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Nephrometry Scoring System Selects Candidates for Radical Nephrectomy versus Nephron Sparing Surgery for Treatment of Renal Masses and Predicts Surgical and Oncological Outcome

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What is already known on this subject

RENAL nephrometry score was one of the first scoring systems created to provide a standardized descriptive system for renal masses based on radiologic findings which are; (Radius, Exophytic or endophytic, Nearness to the collecting system, Anterior or posterior and Location to renal poles). The main target of this scoring system was to put comparative studies between operative results and to give useful standard data of the tumour. However, the prediction of the tumour biology is still debatable.

What does this study add

1) Comparing Application of the Scoring System Preoperatively on CT films and postoperatively on the Specimen to Confirm Accuracy.
2) Cystic Renal Masses Candidate For Surgery Will Be Included.

What may be studied in the future

- Application of RENAL system on multicentric renal tumours.
- Role of the RENAL system in cytoreduction nephron sparing surgeries in metastatic renal tumours.

1. INTRODUCTION/ REVIEW

Currently, prevalence of renal masses increased due to modern technologies and advances of imaging modalities, so, the classic triad of pain, hematuria and palpable renal mass is not present except in advanced cases.(1)
There are multiple treatment options for managing patients with renal cell carcinoma (RCC), particularly for those with a small renal mass. Surgical removal is the gold standard for treatment of localized RCC.(2,3)
Nephron-sparing surgery has become an established surgical treatment for patients with renal tumors, particularly in situations in which preservation of renal parenchyma is critical as in patients having single functioning kidney and bilateral synchronous pathology.(2,3)

Decisions for treatment of renal tumors depend on description of tumor anatomy and the experience of the surgeon. So Alexander Kutikov and Robert G. Uzzo have described the R.E.N.A.L. Nephrometry scoring system in 2009.(7)

RENAL nephrometry score which was one of the first scoring systems originally created with the intention of providing a standardized descriptive system for renal masses based on radiologic findings. The premier and the main target of these nephrometry scoring systems was not to settle down a comparative studies between operative results only, but also to give very useful standard anatomical data of the tumor. However, the value of prediction of the tumor biology still under debate.(7-9)

The element of standardization in R.E.N.A.L. Nephrometry Score comes from the fact that this system depends in its work on the tumor anatomical features as Radius, Exo/Endophytic, Nearness of the tumor the collecting system, Location of the tumor to renal poles and being anterior or posterior.(7)
The R.E.N.A.L. Nephrometry Score consists of (R)adius (tumor size as maximal diameter), (E)xophytic/endophytic properties of the tumor, (N)earness of tumor deepest portion to the collecting system or sinus, (A)nterior (a)/posterior (p) descriptor and the (L)ocation relative to the polar line. The suffix h (hilar) is assigned to tumors that are in contact to main renal artery or vein.(7-9)

Application of R.E.N.A.L. nephrometry scoring preoperatively may be used as a guide to the complexity and choice of surgery in patients with solid and cystic renal masses. It also serves as a tool for patient counselling, with reference to postoperative outcomes.(10,11)
Widespread use of this score may act as communication tools among specialists, such that direct comparisons of data and study results can be achieved.(10_13)

2. AIM/ OBJECTIVES

In that study, we use the RENAL scoring system to assess its predictive value to select candidates for radical nephrectomy versus nephron sparing surgery and approach (open vs minimally invasive).
Evaluation of the surgical complications including intraoperative and postoperative complications.
Pathology result including type of the tumor and its grade, safety margins will be included.
Oncological outcome as cancer specific survival, overall survival, local recurrence and distant metastasis will be an important aim of this study.
Asses the sensitivity of application of the RENAL system on cystic renal lesions.

3. RENAL VASCULAR ANATOMY

Surprisingly, the right (diagram 1 and 3/a) and left (diagram 2 and 4/a) renal arteries feed the right and left kidneys respectively with about 20 % of the total cardiac output. They are originated from each side of the abdominal aorta at the level of the first lumbar vertebra just below the superior mesenteric artery. The right renal artery is slightly more cranial and longer than the left artery. Both right and left renal arteries are divided into the dorsal and ventral branches before reaching the renal hilum.
At a distance of 1 to 1.4 cm away from the right renal hilum, the right renal artery is divided into the dorsal and ventral branches, As regards the left renal artery, the distance will range from 1.3 to 1.7 cm. The right dorsal artery (diagrams 1/b and 3/f) will be divided into three to five interlobar arteries (diagrams 1/c and 3/g) while the right ventral artery (diagrams 1/f and 3/b) divides into four to six interlobar arteries (diagrams 1/g and 3/c). (
Three to six is the count range of the sub branches of the left dorsal branch (diagram 2/b), on the other hand, the left ventral (diagram 4/b) gives out three to four interlobar branches (diagram 4/c).
(Diagram 3/j) shows a third branch rising from the connection between the dorsal and ventral arterial branches, feeding the posterior surface of the kidney. On the other hand, (Diagram 2/f) illustrates the presence of an interlobar artery feeding the anterior surface of the kidney,
All the interlobar arteries then get branched to arcuate arteries (diagrams 1–4/d, 1 and 3/h). From which the interlobular arteries are sub branched (diagrams 1–4/e, 1 and 3/i) feeding whole renal surface. It is to be noted that there is no anastomosis between any of the sub branches of the renal arteries.

A detailed understanding of surgical anatomy is essential to minimize the risk of complications and to maximize perioperative and functional outcomes of partial nephrectomy (PN). In 1901, Max Breodel described the subdivision of the main renal artery into four to five branches, the distribution of which is such that three-quarters of the blood supply is carried anteriorly, while one-quarter runs posteriorly.

Interestingly, in his original study on intrinsic blood vessels of the kidney and their significance in nephrotomy, Breodel defined the renal arteries as end vessels in the strictest meaning of the word, with the anterior segments never crossing over to the posterior side, or vice versa. He strongly highlighted that renal arterial vessels do not anastomose with each other [1].

Subsequent anatomical acquisition supported the hypothesis that each segmental artery supplies a distinct portion of the kidney, confirming the absence of collateral arterial blood supply between the different segments. According to the classic Graves description, the renal parenchyma is subdivided into five segments (apical, upper, middle, lower and posterior), each supplied by its own branch originating from the main renal artery [2,3].
More recent radiological studies have described the presence of so-called pre-segmental arteries originating between the main artery and the segmental branches [4,5].

Interestingly from the surgical point of view, beyond the main renal artery also the posterior and anterior branches show frequently an extraparenchymal tract at the level of the renal hilum [6]. Imaging studies have shown that angio-CT can be used to visualize the renal arterial vasculature, often including the artery or arteries leading to the parenchymal tumour.

Obviously, a detailed knowledge of the classic anatomy of the renal arterial vasculature can play a significant role during both the excisional and the reconstructive steps of PN, improving peri-operative, functional and oncological outcomes (15-18).

Clamping the main renal artery provides the best surgical scenario, helping surgeons to perform the tumour resection and the closure of the parenchymal defect in an ideal bloodless field; however, prolonged ischaemia can be associated with long-term renal function impairment (15-18)
To minimize the effect of warm or cold ischaemia on renal parenchyma, some authors proposed selective clamping of the segmental artery leading to the tumours, preserving the blood flow at a level of the renal segments not involved in the disease [10]; however, the use of near-infrared fluorescence imaging with indocyanine green during robotassisted PN has frequently shown that selective clamping of the segmental arteries does not allow complete ischaemia of the tumour area (15-18). This could be attributable to the location of the tumour involving two or more renal segments or to segmental arterial branches supplying more than a single renal segment. This last hypothesis is not consistent with the classic descriptions of the renal vasculature by Breodel and Graves.

Considering the potential clinical implications of this, researchers performed an anatomical study of the arterial vasculature on the normal kidney of the human cadavers. them aims were: (i) to validate Graves' classification of the renal vasculature; (ii) to verify the absence of collateral arterial blood supply between different renal segments; and (iii) to measure the calibre of the different levels of arteries to predict the potential effect of available haemostasis devices. (15-18)

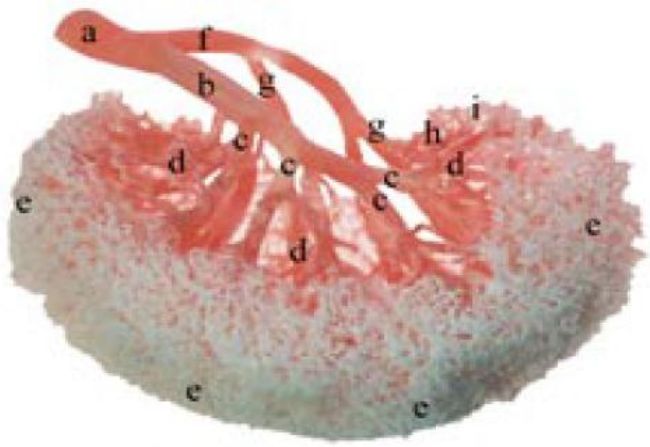

Diagram 1. Posterior view of the right renal artery. a = right renal artery, b = right dorsal branch, c = right dorsal interlobar artery, d = right dorsal arcuate artery, e = right dorsal interlobular artery, f = right ventral branch, g = right ventral interlobar artery, h = right ventral arcuate artery, i = right ventral interlobular artery.

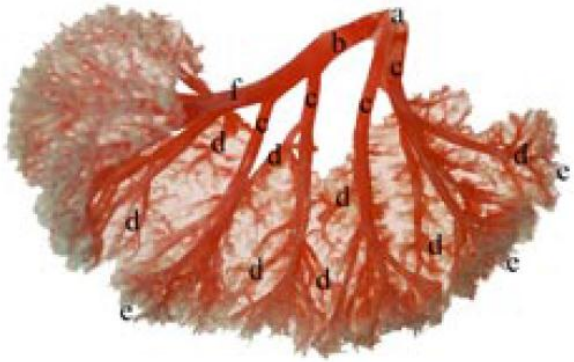

Diagram 2. Posterir view of the left renal artery. a = left renal artery, b = left dorsal branch, c = left dorsal interlobar artery, d = left dorsal arcuate artery, e = left dorsal interlobular artery, f = the interlobar artery coming from the dorsal branch and feeding the anterior surface of the kidney.

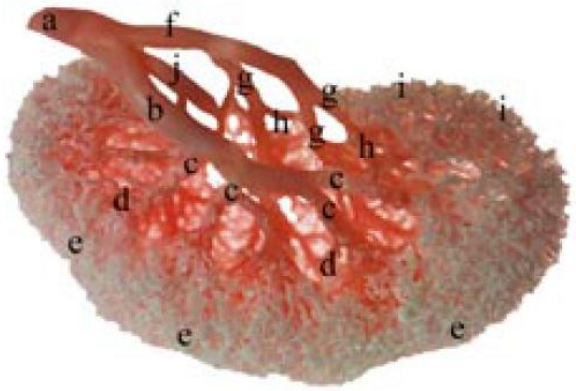

Diagram 3. Anterior view of the right renal artery. a = right renal artery, b = right ventral branch, c = right ventral interlobar artery, d = right ventral arcuate artery, e = right ventral interlobular artery, f = right dorsal branch, g = right dorsal interlobar artery, h = right dorsal arcuate artery, i = right dorsal interlobular artery, j = the third branch coming from the connection between the dorsal and ventral branches.

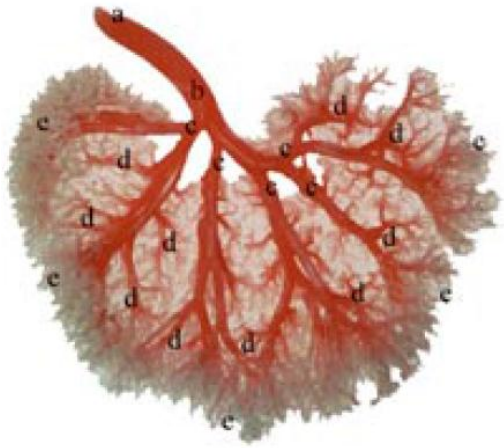

Diagram 4. Anterior view of the left renal artery. a = left renal artery, b = left ventral branch, c = left ventral interlobar artery, d = left ventral arcuate artery, e = left ventral interlobular artery.

Depending on the previously illustrated blood supply of the kidney, the parenchyma of the kidney is anatomically subdivided into five segments as shown in diagram 5.
Apical, upper, middle, lower and posterior are the five renal segments.
The upper, middle and lower segments are generally supplied with the anterior branch of the renal artery.
The posterior and sometimes the lower segments are supplied with the posterior division of the renal artery.
Interestingly, The artery to the apical segment has variant origins, it may arise from the anterior division of the renal artery in 43% of cases, from the junction between the anterior and posterior divisions in 23% of cases, from the renal artery itself or even the aorta in 23% of cases or from the posterior division of the renal artery in 10% of cases. (15-18)

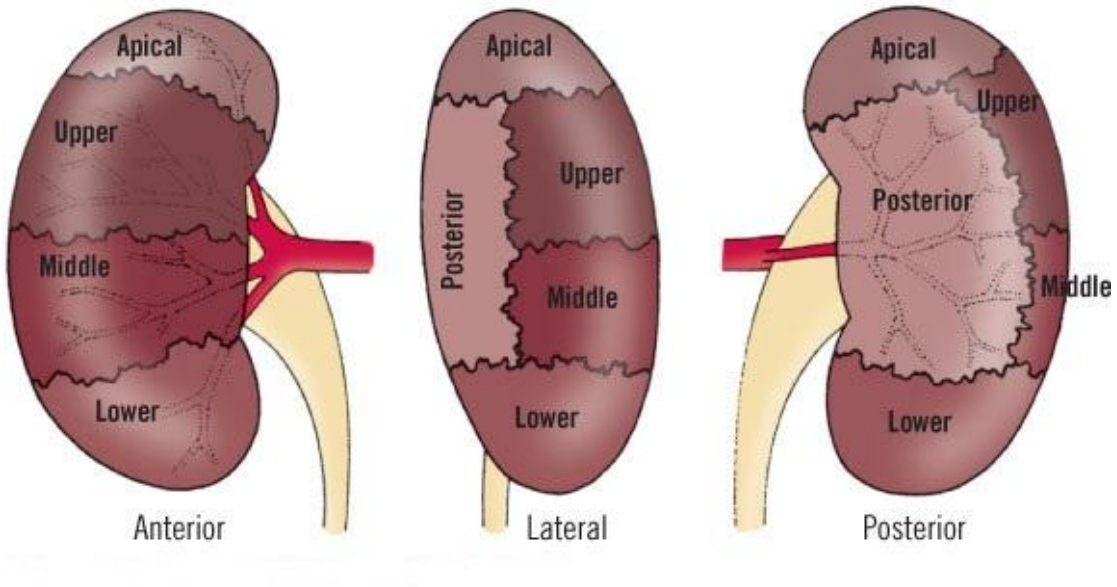

Diagram 5. The segments of the renal parenchyma.(16)

4. Renal cell carcinoma

Renal cell carcinoma (RCC) shows 2-3% of all known malignancies, especially in Western countries. During the last twenty years, the incidence of RCC reached about 4-5% all-over the world. The peak of death rates from RCC was reached in the early 1990s, and then stay as it is or decreased. Male to female ratio of RCC incidence is 1.5:1, with a peak occurrence by the age of 60 and 70 years.
Many risk factors leading to RCC include smoking, obesity and hypertension. Having a first-degree relative with RCC also increases the risk of RCC [27-30].

A number of other factors associated with higher or lower RCC-risk include specific dietary habits, occupational specific carcinogens, acetaminophen and non-aspirin non-steroidal anti-inflammatory drugs, cruciferous vegetables, nephrolithiasis, and viral hepatitis. Effective prophylaxis includes stop cigarette smoking and loosing over weight [29, 30].

The number of incidentally discovered RCCs has increased, thanks to development in diagnostic imaging, especially, Computed tomography (CT) and Ultrasound (U/S). Fortunately, these accidently discovered tumours are usually smaller and of lower stage [31-34].
Histological diagnosis of RCC comprise a broad spectrum of histopathological entities described in the 2016 World Health Organization (WHO) classification [35, 36].
There are three main RCC types: clear cell (ccRCC), papillary (pRCC - type I and II) and chromophobe (chRCC).
The RCC type classification has been confirmed by cytogenetic and genetic analyses [35, 36].
Histological diagnosis includes, besides RCC type; evaluation of nuclear grade, sarcomatoid features, vascular invasion, tumour necrosis, and invasion of the collecting system and peri-renal fat. The WHO/ISUP (International Society of Urological Pathology) grading system has replaced the Fuhrman grading system [35, 36].

Clear cell renal cell cancer (ccRCC) is well circumscribed with a capsule is usually absent. The cut surface is golden-yellow with areas of haemorrhage and necrosis. Loss of chromosome 3p and mutation of the von Hippel-Lindau (VHL) gene at chromosome 3p25 are frequently found, including additional tumour suppressor genes including SETD2, BAP1, and PBRM1; all genes are identified near the VHL gene within a region that is frequently deleted in ccRCC [37].

In general, ccRCC has a worse prognosis compared to pRCC and chRCC [38, 39] even after stratification for stage and grade [40]. The five-year cancer-specific-survival (CSS) rate was 91%, 74%, 67% and 32% for TNM stages I, II, III and IV [41].

Papillary renal cell cancer (pRCC) is the second most commonly type found of RCC. Papillary RCC has traditionally been subdivided into two types [36].
Macroscopically, pRCC is well circumscribed with a pseudocapsule, yellow or brown in colour, and a soft structure. Compared to ccRCC, pRCC has a significantly higher rate of organ-confined tumour (pT1-2N0M0) and a higher five-year CSS rate [43].
Papillary RCC type 1 is more common and generally considered to have a better prognosis than pRCC type 2 [36, 44].

Exophytic spherical growth, pseudo-necrotic changes and pseudo-capsule are typical signs of pRCC type 1. Tumours are fragile. On post-contrast CT, a hypodense central area of tumour surrounded by vital tumour tissue is seen, presented as a serpiginous contrast-enhancing margin on CT [45].

Chromophobe (chRCC) is a pale tan, relatively homogenous and tough, well-demarcated mass without a capsule. Chromophobe RCC cannot be graded (by the Fuhrman grading system), because of its innate nuclear atypia. [35, 36].
Loss of chromosomes Y, 1, 2, 6, 10, 13, 17 and 21 are typical genetic changes [35, 36].
The prognosis is relatively good, with high five-year recurrence-free survival (RFS), and ten-year CSS [46].

Other renal tumours constitute the remaining 10-15% of renal cortical tumours. These include a variety of uncommon, sporadic, and familial carcinomas, some only recently described, as well as a group of unclassified carcinomas. Carcinoma associated with end-stage renal disease; acquired cystic disease-associated RCC Cystic degenerative changes (acquired cystic kidney disease [ACKD]) and a higher incidence of RCC are typical features of ESKD (end-stage kidney disease).
Renal cell cancers of native end-stage kidneys are found in about 4% of patients. Their lifetime risk of developing RCCs is at least ten times higher than in the general population. Compared with sporadic RCCs, RCCs associated with ESKD are generally multicentric and bilateral, found in younger patients (mostly male), and are less aggressive [45, 50].

Although the histological spectrum of ESKD tumours is similar to that of sporadic RCC, the predominant form is pRCC. The remaining tumours are mostly ccRCC [45-50].
A specific subtype of RCC occurring only in end-stage kidneys has been described as Acquired Cystic Disease associated RCC (ACD-RCC) with indolent clinical behaviour, likely due to early detection in patients with ESKD on periodic follow-up
Five to eight percent of RCC is hereditary; to date there are ten hereditary RCC syndromes known, associated with specific germline mutations, RCC histology, and comorbidities. Hereditary RCC syndromes are often suggested by family history, age of onset and presence of other lesions typical for the respective syndromes. Median age for hereditary RCC is 37 years; 70% of hereditary RCC tumours are found in the lowest decile (< 46 years old) of all RCC tumours [47_50].

Hereditary kidney tumours are found in the following entities: VHL syndrome, hereditary pRCC, Birt-Hogg-Dubé syndrome (see Hybrid oncocytoma-chromophobe carcinoma), hereditary leiomyomatosis and RCC (HLRCC), tuberous sclerosis (TS), germline succinate dehydrogenase (SDH) mutation, non-polyposis colorectal cancer syndrome, hyperparathyroidism-jaw tumour syndrome, phosphatase and tensin homolog (PTEN) hamartoma syndrome (PHTS), constitutional chromosome 3 translocation, and familial nonsyndromic ccRCC. Renal medullary carcinoma can be included because of its association with hereditary haemoglobinopathies [48_50].

STAGING AND CLASSIFICATION SYSTEMS

Staging The Tumour Node Metastasis (TNM) classification system is recommended for clinical and scientific use, but requires continuous re-assessment with the latest version published in 2017. A supplement was published in 2012, and the latter's prognostic value was confirmed in single and multi-institution studies.
Tumour size, venous invasion, renal capsular invasion, adrenal involvement, and LN and distant metastasis are included in the TNM classification system.
However, some uncertainties remain:

• The sub-classification of T1 tumours using a cut-off of 4 cm might not be optimal in NSS for localised cancer.

• The value of size stratification of T2 tumours has been questioned
• Since the 2002 version, tumours with renal sinus fat invasion have been classified as pT3a.

• Renal sinus fat invasion might carry a worse prognosis than perinephric fat invasion but is nevertheless included in the same pT3a stage group

• Sub T-stages (pT2b, pT3a, pT3c and pT4) may overlap.

• For adequate M staging, accurate pre-operative imaging (chest and abdominal CT) should be performed [44, 50]