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Research article

Quantitative anatomical analysis of the carpal tunnel in women and men

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A R T I C L E I N F O

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A B S T R A C T

Purpose: The main objective of this study was to identify anatomical differences between men and women in the absolute and relative size of the carpal tunnel (CT), its inner structures, and related external anatomical structures in order to shed light on the higher prevalence of CT syndrome (CTS) in women.
Basic procedures: We have dissected the forearms and hands of ten men and ten women and compared the cross-sectional area (CSA) of the CT between the two sexes. The size of the CT relative to the tendons passing through it, the median nerve (MN), and to hand and wrist size was also compared between men and women.
Main findings: The absolute CSAs of the CT and other parameters were larger in men than in women. The CSA of the CT relative to the length of the capitate bone was also larger in men. However, no significant differences were observed between men and women in the size of the CT relative to its inner structures.
Principal conclusions: The size of the inner structures of the CT are in proportion to that of the CT itself in both sexes. These findings suggest that the etiology of CTS seems to be primarily related to workload and personal traits.

1. Introduction

The compression of the median nerve (MN) inside the carpal tunnel (CT), known as carpal tunnel syndrome (CTS), is currently the most well-known and frequent form of MN neuropathy (Atroshi et al., 1999; Keith et al., 2009), accounting for 90% of all entrapment neuropathies (Aroori and Spence, 1999). CTS typically involves pain or dysesthesia of the first, second and third fingers and weakness of thumb abduction (Franzblau and Werner, 1999; Iyer and Shetty, 2012). The symptoms tend to be worse at night and disappear by the morning. If there is progressive worsening of CTS, it can result in muscle atrophy of the thenar muscles (Rea, 2015).

The CT (Fig. 1) is an osteofibrous outlet formed by the flexor retinaculum (transverse carpal ligament) and the volar radiocarpal ligaments (Drake et al., 2020). The flexor retinaculum is attached to the bone tubercles of the trapezius and scaphoid on the radial side, and to the hook of the hamate and pisiform bones on the ulnar side (Gilroy et al., 2011). It is divided into superficial and deep layers, and the separation between these layers contains the tendon of the flexor carpi radialis muscle (Rea, 2015; Drake et al., 2020). The ulnar aspect of this ligament forms Guyon's canal (Depukat et al., 2014). In most cases, four tendons of the flexor digitorum superficialis muscle (FDS), four tendons of the flexor digitorum profundus muscle (FDP), and a single tendon of the flexor pollicis longus muscle (FPL), pass through the CT, along with the tendon sheaths and the MN (Gilroy et al., 2011; Netter, 2011). Such a large number of structures sharing the same space makes it susceptible to neural compression.

The etiology of CTS is multifactorial and includes personal and physical workload factors (Palmer et al., 2007; Dale et al., 2013), such as the need for a prolonged flexion-extension of the wrist associated with a high hand-force requirement (Van Rijn et al., 2009). Obesity (Shiri et al., 2015), diabetes mellitus (Pourmemari and Shiri, 2016), hypothyroidism (Shiri, 2014), ostheoarthritis and rheumatoid arthritis (Shiri, 2016) are all documented risk factors for CTS. Menopause and pregnancy may also increase the risk of CTS due to edema and hormonal alterations (Padua et al., 2016). Certain anatomical variations can also play a role, including the presence of a reversed palmaris longus muscle, with a proximal tendon originating at the medial epicondyle of the humerus, a distal muscle belly in the forearm, and an insertion at the flexor retinaculum and the pisiform bone (Olewnik et al., 2017; Twoon et al., 2017; Olewnik et al., 2018). Other anatomical variations include a palmaris profundus muscle (Orellana-Donoso et al., 2021), with the tendon below the flexor retinaculum, the presence of lumbrical muscles in the CT (Orellana-Donoso et al., 2021), and a persistent median artery (Osiak et al.,

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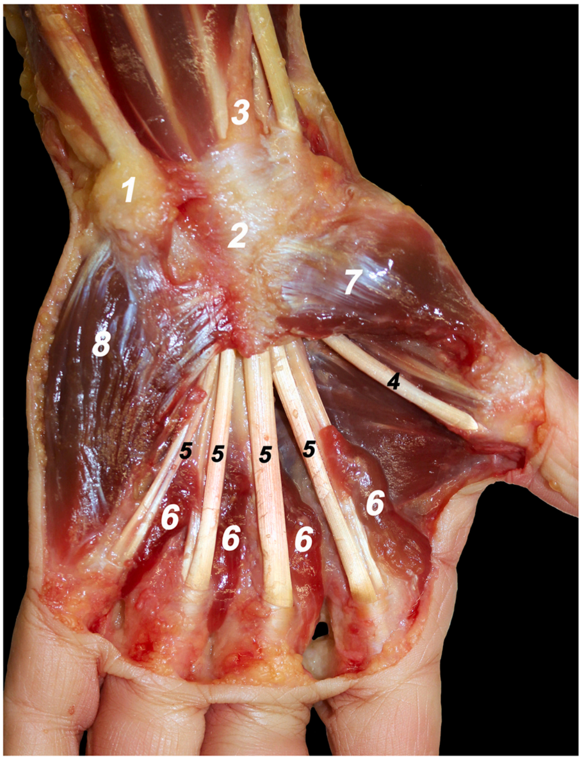

Fig. 1. Palmar view of an anatomical dissection of the carpal tunnel and the inner structures**.** 1 =Pisiform, 2 =Flexor retinaculum, 3 =Median nerve, 4 =Flexor pollicis longus tendon, 5 =Flexor digitorum superficialis and profundus tendons, 6 =Lumbrical muscles, 7 =Thenar muscles, 8 =Hypothenar muscles.

2021; Park et al., 2021; Solewski et al., 2021). The prevalence of CTS varies between studies, although it is generally accepted to be around 3–6%, with higher rates seen in women and in individuals aged 45–60 years (Kuschner et al., 1992; Stevens et al., 1998; Atroshi et al., 1999, 2011; Aroori and Spence, 1999; Franzblau and Werner, 1999; D'Arcy, McGee, 2000; Iyer and Shetty, 2012). In most studies, the probability of CTS is higher in women than in men, with 3:1 being the most common ratio (Solomon et al., 1999; McDiarmid et al., 2000; Papanicolaou et al., 2001; Becker et al., 2002; Bongers et al., 2007; Harris et al., 2013; Jackson et al., 2018; Cazares et al., 2020). The treatment of CTS is generally nonsurgical and includes modification of daily habits, non-steroidal anti-inflammatory drugs (NSAIDs), wrist splints, local corticosteroid injections, ultrasound, and physical therapy. If surgery is indicated, the flexor retinaculum is sectioned to relieve pressure on the median nerve (Huisstede et al., 2014; Padua et al., 2016).

The higher rates of CTS in women have been attributed to several factors, such as hormonal fluctuation or smaller wrist, hand and CT size (McDiarmid et al., 2000; Cazares et al., 2020). There have been many attempts to measure the CT and its related structures with X-rays, computed tomography, magnetic resonance imaging (MRI) and ultrasound. Dekel and Coates (1979) were the first to use X-rays to measure the CT cross-sectional area (CSA) and compare it between sexes. These authors measured the proximal and distal CSA of the CT and found that the absolute size of both measures was smaller in women. Merhar et al. (1986) obtained similar results using computed tomography and additionally found that the distal aspect of the CT was smaller than the proximal. However, these studies only considered the absolute CSA values, without normalizing these values relative to the inner structures of the CT or to related external anatomical structures, such as the hand or wrist.

More recently, several studies have been performed with MRI. Monagle et al. (1999) found that men had larger CSAs than women, and Bower et al. (2006) found that the absolute values of the CT CSA, the CT volume (CTV) and the inner structures of the CT were larger in men than in women, but the CSA and CTV values relative to the inner structures were similar. Also using MRI, Sassi and Giddins (2016) defined relative CT CSA as the CSA divided by the length of the capitate bone, a parameter related to the size of the hand (HS) and observed that this relative CSA was significantly higher in men than women. Lakshminarayan et al. (2019) used ultrasound to measure the CSA of the CT inlet and outlet, normalized these measurements relative to wrist size (WS), and found a smaller ratio in women.

Based on these results, several anatomical features have been proposed to account for the higher rate of CTS in women, primarily their smaller WS (Farmer and Davis, 2008), a smaller CT CSA relative to WS (Lakshminarayanan et al., 2019) and to HS (Sassi and Giddins, 2016). In addition, women have been shown to have a less elastic transverse carpal ligament than men (Li, 2005), which may indicate an inadequate space for the structures contained in the CT. However, no differences between the sexes have been reported in the size of the CT relative to the size of its inner structures (Monagle et al., 1999; Bower et al., 2006; Yao and Gai, 2009).

To the best of our knowledge, only one study has examined the CT using anatomical dissection (Peterson et al., 2013). They found that women have a significantly smaller CT CSA than men, and also a greater depth-to-width ratio. They proposed that the "squarer" CT in women could be associated with compression of the MN. However, they did not calculate the value of these measurements relative to the inner structures of the CT or to external anatomical structures.

In the present study, we have anatomically dissected 20 healthy wrists and compared our findings in men and women. Unlike Peterson et al. (2013), we have also calculated the CT CSA relative to that of its inner structures and, in line with previous studies (Nattrass et al., 1994; Sassi and Giddins, 2016; Lakshminarayanan et al., 2019), to WS and HS. Although these measurements have previously been compared between men and women, the present study is the first to perform a detailed anatomical dissection of cadaveric samples. The main question that we attempted to answer was whether women have a smaller CT relative to the tendons and median nerve contained in the CT. If so, this would indicate that the greater frequency of CTS in women is due to the anatomy of their CT. Our working hypothesis was that the tendons and the MN contained in the CT would be smaller in women and that the ratio of the tendon CSA to the CT CSA or of the MN CSA to the CT CSA would be similar in the two sexes. With this study, we aim to shed light on the question of whether the smaller CT in women is a risk factor for CTS.

2. Material and methods

2.1. CT samples

Macroscopic dissections of the forearm and hand were performed on 20 non-treated human cadavers donated to the Body Donation Service of the University of Barcelona (Barcelona, Spain). All dissections were performed in the Human Embryology and Anatomy Unit of the University of Barcelona. All samples were frozen post-mortem at − 18ºC until 24 h before the study, when they were unfrozen and stored at 4ºC. None of the individuals presented macroscopic signs of CTS, including muscular atrophy or nerve impingement. Ten individuals were men, with a mean age of 80.9 years (range, 62–94), and ten were women, with a mean age of 84.7 years (range, 76–92). Ten of the dissected samples were from the right arm (five men and five women) and ten from the left arm.

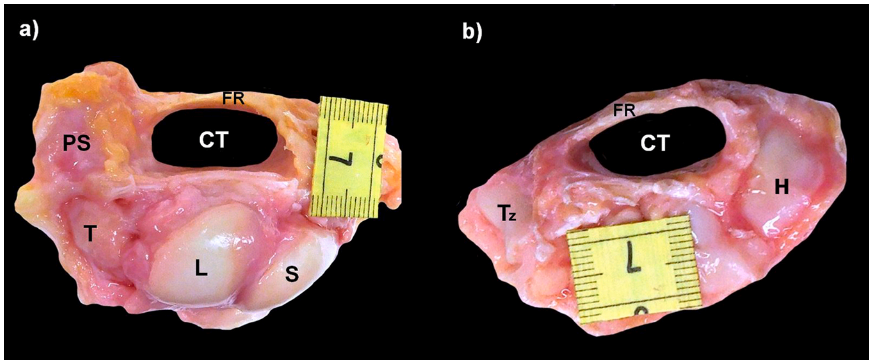

Fig. 2. Proximal (a) and distal (b) view of the carpal tunnel. FR=Flexor retinaculum, CT=Carpal tunnel, PS=Pisiform, T = Triquetrum, L=Lunate, S=Scaphoid, Tz=Trapezium, H=Hamate.

2.2. Anatomical dissections and measurements

All anatomical dissections were performed by the same investigator (PR) to eliminate the possibility of inter-evaluator bias. Before dissection, the anteroposterior diameter and the transverse diameter of the wrist were measured with a digital caliper, and the WS was estimated by multiplying the two values. All epidermis, adipose and connective tissue was then removed, and all muscles were individually dissected and weighed with a precision scale (Sartorius PT610, resolution of 0.1 g). During the dissection, a sample of each tendon passing through the CT was taken and stored on a solution of 5% formaldehyde. The same process was carried out for the MN. The wrist ligaments were then sectioned to separate the carpal bones from the radius and the ulna and from the metacarpal bones, and the CT inlet and outlet were photographed with a Canon EOS-50 digital camera (Fig. 2). After seven days of formaldehyde preservation, the proximal and distal aspects of the tendons that pass through the CT and the proximal and distal aspect of the MN were sectioned in 2 mm segments and each section was photographed.

Table 1 displays the measurements used in the study. The total muscle mass of the forearm and hand muscles (TMM1), the mass of the individual muscles in the CT (FDSM, FDPM and FPLM), and the total mass of all muscles in the CT (TMM2) were calculated for each individual. Also, the percentage of the mass of each muscle in the CT (%FDSM, %FDPM and %FPLM) and the percentage of their total mass (%TMM2) relative to the total mass of the forearm and hand muscles were calculated. The images obtained of the CT inlet and outlet were used to calculate in mm^2 the CSA of the proximal and distal aspects of the CT (PCT-CSA and DCT-CSA) with ImageJ, an open-source image processing program (Abramoff et al., 2004). The values of the PCT-CSA and DCT-CSA were then added together, and the sum divided by 2 in order to calculate the average CT CSA (ACT-CSA) (Fig. 3). The length of the capitate was measured with an electronic caliper in each individual, and this value was used as the HS. Finally, the length of the CT was measured from the proximal to the distal aspects of the flexor retinaculum with a digital caliper, and this value was multiplied by the ACT-CSA to calculate the CTV.

The images of the proximal and distal aspects of the tendons that pass through the CT were used to calculate its proximal and distal CSA in mm^2 (PT-CSA and DT-CSA) with ImageJ. In order to calculate the average CSA of the tendons (AT-CSA) (Fig. 3), the values of the PT-CSA and DT-CSA were added together and divided by 2. These same steps were followed to calculate the proximal and distal CSA of the

Table 1
Abbreviations used in the text, their meaning, and the measurements involved.

ABBREVIATION	MEANING	MEASUREMENTS INVOLVED
ACT-CSA	Average carpal tunnel cross-sectional area	PCT-CSA + DCT-CSA / 2
AMN-CSA	Average median nerve cross-sectional area	PMN-CSA + DMN-CSA / 2
AT-CSA	Average tendon cross-sectional area	PT-CSA + DT-CSA / 2
CSA	Cross-sectional area	
CT	Carpal tunnel	
CTS	Carpal tunnel syndrome	
CTV	Carpal tunnel volume	Carpal tunnel length x ACT-CSA
DCT-CSA	Distal carpal tunnel cross-sectional area	CSA of the CT outlet
DMN-CSA	Distal median nerve cross-sectional area	CSA of the MN at the CT outlet
DT-CSA	Distal tendon cross-sectional area	CSA of the tendons at the CT outlet
FDP	Flexor digitorum profundus	
FDPM	Flexor digitorum profundus mass	
FDS	Flexor digitorum superficialis	
FDSM	Flexor digitorum superficialis mass	
FPL	Flexor pollicis longus	
FPLM	Flexor pollicis longus mass	
HS	Hand size	Length of the capitate bone
MN	Median nerve	
MNV	Median nerve volume	Carpal tunnel length x AMN-CSA
MRI	Magnetic resonance imaging	
PCT-CSA	Proximal carpal tunnel cross-sectional area	CSA of the CT inlet
PMN-CSA	Proximal median nerve cross-sectional area	CSA of the MN at the CT inlet
PT-CSA	Proximal tendon cross-sectional area	CSA of the tendons at the CT inlet
TMM1	Total muscle mass 1	Total muscle mass of the forearm and hand muscles
TMM2	Total muscle mass 2	Total muscle mass of the muscles that pass through the CT
TV	Tendon volume	CT length x AT-CSA
WS	Wrist size	Anteroposterior diameter x transverse diameter of the wrist

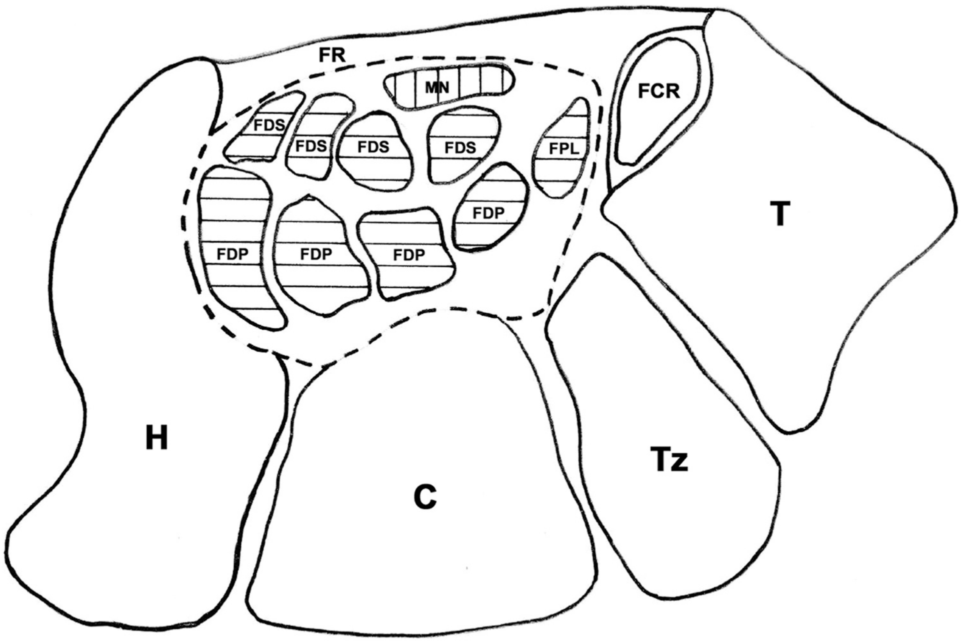

Fig. 3. Drawing of an axial section of the carpal tunnel showing the main measurements taken in this study. Dotted lines indicate the CSA of the carpal tunnel. Horizontal lines indicate the CSA of the tendons in the carpal tunnel. Vertical lines indicate the median nerve. FR=Flexor retinaculum; H=Hamate bone; C=Capitate bone; Tz=Trapezoid bone; T = Trapezium bone; FCR=Flexor carpi radialis tendon; FPL=Flexor pollicis longus tendon; FDP=Flexor digitorum profundus tendons; FDS=Flexor digitorum superficialis tendons; MN=Median nerve.

MN (PMN-CSA and DMN-CSA) and the average CSA of the MN (AMN-CSA) (Fig. 3). Finally, the volume of the tendons that pass through the CT (TV) was calculated by multiplying the CT length by the AT-CSA, and the volume of the MN (MNV) was calculated by multiplying the CT length by the AMN-CSA.

2.3. Quantitative analyses

The measurements obtained in the dissection (Table 1) were compared between men and women: the muscle mass (TMM1, FDSM, FDPM, FPLM, %FDSM, %FDPM, %FPLM, TMM2 and %TMM2); the absolute and relative values of the CT CSA (PCT-CSA, DCT-CSA, ACT-CSA, PCT-CSA/WS, DCT-CSA/WS, ACT-CSA/WS, PCT-CSA/HS, DCT-CSA/HS and ACT-CSA/HS); the absolute and relative values of the CTV (CTV, CTV/WS and CTV/HS); the CSA of the tendons and the MN (AT-CSA and AMN-CSA); the PCT-CSA and DCT-CSA relative to the CSA of the tendons and the CSA of the MN (PCT-CSA/PT-CSA, DCT-CSA/DT-CSA, PCT-CSA/PMN-CSA and DCT-CSA/DMN-CSA); and the CTV relative to the volume of the tendons and the MN (CTV/TV and CTV/MNV).

2.4. Statistical analyses

Sample normality was tested using the Shapiro-Wilk test. To assess for significant differences between men and women, we used the parametric T-test for variables with a normal distribution and the nonparametric Mann-Whitney U test for variables without a normal distribution. All analyses were performed using SPSS (IBM SPSS Statics for Windows, version 24.0). Statistical significance was set at $P \leq 0.05$.

2.5. Ethical note

The research complied with protocols approved by the Use Committee of the University of Barcelona (Institutional Review Board code 00003099) and adhered to the legal requirements of Spain.

3. Results

Tables 2 and 3 show the measurements and results of the quantitative analyses in women and men, respectively, while Table 4 displays the comparisons between men and women. Men had significantly higher values than women for TMM1 (454.3 ± 85.3 g vs 297 ± 76.7 g; $P < 0.001$) and TMM2 (143.3 ± 30.7 g vs 92.2 ± 28.5 g; $P = 0.001$). However, there were no significant differences between men and women for %TMM2 (31.4 ± 1.5 vs 30.6 ± 3.5; $P = 0.88$), TMM2 relative to CT-CSA (0.78 ± 0.18 vs 0.63 ± 0.16; $P = 0.077$) or TMM2 relative to CTV (0.030 ± 0.009 vs 0.025 ± 0.006; $P = 0.146$).

Men also had significantly higher values than women for DCT-CSA (179.7 ± 22.8 mm^2 vs 134.3 ± 17.8 mm^2; $P < 0.001$) and ACT-CSA (188.0 ± 33.8 mm^2 vs 144.3 ± 19.5 mm^2; $P = 0.001$), as well as for PCT-CSA (196.3 ± 55.0 mm^2 vs 154.3 ± 29.1 mm^2; $P = 0.082$), although this difference was not significant. There were no significant differences between men and women for PCT-CSA, DCT-CSA or ACT-CSA relative to WS. However, men had higher values than women for both DCT-CSA and ACT-CSA relative to HS (DCT-CSA/HS: 7.38 ± 0.87 vs 6.21 ± 0.81, $P = 0.006$; ACT-CSA/HS: 7.70 ± 1.20 vs 6.66 ± 0.87, $P = 0.028$). Absolute CTV values were higher in men (4999.3 ± 1240.5 mm^3 vs 3664.9 ± 631.0 mm^3; $P = 0.007$) but there were no differences between men and women for CTV relative to WS or HS.

The values for tendons and median nerve were also significantly higher in men than in women (AT-CSA: 108.6 ± 17.7 mm^2 vs 85.5 ± 19.6 mm^2; $P = 0.013$; AMN-CSA: 13.5 ± 2.3 mm^2 vs 10.9 ± 2.2 mm^2; $P = 0.017$). However, there were no differences between men and women in the size of the CT relative to the size of the tendons (PCT-CSA/PT-CSA, DCT-CSA/DT-CSA) or the size of the median nerve (PCT-CSA/PMN-CSA, DCT-CSA/DMN-CSA). Nor were there differences between men and women in the volume of the CT

Table 2
Results in women.

SAMPLE	AGE	ARM	TMM1	TMM2	%TMM2	ACT-CSA	ACT-CSA/WS	ACT-CSA/HS	CTV	CTV/WS	CTV/HS	AT-CSA	AMN-CSA	PCT-CSA/PT-CSA	DCT-CSA/DT-CSA	PCT-CSA/PMN-CSA	DCT-CSA/DMN-CSA	CTV/TV	CTV/MNV
PR02	92	Left	238.4	79.4	33.3	119.8	0.11	5.99	3274.6	2.94	163.7	131.3	15.6	1.45	1.73	6.22	11.32	0.91	7.67
PR03	89	Left	222.6	65.7	29.5	147.1	0.12	6.51	4067.3	3.29	180.0	76.2	10.4	1.78	2.67	11.24	20.12	1.93	14.12
PR04	87	Left	304.8	103.6	34.0	132.9	0.10	6.65	3727.8	2.93	186.4	89.1	9.9	1.52	1.98	12.86	28.29	1.49	13.45
PR06	80	Left	200.1	43.7	21.8	116.3	0.10	5.67	2467.9	2.05	120.4	77.8	9.8	1.71	1.90	11.69	16.09	1.49	11.83
PR07	88	Left	383.0	124.8	32.6	158.7	0.13	7.42	4675.3	3.85	218.5	102.7	11.5	1.97	1.65	20.75	20.35	1.55	13.83
PR12	78	Right	336.0	110.0	32.7	176.3	0.13	8.48	4424.2	3.17	212.7	69.7	10.0	1.78	1.64	10.89	16.85	2.53	17.59
PR13	82	Right	339.6	101.2	29.8	143.6	0.11	6.30	3465.1	2.75	152.0	64.7	9.4	1.81	1.46	16.48	12.63	2.22	15.35
PR14	91	Right	263.4	79.2	30.1	162.0	0.13	7.33	3505.7	2.85	158.6	73.5	7.9	1.79	1.92	24.30	22.01	2.20	20.54
PR15	84	Right	438.8	137.9	31.4	156.6	0.14	6.52	3772.9	3.43	157.2	91.0	13.3	1.60	1.78	14.69	21.89	1.72	11.76
PR16	76	Right	245.8	76.7	31.2	129.5	0.09	5.75	3267.9	2.34	145.2	79.0	10.9	1.72	1.67	14.94	17.44	1.64	11.89
MEAN			**297.3**	**92.2**	**30.6**	**144.3**	**0.12**	**6.66**	**3664.9**	**2.96**	**169.5**	**85.5**	**10.9**	**1.71**	**1.84**	**14.41**	**18.70**	**18.70**	**18.70**
SD			**76.7**	**28.5**	**3.5**	**19.5**	**0.02**	**0.87**	**631.0**	**0.52**	**30.3**	**19.6**	**2.2**	**0.15**	**0.33**	**5.19**	**4.95**	**4.95**	**4.95**

SD=Standard deviation; TMM=Total muscle mass; ACT-CSA=Average carpal tunnel cross sectional area; WS=Wrist size; HS=Hand size; CTV=Carpal tunnel volume; AT-CSA=Average tendon cross sectional area; AMN-CSA=Average median nerve cross sectional area; PCT-CSA=Proximal carpal tunnel cross sectional area; PT-CSA=Proximal tendons cross sectional area; DCT-CSA=Distal carpal tunnel cross sectional area; DT-CSA=Distal tendon cross sectional area; PMN-CSA=Proximal median nerve cross sectional area; DMN-CSA=Distal median nerve cross sectional area; TV=Tendon volume; MNV=Median nerve volume.

Table 3
Results in men.

SAMPLE	AGE	ARM	TMM1	TMM2	%TMM2	ACT-CSA	ACT-CSA/WS	ACT-CSA/HS	CTV	CTV/WS	CTV/HS	AT-CSA	AMN-CSA	PCT-CSA/PT-CSA	DCT-CSA/DT-CSA	PCT-CSA/PMN-CSA	DCT-CSA/DMN-CSA	CTV/TV	CTV/MNV
PR01	87	Left	391.5	126.5	32.3	166.5	0.11	6.79	3488.0	2.27	142.4	105.1	15.2	1.76	1.64	12.02	13.74	1.58	10.99
PR05	90	Right	457.6	141.0	30.8	177.2	0.11	7.06	6913.9	4.15	275.5	126.6	14.7	1.44	1.91	11.02	25.03	1.57	10.80
PR08	71	Left	525.1	158.9	30.3	170.7	0.11	7.48	4428.6	2.79	194.2	108.9	15.8	1.73	1.57	15.44	13.55	1.86	16.26
PR09	94	Left	314.7	96.0	30.5	170.8	0.12	7.30	4273.8	3.01	182.6	91.6	10.5	1.73	1.92	16.14	18.57	1.49	22.78
PR10	86	Left	531.7	179.4	33.7	190.2	0.12	7.61	4262.2	2.77	170.5	127.5	8.4	1.42	1.73	16.37	26.51	2.39	12.73
PR11	72	Left	552.5	174.0	31.5	176.5	0.11	6.98	4690.9	2.97	185.4	73.8	13.9	1.53	1.90	11.76	14.89	1.40	12.07
PR17	83	Right	475.7	157.7	33.2	182.3	0.13	8.17	3993.6	2.91	179.1	110.2	15.3	1.48	1.91	18.98	22.49	1.65	11.93
PR18	86	Right	389.4	114.0	29.3	156.2	0.12	6.48	4712.6	3.72	195.5	108.6	14.0	1.28	1.41	12.46	19.81	1.44	11.19
PR19	62	Right	361.0	108.1	29.9	271.6	0.17	10.61	6392.7	3.96	249.7	101.4	14.0	2.83	1.93	23.84	14.61	2.68	19.35
PR20	78	Right	544.0	177.8	32.7	218.1	0.14	8.55	6836.3	4.24	268.1	132.2	13.8	1.51	1.64	13.34	16.57	1.65	15.85
MEAN			**454.3**	**143.3**	**31.4**	**188.0**	**0.12**	**7.70**	**4999.3**	**3.28**	**204.3**	**108.6**	**13.5**	**1.67**	**1.76**	**15.14**	**18.58**	**18.58**	**18.58**
SD			**85.3**	**30.7**	**1.5**	**33.8**	**0.02**	**1.20**	**1240.5**	**0.68**	**44.5**	**17.7**	**2.3**	**0.44**	**0.18**	**3.97**	**4.76**	**4.76**	**4.76**

SD=Standard deviation; TMM=Total muscle mass; ACT-CSA=Average carpal tunnel cross sectional area; WS=Wrist size; HS=Hand size; CTV=Carpal tunnel volume; AT-CSA=Average tendon cross sectional area; AMN-CSA=Average median nerve cross sectional area; PCT-CSA=Proximal carpal tunnel cross sectional area; PT-CSA=Proximal tendons cross sectional area; DCT-CSA=Distal carpal tunnel cross sectional area; DT-CSA=Distal tendon cross sectional area; PMN-CSA=Proximal median nerve cross sectional area; DMN-CSA=Distal median nerve cross sectional area; TV=Tendon volume; MNV=Median nerve volume.

Table 4
Comparison of results in women and men.

	TMM1	TMM2	%TMM2	
MEAN (women)	297.3	92.2	30.6	
SD	76.7	28.5	3.5	
MEAN (men)	454.3	143.3	31.4	
SD	85.3	30.7	1.5	
	t = −4.328	t = −3.856	U = 48.000	
P-value	*0.000* *	*0.001* *	0.880	
	ACT-CSA	**ACT-CSA/WS**	**ACT-CSA/HS**	
MEAN (women)	144.3	0.12	6.66	
SD	19.5	0.02	0.87	
MEAN (men)	188.0	0.12	7.70	
SD	33.8	0.02	1.20	
	U = 7.000	t = −0.912	U = 21.000	
P-value	*0.001* *	0.374	*0.028* *	
	CTV	**CTV/WS**	**CTV/HS**	
MEAN (women)	3664.9	2.96	169.5	
SD	631.0	0.52	30.3	
MEAN (men)	4999.3	3.28	204.3	
SD	1240.5	0.68	44.5	
	U = 14.000	t = −1.173	t = −2.046	
P-value	*0.007* *	0.256	0.056	
	AT-CSA	**AMN-CSA**		
MEAN (women)	85.5	10.9		
SD	19.6	2.2		
MEAN (men)	108.6	13.5		
SD	17.7	2.3		
	t = −2.772	t = −2.643		
P-value	*0.013* *	*0.017* *		
	PCT-CSA/ PT-CSA	**DCT-CSA/ DT-CSA**	**PCT-CSA/ PMN-CSA**	**DCT-CSA/ DMN-CSA**
MEAN (women)	1.71	1.84	14.41	18.70
SD	0.15	0.33	5.19	4.95
MEAN (men)	1.67	1.76	15.14	18.58
SD	0.44	0.18	3.97	4.76
	U = 29.000	U = 46.000	t = −0.355	t = 0.057
P-value	0.112	0.762	0.727	0.955
	CTV/TV	**CTV/MNV**		
MEAN (women)	18.70	18.70		
SD	4.95	4.95		
MEAN (men)	18.58	18.58		
SD	4.76	4.76		
	t = −0.015	t = −0.347		
P-value	0.989	0.732		

T = T-test; U=Mann Whitney U test; SD=Standard deviation; TMM=Total muscle mass; ACT-CSA=Average carpal tunnel cross sectional area; WS=Wrist size; HS=Hand size; CTV=Carpal tunnel volume; AT-CSA=Average tendon cross sectional area; AMN-CSA=Average median nerve cross sectional area; PCT-CSA=Proximal carpal tunnel cross sectional area; PT-CSA=Proximal tendons cross sectional area; DCT-CSA=Distal carpal tunnel cross sectional area; DT-CSA=Distal tendon cross sectional area; PMN-CSA=Proximal median nerve cross sectional area; DMN-CSA=Distal median nerve cross sectional area; TV=Tendon volume; MNV=Median nerve volume
*Indicates statistical significance.

relative to the volume of the tendons (CTV/TV) or to the volume of the median nerve (CTV/MNV).

4. Discussion

To date, the anatomical features related to CTS have been examined with X-rays, computed tomography, MRI, and ultrasound to measure the size and configuration of the MN, the bowing of the flexor retinaculum, the CT CSA and the CTV (Nakamichi and Tachibana, 1993; Britz et al., 1995; Cobb et al., 1997; Horch et al., 1997). These previous studies focused on comparing wrists from healthy subjects and from patients diagnosed with CTS. The studies focusing on differences in healthy wrists between men and women generally found a smaller CT CSA in women than in men. For example, Lakshminarayanan et al. (2019) found significant differences between men and women at the CT inlet (0.06 ± 0.01 vs 0.04 ± 0.01, respectively) and at the CT outlet (0.019 ± 0.004 vs 0.008 ± 0.004, respectively). Monagle et al. (1999) also found that men had larger CSAs than women: overall (329 ± 40 mm^2 and 270 ± 25 mm^2); at the inlet (382 ± 78 mm^2 and 333 ± 61 mm^2); and at the outlet (382 ± 65 mm^2 and 265 ± 40 mm^2). Several authors hypothesized that this smaller CT CSA might play a role in the higher incidence of CTS in women (Nattrass et al., 1994; Bower et al., 2006; Peterson et al., 2013; Lakshminarayanan et al., 2019).

In the present study, the absolute values of the CT CSA were calculated by measuring the size of the inlet and that of the outlet and then calculating the CSA. In line with previous studies (Dekel and Coates, 1979; Merhar et al., 1986; Bower et al., 2006; Peterson et al., 2013), we found that women had significantly smaller absolute CSAs, both for the CT (ACT-CSA) and the outlet (DCT-CSA). Similar differences between men and women had also been observed by Monagle et al. (1999) using MRI, while differences were also observed in the proximal CT by Dekel and Coates (1979) using X-rays and by Lakshminarayan et al. (2019) using ultrasound. Taken together, these findings clearly indicate a smaller CT in women, with greater differences between men and women at the outlet and the middle portions of the CT and lesser differences at the inlet. In addition, we have also found that the absolute CTV values were larger in men than in women, which is in line with results obtained by Bower et al. (2006) using MRI.

Other studies have proposed that a smaller CT CSA relative to HS could explain the higher incidence of CTS in women. Sassi and Giddins (2016) found a significantly smaller CT CSA relative to HS in women (11.3 ± 9.0 in men vs 10.9 ± 8.5 in women). In our study, the CT CSA relative to HS was also significantly lower in women although our values for both men and women (7.70 ± 1.20 vs 6.66 ± 0.87) were lower than those reported by Sassi and Giddins (2016). Our finding of a larger CT CSA relative to HS in men could lead us to speculate that a larger part of the CT in women would be occupied by its inner structures. However, further analyses showed that HS was not a reliable surrogate for tendon or MN size, as these structures were also smaller in women than in men. We also compared the CTV relative to HS and found no differences between men and women.

Lakshminarayanan et al. (2019) reported a smaller CT CSA relative to WS in women and speculated that it could be associated with an increased risk of MN entrapment. In our study, in contrast, although the absolute WS was smaller in women, there were no differences between men and women in the CT CSA relative to WS, either at the inlet or the outlet (Table 4).

Women had significantly smaller tendons than men in the present study (Table 4). The FPL, FDS and FDP tendons were thicker and tendon volumes were greater in men than in women, which correlates with the larger muscle mass we observed in men. The MN CSA was also significantly larger in men (Table 4). In contrast, Monagle et al. (1999) and Yao, Gai (2009), using MRI, found no differences between men and women in the MN CSA. Nevertheless, when interpreting these absolute CSA values, we must also take into account the proportion of each structure relative to the others. In the present study, although women had a smaller CT than men, they also had smaller tendons and MN, with no significant differences between men and women in the relative CT CSA values (Table 4). Along these lines, Monagle et al. (1999) also found that the tendons were larger in men but there were no differences in tendon CSA relative to CT CSA (0.37 ± 0.065 in men vs 0.32 ± 0.031 in women). Bower et al. (2006) also found no differences between men and women in the CT CSA and CTV relative to the CSAs of the tendons and MN.

To the best of our knowledge, this is the first study to assess the muscle mass of the forearm in relation to the size of the CT. We hypothesized that a muscular overload in a smaller CT might explain the higher prevalence of CTS in women. As expected, the absolute muscle mass was higher in men than in women, but the proportion of the muscle mass in the CT was similar in both sexes. Furthermore, there were no differences between men and women in the muscle mass relative to the CT CSA or to the CTV, indicating a lack of muscular overload in women.

Differences in measurements between our findings and those of other studies using MRI or ultrasound may be due to an imaging bias. Studies using MRI tended to obtain larger measurements than ours, while studies using ultrasound tended to obtain reduced measurements. Since nerves and other tissues must be isolated to correctly determine size, it is difficult to measure them using imaging techniques. Therefore, we believe that anatomical dissection is the optimal method to measure the size of carpal structures. However, in the present study, we did not evaluate some other features commonly studied in the assessment of CTS. For example, other studies have found that the transverse carpal ligament is less elastic in women than in men although it has a similar thickness, which may explain a reduced tunnel compliance and a reduced palmar bowing in women (Farmer and Davis, 2008; Brett et al., 2014). Nor did we evaluate the shape of the CT, although an association between a squarer CT and CTS was postulated by Peterson et al. (2013). The arch morphology has also been posited as a risk factor for CTS in previous studies (Lakshminarayanan et al., 2019), but we did not include this in the present study. A further limitation of our study was the relatively small sample size, which should be taken into account when drawing conclusions. More anatomical studies with larger samples are warranted to explore the etiology of CTS and its consequent prevention. Finally, because our specimens came from bodies donated to science, ethical constraints did not permit us to have access to clinical data on our specimens or to information such as their right- or left-handedness.

4.1. Conclusions

The results of our quantitative analysis of the CT and its related structures suggest that the higher incidence of CTS in women can be primarily related to workload factors and personal traits. Although the CT CSA in women was smaller than in men, the muscle mass, tendon CSA, MN CSA, WS, and HS were also smaller. The CT outlet in women was smaller relative to HS than in men but still in proportion with the tendon and MN CSA at the outlet. The CTV was also proportional to the size of the inner structures and of the hand in women. Moreover, while the absolute muscle mass was higher in men than in women, the proportion of the muscles was similar in both sexes. The tendons and the MN were both larger in men than in women, but there was no difference in the ratio of tendon size or MN size to CT size. Furthermore, the volume of the CT and of its inner structures were also in proportion in men and in women. Taken together, all these findings indicate that even though the absolute values are smaller in women, the relation between the different parameters are similar in the two sexes.

The data collected in the present study clearly show that the CT in both men and women is in proportion to its inner structures and to related external anatomical structures. Our findings provide anatomical data to support previous MRI studies of the size and proportions of the CT (Monagle et al., 1999; Bower et al., 2006) and indicate that the higher incidence of CTS in women is likely not the result of a disproportionate CT size but may be due to extrinsic factors, such as workload, or to personal features, such as obesity or hormonal imbalance. Our findings are thus of clinical interest since the correction of these extrinsic factors could help prevent CTS in women and ergonomic modifications could become crucial to its treatment.

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Data accessibility statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical statement

The research complied with protocols approved by the Use Committee of the University of Barcelona (Institutional Review Board code 00003099) and adhered to the legal requirements of Spain.

CRediT authorship contribution statement

Patrícia Rodríguez: Data curation, Funding acquisition, Supervision, Methodology, Writing – review & editing. **Aroa Casado:** Data curation, Funding acquisition, Methodology, Supervision, Validation, Writing – review & editing. **Josep Maria Potau:** Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Supervision, Validation, Writing – review & editing.

Declaration of Competing Interest

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

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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