



The transcortical vessel is replacement of cortical capillary or a separate identity in diaphyseal vascularity

Adil Asghar¹, Ravi Kant Narayan¹, Ashutosh Kumar¹, Shagufta Naaz²

Departments of ¹Anatomy and ²Anaesthesiology, All India Institute of Medical Sciences, Patna, India

Received August 5, 2019; Revised October 5, 2019; Accepted October 7, 2019

A recent article published in *Nature Metabolism* “A network of trans-cortical capillaries as a mainstay for blood circulation in long bones” by Grüneboom et al. (2019) [1] is a remarkable description of the bone-vascular network. The discovery of transcortical vessels (TCVs) in long bones has witnessed the enigma of bone vascularity. In the mouse model, they showed hundreds of TCVs originating from bone marrow which travels the whole cortical thickness. They claimed these TCVs to be the same as seen in the human tibia and femoral epiphysis. TCVs express arterial or venous markers, hence are the mainstay of bone vascularity because 80% of arterial and 59% of venous blood passes through them [1]. This new evidence challenges the existence of cortical capillaries in earlier literature.


It is necessary to consider that mice and rats have soft cortical bones which lacks a well-developed Haversian system like humans. In the mouse, the Haversian system exhibit a radial pattern and branch poorly, whereas, in the rat, they are moderately developed. Thus, the organization of cortical vascularization in long bones strongly differs among species [2].

The Brief History of Diaphyseal Vasculature

Leeuwenhoek found several little holes in shin bone of

cow and imagined that bone had small pipes going long ways. Since the last four centuries, we were baffling about diaphyseal vascularity and niche of hemopoietic cells. The controversies exist from the era of Clapton Havers (1691) [3] who discovered nutrient artery. Albinus Bernharbner et al. (1754) [4] proposed the centrifugal vascularity of cortical bone by tiny vessels running in a canal along the long axis of shaft named as Haversian canals, while the oblique or transverse canal was named Volkmann's canal later on. The perfusion techniques like Barium sulfate and Indian ink etc. delineated the three major parts of circulation in bone—medullary vessels, periosteal capillaries, and juxta-articular or juxtaepiphyseal vessels. This concept was well accepted in the early 20th century [5]. The radiographic and microangiographic studies elucidate tiny channels. The hypothesis of osseous circulation has two parallel closed circulatory systems that include three vascular groupings—afferent arteries (nutrient arteries and periosteal arteries), functional vascular lattice, and efferent veins (central veins drained via emissary veins and periosteal veins). Only functional vascular lattice is the site of exchange between blood and bone marrow which include sinusoids of bone marrow and capillaries at other sites [6]. This older view implies there are two separate circulatory systems in long bone for cortex and medulla. Each is possessing its arterial supply, capillary field, and venous drainage. The diaphyseal cortical blood flow is centrifugal and medullary flow is centripetal. Trueta and Buhr [7] examined the question of a possible periosteal arterial supply to the cortex of long bones and explained that diaphyseal cortex survived even if the medullary vessels were completely damaged. They claimed that outer 1/3rd of cortex had periosteal supply and rest inner

Corresponding author:

Adil Asghar 
Department of Anatomy, All India Institute of Medical Sciences, Patna
801505, India
Tel: +91-9911225915, Fax: +91-9911225915, E-mail: dradilasghar2009@gmail.com

Copyright © 2020. Anatomy & Cell Biology

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

two-third had medullary supply via cortical capillaries [7].

Most Accepted Model until the Date

Till now the model of long bone vascularity drawn by Professor Murray Brookes in Gray’s Anatomy (41st edition) [8] mentioned that medullary supply is centripetal and cortical blood supply is centrifugal. Nutrient arteries in adult and periosteal vessels in children are the mainstays of vascularity of long bone. The nutrient artery passes through nutrient foramen and canal to reach the medullary cavity, where they divide into ascending and descending branches as endosteal arteries. These endosteal arteries anastomose with metaphyseal and epiphyseal arteries. The metaphyseal arteries are branches of the nearby systemic artery, and epiphyseal arteries derive from the periarticular anastomosis. The endosteal arteries feed to hexagonal sinusoidal mesh through centripetal branches. They also give centrifugal cortical branches to sustain cortical capillaries in Haversian and Volkmann’s canals. The sinusoidal vasculature of long bone has two types of capillaries–H, and L. H type capillaries found in the metaphyseal region near the growth plate but L capillaries in the diaphyseal region and drain into a central vein. The drainage from medullary sinusoids form central venous sinus and finally drains through nutrient or emissary veins. The periosteal and

muscular arteries nourish periosteal capillary bed and finally drain into systemic veins via periosteal or muscular veins. The longitudinally oblique channels shown as cortical capillaries (transcortical capillaries) emerge through cornet shaped foramina depicted in Murray model (Fig. 1) [8].

Transcortical Circulation of Long Bone Based on Empirical Evidence

The human long bone has a thick cortical shell with well-developed Haversian system of osteon except in children or immature bone at fracture sites. Haversian system is arranged around 15° from the long axis of the bone. The medullary and vascular network in rodents or small mammals are in series or transcortical (Fig. 2) [9], but in human both vascular networks are parallel except in children and immature bone of fracture sites. Throughout the cortex of long bone, there are cortical capillary networks housed in small cortical canals. The transcortical nourishment of bone takes place by capillaries of Volkmann’s canal, and the longitudinal irrigation happens through Haversian vessels. In immature bone of children, these vessels are arranged haphazardly, but as the bone remodels and matures, a more distinct pattern of Haversian system of vessels emerges. Simultaneously, the hemopoietic mesenchymal stromal cells of medullary sinusoids are replaced by nonhemopoietic mesenchymal stromal cells. The cells start to accumulate fat inside, which convert from red to yellow marrow. The fenestrated thin-walled endothelial lining undergoes modification to the closed thick walled capillary. Thus, the medullary flow is reduced significantly and lead to cortical and medullary ischemia. The cortical capillaries com-

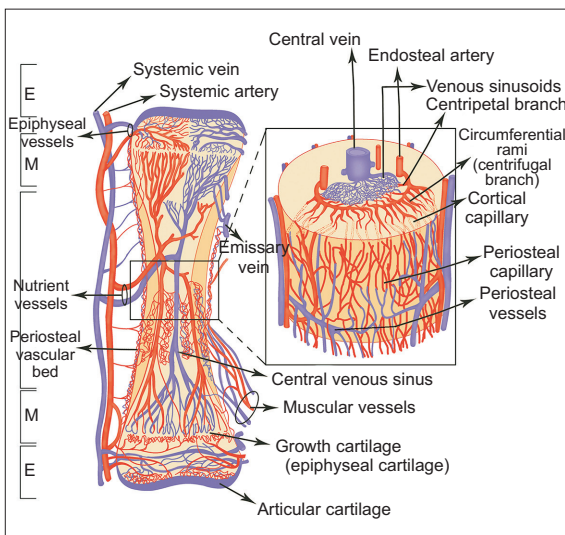


Fig. 1. The blood supply of a long bone. The marrow cavity contains a large central venous sinus, a dense network of medullary sinusoids, and longitudinal medullary arteries and their circumferential rami. E, epiphysis; M, metaphysis; D, diaphysis. Adapted by redrawn from Standerling. Grays anatomy: the anatomical basis of clinical practice, according to the Creative Commons license Elsevier [8].

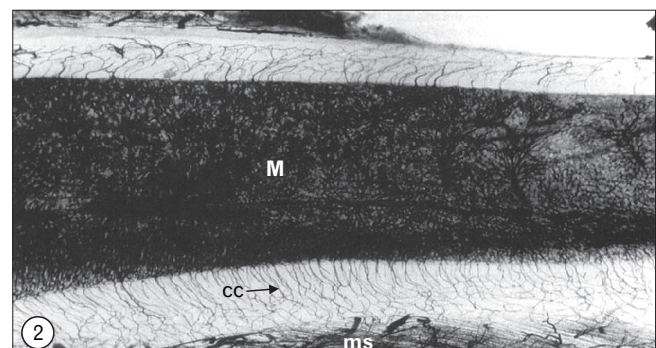


Fig. 2. India-ink-gelatin perfusion of the femoral diaphyseal shaft illustrating the cortical bone canals (cc), the marrow vascular spaces (M), and the surrounding muscle vessels (ms) (×12). Adapted from de Saint-Georges and Miller. Anat Rec 1992;233:169-77 [9], with permission of John Wiley and Son holds the copyright.

pensate the circulation from periosteal vascular bed to medullary sinusoids. Now the major cortical blood supply becomes periosteal [10].

The unearthing of TCVs by Anja Hasenberg et al. can explain the survival of compact bone even after complete damage of either periosteal or medullary systems or infusion of IV fluids through the medullary cavity [1]. Authors have shown bleeding spot on the external surface of the tibia and claimed them as TCVs in human specimens. During the orthopedic procedure, similar hemorrhagic oozes are observed from the bone after periosteal elevation. The major source of bleeding is either from periosteal vascular bed or cortical capillaries, but the new opinion explains it to be the TCVs. Direct vascular connections are also seen in the skull and the tibia, and they perform as a vascular niche for hemopoietic cells. Both kinds of literature were completely wordless about cortical capillaries. Authors are unable to illustrate whether the cortical capillaries are transcortical or they have found morphologically different vessels.

Similarly, the authors did not enlighten the differences between TCVs and other capillaries. Authors have discovered TCVs in the human femoral neck where the medullary cavity hardly extends. But the presence of TCVs may be explainable by direct vascular channels found in the skull. Authors have demonstrated the angiogenesis of TCVs in chronic arthritis models of murine bone. It would be interesting to know the role of TCVs in Perthe's disease and pathogenesis of avascular necrosis of femoral head. Inducing angiogenesis in avascular necrosis of long bone epiphysis especially for femoral head or even in scaphoid and navicular would be a great therapeutic measure. These TCVs will open the door to investigative and the therapeutic models for collagen vascular or immunological disorders of bone and joints in the future.

Assessment of TCVs and cortical capillaries may require further visualization and identification via labeling the vessel wall or filling the vascular network with a contrast product. Vessel wall labeling by the endothelial-specific promoter, immunohistochemistry or intravenous injection of molecules will be helpful. Besides, the functional properties of endothelial cells may be exploited for both types of capillaries detection. Microtomography may be utilized to study the spatial orientation of both capillaries in barium infused decalcified bone. The quantification of both vessels analyzed by three-dimensional micro-computed tomography data sets from barium or Microfil-infused bones. Thus, concrete evidence of TCVs and concomitant existence of cortical capillary will help

to redraw the model of vascularity of long bone in human.

ORCID

Adil Asghar: <http://orcid.org/0000-0002-1404-1298>

Ravi Kant Narayan: <http://orcid.org/0000-0003-2510-6744>

Ashutosh Kumar: <http://orcid.org/0000-0003-1589-9568>

Shagufta Naaz: <http://orcid.org/0000-0001-7845-5708>

Author Contributions

Conceptualization: AA, SN. Data acquisition: RKN, AK. Data analysis or interpretation: RKN, AK. Drafting of the manuscript: AA, RKN. Critical revision of the manuscript: AK, SN. Approval of the final version of the manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Grüneboom A, Hawwari I, Weidner D, Culemann S, Müller S, Henneberg S, Brenzel A, Merz S, Bornemann L, Zec K, Wuelling M, Kling L, Hasenberg M, Voortmann S, Lang S, Baum W, Ohs A, Kraff O, Quick HH, Jäger M, Landgraeber S, Dudda M, Danuser R, Stein JV, Rohde M, Gelse K, Garbe AI, Adamczyk A, Westendorf AM, Hoffmann D, Christiansen S, Engel DR, Vortkamp A, Krönke G, Herrmann M, Kamradt T, Schett G, Hasenberg A, Gunzer M. A network of trans-cortical capillaries as mainstay for blood circulation in long bones. *Nat Metab* 2019;1:236-50.
2. Cowin SC, Cardoso L. Blood and interstitial flow in the hierarchical pore space architecture of bone tissue. *J Biomech* 2015;48: 842-54.
3. Havers C. *Osteologia nova, or, Some new observations of the bones, and the parts belonging to them, with the manner of their accretion, and nutrition, communicated to the Royal Society in several discourses : to which is added a fifth discourse of the cartilages.* London: Printed for Samuel Smith; 1691.
4. Albinus Bernharbner S, Wandelaar J, van Damme D, Verbeek JH, de Groot JW. *B.S. Albini Academicarum annotationum: liber primus [-octavus].* Leidae: apud J&H Verbeek bibliop, 1754.
5. Brookes M, Revell WJ. *Blood supply of bone: scientific aspects.* Berlin: Springer Science & Business Media; 2012.
6. Bridgeman G, Brookes M. Blood supply to the human femoral diaphysis in youth and senescence. *J Anat* 1996;188(Pt 3):611-21.

7. Trueta J, Buhr AJ. The vascular contribution to osteogenesis. V. the vasculature supplying the epiphysial cartilage in rachitic rats. *J Bone Joint Surg Br* 1963;45:572-81.
8. Standring S. *Gray's anatomy: the anatomical basis of clinical practice*. 41st ed. New York: Elsevier; 2015. p.89-91.
9. de Saint-Georges L, Miller SC. The microcirculation of bone and marrow in the diaphysis of the rat hemopoietic long bones. *Anat Rec* 1992;233:169-77.
10. Gurevitch O, Slavin S, Feldman AG. Conversion of red bone marrow into yellow: cause and mechanisms. *Med Hypotheses* 2007;69:531-6.