Persistent Median Artery and Its Implications in Carpal Tunnel Syndrome

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Abstract

Introduction: The median artery is a transient vessel during the embryonic phase responsible for providing most of the blood supply to the embryo's hand. Occasionally, the median artery may not regress and its persistence in the carpal tunnel may result in complications related to compression of the median nerve, which can be a contributing factor to the development of Carpal Tunnel Syndrome (CTS). Thus, our objective was to analyze the persistence of the median artery and its likely association in the development of CTS.

Material and Methods: This is a systematic review of articles indexed in SciELO, PubMed, LILACS, SPRINGERLINK, SCIENCE DIRECT and LATINDEX databases, from November to December 2019. Original studies about persistent median artery (PMA) and studies associating its presence to carpal tunnel syndrome were included. Data collection was performed by two independent reviewers and the interobserver agreement analysis was observed using the Kappa test (Bioestat V 5.0).

Results: At the end of the search, 39 studies were selected, characterized according to the sample, method to assess the anatomical structure and main results. Twelve (30.76%) studies found thrombosed median arteries, whereas eleven (28.20%) studies found large-caliber persistent median arteries. Ten (25.64%) studies also reported an association between the persistent median artery with a bifid median nerve and three (7.69%) demonstrated double median veins associated with PMA.

Conclusion: The results of this review show the most prevalent changes in PMA and their possible contributions to the development of CTS. Thus, knowledge about this condition must be considered during the semiology and surgical procedures of disorders involving the wrist.

Keywords — persistent median artery; carpal tunnel syndrome, anatomical variation.

I. INTRODUCTION

The median artery is a transient vessel during the embryonic phase, which at the beginning of intrauterine life provides most of the blood supply to the embryo's hand. However, with the development of the radial and ulnar arteries, it undergoes involution due to apoptosis on the eighth week of gestation to become a small vessel that accompanies the median nerve [1].

Occasionally, the median artery may not regress and its persistence in the carpal tunnel may result in several complications related to the compression of the median nerve, either directly through its pulsation or indirectly through calcifications, thrombosis, atherosclerosis, aneurysms or trauma in this artery, and may be a contributing factor to the development of important clinical conditions, such as Carpal Tunnel Syndrome (CTS) [2].

CTS is the most common peripheral neuropathy, caused by compression of the median nerve in the wrist, which may result from different reasons that reduce the capacity of the carpal tunnel or increase the volume of its content. In milder cases, patients experience paresthesia and pain in the area of the median nerve innervation. Weakness, atrophy of the muscles of the thenar eminence and persistent hypoesthesia are observed in severe cases, reducing the quality of life of such patients [3].

The incidence of the median artery ranges from 1 to 30% in adult populations and may be higher in neonatal and pediatric populations. This variation may be related to genetic factors, race, age or environmental factors [4]. In addition, topographically, the persistent median artery is closely related to the tendon of the long palmar muscle, often recruited in reconstruction surgeries of other tendons. Therefore, knowledge about this anatomical variation is greatly relevant, especially for surgeons working in this area [5].

It is important to understand the possible variations of this artery in the carpal tunnel, in order to identify an association between the symptomatic scenario reported by the patients and its anatomy, increasing the sensitivity of the differential diagnosis and consequently leading to a more effective treatment. Therefore, this study sought to analyze the persistence of the median artery and its implications for the development of carpal tunnel syndrome.

II. MATERIAL AND METHODS

This is a systematic review with studies found in the following databases: SciELO (Scientific Electronic Library Online); PUBMED (National Library of Medicine); LILACS (Latin American and Caribbean Literature in Health Sciences); SPRINGERLINK; SCIENCE DIRECT and LATINDEX. The electronic search was carried out from November to December 2019. Studies were selected without time restriction, in English and Portuguese. Descriptors were used in a combined way by means of Boolean operators (AND). In SciELO, PUBMED, SCIENCE DIRECT, LILACS, SPRINGERLINK and LATINDEX databases, the combination was considered: "persistent median artery" AND "carpal tunnel syndrome".

To calculate the total number of studies, duplicates were considered as only one study. From the identified studies, those who met the inclusion criteria were selected considering titles and abstracts.

This review included original articles about the presence of persistent median artery and articles that associated its presence to the carpal tunnel syndrome, prioritizing the most relevant studies. Review articles, studies with animal models and those in which reported carpal tunnel syndrome not related to persistent median artery were excluded.

The search was carried out by two independent reviewers, and the interobserver agreement analysis was performed using the Kappa test using the Bioestat V 5.0 software, according to the method of Landis and Koch [6]. The value was K=0.80 (substantial agreement).

The included studies were critically analyzed through an interpretation guide, used to assess their individual quality, based on the studies by Greenhalgh [7] and adapted by Macdermid et al. [8]. Items for assessing the quality of articles are expressed by scores in Table 1, in which 0= absent; 1= incomplete; and 2= complete.

Table 1: Analysis of the quality of the articles investigating the persistent median artery and its relationship with carpal tunnel syndrome.

	Item evaluation criteria												
Study	1	2	3	4	5	6	7	8	9	10	11	12	Total (%)
Acioly, M. et al. (2013)	1	NA	2	NA	1	2	2	NA	1	NA	NA	2	78.57
Akgun, A. et al. (2017)	1	NA	2	NA	1	2	1	NA	NA	NA	NA	2	75.00
Altinkaya, N. et al. (2016)	2	2	2	2	1	0	2	2	1	2	2	1	79.16
Aragão, J. et al. (2017)	2	0	2	2	1	NA	2	2	1	0	0	2	63.63
Areny, M. et al (2012)	1	NA	0	2	1	0	2	1	0	0	0	1	36.36
Ariyo, O. (2015)	2	NA	1	2	1	NA	1	2	1	0	0	2	60.00
Ariyo, O. et al. (2016)	1	NA	1	2	1	NA	2	0	1	0	0	2	50.00
Aulicino, P. (1984)	0	NA	1	2	1	1	1	0	1	0	0	1	36.36
Avenel, M. et al. (2019)	1	NA	0	1	1	2	1	0	0	0	0	2	36.36
Balakrishnan C. (1999)	2	NA	1	NA	1	0	1	NA	NA	NA	NA	0	41.66
Bijannejad, D. et al. (2016)	2	NA	0	NA	1	NA	1	NA	NA	NA	NA	0	40.00
Bilgin, S. et al. (2004)	2	NA	1	NA	2	2	2	NA	2	NA	NA	2	92.85
Boles D. et al. (1982)	1	NA	1	NA	1	1	2	NA	1	NA	NA	1	57.14
Butt, J et al. (2017)	2	NA	1	NA	1	0	2	NA	1	NA	NA	2	64.28
Chen, L. et al. (2017)	1	2	1	NA	2	0	2	NA	2	2	2	2	80.00
Ekiz, T. et al. (2016)	0	NA	1	NA	1	0	1	NA	1	NA	NA	1	35.71
Feintisch, A. et al. (2017)	2	NA	2	NA	1	0	1	NA	1	NA	NA	1	57.14
Feldkamp M et al. (1995)	1	NA	1	NA	1	1	1	NA	1	NA	NA	1	50.00
Fumière E et al. (2002)	1	NA	1	NA	1	1	1	NA	1	NA	NA	1	50.00
Gassner, E. (2002)	1	0	1	1	2	2	2	1	1	0	0	1	50.00
Haladaj, R. et al. (2019)	2	2	1	2	2	NA	2	2	1	2	2	2	90.90
Karaahmet, O. et al. (2016)	1	NA	2	NA	1	0	1	NA	1	NA	NA	1	50.00
Kele, H. et al. (2002)	1	NA	1	2	1	2	2	2	1	NA	NA	2	77.77
Khashaba, A. (2002)	1	NA	1	NA	1	1	2	NA	0	NA	NA	0	42.85
Kopuz, C. et al. (1998)	2	NA	1	2	1	NA	2	1	1	2	2	1	75.00
Krishnamoorthy, L. (1998)	2	NA	1	NA	1	2	2	NA	1	NA	NA	1	71.42
Luyendijk, W. (1986).	2	NA	1	NA	1	2	2	NA	1	NA	NA	2	78.57
Mauersberger, W. et al. (1975)	1	0	1	NA	1	1	2	NA	0	NA	NA	0	37.50
Maxwell, J. et al. (1973)	2	NA	1	2	1	1	1	0	1	NA	NA	0	50.00
Ng, C. et al. (2012)	1	NA	0	NA	1	1	1	NA	0	NA	NA	0	28.57
Pierre-Jerome, C. et al. (2010)	2	1	2	NA	2	0	2	NA	2	2	2	1	80.00
Rzepecka-Wejs, L. et al. (2012)	2	1	2	2	1	2	2	2	1	NA	NA	1	80.00
Salter, M. et al. (2011)	1	NA	1	0	1	0	2	1	1	NA	NA	2	50.00
Schubert, R. (2008).	2	NA	1	0	1	2	1	NA	2	1	0	1	55.00
Srivastava, A. et al. (2015)	0	0	1	NA	2	NA	1	0	1	1	0	1	35.00
Stavros, K. et al. (2016)	1	NA	1	2	1	0	2	2	1	1	0	2	59.09
Vag, T. et al. (2012)	1	NA	2	0	1	0	2	0	1	1	0	2	45.45
Walker, F. et al. (2013)	2	2	2	2	2	0	2	NA	2	2	2	1	86.36
Zeiss, J. et al. (1993)	1	NA	1	0	1	2	1	0	1	1	0	1	40.90

Acronyms: NA, not applicable to paper.
*Assessment criteria: 1. Thorough literature review to define the research question; 2. Specific inclusion/exclusion criteria; 3. Specific hypotheses; 4. Appropriate scope of psychometric properties; 5. Sample size; 6. Follow-up; 7. The authors referenced specific procedures for administration, scoring and interpretation of procedures; 8. Measurement techniques were standardized; 9. Data were presented for each hypothesis; 10. Appropriate statistics-point estimates; 11. Appropriate statistical error estimates; 12. Valid conclusions and clinical recommendations.

III. RESULTS

A summary of the electronic search in the databases is shown in figure 1. Initially, 862 studies were identified, of which 774 were excluded because they did not have relevant data or because they were in duplicates, remaining 88, which were submitted to analysis of the titles and abstracts and verification of inclusion and exclusion criteria. On the full-text analysis, 39 articles [1,3, 4, 9-44] adequately met all inclusion criteria and were selected for this systematic review.

Figure 1. Flowchart of included and excluded studies in this review about the presence of the persistent median artery and its relationship with carpal tunnel syndrome.

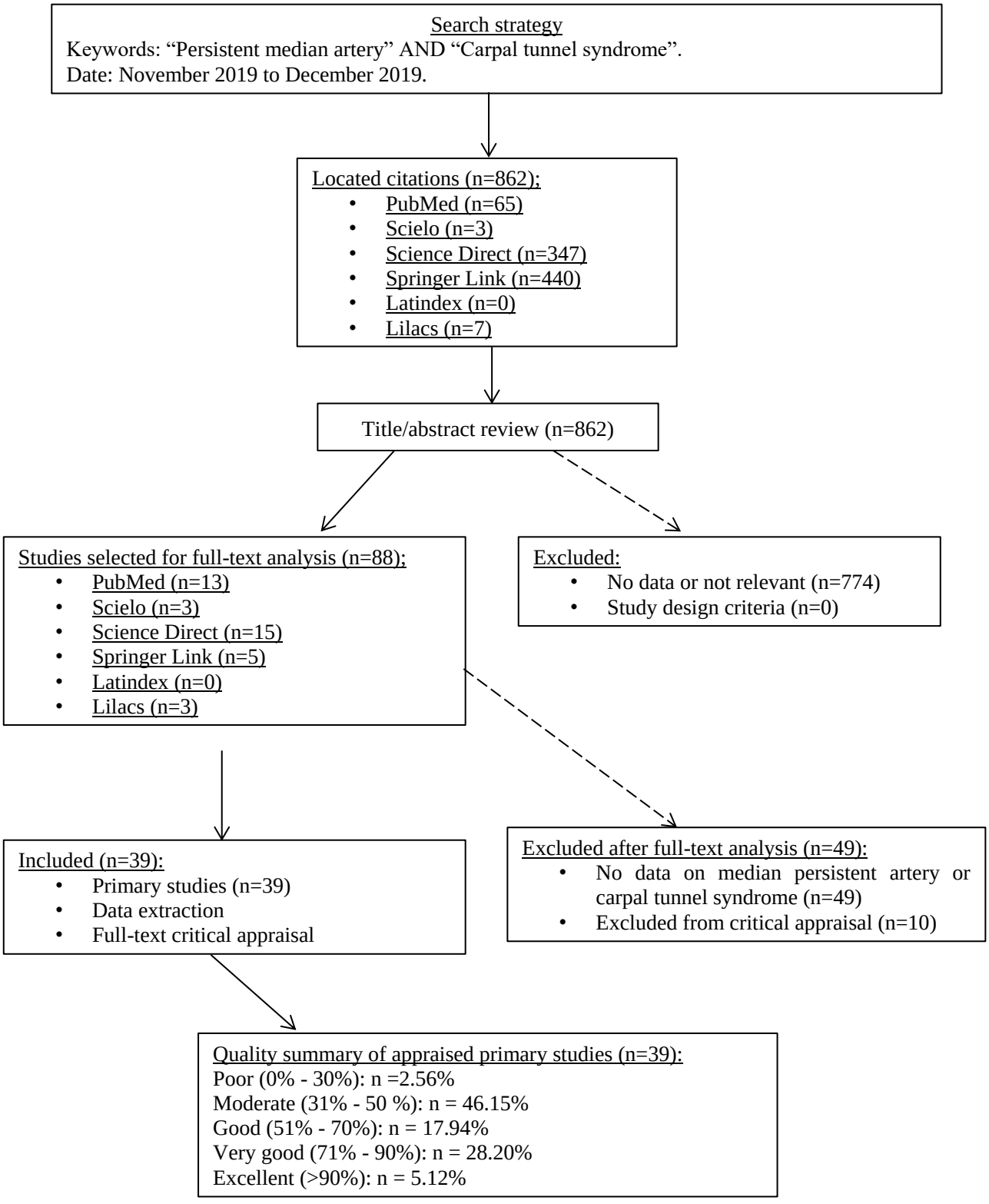
Search strategy
Keywords: "Persistent median artery" AND "Carpal tunnel syndrome".
Date: November 2019 to December 2019.
Located citations (n=862);
PubMed (n=65)
Scielo (n=3)
Science Direct (n=347)
Springer Link (n=440)
Latindex (n=0)
Lilacs (n=7)
Title/abstract review (n=862)
Studies selected for full-text analysis (n=88);
PubMed (n=13)
Scielo (n=3)
Science Direct (n=15)
Springer Link (n=5)
Latindex (n=0)
Lilacs (n=3)
Excluded:
No data or not relevant (n=774)
Study design criteria (n=0)
Included (n=39):
Primary studies (n=39)
Data extraction
Full-text critical appraisal
Excluded after full-text analysis (n=49):
No data on median persistent artery or carpal tunnel syndrome (n=49)
Excluded from critical appraisal (n=10)
Quality summary of appraised primary studies (n=39):
Poor (0% - 30%): n =2.56%
Moderate (31% - 50 %): n = 46.15%
Good (51% - 70%): n = 17.94%
Very good (71% - 90%): n = 28.20%
Excellent (>90%): n = 5.12%

Table 2. Characteristics of studies that assessed the presence of persistent median artery and its possible relationship with carpal tunnel syndrome.

Author (year)	Sample	Method	Main results
Avenel, M. et al. (2019)	2 patients	Angiotomography and Echo Doppler	One patient with CTS presented persistent median artery thrombosis through angiotomography and a second patient presented a color Echo doppler with persistent median artery with thrombosis signs.
Haladaj, R. et al. (2019)	125 upper limbs	Cadaveric dissection	Of the 125 upper limbs, the persistent median artery was found in 5 samples (4%). In the carpal tunnel, the artery was in the anterolateral position (2 cases), anterior position (2 cases) and anteromedial position (1 case) considering the median nerve.
Feintisch, A. et al. (2017)	A 47-year-old female patient	Surgery	A patient with bilateral CTS, presented bilateral persistent median artery (PMA) during an exploration surgery. Unlike previous reports, PMAs were not located dorsally to the flexor retinaculum (FR). Instead, PMAs were interposed between the palmar aponeurosis and FR. Accompanied by two constituent veins.
Akgun, A. et al. (2017)	A 35-year-old women with 8 weeks of pregnancy	Echodoppler	After ultrasound and doppler examination, a case of acute CTS was found due to thrombosis of a persistent median artery and associated bifurcated median nerve during pregnancy.
Butt, J et al. (2017)	A 55-year-old woman submitted to surgery	Surgery	An incidental finding of a large persistent median artery, superficial to the flexor sheath, could have been damaged. It was carefully removed, and the procedure was completed without complications.
Chen, L. et al. (2017)	160 fists	Ultrasound and color Doppler	Among the 160 wrists, a persistent median artery was seen in 12 (7.5%) wrists and a median persistent vein was seen in 9 wrists (5.6%).
Karaahmet, O. et al. (2016)	A 21-year-old male patient	Ultrasound	A patient diagnosed with carpal tunnel syndrome was submitted to an ultrasound examination, where a bifid median nerve with a persistent median artery was observed.
Bijannejad, D. et al. (2016)	An adult male cadaver	Cadaveric dissection	A persistent median artery was observed at the upper left end of an adult male cadaver fixed in formalin, where the persistent median artery originated from the brachial artery and ran distally past the flexor retinaculum. The size of the artery was as large as the radial artery and anastomosed with the superficial palmar arch.
Ekiz, T. et al. (2016)	A 30-year-old healthy man	Ultrasound	A persistent median artery was demonstrated and the presence of two persistent veins, although the patient was asymptomatic, was advised that such variation could influence CTS development.
Aragão, J. et al. (2017)	32 upper limbs from human fetuses	Cadaveric dissection	Among the 32 dissected forearms, the persistent median artery was present in 81.25% (26) of the cases and it was found more frequently in women and on the left side. Regarding the origin, most of the median arteries originated in the common interosseous artery (38.5%) and in the anterior interosseous artery (34.6%).
Stavros, K. et al. (2016)	A patient with CTS symptoms	Ultrasound	A patient who had classic symptoms and a neurological exam for CTS and had an investigation of normal nerve conduction and electromyogram. Neuromuscular ultrasound of the median nerve on the symptomatic side revealed penetration of the nerve by a persistent median artery and vein in the middle of the forearm, with a positive Tinel sonographic signal at this location.

Altinkaya, N. et al. (2016)	84 fists of patients with CTS and 136 fists of healthy individuals	Ultrasound and color Doppler	Of the 84 fists of patients with CTS, 2 (2.4%) had a persistent median artery (both on the right side). Of the 136 control fists, 12 (9%) had unilateral PMA in eight (three on the right and five on the left) and bilateral in two. There was no significant difference between patients with CTS and control groups regarding the frequency of PMA.
Srivastava, A. et al. (2015)	A 38-year-old-men	Ultrasound and angiography	A 38-year-old man with acute pain in his right wrist with a positive Tinel sign. An ultrasound and computerized angiography study confirmed a persistent median artery with thrombosis.
Walker, F. et al. (2013)	1026 fists of 513 Latino hand workers from North Carolina	Ultrasound	A total of 8.6% of the wrists had bifid median nerve and 3.7% of the wrists had PMA regardless of ethnicity, age, sex or type of work subgroup. No definitive association with carpal tunnel syndrome was found. The presence of any anatomical variant was associated with a high probability of co-occurence from another variant on the same wrist or on the contralateral wrist.
Acioly, M. et al. (2013)	A 45-year-old woman	Surgery	During surgery, the transverse carpal ligament was found to be thickened and, after division, a large and patent persistent median artery was identified. The median nerve, which was bifid, was lying deep and laterally in the persistent median artery.
Rzepecka-Wejs, L. et al. (2012)	A 39-year-old woman	Ultrasound	The median nerve was in bifid shape and a persistent median artery was observed between its two parts. The median artery at the wrist level was not likely to generate compression, while its proximal part at the level of the forearm was likely to cause compression.
Vag, T. et al. (2012)	A 40-year-old man	Magnetic Resonance Imaging and Ultrasound	Patient with CTS symptoms demonstrated a persistent median thrombosed artery with compression of the bifid median nerve. High-resolution ultrasound confirmed the diagnosis with atypical ramification of the median artery from the distal radial artery.
Ng, C. et al. (2012)	A 56-year-old woman with distal radial fracture	Open surgery	After open reduction and internal fracture fixation, the carpal tunnel decompression was performed where a persistent median artery was identified. In this patient, there was probable nerve contusion, soft tissue edema, deformity and vasodilation of the persistent median artery secondary to the fracture resulted in acute CTS, considering that the patient reported no similar symptoms before this injury.
Salter, M. et al. (2011)	A 42-year-old woman	Ultrasound and Doppler	High-resolution ultrasound and Doppler revealed a persistent thrombosed median artery and the associated bifurcated median nerve. The patient suffered from continuous wrist pain, not relieved by painkillers. The patient also mentioned mild paresthesia along the radial side of the hand. The thrombus was resolved with anticoagulants.
Schubert, R. et al. (2008)	A 45-year-old patient	Magnetic Resonance Angiography	An atypical vessel was identified as a persistent median artery in distal section, with an occlusive thrombus. The patient underwent vascular surgery due to the symptoms and after 3 months there was an improvement in symptoms.
Bilgin, S. et al. (2004)	4 patients with CTS and mean age of 51 years old	Surgery	Four patients with CTS and persistent median artery underwent open surgery. All four median arteries were patent and only a transverse release of the carpal ligament were performed using a standard anterior open approach for carpal tunnel decompression. No ligation or transposition of the arteries was performed, and all patients were free of symptoms after a few weeks. Only one patient had a slight recurrence 13 months after the procedure.
Kele, H. et al. (2002)	A 37-year-old man	Open surgery	A patient with CTS symptoms underwent open surgery. Upon entering the carpal tunnel, a persistent median artery was found. Below the transverse carpal ligament (flexor retinaculum) the entire

			artery was enlarged (4-5 mm in diameter) and swollen and it was in volar aspect of the bifid nerve, which was integrally related to the perineurium. Both branches of the divided median nerve were compressed by the occluded median artery. The thrombosis stopped directly in front of the location where the median nerve branched.
Fumière E et al. (2002)	A 39-year-old man	Ultrasound and Doppler	The use of Doppler examination confirmed the presence of a persistent left median artery in a patient with CTS. In the proximal part of the carpal tunnel, the artery was larger in size and there was a lateral echogenic structure in the artery. No flow was represented on the Doppler exam, confirming distal thrombosis of the artery.
Gassner EM (2002)	2 patients with CTS and 100 fists of asymptomatic volunteers	Ultrasound and color Doppler	A large persistent median artery of 3 mm in diameter was found in both patients with carpal tunnel syndrome. The results were confirmed in surgery. Among asymptomatic volunteers, a persistent median artery was found in 13 (26%, 10 [20%] unilateral and 3 [6%] bilateral), with an average diameter of 1.1 mm (range 0.5-1,7 mm). In 10 (63%) of the 16 hands, the persistent median artery was associated with high division of the median nerve or with the configuration of a bifid nerve in the carpal tunnel.
Khashaba, A. (2002)	A 43-year-old woman with CTS	Surgery	At the time of surgery, it was found that the transverse carpal ligament was not firm, and a persistent median long thrombosed artery was antero-radial and adhered and compressed the median nerve. The thrombosed vessel extended from its distal trifurcation in the superficial palmar arch to approximately 4 cm in the forearm.
Balakrishnan C. (1999)	A 26-year-old man	Open surgery	After a fracture, hours later the patient complained of a sudden tightness and numbness of the thumb, long and index fingers. In the analysis, a persistent median thrombosed artery was found. The thrombosed vessel was excised, and the patient underwent carpal tunnel decompression. Patient's symptoms improved.
Feldkamp M et al. (1995)	A 63-year-old woman with CTS	Open surgery	During surgery, a large median artery was found pulsating in the carpal tunnel, this pulsation was causing compression of the median nerve. The flexor retinaculum was decompressed, and the median artery was transposed. This is the first reported case of a persistent median artery in a hemodialysis patient who has symptoms contralateral to the vascular access.
Zeiss, J. et al. (1993)	A 28-year-old man with CTS	Magnetic Resonance Imaging and surgery	The patient had a persistent median artery that was the probable cause or at least a contributing factor to CTS. The patient underwent surgery where the retinaculum was released, however, in the following 4 months, symptoms persisted with little improvement. Then, the patient underwent a second surgery, where the median artery was resected, becoming asymptomatic soon after the surgery.
Luyendijk, W. (1986)	A 59-year-old woman	Open surgery	A persistent median artery was observed on both sides of a patient with CTS during carpal tunnel decompression surgery.
Boles D. et al. (1982)	A worker with CTS	Electromyel ogram	The nerve was found to be compressed inside the tunnel by an anomalous median artery. This appears to be the first recorded case of a carpal tunnel syndrome caused by a large persistent anomalous non-thrombosed artery.
Mauersberger, W. et al. (1975)	3 patients	Open surgery	Three patients undergoing carpal tunnel release surgery with symptoms of CTS had persistent median arteries with enough pulse to compress the median nerve, thus developing CTS in the analyzed patients.

Maxwell, J. et al. (1973)	A 43-year-old man with acute CTS	Open surgery	A persistent median artery of 4 mm in diameter was observed, which accompanies the median nerve through the carpal tunnel, and which was integrally related to the perineurium. The thrombosis stopped at a patent arterial arch. The thrombosed section of the 5.2 cm long artery was excised.
Ariyo, O. (2015)	One upper limb	Cadaveric dissection	A persistent median artery was observed. This artery ran inferiorly and was initially positioned posterior to the median nerve. At the junction of the proximal and middle thirds of the forearm, the artery perforated the posteroanterior median nerve and positioned medially to the nerve, a relationship maintained both in the distal forearm and in the carpal tunnel, posterior to the flexor retinaculum.
Ariyo, O. et al. (2016)	An upper limb from a 75-year-old female cadaver	Cadaveric dissection	Two persistent median arteries were observed in the distal forearm. The median artery in both limbs was of the palmar variety, a bilateral division of the median nerve was observed bilaterally. Each PMA crossed its respective radial head of the MN bifid and was positioned centrally between the 2 heads of the MN bifid, maintaining a relationship in the lower course of the forearm and in the passage through the carpal tunnel, posterior to the flexor retinaculum.
Pierre-Jerome, C. et al. (2010)	194 patients (77 men and 117 women) aged between 12-80 years	Magnetic Resonance Imaging	A persistent median artery (MPA) inside the tunnel was observed in 21 (11%) pulses - 10 men and 11 women. Of these, four (19%) cases were presented with coexisting PMA and bifid median nerve inside the tunnel. Statistically, we found that the two variations are not independent characteristics and their covariance is not null.
Kopuz, C. et al. (1998)	60 upper limbs of 30 newborn cadavers	Cadaveric dissection	Of 30 neonatal cadavers in which both forearms were available, the artery was present bilaterally in 4 cases (13.3%), unilaterally in 4 cases (13.3%) and absent bilaterally in 22 cases (73.4%). This provides a frequency of 26.6% per individual. Eight originated from the ulnar artery and four from the common interosseous artery.
Areny, M. et al (2012)	A 22-year-old asymptomatic and healthy man	Ultrasound	A large persistent bilateral median artery was found associated with a median bifid nerve in one wrist. The patient's asymptomatic character was considered surprising, despite the large caliber of his artery.
Aulicino, P. (1984)	A 31-year-old man	Surgery	The arteriogram confirmed the presence of a persistent median thrombosed artery. The artery was thrombosed from its insertion in the superficial arch to a level of approximately 2.5 cm proximal to the crease of the wrist. The length of the thrombosis was approximately 6.5 cm. External diameter of the median artery at the level of thrombosis was approximately 3 mm. A median nerve bifid with an extraligamentous thenar motor branch was also observed.
Krishnamoorth, L. (1998)	A 46-year-old man	Arteriogram	An 18-year-old man had a painful swelling on his right forearm with symptoms of compression on the median nerve. An arteriovenous malformation of the forearm was observed, which was fed by numerous branches of a persistent median artery, with contributing branches of the ulnar artery. After surgery, symptoms improved.

Nineteen (48.71%) of the thirty-nine studies in this review used the image examination method to verify PMA, thirteen (33.33%) studies performed the surgery method, and another six (15.38%) performed their assessments through dissection of dead bodies. Only one (2.56%) study used both the imaging test and surgery.

Twelve (30.76%) studies reported thrombosed median arteries, eleven (28.20%) observed large-caliber persistent median arteries and ten (25.64%) reported the association between PMA with a bifid median nerve. Three (7.69%) authors also demonstrated double median veins associated with the presence of PMA, whereas one (2.56%) reported the presence of only one median vein.

Twenty-five (64.10%) studies showed PMA associated with carpal tunnel syndrome, eight (20.51%) studies did not report a relationship between this variation and CTS symptoms. In six (15.38%) studies, it was not possible to observe symptoms related to CTS, as they were performed on cadaverous pieces.

The most prevalent change in this review was the presence of thrombosis in the persistent median artery, followed by the presence of a large median artery.

IV. DISCUSSION

Median artery during embryogenesis

Several factors may contribute to changes that occur during embryogenesis. There is much evidence that vascular structures form in the limbs not only by the proliferation and migration of endothelial cells in existing vessels, but also by recruiting endothelial precursor cells from the mesenchyme that migrate to the limbs from the somites [45, 46].

As the development of the limb advances, the vascular pattern of the segment becomes increasingly complex and the number of vessels increases in the same measure as the vessel density [47].

During embryogenesis, the primary axial artery is responsible for the origin of the common subclavian, axillary, brachial and interosseous arteries. In this phase, the anterior median and interosseous arteries are the main sources of blood supply to the hand during the first trimester of embryonic development. Right after the eighth week of gestation, the radial and ulnar arteries develop, and the median artery begins to regress. When it does not recede, this vessel is considered a remnant of the primitive arterial architecture, and can also be seen as a contributing factor to the development of carpal tunnel syndrome, since it increases chances of compression of the structures in this region [4, 48].

Aragão et al. [4] analyzed 32 dissected forearms from 16 fetuses with fetal age between 15 to 38 weeks and observed PMA in 81.25% (26) of the cases, more frequently found in women and on the left side. Thus, the results of this study suggest new hypotheses about the time of regression of this artery during the gestational process, since most of the fetuses analyzed showed the persistence of the median artery, with an average gestational age of 30 weeks, that is, well beyond the eighth week reported by the literature as the landmark period of regression of this vessel.

Similar results were reported by Kopuz, et al. [31]. When analyzing 60 forearms of human fetuses, 9 (15%) cases of median arteries were found in cadavers of neonates. However, according to the authors, there is a possibility that this vessel will regress later, in the perinatal period or even in early childhood.

Influence of persistent median artery on carpal tunnel syndrome

Anatomical variations of the carpal tunnel are important to understand its possible implications for CTS. Thus, the presence of a persistent median artery as a cofactor that has to be considered in the development of this syndrome has been evidenced through the scientific literature and, in some cases, there has been a direct link between this disease and the presence of this vessel. However, it cannot always be stated that these changes are associated with their etiology and that they are responsible for pain and paresthesia, considering that asymptomatic patients may have such changes, as well as symptomatic patients may not present this finding [9, 12, 13, 43].

It is widely known that the carpal tunnel is posteriorly constituted by the carpal bones and anteriorly by the flexor retinaculum, which includes the transverse carpal ligament, and structures such as the tendons of the superficial and deep flexor muscles of the fingers pass through it, the long flexor of the thumb, the median nerve and the vessels that supply the region of the wrist, hand and fingers [49].

The tunnel walls are inflexible and its normal pressure varies between 2.5 to 13 mmHg, therefore, when thickness or the number of one of its components increases, it may reduce its cross-sectional area and increase pressure around 20 to 30 mmHg, becoming a critical area [50-52]. In this context, it is believed that the persistence of a median artery inside the carpal tunnel could generate compression on its structures, especially in the median nerve, which could result in nerve compression and consequently predispose CTS [53].

When developing this syndrome, patients mainly experience pain and paresthesia from the first to the third finger and lateral half of the fourth, that generally worsens at night. Individuals in moderate to severe stages may have atrophy of the thenar muscles, as well as decreased strength, mainly for pinching and grasping movements [49].

According to Barfred et al. [54], a persistent median artery with an external diameter greater than 2.0 mm may be able to cause compression on the median nerve. In his study, 239 CTS patients underwent surgery and persistent median arteries of considerable caliber were observed in 4% of cases. PMA is variable in size, with a diameter of 0.8 to 2.7 mm in different cadaveric studies [55,56].

However, the data presented in this review show that the presence of PMA alone would not be able to generate compression on the median nerve, but its association with the formation of thrombi, atherosclerotic processes, calcifications and increased caliber of this vessel would increase the likelihood of the development of symptoms presented by such patients [12, 17, 30].

Studies have observed that the persistent median arteries that were observed during open surgeries in CTS

patients, after the release of the tunnel and transposition of this vessel, there was significant improvements in their symptoms, with only a single recurrence observed 13 months after surgery [9, 19, 24, 30].

However, Zeiss et al. [44] reported the case of a 28-year-old man with CTS who showed persistence of the symptoms with little improvement, even after releasing the carpal tunnel, requiring a second surgery, where PMA was resected, becoming asymptomatic after the procedure. This finding reinforces the hypothesis that the presence of this artery with enough pulse or increased size can be considered a probable cause or contributing factor in the development of this syndrome.

Most studies demonstrate thrombosed PMA as the main finding in scientific research. According to Akgun et al. [10], after resection surgery of a thrombosed PMA, there was a significant improvement in CTS symptoms.

Salter et al. [3] observed that, although thrombosis of this vessel has generated symptoms of paresthesia in the median nerve competence pathway associated with continuous pain in the wrist, not relieved by analgesics, they have improved symptoms after the use of anticoagulants. In addition, after one week, recanalization of the lumen and decrease in the diameter of the affected segment of the persistent median artery resulted in blood flow pattern improvement in the proximal region of the vessel. These findings were confirmed by ultrasound and Doppler exams, demonstrating that early detection of the thrombosed median artery can be treated conservatively, thus avoiding surgical procedures in this area.

Furthermore, the coexistence of PMA and a median bifid nerve has been commonly reported through scientific research. This variation is characterized by the intimate relationship of PMA with this nerve, however these findings were considered independent, and apparently do not influence CTS incidence [9, 12, 13, 37, 38, 43].

Therefore, it is believed that CTS may be caused by several factors and that the contribution that PMA has on this finding should be recognized by the neurologist responsible for the diagnosis. Thus, there should be greater attention mainly to the persistent median veins and the persistent median artery, which may represent new pathogenic factors for CTS when internal thrombi are formed in some pathological conditions.

V. CONCLUSION

It was observed that the potential of PMA by itself to generate compression on the median nerve is an unusual finding, but the knowledge about this vessel and its possible changes such as thrombus formation, atherosclerotic processes, calcifications and increased diameter should be considered, especially before the carpal tunnel is released, since under specific pathological conditions, these findings might be the main causes of CTS.

The most prevalent change in this review was the presence of PMA thrombosis, followed by the presence of a large caliber PMA. However, other studies, especially in vivo studies, are necessary in order to investigate the relationship between PMA, symptoms and degree of CTS.

We believe that the knowledge about this vessel will help doctors to understand the different clinical manifestations of this syndrome, favoring the precise diagnosis and a consequently more effective treatment, avoiding the risk of iatrogenesis during surgical procedures.

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