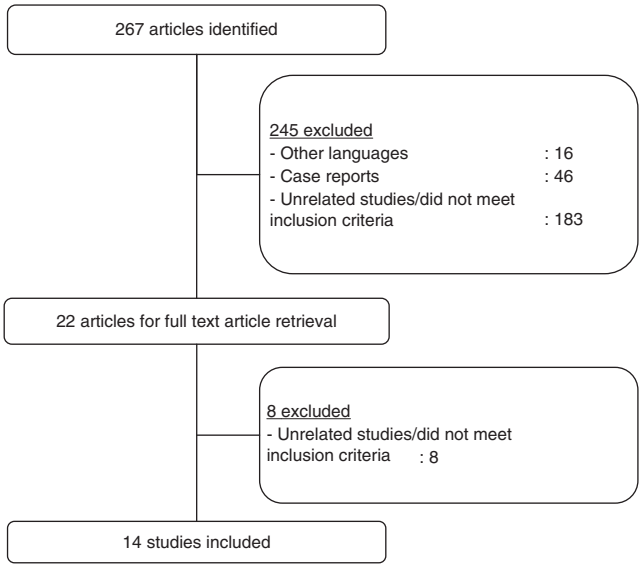

Fig. 1 – The algorithm for selection of studies in this systematic review.

The abstracts of the studies were scrutinized for appropriateness before retrieving the full text of the articles. We searched the bibliographies of all relevant published articles to avoid missing other relevant studies. Fig. 1 summarizes the algorithm used for selection of the studies. Ethics approval was not required for this systematic review as there was no recruitment of subjects or research intervention.

Selection criteria

Inclusion criteria

The search was further refined to achieve a high level of homogeneity across the selected studies. We applied a time restriction to studies published from year 1980 onwards. We included studies about RA which:

1. examined the median nerve characteristics (sonographic and/or electrophysiological),
2. were about CTS,
3. were published in English.

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Exclusion criteria

We excluded case reports and review articles. Studies on peripheral neuropathy which did not provide specific data on the median nerve were not considered either.

Data extraction

The following data were extracted from all studies included in this systematic review: study design, study population including the details of the control arm, sample size, prevalence of CTS in RA, median nerve characteristics in RA (sonographic and electrophysiological), the relationship between the median nerve characteristics and the clinical parameters. The relevant and especially significant statistical values (p and r values) were recorded.

Results

A total of 13 studies.[6,8–19] met the eligibility criteria. Majority of the studies (12/13) were cross-sectional, and there were 5 case-control studies.[9,10,12,13,18] The controls employed by the studies were either healthy individuals[9,10,13,18] or RA patients without symptoms of CTS.[9] Study sample sizes varied from 23[14] to 1070[16] subjects. Two of the studies[11,14] dealt with subclinical CTS i.e. conducted among subjects without signs and symptoms of CTS. Tables 1 and 2 highlight the findings of the selected studies.

Prevalence of CTS in RA

In most studies, the diagnosis of CTS was based on a combination of symptoms (paraesthesia, tingling sensation, pain at the median nerve innervated area), signs (positive Tinel's or Phalen test) and electrophysiological findings. The exact diagnostic criteria and definition of CTS used across the studies were quite diverse. Hammer et al.[12] defined CTS based on a palm-to-wrist median sensory nerve action potential (SNAP) onset latency of >2.0 ms or absence of SNAP and median distal motor latency of >4.9 ms whereas Sim et al.[18] defined CTS as a palm to wrist median nerve latency of less than 50%. The prevalence of CTS in RA ranged from 3.5%[16] to 22.8%.[17] Pooled data from 8 studies[6,8,9,13,15–17,19] with random selection of RA patients revealed that 86 out of 1561 (5.5%) subjects had CTS. Subclinical CTS, on the other hand, had a pooled prevalence of 14.0% (30/215) (Table 2).

Sonographic findings of the median nerve in RA

Cross-sectional area (CSA) of the median nerve was determined using ultrasound scan in 3 of the studies.[11–13] Two out of 3 of these studies[12,13] were of case–control design with healthy individuals as controls. Hammer et al.[11] investigated RA patients without signs and symptoms of CTS. The CSA of the bilateral median nerve of the RA patients without CTS were similar to the healthy controls. The mean (standard deviation) of the right median nerve in asymptomatic RA patients was 8.3 (1.5) mm^2 whereas for the left median nerve was 8.3 (1.4) mm^2.[11] The CSA of the median nerve in CTS patients were significantly higher with a median of 15.7 mm^2 (11.1–21.8).[12]

Electrophysiological findings of the median nerve in RA

Electrophysiological assessment of the median nerve was carried out in 10/13[6,8–10,12,14–16,18,19] of the studies. Details of the NCS in terms of the median nerve velocity, amplitude and latency were provided only by 2 studies i.e. Lanzillo et al.[10] and Calder et al.[15] The former study reported that the median nerve sensory conduction velocity was reduced by 25.2% along the distal nerve segment in 57.5% of RA patients compared to the general population. The amplitude of the sensory responses was significantly reduced at the wrist and elbow in 17.5% and 5% of patients, respectively. Distal latency to the abductor pollicis brevis muscle was significantly slower in 10% of the patients whereas the maximum velocity from the elbow to the wrist was prolonged by 12% in almost a quarter of the subjects. Calder et al.,[10] found that the median nerve SNAP amplitude was significantly lower in the RA and hand osteoarthritis groups compared to the healthy controls ($p < 0.05$) but there were no appreciable differences in the median nerve SNAP conduction velocity and latency between the RA patients and the healthy controls. It is noteworthy that this study had an extremely small sample size with only 8 RA patients.

Correlation between the median nerve characteristics and the clinical parameters

Across the studies, the most frequently assessed clinical parameter was disease duration (9/13 studies)[6,8,11,13–18] as compared to disease activity (4/13 studies).[6,8,9,13] Apart from the above mentioned, the following clinical and laboratory parameters were commonly analyzed by the selected studies; age, height, weight, medications, rheumatoid factor (RF), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Approximately half of these studies were designed to compare the patients' characteristics between RA patients with and without CTS[13,16] or with and without neuropathy.[6,8,17,18] The vast majority of the studies (8/13) disclosed no significant relationship between the median nerve involvement and clinical or laboratory parameters in RA. However, Karadag et al.[13] and Biswas et al.[6] revealed a significant association between disease duration and the occurrence of CTS ($p = 0.036$) and neuropathy ($p = 0.001$), respectively. Likewise, 2 studies found that age was significantly higher among RA patients with CTS[13] and peripheral neuropathy.[18]

Discussion

Rheumatoid arthritis (RA) is often cited in the literature as one of the common etiologies of CTS. This systematic review, however, highlights that the pooled prevalence of CTS in RA was 5.5% which did not differ significantly from the prevalence in the general population which ranged from 2.7 to 5.8%.[20,21] We could have underestimated the prevalence in this regard as a sizable proportion (1070/1561) of the subjects included in the pooled analysis were from a retrospective study.[16] Retrospective studies, in general, are notorious for underreporting due to missing or omitted data.[22,23] In parallel with the aforementioned finding, our pooled prevalence of subclinical CTS of

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Table 1 – Summary of the selected studies of CTS in RA.

Ref.	Test(s)	Study population	Prevalence of CTS in RA *n* (%)	Clinical and laboratory parameters	Findings
Lanzillo et al., 1998	NCS of peripheral nerves	40 RA patients	5 (12.5%)	Age, disease duration, steroid therapy, functional stage	The electrophysiologic findings were unrelated to clinical features of RA.
Sivri et al., 1999	NCS and somatosensorial evoked potential studies	33 RA patients and 20 healthy controls	2 (6%)		No correlation between neuropathy and the clinical variables.
Sakini et al., 2005	NCS, EMG	80 RA patients	8 (22.8%)	Disease duration	There was no association between disease duration and the occurrence of neuropathy.
Hammer et al., 2006	US of the median nerves at the entrance of the carpal tunnel, NCS, Tinel's and Phalen's tests.	7 RA patients with CTS symptoms 5 patients with other forms of arthritis with CTS symptoms Controls: 30 RA patients without symptoms of CTS & 30 healthy controls		Height, weight	CSA of the median nerves were significantly higher in the CTS patients compared with the RA controls and healthy persons; median (range) areas were 15.7 mm^2 (11.1–21.8), 8.5 mm^2 (5.8–11.0) and 8.0 mm^2 (4.9–12.0), respectively ($p < 0.0001$). No significant correlation between CSA of median nerve and clinical parameters in the RA group. Healthy controls had significant correlation between CSA of median nerve and height ($r = 0.6$, $p < 0.001$) and weight ($r = 0.43$, $p = 0.001$)
Agarwal et al., 2008	NCS of peripheral nerves	108 RA patients	11 (10.1%)	Absence of deep tendon jerks, extra-articular manifestations (interstitial lung disease, vasculitis, subcutaneous nodules), disease duration, RF, joint erosions, joint deformities, DMARDs or glucocorticoid intake, and disease activity, abdominal fat pad for amyloid	Absence of deep tendon jerks ($p < 0.005$) and vasculitis ($p < 0.01$) were conspicuous in the neuropathic group. There was no relationship between neuropathy and other parameters.
Aktekin et al., 2009	EMG and NCS of the peripheral nerves	56 RA patients 32 healthy controls	2 (4%)	Corticosteroid therapy, Schirmer's test, RF, disease activity	There was no correlation between electrophysiologic findings and the other study parameters.
Biswas et al., 2011	NCS of the peripheral nerves	74 RA patients	3 (10.3)	Age, disease duration, disease activity, RF, interstitial lung disease, subcutaneous nodules, vasculitis, corticosteroids, DMARDs and joint erosions	Disease duration and RF positivity was significantly higher in patients with neuropathy ($p = 0.001$ for both). No significant difference in other parameters between patients with and without neuropathy.

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Table 1 – (*Continued*)

Ref.	Test(s)	Study population	Prevalence of CTS in RA *n* (%)	Clinical and laboratory parameters	Findings
Calder et al., 2012	NCS of the peripheral nerves, sensory mapping (SM), vibratory and current perception thresholds (VPT and CPT) of the 2nd and 5th digits	7 women with RA 9 healthy women 11 women with hand OA			All SNAP amplitudes were significantly lower for the hand OA and hand RA groups compared with the healthy group ($p < 0.05$). No group differences were found for SNAP conduction velocities, SM, VPT, and CPT.
Karadag et al., 2012	Katz hand diagram, Boston CTS questionnaire, Phalen and Tinel tests. US of wrist joints and carpal tunnel gray scale and power Doppler. Patients with median nerve CSA between 10.0 and 13.0 mm^2 were evaluated with electromyography (EMG)	100 RA patients 45 healthy controls	18 (18%)	Age, gender, body mass index, disease duration, goiter, disease activity, HAQ-DI, ESR, CRP, CTS global assessment, CTS symptom duration, Boston symptom severity score, Boston functional status	In RA group with CTS: age (57 [36–73] vs. 50 [24–76], $p = 0.041$), history of DM (35.3% vs. 6.0%, $p < 0.001$), disease duration (108 [12–396] months vs. 72 [6–360] months, $p = 0.036$), HAQ-DI score (1.93 [0.75–2.87] vs. 1.13 [0–2.75], $p = 0.013$), CTS patient global score (52 [1–97] vs. 25 [0–91], $p = 0.001$), Boston symptom severity (2.81 [1.18–4.17] vs. 2.0 [1.0–4.01], $p = 0.01$) and functional status scores (3.37 [1.37–5.0] vs. 2.25 [1.0–5.0], $p = 0.008$) were elevated compared to patients without CTS.
Sim et al., 2014	NCS, Neuropathic Symptoms Scale (NSS)	30 RA patients with symptoms of peripheral neuropathy	7 (23.3%)	Age, anti-CCP, the type of medication, disease duration, functional status, neuropathic symptoms, ESR, CRP	The mean ages of the patients with and without peripheral neuropathy were 69.4 and 56.5 years, respectively ($p < 0.05$).
Lee et al., 2015	EMG, NCS, Phalen's and Tinel's tests	1070 RA patients	37 (3.5%)	CRP, disease duration	There was no statistically significant correlation between CTS occurrence and duration of RA and CRP levels.

EMG, electromyography; NCS, nerve conduction studies; RF, rheumatoid factor; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; CTS, carpal tunnel syndrome; RA, rheumatoid arthritis; HAQ-DI, Health Assessment Questionnaire – disability index; OA, osteoarthritis; DMARD, disease modifying antirheumatic drug.

14.0% was within the reported range in the general population of 7–16%.[24]

In healthy individuals, the mean CSA of the median nerve at the level of entrance into the carpal tunnel, which has the highest diagnostic sensitivity and specificity for CTS, has been found to be between $7.0 \pm 1.0\,mm^2$ and $10.2 \pm 2.5\,mm^2$.[25–27] The mean CSA of the median nerve in RA patients without signs and symptoms of CTS were similar to healthy controls. This lends credence to the notion that the chronic inflammatory processes in RA do not affect the size of the median nerve despite the close proximity between the median nerve and the wrist joint. However, Yagci et al.[28] had contradicting findings of RA patients having larger CSA of the median nerve despite absence of clinical and neurophysiological evidence of CTS.

No firm conclusions can be made on the electrophysiological changes of the median nerve in RA owing to the paucity of studies in this regard and the conflicting findings of the existing studies. Although Lanzillo et al.[15] revealed that more than half of RA patients without symptoms of CTS had reduced median nerve sensory conduction velocity along the distal nerve segment, this study failed to demonstrate any correlation between the clinical parameters of RA and the electrophysiological findings. Of note, this study had the drawback of not having a control arm and therefore, comparison was made with data from other published studies.

We found that there is no conclusive and convincing proof of association between the clinical or laboratory parameters in RA and the median nerve involvement. Although Karadag et al.,[13] disclosed that age, disease duration and functional

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Table 2 – Summary of the selected studies of subclinical CTS in RA.

Reference	Test(s)	Study population	Prevalence of subclinical CTS in RA *n* (%)	Clinical and laboratory parameters	Findings
Lang et al., 1981	NCS of 6 sensory nerves	23 RA patients	5 (21.7%)	Age, gender, disease duration, stage of disease, RF, ESR.	No significant correlation between neurophysiological/neurological findings and other study parameters.
Hammer et al., 2007	US of the median nerves at the entrance of the carpal tunnel	154 RA patients without signs and symptoms of CTS	10%	Height, weight, age, gender, disease duration, use of prednisolone.	The CSA of the median nerves ranged from 5.0 to 12.8 mm^2, with the 97.5 centile being 11.1 mm^2. The mean cross-sectional areas of the median nerve in patients with RA were similar to those reported in healthy controls. No significant association between CSA of median nerve and all studied parameters except for gender; males were significantly higher (8.8 ± 1.3 mm^2 versus females: 8.0 ± 1.4 mm^2 [*p*, 0.001]

NCS, nerve conduction studies; RF, rheumatoid factor; ESR, erythrocyte sedimentation rate; CTS, carpal tunnel syndrome; RA, rheumatoid arthritis.

scores were higher among the RA patients with CTS, the remaining studies were not in agreement with the above findings. However, numerous studies which investigated the extra-articular manifestations of RA, in general, identified the following factors as predictors in this regard: high disease activity, smoking, antinuclear antibodies and rheumatoid nodules.[29,30]

The studies included in this systematic review were not without their individual limitations. In particular, many had a small sample size, hence limiting the statistical power. Many of the studies did not fully control for confounding factors of CTS such as occupation, the presence of diabetes mellitus and hypothyroidism. Definition of CTS varied substantially across the studies. Misclassification as CTS, particularly among studies that diagnosed CTS solely based on symptoms, was another potential source of error.

In conclusion, the nexus between RA and the median nerve abnormalities or CTS has been overemphasized throughout the literature. Based on this systematic review, a substantial body of research suggests that the prevalence of CTS in RA is similar to the general population without any correlation between the median nerve findings and the clinical parameters of RA.

Conflicts of interest

The authors declare no conflicts of interest.

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REFERENCES

1. Turesson C, O'Fallon WM, Crowson CS, Gabriel SE, Matteson EL. Occurrence of extraarticular disease manifestations is associated with excess mortality in a community based cohort of patients with rheumatoid arthritis. J Rheumatol. 2002;29:62–7.
2. Shapiro JS. The wrist in rheumatoid arthritis. Hand Clin. 1996;12:477–98.
3. Amirfeyz R, Gozzard C, Leslie IJ. Hand elevation test for assessment of carpal tunnel syndrome. J Hand Surg Br. 2005;30:361–4.
4. Golding DN. Rheumatoid neuropathy. Br Med J. 1971;2:169.
5. Bland JD. Carpal tunnel syndrome. Curr Opin Neurol. 2005;18:581–5.
6. Biswas M, Chatterjee A, Ghosh SK, Dasgupta S, Ghosh K, Ganguly PK. Prevalence, types, clinical associations, and determinants of peripheral neuropathy in rheumatoid patients. Ann Indian Acad Neur. 2011;14:194–7.
7. Hart FD, Golding JR, Mackenzie DH. Neuropathy in rheumatoid disease. Ann Rheum Dis. 1957;16:471–80.
8. Agarwal V, Singh R, Wiclaf Chauhan S, Tahlan A, Ahuja CK, Goel D, et al. A clinical, electrophysiological, and pathological study of neuropathy in rheumatoid arthritis. Clin Rheumatol. 2008;27:841–4.
9. Aktekin LA, Gozlukaya H, Bodur H, Borman P, Koz O. Peripheral neuropathy in rheumatoid arthritis patients: an electroneurophysiological study. Turk J Rheumatol. 2009;24:62–6.
10. Calder KM, Martin A, Lydiate J, MacDermid JC, Galea V, MacIntyre NJ. Sensory nerve action potentials and sensory perception in women with arthritis of the hand. J Neuroeng Rehabil. 2012;9:27.
11. Hammer HB, Haavardsholm EA, Kvien TK. Ultrasonographic measurement of the median nerve in patients with rheumatoid arthritis without symptoms or signs of carpal tunnel syndrome. Ann Rheum Dis. 2007;66:825–7.
12. Hammer HB, Hovden IA, Haavardsholm EA, Kvien TK. Ultrasonography shows increased cross-sectional area of the

Please cite this article in press as: Sakthiswary R, Singh R. Has the median nerve involvement in rheumatoid arthritis been overemphasized? Rev Bras Reumatol. 2016. http://dx.doi.org/10.1016/j.rbre.2016.09.001

median nerve in patients with arthritis and carpal tunnel syndrome. Rheumatology (Oxford). 2006;45:584–8.
13. Karadag O, Kalyoncu U, Akdogan A, Karadag YS, Bilgen SA, Ozbakir S, et al. Sonographic assessment of carpal tunnel syndrome in rheumatoid arthritis: prevalence and correlation with disease activity. Rheumatol Int. 2012;32:2313–9.
14. Lang AH, Kalliomaki JL, Puusa A, Halonen JP. Sensory neuropathy in rheumatoid arthritis: an electroneurographic study. Scand J Rheumatol. 1981;10:81–4.
15. Lanzillo B, Pappone N, Crisci C, di Girolamo C, Massini R, Caruso G. Subclinical peripheral nerve involvement in patients with rheumatoid arthritis. Arthritis Rheum. 1998;41:1196–202.
16. Lee KH, Lee CH, Lee BG, Park JS, Choi WS. The incidence of carpal tunnel syndrome in patients with rheumatoid arthritis. Int J Rheum Dis. 2015;18:52–7.
17. Sakini RA, Abdul-Zehra IK, Al-Nimer MS. Neuropathic manifestations in rheumatoid arthritis: a clinical and electrophysiological assessment in a small sample of Iraqi patients. Ann Saudi Med. 2005;25:247–9.
18. Sim MK, Kim DY, Yoon J, Park DH, Kim YG. Assessment of peripheral neuropathy in patients with rheumatoid arthritis who complain of neurologic symptoms. Ann Rehabil Med. 2014;38:249–55.
19. Sivri A, Guler-Uysal F. The electroneurophysiological findings in rheumatoid arthritis patients. Electromyogr Clin Neurophysiol. 1999;39:387–91.
20. Atroshi I, Gummesson C, Johnsson R, Ornstein E, Ranstam J, Rosen I. Prevalence of carpal tunnel syndrome in a general population. JAMA. 1999;282:153–8.
21. de Krom MC, Knipschild PG, Kester AD, Thijs CT, Boekkooi PF, Spaans F. Carpal tunnel syndrome: prevalence in the general population. J Clin Epidemiol. 1992;45:373–6.
22. Dale AM, Harris-Adamson C, Rempel D, Gerr F, Hegmann K, Silverstein B, et al. Prevalence and incidence of carpal tunnel syndrome in US working populations: pooled analysis of six prospective studies. Scand J Work Environ Health. 2013;39:495–505.
23. Gell N, Werner RA, Franzblau A, Ulin SS, Armstrong TJ. A longitudinal study of industrial and clerical workers: incidence of carpal tunnel syndrome and assessment of risk factors. J Occup Rehabil. 2005;15:47–55.
24. Ferry S, Pritchard T, Keenan J, Croft P, Silman AJ. Estimating the prevalence of delayed median nerve conduction in the general population. Br J Rheumatol. 1998;37:630–5.
25. Duncan I, Sullivan P, Lomas F. Sonography in the diagnosis of carpal tunnel syndrome. Am J Roentgenol. 1999;173:681–4.
26. Wong SM, Griffith JF, Hui AC, Lo SK, Fu M, Wong KS. Carpal tunnel syndrome: diagnostic usefulness of sonography. Radiology. 2004;232:93–9.
27. Wong SM, Griffith JF, Hui AC, Tang A, Wong KS. Discriminatory sonographic criteria for the diagnosis of carpal tunnel syndrome. Arthritis Rheum. 2002;46:1914–21.
28. Yagci I, Akdeniz Leblebicier M, Mansiz Kaplan B, Ozturk Gokbakan D, Akyuz G. Sonographic measurements can be misleading for diagnosing carpal tunnel syndrome in patients with rheumatoid arthritis. Acta Reumatol Port. 2016;41:40–4.
29. Nyhall-Wahlin BM, Petersson IF, Nilsson JA, Jacobsson LT, Turesson C. High disease activity disability burden and smoking predict severe extra-articular manifestations in early rheumatoid arthritis. Rheumatology (Oxford). 2009;48:416–20.
30. Turesson C, Jacobsson L, Bergstrom U, Truedsson L, Sturfelt G. Predictors of extra-articular manifestations in rheumatoid arthritis. Scand J Rheumatol. 2000;29:358–64.

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