Examination of the cross-sectional area of the carpal tunnel on fetal cadavers

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SUMMARY

This study aimed to determine the anatomical features of the carpal tunnel (CT) in fetal cadavers and understand the role of etiology in the development of carpal tunnel syndrome (CTS). Seventy hand-wrist regions (35 right, 35 left) of 35 fetal cadavers (24 females; 11 males) that were not exposed to environmental factors and handedness were examined. The contents and cross-sectional area (CSA) of the CT were measured using ImageJ©. The CSA consisting of the flexor tendons and median nerve (MN) in the CT were calculated as a percentage. The results showed that the area covered by the MN and flexor tendons in the CT was significantly smaller in female fetuses ($P<0.05$). There was no significant difference in other ratios between male and female fetuses ($P>0.05$). There was no significant difference in the ratios regarding the CT and contents between the right and left-hand sides ($P>0.05$). It was concluded that the difference in CT anatomy may help explain the variations in the prevalence of CTS among genders. The lack of a difference between the right- and left-hand sides supports the theory that repetitive hand activities, hand dominance, and functional factors play a key role in the development of CTS by causing morphological changes in the CT, MN, and flexor tendons. In our opinion, the examination of CTs that have not been exposed to any environmental effects may provide guidance in understanding the effect of anatomical and morphometric features on the etiology of CTS.

Key words: Carpal tunnel syndrome – Hand – Median nerve – Mononeuropathy – Wrist

INTRODUCTION

The carpal tunnel (CT) is an osteofibrous tunnel which is located between the transverse carpal ligament and the carpal bones. Ten structures pass through the CT. These structures are the median nerve (MN), four tendons of the flexor digitorum superficialis (FDS), four tendons of the flexor digitorum profundus (FDP) and the tendon of the flexor pollicis longus (FPL) (Chammas et al., 2014; Rotman and Donovan, 2002). Carpal tunnel syndrome (CTS) develops due to the compression of the MN under the transverse carpal ligament while passing through the CT (Kim et al., 2013). The etiology of CTS is essentially idiopathic. It

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is also associated with abnormalities in the CT structures (carpal bone deformities, subluxation, distal radius fractures, wrist arthrosis, inflammatory arthritis, acromegaly, etc.). Other factors in the etiology are gender (female), obesity, diabetes mellitus, infection, vibration tools, burns, and hemophilia (Chammas et al., 2014; Newington et al., 2016).

The best-known parameters regarding CT morphometry relate to the cross-sectional area (CSA) of the CT and its contents. It has been shown that morphological changes in the CSA of the CT associated with overuse, profoundly affect the dominant hand (Dec and Zyluck, 2018; Lakshminarayanan et al., 2020; Newington et al., 2016). However, only a few studies have compared CT anatomy and morphometry by hand side. Earlier research has investigated the relationship between CT morphometry and gender. It has been reported that the CSA of the CT and its contents are smaller in women when compared to men (Bower et al., 2006; Pacek et al., 2010; Peterson et al., 2013).

When literature is examined, it can be seen that only a few studies have investigated the CT region in fetal cadavers. Some researchers have focused on the anatomy of the CT in adult cadavers. Adults are more likely to develop CTS as a result of morphological changes that occur in the CT, MN, and FTs due to exposure of environmental factors and overuse of the dominant hand (Bland, 2005; Loh et al., 2019; Marquardt et al., 2016). In the present study, the anatomy of the CT was examined more objectively, because it focused on fetal cadavers that were not exposed to environmental risk factors and handedness. The aim of this study was to determine the anatomical features of CT in fetal cadavers and clarify the role of CT anatomy in the development of CTS. Furthermore, it was planned to establish a basis for future studies by investigating the structure of the CT in the fetal period.

MATERIALS AND METHODS

The sample group consisted of 35 fetal cadavers (24 females; 11 males). The ages of the sample group were determined using the foot length method (Mercer et al., 1987), and it was determined that the fetal cadavers had an intrauterine age of 21.2 to 39.2 weeks. The cadavers were examined in the Anatomy Department of Karadeniz Technical University. The study was approved by a local ethics committee (Protocol number: 2018/72, Decision date: May 25, 2018) and was conducted in accordance with the ethical principles outlined by the Declaration of Helsinki. All cadavers had been embalmed in 10% formaldehyde solution. The upper extremities of the cadavers had no external pathology or anomaly. Gender was identified based on the external morphology of gonads. The cadavers were grouped according to their gender. Each cadaver was assigned a number.

The palmar faces of the wrist and hand were dissected using classical anatomical dissection methods. A consensus was reached on the dissection protocol. The same researcher performed all the dissection and subsequent procedures. All dissections were performed under a surgical microscope (Kaps [SOM]® 62, Asslar, Wetzlar, Germany). After removing the skin and subcutaneous adipose tissue, the transverse carpal ligament forming the roof of the CT was identified.

Following the dissection process, the wrists were cut proximal to the distal wrist fold and separated from the forearm. The hand samples were frozen at -18 °C. The proximal and distal borders of the transverse carpal ligament were determined by the insertions of the transverse fibers at the trapezium, hamate, scaphoid and pisiform. A single section, perpendicular to the CT short axis was obtained with a guillotine mechanism from the determined level. In each hand specimen, a single cut was made concerning a line parallel and equidistant from the proximal and distal borders of the transverse carpal ligament. Thus, all samples were equivalent (Fig. 1). All exposed sections were photographed at a 90° angle to the center of the CT. The images were recorded as the right and left-hand sides for each fetal cadaver.

The images were analyzed using ImageJ©, an image analysis program developed by US NIH Image. The program is Java-based, open-source, enables free ImageJ© software edits and analyzes images and measures area, distance, and angles. It can read many image formats, such as TIFF, GIF, JPEG, and DICOM (Schneider et al., 2012). The im-

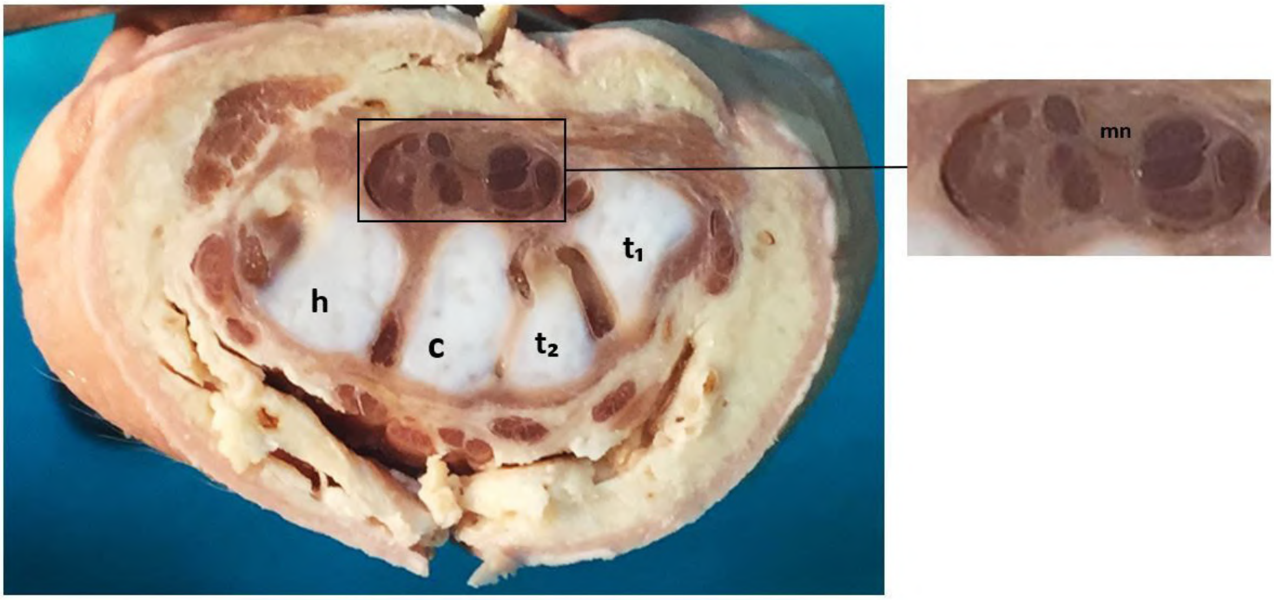

Fig. 1.- Transverse section of the carpal tunnel in a 38.4-week-old male fetus (t_1: trapezium, t_2: trapezoid, c: capitate, h: hamate, mn: median nerve).

ages used in this study were in JPEG format. All measurements were repeated three times by the same researcher.

The arithmetic mean was calculated and recorded as right and left-hand sides for each fetal cadaver.

First, the "Polygon Selection" tool was used to determine the boundaries of CT and MN. Second, the cross-sectional areas of CT and MN were calculated using the "Measure" tool (Fig. 2, Fig. 3).

The areas covered by the tendons were determined using the "Threshold" method to measure the CSAs of the flexor tendons. Calculations were made using the "Measure" tool. Thus, the CSAs of the FPL, FDS, and FDP tendons, and the total flexor tendons were determined (Fig. 4).

Fig. 2.- Determining the borders and measuring the CSA of the carpal tunnel by ImageJ.

Fig. 3.- Determining the borders and measuring the CSA of the median nerve by ImageJ.

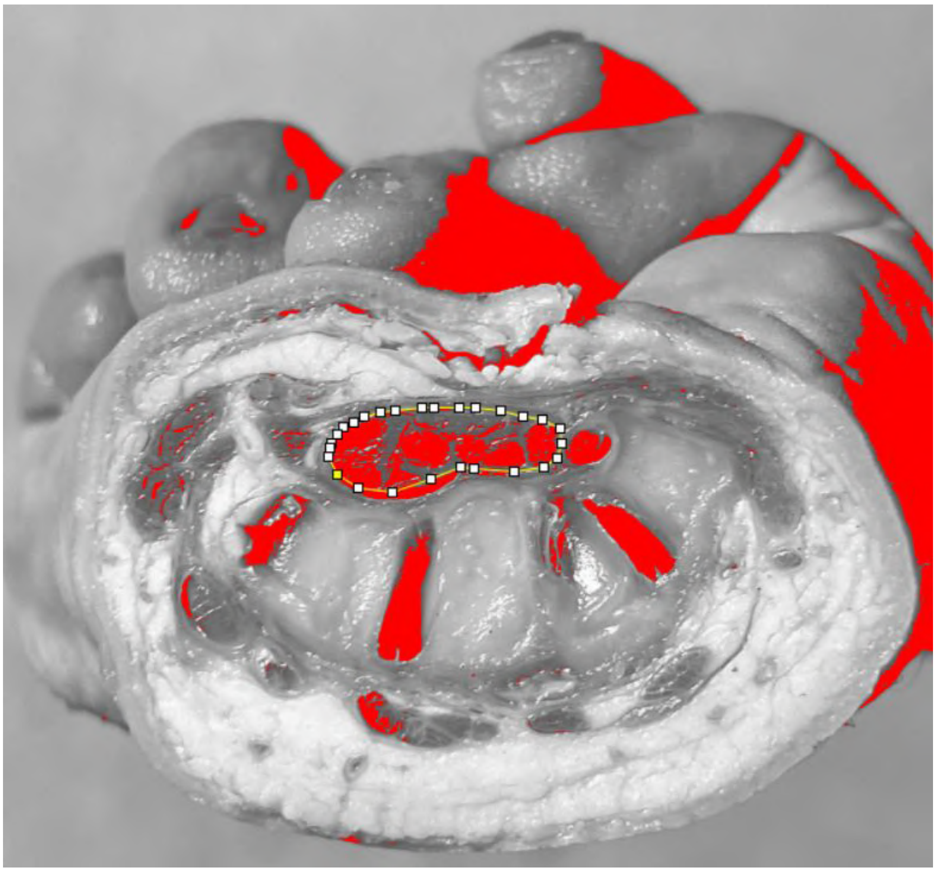

Fig. 4.- Determining and measuring the CSA covered by the all flexor tendons with ImageJ.

The height of the tunnel (CTH) was measured as the maximum length between the dorsal boundary of the transverse carpal ligament and the volar boundary of the capitate bone. The distance between these two points was calculated using the "Measure" tool. The maximum distance between the medial and lateral borders of the tunnel was calculated using the "Measure" tool to obtain the width of the tunnel (CTW).

Ratio calculations were made regarding the CSAs of the CT, MN, and flexor tendons. Thus, the percentage value of the area covered by the nerve and flexor tendons in the tunnel was obtained.

The ratio of the area covered by the MN in the CT (MN/CT) was calculated as follows:

$$MN / CT = CSA_{MN} / CSA_{CT} \times 100$$

The following equation was used to determine the ratio of the area covered by the FPL tendon (FPL/CT), FDS and FDP tendons (FDS.FDP/CT), and all flexor tendons (TFT/CT) in the CT:

$$TFT / CT = CSA_{FT} / CSA_{CT} \times 100$$

The ratio of the total area covered by the MN and all flexor tendons in the carpal tunnel (MN.TFT/CT) was calculated as follows:

$$MN.TFT / CT = MN / CT + TFT / CT$$

The ratio of the empty area outside the CT content (EA/CT) was calculated as follows:

$$EA / CT = 100 - MN.TFT / CT$$

The following equation was used to calculate the CT ratio (CTR):

$$CTR = CTH / CTW$$

The data were analyzed using the Statistical Package for Social Sciences (SPSS 23.0, IBM, Armonk, NY, United States of America) at a significance level of 0.05. Mean and standard deviation (SD) values were used for numerical variables. The Shapiro Wilk test was used for normality testing. The results showed that the data were normally distributed. The data were analyzed using a student's t-test.

RESULTS

This study examined 70 hand-wrist regions (35 right and 35 left) of 35 fetal cadavers. The ratios of the CSAs of the CT, MN and flexor tendons were calculated. The data were compared based on hand side and gender.

There was no difference between intrauterine ages according to gender (p> 0.05) (Table 1). Male fetal cadavers had a significantly higher right MN.TFT/CT ratio than their female counterparts (p<0.05). Female fetal cadavers had a significantly higher right EA/CT ratio than their male counterparts (p<0.05). There was no significant difference in the other parameters between male and female fetal cadavers (p>0.05) (Table 2).

There were no significant differences in the ratios regarding the CT and its content between the right and left-hand sides (p>0.05) (Table 3).

Table 1. Comparison of mean intrauterine ages by gender.

Gender		Intrauterine age (week)		
	n	Min	Max	Mean±SD
Female	24	21.2	39.2	27.68±4.59
Male	11	22.7	38.4	28.83±4.88
Total	35	21.2	39.2	28.04±4.64

Table 2. Comparison of ratio calculations by gender.

Ratio	Right Side (Mean±SD)			Left Side (Mean±SD)		
	Female (n=24)	Male (n=11)	p	F (n=24)	M (n=11)	p
MN/CT	7.401±1.775	8.100±1.938	0.301	7.470±1.756	7.500±1.759	0.963
FPL/CT	5.600±1.474	6.148±9.205	0.281	5.417±1.727	6.098±1.492	0.268
FDS.FDP/CT	37.761±6.558	42.627±9.205	0.082	39.030±6.315	39.196±7.673	0.946
TFT/CT	43.361±6.779	48.754±8.757	0.055	44.451±6.262	45.296±8.720	0.746
NM.TFT/CT	50.762±7.557	56.855±8.482	**0.041***	52.461±7.471	53.451±9.509	0.741
EA/CT	49.237±7.557	43.145±8.481	**0.041***	47.517±7.503	47.414±9.332	0.972
CTR	0.392±0.074	0.372±0.063	0.440	0.419±0.083	0.412±0.097	0.838

CT Carpal tunnel, *CSA* Cross-sectional area, *MN* Median nerve, *FDS* Flexor digitorum superficialis muscle, *FDP* Flexor digitorum profundus muscle, *FPL* Flexor pollicis longus muscle, *TFT* Total flexor tendons, *MN/CT* The proportional value of the CSA covered by the median nerve in the carpal tunnel FPL/CT: The proportional value of the CSA covered by the FPL tendon in the carpal tunnel, FDS.*FDP/CT* The proportional value of the CSA covered by the FDS and FDP tendons in the carpal tunnel, *TFT/CT* The proportional value of the total area covered by all flexor tendons in the carpal tunnel, *NM.TFT/CT* The proportional value of the total area covered by the carpal tunnel contents, *EA/CT* The proportional value of the empty area outside the carpal tunnel contents, *CTR* Carpal tunnel ratio. *p<0.05

DISCUSSION

Research shows that the CSA is an important morphological factor due to the area allocated to the contents of the carpal tunnel (Michelsen and Posner, 2002; Mitchell et al., 2009). It has been shown that the CSAs of the MN and flexor tendons (FTs) are greater larger in people with CTS and that the CSA of the CT, MN, and FTs is are associated with the compression of the MN in the tunnel (Lee et al., 2005; Li et al., 2011; Monagle et al., 1999). In this study the cross-sectional areas of the CT and its contents were measured. The cross-sectional areas covered by the flexor tendons and MN in the CT were calculated as a percentage. The data were compared according to hand side and gender.

Research shows that women are more likely to develop CTS due to smaller hand dimensions and CTs, hormonal factors, and pregnancy (Ablove and Ablove, 2009; Becker et al., 2002; Sassi and Giddins, 2016). Peterson et al. (2013) found that

Table 3. Comparison of ratio calculations by right and left-hand sides.

Ratio	Right Side (n=35)	Left Side (n=35)	
	Mean±SD	Mean±SD	p
MN/CT	7.621±1.829	7.479±1.731	0.740
FPL/CT	5.772±1.376	5.631±1.666	0.701
FDS.FDP/CT	39.290±7.698	39.082±6.665	0.904
TFT/CT	45.056±7.752	44.717±7.003	0.848
NM.TFT/CT	52.677±8.248	52.772±8.035	0.961
EA/CT	47.322±8.247	47.485±7.981	0.933
CTR	0.386±0.071	0.417±0.087	0.111

CT Carpal tunnel, *CSA* Cross-sectional area, *MN* Median nerve, *FDS* Flexor digitorum superficialis muscle, *FDP* Flexor digitorum profundus muscle, *FPL* Flexor pollicis longus muscle, *TFT* Total flexor tendons, *MN/CT* The proportional value of the CSA covered by the median nerve in the carpal tunnel FPL/CT: The proportional value of the CSA covered by the FPL tendon in the carpal tunnel, *FDS.FDP/CT* The proportional value of the CSA covered by the FDS and FDP tendons in the carpal tunnel, *TFT/CT* The proportional value of the total area covered by all flexor tendons in the carpal tunnel, *NM.TFT/CT* The proportional value of the total area covered by the carpal t

female cadavers had smaller CSA of the CT than male cadavers, whereas the latter had smaller CTR than the former. Lakshminarayanan et al. (2019) reported that the height of the carpal arch, and the CSA of the CT were smaller in women at both distal and proximal levels. They concluded that women had a smaller CTR distally, but there were no differences in CTR between men and women proximally. Pacek et al. (2010) examined fresh-frozen hand samples and determined that females had narrower and smaller CTs than their male counterparts. Bower et al. (2006) examined the CSAs of the CT and its contents in healthy individuals. They reported that compared to females, both the CT and its contents were larger in males. However, they found that there was no difference in the ratios between content and tunnel size. Our results showed that the area covered by the structures forming the contents of the CT (MN.TFT/CT) was significantly smaller in female fetuses than in male fetuses ($p<0.05$) (Table 2). This difference in the CT anatomy of fetal cadavers may help explain the variations in the prevalence of CTS among genders.

Zambelis et al. (2010) argue that hand dominance affects the risk for developing CTS and state that right-hand-dominant patients are five times as likely to develop CTS in their right hands, while left-hand-dominant patients are thirteen times as likely to develop CTS in their left hands. Furthermore, Thomsen et al. (2008) showed that CTS had a higher prevalence in the dominant hand. Cobb et al. (1997) calculated the ratio of the volume of the contents of the CT to the volume of the carpal tunnel. They found that this rate was higher in CTS. In another study examining CT and its content, it was seen that the CSA of the CT was not significantly different in individuals with CTS and healthy individuals. However, it was observed that the area covered by the content in the carpal tunnel increased in CTS patients (Oge et al., 2012). Tagliafico and Martinoli (2013) compared the CSA of the MN according to hand side in healthy individuals. They found that there were no differences in CSA of the MN between dominant and non-dominant hands. Asghar et al. (2022) reported that the CSA of the MN in healthy adults was not different according to hand side and hand dominance. Our results showed that the CSAs of the CT and its contents did not differ significantly between the right and left- hand sides ($p>0.05$) (Table 3). Although carpal tunnel syndrome is rarely seen in children, there is no fetal-period evidence that explains the presence of CTS in the dominant hand in adulthood. Druzhinin et al. (2019) examined the CSA of the MN in children. They found that there was no statistically significant difference between right and left sides. In another study measuring the CSA of the MN in children, it was reported that the CSA of the MN increased with age, but no comparison was made according to the hand side. (Cartwright et al., 2012). Given that intrauterine handedness does not affect the morphology of the tunnel, the present study examined the structure of the CT by eliminating the hand dominance factor. The lack of difference between the right and left-hand sides supports the theory that repetitive hand activities, hand dominance, and functional factors play a key role in the development of CTS by causing morphological changes in the CT, MN, and flexor tendons (Lakshminarayanan et al., 2020; Newington et al., 2016). The present study examined the morphometry of CT in the wrists of fetal cadavers, in relation to CTS which is associated with overuse in adulthood. In our opinion, the examination of CTs that have not been exposed to any environmental effects may provide guidance in understanding the effect of anatomical and morphometric features on the etiology of CTS.

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