MODERN SYSTEM OF EVALUATION OF KIDNEY TUMOR (REVIEW)

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Summary. Radiologic evaluation of kidney tumors prior to nephron-sparing surgery is a complex and multifactorial process. New nephrometry scoring systems (PADUA, RENAL, C-index system and DAP nephrometry) have emerged recently that allow for systematic and quantitative assessment of kidney tumors. Nephrometry systems achieve two primary goals: methodological analysis of tumor location and standardization of reporting of tumor data. Secondary goals of nephrometry scoring are to predict success of partial nephrectomy, risk of postoperative complications, and functional and oncologic outcomes.Based on a literature review, the paper presents comparative characteristics of different tumor assessment systems, their advantages and disadvantages.

Keywords: renal cell carcinoma, nephrometry scoring systems, partial nephrectomy.

Surgical removal of the tumor is the “golden standard” of treatment the localized renal cell carcinoma, whereas surgical ablation and active surveillance is the therapy of choice for patients with significant co-morbidity [1].

At the same time, accuracy and clarity of description of the tumor affect, its relation to the structures of the kidney are required for final determination of algorithm of management a patient [2].

According to the final version of standard treatment of the European Association of Urology and the American Urological Association, it is recommended the organ preservation treatment (partial nephrectomy) with

single tumors up to 7 cm in diameter, if this is technically possible [3-4]. The randomized investigation of EORTC showed that after partial nephrectomy because of tumor of T1 stage were received the same cancer results as after radical nephrectomy [5].

Partial nephrectomy can maintain its function, reduce the risk of kidney failure and complications on the part of general health, thus ensuring good performance of overall survival in comparison with radical nephrectomy [6], but is characterized by a high frequency of surgical complications, including hemorrhage, urinary fistula and need of re-operation [7-10].

Peculiarities of the tumor that dictate us the possibility of partial nephrectomy are: diameter, pole location, depth ingrowth, relation to vascular pedicle and hollow system of kidney. Traditionally, surgeons subjectively evaluate possibilities of partial nephrectomy [11].

Affects, which one doctor deems inappropriate for aggressive tactics or even impossible for partial nephrectomy because of its central, endophytic or at the gate location, can be a standard of organ preservation treatment for another doctor [12].

Assessment of renal tumors with the help of radiological method of diagnosis is complex and multifactorial process. New evaluation systems, that were developed recently, can obtain systematic and quantitative assessment of tumor affect of the kidney. Nephrometric evaluation system has two main objectives: primary – methodological analysis of localization the tumor and standardization of data reporting, secondary – definition of success of partial nephrectomy, risk of postoperative complications, and functional and oncological results. Tumor size may limit the indications for partial nephrectomy due to tumor mass and germination in the basic structure of the kidney. The degree of tumor ingrowth has significant effect on the time of ischemia, which is associated with a longer period of tumor removal,

reconstruction of the hollow system, and the frequency of postoperative complications [13-22].

Comparison of tumors with the help of different systems of evaluation differs one from another. Currently are registered nephrometric scoring systems P.A.D.U.A, R.E.N.A.L, system C-index and D-A-P nephrometry, which have advantages and disadvantages, thus it is appropriate to consider separately each of them.

European urologists Ficarra et al. [23] proposed a system for describing tumor of the kidney – PADUA (Preoperative Aspects and Dimensions Used for an Anatomical score).

Assessment of tumor according PADUA – simple anatomical system that combines the most important features of location of the tumor and its relation to the most important structures of kidneys, which allows us to predict the risk of postoperative complications in patients in the risk group undergoing partial nephrectomy.

According to this system, the separation of the tumor is based on five anatomical areas: the tumor is localized to anterior or posterior surface, location (end of kidney and pole), attitude towards both pelvis and to hollow of the kidney, percentage of tumor that grows in the kidney and its maximum diameter (in centimeters).

Anterior or posterior surface of tumor location is determined according to coverage of the kidney with front or rear leaf of renal fascia and is denoted by the letter A (anterior) or P (posterior) (Fig. 1).

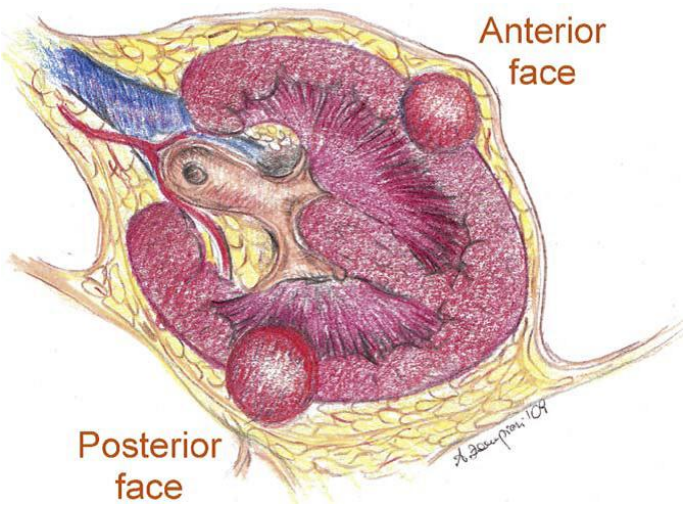


Fig. 1. Definition of anterior and posterior face of the kidney

Polarity of the tumor location indicates its relationship to interpolar area of the kidney, which is defined on images of computed tomography (CT) with axial lines that held perpendicular to the vertical axis of the kidney in the upper and lower pole on the edge of the concentric renal parenchyma, where it is interrupted and passes into adipose tissue or blood vessels (Fig. 2a). Renal sinus appears on CT images in capacity of hypodense area against the background of renal parenchyma. Sinus lines – easily recognizable landmark on CT slices, but they can also be traced on coronary images of magnetic resonance imaging (MRI). One point is given to the tumor if it is located outside interpolar corridor, or less than 50% is in interpolar area, and 2 points – if 50% or more is in interpolar area.

If the tumor is located on the lateral edge, it is assigned a score of 1, if on the medial - 2 points (Fig. 2b).

Relation of tumor to pelvis – another parameter of classification. 1 point is given in case of absence in the tumor process of renal pelvis, and 2 points – while bringing it into the process (Fig. 2c).

The same applies to hollow system of the kidney: 1 point – during the absence of symptoms of involvement in the tumor process, and 2 points – while bringing it into the tumor process (Fig. 2d).

In terms of depth of tumor lesion – 1 point is given to the tumor, which 50% or more has exophytic growth, 2 points – less than 50% exophytic, and 3 points – when fully endophytic tumor (Fig. 2e).

And, finally, evaluation of tumor size according to its maximum diameter: 1 point – if the tumor size ≤ 4 cm, 2 points – size 4,1 - 7 cm, and 3 points – larger than 7 cm (Fig. 2f).

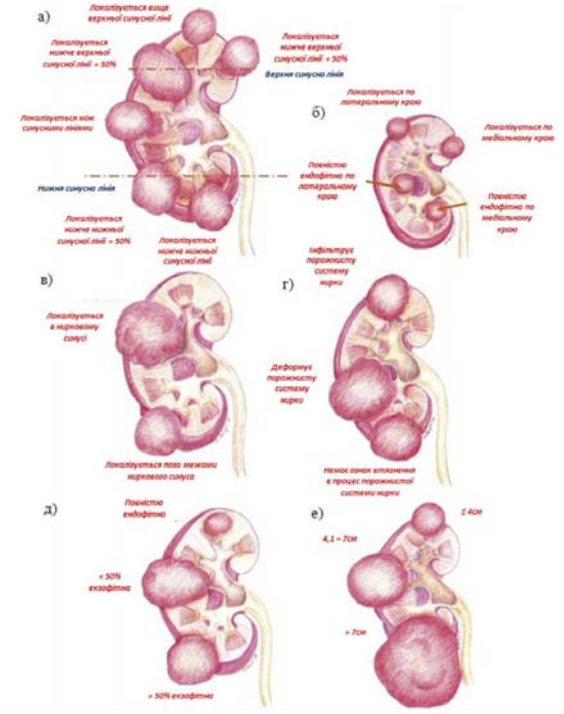


Fig. 2. (a) Longitudinal classification of the tumours; (b) margin location of the tumours; (c) tumour relationship with renal sinus; (d) tumour relationship with urinary collecting system; (e) tumour deepening into the parenchyma; (f) tumour size classification

Outcome assessment in accordance with the system of P.A.D.U.A – index of the sum of all points. This assessment was designed to be an independent predictor of postoperative complications of partial nephrectomy. The level of complications statistically was correlated with the relation of tumor to interpolar area ($p = 0.01$), localization according to the edge of the kidney ($p = 0.005$), attitude toward the hollow system of the kidney or pelvis ($p < 0.001$) and depth of tumor lesion ($p = 0.002$). In contrast, clinically tumor size and interior or

posterior location were not statistically significant predictors for the development of complications ($p = 0.32$ and $p = 0.62$ consequently).

According to this system of evaluation, there are three groups of patients regarding the risk of complications. Fikarra et al. reported that the amount of points more than 8 correlates with increase of complications in case of open partial nephrectomy from 2 to 40%. The risk of complications increases to 14.5% for tumors with P.A.D.U.A 8 - 9 points and 30.6% – for tumors of 10 points or more.

Another anatomical system was developed by American scientists [12], which is a structured, quantitative evaluation system for describing and classifying the most surgically relevant anatomical features of solid renal tumors. An alternative system is called R.E.N.A.L nephrometry score, which is based on the basis of 5 the most important features characterizing renal tumor that can fit for partial nephrectomy.

Each feature of the tumor is designated by the letter of English alphabet, forming an acronym R.E.N.A.L: (R) radius (maximum diameter of the tumor), (E) exophytic / endophytic properties of the tumor, (N) proximity (distance of the nearest edge of the tumor to hollow system of kidney or pelvis, (A) placement (anterior (A) or posterior (P) surfaces), (L) localization (reference to polar lines.) Four of the five components (RENAL) are rated according to the scale from 1 to 3 points. The 5^{th} factor (A) is a suffix that describes what mass of the tumor is mainly located on anterior (A) or posterior (P) surface with relation to the frontal plane of the kidney. Suffix “X” is assigned if the ratio of the tumor to anterior or posterior surface cannot be determined. Additional suffix “H” is used to indicate the location of the tumor at the gate of kidney.

The main feature of the tumor of kidney, according to which most clinicians determine difficulty – is the size of the tumor. This is the most essential characteristic of X-ray examination, which is variable in each case. As part of the system R.E.N.A.L. – (R) radius is measured as the maximum

diameter (in cm.) of the tumor in any plane. According to the TNM classification in 2002, and according to this system of assessment, a score of 1 was allocated to the tumor, which has a diameter of 4 cm or less, 2 points – to the tumor greater than 4 but less than 7 cm, and 3 points – to the tumor with a diameter of 7 cm or more. It is important to emphasize that the largest diameter of the tumor cannot be determined only on the axial sections, coronal and sagittal sections must also be evaluated when determining this feature.

The second variable, that determines the respectability of the tumor, is exophytic or endophytic properties. With more exophytic tumor it is usually easier to perform resection with or without renal ischemia. For quantitative characteristic of this variable tumor of the kidney in R.E.N.A.L system to the tumor, which has 50% or more exophytic pattern of growth, assign 1 point, to the tumor that has less than 50% exophytic growth – 2 points, and completely endophytic (surrounded 360° by renal parenchyma) – 3 points. It is important to note that while, in most cases, tumors have a spherical shape and are arranged symmetrically in kidneys, others – are non-spherically and / or asymmetrically located. If the tumor of kidney distorts normal cortical circuit layer, for ideal quantitative assessment of this variable and for determining the percentage of exophytic is necessary to compare the distance from the apparent edge of the normal surface of kidney to the most endophytic edge of the tumor, i.e. the distance to the most exophytic component (Fig. 3).

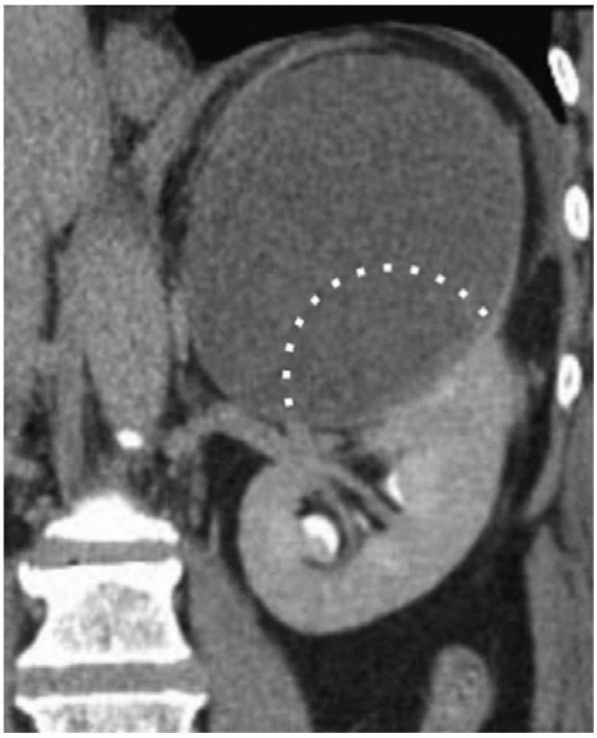


Fig. 3. Broken line demonstrates how expected renal contour is estimated for determination of (E)xophytic/endophytic attribute of R.E.N.A.L. score

The third variable of renal tumors, that is often qualitatively described, is proximity to the pelvis or hollow system of the kidney. As part of the R.E.N.A.L system, in fact, it is the deepest part of the tumor that is relevant in assessing resectability and the need for complex reconstruction of the hollow system. For quantitative assessment of this feature, tumors 7mm or more from the nearest part of the pelvis or the hollow system get 1 point, those that are at a distance of 4 to 7 mm – 2 points, tumors that grow more than or within 4 mm or less from the hollow system or pelvis – 3 points. The value of 4 and 7 mm were used for ease of calculation, similar to the assessment (R) of tumor size.

Anterior or posterior location of renal tumor – the fourth feature of surgical variable. This is particularly important in the choice of surgical approach to the kidney with open surgery (lumbotomical, tranabdominal medial, subcostal, thoracoabdominal), laparoscopic or robotic (transperitoneal, retroperitoneal) or percutaneous ablation.

This variable may be less important in quantitative form as part of the RENAL score, anterior / posterior locations of the tumor are indicated by nonnumeric suffixes that describe whether the tumor is situated primarily on the anterior or posterior surface of the kidney according to the frontal plane. This feature is the best assessed on axial images using conventionally drawn line, drawn parallel to the intrarenal structures that divide in two renal parenchyma, as shown in Fig. 4.

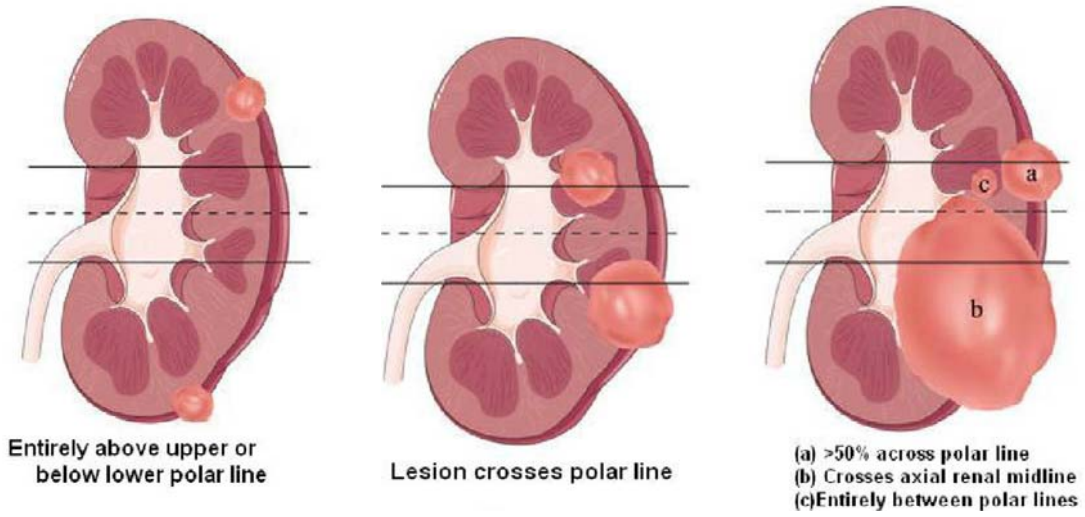
Fig.4. Line drawn to divide kidney for anterior and posterior designations

When the tumor arises from the kidney so that anterior or posterior its location cannot be determined, it is assigned the suffix “X”. It is important to note that the A / P suffix is used at the end of nephrometrical sum (i.e. 9A – the tumor with the sum of points 9 on the anterior surface).

The last feature is determination of relationship of the tumor to the surgical anatomy of the kidney (upper, middle or lower segment). This system evaluates the ratio of the tumor to polar lines. Polar lines of the kidney are on edges of medial lip where renal parenchyma continues in the renal fat of sinuses, blood vessels or hollow system. Polar lines are the best seen in the frontal plane (Fig. 5).

Fig. 5. Scoring of (L)ocation component of R.E.N.A.L. – NS determined in relation to upper or lower polar line.

The tumor that is situated completely over the upper polar line or below the lower polar line is assigned a score of 1 (Fig. 6a). If the polar line partially intersects the tumor – 2 points (Fig. 6b). The tumor, which more than 50% of its diameter is in interpolar area or entirely in it, is assigned 3 points (Fig. 6c).



a b c

Fig. 6. Polar lines (solid lines) and axial renal midline (broken line) are depicted on each sagittal view of kidney.

Overall evaluation R.E.N.A.L nephrometry score system is given in Table 1.

Table. 1. R.E.N.A.L. Nephrometry Score with scoring of (L)ocation component.

	1pt	2pts	3 pts
(R)adius (maximal diameter in cm)	≤4	>4 but < 7	≥ 7
(E)xophytic/endophytic properties	≥ 50%	<50%	Entirely endophytic
(N)earness of the tumor to the collecting system or sinus (mm)	≥7	>4 but <7	≤4
(A)nterior/Posterior	No points given. Mass assigned a descriptor of a, p, or x		
(L)ocation relative to the polar lines* * **suffix "h" assigned if the tumor touches the main renal artery or vein**	Entirely above the upper or below the lower polar line	Lesion crosses polar line	>50% of mass is across polar line (a) or mass crosses the axial renal midline (b) or mass is entirely between the polar lines (c)

Regarding the location of the tumor in the gate of kidney, that is important, as part of evaluation system of nephrometry only to tumors related to the main renal artery or vein, add the suffix "H" (Hilar) to (L) component.

Tumors that received the sum under the R.E.N.A.L system from 4 to 6 points belong to low degree, from 7 to 9 – medium and 10 to 12 –high degree of complexity of partial nephrectomy, respectively, with the addition of suffixes according to the location relative to the surface and gates of kidney.

For example, if there is a tumor up to 4 cm, more than 50% of exophytic nature of growth, in the lateral edge (distance to the hollow system is more than 7 mm), on the anterior surface, in the upper segment of the kidney, then the sum will look like (1+1+1+A+1=4A).

If to make a comparative analysis, the P.A.D.U.A system estimates the ratio of tumor to renal pelvis and to hollow system of the kidney as two independent factors. Germination in hollow system of the kidney can assume making the special reconstruction. The proximity to the renal pelvis is usually

associated with an increased risk of ligation of major vascular of kidney and a big injury of kidney. The R.E.N.A.L. system involves determining the distance to the hollow system of the kidney or to renal pelvis as one factor. In this regard, the system attaches less importance to the proximity of the tumor to kidney structures overall. For example the value of proximity of tumors from 4 to 7mm are designed for ease of evaluation (they reflect the criteria of TNM size), and not for evidence that these distances can affect the success of partial nephrectomy. Both systems do not take into account the specific location of the tumor, which may directly affect the efficiency of resection.

One of the most important features of the tumor of kidney is medial / lateral location. This feature can only dictate the possibility for making partial nephrectomy because medially located tumors can be very difficult for resection. Anterior / posterior located tumors may also limit the indications for resection, especially for laparoscopic. It is necessary to conduct further studies to show how assessment of the tumor by these systems correlates with successful partial nephrectomy.

Another difference between R.E.N.A.L. and P.A.D.U.A. systems is in determining the interpolar area. In the R.E.N.A.L. system interpolar area is bounded by cortical layer on the medial surface of the kidney. Renal sinus may extend up to 1-2 cm from this level. The P.A.D.U.A. system determines interpolar area between lines passing through the upper and lower edges of the hollow system of the kidney. This difference is surgically important because anatomical distance of 1-2 cm from the gate of kidney can change the course of operation from partial nephrectomy to radical nephrectomy. Tumors that are in interpolar area according to R.E.N.A.L. system are less likely to their resection.

All systems of evaluation have advantages in terms of systematic characteristic of tumor features. R.E.N.A.L. system has advantages over P.A.D.U.A system in terms of the final point. Evaluation by R.E.N.A.L. system gives a detailed analysis of various features of the tumor. Evaluation by

P.A.D.U.A system is the sum of points and not separately detailed description. In this respect, it does not give optimal data that is under analysis [11].

Unfortunately, there is no single definition of important anatomical features. For example, centrally located tumor was defined as completely surrounded by normal renal parenchyma [24], at least 60% endophytic [25], which spread into renal sinus [26], situated less than 5 mm from the hollow system or related to it or pelvis of the kidney. In this regard were developed two new evaluation systems which provide a quantitative description of the central tumor based on two-dimensional cross-sectional images of computed tomography (CT).

The system of evaluation of tumor C-index was registered in 2010 by Simmons and others [27]. C-index provides an evaluation based on determination of diameter of the tumor and its distance from the edge to the center of the kidney. Method of evaluation C-index allows the use of standard 2D computed tomography in cross sections and can be calculated easily using standard database software with automated calculations [11].

Evaluation of C-index begins with determination of size of the kidney in transverse and longitudinal direction. Calculate the middle of the kidney. The next step is to determine the size of the tumor in its largest diameter and its center. Then the distance from the center of the tumor to the center of the kidney (index “c”) is determined according to lines drawn perpendicular to each other, using the Pythagorean Theorem. Finally, the distance “c” is divided by the radius of the tumor and thus is calculated C-index (Fig. 7).

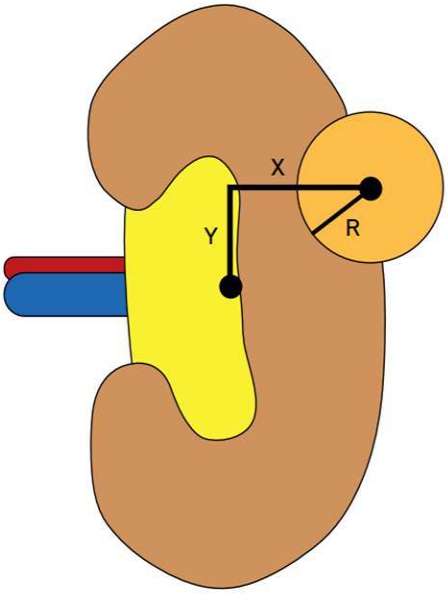


Fig. 7. C-index measures vertical (y) and horizontal (x) distance and tumor radius (R).

The methodology of mathematical calculation of C-index allows determining properties of location of the tumor. If the C-index = 0, then the tumor is located directly in the center of the kidney. If the C-index = 1, the tumor with its edge is adjacent to its center. Tumors, in which the C-index is greater than 1, are located far from the center of the kidney.

Indicator of C-index depends on the diameter of the tumor and its distance from the center of the kidney. For example, if two tumors with the largest diameter of 2 and 4 cm, the edge of which is just 2 cm from the center of the kidney, one would expect that the larger the tumor was, the higher the risks involved in removing than with smaller tumors, and therefore have a lower value of C-index. This can be explained mathematically: C-index tumor, diameter 2 cm is equal to 3 (“c” = 3 cm, radius = 1 cm), C-index tumor, diameter 4 cm is equal to 2 (“c” = 4 cm, radius = 2 cm).

C-index correlates with the frequency of postoperative complications of partial nephrectomy, which was confirmed in multivariate analysis [20]. It can also improve functional results, as it was shown that on the decrease in

glomerular filtration rate after laparoscopic resection of the kidney affected the tumor diameter and C-index. Upon further analysis, only C-index, and not the size of the tumor, involved the decline of the kidney function. Since the measure of C-index of 2,5 and less, in 2,2 times increased the risk of functional impairment for more than 30%.

It is difficult to directly compare the C-index with other evaluation systems, as they are fundamentally different. C-index shows a single point based solely on the tumor size and the depth of invasion into the kidney. C-index does not provide the description of spatial data about the location of the tumor and, therefore, is limited concerning comparison with nephrectomic systems. The main purpose of C-index is to provide information about the proximity of the tumor to the center of the kidney.

Another evaluation system, proposed by Simmons et al [28] in 2012, is "Diameter-Axial-Polar Nephrometry".

Methodology of D-A-P Nephrometry is that all measurements are carried out manually on axial slices of contrast computer tomography. It is performed by 4 steps:

1) measure the tumor size in its largest diameter. Tumors up to 2.4 cm are assigned 1 point, from 2.4 to 4.4 cm – 2 points, and more than 4.4 cm – 3 points;

2) measure the distance from the center of the kidney to the nearest edge of the tumor. If the distance is more than 1.5 cm – is assigned 1 point, less than 1.5 cm – 2 points and 3 points if the tumor blocks the central part. If the distance from the edge of the tumor and the central point is in the range from 0 to 2 mm, such tumor is centrally located and is assigned 3 points.

3) measure the median plane by determining the length of the kidney from the upper to the lower edge. The sum is divided in two and is the median line. If the tumor is located further than 2cm from the line – is assigned 1 point, less than 2 cm – 2 points and 3 points – when the line passes through the tumor.

4) the final result of D-A-P is calculated by adding points for the diameter, relation to the axis of the kidney and the median plane (Fig. 8).

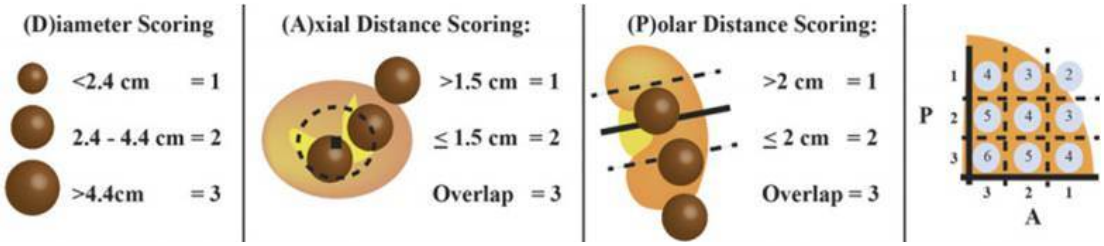


Fig. 8. DAP nephrometry scoring. Combined A and P scores indicate tumor location and centrality.

For example, the tumor 1 (axial) + 1 (polar) is localized away from the axial line of the kidney and the central plane, i.e. the superficial tumor is located at the pole of the kidney; the tumor 3 (axial) + 3 (polar) is localized on the axial line and the central plane of the kidney, i.e. the tumor is centrally located; the tumor 3 (axial) + 1 (polar) is localized on the axial line of the kidney, but away from the central plane, i.e. the tumor is on the axial line in the pole of the kidney. Example of measuring features of tumors location according to D-A-P nephrometry is shown in Fig. 9.

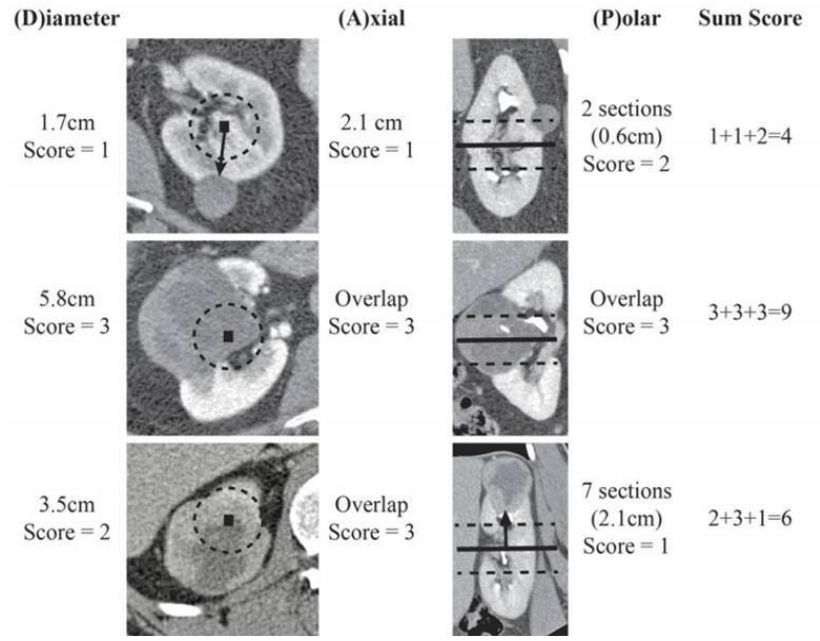


Fig. 9. DAP nephrometry scoring. 1.7 cm tumor 2.1 cm from axial reference point and 2 image sections (0.6 cm) superior to equatorial plane is

scored as 1 + 1 + 2 = 4. Tumor 5.8 cm overlapping axial reference point and in equatorial plane is scored as 3 + 3 + 3 = 9. Tumor 3.5 cm overlapping axial reference point and 7 image sections (2.1 cm) superior to equatorial plane is scored as 2 + 3 + 1 = 6.

In the investigation has been reliably shown correlation between preservation of renal parenchyma after resection, renal ischemia time and volume of blood loss during partial nephrectomy and all three parameters of evaluation of D-A-P system ($p < 0{,}001$), so it is a step forward in the development of optimized system of nephrectomy . In comparison with R.E.N.A.L. and C-index, D-A-P methodology is simpler and less volatile. Format of D-A-P evaluation is easier to interpret and intuitive to understand.

Conclusion. Surgeons in its arsenal have various ways of partial nephrectomy, based on their own experience and knowledge, but the results and complication rate may vary. Adding to calculation of average measures of nephrectomy for a particular cohort of patients will allow comparing data obtained by different researchers. Evaluation of nephrometric indicators can improve results of partial nephrectomy by predicting risk of occurrence of complications, assessment of functional and oncological results because they combine several characteristics of the tumor in one analysis. There are no investigations that would have analyzed the dependence of oncological results from the initial nephrometric indexes. TNM classification is the basis for predicting results, but it is possible that nephrometric indexes could provide additional information. In this connection evaluation systems would be useful for “sub-staging”, which will increase the accuracy of TNM classification. Also the use of nephrometric indexes will promote academic reporting, as this would allow the comparison of more similar groups. It is important to conduct both retrospective and prospective investigations to assess these possibilities [11].

Thus investigations that used nephrometric system of evaluation showed their feasibility, which allows objectively predict the risk of complications of partial nephrectomy. This assessment provides important information for planning of treatment, patient counseling and appropriate comparison of groups after partial nephrectomy. However, anatomic assessment should always be considered together with clinical data, patient characteristics and experience of the surgeon to choose the best treatment option for each patient [6, 29].

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