

Determinants of Remission in Medically Treated Carpal Tunnel Syndrome: Study from Central India

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Abstract

Background: The factors associated with the spontaneous remission (SR) of symptoms in carpal tunnel syndrome (CTS) are not well known. **Objectives:** To look for determinants of SR in medically treated, electrophysiologically proven patients of CTS. **Methods:** We revisited the medical records and nerve conduction study data of 130 hands with CTS and divided them into two groups as per the absence or persistence of the symptoms when contacted after a median time lapse of 3 years following the diagnosis. **Results:** SR occurred in 46.1% of the hands. Higher odds of SR were linked with female gender, symptoms restriction to lateral fingers, symptom duration <10 months, mildly delayed median motor and sensory distal latencies, and median sensory amplitude >20 μ V. We developed a seven-point scale, on which a score of ≥ 4 had a strong association (odds ratio 4.31) with SR. **Discussion and Conclusion:** No single risk factor, standalone, can predict SR in patients with CTS, which could lead to an invasive treatment (Surgery or local injection) to them. We propose that patients scoring ≥ 4 on our 7 point scale should be treated medically for the initial 10 months after the symptom onset.

Keywords: Carpal tunnel syndrome, grading scale, nerve conduction, prognostic factors, outcome

INTRODUCTION

Carpal tunnel syndrome (CTS) is a common neurological disease with the prevalence of 2.7%–5.8% in general population.^[1,2] It is reported to be the most common entrapment neuropathy seen in a hospital setting.^[3] The disease is thought to be progressive in nature,^[4] more rapid progressions been linked with advancing age,^[5] neurophysiological severity,^[6] hypothyroidism, male sex,^[5] and diabetes.^[7] Accordingly, the surgical release of the median nerve compression at wrist has emerged as the definitive therapy with some suggesting operating on within 2 weeks of the symptom onset (Grade B, Level I and II)^[8,9] Contrasting with the above is the recommendation of delaying the surgery for 6–9 months based on the findings of couple of epidemiological studies^[10-12] highlighting spontaneous regression of the symptoms in up to 47% of the patients.

Furthermore, scrutiny of the published data reveals that 23%–60% of the patients undergoing surgical intervention develop adverse effects such as a painful scar and pillar pain.^[13,14] Thus, the dilemma of the risks of overtreatment and the fear of disability with undertreatment hovers on the primary

care physician treating a patient of CTS. For addressing this dilemma attempts have been made to identify the patients destined for spontaneous remission (SR).^[11,12,15] Normal or mildly abnormal nerve conduction study (NCS),^[16] young age, and shorter duration of the symptoms are linked with higher chances of SR.^[12] However, review of data reported by Mühlau *et al.* show that only 5 out of 16 (31%) medically treated young patients have a natural cure.^[11] Another study has reported SR of symptoms in 8 out of 20 (40%) patients with mild NCS abnormality while remaining 12 worsened.^[17] The same study found the mean age of the spontaneously remitting patients to be higher than those who worsened (61 vs. 50 years). This suggests that in a given patient, it is hard to ascertain the chances of SR-based on any single parameter.

We, therefore, sought to identify, retrospectively, the demographic, clinical, and/or NCS parameters, single or a

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combination thereof, associated with SR of the symptoms, in the cohort of the patients diagnosed at our laboratory and treated medically by their individual treating physician. The outcome measure was remission of symptom at or before 10 months of diagnosis of CTS.^[10-12] We hypothesized that patients with low risk for developing CTS would have higher odds of SR.

MATERIALS AND METHODS

This study was conducted at the Neurology Department of SAIMS Medical College and Postgraduate Institute, Indore. In our laboratory, the hands are evaluated for CTS using standard techniques^[18] with Nicolet Viking IV (version 12). The skin temperature of the body part, under evaluation, is measured using a probe connected to the machine and is maintained at 31°C using a commercial hot air blower. The median motor conduction is performed with surface disk electrodes applied over abductor pollicis brevis, and motor distal latency (MDL) is measured over a distance of 8 cm. The baseline to the negative amplitude of the compound muscle action potential (MMA) is measured. The median sensory nerve is examined antidromically using ring electrodes applied to the middle finger. The onset latency of median sensory nerve action potential (SDL) is measured at 14 cm, and the amplitude of the sensory nerve action potential (MSA) is measured from baseline to the negative peak. The latency difference over 14 cm between antidromically obtained median/ulnar sensory action potentials (SNAP) is studied over ring finger.

In our laboratory, based on our normative data, MDL of more than ≥ 4.2 ms, SDL of more than ≥ 3.4 ms and MSA of $< 20 \mu V$ is taken as abnormal. The median and ulnar SNAP latency difference over ring finger (at 14 cm) of more than 0.5 ms is considered abnormal. We apply Bland's criteria for the grading of severity of the CTS,^[19] which stratifies the syndrome into mild, moderate, severe, and very severe based on the values of MDL and normal or abnormal SNAP.

The Boston Carpal Tunnel Questionnaire (BCTQ),^[20] that looks at the symptoms and functional deficits, has become standard for the evaluation of the treatment outcome. According to BCTQ, complete disappearance of the symptom without any functional deficit correlates with the best result. The outcome (remission or nonremission) was determined telephonically, for which we designed a questionnaire, in Hindi, modified from BCTQ so as to include the course of the disease and treatment details.

Study population

Two hundred and ten patients were referred to our laboratory for the evaluation of the suspected CTS between January 2010 and December 2014. The medical records and the raw data of the NCS findings of these patients were reviewed. Body mass index (BMI), at the time of the first contact, was calculated according to the previously described method.^[21] The gender, age in years (y), and duration of the symptoms at the time of referral for to our laboratory in months (mo.) was noted.

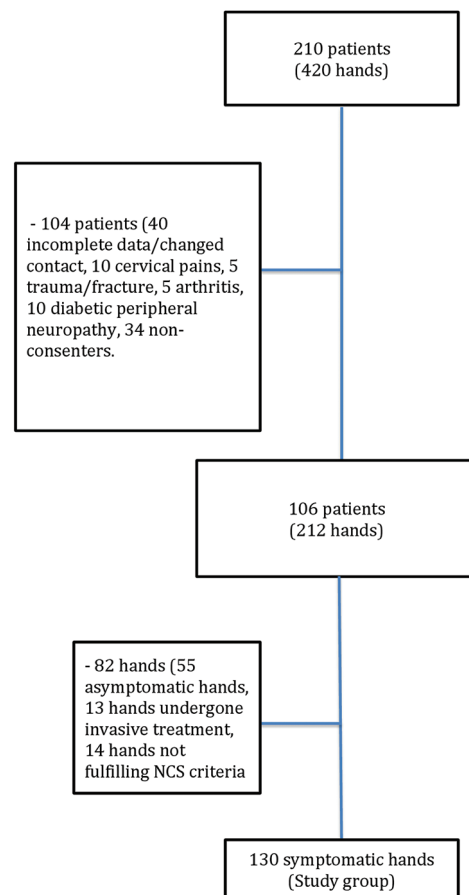


Figure 1: Patients excluded from the study

Attempts were made to reach them through the telephone between June 2016 and January 2017 by one of the authors (RD). After explaining the purpose of the call, telephonic consent was sought. They were requested to respond to the standard questionnaire and the information about the course of the symptoms; current functional status and treatment details were obtained and recorded in the study pro forma.

Those satisfying following criteria were included for further analysis.

Inclusion criteria

One hundred and thirty symptomatic hands from 106 patients fulfilled the following study inclusion criteria:

- The presence of sensory symptoms in hand/s, persisting for ≥ 4 weeks before the NCS evaluation. The symptoms were required to involve one or more of lateral three fingers and also either nocturnal appearance or precipitation/aggravation by any maneuvers leading to median nerve compression at wrist; plus
- One of the above mentioned NCS abnormalities.

Exclusion criteria

Patients ($n = 104$) with following conditions were excluded (a) history suggestive of cervical radiculopathies, (b) trauma to the symptomatic limb, (c) diabetes with symptoms or NCS findings

suggestive of peripheral neuropathy, (d) received invasive treatment (local steroid injections or surgery), (e) history of arthritis, (f) Not be contacted (e) symptomatic hands with normal NCS findings, and (f) refusal to participate in the study [Figure 1].

Definitions:

- SR - Complete disappearance of symptoms without any functional deficit. The symptoms must remit on medical management, and the remission should last for ≥ 6 months^[15]
- Nonremission - Symptoms in the previous 6 months from the date of the telephonic contact or recurring intermittently with intervening period of lesser than 6 months and/or those with functional deficits (with or without symptoms)
- Asymptomatic - Never had symptoms
- Medical management - Nonsteroidal anti-inflammatory medication, local splints, physiotherapy, and vitamins
- Concomitant medical conditions: Presence of diabetes and/or hypothyroidism.

Data management

The study population was grouped according to treatment outcome (remitters vs. nonremitters). The groups were conceived such that patients with known high risk for CTS separate out from the rest.^[16,21-23] Thus, the demographic data were grouped according to gender, age (below vs. above 45 years), BMI (below or above 24), presence or absence of concomitant medical conditions, namely, diabetes and/or hypothyroidism. Symptoms were grouped as per their duration (below or above 10 months) and distribution-lateral (restricted to the lateral three finger) or beyond (symptoms in the hand or forearm in addition to one or more of the lateral three fingers). The median NCS parameters were divided according to MDL (≤ 5.9 vs. > 5.9 ms), MMA (≥ 6.1 vs. ≤ 6 mV), MSA (≥ 20 vs. < 20 μ V), SDL (≥ 3.4 vs. < 3.4 ms). Hands with the Bland score of 1–3 and 4–6 were divided into two separate groups. As the hands with normal NCS findings were not included in the study, none of our patients fell into Bland grade zero.

Statistical analysis

The statistical analysis was done using free online software^[24,25] and Microsoft Excel 2010.^[26]

The categorical variables were presented as a percentile. Deploying “N-1” Chi-squared test we compared the means.

The relationship between the variables and the outcome (remission and nonremission) odds ratio (OR) was calculated at 95% confidence interval (CI) by drawing a 2×2 contingency table. As and when necessary, the significance level was evaluated further with two-tailed Fisher’s exact test. The significance level was set at $OR = > 1$ and $P \leq 0.05$.

The Institutional Scientific and Research Committee approved the study and a telephonic consent was taken from all the responders.

RESULTS

The summary of the results is provided in Table 1.

The median time elapsed between the diagnosis and telephonic contact was 3 years (maximum-6 years, minimum-1 years). At this time, spontaneous remission was reported in 46.1% (60 of 130 hands), the difference between the frequency of remitters and nonremitters was not significant (proportion of mean, $P = 0.2$).

Patient-related variables and the outcome

The mean age of the study population was 46.4 years (minimum 24 and maximum 75 years), of remitters was 46.2 years, and that of nonremitters was 46.5 years. We had almost equal number of patients in the two age groups of below and above 45 years (66 vs. 64; $P = 0.8$). The number of symptomatic hands was more in females (73 vs. 27%) and persons with high BMI (61.5 vs. 38.5); 27.7% of the hands belonged to the persons having concomitant medical issues. No higher odds were found between spontaneous remission and younger age (OR 0.8), lower BMI (OR 0.99), or absence of concomitant medical conditions (OR 0.94). Female gender showed slightly higher odds (OR 1.2, CI 0.5–2.6, two-tailed $P = 0.5$) for remission on medical therapy.

The pattern of the distribution of the symptoms showed weak odds with SR, those with symptoms restricted to the lateral three finger showed higher rates of spontaneous remission (49 vs. 44%, OR 1.22, CI 0.6–2.4, two-tailed $P = 0.6$).

The median duration of symptoms of our study population was 12 months (mean 24.16 ± 28.93 months). We had forty patients having CTS in bilateral hands ($n = 80$ hands), whereas fifty patients had unilateral hand symptoms ($n = 50$ hands). Forty-one (31.5%) hands were symptomatic for 10 months or less (median 6 months) while remaining 89 hands were symptomatic for longer than 10 months (median 24 months). Shorter duration of the symptoms, at presentation, had significant higher odds of spontaneous remission (OR 9.47 CI 3.8–23.1, two-tailed $P = < 0.0001$).

Nerve conduction study-related variables and the outcome

The sensory conduction parameters showed higher odds with SR than those of motor conduction.

The values of MMA failed to show any correlation with the outcome, while MDL of ≤ 5.9 ms showed higher odds for SR (OR 1.85, CI 0.9–3.7) but did not show statistical significance on two-tailed Fishers’ Exact test ($P = 0.11$).

Odds for SR were found to be high for the hands with shorter SDL (≤ 3.4 ms) and higher MSA (> 20 μ V). Between them, the odds of the SDL (OR 2.53, CI 1.1–5.6) showed greater significance on two-tailed Fishers’ exact test ($P = 0.02$).

Eighty-three hands (63.8%) of our study had mild-to-moderately severe CTS according to the Bland’s grading system and had significant odds of a better outcome (OR 2.5 CI 1.1–5.3, two-tailed $P = 0.01$).

On closer scrutiny of our results, we noticed that for computing the odds of remission, for a given patient, neither

Table 1: The clinical and electrophysiological characteristics of the study population

Variables	Total, n (%)	Remission n (%)	No remission n (%)	Statistical analysis	
				OR (95% CI)	P
Total hands	130	60 (46.1)	70 (53.9)		
Patient related variables					
Age in years					
≤45	66 (50.7)	29 (43.9)	37 (56.1)	0.83 (0.4-1.66)	
>45	64 (49.3)	31 (48.4)	33 (51.6)		
Gender				1.20 (0.5-2.62)	
Female	95 (73)	45 (47.3)	50 (52.6)		
Male	35 (27)	15 (42.8)	20 (57.2)		
BMI				0.99 (0.48-2.01)	
≤24	50 (38.5)	23 (46)	27 (54)		
>24	80 (61.5)	37 (46.2)	43 (53.8)		
Concomitant medical condition				0.94 (0.43-2.03)	
Without	94 (72.3)	43 (45.7)	51 (54.3)		
With	36 (27.7)	17 (47.2)	19 (52.8)		
Symptoms					
Duration of symptoms (months)				9.47 (3.8-23.1)	<0.0001 (S)
≤10	41 (31.5)	33 (80.4)	8 (19.6)		
>10	89 (68.5)	27 (30.3)	62 (69.7)		
Pattern of distribution					
Lateral three fingers	55 (42.3)	27 (49)	28 (51)	1.22 (0.6-2.4)	
Beyond	75 (57.7)	33 (44)	42 (56)		
NCS related variables					
Median MDL (ms)				1.85 (0.9-3.7)	
≤5.9	74 (56.9)	39 (52.7)	35 (47.2)		
>5.9	56 (43.1)	21 (37.5)	35 (62.5)		
MMA (mV)				0.62 (0.2-1.5)	
>6.1	104 (80)	46 (44.2)	58 (55.8)		
≤6	25 (20)	14 (56)	11 (44)		
MSA (μV)				1.63 (0.7-3.5)	
≥20	35 (26.9)	19 (54.2)	16 (45.8)		
<20	95 (73.1)	40 (42.1)	55 (57.9)		
SDL (ms)				2.53 (1.14-5.6)	0.02 (S)
≤3.4	95 (73.1)	38 (40)	57 (60)		
>3.4	35 (26.9)	22 (62.8)	13 (37.2)		
Neurophysiological grading (Bland)				2.52 (1.19-5.3)	0.015 (S)
Grade 1-3	83 (63.8)	45 (54.2)	38 (45.8)		
Grade 4-6	47 (36.1)	15 (31.9)	32 (68.1)		
Our score					
Score out of 7 point scoring system				4.31 (2-9.03)	0.0001 (S)
4-7	58 (44.7)	38 (65.5)	20 (34.5)		
0-3	72 (55.3)	22 (30.5)	50 (69.5)		

S = Statistically significant, MDL = Motor distal latency, OR = Odds Ratio, SDL = Sensory distal latency, CI = Confidence interval, MMA = Median motor amplitude, n = Number in each group, MSA = Median sensory amplitude, BMI = Body mass index, NCS = Nerve conduction study

a patient-related nor any of the NCS-associated parameter can be applied in isolation. For example, 19.6% of hands with short duration of symptoms failed to remit, whereas 30.3% of those with symptoms longer than 10 months remitted spontaneously. Similarly, almost 46% of the hands with Bland score 1–3 did not remit spontaneously. This is further highlighted by the results of the regression analysis [Table 2], in which only the duration of the symptom appeared to be associated with the higher odds of remission.

We, therefore, attempted to develop a seven-point scale taking into the consideration all those seven variables (gender, distribution of the symptoms, symptom duration, MDL, SDL, MSA, and Bland's severity grade), which showed positive statistical odds (OR >1) with SR. One point was assigned for the presence of each of the following factors-female gender, symptoms restricted to the lateral three fingers, symptoms duration of <10 months, MDL ≤5.9 ms, SDL ≤3.4 ms, MSA >20 μV, and Bland grade 1–3. Value other than the above, for any of the parameter, was scored zero. The scheme

Table 2: Binary logistic regression of remission versus variables

Variables	OR	95% CI	χ^2	P
Age	1.00	0.90-1.08	0.03	0.85
Gender	0.47	0.13-1.69	1.33	0.25
BMI	0.99	0.90-1.08	0.01	0.90
Concomitant medical condition	2.09	0.5-7.7	1.27	0.26
Duration of symptoms	0.84	0.78-0.91	51.16	0.0001
Pattern of distribution	0.80	0.2-3.14	0.09	0.75
MDL	1.01	0.60-1.71	0.00	0.95
MMA	0.94	0.78-1.12	0.44	0.50
MSA	1.00	0.95-1.06	0.11	0.73
SDL	0.85	0.47-1.54	0.28	0.59
Neurophysiological grading (bland)	1.01	0.42-2.46	0.00	0.96

OR = Odds ratio, CI = Confidence interval, BMI = Body mass index, MDL = Motor distal latency, MMA = Median motor amplitude, MSA = Median sensory amplitude, SDL = Sensory distal latency

of scoring was based on Kaplan's scoring method^[15] and was modified by us. The net score was summed up which ranged between 0 and 7, that is, higher the number of positive predictors higher the scores. The score was calculated for each hand, and they have been regrouped accordingly into those with score 0–3 ($n = 72$) and 4–7 ($n = 58$). The group with the score of ≥ 4 showed higher odds of spontaneous remission (OR 4.3 CI 2–9, two-tailed $P < 0.0001$). The trend, according to this score, suggests that there exists a cutoff at the score of 3 so that those with scores higher than this experience remission in a higher percentage [Figure 2].

DISCUSSION

Our study looks into several clinical and electrophysiological variables and their ability to predict spontaneous remission in the medically treated hands of the patients with CTS.

As reported previously,^[21,23] we too found a preponderance of hands belonging to female gender (73% vs. 27%) and the persons with high BMI (61.5% vs. 38.5%). Previous work reports that female sex,^[27] male sex,^[5] overweight,^[27] the age beyond 50 years,^[5,15] and presence of concomitant illness respond poorly^[27] to conservative therapy. In our study, 46.1% of the hands with CTS achieved spontaneous symptoms remission on the medical treatment. These findings are in line with that of DeStefano *et al.*, who report improvement on conservative treatment in 52% of their patients.^[27] Attempts to identify prognostic factors associated with a good outcome of medically treated patients have been made previously. A multiperspective study found young age to be associated with spontaneous remissions.^[12] Kaplan *et al.*^[15] studied the predictive factors for outcome of CTS and found age beyond 50 years to be linked with the poor outcome if treated conservatively. However, a meta-analysis of the published work has found conflicting evidence for association of age and CTS.^[9] We did not find any correlation between age, BMI, concomitant medical condition with the outcome.

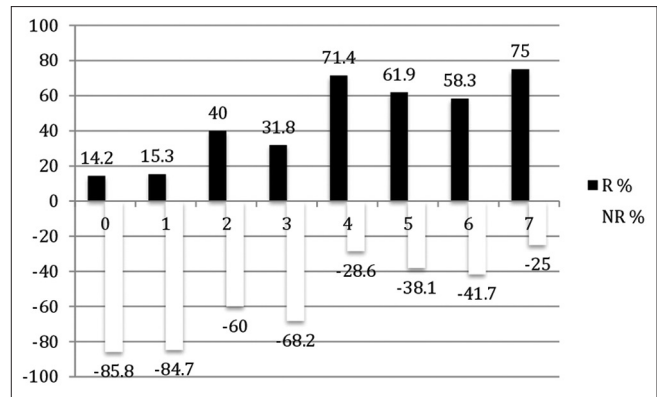


Figure 2: Outcome scale for predicting spontaneous remission. R: Remission, NR: No remission, NR is arbitrarily marked negative for graphical presentation. Remission percentages are marked above the baseline; No remission percentages are marked below the baseline. 7 scale scoring with one point for presence of each of the below-Female gender. Symptom restricted to lateral three fingers. Symptom duration < 10 months, MDL ≤ 5.9 ms, SDL ≤ 3.4 ms, MSA > 20 μ V, Bland grade 1 to 3

Our results indicate that female gender, duration of < 10 months, MDL < 5.9 ms, MSA > 20 μ V, SDL of < 3.4 ms, symptoms restricted to lateral three fingers, and Bland's grade 1–3 are associated with higher odds of spontaneous remission. The correlation of younger age with spontaneous remission has been reported previously.^[12] The association of short duration of symptoms with better outcome had been found by earlier workers.^[11,12,15] Association of better outcome and shorter duration is not surprising in the light of the fact that a recent study has found significant thickening and neovascularization in the patients of CTS if the duration of the symptoms is more than 7 months.^[28,29] There are conflicting reports about the correlation of severity of the NCS findings with clinical symptomatology and the outcome. Mühlau *et al.*^[11] studied 157 patients with CTS and found no correlation of severity of the MDL with the prognosis. In contrast, Bland^[19] and Padua *et al.*^[16] have found NCS to be of prognostic value such that more the severity worst being the outcome.

However, it is interesting to note that none of these factors, in its own right, is a robust predictor of a better outcome. A glance at the Table 1 will reveal that almost 52% of female, 60% of those with short SDL, 45% of mild-to-moderate CTS (Bland's grade 1–3), 51% of those with restricted symptoms, and 19% with symptoms duration of lesser than 10 months actually fail to remit spontaneously.

We, therefore, tried to examine the association of combination of the good predictors with odds of spontaneous remission. According to this seven-point scale, each hand was regrouped into those with score 0–3 ($n = 72$) and 4–7 ($n = 58$). The scale thus obtained [Figure 2] shows a significant correlation of high score with a better outcome on medical management such that 65.5% (38 out of 58 hands) of those with score ≥ 4 showing spontaneous remission of the symptoms.

CONCLUSION

It seems reasonable to treat participants of CTS, conservatively for first 10 months after symptom onset, more so when they have four or more out of the seven favorable factors. Based on our data, it would be reasonable to suggest to apply our score (good outcome predictor score) before deciding on the invasive intervention for CTS and also to consider conservative management if the score is ≥ 4 .

Our study has limitations of being retrospective in nature and having a small sample size. The proposed seven-point scale for calculating chances of spontaneous remission need to be validated in a prospective study with effective blinding.

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Conflicts of interest

There are no conflicts of interest.

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