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RESEARCH

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Analysis of the frequency of Martin–Gruber anastomosis in patients with carpal tunnel syndrome

Hager El-Shehawy Mohamed[1*], Samia M. Abdel-Monem[2], Gamal Abdel-Ghafaar Hammad[2] and Marwa Yahia Mahgoub[2]

Abstract

Background: Martin–Gruber anastomosis (MGA) is one of the most common anomalous innervations of the upper limb. It may alter the usual clinical picture and electrophysiological characteristics of median nerve (MN) injury or ulnar nerve (UN) injury.

Aim: To determine the mutual relation between MGA and carpal tunnel syndrome (CTS) regarding their association and to explore whether certain patterns of MGA are more prevalent in patients with CTS.

Methods: This study included 100 forearms of 64 subjects. They were 37 subjects complaining of unilateral or bilateral clinical symptoms of idiopathic CTS according to the criteria of the American Academy of Neurology and 27 subjects healthy or having traumatic lesions in either the upper or lower limbs with no neurological disorders. Electrophysiological studies of the MN and UN for the confirmation of CTS as well as the validation of MGA were done.

Results: By electrophysiological examination, MGA was encountered in 22% forearms of all the studied groups, mostly females. MGA type II and type III were the commoner types, each occurring in 40.9%, while type I and type IV each occurred in 9.1%. MGA type II was prevalent in the control group, while type III associated subjects with only clinical CT symptoms.

Conclusion: MGA is not prevalent in patients with CTS. Different types of MGA are present in CTS, but MGA was not implicated in the occurrence, severity, or electrodiagnostic features of CTS.

Keywords: Martin–Gruber anastomosis, Carpal tunnel syndrome, Median nerve, Ulnar nerve, Nerve conduction studies

Background

Considering anomalous innervations of peripheral nerves are important in the routine electrophysiological assessment of any patient [1]. Missing these anomalous innervations may easily be mistaken for technical pitfalls or even for an actual pathology [2].

Upper limb is one of the most common sites for anastomosis between its nerves especially the MN and UN. This consists of crossings of axons producing variations in the innervation of the muscles in the upper limbs, mainly the motor part of the intrinsic muscles of the hand [1].

A better knowledge of the anatomical variations of these nerves helps to understand both anatomic variations and paradoxical complaints of sensory and/or motor loss of patients [3].

The most frequent anastomosis between the MN and UN in the forearm are the Martin–Gruber anastomosis (MGA) and the Marinacci anastomosis (MA) [4].

*Correspondence: hagerelshahawy28887@gmail.com

[1] Toukh Central Hospital, Toukh, Egypt
Full list of author information is available at the end of the article

MGA is one of the most common anomalous innervations present in the body, presenting in the upper limb. A Swedish anatomist Martin was the first one who described this anastomosis in 1763, followed by Gruber in 1870 [2].

This anomaly is formed from the cross-over of median-to-ulnar motor nerve fibres. It can take place from the trunk of the median nerve (MN) or from one of its branches in the forearm, mainly the anterior interosseous nerve [5].

MGA might lead to underestimation in the CTS severity or misinterpretation of electrophysiological data. Patients with CTS and MGA type III present a near normal proximal motor latency of the MN in the presence of prolonged DML, resulting in an apparently faster CV. In addition, patients with MGA and CTS might have the partial or complete sparing of the thenar muscles due to the crossover of fibres to the UN. In particular, the detection of a positive onset or an increased CV can be an important supporting feature in patients with a combined CTS and MGA III [5].

MGA can be diagnosed electrophysiologically by detecting the presence of certain differences in the compound muscle action potentials (CMAP) recorded from the intrinsic hand muscles when the MN and UN are stimulated electrically at the wrist and elbow [6].

The aim of our study was to determine the mutual relation between MGA and CTS regarding their association and to explore whether certain patterns of MGA are more prevalent in patients with CTS.

Patients and methods

This is a cross-sectional study that included 100 forearms from 64 subjects who attended the Electromyography and Nerve Conduction Lab for electrophysiological evaluation, at the Rheumatology, Rehabilitation, and Physical Medicine Department of Benha University Hospital.

These subjects were classified into two groups:

Group I: Including patients complaining of unilateral or bilateral clinical symptoms of CTS, according to criteria of the American Academy of Neurology (1993) [7]. These patients will be further subdivided according to electrophysiological findings (group IA and group IB).

The clinical diagnostic criteria of CTS based on the American Academy of Neurology (1993) [7]:

- Paraesthesia, pain, swelling, weakness, or clumsiness of the hand provoked or worsened by sleep, sustained hand or arm position, or repetitive action of the hand or wrist that is mitigated by a change in posture or by shaking of the hand
- Sensory deficits in the median nerve-innervated regions of the hand
- Motor deficit or hypotrophy of the median nerve-innervated thenar muscles
- Positive provocative clinical tests (positive Phalen's manoeuvre and/or Tinel's sign)

The clinical diagnosis of CTS was made when criterion 1 and one or more of criteria 2–4 were fulfilled.

Group II: Including healthy subjects or those suffering from traumatic lesions in either the upper or lower limbs and having no neurological disorders. The healthy forearms were examined.

To be included in this study, certain criteria were required; otherwise, some patients were excluded. These criteria were justified by a careful clinical examination.

– Inclusion criteria:

- Age $\geq$ 20 to $\leq$ 60 years old.
- Idiopathic CTS.

– Exclusion criteria:

- Age < 20 years and > 60 years old.
- Patients with well-known axonal neuropathies.
- Patients with well-known peripheral polyneuropathies.
- All patients with well-known chronic diseases that may affect the nervous system (DM, autoimmune diseases, hypothyroidism, or thyrotoxicosis).

Subjects of both groups were subjected to the following:

– A detailed history taking and full-clinical and musculoskeletal examination of the upper limbs with the assessment of CTS provocative tests
– Electrophysiological studies carried out using a Neurowerk EMG unit with a four-channel evoked potential/EMG measuring system (SIGMA Medizin-Technik GmbH Germany) [6]. The electromyographer was blind to data about MGA.

Nerve conduction studies

1) Motor nerve conduction study of the MN and UN, stimulating both nerves at the wrist and elbow while recording from the abductor pollicis brevis (APB),

abductor digiti minimi (ADM), and 1st dorsal interosseous (FDI) muscles for each nerve.
  - Measurements included the amplitude of the CMAP measured from the first negative peak to the next positive peak expressed in millivolt (mV).
2) MN and UN nerves forearm motor conduction velocities (CVs): the CVs defined in m/s^2 are calculated by dividing the forearm skin distance between the distal and proximal sites of stimulation for each nerve by the difference between the onset of the proximal and distal responses in ms (proximal and distal CMAPs latencies).
3) Sensory nerve conduction study of the MN and UN nerves: stimulating both nerves at the wrist while recording at the interphalangeal (IP) joint of digits 2 or 3 for the MN, and the IP joint of digit 5 for the UN.
  - Measurements included the amplitude of the sensory nerve muscle action potential (SAP) measured from the first negative peak to the baseline, expressed in μV and the onset latency in msec.

- Electrophysiological findings in CTS: electrophysiological findings of CTS were graded and classified according to Bland's neurophysiological grading scale (9).

Bland's neurophysiological grading scale [8]

Grade 0: Normal.

Grade 1: Very mild, CTS demonstrable only with most sensitive tests.

Grade 2: Mild, sensory nerve CV slow on finger/wrist measurement, normal terminal motor latency.

Grade 3: Moderate, sensory potential preserved with motor slowing, distal motor latency to abductor pollicis brevis (APB) < 6.5 ms.

Grade 4: Severe, sensory potentials absent but motor response preserved, distal motor latency to APB < 6.5 ms.

Grade 5: Very severe, sensory potentials absent but motor response preserved, distal motor latency to APB > 6.5 ms.

Grade 6: Extremely severe, sensory, and motor potentials effectively unrecordable, surface motor potential from APB < 0.2 mV amplitude.

Electro diagnostic findings of MGA

These are dependent on the CMAP amplitude of MN and UN [2].

- *MGA type I* (the median to-ulnar cross-over innervates the ADM muscle): The amplitude of the UN CMAP recorded from the ADM muscle on below-elbow stimulation is lower than that recorded on wrist stimulation by more than 10%. To confirm the presence of MGA, an ADM muscle CMAP will be seen on proximal stimulation of the MN that was not present on wrist stimulation.
- *MGA type II* (the median to-ulnar cross-over innervates the FDI muscle)*:* There is a drop in the CMAP amplitude of the FDI muscle between the wrist and below-elbow sites. To confirm the presence of MGA, MN stimulation at the wrist, and antecubital fossa while recording the FDI, a higher amplitude of the CMAP on proximal stimulation than on wrist stimulation is present.
- *MGA type III* (the median to-ulnar cross-over innervates one of the ulnar-innervated thenar muscles (i.e., adductor pollicis or deep head of the flexor pollicis brevis): Recording a CMAP from the ADM muscle after UN stimulation is normal. MN stimulation while recording from the thenar muscles, the amplitude of the MN CMAP at the antecubital fossa stimulation is larger than that obtained with wrist stimulation unlike the usual pattern of a higher-amplitude CMAP with distal stimulation. To confirm the presence of MGA, stimulation of the UN at the wrist, below-elbow, and above-elbow, while recording the APB muscle, the UN CMAP amplitude at the below-elbow stimulation is substantially lower than that obtained at wrist stimulation.

Type IV MGA was the presence of two or more of the previous three types in the same forearm [6].

Statistical analysis

The collected data was revised, coded, tabulated, and introduced to a PC using Statistical Package for Social Sciences (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Data were presented and suitable analysis was done according to the type of data obtained for each parameter.

The Kolmogorov–Smirnov test was done to test the normality of data distribution. The mean and standard deviation (±SD) were used to describe parametric data, while for the median and range, Mann–Whitney test (*U* test) and the Kruskal–Wallis, were used to describe non-parametric numerical data. The frequency and percentage were used to describe non-numerical data. Analytical statistics tests used were the Student *t* test, chi-square tests, Fisher's exact test, and the ROC curve (receiver operating characteristic). Probability of results was adjusted as all tests were 2-sided and a *P* value > 0.05 was considered statistically significant.

Sample size was calculated by the G*Power (Version 3.1.9.2) (Faul et al. 2007) and published study by Saba

et al. 2018 with respect to prevalence of MGA reported as 26%. Using confidence limits of 5%, power of 80%, exact proportion, sign test, required minimal sample size is 30 at each group. To increase the power of the study, sample size was increased to 40 control and 60 CTS cases [9].

Results

This study included 100 forearms from 64 subjects, divided into two groups.

- Group I included 60 forearms from 37 patients with clinical symptoms of carpal tunnel syndrome (CTS). These patients' ages ranged between 20 and 60 years (mean ± SD) and their disease duration ranged between 3 months and 5 years (median = 1 year). Fourteen cases had unilateral CTS, while 23 cases had bilateral affection. Electrophysiological testing for clinical CTS cases (9) showed that 19/60 hands (31.7%) had a normal study, while 41/60 hand (68.3%) had an abnormal study (20% had a mild CTS grade, 21.7% had a moderate CTS grade, while 26.7% had a severe CTS grade). Consequently, these patients, were designated as CTS cases (group IA) and CTS patients (group IB).
- Group II included 40 forearms from 27 subjects, healthy or with traumatic lesions of either the contralateral upper limb or lower limbs, where the healthy forearms were examined. Fourteen subjects had normal unilateral forearms and 13 subjects had bilateral normal forearms. Their ages ranged between 20 and 60 years (mean ± SD).

Table 1 Comparisons between group I and group II regarding demographic and anthropometric data

Variables			Control Number = 40	Cases Number = 60	*P*
Age (years)		**Mean ± SD**	39.7 ± 9.6	39.9 ± 9.7	0.896
Gender	**Males**	***N* (%)**	8 (20%)	6 (10%)	0.158
	Females	***N* (%)**	32 (80%)	54 (90%)	
Weight (kg)		**Mean ± SD**	75.3 ± 11.7	77.2 ± 8.1	0.335
Height (cm)		**Mean ± SD**	166 ± 5.2	165.5 ± 5.3	0.698
Body mass index (kg/cm^2)		**Mean ± SD**	27.3 ± 4	28.2 ± 2.7	0.212

T test Student test, *P value* probability value, *SD* standard deviation, *p > 0.05* insignificant difference

There were no statistically significant differences between CTS cases and controls regarding their demographic and anthropometric data ($p > 0.05$) (Table 1).

By electrophysiological examination, MGA was found in 22/100 (22%) of all the studied groups, 17 females (77.3%) and 5 males (22.7%), 3 bilateral (13.6%), and 16 unilateral (72.7%).

MGA was found in 2 cases (10.5%) of group IA, in 6 cases (14.6%) of group IB, and in 14 cases (35%) of the controls (group II) (Fig. 1).

There were no statistically significant differences among the subjects with and without MGA regarding their mean age, gender, mean weight, mean height, mean BMI, and mean MN forearm CV ($p > 0.05$ each) (Table 2).

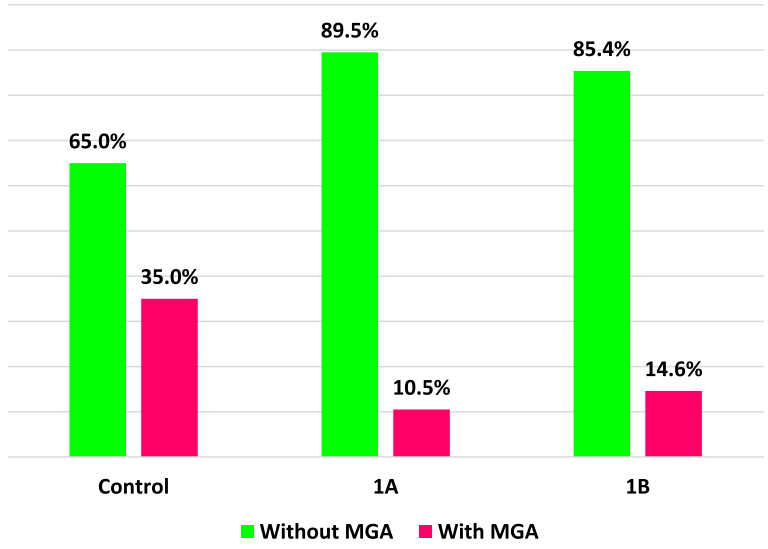

Fig. 1 Bar chart showing the distribution of MGA among the studied groups

Table 2 Comparison between studied subjects with and without MGA

Variables			Subjects				*p*
			With MGA		Without MGA		
			Number = 22		Number = 78		
Age (years)		**Mean ± SD**	40.0	11.0	39.8	9.2	0.945
Gender	**Males**	***N* (%)**	5	22.7%	9	11.5%	0.182
	Females	***N* (%)**	17	77.3%	69	88.5%	
Weight (kg)		**Mean ± SD**	76.6	12.1	76.4	9.0	0.939
Height (cm)		**Mean ± SD**	166.3	7.6	165.5	4.4	0.563
Body mass index (kg/cm^2		**Mean ± SD**	27.7	3.9	27.9	3.1	0.810
MN forearm CV (m/s)		**Mean ± SD**	54.940	6.5754	56.772	8.6575	0.385

MGA Martin–Gruber anastomosis, *N* number, *P value* probability value, *SD* standard deviation, *MN* median nerve, *CV* conduction velocity, *p > 0.05* = insignificant difference

Table 3 Comparisons among CTS patients (group IB) with and without MGA regarding their studied data

Variables			Group IB				
			Number = 41				
			With MGA		Without MGA		*p*
			n = 6		*n* = 35		
Age (years)		**Mean ± SD**	43.0	±11.3	41.8	±8.6	0.759
Gender	**Males**	***N* (%)**	1 (16.7%)		0 (0%)		0.146
	Females	***N* (%)**	5 (83.3%)		35 (100%)		
Left	***N* (%)**		3 (50%)		17 (48.6%)		0.948
Right	***N* (%)**		3 (50%)		18 (51.4%)		
Weight (kg)		**Mean ± SD**	86.0	± 14.6	76.7	± 6.5	**0.012***
Height (cm)		**Mean ± SD**	169.7	± 12.6	164.3	± 2.6	0.124
Body mass index (kg/cm^2)		**Mean ± SD**	29.8	± 3.3	28.4	± 2.8	0.278
MN forearm CV (m/s)		**Mean ± SD**	49.5	± 5.4	57.6	± 8.2	**0.042***

MGA Martin–Gruber anastomosis, *N* number, *P value* probability value, *SD* standard deviation, *MN* median nerve, *CV* conduction velocity, *p > 0.05* = insignificant difference

The mean weight was significantly higher ($p = 0.012$), while the MN forearm CV was significantly lower ($p = 0.042$) in CTS patient with MGA compared to patients without MGA. Otherwise, there were no statistically significant differences among group IB patients with and without MGA regarding their studied data ($p > 0.05$) (Table 3).

There were no statistically significant differences among different CTS patients' electrophysiological parameters regarding the presence of MGA ($p > 0.05$ each) (Table 4).

There were no statistically significant differences among different CTS grades regarding the presence of MGA ($p > 0.05$ each).

There were no statistically significant differences among CTS cases (group 1A) with and without MGA regarding their mean age, gender, mean weight, mean

Table 4 Comparisons among CTS patients (group IB) with and without MGA regarding their electrophysiological parameters

Variables	Group IB		
	Number = 41		
	With MGA	Without MGA	*p*
	n = 6	*n* = 35	
Distal latency Median range	**4.55–3.9**	**4.6–8.9**	**0.5752**
Proximal latency Median range	**8.65–4.5**	**8.6–9.7**	**0.6974**
CV Median range	**52.3–14.8**	**55.3–33.1**	**0.1048**

MGA Martin–Gruber anastomosis, *N* number, *P value* probability value, *p* > 0.05 = insignificant difference, *IB* CTS patients who had carpal tunnel symptoms and an abnormal nerve conduction study

height, mean BMI, and mean MN forearm CV ($p > 0.05$) (Table 5).

MGA was predominant in the subjects without CTS (the control group). MGA type I was found in 2 forearms (9.1%), type II in 9 forearms (40.9%), type III in 9 forearms (40.9%) and type IV in 2 forearms (9.1%). Type II was most prevalent in the control group, while type III associated CTS patients (group IB); (Fig. 2).

– The receiver operating characteristic (ROC) curve was conducted for discrimination of median nerve CV between subjects with and without MGA. A poor AUC was found (AUC = 0.575). At best CV cut-off value of 54.4 m/s, the sensitivity was 61.8%, the specificity was 6%, the PPV was 30.4%, the NPV was 84.8% and the accuracy was 60.4%.

Discussion

MGA anastomosis is the main factor causing or inducing difficulties during surgical procedures. Complications of diagnosis of CTS, cubital tunnel syndrome, peripheral lesions, and neuropathies may result from the presence of MGA [10].

Many studies demonstrated the importance of detecting MGA in CTS and its reflection on the medical and surgical treatment of these conditions [5].

The aim of this study was to evaluate the frequency of MGA between the MN and UN in a sample of healthy

Table 5 Comparisons among CTS cases (group IA) with and without MGA regarding their studied data

Variables			1A				
			Number of forearm = 19				
			With MGA		Without MGA		*p*
			n = 2		*n* = 17		
Age (years)		Mean ± SD	26.0	7.1	36.7	9.8	0.157
Gender	Males	*N* (%)	1 (50.0%)		4 (23.5%)		0.421
	Females	*N* (%)	1 (50.0%)		13 (76.5%)		
Side	Left	*N* (%)	1 (50.0%)		10 (58.8%)		0.811
	Right	*N* (%)	1 (50.0%)		7 (41.2%)		
Weight (kg)		Mean ± SD	75.0	7.1	75.4	6.9	0.938
Height (cm)		Mean ± SD	164.5	0.7	166.6	5.3	0.582
Body mass index (kg/m2)		Mean ± SD	27.7	2.9	27.2	2.2	0.744
MN forearm CV (m/s)		Mean ± SD	56.80	–	54.25	9.52	0.799

MGA Martin–Gruber anastomosis, *N* number, *P value* probability value, *SD* standard deviation, *MN* median nerve, *CV* conduction velocity, $p > 0.05$ = insignificant difference, *group IA* CTS cases who had symptoms of carpal tunnel syndrome and normal nerve conduction study

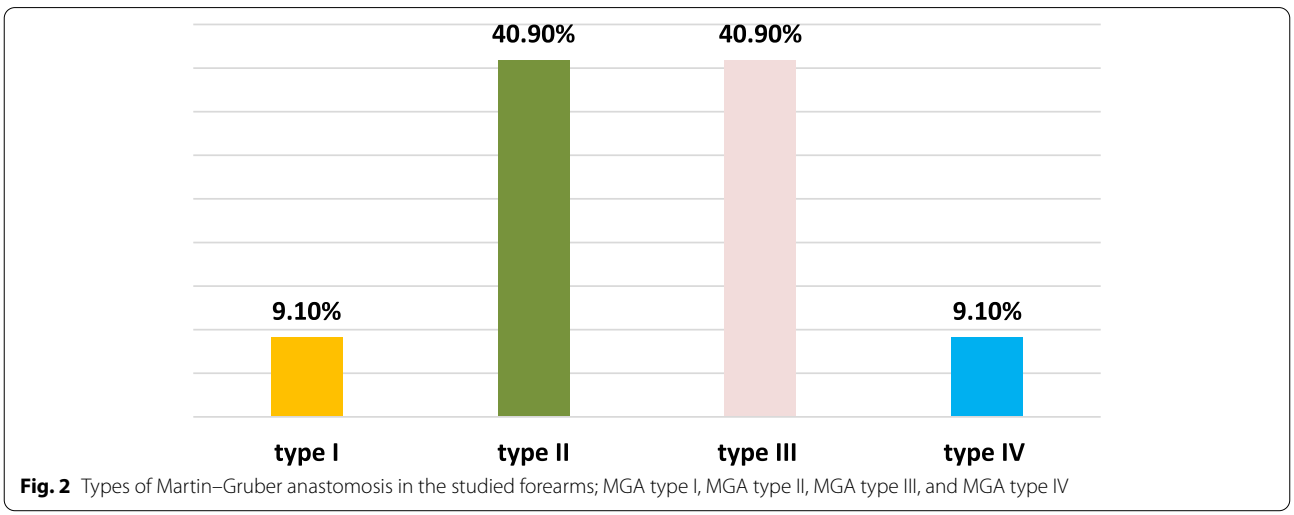

Fig. 2 Types of Martin–Gruber anastomosis in the studied forearms; MGA type I, MGA type II, MGA type III, and MGA type IV

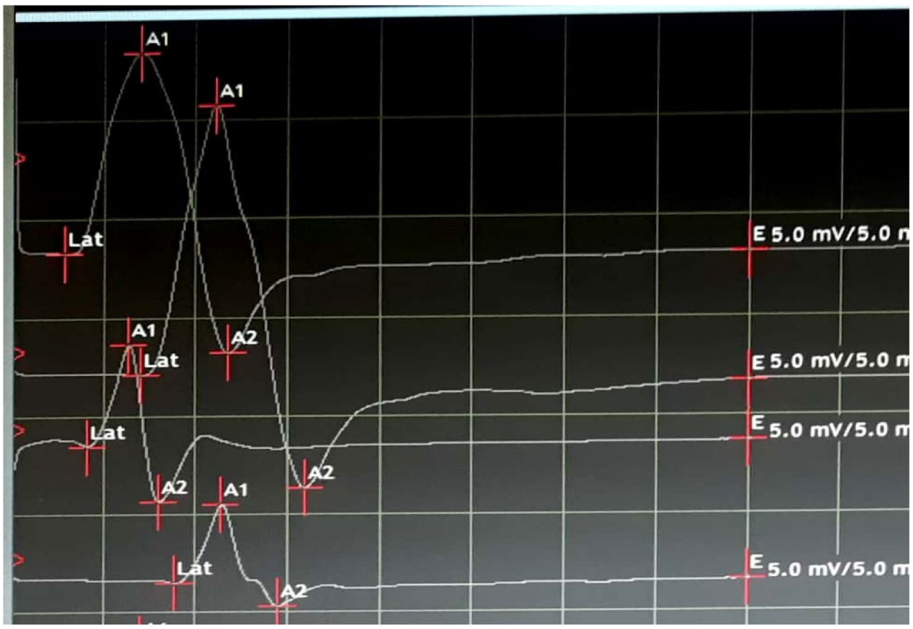

Fig. 3 A case of MGA type III, where the electrical stimulation of the median nerve while recording from the APB muscle showed a higher amplitude of the CMAP with proximal stimulation (19.4 mv) than with distal MN stimulation (15.2 mv). To confirm the presence of MGA, electrical stimulation of the ulnar nerve is done at the wrist, at the below-elbow, while recording from the APB muscle

subjects compared to patients with CTS and to analyse the pattern of this anastomosis in CTS patients.

In our study, by electrophysiological examination, MGA was found in 22% of all the studied groups. The same results had been found in other reports, with the same range of prevalence of MGA present in other studies, which varied from 3.3 to 40% [6, 11, 12]. A recent study of MGA in the Indian population found the prevalence to be 21.4% [13].

However, the wide variation of the prevalence of MGA among different studies could be attributed to the presence of different electrophysiological diagnostic criteria of MGA. Some studies required changes in the amplitude between the distal and proximal stimulation sites by more than 1 mV [5] (Fig. 3).

In our results, MGA was more prominent in females 77.3% vs 22.7% of males. Other reports revealed no statistically significant difference between males and females regarding the frequency of MGA except for MGA to FDI (type II) which was significantly higher among women. This could be explained by the high percentage of women in comparison to men (69% vs 31%) in their studies [6].

In Erdem et al.'s study [13], no significant difference was also found regarding the frequency of MGA between males and females. They attributed this to the autosomal dominant inheritance of MGA [14].

The same result of a non-significant difference between the prevalence of MGA in males and females was found by Sur et al. (2021) [13].

Our results found that MGA had more a unilateral occurrence of 72.7% vs 13.6% who were bilateral. This agreed with another study that found 46% of their subjects had MGA bilaterally while 54% had MGA in only one forearm [13]. Other reports found that MGA was present bilaterally in 13% of subjects [6].

The current study MGA was predominant in the healthy control group. It was found in 35% of the controls group, 10.5% of cases with only clinical CTS symptoms, and in 14.6% of CTS patients, thus, MGA had no impact on the occurrence of CTS.

Several studies were implemented on the prevalence and characteristics of the MGA among healthy subjects [12, 15, 16], whereas subjects with MN or UN injuries were often excluded. Many studies have revealed the effects of such communication in a population of patients affected by CTS [4, 17, 18].

Regarding types of MGA in our study, type II and III of MGA were the most prevalent among our studied population. MGA type II and type III were found in 40.9% forearms each, while type I and type IV in 9.1% forearms each. Type II was most prevalent in the control group, while type III associated predominantly CTS patients [5]. The predominance of MGA type III was demonstrated by all studies that targeted CTS may be explained by the

demonstration of MGA type III reported by our traditional NCS study protocol of CTS.

These results agreed with another study that found MGA type II was the most commonly encountered subtype in 74% of subjects. Other studies also reported that type II MGA was the most frequent type in healthy subjects [6, 13].

Our results found no statistically significant differences between CTS patients with MGA and other MGA subjects with only CTS symptoms regarding the mean weight, height, BMI, side affected, disease duration, and MN forearm CV as well as the presence of MGA (14.6% vs 10.5%).

Of interest, a study on 63 consecutive patients with bilateral CTS reported that the association between MGA and CTS is not rare. Signs of MGA were encountered in 25% of patients, so additional electrophysiological changes may appear with the risk of the underestimation of CTS or even false-negative results on NCS [18].

In our study, there were no statistically significant differences between CTS patients with MGA and those without MGA regarding MN proximal motor latency, distal motor latency and the forearm CV.

Our results disagreed with other studies that had specific electrophysiological features in CTS patients with MGA. Di Stefano et al. [5], reported the presence of a delayed distal latency with a near normal proximal latency and a consequent faster CV in their MGA-CTS. The insignificance of our results may be related to the few cases of MGA-CTS in our study.

In our study, in CTS patients with MGA compared to patients without MGA the mean weight was significantly higher, while the MN forearm CV was significantly lower; otherwise, there were no statistically significant differences between both groups. This is different from expected because other studies have higher numbers of patients.

The current study revealed no statistically significant differences among different CTS grades regarding the presence of MGA.

It is important for orthopaedic and neurosurgeons to be aware of this anatomic variation in order to explain paradoxical motor and sensory losses in patients [19].

Limitations of the current study were due to the small number of the CTS group and missing comparative studies to verify CTS in all cases.

The small number of the CTS group with MGA which was analysed by using non-parametric statistical tests which are more sensitive in small groups to demonstrate the affection of MGA on NCS of CTS.

Further studies are recommended using ultrasound techniques for the pathway of the MN fibres.

Conclusion

MGA is not prevalent in patients with CTS. Different types of MGA are present in CTS, but MGA was not implicated in the occurrence severity or electrodiagnostic features of CTS.

Abbreviations

APB: Abductor pollicis brevis; ADM: Abductor digiti minimi; AUC: Area under the ROC curve; BMI: Body mass index; CTS: Carpal tunnel syndrome; CMAP: Compound muscle action potential; CV: Conduction velocity; DM: Diabetes mellitus; EMG: Electromyography; FDI: 1st dorsal interosseous; MGA: Martin–Gruber anastomosis; MA: Marinacci anastomosis; MN: Median nerve; Ms: Millisecond; mV: Millivolt; NCS: Nerve conduction study; ROC: Receiver operating characteristic; UN: Ulnar nerve; SAP: Sensory nerve muscle action potential.

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Authors' contributions

Conception and design were done by Dr. SMA, Dr. GAH, and Dr. MY. Clinical examination was done by Dr. MY and Dr. HE. Electrophysiological study was done by Dr. MY and Dr. HE. Data collection, processing, and analysis were done by Dr. SMA, Dr. GAH, Dr. MY, and Dr. HE. Writing the manuscript was done by Dr. SMA, Dr. MY, and Dr. HE. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All authors of the manuscript have read and agreed to its content and are accountable for all aspects of the accuracy and integrity of the manuscript in accordance with ICMJE criteria.

That the article is original, has not already been published in a journal, and is not currently under consideration by another journal.

The present study is conducted in agreement with the guidelines of the Declaration of Helsinki with written informed consent obtained from all patients prior to their participation in the study. This study is approved by the Research Ethics Committee, Benha University Faculty of Medicine, Egypt, MS 1512019, date: 15 January 2019.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Toukh Central Hospital, Toukh, Egypt. [2]Rheumatology, Rehabilitation & Physical Medicine Faculty of Medicine, Benha University, Banha, Egypt.

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