




Anatomical study about the variations in renal vasculature

Alberto García-Barrios^{1, 2}, Ana I. Cisneros-Gimeno^{1, 2}, Andrea Celma-Pitarch¹,
Jaime Whyte-Orozco^{1, 2}

¹Department of Human Anatomy and Histology, School of Medicine, University of Zaragoza, Spain

²Medical and Genetic Research Group (GIIS099) IIS Aragón, Zaragoza, Spain

[Received: 14 April 2023; Accepted: 10 May 2023; Early publication date: 5 June 2023]

Background: Renal vascularization is classically described as a renal artery and vein. However, this vascular pattern presents numerous anatomical variations in terms of their number, origin and course due to ontogenetic alterations. The aim was to carry out a descriptive study of the renal vascular pattern observed during the dissection of cadavers intended for teaching purposes.

Materials and methods: A descriptive and observational study of renal vascular anatomy was carried out by dissecting 16 renal blocks from 8 cadavers donated to science and used for teaching at the Faculty of Medicine of the University of Zaragoza.

Results: The prevalence of arterial variations was 75% (56.3% for polar renal arteries, 12.5% for pre-hilar branching and 6.25% for double communicating arterial arch) and venous was 62.5% (12.5% for polar renal veins, 25% for late venous confluence, 6.25% for triple renal vein and 18.75% for double circum-aortic renal vein).

Conclusions: We conclude that the renal vascular anomalies occur with high frequency; for this reason, knowledge of these anomalies is extremely important for the correct planning of numerous medical-surgical activities. (Folia Morphol 2024; 83, 2: 348–353)

Keywords: renal artery, renal vein, vascular variation, anatomical variants, polar artery, circum-aortic renal vein, renal vascular arch, renal surgery

INTRODUCTION

In classical anatomical terminology, the renal vasculature is generally described by a renal artery and a renal vein, a branch originating from the abdominal aorta and tributary to the inferior vena cava, respectively. The arterial supply of the kidney arises bilaterally and anteriorly from the abdominal aorta at the level of the lumbar vertebrae L1 and L2, approximately one centimetre below the exit of the superior

mesenteric artery and, at a variable distance from the renal hilum, divides into its two terminal branches, the anterior or prepyelic artery (AP) and the posterior or retropyelic artery (RP), which in turn divide into segmental branches. In addition, collateral branches are distributed from this renal artery that will give rise to the inferior suprarenal arteries and branches for the renal capsule and proximal part of the ureter [20, 31]. On the other hand, the venous return is

Address for correspondence: Dr. Ana I. Cisneros-Gimeno, Department of Human Anatomy and Histology, School of Medicine, University of Zaragoza, C/Domingo Miral, s/n, 50009 Zaragoza, Spain; tel: +34 976761688, e-mail: aicisner@unizar.es

This article is available in open access under Creative Commons Attribution-Non-Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0) license, allowing to download articles and share them with others as long as they credit the authors and the publisher, but without permission to change them in any way or use them commercially.

responsible for draining blood from venous branches homonymous with the arteries of both kidneys into the inferior vena cava where it empties approximately at the level of the second lumbar vertebra. Generally, they are located in an anterior position with respect to the artery and follow a reverse trajectory to the latter [16].

However, this described vascular pattern presents numerous anatomical variations in terms of their number, origin and course. It is considered that variations in the renal arteries, in general, are found in about 35% of cases, while alterations in the renal veins, which are less frequent, occur in 18% of the observed cases [7, 9].

Knowledge of the normality and variations in the vascular system of the kidney is extremely important for proper medical-surgical care, especially when planning various interventions (renal transplantation, angiography and/or aneurysm repair, among others) and knowing the pathologies associated with these alterations (hydronephrosis, varicocele or orthostatic proteinuria due to venous compression) [23, 33].

Anatomical variations of the renal vessels are considered one of the most prevalent vascular anomalies, both arterial and venous, occurring in approximately 35% and 18% of individuals, respectively [7, 9]. Incidence varies according to ethnicity, ranging from 4% to 61.5% [11, 12] in the renal arterial system and between 8 and 38.8% in the venous system [6]; the number of accessory arteries, between 3% and 30% unilaterally and 10% bilaterally [1, 4, 27, 29, 36], and accessory veins, more frequent in the right renal vein (16.6%) compared to the left (2.1%) [15]; and the method of study, computed tomography or dissection [12]).

Embryological development plays a major role in its prevalence, with an association between the presence of accessory renal vessels and evidence of arrested uniform development of the kidney [37]. Organs that migrate extensively during development, such as the kidneys, may retain vessels from their initial location or incorporate new vessels from the invaded region. Initially, the permanent primordial kidneys are located in the pelvis in close proximity to each other and, as the embryo grows, they gradually separate and relocate in the abdomen, reaching their usual position by the ninth week of gestation. During the early stage, the renal arteries originate from the common iliac arteries and as the kidneys ascend they receive new branches from the distal aorta. When the

kidneys are located in their adult position they receive most of their arterial branches from the abdominal aorta. Thus, as a rule, the caudal branches from the initial renal vessels involute and disappear, while the cranial branches from the abdominal aorta become the permanent renal arteries [21]. This could explain the cases of accessory renal vessels arising from iliac, sacral or inferior mesenteric arteries, as they could be considered as persistence of primitive renal arteries.

The main objective of this study was to carry out a descriptive study of the vascular patterns observed in the dissection of 16 renal blocks belonging to cadavers destined to teaching for the Degree of Medicine.

MATERIALS AND METHODS

A descriptive and observational study of renal vascular anatomy was carried out by dissecting renal blocks belonging to the bodies donated to science, and used for teaching the Degree of Medicine, from the Department of Human Anatomy and Histology of the Faculty of Medicine in the University of Zaragoza.

The study in cadavers was carried out by dissecting a total of eight cadavers, previously destined for use in teaching, aged between 70 and 99 years, of which 5 were male (62.5%) and 3 were female (37.5%), obtaining a total of 16 renal blocks (8 left and 8 right kidneys).

During the dissection protocol, both renal structures were studied as a block, to subsequently study them individually and assess the presence of arterial variations for comparison with those described in the literature.

RESULTS

Dissection showed the presence of different anatomical variations related to the vascular supply of the kidney, while renal anatomy showed no alterations in size, position and structure in any of the cases studied.

The main variations observed are classified in Table 1, their prevalence in Table 2 and some of them are shown in Figures 1 and 2.

In addition, the following table shows the percentage values of the vascular anatomical variations found in relation to the number of dissected renal structures (Table 2).

DISCUSSION

The presence of variations in the renal vascular system is considered of utmost importance, being

Table 1. Classification of variations in renal vascularisation

| | Arterial anomalies | | Venous anomalies | |
|--------|--|--|--|--|
| | Right | Left | Right | Left |
| Case 1 | Superior polar artery | Perforant superior polar artery | <ul style="list-style-type: none"> • Superior polar vein • Gonadal vein inflow to VR • Late venous confluence | Double crossed circumaortic renal vein |
| Case 2 | Superior polar artery | – | Late confluence of 2 branches | – |
| Case 3 | Perforant superior polar artery | – | Late confluence of 3 branches | Late confluence of 4 branches |
| Case 4 | Superior polar artery arising from renal artery | <ul style="list-style-type: none"> • Upper aortic polar artery with suprarenal branch • Prepyelic with ureteral branch | V. polar inferior tributary of VR | RV upper branch tributary adrenal vein |
| Case 5 | <ul style="list-style-type: none"> • Prehilar branching • Inferior polar artery | Double polar aortic artery: superior and inferior | – | Double crossed circumaortic renal vein |
| Case 6 | – | – | – | Double crossed circumaortic renal vein |
| Case 7 | – | – | – | Triple renal vein |
| Case 8 | <ul style="list-style-type: none"> • Double polar aortic artery: superior and inferior • Double communicant vascular arch vascular: anterior and posterior | Pre- and retropyelic pre-hilar branching | – | – |

Table 2. Prevalence of renal vascular variations

| | n = 16 | Right | Left | Total | |
|----------|------------------------------------|-------|-------|-------|-----------|
| | | | | N | Freq. (%) |
| ARTERIAL | Superior polar artery | 62.5% | 37.5% | 8 | 50% |
| | Inferior polar artery | 25% | 12.5% | 3 | 18.75% |
| | Double communicating arterial arch | 12.5% | 0% | 1 | 6.25% |
| | Prehilar ramification | 12.5% | 12.5% | 2 | 12.5% |
| VENOUS | Superior polar vein | 12.5% | 0% | 1 | 6.25% |
| | Inferior polar vein | 12.5% | 0% | 1 | 6.25% |
| | Double circumaortic renal vein | 0% | 37.5% | 3 | 18.75% |
| | Triple renal vein | 0% | 12.5% | 1 | 6.25% |
| | Late venous confluence | 37.5% | 12.5% | 4 | 25% |

essential for radiologists, surgeons and urologists to have a global anatomical vision that allows them to establish a good approach and surgical plan for different pathologies of the renal-ureteral system.

In this study we have observed the presence of anatomical polymorphisms of the vascularisation of the kidney in a total of 16 renal structures (8 left and 8 right). Of the total number of renal blocks dissected in the study, we identified 75% and 62.5% of variations at the arterial and venous levels, respectively. These results reflect a higher frequency than previous

studies, such as Cruzat et al. [7] who reported a prevalence of 35% of arterial variations, Gebremickael et al. [10] who described their presence in 38.5% of the Ethiopian population and Budhiraja et al. [3] with an incidence of 59.5% of variations with respect to normality in the Indian population. On the other hand, the venous anomalies observed in our study (62.5%) are higher than those described in the investigations by Ferreira et al. [9] and Mendez et al. [20] (18% and 31.9% respectively).

The pattern of arterial variations was more common on the right side (64.3%) than on the left (35.7%), while venous anomalies were equally distributed on both sides. These data are similar to those shown by Özkan et al. [25] and Ugurel et al. [35] in two renal helical CT angiographic investigations in a total of 855 and 100 patients respectively.

The vascular anatomical variations in the kidney with the highest incidence are the polar renal arteries. In fact, in the present study, this tendency was observed in 56.3% of the renal structures (in 9 of the 16 dissected kidneys), a higher percentage than that obtained by Satyapal et al. [30] of 27.7%, a result that is within the average mean prevalence of polar renal artery (RA) described by other authors such as Khamanarong et al. [17] and Çınar & Türkvatan [5] (17% vs. 31.3%).

Furthermore, supernumerary RAs can be divided according to their point of entry into the kidney, into

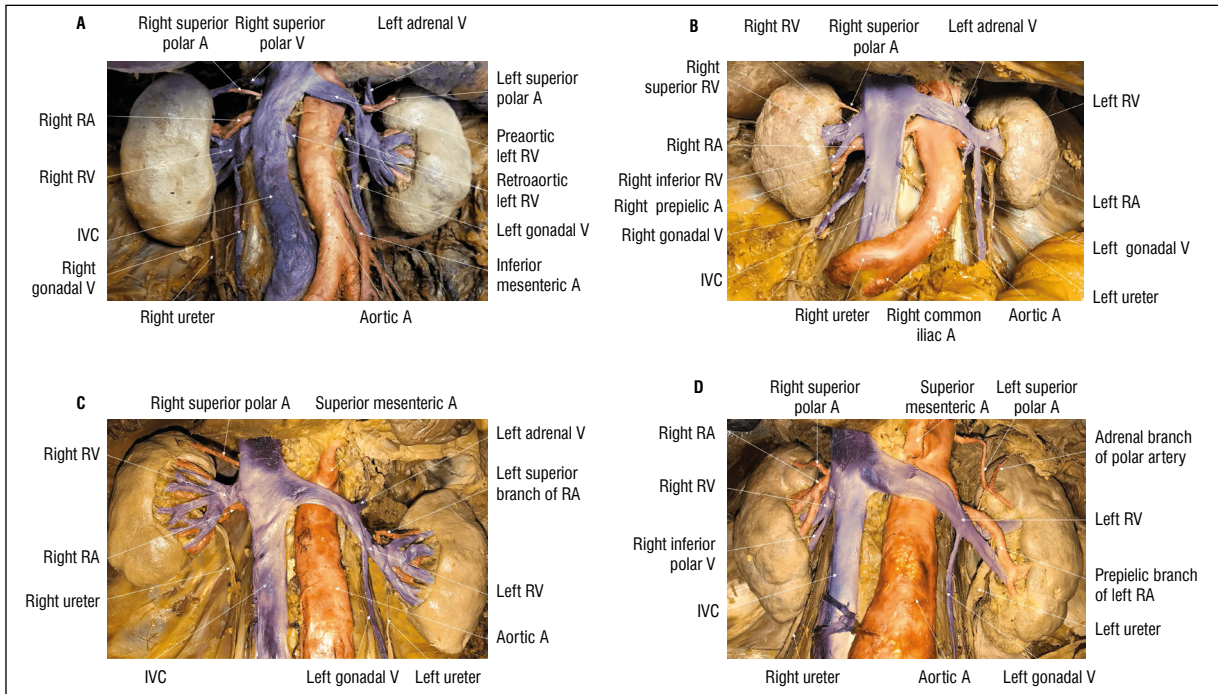


Figure 1. A. Case no. 1; B. Case no. 2; C. Case no. 3; D. Case no. 4. Right and left superior perforating polar artery. Right superior polar vein. Right late venous confluence. Double left circumaortic renal vein. Ao — aorta artery; IMA — inferior mesenteric artery; RRA — right renal artery; LRA — left renal vein; RKV — right renal vein; IVC — inferior vena cava.

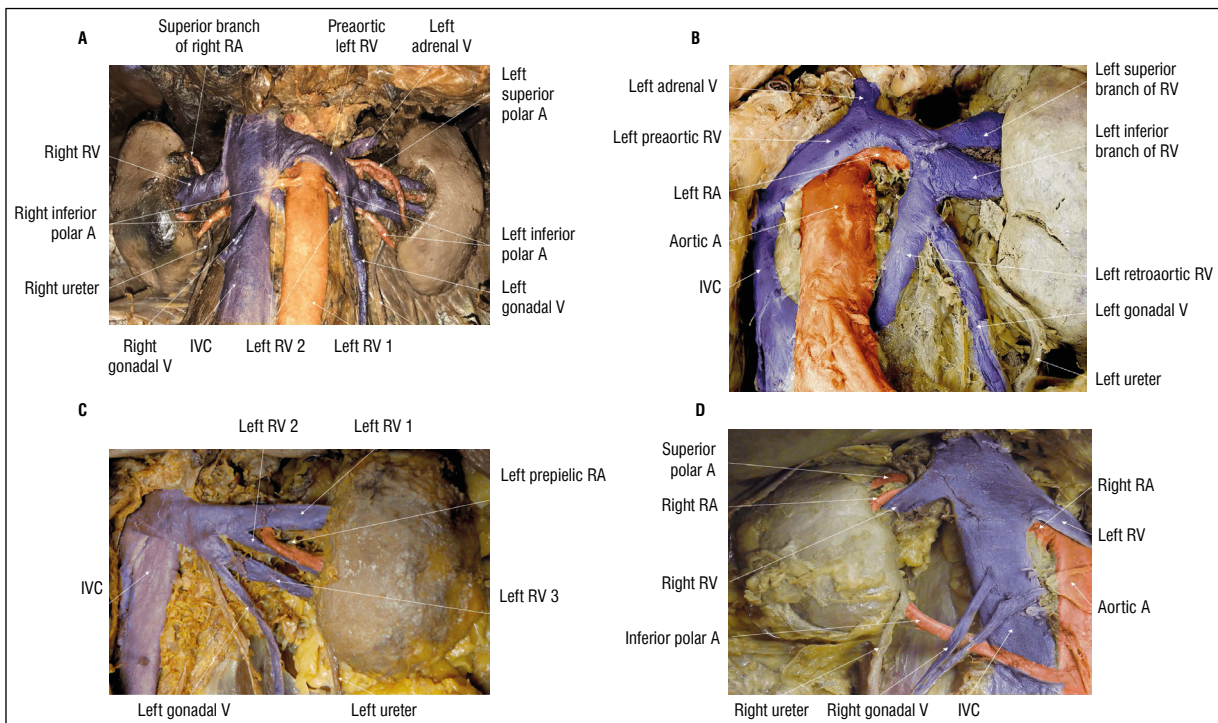


Figure 2. A. Case no. 5; B. Case no. 6; C. Case no. 7; D. Case no. 8. Right and left superior perforating polar artery. Right superior polar vein. Right late venous confluence. Double left circumaortic renal vein. Ao — aorta artery; IMA — inferior mesenteric artery; RRA — right renal artery; LRA — left renal vein; RKV — right renal vein; IVC — inferior vena cava.

superior and inferior polar arteries. In this regard, our study found a higher incidence of superior polar arteries compared to inferior ones (72% vs. 28%); data that differ from those obtained by Gebremickael et al. [10], who found a lower prevalence regardless of whether their entry point was inferior or superior and, in turn, highlighted a somewhat lower frequency of superior polar RAs compared to inferior ones (9.2% vs. 11.7%). Similarly, these supernumerary arteries may originate from the aorta or the main RA. Talovic et al. [34] described a higher prevalence of aortic versus renal origin, a result similar to that obtained in this study (82% Ao vs. 18% RA).

At the venous level, it is necessary to differentiate renal variations according to whether they occur on the right or left side. Several studies [5, 18, 26] have shown that multiple renal veins (RV) are more common on the right side, especially polar RV with a percentage of 24% described by Raman et al. [26], a result similar to that obtained in our study of 25%. In contrast, on the left side, the presence of multiple veins is not frequent, but a double circumaortic renal vein is found, also called "renal collar" by authors such as Sousa-Rodrigues et al. [32] and Haladaj et al. [13]. Beckmann et al. [2] described an incidence of 11% of renal collars compared with the 37.5% found in our study. Recognition of the retroaortic RV is essential, as this vessel may be mistaken during dissection of the interaortic and para-aortic canal as a lumbar vein or a variant of the gonadal vein and may be injured; moreover, it has been associated with the development of secondary renal venous hypertension due to the difficulty of drainage [28].

In our study, the rate of early branching of the main RA is 12.5% (6.25% on each side). This prevalence is within the range described in articles such as Özkan et al. [25], Holden et al. [14] and Raman et al. [26] on pre-hilar renal arterial branching, with a frequency of between 8.12 and 21%. This variability may be due to the distance from which early branching was considered, as in some cases a division within 1.5 cm from the RA exit was considered early branching [5], while in other cases 2 cm was considered early branching [26] or even certain studies did not specify the exact distance [14, 25].

Similarly, at the venous vascular level, late confluence of venous branches has also been observed in 25% of renal anatomical structures, 18.75% on the right side and 6.25% on the left. However, after

review of numerous studies on variations in renal vascular anatomy, late RV confluence was identified in only a small number of cases, including Raman et al. [26], who described a prevalence of such variation of 10% on the right side and 17% on the left, and Çınar and Türkvatın [5], with a frequency of 4.1% and 3.2%, respectively.

CONCLUSIONS

A large number of variations of the renal vasculature have been observed; therefore, knowledge of the renal vasculature and its possible variations is extremely important during the planning of medical-surgical activities, especially uro-radiological ones, such as angiographic interventions, transplantations, renovascular reconstructions or partial renal resections.

ARTICLE INFORMATION AND DECLARATIONS

Acknowledgments

The authors sincerely thank those who donated their bodies to science so that anatomical research could be performed. Results from such research can potentially increase mankind's overall knowledge that can then improve patient care. Therefore, these donors and their families deserve our highest gratitude.

Conflict of interest: None declared.

REFERENCES

1. Aristotle S, Felicia C. Anatomical study of variations in the blood supply of kidneys. *J Clin Diagn Res.* 2013; 7(8): 1555–1557, doi: [10.7860/JCDR/2013/6230.3203](https://doi.org/10.7860/JCDR/2013/6230.3203), indexed in Pubmed: [24086837](https://pubmed.ncbi.nlm.nih.gov/24086837/).
2. Beckmann CF, Abrams HL. Circumaortic venous ring: incidence and significance. *AJR Am J Roentgenol.* 1979; 132(4): 561–565, doi: [10.2214/ajr.132.4.561](https://doi.org/10.2214/ajr.132.4.561), indexed in Pubmed: [106686](https://pubmed.ncbi.nlm.nih.gov/106686/).
3. Budhiraja V, Rastoi R, et al. Anatomical variations of renal artery and its clinical correlations: a cadaveric study from central India. *J Morphol Sci.* 1979; 30: 228–233.
4. Cho Y, Yoon SP. Bilateral inferior renal polar arteries with a high origin from the abdominal aorta. *Folia Morphol.* 2021; 80(1): 215–218, doi: [10.5603/FM.a2020.0040](https://doi.org/10.5603/FM.a2020.0040), indexed in Pubmed: [32301105](https://pubmed.ncbi.nlm.nih.gov/32301105/).
5. Çınar C, Türkvatın A. Prevalence of renal vascular variations: evaluation with MDCT angiography. *Diagn Interv Imaging.* 2016; 97(9): 891–897, doi: [10.1016/j.diii.2016.04.001](https://doi.org/10.1016/j.diii.2016.04.001), indexed in Pubmed: [27178758](https://pubmed.ncbi.nlm.nih.gov/27178758/).
6. Covantsev S, Mazuruc N, Belic O. Renal veins: developmental variations and clinical significance. *Online J Health Allied Scs.* 2017; 16(4): 12.

7. Cruzat C, Olave E. Irrigación renal: multiplicidad de arterias. *Int J Morphol.* 2013; 31(3): 911–914, doi: [10.4067/s0717-95022013000300022](https://doi.org/10.4067/s0717-95022013000300022).
8. Dorland NW. *Dorland's Illustrated medical dictionary.* 30th ed. Saunders, Philadelphia 2003.
9. Arquez HF. Bilateral anatomical variations of renal and testicular vessels. *CES Med.* 2014; 28(2): 273–281.
10. Gebremickael A, Afework M, Wondmagegn H, et al. Renal vascular variations among kidney donors presented at the national kidney transplantation center, Addis Ababa, Ethiopia. *Transl Res Anat.* 2021; 25: 100145, doi: [10.1016/j.tria.2021.100145](https://doi.org/10.1016/j.tria.2021.100145).
11. Gulas E, Wysiadecki G, Cecot T, et al. Accessory (multiple) renal arteries — differences in frequency according to population, visualizing techniques and stage of morphological development. *Vascular.* 2016; 24(5): 531–537, doi: [10.1177/1708538116631223](https://doi.org/10.1177/1708538116631223), indexed in Pubmed: [26945775](https://pubmed.ncbi.nlm.nih.gov/26945775/).
12. Gulas E, Wysiadecki G, Szymański J, et al. Morphological and clinical aspects of the occurrence of accessory (multiple) renal arteries. *Arch Med Sci.* 2018; 14(2): 442–453, doi: [10.5114/aoms.2015.55203](https://doi.org/10.5114/aoms.2015.55203), indexed in Pubmed: [29593819](https://pubmed.ncbi.nlm.nih.gov/29593819/).
13. Haładaj R, Polguy M, Wysiadecki G, et al. Circumaortic left renal vein (circumaortic renal collar) associated with the presence of vascular anomalies: a case series and review of literature. *Folia Morphol.* 2019; 78(2): 437–443, doi: [10.5603/FM.a2018.0090](https://doi.org/10.5603/FM.a2018.0090), indexed in Pubmed: [30280373](https://pubmed.ncbi.nlm.nih.gov/30280373/).
14. Holden A, Smith A, Dukes P, et al. Assessment of 100 live potential renal donors for laparoscopic nephrectomy with multi-detector row helical CT. *Radiology.* 2005; 237(3): 973–980, doi: [10.1148/radiol.2373041303](https://doi.org/10.1148/radiol.2373041303), indexed in Pubmed: [16304115](https://pubmed.ncbi.nlm.nih.gov/16304115/).
15. Hostiuc S, Rusu MC, Negoii I, et al. Anatomical variants of renal veins: a meta-analysis of prevalence. *Sci Rep.* 2019; 9(1): 10802, doi: [10.1038/s41598-019-47280-8](https://doi.org/10.1038/s41598-019-47280-8), indexed in Pubmed: [31346244](https://pubmed.ncbi.nlm.nih.gov/31346244/).
16. H OI, A MI, A GS. Vena renal izquierda recurrente retroaórtica: reporte de una rara variación. *Int J Morphol.* 2011; 29(2): 339–343, doi: [10.4067/s0717-95022011000200005](https://doi.org/10.4067/s0717-95022011000200005).
17. Khamanarong K, Prachaney P, Utraravichien A, et al. Anatomy of renal arterial supply. *Clin Anat.* 2004; 17(4): 334–336, doi: [10.1002/ca.10236](https://doi.org/10.1002/ca.10236), indexed in Pubmed: [15108340](https://pubmed.ncbi.nlm.nih.gov/15108340/).
18. Koc Z, Ulasan S, Oguzkurt L, et al. Venous variants and anomalies on routine abdominal multi-detector row CT. *Eur J Radiol.* 2007; 61(2): 267–278, doi: [10.1016/j.ejrad.2006.09.008](https://doi.org/10.1016/j.ejrad.2006.09.008), indexed in Pubmed: [17049792](https://pubmed.ncbi.nlm.nih.gov/17049792/).
19. Méndez López V, Casado Méndez PR, Labrada RL, et al. Anatomic variants of the polar arteries of the kidney. *Rev Med Electron.* 2014; 36(suppl. 1): 720–728.
20. Méndez Lopez V, Casado P, Méndez H, et al. Anatomical variants of the renal veins. *Rev Méd Electrón.* 2016; 38(6): 817–825.
21. Moore K, Dailey A, Agur A. *Anatomía con orientación clínica.* 5th ed. Wolters Kluwer, Barcelona 2015.
22. Moore KL, Persaud TVN, Torchia MG. *Embriología Clínica.* 8th ed. Elsevier Saunders, Barcelona 2009.
23. Nathan H. Observations on aberrant renal arteries curving around and compressing the renal vein. *Circ J.* 1958; 18(6): 1131–1134, doi: [10.1161/01.cir.18.6.1131](https://doi.org/10.1161/01.cir.18.6.1131).
24. Netter FH. *Atlas de Anatomía Humana.* 4th ed. Masson, Barcelona 2007.
25. Ozkan U, Oğuzkurt L, Tercan F, et al. Renal artery origins and variations: angiographic evaluation of 855 consecutive patients. *Diagn Interv Radiol.* 2006; 12(4): 183–186, indexed in Pubmed: [17160802](https://pubmed.ncbi.nlm.nih.gov/17160802/).
26. Raman SS, Pojchamarnwiputh S, Muangsomboon K, et al. Surgically relevant normal and variant renal parenchymal and vascular anatomy in preoperative 16-MDCT evaluation of potential laparoscopic renal donors. *AJR Am J Roentgenol.* 2007; 188(1): 105–114, doi: [10.2214/AJR.05.1002](https://doi.org/10.2214/AJR.05.1002), indexed in Pubmed: [17179352](https://pubmed.ncbi.nlm.nih.gov/17179352/).
27. Rao M, Bhat S, Venkataramana V, et al. Bilateral prehilal multiple branching of renal arteries: a case report and literature review. *Kathmandu Univ Med J.* 2006; 4(3): 345–348, indexed in Pubmed: [18603933](https://pubmed.ncbi.nlm.nih.gov/18603933/).
28. Rodríguez-Blas AI, Díaz-García JD, Salinas-Ramos CR, et al. Vena renal izquierda retroaórtica. *Rev Hosp Jua Mex.* 2016; 83(3): 109–112.
29. Saldarriaga B, Pinto S, Ballesteros L. Morphological expression of the renal artery: a direct anatomical study in a colombian half-caste population. *Int J Morphol.* 2008; 26(1): 31–38, doi: [10.4067/s0717-95022008000100005](https://doi.org/10.4067/s0717-95022008000100005).
30. Satyapal KS, Haffeejee AA, Singh B, et al. Additional renal arteries: incidence and morphometry. *Surg Radiol Anat.* 2001; 23(1): 33–38, doi: [10.1007/s00276-001-0033-y](https://doi.org/10.1007/s00276-001-0033-y), indexed in Pubmed: [11370140](https://pubmed.ncbi.nlm.nih.gov/11370140/).
31. Schünke M, Schulte E, Voll M. *Prometheus. Texto y Atlas de Anatomía.* Editorial Médica Panamericana, Barcelona 2007.
32. Rodrigues CFS, Alcântara FS, Rocha AC, et al. Persistencia del collar venoso renal. *Int J Morphol.* 2013; 31(2): 500–504, doi: [10.4067/s0717-95022013000200023](https://doi.org/10.4067/s0717-95022013000200023).
33. Sumalatha T, Pushpamala N. Accessory renal arteries: a cadaveric study. *Indian J Anat.* 2018; 7(5): 528–532, doi: [10.21088/ija.2320.0022.7518.12](https://doi.org/10.21088/ija.2320.0022.7518.12).
34. Talović E, Kulenović A, Voljević A, et al. Review of the supernumerary renal arteries by dissection method. *Acta Med Acad.* 2007; 36(2): 59–69.
35. Ugurel MS, Battal B, Bozlar U, et al. Anatomical variations of hepatic arterial system, coeliac trunk and renal arteries: an analysis with multidetector CT angiography. *Br J Radiol.* 2010; 83(992): 661–667, doi: [10.1259/bjr/21236482](https://doi.org/10.1259/bjr/21236482), indexed in Pubmed: [20551256](https://pubmed.ncbi.nlm.nih.gov/20551256/).
36. Urban BA, Ratner LE, Fishman EK. Three-dimensional volume-rendered CT angiography of the renal arteries and veins: normal anatomy, variants, and clinical applications. *Radiographics.* 2001; 21(2): 373–86; questionnaire 549, doi: [10.1148/radiographics.21.2.g01mr19373](https://doi.org/10.1148/radiographics.21.2.g01mr19373), indexed in Pubmed: [11259702](https://pubmed.ncbi.nlm.nih.gov/11259702/).
37. Young AH, Thompson P. Abnormalities of the renal arteries, with remarks on their development and morphology. *J Anat Physiol.* 1903; 38(Pt 1): 1–14.1, indexed in Pubmed: [17232579](https://pubmed.ncbi.nlm.nih.gov/17232579/).