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Ultrasonographic changes of the median nerve in patients with end-stage renal failure and comparing it with a control group

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Carpal Tunnel Syndrome (CTS) is characterized by median nerve entrapment in the wrist. CTS is diagnosed by clinical symptoms, which are confirmed by electrodiagnostic studies. This study aimed to assess median nerve cross-sectional area and elastography in chronic hemodialysis patients. This case-control study was conducted on end-stage renal failure (ESRD) patients undergoing hemodialysis at Rasool Akram Hospital's Dialysis Unit. The healthy companions of the patients were included as control group. An experienced rheumatologist used a supersonic device with linear array probes and dynamic scanners (5-22 MHz) to perform the sonography. The current study was conducted on both hands. There was no statistically significant difference between 30 patients and 30 healthy individuals regarding age, weight, and body mass index. The cross sectional area of median nerve in both hands was increased in the dialysis group compared to the control group. However, it was significantly higher in the patient group's right hand than in the control group (P = 0.031). Considering the causes of ESRD and parathormone levels, the cross-sectional area and mean right and left median nerve elastography were not different between the two groups. The results showed that the patient group had a larger right and left median nerve cross-sectional area than the control group. However, the median nerve elastographic indices did not differ between dialysis patients and healthy individuals.

***Keywords*:** Median nerve; Cross-sectional area of median nerve; Elastography; Chronic hemodialysis; Ultrasonography

Introduction

Carpal tunnel syndrome (CTS) is the most common neurological disorder in humans. The median nerve passes through the wrist in an anatomical area known as the carpal tunnel. The elastic rope of the flexor retinaculum from the anterior part surrounds the oval canal. Wrist bones cover the posterior region [1-4]. Increased pressure on the median nerve causes CTS. Clinical trials and electro-physiological evaluation are required to confirm it. According to some studies, the prevalence of CTS is about 2.7% of the general population. The prevalence rate in women is nearly double that of men [5-9]. Pathological examinations reveal increased growth and pressure in the tissue surrounding the nerve [10-12]. Edema of the

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nervous system raises pressure and causes venous congestion, stasis, and nerve ischemia—the stress in the carpal tunnel triples during wrist extension and passive flexion [13, 14].

Genetics, tenosynovitis caused by systemic disorders, increased flexor retinaculum thickness, muscular hypertrophy, canal infiltrative diseases (such as amyloidosis, myeloma, myxedema, bone involvement due to tumor tissue), long flexor tendon synovitis due to increased workload, joint fluid retention, systemic inflammation, bad behavioral habits (severe flexion of the wrist while sleeping, studying, or driving), and occupation (cumulative trauma in certain occupations) are important etiologies of CTS [14-16].

CTS has various symptoms, but the most common clinical manifestations are pain and numbness in the median nerve territory. Neuro-physiological studies show a decrease in nerve conduction velocity due to demyelination from the pressure on the median nerve. Some studies have explored independent risk factors like obesity, female gender and age over 40 [17]. Additionally the utilization of oral contraceptive pills, smoking, premature menopause are recognized as other risk factors [17]. CTS is the most common complaint among hemodialysis patients. Three factors cause CTS in hemodialysis patients: the local effect of arteriovenous fistula (AVF) with edema and increased venous blood pressure, uremic polyneuropathy resulting from chronic renal failure in diabetic patients, and amyloidosis induced by β2-microglobulin deposition [18]. The prevalence of hemodialysis patients experiencing carpal tunnel syndrome (HD-CTS) has risen substantially due to advancements in the hemo-dialysis technique [19]. However, reports differ on the optimal cross-sectional area cutoff for diagnosis and the sensitivity and specificity of this condition [20]. CTS prevalence has been reported in approximately 5% of chronic renal failure patients undergoing hemodialysis. Moreover, more than 50% of patients who undergoing hemodialysis for over 20 years experience the impact of CTS [21,22]. Clinical symptoms of CTS in hemodialysis patients are similar to those of idiopathic CTS.

Nonetheless, the clinical outcomes of surgery vary [23, 24]. CTS is diagnosed based on clinical symptoms, but other tests, such as electro-physiological evaluation and ultrasound, may be used to confirm the diagnosis. Ultrasonography takes less time and causes less patient discomfort, making it a more cost-effective method as a first-line modality for confirming a potential suspected CTS case. Ultrasound findings, such as determining the median nerve cross-sectional area at the tunnel's entrance and exit and the flexor retinaculum, are used to diagnose CTS on a grayscale [25, 26]. Ultrasound elastography (USE) is a tissue stiffness imaging technology first described in the 1990s [27]. In recent years, this method has been gradually developed and used for quantitative tissue stiffness evaluation. Elastography methods use changes in soft tissue elasticity due to specific pathological or physiological processes. For example, many solid tumors are mechanically distinct from the surrounding healthy tissue. In addition, fibrosis in chronic liver diseases stiffens liver tissue, exceeding the normal rigidity of normal organ. Therefore, elastographic techniques can be a promising modality for detecting abnormally stiff tissues. USE has recently been used to evaluate liver fibrosis and characterize breast lesions [28, 29]. Documentation is scarce on the use of USE in Iranian patients with chronic hemodialysis. The present study aimed to compare and investigate median nerve cross-sectional area and elastography in chronic haemodialysis patients with a control group.

Materials and Methods

This case-control study was conducted on hemodialysis patients referred to Rasool Akram Hospital's Dialysis Unit. The research was conducted over a year. Patients with end-stage renal disease (ESRD) who underwent regular hemo-dialysis three times a week for four hours per session for at least six months were included, with permission from the Ethics Committee of Iran University of Medical Sciences (IR.IUMS.FMD. REC.1400.033).

The study excluded patients with systemic inflammatory diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) as the cause of renal failure, as well as hypo-thyroidism, and acromegaly. The control group consisted of healthy patients' companions who volunteered to participate and provided written consent. All patients had a thorough history and laboratory evaluation, which included a CBC,

serum BUN and creatinine, serum calcium, phosphate, and stable parathormone (PTH) or iPTH levels. A skilled rheumatologist utilized a supersonic device with linear array probes and dynamic scanners (5-22 MHz) to perform a sonographic evaluation on both hands of hemodialysis patients and healthy candidates. The data was analyzed using the SPSS software version 22. The variables were first assessed using the Kolmogorov-Smirnov test. The quantitative data were expressed as mean and standard deviation (SD), whereas the qualitative data were expressed as frequency and percentage. The chi-square test, Mann-Whitney U, and t-test were used for inter-group comparisons. The significance level in all the tests was $P < 0.05$.

Results

In our study at Rasool Akram Hospital, 60 patients were referred, 30 of whom were on dialysis. They were assigned to the patient group, while the remaining 30 individuals were healthy and assigned to the control group. Various indices were compared between the two groups, and the data presented in Table 1 revealed no statistically significant difference in age, weight, and body mass index (BMI) between the groups. The cross-sectional area of the median nerve in the right hand of chronic dialysis group was significantly higher than than the control group ($P = 0.031$). In both hands, elastography showed no difference in the median nerve (Table 2). There was no significant difference in mean median nerve cross-sectional area or elastography in both hands at different PTH levels (Table 3). Patients with ESRD divided into 2 subgroups (diabetic and non

Table 1: Distribution of demographic characteristics of participants in the study groups

Variables		Studied groups		P-value
		Patients (n=30)	Healthy people (n = 30)	
Age (years)		61.05	58.14	0.314
Gender	Male	19	16	0.113
	Female	11	14	
Weight (kg)		68.62	71.14	0.113
Height (cm)		166	163	0.592
Body mass index (kg/m^2)		25.09	26.14	0.078

Independent Samples Test was used. The value of $P < 0.05$ was considered significant.

Table 2: Cross-section of the median nerve at elastography in the study groups

Variables			Studied groups		P-value
			Patients (n = 30)	Healthy people (n = 30)	
Cross section of median nerve	Right		9.16 ± 2.72	7.81 ± 2.37	0.031
	Left		8.88 ± 2.45	8.20 ± 2.20	0.223
Median nerve elastography	Right	First turn	70.63 ± 82.64	58.87 ± 37.31	0.647
		Second turn	72.46 ± 66.10	72.09 ± 72.28	0.842
		Average	71.55 ± 70.94	65.48 ± 46.24	0.807
	Left	First turn	50.20 ± 36.17	48.74 ± 38.99	0.673
		Second turn	59.87 ± 47.65	66.27 ± 80.71	0.433
		Average	55.04 ± 38.46	57.51 ± 55.23	0.496

Mann-Whitney U test was used. The value of $P < 0.05$ was considered significant.

Table 3: Cross-section of the median nerve at elastography in the patient groups according to different levels of PTH

Variables			Levels of PTH			P-value
			0-150 (n = 3)	150-300 (n = 11)	> 300 (n = 16)	
Cross section of median nerve	Right		8.42 ± 2.15	8.74 ± 2.55	9.58 ± 2.99	0.567
	Left		8.27 ± 0.21	8.51 ± 2.36	9.25 ± 2.75	0.942
Median nerve elastography	Right	First turn	74.73 ± 44.96	40.33 ± 24.14	90.70 ± 106.9	0.301
		Second turn	69.86 ± 38.34	68.47 ± 62.56	75.69 ± 74.95	0.629
		Average	72.30 ± 28.42	54.40 ± 40.62	83.19 ± 90.30	0.652
	Left	First turn	39.80 ± 40.90	43.55 ± 28.91	56.61 ± 40.46	0.560
		Second turn	38.70 ± 23.49	57.23 ± 39.40	65.66 ± 56.13	0.656
		Average	39.25 ± 31.28	50.39 ± 28.79	61.19 ± 45.50	0.774

PTH, parathyroid hormone
The Kruskal-Wallis test was used. The value of $P < 0.05$ was considered significant.

diabetic). Further analysis revealed significant differences in the elastography of the median nerve between the two groups in both hands The diabetic group's median nerve cross-sectional area was also larger in the right hand, as shown in Table 4.

Table 4: Cross-section of the median nerve at elastography in diabetic and non-diabetic subgroups in the ESRD group

Variables			ESRD groups		P-value
			Diabetics patients (n= 17)	Non- diabetics patients (n = 13)	
Cross section of median nerve	Right		10.02 ± 2.55	8.05 ± 2.62	0.050
	Left		9.34 ± 2.63	8.28 ± 2.14	0.238
Median nerve elastography	Right	First turn	96.59 ± 10.1	36.69 ± 21.28	0.030
		Second turn	87.77 ± 79.17	52.44 ± 37.87	0.120
		Average	92.18 ± 86.52	44.56 ± 27.94	0.046
	Left	First turn	60.31 ± 38.21	36.98 ± 29.68	0.070
		Second turn	74.94 ± 52.67	40.17 ± 32.34	0.035
		Average	67.62 ± 42.11	38.58 ± 26.32	0.029

ESRD, end satge renal damag
Mann-Whitney U test was used. The value of P less than 0.05 was considered significant.

Discussion

The study aimed to evaluate the ultrasonic indices of the median nerves in the right and left hands of patients who underwent chronic hemodialysis. The results were compared with a control group. Ultrasound is an effective tool for detecting entrapment neuropathy as it can visualize changes in nerve size and echotexture. Additionally, it can recognize nerve fascicles hypertrophy or complete disorganization and detect nerve thickening and stiffening, which may not be evident during a physical examination. Ultrasound is, therefore, more precise in identifying nerve thickness changes and subsequent damages [30,31].

Research has found that the size of the median nerve upon entering the wrist is the most reliable indicator of CTS. This is because when the median nerve becomes compressed in the wrist, it leads to swelling and an increase in size (also known as cross-sectional area or CSA) of the nerve, as is visible in a 2D ultrasound image. The

accumulation of fluid and growth of fibrous tissue in the wrist are the primary causes of CTS [32, 33]. The most importantl parameter for diagnosis of CTS is when the median nerve cross-sectional area is greater than 10 mm2 [34].

The study revealed that among chronic dialysis patients and healthy controls, the median nerve's average cross-sectional area was below 10 mm2. Nevertheless, a few patients recorded higher values. Specifically, 10 out of 30 patients had a cross-section exceeding 10 mm2 in their right hand, and six in their left. In contrast, only three patients in the control group exceeded this threshold. It is important to note that the presence or absence of CTS in these patients requires further verification. CTS is a widespread ailment impacting many individuals. Numerous factors contribute to the development of CTS, such as being female gender, obesity, diabetes, hypothyroidism, rheumatoid arthritis, and having a family history of this condition. One theory supposed increased pressure within the carpal tunnel may cause vascular trauma, ultimately damaging the median nerve and leading to CTS. While the cause of CTS remains unknown in most cases, ultrasound scans may uncover hypertrophy of the flexor digitorum profundus muscle in some patients, which could displace muscle tissue and contribute to CTS [35, 36]. In a study conducted by Miyamoto et al. [37] , the elasticity and cross section area values of median nerve of 22 healthy individuals (44 hands) and 31 individual with CTS wer examined. The results revealed that the cross-sectional area and elasticity of the median nerve in CTS patients were significantly higher than in normal subjects ($P < 0.01$). In our study, we found that the cross-sectional area of dialysis patients was significantly higher than that of the control group, particularly in the right hand ($P = 0.031$). Our study showed no significant difference in left and right median nerve elastographic indices between the two groups in almost all parts.

Conclusions

According to the study, the patient group exhibited higher cross-sectional areas of the right and left median nerves than the control group. The research found no significant difference in the elastographic indices between dialysis patients and healthy individuals.

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Conflict of Interest

The authors state that they have no conflicts of interest.

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