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TITLE: Anatomical variations of the renal arterial vasculature: An Australian perspective

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RUNNING TITLE: Renal arterial variations in Australia

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ABSTRACT:

Introduction: Variations of the renal arteries have been studied and published across various population groups, but similar information for the ethnically diverse nation of Australia is lacking. This study describes the pattern of renal artery anomalies in a section of the Australian population based on computed tomography (CT) angiograms of the abdomen and cadaveric dissection.

Methods: The renal arterial vasculature of 594 kidneys from 300 subjects (28 cadavers, 272 CT) was studied. The number and pattern of renal arteries were categorised on the basis of laterality, point of origin and termination in the kidney (superior pole, hilum, inferior pole), symmetry and sex.

Results: Multiple renal arteries were discovered in 22% of subjects and 12.12% of kidneys. The most common pattern observed was the presence of one variant renal artery (93.1%), compared to the finding of two (5.6%) and three (1.4%) multiple arteries. The aorta was the most frequent site of origin for anomalous vessels, whilst the hilum was the predominant point of entry. No significant difference was established between left and right-sided kidneys (13.8% versus 12.5%; $p = 0.627$); however, unilateral distribution was more common than bilateral additional renal arteries (16.7% versus 3.4%; $p < 0.01$), and variations amongst males were more than females (27.2% versus 15.2%; $p < 0.05$). A higher rate of multiple renal arteries was noted in cadaveric dissections compared to CT images (46.4% versus 19.5%; $p < 0.01$).

Conclusions: These findings provide application of an evidence-based teaching tool that facilitates education regarding renal arterial variations in Australia.

Key words: renal artery; renal vasculature; kidney; multiple; variation

INTRODUCTION

The traditional teaching of renal arterial variations provided in standard anatomical textbooks describes these structures as vessels existing in addition to the normal, single, high-calibre main renal artery and presence of anomalous vessels. 25-30%[1-3]. This frequent rate of incidence reflects the manner in which the renal blood supply is continually changed during embryonic and early foetal life as a result of migration of kidneys cranially from the pelvis to where they receive new branches from a more superior aspect of the aorta The preceding caudal vessels then usually regress and disappear, but failure to regress leads to anomalous renal arteries[4].

Numerous terms have been utilised in reference to these anomalous arteries, including "aberrant", "abnormal", "accessory", "additional", "extra", "multiple", "supernumerary"; and "supplementary"[1,3,5]. Whilst the literature has attempted to amalgamate these different names, alternate perspectives have been promoted regarding their use in recent times[5-7]. Papaloucas and colleagues[6] recommend adopting the universal terminology of 'additional' as proposed by Satyapal et al.[7] to describe all renal arterial anomalies for greater clarity.

By contrast, the use of 'multiple' is encouraged as opposed to 'additional' to reinforce the significance of these vessels as independent vascular entities[7]. Such a notion highlights the clinical importance of this structural anomaly and how they are inextricably linked to a key anatomical principle, that being additional renal arteries act as end arteries. Functionally, this means that they are responsible for the segmental blood supply of a particular portion of the renal parenchyma, in the absence of collateral circulation[5,8]. The term 'additional' may be perceived as something which can be dispensed with as a non-essential structure. However, given that these arterial structures are end arteries, disease, obstruction or their ligation result in diminished blood supply to the segmental tissue. Hence, the term multiple will be adopted throughout this article.

Some examples of their clinical relevance include intraoperative injury or ligation, and occlusion at their origin during endovascular procedures; or stenosis caused by atherosclerosis, fibromuscular dysplasia or vasculitis. The sequential repercussions begin with ischemic injury and focal necrosis, which subsequently leads to a reduction in renal function in addition to resultant renovascular hypertension[9]. As such, awareness of their existence and a clear attempt to preserve them is essential.

Yammine[10] recently recommended applying the concept of evidence-based anatomy to the study of anatomical variations to ensure safe medical practice. This relates directly to additional renal arteries, encouraging a shift towards the use of research based teaching resources that are specific to population groups of interest, rather than following generalised incidence rates as

stated in textbooks. Variations of the renal arteries have been studied extensively both in original research articles and case reports, using kidneys from cadavers, radiological investigations and surgical patients, or various combinations of these modalities of data.

Previous findings indicate substantial variability in incidence beyond standard teaching, ranging from 4%[11] to 61%[12]. The breadth of these data spans studies with samples from 32 different population groups as reported in a recent publication indicating that considerable ethnic diversity exists not only between, but also within, these populations[5].

Determination of the presence of variations according to sex, laterality and symmetry in a given study has occurred inconsistently. Furthermore, investigations into whether differences exist for each of these subsets of data based on statistical comparisons are rare. However, pooled results for each variable are available, which reveal specific trends. With regards to sex, variations tend to occur more commonly in males[12-16] have shown that no difference exists between the two sexes.

Most studies show that there is no difference on the basis of laterality[5,12,13,15-17]. However, there is disagreement in the literature with some evidence pointing towards a statistically significant predominance of variations in both the left[7] and right[18,19] kidneys. Whilst few studies have examined symmetry amongst their included variables, the presence of bilateral renal arterial variations has been shown to range between 10.2%[7,20] and 16%[9].

Despite the large volume of previous relevant work examining the relation between ethnicity and renal artery variation showing significant variability across different nationalities, data is still lacking for the ethnically diverse Australian population[21]. This study aims to redress this by conducting a systematic investigation incorporating a thorough description of the variations in the renal arterial vasculature variations by cataloguing the presence of multiple renal arteries from both cadaveric and CT samples in an Australian population.

MATERIALS AND METHODS

Participants and study design

Three hundred subjects (164 females, 136 males; mean age 66 years; range 22–99 years) were sampled by abdominal CT angiograms (n=272) and cadaveric dissection (n=28), providing a total of 594 kidneys (297 right, 297 left). Cross-institutional approval by the St John of God Hospital Ballarat, University of Melbourne Health Sciences; and University of Notre Dame Australia Human Research Ethics Committees was obtained for this investigation. Given the retrospective design of the study, consent requirements were satisfied using a standardised hospital-based waiver signed by all patients for use of the radiological images and the well-established body donor program in accordance with Australian Federal and State Law through the University of Melbourne for cadavers.

Sample size calculation

Previously detected prevalence rates of renal arterial variations provided the basis for the power calculations, those being 11.2%[5], 36.1%[17] and 59.5%[22]. A sample size between 152 and 364 would provide an alpha level of 0.05 which was considered sufficient.

Inclusion and exclusion criteria

Selected abdominal CT angiograms, undertaken for varied clinical indications, had to demonstrate adequate arterial phase coverage of the abdominal aorta, associated arterial branches and the iliac arteries. Inclusion of cadavers was dependent upon being newly donated and thus available for complete dissection. Exclusion criteria relevant to both data sets were incomplete demographic data, the presence of renal pathology that distorted the gross anatomy of a kidney's vasculature (for example renal cell carcinoma or crossed fused ectopic and horseshoe kidney); and previous donor nephrectomy or recipients of renal transplantation. CT scans which were duplicates or displayed inadequate arterial phase coverage were also excluded.

Classification of renal arterial variations

Multiple renal arteries, identified as being independent of the main renal artery, were categorised according to the Merklin and Michels classification system[5,9,17,22]. This system outlines these anatomical variants based on origin, including the abdominal aorta and the main renal artery as well as other sources (for example the common iliac artery) and point of termination in the kidney, whether they are superior polar, inferior polar or hila(9).

Data collection

The retroperitoneum was visualised by standard anterior dissection of the abdominal cavity at the University of Melbourne's Department of Anatomy and Neuroscience under the supervision of experienced prosectors. New cadavers were selected for complete dissection ensuring the

relevant renal anatomy had not been distorted. Consecutive CT abdominal and pelvic angiograms were accessed retrospectively via the PACS (Picture Archiving and Communication System, Siemens) program and Visage software (Visage 7 Imaging Platform) at the St John of God Hospital Ballarat. These images had been collected using a 128-slice multi-detector CT scanner (SOMATOM Definition Edge, Siemens) after the injection of iodine-containing contrast medium as per hospital protocols. Consecutive selected scans spanned a four-year period from July 17, 2011 to July 17, 2015 and were reviewed by a current practicing radiologist. Variables collected for each kidney included the number of renal arteries, their points of origin and termination and sex.

Statistical analysis

Incidence rates for each of these variables were recorded using Microsoft Excel. Statistical comparisons based on laterality (left kidney, right kidney), sex (female, male), symmetry (unilateral, bilateral) and data sets (CT angiogram, cadaveric dissection) were undertaken using chi-square analyses (SPSS software, IBM SPSS Statistics for Windows, Version 22.0). An alpha level of 0.05 was set as the level of significance.

RESULTS

Renal arterial variations were identified in 66 of the 300 participants (22%) and 72 of the 594 kidneys (12.12%) examined in this study. Out of the 72 kidneys with variations present, 67 (93.1%) had one multiple renal artery, four (5.6%) had two multiple arteries and one had three multiple arteries (1.4%) (Fig. 1). Table 1 summarises the distribution of normal and multiple renal arteries for left-sided and right-sided kidneys. Findings for laterality demonstrated that of the 297 left-sided and right-sided kidneys 37(12.5%) and 41 (13.8%) were found to have multiple renal arteries respectively. No statistically significant difference was found on the basis of laterality ($p = 0.071$) (Table 2).

All subjects had at least one single, dominant renal artery originating from the abdominal aorta. In the majority of cases multiple renal arteries were found to originate from the aorta. Eight participants (5 left, 3 right) were found to have the multiple artery originating from the main renal artery itself. One participant had a right-sided multiple renal artery with its origin at the common iliac artery, supplying the inferior pole of the right kidney (Table 1).

The hilum was the predominant point of termination for renal arterial variations, with a total of 38 (19 left, 19 right) multiple hilar arteries having been detected. Multiple superior polar arteries were encountered on 24 occasions (8 left, 16 right), whereas the inferior pole received additional blood supply in 16 participants (10 left, 6 right). Amongst the 294 participants possessing two kidneys, 49 (16.7%) were found to have unilateral variations, whereas a significantly smaller number of only 10 (3.4%) had multiple renal arteries bilaterally ($p < 0.01$) (Table 2, Fig. 2).

A greater proportion of males possessed multiple renal arteries when compared to their female counterparts ($p < 0.05$) (Table 2). Specifically, of the 136 male participants 37 (27.2%) demonstrated the presence of variations, whereas multiple renal arteries were detected in only 25 (15.2%) of the 164 females. When comparing modalities of data collection, a significantly greater number of variations were found in the cadaveric dissections as opposed to the CT images (46.4% vs. 19.5%, $p < 0.01$) (Table 2).

DISCUSSION

This study used both cadaveric dissections and retrospectively reviewed radiological data from CT angiograms to determine the incidence and pattern of renal arterial variations within an Australian based population. We used an evidence-based approach, as recommended by Yammine[10], by supplementing this data collection with statistical comparisons to profile differences between the specific variables of laterality, symmetry, sex; and data type. We found additional renal arteries in 22% of participants and 12.12% of the kidneys examined. This result reflects the standard teaching within primary anatomy based educational resources that state renal arterial variations present with a common incidence of 25-30%[1-3]. Further, these findings also support the collective results demonstrated in independent literature reviews by Natsis et al[5], Satyapal et al.[7]; and Merklin and Michels[9] of 23.3%, 28.1%; and 28% respectively.

Despite similarities in the mean number of multiple renal arteries between the current and aforementioned studies, the literature demonstrates distinct differences have been identified on the basis of ethnic diversity. In an extensive review article covering the thirty-one major countries studied to date Natsis et al.[5] reported on findings ranging from an incidence as low as 4%[11] in a Malaysian sample, to 61.5%[12] in a Brazilian population. Overall, previous work points towards clear variability existing between population samples.

Given this trend and Australia's ethnic diversity, as demonstrated in the most recent census data showing 28.2% of the country's inhabitants were born overseas[21], it is thus an interesting population to examine. One would have expected a higher variation in a cross section of Australia's inhabitants reflecting this ethnic diversity. However, in this investigation renal arterial variations are comparable to previous studies.

Previously reported limitations (for example insufficient sample size in addition to a lack of inclusion criteria, clear renal artery definitions, standardisation of methodology; and statistical analyses) concerning study design could explain the outlying differences observed in population incidence rates. In particular, the lack of non-standardised definitions for renal arterial variations, influencing which vessels are selected as samples, as well as varied modalities and methods of data collection[5,10] may mean that the results ascertained for different populations may, in fact not be directly comparable.

The current study attempted to overcome the methodological differences outlined above in a number of ways. Firstly, the novel approach of sample size calculations were utilised to ensure adequate power, which is a technique overlooked by all previous studies on this topic. Further, a clear and accepted classification system for describing the variations was adopted, in a standardised sampling process with clearly defined inclusion and exclusion criteria. Lastly, all key variables (that is, laterality, sex and symmetry) that had been explored inconsistently across

previous studies were selected and compared statistically, to ensure epidemiological completeness for this population sample.

It is possible that a molecular explanation may underpin observed differences in variations across respective ethnic groups on a genetic level[5]. For example the production of vascular endothelial growth factor (VEGF), which is present in embryonal arteries and known to play a primary role in the proliferation of blood vessels at this early stage of development, is heavily influenced by genetic and physiologic controls[23].

The number of multiple renal arteries detected for a given kidney in this study reached a maximum of three in one individual/subject (1.4%). Of the remaining subjects four possessed two vessels (5.6%) and 93.1% were found to have one multiple artery. This is in accord with the literature, which shows that multiple renal arteries usually range from one to three[5,24]. Interestingly, cases of four[9,20,24,25] and five[20,26] arteries per kidney have been documented in previous reports, in addition to the presence of seven[25] and ten[26] renal arteries in both kidneys for a single individual.

Clinical implications associated with multiple renal arteries are both medical and surgical in nature. From a medical perspective renal artery stenosis caused by atherosclerosis or other vascular diseases, such as fibromuscular dysplasia, pseudoaneurysms, spontaneous renal artery dissection and vasculitis (for example Takayasu's arteritis), are capable of impairing any additional vessel thus impeding segmental blood supply and causing ischaemic nephropathy[7,27]. In the case of bilateral renal artery stenosis involving multiple small arteries, the risk of renal organ failure is significant enough to warrant surgical intervention[27].

Surgically, multiple renal arteries are considered a relative contraindication to transplantation, an associated increase in operating time and a greater risk of complications, such as haemorrhage and infarction, arterial thrombosis, stenosis at suture lines; and graft failure[27,28]. As such, preoperative assessment with CT imaging plays an important role in identification of the presence and number of these variant vascular structures to prevent operative injuries during laparoscopic surgery with limited visibility and facilitates better surgical planning[27].

Multiple renal arteries primarily originated from the aorta in the present study, with the exception in eight samples taking their origin from the main renal artery and in one case branching from the common iliac artery. The literature reports a number of alternative points of origin for multiple renal arteries. In addition to the main renal artery[22] and common iliac artery[9] as shown in the current investigation, other sites have included the celiac trunk, inferior and superior mesenteric arteries, thoracic aorta, suprarenal artery, contralateral kidney, splenic, right hepatic, inferior phrenic, twelfth intercostal, lumbar, middle sacral, gonadal; and right colic

arteries[5,9]. Variations in origin principally relate to surgical applications. In the context of correcting abdominal aortic aneurysms, endovascular stents and aortic grafts must be constructed in a personalised manner to suit the specific arterial anatomy of the individual. In doing so the patency of the multiple arteries is guaranteed, preventing occlusion of the renal ostium at the aorta, which should be confirmed by performing a completion angiogram following the procedure[29].

The point of termination for multiple renal arteries in this study was found to be the hilum of the kidney in 48.7% of cases, whereas the inferior and superior poles received these vessels at a rate of 20.5% and 30.8% respectively. Studies do however indicate that multiple renal arteries enter both poles in previous investigation which reported inferior polar variations are more common in Caribbean and British population samples[17,20]. Inferior polar arteries appear to be of greater clinical significance than superior polar arteries for two important reasons. Firstly, the upper part of the ureter receives critical blood supply from a branch of the inferior polar artery if one is present[9,17]. Damage to this vessel will result in ureteric necrosis and subsequent paralysis, or the development of urinary leak[9,17].

Secondly, there is a reported risk of ureteropelvic obstruction occurring if the inferior polar artery originates from the aorta and passes the ureter either anteriorly or posteriorly[9,17]. Consequently, this can lead to the development of hydronephrosis which in time has the potential to progress to pyelonephritis[9,17].

The current study showed left-sided and right-sided variations were present to a similar extent, being detected at rates of 12.5% and 13.8% respectively ($p = 0.071$). Despite the inconsistencies evident in previous work, these results agree with the majority of the literature[5,12,13,15-17] which indicates that there is no difference based on laterality. The lack of dominance regarding left or right-sided variations suggests alternative criteria should be considered when it comes to surgical decision-making, such as in the case of donor nephrectomies.

Whilst limited data is available regarding symmetry of variations across both kidneys in a given individual, it has been shown that bilateral variations are less common than unilateral findings generally occurring between 10.2%[7,20] to 16%[9]. In this study, bilateral variations were present in 3.4% of the participants who possessed two kidneys. This result was significantly less than the 16.7% of subjects with unilateral variations ($p < 0.01$), reflecting trends in earlier studies.

This study found multiple renal arteries to be significantly more prevalent in males compared to females ($p < 0.05$), supporting previous observations[7,13,14]. By contrast, Natsis et al.[5] indicated that there is no difference on the basis of sex. Awareness of a higher incidence of variations in

males is of note clinically as men are more likely to undergo kidney transplantation since they are affected by end-stage renal disease more commonly than females[28].

The efficacy of CT angiograms in detecting additional renal arteries is well established[24]. Despite this demonstrated utility, the comparison between modalities of data collection in this study demonstrates that variations were significantly more common amongst cadaveric dissections as opposed to CT angiograms ($p < 0.01$), as reflected elsewhere in the literature[5,30,31]. It is possible that this difference was due to the variation between data sample sizes, which specifically included 272 CT angiograms compared to 28 cadaveric dissections. However, the limited availability of cadavers at the time of this investigation required a greater proportion of the data to be sampled with radiological imaging. Alternatively, some multiple vessels potentially may have been missed during assessment of the CT images despite being assessed by a skilled reviewer. Whilst this explanation is unlikely, it is still possible particularly in the case of small additional arteries. This was shown in one particular investigation whereby two particular diminutive arteries, measuring less than 2 mm in diameter, were missed on CT by all three expert reviewers in comparison to intraoperative observations[31].

These results need to be interpreted within the appropriate context. The current study included a small population sampling from one state in Australia and unfortunately, due to lack of information on the subjects' ethnicity we were unable to compare variations on the basis of ethnicity between subjects in this study with other population groups. Further, the current investigation did not explore morphometric data, as the focus of our investigation was to determine the presence and profile of variations amongst subjects. Following the suggestion of Yammine[10], further work should be directed towards pooling results throughout the current literature by means of a meta-analysis to more accurately reflect population statistics.

The incidence of renal arterial variations in the Australian population examined in this study was 22%, consistent with the available body of literature. From a clinical perspective, since the presence of these structures is so common, there is a small chance they may be missed on CT angiography; and functionally they act as end arteries, in the intraoperative setting it would be safest to assume renal arterial variations are present until proven otherwise upon careful dissection. We believe that this study will encourage further research towards an evidence-based teaching content of anatomical variations in the Australian context.

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383 **CONFLICT OF INTEREST**

384 None declared.

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493 **FIGURE LEGENDS**

494

495 **Fig. 1** Cadaveric dissection identifying a single, unilateral multiple renal artery arising from the
496 aorta and supplying the lower pole of the left kidney

497

498 **Fig. 2** Arterial phase coronal maximum intensity projection (MIP) computed tomography (CT)
499 image demonstrating bilateral multiple arteries. Both multiple vessels originate from the aorta,
500 supplying the superior pole of the left kidney and hilum of the right kidney

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502 **TABLES**

503

504 **Table 1.** Renal artery variations in left and right-sided kidneys.

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	CT	Cadaveric	Total
LEFT KIDNEY			
Point of Origin	270	27	297
Aortic	270	27	297
Renal artery	3 (1.1%)	2 (7.4%)	5 (1.7%)
Point of Termination			
Superior Polar	3	5	8
Hilar	270	27	297
Single artery	255 (94.4%)	23 (85.2%)	278 (93.6%)
Two arteries	15 (5.6%)	4 (14.8%)	19 (6.4%)
Inferior Polar	5	5	10
RIGHT KIDNEY			
Point of Origin	272	25	297
Aortic	272	25	297
Renal artery	3 (1%)	0	3 (1%)
Common iliac artery	1 (0.4%)	0	1 (0.34%)
Point of Termination			
Superior Polar	8	8	16
Hilar	272	25	297
Single artery	256 (94%)	22 (88%)	278 (93.6%)
Two arteries	16 (5.9%)	3 (12%)	19 (6.4%)
Inferior Polar	4	2	6

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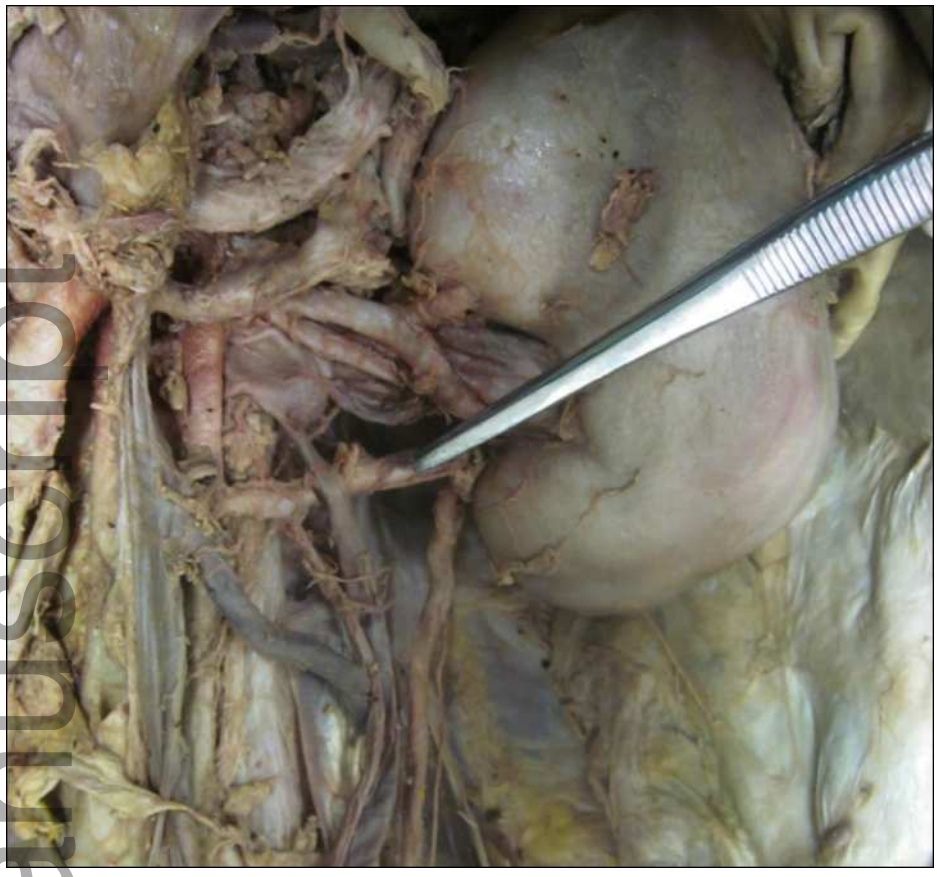
Table 2. Differences in the presentation of variations in renal arteries based on laterality (left vs. right), sex (female vs. male), symmetry (unilateral vs. bilateral) and data modality (CT vs. cadaveric) with an alpha value set at $p < 0.05$.

Variable	Number of Variations	p-value
Laterality		
Left-sided	37/297 (12.5%)	0.627
Right-sided	41/297 (13.8%)	
Sex		
Female	25/164 (15.2%)	0.011*
Male	37/136 (27.2%)	
Symmetry		
Unilateral	49/294 (16.7%)	< 0.001*
Bilateral	10/294 (3.4%)	
Data Modality		
CT	53/272 (19.5%)	0.001*
Cadaveric	13/28 (46.4%)	



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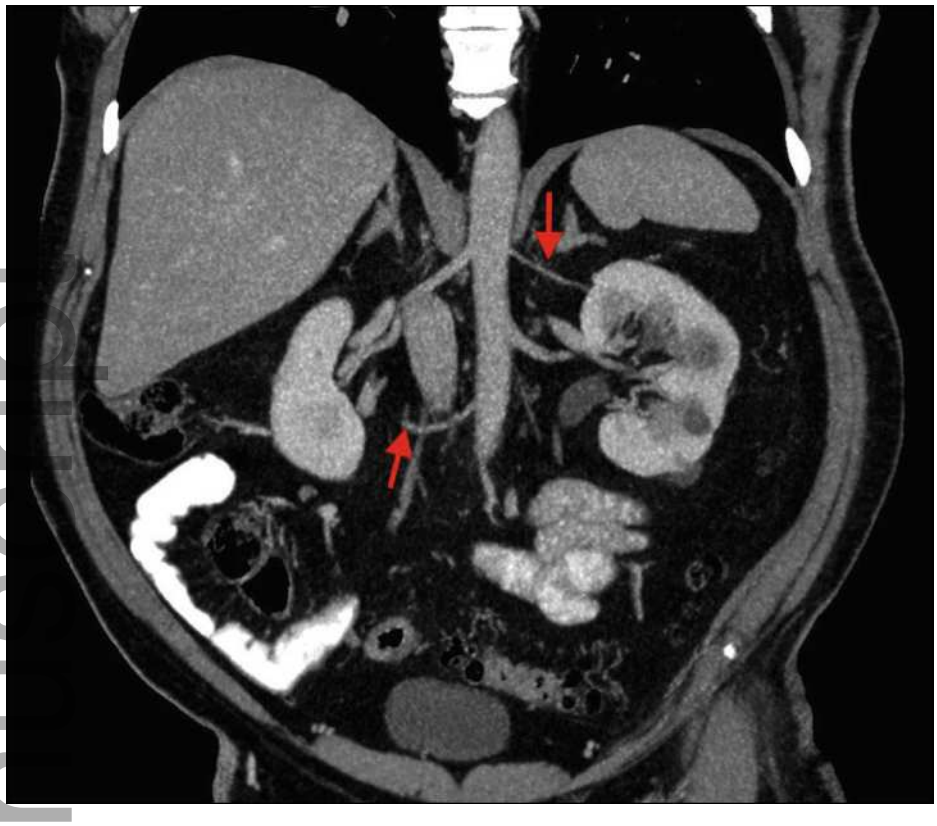

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