Anatomical variations of extra-parenchymal renal arteries in Vietnamese adults

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Article History
Received: 22 April 2020
Reviewed: 23/April/2020 to 29/May/2020
Accepted: 30 May 2020
E-publication: 6 June 2020
P-Publication: July - August 2020

Citation

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General Note
Article is recommended to print as color digital version in recycled paper.

ABSTRACT
Background: The anatomy of renal arteries has great significance in specific urology therapies. This study characterized the morphology of the extra-parenchymal renal artery, verified whether the main renal artery has a predominant branching pattern.

Materials and methods: Forty kidneys from 20 cadavers were obtained. The kidneys were removed from the body and micro-dissected the parenchyma to reveal the renal artery.

Results: The majority of kidneys have one main renal artery (90%). The upper and lower renal aberrant renal artery, which arises from the abdominal aorta, appears in 5% and 2.5% of the observed kidneys,
respectively. The renal artery often branches outside the renal sinus (77.78%). The renal artery can be classified into three groups: group I (the main renal artery separates into two divisions – anterior and posterior division, 52.78%), group II (the main renal artery gives “early” lateral branches before dividing into two end divisions, 25.00%), group III (the main renal artery separates into more than two primary divisions – trifurcating, quad-furcating, 22.22%). In group I, the anterior division has four branching patterns: bifurcating (47.37%), trifurcating (26.32%), quad-furcating (10.53%) and ladder-like dividing (15.79%); the posterior division has two branching patterns: ladder-like dividing (78.95%) and bifurcating (21.05%). Overall, the anterior division supplies blood to a broader area than the posterior division does. Conclusions: The branching of the human renal artery is diverse, and the division into five segmental arteries becomes inappropriate in a large proportion of cases.

Keywords: Anatomy, renal artery, extra-parenchymal, blood supply.

1. INTRODUCTION

Many minimally invasive renal surgeries and kidney transplantation demand more specific and precise knowledge of the extra-parenchymal morphology of the renal artery. Anatomical variations of the renal artery at the hilum level may pose a challenge to survival and complication in transplant surgery (Coen and Raftery, 1992; Benedetti et al., 1995). The details in vascular division allow the physician to better access to a certain extent of renal parenchyma, especially in laparoscopic partial nephrectomy and angiographic interventions.

The first primary pattern of renal vascular segmentation was produced by Graves, using cast injected with plastic and contrast angiography of post-mortem specimens since 1954. The renal artery has been perceived to divide into five segmental arteries. Consequently, the kidney is described as having five segments, which are supplied by their end segmental arteries: apical, upper, middle, lower, and posterior (Graves, 1954). This classification has widely become a teaching and learning model. However, the five segmental renal arteries hypothesis did not encompass extra-parenchymal division, and branching pattern as well as the vascular variants. Subsequent researches show many variations in number and branching pattern of renal arteries, along with the blood supply model of renal parenchyma (Fine and Keen, 1966; Sampaio and Passos, 1992; Shoja et al., 2008; Daescu et al., 2012). Considering those variations, a constant pattern of the renal arterial branching seems unsatisfactory. To provide additional anatomical information in detail of the renal artery, its branching pattern, and characteristics of renal parenchyma’s blood supply, we observed renal arteries from extra-renal to intra-sinus parts. The study verified whether the renal artery has a predominant branching pattern and investigated the blood supply of the specific renal parenchymal partitions.

2. MATERIALS AND METHODS

Anatomical Donor and Preservation

To characterize the morphology of the extra-parenchymal parts of the renal arteries, we observed the extra-sinus parts on the cadaver’s body, then removed the kidneys and micro-dissected the parenchyma to reveal intra-sinus part. Forty kidneys from 20 fixed cadavers were obtained. These anatomical donors had been prepared for the use in the formal course in gross human anatomy in the Department of Anatomy at the University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam, from years 2015 to 2017. All guidelines are followed regarding the use and care of cadaveric material, as well as all regulations set forth by the Vietnamese Anatomical Education Program. There is 12 male and eight female cases, the mean life-time age of the corpses was 68.30 ± 13.05 years. We excluded all cases that have congenital or acquired anatomical abnormalities, which had changed the genuine characteristics of the kidneys or renal vascular (renal tumor, adrenal tumor, renal injury...). The cadavers damaged due to preservation or dissection also were eliminated.

The embalming procedure is a 2-phase procedure beginning within the first 24 hours after death. The first step of the first phase of the embalming procedure is an injection of 18 L mixture composed of 37% Formalin (2 L); 1 M Phenol (1 L); Glycerin 1 L, 90% Alcohol (2 L) and water (12 L). Three days following injection, cadavers are placed into 300 L of a solution composed of 37% Formalin (2 L), 1 M Phenol (3 L), and water (295 L). The specimen remains submerged in the vat for a minimum of 4 months. We accessed the abdominal cavity using midline incision. The peritoneum with the stomach, the intestine, was lifted to approach the retroperitoneal space. We excised and cleared the fat and fibrous tissue around kidneys, adrenal glands, abdominal aorta for better visualization of the kidneys along with their extra-sinus vascular. Arteries from both sides were examined carefully. At this level, we observed the number of renal arteries, the appearance of accessory renal arteries. We continued exploring the anatomy of intra-sinus renal arteries. Two kidneys with their vascular, ureters and aorta were excised from the body en-bloc. We curetted the kidney's
parenchyma carefully to uncover the renal sinus and investigated the branches of the main renal artery (MRA). The pelvis and calyces were preserved to observe the interrelation with arterial divisions.

Furthermore, the diameter of the MRAs and their first divisions were measured. To obtain the diameter of those circular structures, we flattened the arteries with a Kelly straight forceps, then measured the width of the arteries between two grips. The measured data was the haft circumference (P). Using the formula "d = 2P/ \pi", we calculated the outer diameter of the vascular.

**Measurements**

Using a caliper with a center distance attachment, the data were saved and evaluated using SPSS 14.0. The following data were recorded: (1) biometric variables of the hepatic veins and the IVC; (2) morphologic variables of the common trunk of the middle and left hepatic veins. Results were expressed as mean length (or diameter) in millimeters (mm) ± mm standard deviation (SD).

**Photography**

Digital photography of the external features of the livers and veins was done using a NIKON D3100 SLR Camera (B&H Foto & Electronic Corporation, NY) equipped with an 18-55 mm VR NIKKOR Macro lens and a Nikon 49 mm f/2.8G AF-S DX NIKKOR 2200 VR Micro lens.

3. RESULTS

**General characteristics**

The majority of kidney had 1 MRA (90%). In 10% of cases, the kidney presented 2 MRAs. There was not any case that had 2 MRAs on both sides simultaneously. There were no statistically significant differences in the number of the MRA between the left and right sides (p > 0.05). Furthermore, there are 5.00% of kidneys had one upper polar artery, and 2.50% of kidneys had one lower polar artery arising from the aorta. Those aberrant renal arteries were not presented simultaneously in the same kidney.

**The branching position of the renal artery**

Among the kidneys which had 1 MRA, the position where the arteries divided into main divisions, run anterior and posterior to the pelvis, was extra-sinus in 77.78% of cases and intra-sinus in 22.22% of cases. No significant difference was found between left and right sides (Fisher’s exact test, p = 0.691) (Table 1 and Figure 1).

<table>
<thead>
<tr>
<th>Position</th>
<th>Right Renal</th>
<th>Left Renal</th>
<th>Both Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extra-sinus</td>
<td>15 (83.33%)</td>
<td>13 (72.22%)</td>
<td>28 (77.78%)</td>
</tr>
<tr>
<td>Intra-sinus</td>
<td>3 (16.17%)</td>
<td>5 (27.78%)</td>
<td>8 (22.22%)</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>18</td>
<td>36</td>
</tr>
</tbody>
</table>

**Figure 1** The branching position of the renal artery: a. Extra-sinus. b. Intra-sinus.
The branching pattern of the main renal artery
Renal artery branches very incidentally. We cured the parenchymal, which covered the renal sinus meticulously then observed the branching pattern. In general, the MRAs split into the primary divisions which ran anterior, and the others ran posterior to the pelvis. From these primary divisions, the arteries may continue to divide into smaller branches before reaching the parenchymal. Moreover, in some kidneys, before splitting into the primary end divisions, the MRAs gave some "early" lateral branches (ELBs), which supplied for a part of renal tissue. Based on those characteristics, we classified the kidney, which had one MRA, into three groups (Figure 2):

**Group I**: account for 52.78% of cases, renal artery splits into two primary divisions, anterior division (AD) runs anterior to the pelvis, and posterior division (PD) runs posterior to the pelvis.

**Group II**: account for 25.00% of cases, renal artery gives "early" lateral branches before splitting into two primary end divisions, AD and PD.

**Group III**: account for 22.22% of cases, renal artery splits into more than two primary divisions (trifurcating, quad-furcating).

The majority of the renal arteries were classified into group I. The arteries in group II, and group III were nearly equal and accounted for almost half of cases.

Figure 2 The groups of the main renal artery. Arrow: “early” lateral branch.

Characteristics of renal arteries in group I
The ADs had many branching forms before their end arteries entering renal tissue (Figure 3):

Figure 3 Main renal arteries in group I. Anterior division branching forms: a. Bifurcating b. Trifurcating c. Ladder-like dividing.
Bifurcating (47.37%): The ADs split into two arteries, which were usually nearly equal in diameter. Those branches often continued to divide into many smaller arteries before going to renal parenchyma. In this branching pattern, the anterior renal parenchyma was easy to separate into superior and middle segments, as in Graves’s classification.

Trifurcating (26.32%): The ADs split into three arteries and entered the renal tissue or give smaller branches.

Quad-furcating (10.53%): The ADs split into four arteries at the same point.

Ladder-liked dividing (15.79%): The ADs gave many side branches on the way run downward and give end arteries supply for the lower pole. In this branching pattern, the anterior renal parenchyma was hard to separate into suitable upper and middle segments.

The PDs had two branching patterns: Ladder-liked dividing (78.95%): the PDs gave many side branches. The PDs often ran downward. Furthermore, those divisions sometimes split a branch, ran upward, and supplied for the upper pole. This branch may enter the renal tissue posterior to the pelvis, or curved around to provide blood for the anterior region of the upper pole.

Bifurcating (21.05%): The PDs split into two arteries sequentially. In this pattern, the posterior renal parenchyma can be considered to divide into many smaller segments.

Characteristics of renal arteries in group II
Among 9 cases in group II, 8 MRAs (88.9%) had 1 ELB, and 1 case (11.11%) had 2 ELBs, before splitting into two end divisions, AD and PD (Figure 4). In most cases with 1 ELB, this side branch often anterior to the pelvis in the renal sinus (7 cases). The blood supply region of those ELB was variable, from a little tissue to half of the anterior parenchyma. Many ELB supplied for a partition in the upper half of anterior parenchyma (6 cases).

Figure 4 Main renal arteries in group II.

In one case with 2 ELBs, one branch ran anterior to the pelvis, supplied for the middle of anterior renal parenchyma, and the other ran posterior, supplied for lower pole.

Characteristics of renal arteries in group III
In 7 MRAs trifurcating, 85.71% of arteries had two branches run anterior, and one branch run posterior to the pelvis, 14.29% of arteries had one branch run anterior, and two branches run posterior to the pelvis. Moreover, in 2 cases, the MRAs had split the ELBs before giving those three end arteries (Figure 5). There was 1 MRA quad-furcating. Two branches ran anterior to the pelvis, bifurcated into smaller arteries. One branch ran posterior to the pelvis, ladder-liked divided. The other branch ran along the upper edge, slightly tilted backward, supplying blood for the upper pole.

The kidney had multiple main renal arteries
There were 4 cases of kidney having 2 MRAs. When entering the renal hilum, in the renal sinuses, one artery ran anterior, and one artery ran posterior to the renal pelvis. Therefore, these two arteries can be considered similar to the form of one MRA with the very “early” position of splitting into ADs and PDs (at the abdominal aorta). Especially, although there were only 4 cases, the anterior renal artery had four branching forms: bifurcating, trifurcating, quad-furcating, and ladder-liked dividing (each kidney has its form). The posterior artery also had two branching forms, bifurcating and ladder-liked dividing.
The blood supply of renal parenchyma
We divided the renal parenchyma into four partitions: upper pole, lower pole, and the remain anterior, posterior parts labeled as middle anterior and middle posterior (Table 2 and Figure 6).

Table 2 The blood supply of renal parenchyma.

<table>
<thead>
<tr>
<th>Partition</th>
<th>Blood source</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper pole</td>
<td>Anterior vessels</td>
<td>23</td>
<td>57.50</td>
</tr>
<tr>
<td></td>
<td>Posterior vessels</td>
<td>7</td>
<td>17.50</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>10</td>
<td>25.50</td>
</tr>
<tr>
<td>Lower pole</td>
<td>Anterior vessels</td>
<td>19</td>
<td>47.50</td>
</tr>
<tr>
<td></td>
<td>Posterior vessels</td>
<td>10</td>
<td>25.00</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>11</td>
<td>27.50</td>
</tr>
<tr>
<td>Middle anterior</td>
<td>Anterior vessels</td>
<td>39</td>
<td>97.50</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>1</td>
<td>2.50</td>
</tr>
<tr>
<td>Middle posterior</td>
<td>Posterior vessels</td>
<td>39</td>
<td>97.50</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>1</td>
<td>2.50</td>
</tr>
</tbody>
</table>
In kidneys having aberrant renal arteries, these additional arteries supplied blood for relatively modest parenchyma; the upper or lower poles were also received blood from the branches of the MRAs. Therefore, we described only the blood supply characteristics of the MRA.

We assumed that the parenchyma is supplied blood from the anterior, posterior vessels, or both. Anterior vessels mean all branches arising from the ADs, included ELBs running in front of the pelvis when entering the renal sinuses. In some cases, there was a branch arising from ADs, then climbing up to the pelvis, going backward, and entering the renal tissue at a position posterior to the pelvis. It was still considered as anterior vessels. With the kidneys having two MRAs, anterior vessels referred to branches arising from the anterior artery. Posterior vessels were considered similarly.

The diameter of the main renal artery and its primary divisions
The MRA measured 5.39 ± 0.80 mm, varied between 4.28 and 8.71 mm, at the position just before branching. No significant difference was found regarding the left and right sides, p = 0.310. Among group I, the diameter at the origin of the AD was 4.50 ± 0.90 mm, varied between 3.12 and 7.13 mm. The diameter at the origin was 3.92 ± 0.74 mm, varied between 1.99 and 5.09 mm. The AD was significantly bigger than the PD, p = 0.017. Among group II, the diameter at the origin of the anterior and PD was 3.79 ± 0.65 and 3.79 ± 0.43, respectively. Among group III, the diameter of the primary branch of the trifurcating artery was 530 ± 1.07 mm, and one of quad-furcating was 6.79 ± 0.36 mm.

4. DISCUSSION
General characteristics
The morphology of the renal artery has been described in many ways. Along the time, many terms were established. In our study, based on the origin, course, and blood supply region of the vascular, we define in (Figure 7 and Table 3).
Main renal artery: the artery arises from aorta, goes along the renal peduncle to enter the hilum, and has a relatively big size and supply for a vast region of renal tissue. As this definition, the kidney may have many MRAs.
Upper and lower aberrant renal artery: the artery enters the renal upper or lower pole, often arises from aorta, usually has a small size, supply for a small area of the renal pole.
Accessory renal artery: the artery does not go along the renal peduncle, arises from arteries other than the aorta, or have a relatively small size and supply for a modest region of renal tissue.

Figure 7 The terminology of renal arteries. a. Two main renal arteries. b. Upper aberrant renal artery (arrow). c. Accessory renal artery (arrow).

The differentiation in several MRA, as well as the appearance of the aberrant artery, has been mentioned by many authors. Sampaio and colleagues described up to 12 types of hilum and polar renal arteries (Sampaio et al., 1992). The constant point of all studies is that the kidney with one MRA was the most common (Figure 8).
Table 3 The number of main renal arteries.

<table>
<thead>
<tr>
<th>Author</th>
<th>One artery (%)</th>
<th>Two arteries (%)</th>
<th>More than two (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampaio and Passos (Sampaio et al., 1992)</td>
<td>84.2</td>
<td>13.5</td>
<td>2.3</td>
</tr>
<tr>
<td>Kyle J. W. et al. (Weld et al., 2005)</td>
<td>87.7</td>
<td>12.3</td>
<td>_</td>
</tr>
<tr>
<td>Rocco et al. (Rocco et al., 2015)</td>
<td>86.6</td>
<td>11.43</td>
<td>1.96</td>
</tr>
<tr>
<td>Our study</td>
<td>90.00</td>
<td>10.00</td>
<td>_</td>
</tr>
</tbody>
</table>

Figure 8 The presence of the aberrant renal artery.

The branching position of the renal artery

Daescu and colleagues found that 81.67% of renal arteries divided before entering the hilum, 10.00% at the hilum, and 8.33% inside the renal sinus (Daescu et al., 2012). Our study showed a similar finding with the majority of renal artery branching outside the sinus (77.78%). The number of arteries branching intra-sinus was smaller but still accounted for a relatively high proportion (22.22%). Understanding the branching position is required in surgeries that need to show the vessel’s supply for partial renal tissue.

The branching pattern of the main renal artery

The MRA divides into end branches, which do not anastomose with their neighbors once it has split, as in other previous studies. Therefore, in clinical practice, damaging or occlusion of a branch can cause necrosis of the corresponding parenchyma. Many authors have described the morphology of renal arteries (Graves, 1954; Weld et al., 2005; Shoja et al., 2008; Budhiraja et al., 2010; Daescu et al., 2012). However, these studies have a way of classifying and describing branching forms of renal arteries by their own methods. This shows the diversity of renal artery branching patterns, and there has not been a comprehensive method to characterize the artery. In this study, we relied on the number of primary branches, ELBs, and the characteristics of their blood supply partitions to place renal arteries into three groups.

In general, all studies have shown that the MRAs mostly bifurcated. In our study, 77.78% of arteries split into two divisions, with or without ELBs, the remains divided into 3 and 4 branches, 19.44% and 2.78%, respectively. Daescu reported similar results with the majority of arteries to give two branches, 70.00%, and the number of arteries gives 3 or 4 branches account for 23.33 and 6.67% of cases (Daescu et al., 2012).

Characteristics of primary divisions of main renal arteries (Figure 9). In group I, the divisions which run anterior to renal pelvis had predominantly bifurcating form (47.37%); the trifurcating, quad-furcating, or ladder-like form was less common. In contrast, the PDs had ladder-like form predominantly (78.95%). Less than half of the ADs bifurcated. The other types, especially the ladder-like form, make it difficult to appropriately classify the anterior renal parenchyma into upper and middle segments. In 1966, Fine and Keen (Fine et al., 1966) described the branching patterns of PDs, in which the ratio of the ladder-like types, bifurcating, and trifurcating were 50%, 30%, and 10%, respectively. Meanwhile, we have only recorded two types: the ladder-like (78.95%) and the bifurcating form (21.05%). The difference may be due to the lower number of samples. Both studies agreed that ladder-like is the most common type for the PD. The blood supply of renal parenchyma (Table 4).
Figure 9 The branching forms of the primary divisions of main renal arteries in group I.

Table 4 Comparison of blood supply of renal parenchyma.

<table>
<thead>
<tr>
<th>Partition</th>
<th>Blood source</th>
<th>Our study (%)</th>
<th>Sampaio and Aragao (Sampaio and Aragao, 1990)(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper pole</td>
<td>Anterior vessels</td>
<td>57.50</td>
<td>13.40</td>
</tr>
<tr>
<td></td>
<td>Posterior vessels</td>
<td>17.50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>25.50</td>
<td>86.60</td>
</tr>
<tr>
<td>Lower pole</td>
<td>Anterior vessels</td>
<td>47.50</td>
<td>62.20</td>
</tr>
<tr>
<td></td>
<td>Posterior vessels</td>
<td>25.00</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>27.50</td>
<td>37.80</td>
</tr>
<tr>
<td>Middle anterior</td>
<td>Anterior vessels</td>
<td>97.50</td>
<td>100.00</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>2.50</td>
<td>_</td>
</tr>
<tr>
<td>Middle posterior</td>
<td>Posterior vessels</td>
<td>97.50</td>
<td>100.00</td>
</tr>
<tr>
<td></td>
<td>Both</td>
<td>2.50</td>
<td>_</td>
</tr>
</tbody>
</table>

In general, the AD supplied to a broader portion than the PD. AD supplied to the upper pole in 83.00% of the kidney and the lower pole in 75.00% of cases. Meanwhile, the PD only provided to the upper pole in 43.00% of cases and the lower pole in 52.50% of cases. Moreover, in group I, the diameter of the AD is larger than the PD. Compared to the study of Sampaio and Aragao (Sampaio et al., 1990), our research has a certain similarity in blood supply to the anterior and posterior medial portion. Most of the anterior and posterior medial regions are supplied blood from the ADs and PDs, respectively. This is understandable, considering the relative location of these renal parenchyma areas and the arteries. However, we noted a particular case, in which the anterior and posterior medial renal parenchyma were supplied by both AD and PD. Each branch blood provided to half of these portions. The blood supply to the upper and lower poles was significantly different between the two studies. In our study, the majority of the upper pole was supplied only by AD (57.50%), and 25.00% of the kidney was supplied by both AD and PD. However, Sampaio and Aragao found that 86.6% of the upper poles were supplied by blood from two branches, one originated from the AD and one from the PD. For the lower pole, both studies showed that a high proportion of this portion was supplied by only the AD. Sampaio and Aragao did not report any cases where the lower pole was provided only by the PD, while we recorded the rate of 25.00%.

In 1954, based on the branching pattern of the MRA, Graves divided the kidney into five segments: the apical, upper anterior, middle anterior, lower, and posterior segments. Graves found that the AD branched into the upper, middle and lower segmental arteries, the PD supplied the posterior segment, and the apical segment usually arises from AD (Graves, 1954). In 1963, David Sykes investigated 71 renal casts and found that only 83.1% of renal artery branched into five segmental arteries, corresponding to Graves's study (Sykes, 1963). In 2008, Shoja and colleagues showed that the peri-hilar morphology of the MRA demonstrated high individual variability, and at least ten “infrequent” types were found. In 2019, Macchi and colleagues identified a mean of 6.3 (range
from 4 to 8) avascular fissures, indicating a mean of 7.3 renal segments, using the vascular casts, CT angiography images, and 3D printed casts (Macchi et al., 2019).

In this study, we observed that the MRA branches very incidentally. We also recognize many morphologies as David Sykes or Shoja. Furthermore, the AD can split with the ladder-like pattern, without creating clearly segmental arteries. The middle anterior portion can also be received blood from the PD. The middle posterior portion can be received blood from the AD in a few cases. Therefore, the division of the MRA into five segmental arteries becomes inappropriate in a large proportion of cases.

5. CONCLUSION
The kidney may have 1 MRA (90.00%) or multiple MRAs (10.00%); 5.00% of cases have one upper aberrant artery, and 2.50% of cases have one lower aberrant artery, arise from aorta. The MRA divided into primary divisions in extra-sinus (77.78%) or intra-sinus (22.22%). Main renal arteries can be classified into three groups: Group I: renal artery branches into 2 primary divisions, AD and PD (52.78%). Group II: The renal artery gives ELBs before splitting into AD and PD (25.00%). Group III: renal artery branches into more than 2 primary divisions (trifurcating, quad-furcating) (22.22%). The AD branches by four types: bifurcating, predominantly (47.37%), trifurcating (26.32%), quad-furcating (10.53%) and ladder-like form (15.79%). The PD branches by two types: ladder-like, predominantly (78.95%), bifurcating (21.05%). The diameter of the AD is bigger than the posterior one. The blood supply portion of the ADs is larger than the PDs. The main renal artery branches highly diverse and the classification into five segmental arteries become inappropriate in a large proportion of cases.

Abbreviations
MRN: main renal artery
AD: anterior division,
PD: posterior division,
ELB: "early" lateral branch.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

Informed consent
Informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval for study protocol
The study was approved by the Medical Ethics Committee of HCH University of Medicine and Pharmacy (ethical approval code: 0212–HCHUMP).

REFERENCE

