ORIGINAL ARTICLE



Persistent median artery: paedogenesis of the antebrachial arterial system in the human body

Shinnosuke Yamada¹ · Kyutaro Kawagishi² · Takaya Ishii¹ · Hidenobu Miyaso³ · Hirotaka Yoshioka¹ · Yoshiharu Matsuno⁴ · Yasutake Mori¹ · Jun Kosaka¹

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Abstract

The persistence of the median artery in adult life, a remnant of the early brachial artery in the embryonic stage, has been reported in many anatomical and clinical studies. Herein, we aimed to investigate the prevalence and origin of the median artery in cadavers. We examined 53 adult Japanese cadavers and carefully dissected 106 upper limbs, and the arterial systems in the forearms and hands were observed macroscopically. We found the palmar type of the median artery on 106 sides in 53 cadavers, and found that it passes through the carpal tunnel and forms the superficial palmar arch in the hand in only two cadavers. The antebrachial type, ending in the forearm before reaching the wrist joint, was detected on 63 sides in 44 cadavers. The proportions of the origins of the median artery examined in this study were as follows: originating from the common interosseous artery (CIA) on 15 sides (23%), anterior interosseous artery (AIA) on 9 sides (14%), ulnar artery (UA) on 16 sides (24%), and CIA–UA trunk on 26 sides (39%). None arose from other arteries in the upper limbs. Based on our results and the current theory on vascular development, we conclude that the term 'persistent median artery' must be strictly used for the one that arises from the arteries in the forearm except for the radial artery, and the presence of this ontogenetic remnant can be interpreted as paedogenesis in the human body. We also describe that the increasing trend in the incidence of the median artery since the nineteenth century, as pointed out by a few researchers, may represent 'nearly neutral evolution' at the phenotypic level in human populations.

Keywords Anatomical variation · Heterochrony · Neutral evolution · Paedomorphosis

Shinnosuke Yamada syamada@iuhw.ac.jp

- ¹ Faculty of Medicine, School of Medicine, International University of Health and Welfare, Narita Campus, Kozunomori 4-3, Narita City, Chiba Prefecture 286-8686, Japan
- ² Department of Anatomy and Structural Science, Faculty of Medicine, Yamagata University, Iidanishi 2-2-2, Yamagata City, Yamagata Prefecture 990-9585, Japan
- ³ Department of Anatomy, Tokyo Medical University, Shinjuku 6-1-1. Shinjuku-Ku, Tokyo 160-8402, Japan
- ⁴ Basic Medicine Research Centre, International University of Health and Welfare, Narita Campus, Kozunomori 4-3, Narita City, Chiba Prefecture 286-8686, Japan

Introduction

Heterochrony—changes in the timing or rates of the development of morphological traits or both during ontogeny is a significant concept in developmental and evolutionary biology, with the increased and decreased degrees of development called 'paramorphosis' and 'paedomorphosis', respectively (Reilly et al. 1997; McNamara 2012). Both the 'paramorphic' and 'paedomorphic' processes occurring during ontogeny seem to have been involved in the evolution of human traits (Bufill et al. 2011), and paedomorphic traits, defined under the term 'neoteny', have been detected in the human body in previous studies (Shea 1989; Godfrey and Sutherland 1996; Somel et al. 2009).

The 'persistent median artery', a remnant of the early brachial artery in embryonic life, has been reported to be present in the human forearm by several studies (Adachi 1928; Henneberg and George 1992a; Aragão et al. 2017). In the forearm, the brachial artery branches at the elbow joint into

the ulnar artery (UA) and radial artery, which anastomose in the hand to form the superficial and deep palmar arches, and the common interosseous artery (CIA), including the anterior and posterior interosseous arteries, branches from the UA. The persistent median artery is occasionally found as an extra artery originating from one of these arteries in the forearm and running parallel to the median line of the forearm. This artery mostly disappears proximal to the carpal tunnel but rarely passes through the carpal tunnel and joins the palmar arch. A few previous researchers investigated or reviewed the anatomical characteristics of the persistent median artery, i.e. its origin, course, and prevalence, but most of their observations have been inconclusive and remain disputed (Rodríguez-Niedenführ et al. 1999; Kodama 2000; Solewski et al. 2021). Several researchers have traditionally identified this extra artery running parallel to the median line of the forearm as the persistent median artery without considering its developmental homologue and the process underlying its development (Henneberg and George 1992a; Matsunaga et al. 2001; Elhossiny et al. 2023). Therefore, in this study, we first describe the persistent median artery based on our macroscopic results, and then discuss its significance in developmental biology and human evolution.

Materials and methods

In the present study, we examined 53 adult Japanese cadavers (32 males and 21 females, aged: 50–100 years). We carefully dissected 106 upper limbs (right: 53, left: 53), and the arterial systems in the forearms and hands were observed macroscopically. Initially, the presence of the median artery was assessed and then its origin and termination were investigated. The cadavers were embalmed with an aqueous solution of 3.7% formaldehyde and 34.0% ethanol. None of the upper limbs showed evidence of previous surgical procedures or trauma to the examined region. The definitions of the two morphotypes of the median artery are as follows: the median artery passing through the carpal tunnel is a 'palmar type', and the one ending before reaching the wrist joint is an 'antebrachial type' (Rodríguez-Niedenführ et al. 1999).

Results

The prevalence of the persistent median artery in the forearm, recorded in this study, is listed in Table 1. A total of 66 median arteries (right: 31, left: 35) were found in 44 cadavers (25 males and 19 females) in their examined upper limbs (Table 2). The arteries were bilateral in 22 cadavers and

Table 1 Prevalence rate of the persistent median artery

	Palmar ty	pe (%)	Antebrachial type (%)			
	Left	Right	Left	Right		
Male (64)	1.6 (1)	1.6 (1)	31.3 (20)	29.7 (19)		
Female (42)	-	2.4 (1)	33.3 (14)	23.8 (10)		
Total (106)	0.9 (1)	1.9 (2)	32.1 (34)	27.4 (29)		

Arabic numerals in parenthesis represent the sample size

unilateral in 22 cadavers (9 on the right and 13 on the left). The cadavers under examination did not exhibit co-variants in muscles, related nerves, and other arterial variants. The median arteries found in this study were located beneath the flexor digitorum superficialis and ran parallel to the median nerve (Figs. 1 and 2). These median arteries nourished the flexor digitorum superficialis (n=38), flexor digitorum profundus (n=7), pronator teres (n=7), flexor pollicis longus muscle (n=2), palmaris longus muscle (n=2), and the median nerve (n=16). We found no median artery penetrating the anterior interosseous or median nerve (Matsunaga et al. 2001; Buch et al. 2019).

Only two cadavers revealed the presence of the palmar type of the median artery (Fig. 1 and Table 2). The median artery arose from the CIA–UA trunk (branching point between the CIA and UA) bilaterally in the male cadaver and originated from the UA only on the right side of the female cadaver. These arteries run parallel to the median nerve and pass through the carpal tunnels. Finally, these arteries merged with the UA to form the superficial palmar arterial arch in both cadavers.

The remaining 63 median arteries were of the antebrachial type (Fig. 2 and Table 2). The origins of these median arteries varied, although all arteries ran parallel to the median nerve and penetrated neither the median nor the anterior interosseous nerve. The antebrachial types identified in this study arose from the CIA (n=15), AIA (n=9), UA (n=16), and CIA–UA trunk (n=26) (Table 3). The median arteries terminate irregularly in each forearm.

Discussion

Definition of the 'persistent median artery' as the ontogenetic remnant

A persistent median artery has been reported by many previous researchers who have described the presence, course, size or variations of the median artery (Adachi 1928; Henneberg and George 1992a, b; Sañudo et al. 1994; Kopuz

Persistent median a					

0		Persistent median arteries found in this study					Table 2 (continued)			
Sex	Side	Туре	Origin	Blood supply	Age	Sex	Side	Туре	Origin	Blood supply
М	R	Pal	CIA-UA trunk	_	78	F	R	-	_	_
	L	Pal	CIA-UA trunk	_			L	Ant	UA	FDP
F	R	Pal	UA	_	72	Μ	R	Ant	UA	MN
	L	Ant	UA	РТ			L	Ant	UA	MN
М	R	Ant	CIA-UA trunk	FDS	80	F	R	Ant	CIA-UA trunk	-
	L	-	_	_			L	Ant	CIA-UA trunk	-
F	R	Ant	AIA	FDS, FDP, MN	76	Μ	R	Ant	UA	FDS
	L	_	_	_			L	Ant	CIA	FDS
F	R	Ant	CIA	FDS	50	Μ	R	-	-	-
	L	_	_	_			L	Ant	UA	FDS, MN
М	R	_	_	_	53	F	R	Ant	AIA	_
	L	Ant	CIA-UA trunk	FDS			L	Ant	AIA	_
F	R	_	_	_	79	F	R	Ant	CIA-UA trunk	FDS
		Ant	AIA	FDS			L	Ant	CIA-UA trunk	MN, PT
М	R	Ant	UA	FDS	94	М	R	-	-	_
	L	Ant	CIA				L	Ant	CIA	FDP
М		Ant			89	F	R	Ant	CIA	FDS
							L	_	_	_
F			_	_	90	М	R	Ant	AIA	FDS, MN
				_				_	_	_
F				FDP. PT	73	F		Ant	CIA-UA trunk	РТ
								_	_	_
F			_		77	М		Ant	CIA-UA trunk	FDS
-										FDS
м					80	М				FDS
										FDS
F					67	F				FDS
								_	_	_
м					91	М		Ant	CIA-UA trunk	FDS
										_
м					98	м				FDS
IVI					20	111				FDS
F					80	м				FDS
1					00					FDP, FPLM
м					62	м				MN
IVI					02	111				FPLM, MN
м					73	м				FDS
IVI					75	111				FDS, MN
Б							L	Ant		
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IVI					FPLM	flexor p	ollicis lo	ngus mus	cle, PLM palmar l	
F					pronat	or teres,	MN med	ian nerve		
H	R	-	-	-						
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Table 7 Da -----... а : th:

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73

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CIA-UA trunk

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UA

MN

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FDS, MN

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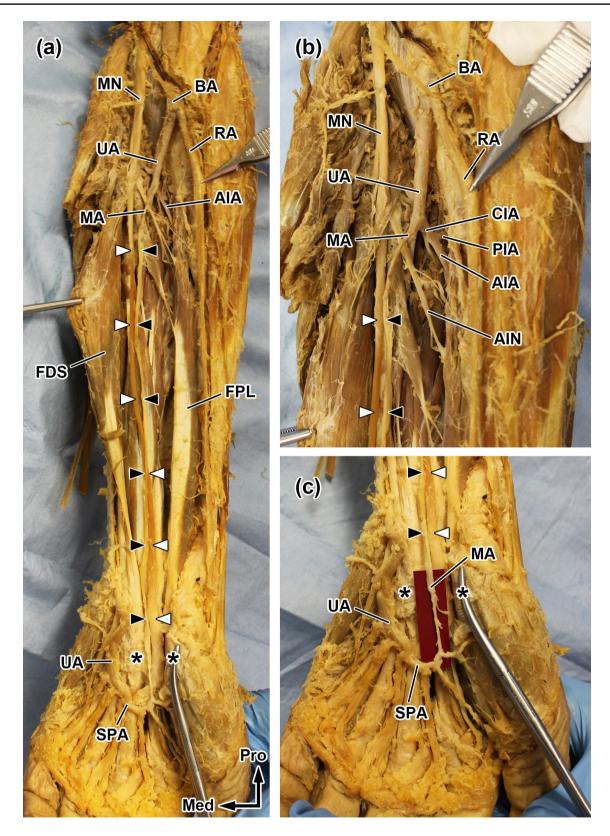


Fig. 1 Palmar type of the persistent median artery (MA). (a) The whole image of the palmar type. (b) Image depicting the origin of the MA. (c) Image showing the superficial palmar arterial arch (SPA), continuous with the MA. Asterisks show the flexor retinaculum, which is opened and excised. Black and white arrowheads represent

the paths of the MA and median nerve (MN), respectively. AIA anterior interosseous artery, AIN anterior interosseous nerve, BA brachial artery, CIA common interosseous artery, FDS flexor digitorum superficialis, FPL flexor pollicis longus, PIA posterior interosseous artery, RA radial artery, UA ulnar artery

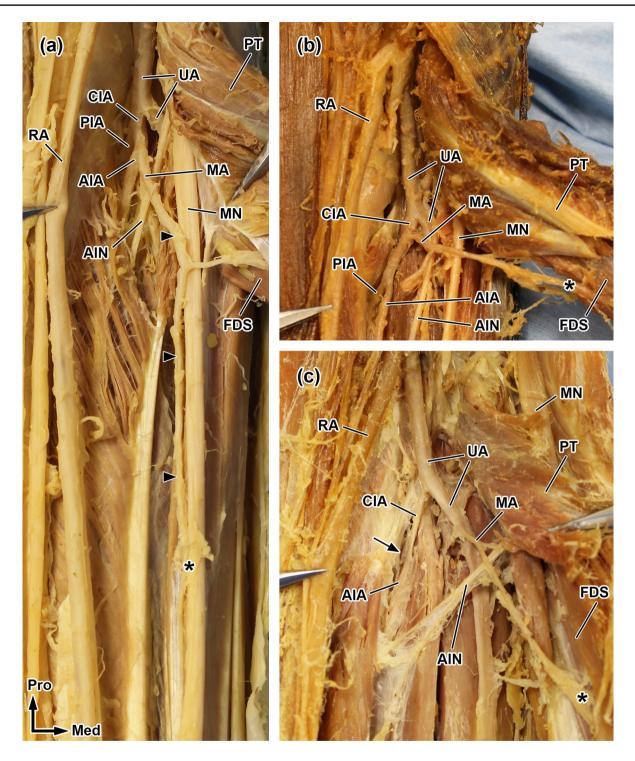
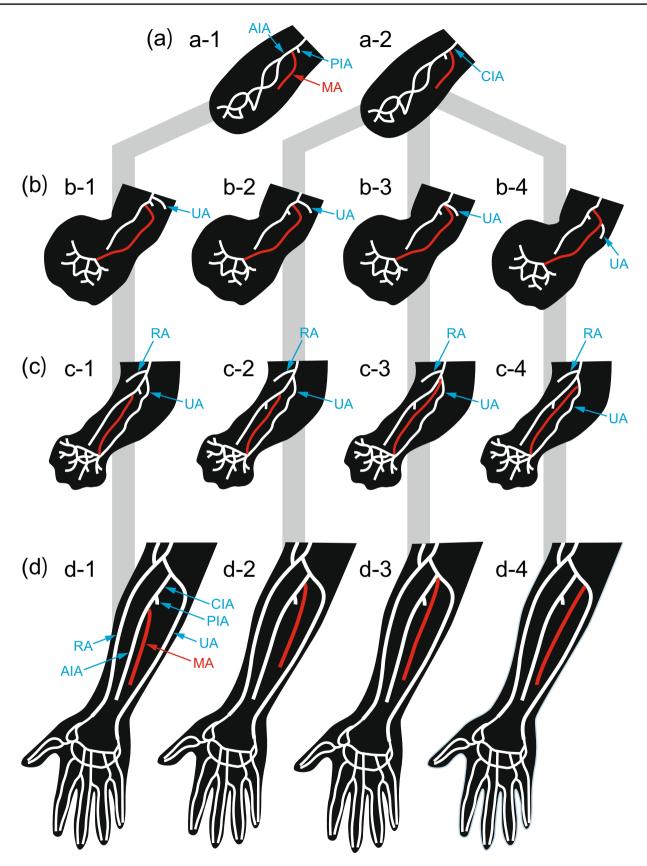


Fig. 2 Various origins of the antebrachial type of the persistent median artery (MA). (a) Image depicting the MA originating from the anterior interosseous artery (AIA). (b) Image showing the MA originating from the common interosseous artery (CIA). (c) An image of the MA, originating from the ulnar artery (UA). Asterisks show the terminal part of the MA. Arrowheads represent the path of

the MA. The arrow in (c) indicates the branching point between the AIA and posterior interosseous artery (PIA). The image of the antebrachial type originating from the CIA–UA trunk is not shown. *AIN* anterior interosseous nerve, *BA* brachial artery, *FDS* flexor digitorum superficialis, *MN* median nerve, *PT* pronator teres, *RA* radial artery



◄Fig. 3 Ontogenetic development of the persistent median artery (MA) with different origins. Drawings of the forearm (MA drawn in red), modified from DeSesso (2017). (a) Drawings depicting the initiation of the MA formation. (b) Drawings showing the MA, continuous with the coalescence of capillaries in the limb bud, and then the ulnar artery (UA) emerges. (c) Drawings of the UA merging with the coalescence of capillaries and the MA, while the radial artery (RA) begins to be formed. (d) As the development proceeds, the MA and anterior interosseous artery (AIA) regress. On the contrary, the RA and UA merge with the capillary plexus in the hand and form the palmar arterial arch. *CIA* common interosseous artery, *PIA* posterior interosseous artery

Eid et al. 2011; Jelev and Georgiev 2011; Potu et al. 2011; Singla et al. 2012; Agarwal et al. 2013; Klimek-Piotrowska et al. 2013; Ariyo and Shea 2016; Patnaik and Paul 2016; Cheruiyot et al. 2017; Carry et al. 2018; Haładaj et al. 2019; Alexander et al. 2020; Elhossiny et al. 2023). However, most of these findings remain disputed, and there is little consensus regarding this anomalous artery. Plausible knowledge regarding the median artery based on the results of previous studies includes the following: (1) the median artery is the remnant of the antebrachial artery of the foetuses (Singer 1933; Rodríguez-Niedenführ et al. 2001); (2) the palmar and antebrachial morphotypes, which differ in terms of whether they pass through the carpal tunnel, have been described, and the prevalence of the former is lower than that of latter (Huelin et al. 1979; Srivastava and Pande 1990; Rodríguez-Niedenführ et al. 1999; Solewski et al. 2021); and (3) the prevalence of the median artery in foetuses or neonates is higher than that in adults (Kopuz et al. 1997; Aragão et al. 2017; Solewski et al. 2021). Most previous researchers have sporadically reported an extra artery running parallel to the median nerve in the forearm as the 'persistent median artery'; therefore, we had no way to confirm the developmental homologue of this anomaly artery, which is one of the reasons why we faced some difficulties in elucidating the process underlying the persistence of the median artery.

The prevalence of the palmar type is significantly lower than that of the antebrachial type (Table 1). The origins of the median artery are varied (Table 2), including from the CIA (22.7%), AIA (13.6%), UA (24.2%), and CIA-UA trunk (39.3%): however, we found no cadaver with the median artery arising from the radial or brachial artery, which was reported by previous studies (Nakane and Igawa 1955; Henneberg and George 1992a; Wood et al. 1997; Rodríguez-Niedenführ et al. 1999; Elhossiny et al. 2023). The prevalence rate of the median artery arising from the radial artery is much lower than that of those with other origins (Table 3), and this type of median artery has rarely been reported hitherto (Matsunaga et al. 2001; Tsuruo et al. 2006; Natsis et al. 2009; Patnaik and Paul 2016; Aragão et al. 2017). Our results reveal that most median arteries originate from the interosseous or ulnar artery and end proximal to the wrist joint. In contrast, the palmar type of the median artery and the median artery originating from the radial artery are extremely rare. Hence, we can consider the two morphotypes of the median artery to represent the degree of regression of the artery during ontogeny, because the median artery is usually fused with the interosseous or ulnar artery at an early embryonic stage. Therefore, we propose that the 'persistent median artery' is the remnant of the early brachial artery (Fig. 3), and the 'persistent median artery' reported in some previous studies should be excluded because it is not the remnant of the median artery in the early embryonic stage. The current theory, widely accepted in textbooks, attributes the vascular development of the upper limb to sprouting angiogenesis (Singer 1933; DeSesso 2017). First, vascular development begins at stage 12 (embryonic day 26) and the capillary plexus appears in the limb bud. Then, the AIA (with a branch forming the posterior interosseous artery) exists as the main axial artery in the limb, terminating in the capillary plexus (Hubmer et al. 2004). In later stages, the median artery branched from the main brachial artery and became the main artery of the forearm (Fig. 3a). In the subsequent stages, the UA arises via sprouting angiogenesis (Fig. 3b), and the radial artery begins to arise from the brachial artery (Fig. 3c). Finally, the ulnar and radial arteries become dominant, forming the superficial and deep palmar arches in the hand region, whereas,

Authors	Origins of the median artery (%)								
	CIA	AIA	UA	RA	CIA-UA trunk				
Rodríguez-Niedenführ et al.	7 ^a (2)	$14^{a}(4)$	17 ^a (5)	3 ^a (1)	59 ^a (17)				
(1999)	12 ^b (10)	55 ^b (46)	-	2 ^b (2)	31 ^b (26)				
Matsunaga et al. (2001)	24 (23)	33 (32)	22 (22)	1(1)	20 (20)				
Cheruiyot et al. (2017)	57 (21)	35 (13)	8 (3)	-	-				
This study	23 (15)	14 (9)	24 (16)	-	39 (26)				

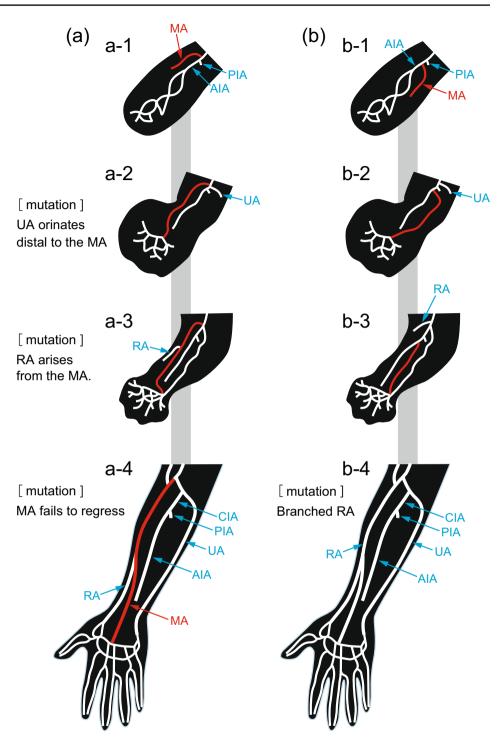
AIA anterior interosseous artery, CIA common interosseous artery, CIA-UA trunk branching point between the common interosseous artery and ulnar artery, RA radial artery, UA ulnar artery

^aValue of the palmar type

^bValue of the antebrachial type, Arabic numerals in parenthesis represent the sample size

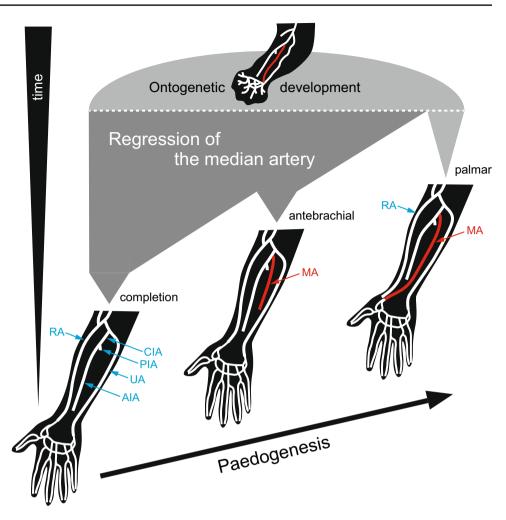
Table 3Prevalence rates of themedian artery, as reported in theprevious studies

Fig. 4 Drawings of presumed model regarding the ontogenetic process of the persistent median artery (MA; drawn in red) originating from the radial artery (RA), reported by the previous studies. (a) Drawings depicting the case of the persistent MA originating from the RA. (b) Drawings showing the case of branched RA. *AIA* anterior interosseous artery, *CIA* common interosseous artery, *PIA* posterior interosseous artery, *UA* ulnar artery



the median artery undergoes partial or complete regression (Fig. 3d). We can describe the 'persistent median artery' as a remnant of partial regression, branched from the various antebrachial origins, i.e. the AIA (Fig. 3a-1, b-1, c-1, d-1), CIA (Fig. 3a-2, b-2, c-2, d-2), CIA–UA trunk (Fig. 3a-2, b-3, c-3, d-3), and UA (Fig. 3a-2, b-4, c-4, d-4). Herein, we propose that the median artery branching from the radial artery is not a remnant of regression because it is unfeasible for the

median artery to originate from the radial artery during normal vascular development (Fig. 4). If the persistent median artery branches from the radial artery, at least three mutations must have occurred during ontogeny (Fig. 4a-1, a-2, a-3, a-4). However, if the medial branch of the radial artery has been misidentified as a persistent median artery, only one mutation is required (Fig. 4b-1, b-2, b-3, b-4). Another theory regarding the vascular development of the upper limb **Fig. 5** Paedogenesis of the arterial system in the human forearm. The morphotypes of the persistent median artery (MA; drawn in red) are formed owing to the differences in the degree of the regression of the median artery, and their formation is interpreted as the paedogenesis of arterial systems in the forearm. *AIA* anterior interosseous artery, *CIA* common interosseous artery, *RA* radial artery, *UA* ulnar artery



proposed by Rodríguez-Niedenführ et al. (2001) claims that the arterial pattern of the upper limb develops from an initial capillary plexus via the enlargement and differentiation of selected parts. The theory further states that the median artery is one of the early main vessels in the limb bud, and the radial artery is the main artery formed later, implying that regardless of the validity of these theories, our explanation is reasonable. Additionally, the persistent median artery originating from the radial artery, as reported in previous studies (Henneberg and George 1992a; Wood et al. 1997; Rodríguez-Niedenführ et al. 1999; Elhossiny et al. 2023), has the following common features: (1) its prevalence rate is much lower than that of those having other origins; (2) it runs in the superficial muscle layer of the forearm (superficial to the flexor digitorum superficialis); and (3) it joins the palmar arch, and its antebrachial type has never been found. These findings support our hypothesis that the persistent median artery branching from the radial artery is not the true 'persistent median artery'. Therefore, we must use the term 'persistent median artery', implying the remnant of the early main artery in the upper limb, for the median arteries originating from the arteries of the forearm except for the radial artery, as the medial branch of the radial artery is likely to have been misidentified as the median artery.

Evolutionary trend regarding the persistent median artery

Many previous studies have traditionally considered that the median artery in adults is formed by the regression of the median artery present in the early stage of ontogeny (Henneberg and George 1992a; Rodríguez-Niedenführ et al. 1999). Several studies have provided the following evidence to support this idea: (1) the median artery is the transitory vessel representing the arterial axis of the human forearm during the early embryonic stage (Singer 1933; Rodríguez-Niedenführ et al. 2001), (2) the prevalence of this artery in foetuses is higher than that in adults (Kopuz et al. 1997; Aragão et al. 2017; Solewski et al. 2021), and (3) the median artery may continue to regress progressively even after birth because of the probability of its regression by 4.4% every 1-year (Carry et al. 2018). The two morphotypes (the palmar and antebrachial types) of the median artery have been reported previously (Rodríguez-Niedenführ et al. 1999; Kodama 2000; Matsunaga et al. 2001; Solewski et al. 2021). In this study, we found both morphotypes (Figs. 1 and 2) and that the morphology of the antebrachial type is irregular (Fig. 2). The different morphologies of the antebrachial type, which terminated around the wrist joint, midpoint of the forearm, or elbow joint, are thought to represent the degree of regression of the median artery during ontogeny, indicating that the persistent median artery is not a simple vestigial organ in the human body. Therefore, the 'persistent median artery' is undoubtedly a remnant of the median artery in embryonic life, with its two morphotypes, including the antebrachial type with unstable length, indicating that the morphological differences in this artery are caused by the degree of its regression during ontogeny. Additionally, the prevalence of the persistent median artery, including the palmar and antebrachial types, maintains a certain percentage within human populations (Table 3). These findings indicate that the persistence of the median artery can be interpreted as paedogenesis, an intraspecific heterochrony generated owing to the truncated development (Reilly et al. 1997) of the arterial system in the forearm (Fig. 5).

Several researchers have indicated that the prevalence of

this phenomenon has been increasing in human populations since the nineteenth century. Henneberg and George (1995)

reported a twofold increase in the presence of a median

artery in Southern Africa from 1900 to 1990. Lucas et al.

(2020) reviewed previous studies on the median artery and

statistically analysed its prevalence since the nineteenth

century. They concluded that the prevalence of the persis-

tent median artery increased over time, from approximately

10% in people born at the end of the nineteenth century

to approximately 30% by the end of the twentieth century.

They further concluded that this morphological trend rep-

resents a microevolutionary change in the internal anatomy

of the human body caused by damage to a specific gene that

regulates the regression of the persistent median artery. If

their hypothesis is correct, the paedogenesis of the persis-

tent median artery contributes to the morphological evolu-

tion of the antebrachial artery system in the human body.

They assumed the causes of the prevalence of the persistent

median artery to be either of the following: (1) an environ-

mental insult around the foetus caused by the healthcare for

the mother or (2) mutations damaging the genes regulat-

ing the regression of the median artery. They favoured the

former and attributed the increase in the prevalence of the

persistent median artery to the improvement in healthcare

provided to pregnant women globally over the last 125 years.

If this explanation is valid, the increasing trend of the preva-

lence of the persistent median artery is not 'biological evolu-

tion' but must be categorised as 'environmental variation' or

'hereditary disease (if the germ cells are also damaged)'. The

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however, they did not explain the pressures concretely. We believe it is impossible to describe this evolutionary trend to be based on natural selection because the persistent median artery renders almost no benefit toward increasing the 'fitness' of individuals but carries a small risk of causing carpal tunnel syndrome (Maxwell et al. 1973; Lisanti et al. 1995; Kele et al. 2002; Bilgin et al. 2004; Osiak et al. 2021; Townsend et al. 2022). However, these findings imply that the persistent median artery is a mildly detrimental mutation for humans; therefore, this evolutionary trend of the median artery may be interpreted as an example of the 'nearly neutral evolution' at the phenotypic level. In this case, the prevalence of the persistent median artery must have been increased by genetic drift, although there is no evidence that genetic drift is working in the examined populations. However, previous studies have provided little information.

Townsend et al. (2022) reported a high prevalence rate of persistent median arteries in patients with carpal tunnel release, concluding that their results coincide with the microevolutionary change reported by Lucas et al. (2020) compared with the results of similar previous studies in living patients. However, they mentioned that their cohort comprised patients from a limited region; therefore, the possibility that the prevalence of the persistent median artery could vary between different races or populations remains. Solewski et al. (2021) investigated the prevalence and anatomical characteristics of the median artery by reviewing the literature, detecting a higher prevalence of the palmar type in a few regions, such as South Africa, Brazil and South America, than in others. Other studies have reported that the palmar type is also highly prevalent (>10%) in Kenya, Great Britain, Israel, Malaysia, and India (Pecket et al. 1973; Mansor et al. 1999; Rodríguez-Niedenführ et al. 1999; Nayak et al. 2010; Cheruiyot et al. 2017). These results indicate a high prevalence of the persistent median artery worldwide and suggest that the frequency of this mutation increases within a local population. Generally, as the size of the population decreases, genetic drift affects the gene pool in the population relatively more strongly; therefore, we presume that the persistent median artery is spreading in the local population in specific regions. Alternatively, the increasing trend of the prevalence of the persistent median artery since the end of the nineteenth century may be attributed to the advances in our anatomical knowledge and techniques. To negate this possibility, we need to conduct further research, continued for a long time in a specific region, regarding the prevalence of the persistent median artery in a particular racial group.

Other important factors affecting the prevalence of the persistent median artery could be the differences among human races or living environments (Townsend et al. 2022), as these are closely associated with the characteristics of local populations. Henneberg and George (1992a,

b) reported no differences in the prevalence of this artery between white and black people living in southern Africa; however, Carry et al. (2018) concluded that the prevalence of this artery is significantly different between African American and non-African American racial groups. These findings remain disputed; therefore, a comprehensive study with substantial results is needed.

Conclusions

The persistent median artery is the remnant of the main brachial artery in embryonic life and usually originates from the CIA, AIA, UA, and CIA–UA trunk. The presence of this artery results from the paedogenesis of the antebrachial arterial system. The increasing trend of the prevalence of the persistent median artery in human populations, as reported in previous studies, may be interpreted as 'nearly neutral evolution' at the phenotypic level.

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Author contributions S.Y. carried out the collection and analyzation of the data, writing and editing the original draft. K.K. also collected the data and wrote the original draft. T.I., H.M., H.Y., Y.Ma. and Y.Mo. collected the data. J.K. wrote and edited the original draft. Project administration has been done by K.K. and J.K.

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Data availability The data that support the findings of this study are available from the corresponding author, S.Y., upon reasonable request.

Declarations

Conflict of 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.

Ethical approval and consent of participation This study was approved by the Research Ethics Review Committee of the International University of Health and Welfare (IUHW) (23-Im-043). All the donors agreed to donate their bodies to the International University of Health and Welfare for medical education and research in their living will.

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