Review Article

Study of Median Nerve Variations and Its Clinical Implications at the Distal Part of Upper Limb: A Review

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Citation Bakhshi Kashi M, Behnejad M, Loghman A, Zamani-Badi T, Nikzad H.Study of Median Nerve Variations and Its Clinical Implications at the Distal Part of Upper Limb: A Review. Anatomical Sciences Journal. 2022; 19(1):1-10.

Article info:
Received: 29 Jan 2017
Accepted: 19 Dec 2021
Available Online: 01 Jan 2022

Keywords:
Median Nerve, Variation, Upper Limb, Clinical Implication

ABSTRACT

Introduction: Median Nerve (MN) originated from medial and lateral cords of Brachial Plexus and can be affected by anatomical variations, which may lead to several diagnostic and therapeutic mistakes. This paper aimed to study MN variations investigated by cadaveric studies.

Methods: This study is based on research in electronic databases. The full text of all relevant papers has been studied to extend our data.

Results: variation of MN distribution in the palm, variation of MN innervation patterns, communication between MN and (Ulnar Nerve) UN and their branches in the forearm, communication between MN and UN and their components in the palm, variation in the course of MN are main MN variation categories containing several subgroups. However, communication between the third common digital nerve of MN and the fourth common digital nerve of UN is the most common MN variation at the distal of upper limbs.

Conclusion: decompression of MN entrapped in the carpal tunnel can be considered the essential clinical challenge resulting from MN variations, especially variations including the third common digital nerve.

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1. Introduction

Lateral (C5,6,7) and medial (C8, T1) cords of brachial plexus (BP) give two main median nerve (MN) roots uniting anterior to the axillary artery to form MN [1]. This formation pattern follows the BP embryological development basis in which the upper limb buds are included in the cervicothoracic segments (C5-T1) region and develop through the upper limb mesoderm and pierces it as ventral rami of the spinal cord [2].

After forming anterolaterally to the brachial artery, MN distally runs and crosses to the medial side of the brachial artery. Interestingly, branches supplying the elbow joint are reported as a single division of MN in the arm and axilla. The medial aspect of the brachial artery and heads of pronator teres are entrance and exit points that MN passes through them within the cubital fossa. Then MN runs between flexor digitorum superficialis and profondus to hand while passes deep to Palmaris longus and flexor retinaculum. The distal edge of the flexor retinaculum is the point at which the recurrent branch derives from the lateral side of the MN trunk supplying three Thenar muscles. Then, it runs around the flexor retinaculum. After passing between the flexor pollicis brevis and abductor pollicis brevis, its pathway ends in the medial edge of the opponens pollicis muscle, and then two main ramus derive from MN. The lateral ramus (first Common Digital Nerve [CDN]) supplies the thumb and lateral side of an index by two Proper Palmar Digital Nerves (PPDN), which the nerve to the radial side of the index innervates the first lumbrical muscle. The medial ramus divides into two (second and third) CDN supplying medial aspects of the index and adjacent sides of the middle digit and lateral side of the ring digit, and the second CDN supplies the second lumbrical muscle [1, 3].

Behnejad et al. [4] studied MN variations in the proximal part of the upper limbs. However, the complications involved in MN distal to cubital fossa are common and have clinical importance; for example, entrapment of MN in the carpal tunnel is the most common entrapment neuropathy in the clinical setting [5-7]. Still, anatomical variations from unremarkable abnormality to noticeable changes with diagnostic and therapeutic clinical importance can affect every part of the human body. MN variations also are common and are investigated and reported by many authors [8-14].

This survey aims to study median nerve variations and their clinical implications in the distal part of the upper limb to help surgeons, electrophysicians, and radiologists better know MN anatomy and anomaly to decrease iatrogenic mistakes.

2. Materials and Methods

This study is based on data published about MN variation from 1990 to 2020. Pubmed, Science Direct, and Google Scholar were researched to obtain relevant data by the following keywords: "Median nerve," "Brachial plexus," "Carpal tunnel," and MeSH phrases made from the terms "Variation," and "Cadaveric study." We limited our research to dissection investigations. After downloading articles, we again searched associated references of pieces of literature to increase our data. Case reports, multiple cadaveric studies, and review articles were chosen for this study, and we didn't apply any limitations. After reading the full text of all papers, we classified MN variations as reported in this paper.

3. Results

We categorized MN variations and coexistence anomalies into five groups as reported. Communication between the 4th common digital nerve of UN to the 3rd CDN of MN is the most common MN variation at the distal of the upper limb. The total numbers of cases with variation in the distribution of MN are 327 cases (Table 1).

4. Discussion

MN anatomy distal to cubital fossa doesn't wholly match with related anatomy textbooks explanations and its different anatomy reported by many authors [8, 14, 15-41]. The MN anomalies have spread spectrum in type and prevalence [8-10, 13, 37]. Notably, the prevalence of variation investigated in dissection studies is more common than in surgical observation, probably because of limitations on patient dissection [10, 13, 42-44]. We mention coexistence anomalies in the separation part because MN variation can be attributed to other coexistence variations disrupting normal MN development [9, 15, 32]. Variations in the distribution of MN were reported in 252 cases, including different types of variations. Of 327 patients, 113 can be categorized in one of Lanz's classification groups (Tables 2, 3, 4 and 5). However, the new variations compiled from cadaveric observations can be classified into five groups:

I) Variation in the distribution of MN in palm (Table 5)

II) Variation in MN innervation pattern (Table 5)

III) Communicating branches between MN and UN in the forearm (Table 6)

IV) Communicating branches between MN and UN in palm (Tables 7, 8, 9, 10 and 11)

V) Variation in the course of MN (Table 12)

Lanz's classification contains (Tables 2, 3 and 4):

I) Variation of thenar branch course

II) Accessory branches derived from MN at the distal of carpal tunnel

III) High division of MN

IV) Accessory branches derived from MN at the proximal part of carpal tunnel

The prevalence of MN variation described by Lanz's groups (I-IV) were 46%, 7.5%, 2.9%, and 2.9%, respectively [13]. However, our study verifies the high prevalence of Lanz I, too.

Entrapment of MN beneath the flexor retinaculum presented by carpal tunnel syndrome, including some symptoms (such as numbness and weakness) and signs (such as Tinel sign and Phalen sign). These signs and symptoms can be alleviated by decompressing MN via endoscopic or open surgeries [45-48]. Unfortunately, injury to the third common digital nerve (TCDN) is the most common post-carpal tunnel release operation complication [49]. Despite the clinical importance of the TCDN branching pattern, its variations had not been reported since Engineer et al. [14] classified variations of TCDN into three groups:

1) TCDN originates from MN proximal to the distal edge of the TCL

2) TCDN originates from MN distal to TCL but proximal to superficial palmar arch

3) TCDN originates from MN distal to TCL and superficial palmar arch

Notably, all TCDN variations may be vulnerable to damage by open carpal tunnel surgeries. Types 2 and 3 may potentially risk injury in endoscopy techniques. Despite visualization limitations, the Agee endoscopic surgery technique can preserve TCDN and its three types of variations from possible damage if done by a professional surgeon [14].

High bifurcation and trifurcation of MN are common variations of MN distribution [17]. Amadio documented high bifurcation MN in 9 cases in carpal tunnel decompression surgery [50]. Abnormal origination of recurrent branches is another variation of MN distribution, increasing the risk of MN injuries in carpal tunnel decompression [17].

Supplying all lumbricals from UN is highly associated with the presence of MGA in the forearm [23]. Originating the third lumbrical muscle nerve from MN is a rare variation reported by some authors [17, 51]. However, proximal UN injuries with incomplete clawed-hand must be considered as the presence of MGA [52]. Linell [53] reported one hand in which the UN supplied two sides of the ring finger and three hands in which the UN innervated the medial side of the middle finger. However, all variations associated with MN innervations patterns may disrupt post-trauma evaluations.

Martin-Gruber anastomosis was first described by Swedish anatomist Martin (1763) [54] and Gruber (1810) [55], is a connection between MN and UN in the forearm, and it can be classified into seven subtypes as documented in the previous part (Table 5). MGA has been seen in the primate's elbows too. The MGA reveals a common trunk supplying the flexor compartment of the forearm in embryological life [56]. Examination of family members with MGA variations indicated some genetic features of this variation, and an Autosomal Dominant pattern was suggested for it [57]. Some hypotheses consider the role of chromosome 21 in this variation. Srinvasan and Rhodos [58] reported MGA bilaterally in fetuses carrying an extra 21 chromosomes (21 trisomies). Prevalence of MGA follows a difference statistically high prevalence of MGA was reported by Erdem et al. [59], Amoiridis [60], Lee et al. [29], and medium prevalence was reported by Shu et al. [25], and Nakashima [24] and low prevalence of this variation was documented by de Alemida et al. [61] and Prates et al. [62]. These different ranges can be explained by the different methodology used for studies and genetic variation between examined target populations [26]. Notably, MGA can change the clinical manifestations of patients suffering from pronator syndrome by changing muscle innervation patterns and sensory distribution [28, 63].

Marinacci anastomosis, called Martin-Gruber reverse anastomosis too, was first reported in a patient who

Table 1. Variation in CDN distribution

Variable	Variations	No(%)	Authors
Variation in CDN[1] distribution	CDN originated from MN proximal to carpal tunnel	8(2.44)	Krol 2005 [11], Sanudo 1994 [20], Sundaram 2008 [21], Agarwal 2014 [9]
	3rd CDN originates from MN within the carpal tunnel proximal to the distal edge of the TCL[2]	3(0.91)	Engineer 2008 [14]
	3rd CDN originates from MN distal to the TCL but proximal to the superficial palmar arch	14(4.28)	Engineer 2008 [14]
	3rd CDN originates distal to the TCL and at or distal to the superficial palmar arch	3(0.91)	Engineer 2008 [14]

1: Common Digital Nerve
2: Transverse Carpal Ligament

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Table 2. Lanz's classification

Variable	Variations	No(%)	Authors
Lanz	I	76(23.24)	Agarwal 2014 [10], Mizia 2011 [15], Barbe 2005 [10]
	II	12(3.66)	Agarwal 2014 [9], Mizia 2011 [15], Stancic 1995 [16]
	III	19(5.81)	Agarwal 2014 [9], Barbe 2005 [10], Vashishtha 2011 [17], Mizia 2011 [15], Krol 2005 [11], Won 2009 [18], Campos 2009 [19]
	IV	6(1.83)	Agarwal 2014 [9], Mizia 2011 [15], Stancic 1995 [16]

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Table 3. Variation in recurrent branch distribution

Variation	Variables	No(%)	Authors
Variation in recurrent branch distribution	MN with more than one recurrent branches	30(9.17)	Agarwal 2014 [9], Vashishtha K. 2011 [17], Kozin 1998 [22], Sanudo 1994 [20]
	The recurrent branch originated from the anterior aspect of MN	69(21.10)	Vashishtha K. 2011 [17], Kozin 1998 [22], Mizia 2011 [15]
	The recurrent branch originated from the anteromedial aspect of MN	13(3.97)	Vashishtha V. 2011 [17], Stancic 1995 [16], Kozin 1998 [22], Mizia 2011 [15]

ANATOMICAL SCIENCES

Table 4. Abnormal division of MN

Variable	Variations	No(%)	Authors
Abnormal division of MN	High PCN[1] origin	1(0.30)	Sanudo 1994 [20]
	Trifurcation of MN	23(7.03)	Vashishtha 2011 [17]
	Bifurcation of MN to its digital branches just proximal to the distal border of FR[2]	27(8.25)	Vashishtha 2011 [17]
	Trifurcation (with thenar) at or just proximal to the distal border of FR	22(6.72)	Vashishtha 2011 [17]
	Trifurcation (with thenar) distal to the lower border of FR	1(0.30)	Vashishtha 2011 [17]

1: Palmar Cutaneous Nerve
2: Flexor retinaculum

B) Variation in MN innervation patterns:

The total numbers of cases with variation in the innervation of MN are 17 cases.

Table 5. Variation in MN innervation patterns

Variations	No(%)	Authors
All lumbricals from UN[1]	6(35.29)	Taams 1997 [23]
UN innervated 3 lumbricals	1(5.88)	Taams 1997 [23]
MN innervated 3 lumbricals	6(35.29)	Vashishtha 2011 [17]
Two and a half digital innervations pattern	2(11.76)	Vashishtha 2011 [17]
MN innervate lateral 3 digits	1(5.88)	Vashishtha 2011 [17]
Deep head of FPB[2] innervations from both MN and UN	1(5.88)	Vashishtha 2011 [17]

1: Ulnar Nerve
2: Flexor Pollicis Brevis

C) Communicating branch between MN and UN and their components in the forearm:

The total number of cases with a communicating branch between MN and UN and their branches in the forearm is 260.

Table 6. Communicating branch between MN and UN and their components in the forearm

Type of Anastomosis	Subtype	No(%)	Authors
MGA[1]	Between AIN[2] and UN	80(30.76)	Nakashima 1993 [24], Shu 1998 [25], Ballesteros 2014 [26], Sarikcioglu 2003 [27], Felippe 2012 [28], Lee 2005 [29], Taams 1997 [23], Marc Rodriguez-Niedenfuhr 2002 [30], Rodriguez-Niedenfuhr 2002 [31]
	Between MN trunk and UN	22(8.46)	Nakashima 1993 [24], Shu 1998 [25], Ballesteros 2014 [26], Sarikcioglu 2003 [27], Felippe 2012 [28], Lee 2005 [29], Marc Rodriguez-Niedenfuhr 2002 [30], Rodriguez-Niedenfuhr 2002 [31]
	Between muscular branches of FDP[3] and UN	42(16.15)	Nakashima 1993 [24], Shu 1998 [25], Ballesteros 2014 [26], Lee 2005 [29], Taams 1997 [23], Narayana 2004 [32]
	Anastomotic branches arose from both MN and UN or their branches (AIN, branch to FDP)	7(2.69)	Nakashima 1993 [24], Shu 1998 [25]
	Between a branch of MN for superficial forearm flexor muscles and UN	27(10.38)	Marc Rodriguez-Niedenfuhr 2002 [30], Ballesteros 2014 [26], Taams 1997 [23], Rodriguez-Niedenfuhr 2002 [31]
	One communicating branches from MN to UN (MGA)	77(29.61)	Marc Rodriguez-Niedenfuhr 2002 [30], Felippe 2012 [28], Ballesteros 2014 [26], Rodriguez-Niedenfuhr 2002 [31]
	Two communicating branches from MN to UN (MGA)	4(1.53)	Marc Rodriguez-Niedenfuhr 2002 [30], Rodriguez-Niedenfuhr 2002 [31]
Marinacci anastomosis	From UN to MN (with one branch)	1(0.38)	Felippe 2012 [28]

1: Martin-Gruber Anastomosis
2: Anterior Interosseous Nerve
3: Flexor Digitorum Profundus

D) Communicating branch between MN and UN and their components in palm:

The total number of cases with a communicating branch between MN and UN and their branches in palmar is 602.

Table 7. Communicating branch between MN and UN in palm

Between branches of UN and MN		
Variations	**No(%)**	**Authors**
Between the deep branch of the UN and the recurrent branch of MN	13(2.15)	Ajmani 1996 [33]
From 4th CDN of UN to 3rd CDN of MN (Berrettini anastomosis)	201(33.38)	Peter 2000 [34], Ferrari 1991 [35], Stancic 1999 [16], Tagil 2007 [36], Peter 2002 [34]
From 3rd CDN of MN to 4th CDN of UN (Berrettini anastomosis)	9(1.49)	Peter 2000 [34], Ferrari 1991 [35], Tagil 2007 [36], Peter 2002 [34], Loukas 2007 [37]
Between 3rd CDN of MN and 4th CDN of UN perpendicularly (Berrettini anastomosis)	13(2.15)	Peter 2000 [34], Tagil 2007 [36], Peter 2002 [38], Loukas 2007 [37]
From 4th CDN of UN to 3rd and 2nd CDN of MN	22(3.65)	Loukas 2007 [37]
From 4th CDN of UN to 4th and 3rd PPDN of MN	15(2.49)	Loukas 2007 [37]
From 3rd CDN of MN to 4th PPDN[1] of UN	33(5.48)	Loukas 2007 [37]
3rd CDN of MN to both PPDN branches of UN and 4th CPD of UN	1(0.166)	Sirasanagandla 2013 [39]

1: Proper Palmar Digital Nerve

Table 8. Communicating branch between MN and UN trunk

Variable	Variations	No(%)	Authors
Between UN and MN trunk	From MN to UN	8(1.32)	Bas 1999 [40], Loukas 2007 [37]
	From UN to MN	26(4.31)	Bas 1999 [40], Loukas 2007 [37], Vashishtha K. 2011 [17]
	Between MN and UN perpendicularly	4(0.66)	Loukas 2007 [37]
	Multiple communicating branches from both UN and MN	23(3.82)	Bas 1999 [40], Loukas 2007[37], Kawashima 2004 [41], Tagil 2007 [36], Vashishtha K. 2011 [17]

Table 9 Communicating branch between MN and its branches

Variable	Variations	No(%)	Authors
Between MN and its branches	From the major component of MN to 3rd CDN (in one case with a high division of MN)	1(0.166)	Krol 2005 [11]
	Between 1st and 2nd PPDN of thumb	5(0.83)	Agarwal 2014 [9]
	Between 1st and 2nd CDN	3(0.49)	Agarwal 2014 [9]
	Between PPDN of thumb and PPDN of index	1(0.166)	Agarwal 2014 [9]
	Between the palmar cutaneous branch and the recurrent branch of MN	1(0.166)	Kozin 1998 [22]

Table 10. Communicating branch from UN to MN branches

Variable	Variations	No(%)	Authors
From UN to MN branches	From UN to 3rd CDN of MN	180(29.9)	Loukas 2007 [37], Krol 2005 [11], Kawashima 2004 [41]
	From UN to 1st and 2nd CDN and MN itself	6(0.99)	Loukas 2007 [37]
	One branch from UN to 7th PPDN of MN	1(0.166)	Kawashima 2004 [41]
	From 3rd CDN to UN	10(1.66)	Engineer 2008 [14]

Table 11. Communicating branch from MN to UN branches

Variable	Variations	No(%)	Authors
From MN to UN branches	From MN to 4th CDN of UN	24(3.98)	Kawashima 2004 [41]
	From the MN to the PPDN supplying the medial half of the 5th digit	2(0.33)	Loukas 2007 [37]

E) Variation in the course of MN:

The total numbers of cases with variation in the course of MN are 50 cases.

Table 12. Variation in the course of MN

Variations	No(%)	Authors
MN anterior to ulnar bursa in carpal tunnel	1(2)	Vashishtha K. 2011 [17]
Transligamentous MN (in a fascial canal)	2(4)	Vashishtha K. 2011 [17], Vashishtha 2010 [42]
PCN entered a tunnel in TCL	1(2)	Naff 1993 [43]
PCN course under FR	1(2)	Mogra 2014 [8]
Transligamentous thenar branch	45(90)	Agarwal 2014 [9], Kozin 1998 [22], Vashishtha K. 2011 [17], Stancic 1995 [16], Mizia 2011 [15]

F) Coexistence variations:

The total numbers of cases with other MN variations are 18 cases.

Table 13. Coexistence variations

Variations	No(%)	Authors
PMA[1]	11(61.11)	Agarwal 2014 [9], Mizia 2011 [15], Krol 2005 [11], Sanudo 1994 [20], Barbe 2005 [10]
The median nerve formed a ring enclosing the median artery	1(5.55)	Sanudo 1994 [20]
Gantzer's muscle	3(16.66)	Narayana 2004 [32], Campos 2009 [19], Won 2009 [18]

presented with MN trauma, and despite forearm flexor muscle denervation, hand muscle function was normal [64]. However, communicating branch from UN to MN (Marinacci anastomosis) is a rare variation, and Kimura et al. [65] didn't report any UN to MN communication in their electrophysiological examinations.

Palmar communication between MN and UN is the most common variation of MN and can be categorized into five subtypes as presented. Communicating branches often arose from UN to MN and were reported by some authors [23, 56, 57, 66]. However, the crucial role of these connections is in changing the pattern of sensory loss when MN or UN is compressed, which may lead to clinical mistakes [67].

Petro Berrettini [68] was the first man to paint the superficial palmar communication between UN and MN in the anatomy atlas. The Berrettini anastomosis can be categorized into three groups, as reported in the previous part (Table 4). However, some authors believed that Berretin anastomosis must be considered a normal anatomic discovery, and even in some papers, this anastomosis has been seen in all cases [69, 70].

Don Griot et al. [34] emphasized the advantage of Berretin anastomosis knowledge for surgeons performing carpal tunnel release, Dupuytren fasciotomy, and flexor tendons surgeries. Because of the high prevalence of UN and MN communications and their possible role in either diagnostic or therapeutic mistakes, some studies should be done to evaluate the relation of these variations and their potential clinical manifestation.

Subligamentous, Extraligamentous, and Transligamentous (rather than transverse carpal ligament) are pathways in which the thenar branch of MN passes through them to reach the thenar muscle and are explained by some authors [9, 15, 17]. Recurrent branches of MN passed through the transverse carpal ligament have critical importance in carpal tunnel release and loss of motor function in possible injuries that may lead to adverse iatrogenic morbidity [22].

PMA is the most common coexistence anomaly with MN variations reported by some authors [11, 15, 20] (Table 13). Because of the involution of PMA in embryologic life, it is not seen in adults usually [71]. However, Gassner [72] reported PMA in 16% of 100 hands studied by color Doppler ultrasonography in 50 asymptomatic volunteers. PMA is commonly associated with high division of MN [9-11, 44]. Most people with PMA seem asymptomatic [72], but some suffer from carpal tunnel syndrome secondary to PMA thrombosis [73, 74].

Incomplete superficial palmar arch is another significant coexistence anomaly, and its possible simultaneous neural variations must be considered by surgeons performing vascular grafts or repairing vascular surgeries [39]. The Gantzer's muscle (flexor digitrum profundus with two accessory heads) and simultaneous neural variations can cause a clinical condition called anterior interosseous syndrome [75]. The knowledge of these variations reported in the paper may be helpful for all specialists concerned about MN surgery, electrophysicion, and radiologic evaluation.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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