3 months of euthyroid state after treatment were (6.33±4.75 IU/mL, 15.52±4.86 pmol/L, 4.06±0.62 Pmol/L) for TSH, FT4, FT3 respectively (P =0.001). The comparison between right and left median nerves motor and sensory functions before and after treatment showed a significant change (P < 0.001). Initial values of right median nerve distal and proximal CSA were 12.5±2.4 mm$^2$ and 9.6±0.5 mm$^2$ respectively while on the left side values were 12.4±2.4 mm$^2$ and 9.9±0.5 mm$^2$ respectively. After treatment, values changed to 12.0±2.4 mm$^2$ (distal) and 0.096±0.004 mm$^2$ (proximal) on the right side and 12.0±2.3 mm$^2$ (distal) and 9.8±0.5 mm$^2$ (proximal) on the left side. 25 patients (62.5 %) showed significant electrophysiological and radiological improvement with hormonal control. While fifteen patients (37.5%) were still suffering manifestations of carpal tunnel syndrome even after hormonal control.

CONCLUSION: The median nerve cross sectional area can be used as a guide for selection of patients that may benefit from a surgical release even before commencement of medical treatment.

Key words: Hypothyroidism; Carpal Tunnel Syndrome; Ultrasonography; Median Nerve

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ABSTRACT

BACKGROUND: We evaluated the efficacy of ultrasonography in newly diagnosed hypothyroid patients suffering manifestations of median nerve entrapment before and after hormone replacement therapy.

METHODS: Forty patients with a mean age of 47.8±12 years diagnosed with hypothyroidism were included in this study. Electrodiagnostic workup and ultrasonographic assessment of both right and left median nerves were done at the initial time of diagnosis and 3 months of euthyroid state after hormone replacement.

Results: Thyroid hormones at the initial time of diagnosis were (48.38±30 IU/mL, 7.59±2.98 pmol/L, 1.79±0.81 pmol/L) and 3 months of euthyroid state after treatment were (6.33±4.75 IU/mL, 15.52±4.86 pmol/L, 4.06±0.62 Pmol/L) for TSH, FT4, FT3 respectively (P =0.001). The comparison between right and left median nerves motor and sensory functions before and after treatment showed a significant change (P < 0.001). Initial values of right median nerve distal and proximal CSA were 12.5±2.4 mm$^2$ and 9.6±0.5 mm$^2$ respectively while on the left side values were 12.4±2.4 mm$^2$ and 9.9±0.5 mm$^2$ respectively. After treatment, values changed to 12.0±2.4 mm$^2$ (distal) and 0.096±0.004 mm$^2$ (proximal) on the right side and 12.0±2.3 mm$^2$ (distal) and 9.8±0.5 mm$^2$ (proximal) on the left side. 25 patients (62.5 %) showed significant electrophysiological and radiological improvement with hormonal control. While fifteen patients (37.5%) were still suffering manifestations of carpal tunnel syndrome even after hormonal control.

CONCLUSION: The median nerve cross sectional area can be used as a guide for selection of patients that may benefit from a surgical release even before commencement of medical treatment.

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INTRODUCTION

Hypothyroidism is a clinical disorder due to the deficiency of the thyroid hormone. This Hormone is a key regulator of cellular
metabolism in our body. This deficient state is estimated to affect 3.8 – 4.6 % of the general population, with a fourfold affection in women[3]. Peripheral nerve dysfunction is a well-documented feature of clinical hypothyroidism. Thyroid hormones deficiency causes sensory neuropathy by affecting different peripheral nerves especially the median nerve[4].

The mechanism involved in the development of neuropathy in hypothyroidism still remains unclear[5,8]. Mononeuropathies secondary to compression caused by deposition of mucopolysaccharide or mucinous deposits in the soft tissues surrounding the peripheral nerves and a polyneuropathy due to either a demyelinating process or primary axonal degeneration are the most commonly proposed mechanisms of peripheral nerve dysfunction in hypothyroidism[5,7]. Myelin structure abnormalities and dysfunction of axonal-oligodendrogial processes may also be responsible for neuropathy in patients with hypothyroidism[5,7]. Also, hypothyroidism produces alterations of fluid balance and peripheral tissue edema, which may lead to CTS development[6].

Carpal tunnel syndrome (CTS) is the most frequent entrapment syndrome of the upper limb; it arises owing to compression of the median nerve at the wrist, which leads to an enlargement of the median nerve cross-sectional area (CSA)[8]. An early diagnosis based on clinical and electrodiagnostic findings is essential to preventing permanent nerve damage and functional sequelae[6,7]. Consequently, treatment of hypothyroidism may help to reduce or cure CTS complaints[9]. Ultrasonography has emerged as an important diagnostic investigation for CTS[10-12]. A number of ultrasonographic changes have been demonstrated in CTS including swelling of the median nerve, flattening of the nerve, palmar bowing and thickening of the flexor retinaculum and changes in the median nerve appearance[12]. The most commonly described abnormality has been enlargement of the median nerve cross sectional area (CSA) usually proximal to the carpal tunnel[12]. The aim of this study is to evaluate the efficacy of ultrason in newly diagnosed hypothyroid patients suffering manifestations of median nerve entrapment before and after hormone replacement therapy.

**METHODS**

**Patients**

Patients with hypothyroidism were recruited from the internal medicine, neurology and general surgery outpatient clinics at Al-Hussein University hospital and the outpatient clinic of neurological surgery at Ainshams University hospital. Out of these patients, forty patients with carpal tunnel syndrome were selected according to an empirical electrophysiological assessment (irrespective of whether they had neurological complaints or not) during the period from March 2013 to January 2015. As they were newly diagnosed, none of these patients received any medical treatment for hypothyroidism and they had neurological complaints or not during the period from March 2013 to January 2015. As they were newly diagnosed, none of these patients received any medical treatment for hypothyroidism and underwent the initial electrodiagnostic evaluation according to standard techniques and median nerve ultrasonography. Thereafter, all patients received appropriate doses of thyroxine treatment for hypothyroidism and were monthly followed up for FT4, FT3 and TSH levels throughout a 3 month period after they have achieved euthyroid state. At the end of this period, patients underwent control electrodiagnostic and ultrasonographic evaluation.

### Table 1 Patients characteristics

|              | Male       | Female  | Total |  |
|--------------|------------|---------|-------|---|
| N(%)         | 10(25%)    | 30(75%) | 40    |  |
| Age Mean ±SD| 49±12      | 47±12   | 47.8±12 |  |
| Range        | 30-65      | 25-65   | 25-65 |  |
| Response to treatment | Maintained on medical treatment 2(20%) | Kept on medical treatment 8(26.7%) | Kept on medical treatment 17(56.7%) |  |
| Referred for surgery | 0 | 5 | 5(16.5%) |  |

### Table 2 Thyroid hormones before and after hormone replacement therapy (HRT).

|                | Minimum | Maximum | Mean±SD | T  | P     |
|----------------|---------|---------|---------|----|-------|
| TSH before HRT uIU/ml | 16.5   | 125     | 48.3±30 | 9.099 | 0.000 |
| TSH after HRT uIU/ml  | 0.5    | 25      | 6.3±4.75 |  |
| FT4 before HRT pmol/L | 2.3   | 15      | 7.59±2.98 |  |
| FT4 after HRT pmol/L  | 9.5    | 26      | 15.52±4.86 |  |
| FT3 before HRT pmol/L | 0.7 | 3.10    | 1.79±0.81 | 4.0±6.2 | 24.612 | 0.000 |
| FT3 after HRT pmol/L  | 2.9    | 5.30    | 4.0±6.2 |  |

**Electrodiagnostic Evaluation**

The electrodiagnostic studies were performed according to standard techniques[15,16]. Motor nerve conduction studies included the determination of conduction velocity, amplitudes and latencies after stimulation of the median nerve. Sensory nerve conduction studies included the antidromic determination of conduction velocity, latencies and amplitude of the sensory nerve action potential of the median nerve. A carpal tunnel syndrome was diagnosed when the median nerve distal motor and/or sensory latencies exceeded 4.4 and 3.5 ms, respectively[16]. Distance between stimulation site and active electrode was 14 cm for median nerve sensory study.

**Ultrasonographic Examinations**

All sessions were performed using a 13- to 14– MHz machine. Patients were seated near the examiner with their arms stretched; hands in a supine position, wrists resting on a flat surface and fingers were semiflexed. To avoid causing any artificial nerve deformity no additional force was applied other than the weight of the probe. Cross-sectional area (CSA) of the median nerve was measured at the distal wrist (CSA-D), and proximal forearm (CSA-P). The CSA of
median nerve was measured at the proximal inlet of carpal tunnel at level of the pisiform bone as a landmark and 12 cm proximal in the forearm by tracing a continuous line around the inner hyperechoic rim of the median nerve with electronic calipers. The CSA was measured 3 times, and the average value was used for analysis.

The examining radiologist was not permitted to ask the patients about symptoms. The only information provided to the examining radiologist was a written request from the referring neurologist that the patient will be examined for the presence of median nerve thickening. Ultrasonographic assessment was performed without knowledge of the clinical and electrodiagnostic test results.

**Statistical analysis**

Statistical analyses were performed by using SPSS Statistics 17.0, Release 17.(Aug 23, 2008). Data are reported as mean ± standard deviations. The Paired –Samples T Test was used to evaluate differences in the pre and post treatment values. Kruskal –Wallis H test was used to evaluate differences between more than two groups of nonparametric data.

**RESULTS**

There were 30 female patients (75%) with a mean age of 47 years (ranging from 25 to 65 years) and 10 male patients (25%) with a mean age of 49 years (ranging from 25 to 65 years). The pertinent values of thyroid hormones at the initial time of diagnosis and those detected months after treatment and restoration of the euthyroid state were compared. Table 1 shows the clinical and electrodiagnostic test results. The mean ± standard deviation values of thyroid hormones at the initial time of diagnosis and those detected months after treatment and restoration of the euthyroid state were compared.

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**Table 3** Motor conduction parameters of tested median nerve before and after hormone replacement therapy (HRT).

|                | Minimum | Maximum | Mean ±SD | P  |
|----------------|---------|---------|----------|----|
| RT. Median N Motor distal latency (m/sec) before HRT | 4.42    | 6.70    | 5.01±0.70 | 0.000 |
| RT. Median N Motor distal latency (m/sec) after HRT | 3.10    | 6.20    | 4.00±0.58 | 0.000 |
| IT. Median N Motor distal latency (m/sec) before HRT | 4.30    | 6.90    | 4.81±0.56 | 0.000 |
| LT. Median N Motor distal latency (m/sec) after HRT | 3.50    | 6.30    | 4.17±0.47 | 0.000 |
| RT. Median N Motor NCV(m/sec) before HRT | 37.00   | 50.00   | 43.92±2.9  | 0.000 |
| RT. Median N Motor NCV(m/sec) after HRT | 45.00   | 54.00   | 49.37 ±2.26 | 0.000 |
| LT. Median N Motor NCV(m/sec) before HRT | 37.00   | 50.00   | 43.35±3.31 | 0.000 |
| LT. Median N Motor NCV(m/sec) after HRT | 45.00   | 53.00   | 48.62±2.2  | 0.000 |
| RT. Median N Motor amplitude(µVolt) before HRT | 3.00    | 7.00    | 5.01±1.2   | 0.000 |
| RT. Median N Motor amplitude(µVolt) after HRT | 4.00    | 7.90    | 6.17±1.05  | 0.000 |
| LT. Median N Motor amplitude(µVolt) before HRT | 3.00    | 7.10    | 5.04±1.19  | 0.000 |
| LT. Median N Motor amplitude(µVolt) after HRT | 4.20    | 7.50    | 6.15±1.05  | 0.000 |

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**Table 4** Sensory conduction parameters of tested median nerve before and after hormone replacement therapy (HRT).

|                | Minimum | Maximum | Mean ±SD | P  |
|----------------|---------|---------|----------|----|
| RT. Median N Sensory distal latency (m/sec) before HRT | 3.50    | 6.00    | 4.41±0.71 | 0.000 |
| RT. Median N Sensory distal latency (m/sec) after HRT | 2.00    | 7.00    | 3.01±0.51 | 0.000 |
| IT. Median N Sensory distal latency (m/sec) before HRT | 3.40    | 6.00    | 4.43±0.75 | 0.000 |
| LT. Median N Sensory distal latency (m/sec) after HRT | 2.00    | 5.00    | 3.54±0.59 | 0.000 |
| RT. Median N Sensory NCV(m/sec) before HRT | 29.00   | 47.00   | 37.87±5.30 | 0.000 |
| RT. Median N Sensory NCV(m/sec) after HRT | 40.00   | 54.00   | 45.15±3.22 | 0.000 |
| LT. Median N Sensory NCV(m/sec) before HRT | 30.00   | 47.00   | 37.16±4.02 | 0.000 |
| LT. Median N Sensory NCV(m/sec) after HRT | 37.00   | 52.00   | 44.62±2.23 | 0.000 |
| RT. Median N Sensory amplitude(µVolt) before HRT | 8.00    | 29.00   | 21.97±5.33 | 0.000 |
| RT. Median N Sensory amplitude(µVolt) after HRT | 12.00   | 33.00   | 25.85±4.93 | 0.000 |
| LT. Median N Sensory amplitude(µVolt) before HRT | 8.00    | 29.00   | 22.42±5.64 | 0.005 |
| LT. Median N Sensory amplitude(µVolt) after HRT | 13.00   | 32.00   | 26.02±5.20 | 0.005 |

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**Table 5** Distal and proximal cross area (CSA) of median nerve before and after hormone replacement therapy (HRT).

|                | Minimum | Maximum | Mean ±SD | P  |
|----------------|---------|---------|----------|----|
| RT. DTS CSA (mm²) before HRT | 9.1     | 17.0    | 12.5±2.4  | 0.0001 |
| RT. DTS CSA (mm²) after HRT | 9.0     | 16.5    | 12.0±2.4  | 0.0001 |
| IT. DTS CSA (mm²) before HRT | 9.5     | 18.0    | 12.4±2.4  | 0.0001 |
| IT. DTS CSA (mm²) after HRT | 9.0     | 16.5    | 12.0±2.3  | 0.0001 |
| LT. DTS CSA (mm²) before HRT | 8.5     | 11.0    | 9.6±0.5   | 0.202  |
| LT. DTS CSA (mm²) after HRT | 8.6     | 11.0    | 9.6±0.4   | 0.0001 |
| RT. PXL CSA (mm²) before HRT | 9.4     | 11.4    | 9.8±0.5   | 0.030  |
| RT. PXL CSA (mm²) after HRT | 9.4     | 11.4    | 9.8±0.5   | 0.030  |

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**Table 6** Comparison between CSA of median nerve before and after HRT as regards to patient’s outcome.

|                | Responded to HRT | Maintained on HRT | Referred for surgery | χ² | P  |
|----------------|------------------|-------------------|----------------------|----|----|
| LT. DTS CSA (mm²) before HRT | 11.6±1.8 | 12.8±2.9 | 15.9±0.9 | 9.001 | 0.007 |
| LT. DTS CSA (mm²) after HRT | 11.4±1.5 | 12.4±2.9 | 15.3±0.6 | 9.836 | 0.007 |
| LT. PXL CSA (mm²) before HRT | 9.7±0.2 | 10.0±0.6 | 10.8±0.4 | 11.139 | 0.004 |
| LT. PXL CSA (mm²) after HRT | 9.6±0.2 | 9.8±0.5 | 10.6±0.7 | 8.604 | 0.014 |
| RT. DTS CSA (mm²) before HRT | 11.6±1.7 | 13.2±2.5 | 16.0±1.0 | 12.618 | 0.002 |
| RT. DTS CSA (mm²) after HRT | 11.2±1.8 | 12.3±2.7 | 15.5±1.0 | 9.642 | 0.008 |
| RT. PXL CSA (mm²) before HRT | 9.5±0.4 | 9.6±0.5 | 10.1±0.4 | 5.021 | 0.081 |
| RT. PXL CSA (mm²) after HRT | 9.5±0.4 | 9.5±0.5 | 10.1±0.5 | 5.394 | 0.067 |
4.41±0.71 m/sec before commencement of hormonal replacement therapy to 3.41±0.51 m/sec after maintenance of the euthyroid state. Moreover, the mean left median nerve sensory distal latency changed from 4.43±0.75 m/sec to 3.5±0.59 m/sec.

As detailed in Table 5, the ultrasonographic assessment revealed a statistically highly significant reduction in distal median nerve cross sectional area (CSA-d) after constitution of an euthyroid state. The mean CSA-d changed from 12.5±2.4 mm$^2$ to 12.0±2.4 mm$^2$ on the right side and from 12.4±2.4 mm$^2$ to 12.0±2.3 mm$^2$ on the left side. On the other hand, the change in proximal median nerve cross sectional area (CSA-p) was much less statistically significant.

Twenty five patients (62.5 %) had satisfactory electrophysiological, ultrasonographic and clinical (if complaining) improvement after 3 months of restoration of an euthyroid state, while fifteen patients (37.5%) failed to achieve such improvement. Out of these 15 patients, 10 (25%) patients of those with carpal tunnel syndrome were maintained on hormone ± nonhormonal treatment for an extended period to get improved. On the contrary, five patients (12.5%) continued to suffer from intractable symptoms of carpal tunnel syndrome despite receiving available nonsurgical treatment modalities and they were referred for surgical release of the carpal tunnel according to standard techniques (Table 1). Of these five patients, three patients refused the option of surgery and preferred to continue on trials for non-surgical control while the remaining two patients were operated upon with a satisfactory post-operative outcome. As shown in Table 6, the patients who responded to hormonal replacement therapy (HRT) had smaller CSA-d ($p<.005$) on both sides than those who partially responded to therapy and who were referred for surgery.

**DISCUSSION**

Carpal tunnel syndrome (CTS) is a combination of signs and symptoms due to compression and trapping of the median nerve at the wrist. It is the most commonly reported peripheral nerve entrapment syndrome. A few studies performed in the United States revealed that CTS accounts for 0.2% of all ambulatory care visits[16] and over 500,000 carpal tunnel releases in 2006[17]. One earlier study reported that in 52% of hypothyroid patients with peripheral nervous system involvement, entrapment neuropathy was the commonest (35%) and axonal neuropathy was recorded in 9% of these patients[20].

In this study, all our selected hypothyroid patients had significantly higher TSH levels and significantly lower FT4 and FT3 levels before hormone replacement therapy. Also, a significant number of our patients showed nerve conduction abnormalities. At the initial time of assessment, all patients had electrophysiological evidence of carpal tunnel syndrome. In our patients, there were higher sensory and motor distal latencies with lower both motor, sensory nerve conduction velocities and lower motor and sensory median nerve amplitudes. These findings were compatible with other investigators that revealed similar involvement of the motor portion of the median nerve and slowing of the nerve conduction velocities in different peripheral nerves but they did not mention the individual values of measured parameters like sensory distal latencies and sensory nerve conduction velocities[20, 21].

Some studies revealed that despite obtaining an euthyroid state, most patients with diagnosis of primary hypothyroidism continue to experience symptoms and electrophysiological signs of carpal tunnel syndrome[16, 22]. In the current study, all patients were newly diagnosed cases with hypothyroidism and the carpal tunnel syndrome symptoms and/or signs and they showed a significant improvement of symptoms and electrodiagnostic findings in 62.5% of patients ($n=25$) after their thyroid functions were normalized with hormonal replacement therapy. This was compatible with the results of Kececi and Degirmenci[13], in their study, they found that 13 out of 15 patients with newly diagnosed hypothyroidism associated with carpal tunnel syndrome improved after 3 months of appropriate hormone replacement treatment. Also, Arafat and his colleagues[23] concluded that 84.2% ($n=48$) of their patients had improvement in their median nerve functions after hormonal treatment, while 15.8% ($n=9$) still had carpal tunnel syndrome symptoms. This variation of response to treatment may be related to severity, duration and treatment regimens of carpal tunnel syndrome.

Currently, carpal tunnel syndrome is typically diagnosed by history taking, physical examination and electrodiagnostic results[24, 25]. Although this approach is effective for localizing the site of pathology and determining the severity of the condition, electrodiagnostic study has its own limitations: it does not provide information about structures surrounding the nerve, it does not allow visualization of abnormalities intrinsic to the nerve, and it is painful[26]. Over the past years, high-resolution ultrasonography has been proposed as a useful tool for the diagnosis of CTS[27-29]. The attraction of ultrasonography for diagnosis of CTS lies in its wide availability, lower cost, noninvasiveness, and shorter examination time[29]. The measurement of cross-sectional area (CSA) of the median nerve at the wrist is the most widely used ultrasonography method in CTS diagnosis. Normal ranges for median nerve area at the distal wrist crease have varied among reports, ranging from 7.2 to 9.8 mm$^2$[29-32], the values for diagnosing CTS range from 9 to 15 mm$^2$[33]. The sensitivity and specificity range from 70 to 88% and 57 to 97%, respectively[34]. In our study, the means of distal CSA were 12.5 and 12.4 mm$^2$ in right and left median nerve respectively, ranging from 9 to 17 mm$^2$. Also, Tengfei et al[34], reported that, the mean inlet CSA was 8.7 mm$^2$ in healthy controls and 14.6 mm$^2$ in CTS. Additionally, Andrea et al[35], reported that distal CSA was 16.8 mm$^2$, Seok et al[36] found that the distal CSA were significantly different from mild, moderate to severe (13.5 mm$^2$, 14.67 mm$^2$ and 18.74 mm$^2$) cases of carpal tunnel syndrome respectively. In the current study, the means of proximal CSA were 9.6 and 9.9 mm$^2$ in right and left median nerve respectively, ranging from 8.6 to 11.4 mm$^2$. Seok et al[37] reported that proximal CSAs for mild, moderate and severe were 7.14 mm$^2$, 6.57 mm$^2$ and 6.39 mm$^2$. Moreover, Andrea et al[38] found only a small difference in proximal CSA between the patients (9.5 mm$^2$ ± 1.9) and the control subjects (8.7 mm$^2$ ± 1.6) and the proximal nerve to be slightly larger in the patients. These different results may be related to several personal risk factors such as age, sex, BMI, external wrist dimensions, severity and duration of hypothyroidism. However, these results indicate that the distal CSA may be much more useful in the diagnosis of CTS than proximal CSA and this conclusion is consistent among most studies, including ours. Furthermore, three months of euthyroid state after hormone replacement therapy, we found significant reduction in distal CSA ($p=.0001$), and much less significant reduction in proximal CSA ($P=.03$). This means that the distal CSA is not only significant in the diagnosis of CTS but also it is important in the follow up after hormonal therapy and it may differentiate between symptoms of CTS and presence of other pathologies.

Surprisingly, we found that the 25 patients (62.5%) who showed clinical and/or electrophysiological improvement after 3 months of euthyroid state had smaller distal CSA (less than 11.6 ± 1.8 mm$^2$). While, the 10 patients who required extended time to be cure recorded large distal CSA (ranging from 12.8 ± 2.9 mm$^2$ to 13.2 ± 2.5 mm$^2$). In contrast, the remaining 5 patients with intractable CTS symptoms
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who were referred for surgery had larger distal CSA (more than 15.9 ± 0.9 mm²) (Table 6). This suggests that the mechanism leading to carpal tunnel syndrome in patients with hypothyroidism might be reversible at early stages; on the other hand irreversible cases might have longer duration of disease or might present etiologies other than hypothyroidism. Long term accumulation of mucinous tissue is a possible cause of irreversibility[22]. Moreover, this may reflect that a large distal CSA of more than 15.5 mm² may be a guide as a significant criterion for selection of patients that may be offered surgical treatment even before initiation of hormonal therapy whenever applicable.

CONCLUSION

With hormonal replacement therapy, carpal tunnel syndrome can be controlled in patients with hypothyroidism within three months of euthyroidism. In addition, in patients having a symptomatic median nerve entrapment, the median nerve cross sectional area can be used as a guide for selection of patients that may benefit from a surgical release even before commencement of medical treatment.

ETHICS STATEMENT

All patients were informed about the content of the study and gave their written approvals before enrollment. All procedures were performed in accordance with the ethical standards of Al-Azhar University’s committee on human experiments.

Author Contribution
Osama A. Khamis, Hegazy M Altamimy, Salama S. Abdellatif, Hossam I. Abdul-Hamied, Ahmed Abdelfattah Mostafa and Ahmad E D Elayouty contributed equally to the manuscript.

REFERENCES

1 Adikesavan B, Gowdhaman N, Vishwanatha R et al. A Study of Nerve Conduction Velocity in Newly Diagnosed Hypothyroid Females. World Journal of Medical Sciences.213; 9 (4): 198-201.
2 Nebuchennykh M, Loseth S, Mellegren S. Aspects of peripheral nerve involvement in patients with treated hypothyroidism. European Journal of Nutrition.2010; 1, 67-72.
3 Shirabe T, Tawara S, Terao A et al. Myxedematous polyneuropathy. A light and electron microscopy study of the peripheral nerve and muscle. J. Neurol. Neurosurg. Psychiatry. 1975;38: 241-7.
4 Rao SN, Katiyar BC, Nair KR et al. Neuromuscular status in hypothyroidism. Acta Neurol Scand.1980; 61: 167-77.
5 Kececi H, Degermenci Y. Hormone replacement therapy in hypothyroidism and nerve conduction study. Clinical Neurophysiology.2006; 36: 79-83.
6 Ferracci F, Carnevale A. The neurological disorder associated with thyroid autoimmunity. J. Neurol.2006; 253(8): 975-84.
7 Deniz Y, Ede F, Filiz K. The effects of hypothyroidism on strength duration properties of peripheral nerve. J. Neurological Sciences.2010; 294(1-2): 89-91.
8 Gelberman RH, Eaton R, Urbanik JR. Peripheral nerve compression. Instr Course Lect.1994; 43:31–53.
9 Kok YC, John G, Khean JG, Tunku SA. Ultrasonography in the evaluation of carpal tunnel syndrome: Diagnostic criteria and comparison with nerve conduction studies. Neurology Asia.2011; 16(1) : 57 – 64.
10 Merle, E.D.D. Spectrophotometric techniques. In Fundamentals of Clinical Chemistry. Tietz WW Fifth edition.2001; Ch 3 P. 56 Sanders Company Philadelphia
11 Murray R. Aspartate and Alanine aminotransferase. Clin Chem. The C.V. Mosby Co. St Louis/Toronto. Princeton1984; 1112-16.
12 Donald B. and George G. Methods for determination of vitamin B12 and Folic acid. In Fundamentals of Clinical Chemistry. Tietz WW Fifth edition.2001; Ch 28 P: 559-62 Sanders Company Philadelphia.
13 Pease C and Byfield P. free thyroid hormone assays and thyroid functions. Ann. Clin. Biochem.1986; 23: 230-237.
14 Wondisford F., Magner J. and Weintraub B. chemistry and biosynthesis of thyrotropin. In Braverman L.E. and Utiger R.D. eds. Werner and Ingbar , the thyroid, 7th ed. Philadelphia Lippincott-Raven.1996:190-207.
15 Ferreira AA, Nazario JC, Periera PJ et al. Effects of experimental hypothyroidism on myelin sheath structural organization. J. Neurocytol.2004; 33(2): 225-31.
16 Kimura G. Assessment of individual nerves. Electrodiagnosis in diseases of nerve and muscle: Principles and practice Edition 3. New York: Oxford University Press.2001; 130-77.
17 Fatemeh Abshiramehchi, Bagher Zaki, Keyvan Basiri et al. A comparison of the ultrasonographic median nerve cross-sectional area at the wrist and the wrist-to-femoral ratio in carpal tunnel syndrome. J Res Med Sci.2014;19(12): 1113–17.
18 Schappert SM, Rechtsteiner EA. Ambulatory medical care utilization estimates for 2006. Natl Health Stat Report.2009; 6:1–29.
19 Cullen KA, Hall MJ, Golosinskiy A. Ambulatory surgery in the United States, 2006. Natl Health Stat Report.2009; 28:1–25.
20 Khedr EM, El-toony LF, Tarkhan MN et al. Peripheral and central nervous system alterations in hypothyroidism: Electrophysiological findings. Neuropsychobiology.2000; 41(2): 88-94
21 Kececi H, Degermenci Y. Hormone replacement therapy in hypothyroidism and nerve conduction study. Clinical Neurophysiology.2006;36; 79-83.
22 Nebuchennykh M, Loseth S, Mellegren S. Aspects of peripheral nerve involvement in patients with treated hypothyroidism. European Journal of Nutrition.2010;1; 67-72.
23 Arafa A. Kasem, Sabry M, Fathy, Doaa A. Shahnin et al. (2014) Carpal tunnel syndrome in hypothyroid patients: The effect of hormone replacement therapy. American Journal of Internal Medicine.2014;2(3): 54-8
24 Wong SM, Griffith JF, Hui AC et al. Carpal tunnel syndrome: diagnostic usefulness of sonography. Radiology.2004;232:93–9
25 Cartwright MS, Hobson-Webb LD, Boon AJ et al. Evidence-based guideline: neuromuscular ultrasound for the diagnosis of carpal tunnel syndrome. Muscle Nerve.2012;46:287–93
26 Cartwright MS, Passmore LV, Yoon JS et al. Cross-sectional area reference values for nerve ultrasonography. Muscle Nerve.2008;37:566–71.
27 Kele H, Verheggen R, Bitterman H et al. The potential value of ultrasonography in the evaluation of carpal tunnel syndrome. Neurology.2003;61:389–391.
28 Visser LH, Smith MH, Lee ML et al. High resolution sonography versus EMG in the diagnosis of carpal tunnel syndrome. J Neurosurg Psychiatry.2008; 79:63–7.
29 Cartwright MS, Shin HW, Passmore LV et al. Ultrasonographic reference values for assessing the normal median nerve in adults. J Neuroimaging.2009;19:47–51.
30 Barthala L, Kumar P, Kumara K et al. Ultrasonographic cross-sectional area normal values of the ulnar nerve along its course in the hand with electrophysiological correlations in 100 Asian subjects. Muscle Nerve.2013;47:673–6.
31 Sugimoto T, Ochi K, Hosomi N et al. Ultrasonographic reference sizes of the median and ulnar nerves and the cervical nerve roots in healthy Japanese adults. Ultrasound Med Biol.2013;39:1560–70.
32 Won SJ, Kim BJ, Park KS et al. Reference values for nerve ultrasonography in the upper extremity. Muscle Nerve 2013;47:864–71
33 Beekman R, Visser L.H. Sonography in the diagnosis of carpal tunnel syndrome: a critical review of the literature. Muscle Nerve.2014;27:26–33.
34 Tengfei Fu, Marlin Cao, Fang Liu et al. Carpal Tunnel Syndrome Assessment with Ultrasonography: Value of Inlet-to-Outlet Median Nerve Area Ratio in Patients versus Healthy Volunteers. PLoS One. 2015;10(1): e0116777.

35 Andrea S. Klauser, Ethan J. Halpern, Tobias et al. Carpal Tunnel Syndrome Assessment with US: Value of Additional Cross-sectional Area Measurements of the Median Nerve in Patients versus Healthy Volunteers. Radiology. 2009;250:1.

36 Seok Kang, Hee Kyu Kwon, Ki Hoon Kim et al. Ultrasonography of Median Nerve and Electrophysiologic Severity in Carpal Tunnel Syndrome. Ann Rehabil Med. 2012; 36: 72-9.

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