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Research paper

Median nerve ultrasound cross sectional area and wrist-to-forearm ratio in relation to carpal tunnel syndrome related axonal damage and patient age

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ABSTRACT

Objective: Primary objective was to retrospectively examine the effects of patient age and carpal tunnel syndrome (CTS) related axon loss on median nerve (MN) high resolution ultrasound (HRUS) in younger and older patients. HRUS parameters evaluated in this study were MN cross sectional area at the wrist (CSA) and wrist-to-forearm ratio (WFR).
Methods: The material comprised 467 wrists of 329 patients. The patients were categorized into younger (<65 years) and older (≥65 years) groups. Patients with moderate to extreme CTS were included in the study. Axon loss of the MN was assessed by needle EMG and graded by the interference pattern (IP) density. The association between axon loss and CSA and WFR was studied.
Results: The older patients had smaller mean CSA and WFR values compared to the younger patients. CSA correlated positively to the CTS severity only in the younger group. However, WFR correlated positively to CTS severity in both groups. In both age groups, CSA and WFR correlated positively with IP reduction.
Conclusions: Our study complemented recent findings on the effects of patient age on the CSA of the MN. However, although the MN CSA did not correlate with the CTS severity in older patients, the CSA increased in respect to the amount of axon loss. Also, as a new result, we presented the positive association of WFR with CTS severity among older patients.
Significance: Our study supports the recently speculated need for different MN CSA and WFR cut-off values for younger and older patients in assessing the severity of CTS. With older patients, WFR may be a more reliable parameter to assess the CTS severity than the CSA. CTS related axonal damage of the MN is associated to additional nerve enlargement at the carpal tunnel intel site.

1. Introduction

Carpal tunnel syndrome (CTS) is the most common peripheral nerve entrapment neuropathy (Sadosky et al., 2008). In addition to clinical evaluation, electrodiagnostic studies (EDX) has for many decades been the gold standard method for assessing the diagnosis and severity of CTS (Werner and Andary, 2011). Lately, however, the capability of high-resolution ultrasound (HRUS) to diagnose and grade CTS has been the subject of intensive research. Different HRUS-based methods, such as measuring the cross sectional area (CSA) of the median nerve (MN) at the wrist and calculating the wrist-to-forearm ratio (WFR), have been introduced (Hobson-Webb et al., 2008; Visser et al., 2008; Yoshii et al., 2020). Many previously published studies agree that CSA has good sensitivity and specificity in diagnosing CTS; however, there have been contradictory results regarding its reliability in grading the severity of CTS (Chen et al., 2016; El Habashy et al., 2017; El Miedany et al., 2004; Elnady et al., 2019; Martikkala et al., 2021a; Mhoon et al., 2012).

Recently, the effect of patient age on the reliability of HRUS in diagnosing and grading CTS has been studied and discussed. It seems that CSA measurement of the MN is more reliable for diagnosing and grading CTS in younger patients than it is in older patients (Gregoris and Bland, 2019; Miwa and Miwa, 2011; Moschovos et al., 2019; Mulroy and Pelosi, 2019). However, in a study by Roghani and coworkers, CSA also showed excellent diagnostic accuracy among patients 60 years and older (Roghani et al.,

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2018). In their large-scale study, Gregoris and Bland estimated CSA would no longer be reliable in assessing CTS or its severity in patients 63 years and older. Gregoris and Bland also speculated that CTS in older patients could be a totally different disease entity with a different pathogenesis compared to CTS in younger patients. (Gregoris and Bland, 2019) However, the specific pathophysiological mechanisms have not yet been comprehensively reported.

The possible effect of axon loss on CSA changes in CTS has also been speculated. Bayrak and coworkers used the motor unit number estimation (MUNE) method to determine axon loss in the MN and found a negative correlation between the MUNE and CSA (Bayrak et al., 2007). In addition, nerve conduction studies (NCS) have also been used to assess axon loss in CTS (Deng et al., 2018; Moon et al., 2017). In these studies, HRUS has been shown to discern axonal degeneration from simple demyelination in CTS by means of increased CSA.

We are unaware of previous studies that have evaluated the association between CSA and WFR and axon loss in CTS using needle EMG, which is considered to be the key method to assess denervation (Kimura, 1984). In the present study we evaluate potential relation between axon loss based on needle EMG and sonographic nerve size in CTS across different age groups.

2. Material and methods

The material for this retrospective study was gathered from the medical records of patients who were referred to our laboratory due to a suspicion of CTS between January 2017 and December 2019.

2.1. Patient selection

Patients were referred to EDX because of clinically suspected CTS. Data of the wrists with NCS based moderate to extreme CTS were included in the study. Exclusion criteria were previously operated MN entrapment, EMG findings in the current EDX indicating radiculopathy in nerve roots C7 to Th1, signs of polyneuropathy or findings indicating a more proximal MN lesion than the wrist. In addition, wrists that showed a bifid MN in HRUS were not included in the study. Moreover, only wrists with moderate to extreme CTS were included, as axon loss is uncommon in mild CTS (Stevens, 1997; Werner and Andary, 2011).

Patients were categorized into a younger group (<65 years) and an older group (≥65 years). We decided on the cutoff point according to the previous literature (Gregoris and Bland, 2019; Moschovos et al., 2019).

2.2. Electrodiagnostic studies

The routine EDX of the upper limb performed on all patients consisted of both NCS and needle EMG. EDX measurements were conducted by an experienced clinical neurophysiologist or experienced clinical neurophysiology resident. Prior to EDX, the hand was warmed to ensure the correct nerve conduction velocities. The CTS was diagnosed by an MN sensory nerve action potential (SNAP) conduction velocity of more than 10 m/s slower than the ulnar. If the MN SNAPs were absent, a prolonged MN distal motor latency, in addition to absence of signs in EDX indicating a more proximal lesion, was interpreted to indicate CTS (Padua et al., 1997). The devices used were the Cadwell Sierra Summit Electrodiagnostic Solution (Cadwell Industries Inc., Kennewick, WA, USA) and the Dantec Keypoint EMG Workstation (Natus Medical Inc., San Carlos, CA, USA). Sensory NCS were performed antidromically in the median (wrist to digits 2, 3, and 4), radial, and ulnar nerves. Motor NCS were performed in the median (registered from the abductor pollicis brevis (APB) muscle) and ulnar nerves. Distances between stimulating and recording electrodes were standardized at 8 cm in the motor NCS. Needles used in EMG were Ambu Neuroline Concentric 30 × 0.35 mm (1.2″ x 28 G) and 38 × 0.45 mm (1.5″ x 26 G). Needle EMG was performed in several upper limb muscles from the myotomes C5 to T1, including APB, in order to exclude C8/Th1 nerve root lesion or more proximal median nerve lesion than CTS.

Based on the NCS findings, the wrists were assigned to three CTS classes according to severity (moderate, severe, and extreme CTS). The classification was based on the study by Padua et al. (1997) and the internal reference values of our laboratory. In moderate CTS, the MN sensory velocity was ≥ 10 m/s slower than the ulnar, and MN distal motor latency was ≥ 4.2 ms. In severe CTS, the sensory responses were absent, and the MN distal motor latency was ≥ 4.2 ms. In extreme CTS, both sensory and motor responses were absent. (Padua et al., 1997).

In needle EMG of the APB, spontaneous activity, morphology of the motor unit potentials (MUPs), and recruitment of the MUPs during maximal voluntary contraction (the interference pattern, IP) were estimated. The reduction of the IP was categorized on a four-grade scale from 0 to 3, where 0 is normal, 1 is mildly reduced, 2 is moderately reduced and 3 is severely to extremely reduced IP (Stålberg et al., 2019; Sanders et al., 1996). The amount of spontaneous activity, if any, was graded from 1 to 4 (Michell, 2013). In order to obtain a true neurogenic recruitment pattern, an incomplete interference pattern was interpreted as being reduced (IP 1 to 3) only when motor unit potentials had a high amplitude and long duration and/or were polyphasic.

2.3. HRUS

Median nerve HRUS was performed right after the EDX study by the same examiner who performed the EDX. The examiner was not blinded to the EDX data or clinical information. The HRUS device used was a GE Healthcare Logiq E9 (GE Healthcare, Milwaukee, WI, USA) with a 12.0 MHz ML 6–15-D linear transducer. The CSA of the MN was measured by a single measurement in the transversal plane at the site of the carpal tunnel inlet, where the median nerve was at its largest, and at the distal third of the forearm. The CSA was measured with freehand tracing inside the epineurium. The WFR was calculated by dividing the wrist CSA by the forearm CSA. A total of 16 wrists in the younger group and 18 wrists in the older group lacked a forearm CSA measurement. In addition, 15 wrists in the younger group and 17 wrists in the older group lacked the needle EMG results. The wrists that lacked the forearm CSA were not included in the WFR analysis but were included in the analysis of the wrist CSA. The wrists that lacked the needle EMG results were included in other statistical analyses than those related to EMG correlations and IP group assessments.

2.4. Statistical analyses

Statistical analyses were performed using IBM SPSS version 26 (SPSS Inc, Chicago, IL, USA). Spearman's correlation was used to study the significance of correlations. Mann-Whitney *U* test and Independent-Samples Kruskal-Wallis test were used to define the differences between groups.

3. Results

Patient characteristics are presented in Table 1. Patients in the older group had more wrists with more severe CTS than patients in the younger group. The different CTS severity groups were more evenly distributed in the older group, whereas moderate CTS was

Table 1
The mean patient age, number of patients, number of men and women, and number of wrists included in the study in total and in the younger and older subgroups. SD, standard deviation.

	Younger group (<65 years)	Older group (≥65 years)	Total
Mean age (years)	49 (SD ± 10.6)	77 (SD ± 6.9)	61 (SD ± 16.5)
Patients included	192	137	329
Men	69	47	116
Women	123	90	213
Wrists included	267	200	467

emphasized within the younger group. The distribution of the wrists in different CTS categories is presented in Tables 2 and 3.

3.1. Association between patient age and CSA and WFR

In general, the median CSA and WFR values of the older group were smaller than the values of the younger group (Tables 2 and 3). The difference in the mean CSA and WFR values between the two age groups was significant when tested in the entire study material ($p < 0.001$ for CSA and $p = 0.006$ for WFR) and when tested separately in the groups of moderate CTS ($p < 0.001$ for CSA and $p = 0.005$ for WFR) and severe CTS ($p < 0.001$ for CSA and $p = 0.034$ for WFR). The difference was not significant in extreme CTS.

In the entire study material, patient age showed a slight negative correlation to CSA ($p < 0.001$, $r = -0.208$) and to WFR ($p = 0.001$, $r = -0.159$). The correlations were also significant in the moderate ($p < 0.001$, $r = -0.196$ for CSA and $p < 0.001$, $r = -0.197$ for WFR) and severe CTS groups ($p < 0.001$, $r = -0.492$ for CSA and $p < 0.001$, $r = -0.240$ for WFR).

The association between CSA and WFR and CTS severity was first tested without dividing the study material into the two age groups. In this setting, the CSA showed a weak positive correlation to CTS severity ($p = 0.013$, $r = 0.115$), whereas WFR did not associate with CTS severity. After this, the associations were retested separately in the two age groups. In the younger group, the CSA correlation was slightly stronger and WFR also showed a slight positive correlation with CTS severity ($p < 0.001$, $r = 0.289$ and $p = 0.024$, $r = 0.142$, respectively). In the older group, CSA did not correlate to CTS severity, but a slight correlation between CTS severity and WFR was seen ($p = 0.033$, $r = 0.158$).

3.2. Association of IP density and spontaneous activity to CSA and WFR

The older group had more cases of more severe CTS than the younger group ($p = 0.001$). Subsequently, the IP was reduced more often and more severely in the older group. To eliminate the possible biasing factor of an uneven distribution of CTS severity between the age groups, the distribution of the IP in the two age groups was compared within the moderate CTS. Fig. 1 demonstrates that IP reduction in the older group was still seen more often than in the younger group. Moreover, the IP was normal less often in the older group than in the younger group. The moderate CTS group was chosen for this comparison because the number of wrists was the highest of all the CTS groups in both age groups, and the different IP groups were most evenly distributed (Tables 4 and 5).

In general, combining the moderate and severe CTS groups and both age groups, the CSA ($p = 0.022$) and WFR ($p = 0.016$) were larger in cases showing findings of neurogenic lesion in the APB compared to those in which the EMG findings were normal.

In the younger group, both CSA and WFR correlated positively with IP reduction ($p = 0.001$, $r = 0.214$ for CSA and $p = 0.005$, $r = 0.183$ for WFR). There was also a significant difference in the mean CSA and WFR values between the groups IP0 and IP1 ($p = 0.020$ for CSA and 0.025 for WFR) as well as IP0 and IP2 ($p = 0.006$ for CSA and $p = 0.014$ for WFR) as shown in Fig. 2. Unfortunately, in the younger group, the material was too unevenly distributed regarding the CTS and IP severity groups to reliably study the relation of IP and CSA/WFR in the different CTS severity categories (Table 4). The CTS severity and IP groups were, however, more evenly distributed in the older group, and could therefore be studied in more detail.

In the older group, IP reduction also correlated positively with CSA and WFR ($p = 0.018$, $r = 0.174$ for CSA and $p = 0.005$, $r = 0,215$ for WFR). The likewise correlation was also found within the moderate CTS group ($p = 0.021$, $r = 0.244$ for CSA and $p = 0.015$, $r = 0.265$ for WFR), again limiting the possible biasing factor of the increasing CTS severity. Regardless of the correlation, CSA did not differ statistically significantly between the IP groups. WFR, however, was significantly smaller in the IP0 group than in the IP3 group ($p = 0.002$, Fig. 2). There was a nearly significant difference between the IP1 and IP3 groups ($p = 0.073$) as well as between the IP2 and IP3 groups ($p = 0.066$). Again, this finding could be reproduced within the moderate CTS group; there was a statistically significant difference between the IP0 and IP3 groups ($p = 0.002$), the IP1 and IP3 groups ($p = 0.016$), and between the IP2 and IP3 groups ($p = 0.029$). In the older group, the MN motor

Table 2
Cross sectional area (CSA) mean, minimum, and maximum values in the two age groups.

CTS	CSA							
	Younger group (<65 years)				Older group (≥65 years)			
	N	mean	min	max	N	mean	min	max
moderate	222 (83%)	15.1	7	52	102 (51%)	13.3	7	28
severe	38 (14%)	19.5	10	34	61 (30%)	13.7	8	29
extreme	7 (3%)	18.1	14	29	37 (19%)	15.4	9	25
total	267	15.8	7	52	200	13.8	7	29

N, the number of wrists and the percentage from the total; CSA, cross sectional area (mm^2); CTS, carpal tunnel syndrome severity (moderate: Median nerve (MN) sensory velocity ≥ 10 m/s slower than the ulnar and MN distal motor latency ≥ 4.2 ms, severe: sensory responses absent and the MN distal motor latency ≥ 4.2 ms, extreme: both sensory and motor responses absent).

Table 3
Wrist-to-forearm ratio (WFR) mean, minimum, and maximum values in the two age groups.

CTS	WFR							
	Younger group (<65 years)				Older group (≥65 years)			
	N	mean	min	max	N	mean	min	max
moderate	212 (84%)	2.39	1.17	4.89	96 (53%)	2.17	1.14	4.50
severe	32 (13%)	2.76	1.27	5.50	53 (29%)	2.30	1.00	4.83
extreme	7 (3%)	2.79	2.11	4.14	33 (18%)	2.41	1.50	3.80
total	251	2.45	1.17	5.50	182	2.25	1.00	4.83

N, the number of wrists and the percentage from the total; WFR, wrist-to-forearm ratio ($CSA_{wrist}/CSA_{forearm}$); CTS, carpal tunnel syndrome severity (moderate: Median nerve (MN) sensory velocity ≥ 10 m/s slower than the ulnar and MN distal motor latency ≥ 4.2 ms, severe: sensory responses absent and the MN distal motor latency ≥ 4.2 ms, extreme: both sensory and motor responses absent).

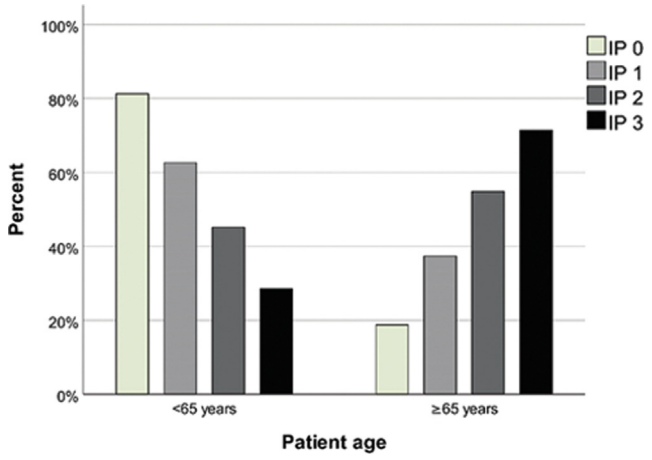

Fig. 1. Percentages of wrists in different interference pattern density (IP) groups according to patient age in the moderate carpal tunnel syndrome (CTS). In the younger group, the IP density was more often normal, whereas in the older group it was more often reduced ($p < 0.001$). The density of the IP was scored as follows: 0: normal; 1: slightly reduced; 2: moderately reduced; 3: severely to extremely reduced.

amplitude had a slight negative correlation to the wrist CSA ($p = 0.040$, $r = -0.146$) and WFR (0.021, $r = -0.172$).

Spontaneous activity was detected in 35 APB of the younger patients and in 71 APB of the older patients. The amount of spontaneous activity, however, did not correlate significantly with CSA or WFR. There were no significant differences in the CSA or WFR values between the different groups of spontaneous activity, even when studied separately in the two age groups.

4. Discussion

In our present study, we have shown that both patient age and degree of median nerve axon loss are associated with the ultrasound parameters used in CTS. Moreover, axon loss was found to be more common among older patients.

In concordance with the previous literature (Gregoris and Bland, 2019; Martikkala et al., 2021b; Moschovos et al., 2019) the mean values of both CSA and WFR were, in general, smaller in older patients than in younger patients. We used NCS to divide CTS into different severity categories (Padua et al., 1997), and the age difference was also found within the moderate and severe CTS categories. The association between age and CSA was emphasized in the severe CTS category, implying that patient age is even more strongly associated with smaller CSA in severe CTS. This might explain why CSA does not correlate to CTS severity in elderly. In the previous literature, several interpretations have been given as to why CTS is often more severe and CSA smaller in older patients than in younger patients. One explanation is that the pathophysiology of CTS is different in the older population (Miwa and Miwa, 2011). This could explain the smaller CSA in older patients compared to younger ones. In the entire study material, there was a slight increase between the NCS based CTS severity and CSA, but not between CTS severity and WFR. Interestingly, when studied separately in the younger and older groups, WFR increased with CTS severity in both age groups. WFR even had approximately the same correlation coefficient amongst older patients than amongst younger patients. To our best knowledge, a WFR increasing with CTS based severity in older patients has not previously been reported. Although the associations between CTS severity and HRUS have been extensively evaluated, many previous studies have focused solely on the CSA, whereas the effect of age on WFR has been studied to a much lesser extent. In one study that evaluated the relationship between WFR and CTS categories, no significant correlation was found (Moschovos et al., 2019). This finding might have been due to different rules for categorizations, which we will discuss later.

Miwa and Miwa (2011) found the severity of CTS to increase with advancing age, which was also seen in our study. Furthermore, axon loss was also more frequent among older patients, even if the study material was limited to moderate CTS. Thus, it could be speculated that the nerves of older patients could be more prone to acquire axonal damage in relation to CTS. Indeed, aging by itself can cause slight denervation and reinnervation changes (Michell, 2013). It has previously been speculated that CTS in the older pop-

Table 4
The distribution of the interference pattern density (IP) groups according to carpal tunnel syndrome (CTS) severity in the younger group.

CTS severity	**Severity of the interference pattern reduction**				
	IP0	**IP1**	**IP2**	**IP3**	**Total**
Moderate	130	62	14	2	208
Severe	4	19	11	3	37
Extreme	0	0	2	5	7
Total	134	81	27	10	252

CTS, carpal tunnel syndrome severity (moderate: Median nerve (MN) sensory velocity ≥ 10 m/s slower than the ulnar, and MN distal motor latency ≥ 4.2 ms, severe: sensory responses absent and the MN distal motor latency ≥ 4.2 ms, extreme: both sensory and motor responses absent). The density of the interference pattern (IP) (IP0: normal, no reduction; IP1: slightly reduced interference pattern; IP2: moderately reduced interference pattern; IP3: severely to extremely reduced interference pattern).

Table 5
The distribution of the interference pattern (IP) groups according to carpal tunnel syndrome (CTS) severity in the older group.

CTS severity	Severity of the interference pattern reduction				
	IP0	IP1	IP2	IP3	Total
Moderate	30	37	17	5	89
Severe	5	20	22	10	57
Extreme	0	1	5	31	37
Total	35	58	44	46	183

CTS, carpal tunnel syndrome severity (moderate: Median nerve (MN) sensory velocity ≥ 10 m/s slower than the ulnar, and MN distal motor latency ≥ 4.2 ms, severe: sensory responses absent, and the MN distal motor latency ≥ 4.2 ms, extreme: both sensory and motor responses absent). The density of the interference pattern (IP) (IP0: normal, no reduction; IP1: slightly reduced interference pattern; IP2: moderately reduced interference pattern; IP3: severely to extremely reduced interference pattern).

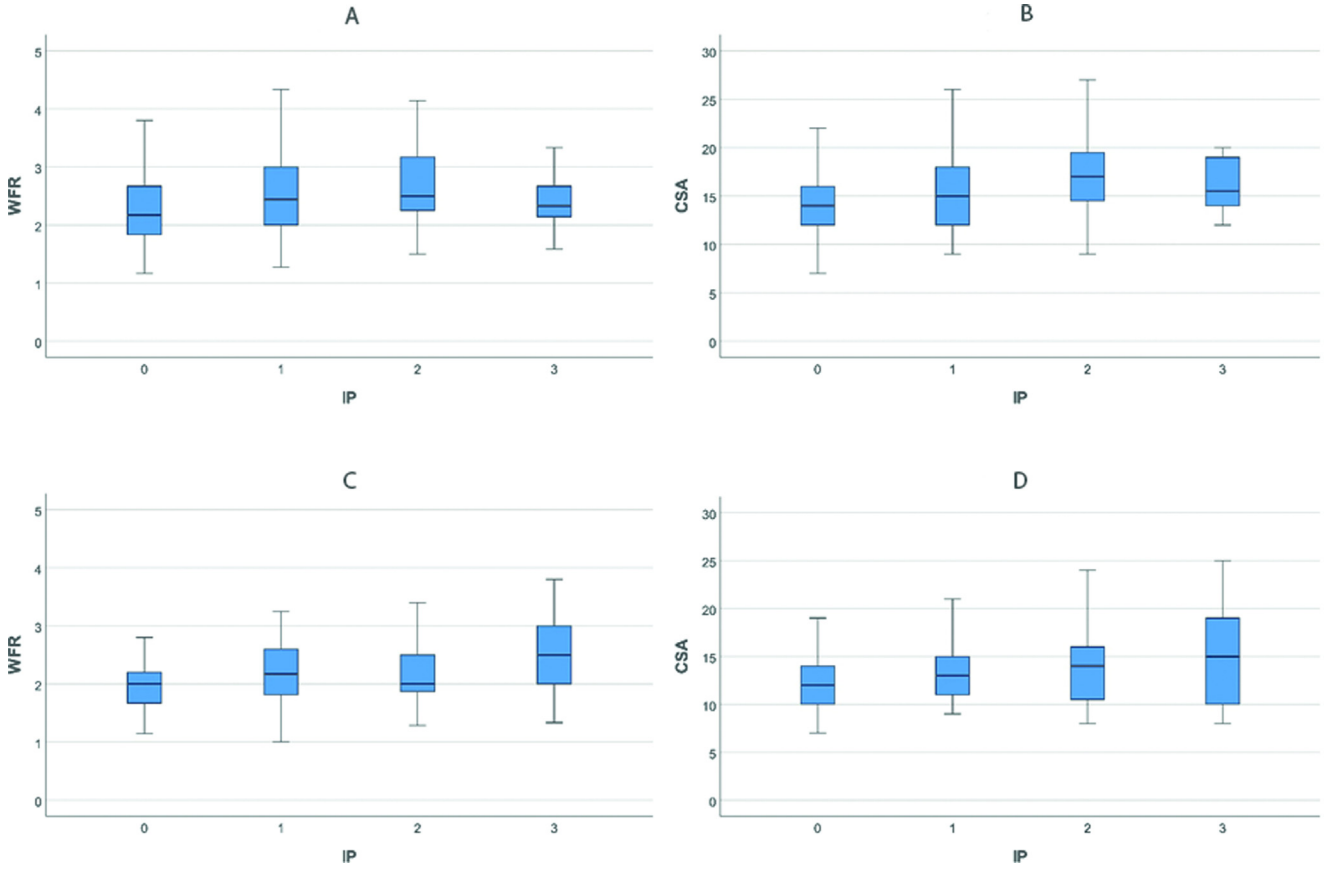

Fig. 2. wrist-to-forearm ratio (WFR) and cross sectional area (CSA) in relation to interference pattern (IP) density in the younger and older groups. The density of the IP was scored as follows: 0: normal; 1: slightly reduced; 2: moderately reduced; 3: severely to extremely reduced IP. The box represents the first and third quartile, the thick line within the box indicates the median and the bars show the minimum and maximum values of WFR/CSA.

ulation could be a separate entity (Gregoris and Bland, 2019). The predisposition of this population to acquire axonal loss in relation to CTS could be related to this speculation. However, it does not explain why the CSA and WFR are smaller in older patients compared to younger patients, since axon loss is associated with increasing CSA and WFR. The WFR seems to behave differently in relation to IP reduction in older and younger patients as can be seen in the box plots of Fig. 2. In older patients, there is a linear growth in WFR and CSA, whereas in younger patients the growth follows more of a dome shape.

Spontaneous activity was not associated with either CSA or WFR. Thus, it seems that acute axonal damage might not cause dramatic changes in the CSA or WFR. However, the ongoing changes in the damaged nerve are dynamic and the changes seen in an EMG only reflect a momentary state. Therefore, spontaneous activity may alter in respect to the balance of nerve sprouting and ongoing axonal damage at a certain moment, which may cause bias. Also, fibrillations are a manifestation of muscle fiber instability due to various reasons, not axonal damage alone.

According to our results, it can also be questioned whether the grading method of CTS severity has some effect on the variation of previous literature regarding the usability of CSA and WFR in CTS grading. For example, the study by Moschovos et al. (2019) utilized needle EMG in the assessment of CTS severity, whereas in most studies CTS severity has been mainly categorized based solely on NCS (Bayrak et al., 2007; Deng et al., 2018; El Habashy et al., 2017; El Miedany et al., 2004; Elnady et al., 2019; Gregoris and Bland, 2019; Miwa and Miwa, 2011; Mulroy and Pelosi, 2019; Padua et al., 1997; Wee and Simon, 2020). In their study, Moschovos et al. (2019) considered CTS always severe if signs of neurogenic lesion were found in the APB muscle. The findings of our study, however, show that there can be neurogenic lesion in the APB muscle even in moderate CTS when graded by NCS, and this is emphasized in older patients. Therefore, some of the

patients that would have been in the moderate CTS group in studies based solely on NCS were most likely considered to be in the severe group in the study by Moschovos et al. (2019). Moreover, including the neurogenic lesions of the APB in the classification of CTS may lead to an unequal distribution of the study material between the older and younger groups, as neurogenic lesions are more often presented in older patients. It could be questioned, therefore, whether it would be preferable to include the needle EMG of the APB in future studies in addition to the previously suggested partition of younger and older patients, as we have shown that the axon loss also affects the CSA and WFR in CTS. In addition, the cut-off value of the MN distal motor latency to discriminate moderate CTS from mild CTS often varies in different studies, which also limits their comparability.

Our study has several limitations that should be addressed. First, although EMG is an established method to assess axonal damage that has been reported to be reasonably reproductive and clinically reliable, it is eventually a subjective parameter (Daube and Rubin, 2009). However, a quantitative MUP analysis would have given quantitative parameters to replace the subjective evaluation of the morphology of the motor unit potentials. Second, the IP may be reduced due to demyelination in addition to axonal damage. Demyelination might also play a role in increasing CSA and WFR, as reported in the previous literature. (Rubin and Dimberg, 2018; Özişler and Akyüz, 2021). Even though signs of neurogenic lesion in the APB were required to determine that IP reduction was associated with axonal loss, it does not exclude coincidental demyelination at the entrapment site, which may potentially enforce the IP reduction. However, as presented in the results, the median CSA was significantly larger in the group of wrists in which a neurogenic lesion was detected in the APB when compared to the group in which the EMG of the APB was normal. Furthermore, a negative correlation between the objective MN CMAP amplitude and wrist CSA was found in the group of older patients, which supports the EMG finding. Third, the duration of the CTS related symptoms was not accessible due to the retrospective study design. The pathophysiology of the nerve entrapment changes in association with entrapment duration (Rempel and Diao, 2004), which may also affect the HRUS findings and limit the comparability of the CTS severity groups and patient age. Finally, the wrist CSA was only measured at the intel site. It is, however, also possible that in some cases MN CSA only increases in the distal side of the transverse ligament. Other factors that may be considered as limitations of the study are single center design, modest sample size in CTS severity subgroups, heterogeneity of patient characteristics and lack of blinding in the EDX testing and HRUS assessment.

4.1. Conclusions

Our study complements the recently published findings on the effects of patient age on the median nerve CSA, and on its reliability in assessing the severity of CTS. As a new finding, we present a positive association between WFR and CTS severity amongst older patients, indicating that WFR could be a more reliable HRUS parameter than CSA when assessing the severity of CTS in older patients. Although the MN CSA does not correlate with the severity of CTS in older patients, the CSA seems to increase in respect to the amount of axon loss, irrespective of patient age. Nevertheless, associations between axon loss and HRUS parameters are modest and are unlikely to be suitable for clinical work. Therefore, NCS and EMG both remain the optimum tools to assess the degree of axonal loss. Different ultrasound parameter cut-off values in older and younger patients with CTS could improve diagnostic accuracy in the assessment of CTS severity.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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