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Upper limb arterial development theories used to explain arterial variations in adults

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Abstract. The formation of the upper limb arterial pattern takes place in several stages during the embryonic development. The arterial variations observed in the adult population are thought to occur during the developmental stages because of the primitive arteries failing to form or recede, as well as unusual origins of native vessels. Two contrasting theories of upper limb arterial development have been suggested, one by Singer, 1933 who suggested that the upper limb arteries develop from a single axial trunk, and the other by Rodriguez-Niedenfuhr et al., 2001 who suggested that the upper limb arteries develop from a capillary plexus. While the two theories describe the development process differently, the two theories are cited in an interchangeable manner, raising questions about which of the two theories is accepted as correct by the authors. This review seeks to record and compare the utilization of both theories. A literature search for articles and case reports between 2002 and 2022 was conducted, using several search engines, including ResearchGate, Google Scholar, PubMed, Medscape and Science Direct. 38 articles were used in this review. The chi-square test did not pick up any significant differences in the use of the two theories (P=0.223). We conclude that neither of the two theories is preferred by authors as they are almost equally cited. These results suggest that confusion remains as to which of the two theories is accepted. Further research on the upper limb arterial development is necessary to establish the accuracy of the two existing theories.

Keywords: embryonic, arterial development, arm, forearm.

INTRODUCTION

The development of the arterial pattern of the upper limb is said to arise during several embryonic stages. The seventh intersegmental artery gives rise to a single axial artery, which then gives rise to the arteries of the upper limbs (DeSesso, 2017). According to Singer, 1933, the upper limb arteries arise from a single axial artery, which represents the brachial and interosseous arteries (Singer, 1933) (Fig. 1). However, the above description by Singer, 1933 was not based on his own study but rather on the study conducted by Senior, 1926. Nonetheless, this theory is still commonly known as Singer's (1933) theory in literature to date. Contrary to Singer's (1933) theory of a single axial arterial trunk, a study by Rodriguez-Niedenfuhr et al., 2001 utilised 112 human

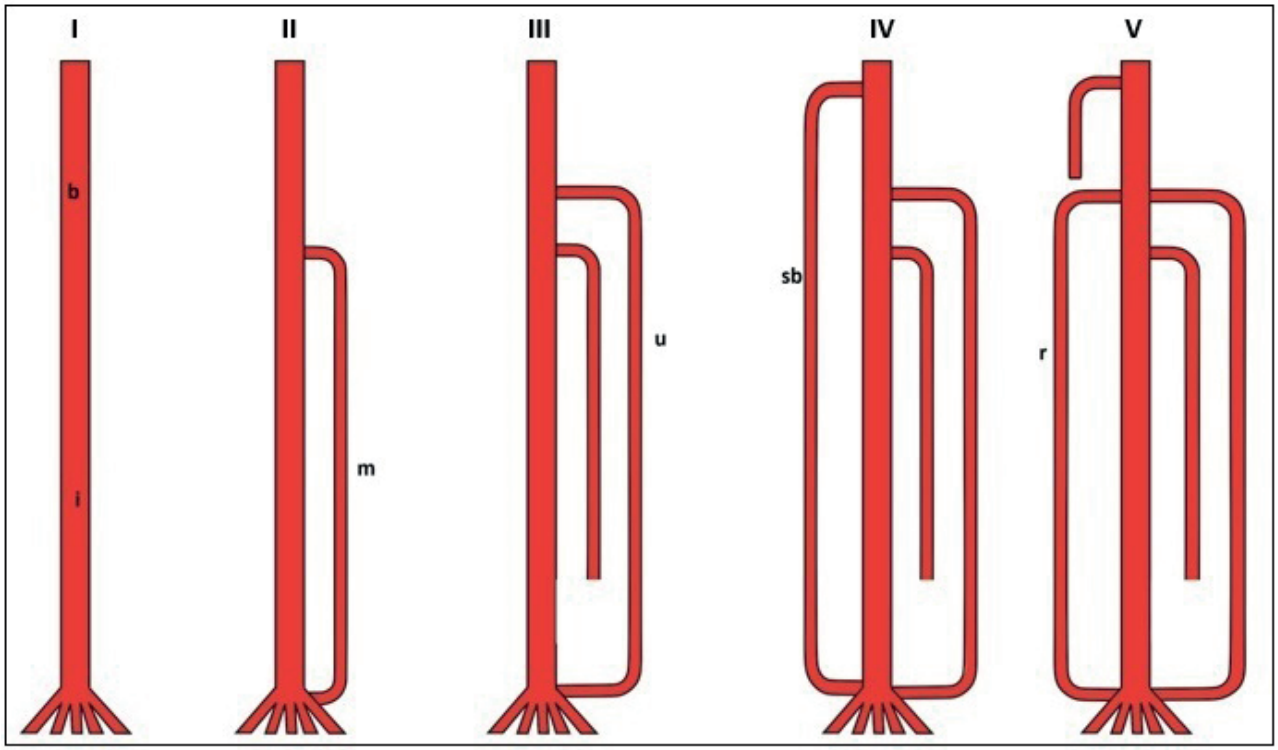

Figure 1. An illustrative diagram showing the theory of the embryonic development of the upper limb arterial pattern proposed by Singer, 1933 (Adapted from Rodriguez-Niedenfuhr et al., 2003).

embryos and concluded that the upper limb arteries arise as an initial capillary plexus from the dorsal aorta during the 12th embryonic stage (26–30 days) of development (Fig. 2). The definite arteries of the upper limb arise from stage 14 (31–35 days), starting with the subclavian artery through to stage 23 (56–60 days), where the radial artery is completely defined. The above authors challenged Singer's (1933) theory as it was based on data from a previous study by Senior, 1926, without the consideration of embryonic material (Rodríguez-Niedenführ et al., 2001, Rodriguez-Niedenfuhr et al., 2003). Additionally, Rodriguez-Niedenfuhr et al., 2001 argued that the theory proposed by Singer, 1933 was limited as it was able to explain those cases in which the radial artery originated above the elbow level but was unable to explain other variations like an ulnar artery arising above the elbow level. In agreement with Rodriguez-Niedenfuhr's et al. 2001 theory, another study showed that an early anterior limb bud receives vascular supply from the fifth to the nineth pairs of cervical intersegmental arteries that arise from the aorta (DeSesso, 2017). The above authors noted that the seventh cervical intersegmental artery persists for the development of the upper limb arteries.

Currently, there seems to be no consensus in the literature regarding which of the above two theories (Singer, 1933 and Rodriguez-Niedenfuhr et al., 2001) is most accepted as authors quote one or the other. In addition, very few studies have been done on the embryos to support or dispute the above two theories of upper limb arterial development, with most of the studies simply referring to a few available previous studies. Knowledge of the upper limb arterial development is crucial as the variations observed in the adults are thought to occur during the developmental stages due to unusual origins of native vessels or primitive arteries failing to form or recede (Ciervo et al., 2001, Chrysoglou et al., 2022). This review seeks to record and compare the use of the two upper limb arterial development theories to establish which one is most accepted by most of the authors as accurate. This information will help to establish the common ground in explaining the upper limb arterial variations observed during surgical procedures and inform the direction of future research on the subject.

MATERIALS AND METHODS

A literature search for articles and case reports between the years 2002 and 2022, describing the developmental basis of the variations observed in the upper limb

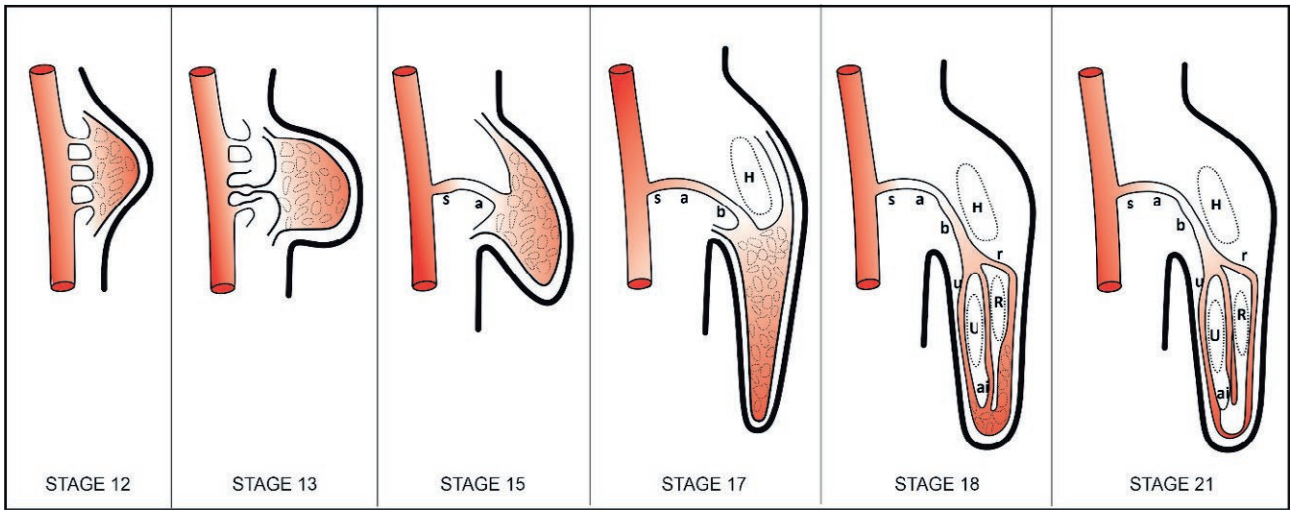

Figure 2. An illustrative diagram showing the theory of the embryonic development of the upper limb arterial pattern proposed by Rodriguez-Niedenfuhr et al., 2001 (Adapted from Rodriguez-Niedenfuhr et al., 2003).

arteries, was conducted. A total of thirty-eight (n=38) articles were used in the current review. The keywords for search included variations of the axillary artery, brachial artery, radial artery, and ulnar artery. The search engines included: (i) ResearchGate, (ii) Google Scholar (iii) PubMed (iv) Medscape and, (v) Science Direct. The references from the articles were assessed to find other relevant articles. Articles describing upper limb arterial variations with a description of the embryonic development were included, while those articles describing upper limb arterial variations without a description of the embryonic development were excluding.

RESULTS

Variations of the axillary artery and their embryonic developmental basis

Variations of the axillary artery accounted for 34,15% of upper limb arterial variations in this literature search. The most variable branch of the axillary artery is the subscapular artery. The variabilities of the subscapular artery include trunk formations with other branches and origin from the second instead of the third part of the axillary artery. The most encountered trunk formation is the common trunk of the subscapular artery and the lateral thoracic artery. The above variation was recorded in six of the 11 articles that reported the variations of the axillary artery in the current review (Sreeja and Leo Rathinaraj, 2014, Singh et al., 2020, Tiwari and Afroze, 2020, Chakraborty and Sarkar, 2019, Ovhal et al., 2021, Yang et al., 2021). All six authors described this variation as arising from either the persistence, enlargement or differentiation of certain branches of the capillary plexus in accordance with Rodriguez-Niedenfuhr's et al., 2001 theory. The remaining five of the eleven authors recorded arterial trunks, which included a common trunk from which the subscapular, anterior and posterior circumflex humeral arteries arise from and a common trunk from which the subscapular and posterior circumflex humeral arteries arise from (Ovhal et al., 2021, Yang et al., 2021, Astik and Dave, 2012, Singh, 2017, Padmalatha et al., 2018). All five of the above authors described the common trunk for the subscapular, anterior and posterior circumflex humeral arteries and the common trunk for the subscapular and posterior circumflex humeral arteries as arising from the unusual pathways that embryonic vessels follow, or the failure of capillaries from the primitive capillary plexus to form or recede as they should, in accordance with Rodriguez-Niedenfuhr's et al., 2001 theory. One of the above authors (Padmalatha et al., 2018) used Singer's (1933) illustrations while describing the trunk formation according to Rodriguez-Niedenfuhr's et al., 2001 theory in explaining the embryonic basis of these trunk formations, adding to the confusion of the acceptance of one or the other of the two theories. Two authors (Naveen et al., 2014, Saeed et al., 2002) described the two trunks to be due to the sprouting of vessels at unusual locations, as well as the persistence of sprouted vessels that are meant to regress in accordance with Singer's (1933) theory.

Variations of the brachial artery and their embryonic developmental basis

The variations of the brachial artery include high bifurcation, superficial and accessory brachial arteries.

The high bifurcation of the brachial artery is when this artery bifurcates into its terminal branches proximal to the level of the intercondylar line (Tsoucalas et al., 2020). This variation of the brachial artery has an incidence of 14,63%. Six authors reported on the high bifurcation of the brachial artery and the basis of its embryonic development (Kumar and Rathnakar, 2014, Mehta et al., 2008, Deka, 2018, Balasubramanian et al., 2018, Jadhav and Pawar, 2018, Sophia et al., 2021). Three of the above six authors (Mehta et al., 2008, Deka, 2018, Balasubramanian et al., 2018) described this variation as the sprouting of the terminal branches of the brachial artery at a level higher than the usual point of sprouting, resulting in the high bifurcation of the brachial artery, in line with Singer, 1933. However, one of the above three authors (Balasubramanian et al., 2018), while using Singer's (1933) theory to describe the high bifurcation of the brachial artery utilised Rodriguez-Niedenfuhr's et al., 2001 illustrations, which is contrary to Singer's (1933) theory as it depicts the basis of development arising as a capillary plexus which undergoes elongation and differentiation in the limb bud as opposed to the sprouting process from the axial artery described by Singer, 1933. As explained above, the combination of the two theories by the authors poses a contradiction as the two theories differ in explaining the upper limb arterial pattern of development. Three of the six authors (Kumar and Rathnakar, 2014, Jadhav and Pawar, 2018, Sophia et al., 2021) described the high bifurcation of the brachial artery as the persistence of the proximal part of the radial artery and the failure of an established connection with the brachial artery at the level of the ulnar artery, resulting in the high bifurcation of the brachial artery in line with Rodriguez-Niedenfuhr et al., 2001. Two of the abovementioned six authors (Kumar and Rathnakar, 2014, Sophia et al., 2021) described the high bifurcation according to Singer, 1933 but cited Rodriguez-Niedenfuhr et al., 2001, while one author (Jadhav and Pawar, 2018) cited Rodriguez-Niedenfuhr et al., 2001. However, the description of the actual developmental process was that of Singer, 1933 for all of the abovementioned six authors.

Superficial brachial artery

The superficial brachial artery is a brachial artery that runs superficial to the median nerve instead of running deep to this nerve (Sharma et al., 2009, Shetty et al., 2022). This variation has an incidence of 12, 20%. It was reported by five authors (Sharma et al., 2009, Nkomozepi et al., 2017, Kachlik et al., 2011a, Lalit and Piplani, 2021, Yang et al., 2008). The abovementioned authors suggested that under normal developmental circumstances, the brachial artery that passes deep into the median nerve is given hemodynamic preference over the one passing superficially to the median nerve, as it becomes obliterated at a later stage. However, in the case of the persistent superficial brachial artery, in accordance with Singer's (1933) theory, this artery receives hemodynamic preference, and the deep brachial artery gets obliterated instead. While all five authors described the variation in accordance with Singer's (1933) theory, two of the five (Kachlik et al., 2011a, Lalit and Piplani, 2021) stated and quoted Rodriguez-Niedenfuhr et al., 2001 while using Singer's (1933) theory to describe the variation.

Accessory brachial artery

The accessory brachial artery is a rare variant artery which originates from the brachial artery in the upper one third of the arm and, in some cases, from the axillary artery with an incidence of 7,32% (Kachlik et al., 2011b). The accessory brachial artery rejoins the brachial artery before it bifurcates in the cubital fossa into the ulnar and radial arteries (Kachlik et al., 2011b). Three authors reported the accessory brachial artery (Kachlik et al., 2011b, Elnaiem et al., 2022, Chakravarthi et al., 2014). The above authors described the accessory brachial artery as sprouting from the superficial brachial artery, which is also a vestigial artery as described above. Furthermore, it was suggested that on some occasions, this variation may arise due to the persistence of another cervical intersegmental artery in addition to the persisting seventh cervical intersegmental artery. Two of the above three authors (Chakravarthi et al., 2014, Elnaiem et al., 2022) who described the accessory brachial artery, based their descriptions on Singer's (1933) theory, while one author (Kachlik et al., 2011b) based the description on Rodriguez-Niedenfuhr's et al., 2001 theory.

High origin of radial artery and its embryonic developmental basis

A high origin radial artery is one that originates proximal to its usual point of origin in the cubital fossa from either the axillary artery or from the brachial artery in the upper part of the arm (Rodriguez-

Baeza et al., 1995). This high origin of radial artery has an incidence of 19,51%. Eight authors reported on the high origin of the radial artery (Pelin et al., 2006, Konarik et al., 2009, Shiny Vinila et al., 2013, Gandhi and Lakshmi, Ghosh and Chaudhury, 2018, Nasr, 2012, Klimek-Piotrowska et al., 2013, Haładaj et al., 2018). Seven of the above eight authors (Pelin et al., 2006, Konarik et al., 2009, Shiny Vinila et al., 2013, Gandhi and Lakshmi, Ghosh and Chaudhury, 2018, Nasr, 2012, Klimek-Piotrowska et al., 2013) described this variation as arising because of non-regression of the proximal part of the superficial brachial artery. During development, the distal part of the superficial brachial artery gives rise to the radial artery, while the proximal part undergoes regression. Failure of this regression results in the radial artery arising from the proximal part of the embryonic superficial brachial artery instead of the distal part and, therefore, adopting a high origin in accordance with Singer's (1933) theory. However, three of the above authors (Gandhi and Lakshmi, Ghosh and Chaudhury, 2018, Klimek-Piotrowska et al., 2013) cited Rodriguez-Niedenfuhr et al., 2001, despite using Singer's (1933) theory. One of the above authors (Haładaj et al., 2018) described this variation using both theories, firstly as arising due to the selective differentiation and remodelling process that the primitive plexus undergoes in accordance with Rodriguez-Niedenfuhr et al., 2001, and secondly, due to the persistence of the connection between the proximal part of the superficial brachial artery and the axial artery in accordance with Singer's (1933) theory.

High origin of ulnar artery and its embryonic developmental basis

A high origin of the ulnar artery has an incidence of 12,20%. Five authors reported on the high origin of the ulnar artery in the current review (Vollala et al., 2011, Krishnamurthy et al., 2006, Bhat et al., 2008, Bozer et al., 2004, Ghosh et al., 2016). Three of the above five authors described this variation as occurring due to an establishment of a connection between the ulnar artery and the axial artery in the arm proximal to the usual point of connection of the ulnar artery and the axial artery (Vollala et al., 2011, Krishnamurthy et al., 2006, Ghosh et al., 2016). The above authors further suggested that hemodynamic preference of the ulnar artery origin given to the superficial over the deep arterial system results in the persistence of embryonic vessels as described by Singer,1933. While two of the above authors (Bhat et al., 2008, Bozer et al., 2004) described this variation to be due to one of the capillary buds from the axillary artery persisting instead of following the proposed selective enlargement or regression of the primitive capillary plexus as described by Rodriguez-Niedenfuhr et al., 2001. While the above authors cited Rodriguez-Niedenfuhr et al., 2001, the embryonic description was that of Singer,1933.

Table 1 summarises the upper limb arterial variations and the developmental theories used to describe the variations.

CONCLUSION

The chi-square statistical test did not pick any statistically significant difference in the number of authors who used either of the two theories (P=0.223). We conclude that none of the two theories is preferred over the other as the two theories are almost equally used in the literature. A small fraction of the authors used both theories, whereby the description of one theory was used but illustrated with the diagrams of the other theory, suggesting that the selection of one or the other theory is more of convenience than the belief in its correctness. It is also apparent that the majority of the authors used Rodriguez-Niedenfuhr's et al., 2001 theory to describe the variations of the axillary artery, while the majority of authors used Singer's (1933) theory to describe the variations of the brachial artery, further strengthening the idea of convenience than correctness in the selection of the use of the two theories. The equal use of the two theories illustrates the confusion around this subject, suggesting that more research is necessary for better scientific basis of the development of upper limb arteries. Such research can aid in explaining the multiple upper limb arterial variations observed and probably the prediction of the frequency of occurrence of specific ones for precautionary measures during surgery.

It is our suspicion that the scarcity of data around this subject could be due to ethical issues regarding the access to human embryos. More scientific debate on this subject and its ethical issues could help paving a way forward in further exploring the embryonic bases of arterial variations and racial differences in upper limbs arterial branching patterns.

AUTHOR CONTRIBUTIONS

Conceptualization: AT Sebelebele and NK Xhakaza. Drafting of the manuscript: AT Sebelebele. Critical revision of the manuscript: NK Xhakaza. Approval of the final version of the manuscript: Both authors.

Table 1. Summary of upper limb arterial variations and their description according to the two theories.

Arterial variations of the upper limb			
Variation		Arterial development theory	
	Author	Singer, 1933	Rodríguez-Niedenfuhr et al., 2001
Common Trunk for Subscapular Artery and Lateral Thoracic Artery	Sreeja and Leo Rathinaraj, 2014		×
	Singh et al., 2020		×
	Tiwari and Afroze, 2020		×
	Chakraborty and Sarkar, 2019		×
	Ovhal et al., 2021		×
	Yang et al., 2021		×
Subscapular-Bi-circumflex Humeral Trunk	Naveen et al., 2014	×	
	Yang et al., 2021		×
	Padmalatha et al., 2018	×	×
	Astik and Dave, 2012		×
Common Trunk for Subscapular Artery and Posterior Circumflex Humeral Artery	Singh, 2017		×
	Saeed, 2002	×	
	Ovhal et al., 2021		×
	Yang et al., 2021		×
High Bifurcation Brachial Artery	Kumar and Rathnakar, 2014		×
	Mehta et al., 2008	×	
	Deka, 2018	×	
	Balasubramanian et al., 2018	×	×
	Jadhav and Pawar, 2018	×	×
	Laishram et al., 2021		×
Superficial Brachial Artery	Lalit and Piplani , 2021	×	×
	Nkomozepi et al., 2017	×	
	Sharma et al., 2009	×	
	Yang et al., 2008	×	
	Kachlik et al., 2011	×	×
Accessory Brachial Artery	Chakravarthi et al., 2014	×	
	Kachlik, 2011		×
	Elnaiem et al., 2022	×	
High Origin Radial Artery	Pelin et al., 2006	×	
	Konarik et al., 2009	×	
	Shiny et al., 2013	×	
	Gandhi and Lakshmi, 2018	×	×
	Ghosh and Chaudhury, 2018	×	×
	Nasr, 2012	×	
	Klimek-Piotrowskaet et al., 2012	×	×
	Haladji et al., 2018	×	×
High Origin Ulnar Artery	Vollala et al.,2011	×	
	Krishnamurthy et al., 2006	×	
	Bhat et al., 2008		×
	Bozer et al., 2004		×
	Ghosh et al., 2016	×	

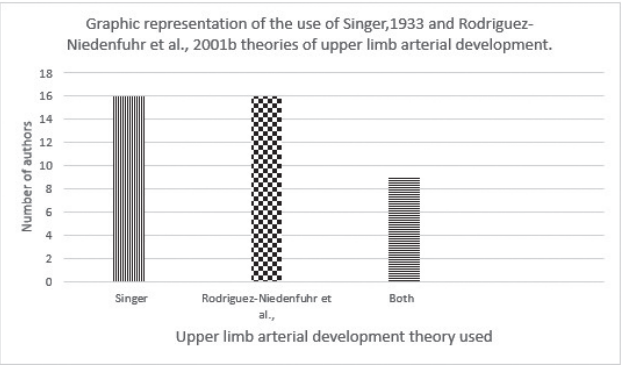

Figure 3. Graphic representation of the use of Singer, 1933 and Rodriguez-Niedenfuhr et al., 2001 theories of upper limb arterial development.

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