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The diagnostic value of ultrasound examination in cases of diagnostic kidney oligobiopsy in children

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Summary

Background: Biopsy is an invasive method of taking tissue samples which are estimated microscopically. Oligobiopsy is performed in adults and children in the course of renal diseases, both in diagnostic process and in evaluation of treatment results. More precise sampling is possible when a biopsy is performed under ultrasound guidance.

The aim of the study is to evaluate diagnostic effectiveness of renal ultrasound in cases of biopsies in children on the basis of analyses of histopathologic results, complications and learning curve assessed with relation to procedure duration.

Material/Methods: In the Radiology Department in Zabrze, renal ologobiopses were performed in 174 children from the Pediatric Department, 88 girls and 86 boys. The age ranged from 4 to 19 years, mean 12 years. The biopsies were performed under general anesthesia with an automatic "gun" under ultrasound guidance.

Results: Biopsy effectiveness was estimated after the diagnostic material was collected. Our material included 22 samples with less than 6 glomeruli (12.6%), only in 6 children (3.5%) the final diagnosis was not established (including 2 samples without tissue material). Minor complications accounted for 65.5% of all biopsies and major ones 3.4%. A statistic correlation between the procedure duration and the date of examination was found; no correlation between the date and the number of glomeruli in a sample was discovered.

Conclusions: The value of ultrasound examination in renal biopsy in children is very high. The percentage of complication is low, which makes the procedure safe. The biopsy duration depends on the examiner's experience, and the number of glomeruli on the degree of renal disease advancement.

Key words: ultrasound-guided biopsy • oligobiopsy • postbiopsy complications

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Background

The term *biopsy* itself originates from a Greek word βιοσ *(bios)* – the meaning of which is related to biological life and living organisms; now it means a special diagnostic procedure type. It is an invasive method of collecting biological material from pathologic tissues, which is then assessed morphologically by light microscopy (histological or cytological investigation) or under an electron microscope. The biological material obtained with this method can also be used for investigations other than morphological ones (e.g. virological, bacteriologi-

cal, biochemical, etc.). Various biopsy types can be distinguished:

- Fine needle aspiration biopsy (FNAB) – used for collection of cellular material (for cytology) with a fine needle of external diameter up to 1 mm (above 19 G), regarded as atraumatic. The cellular material is collected under the pressure in a syringe connected to the biopsy needle. FNAB is applied in cytological diagnostics of i.a. breast, lung and thyroid tumors.
- Thick needle biopsy (oligobiopsy) – is used for collection of cylindrical tissue specimens with a special cutting needle above 1 mm in diameter (below 19 G, usually 14 or 16 G, which corresponds to 1.62 and 1.29 mm, respectively). A tissue or organ specimen obtained in this way is subjected to histological assessment. The method is associated with complications described in the literature. It is used for detailed assessment of lesions, including tumors, as well as organs such as liver and kidneys.
- Section biopsy – involving collection of the histological material from the lesion or organ by open surgery.
- Drill biopsy – used in orthopedics. The biopsy material is obtained mechanically with special drills (trephines).
- Exfoliative and abrasive biopsy – used most frequently in skin diseases and in gynecology (endometrium specimens).

Except for FNAB (fine needle aspiration biopsy) where the collected material is assessed by cytopathological methods, the other biopsy types provide material for histological investigations. Historically, the term *biopsia* was introduced in 1879 by a French dermatologist Ernest H. Besnier as, in a sense, an opposite to *autopsia*, used to denote postmortem examination and examinations of cadaverous tissues. Collection of tissues from a living organism – biopsy – was introduced in the mid-19th century as a diagnostic procedure. Before that, pathologists had learned to assess microscopic images of tissues obtained from cadavers. Indeed, the examined tissues, both those collected by biopsy and obtained on autopsy, are in most cases no longer living tissues after special processing enabling to visualize their structure under the microscope [1–3].

Edward Stanley performed the first aspiration biopsy of the liver to exclude cancer in 1833, and Sir James Paget in 1853 gave a series of lectures concerning the use of aspiration biopsy in tumor diagnostics. The case of 1887, when Rudolph Virchow in Berlin diagnosed squamous epithelial carcinoma of the larynx (*Kasierkrebs*) in the crown prince, and then emperor Friedrich III, became famous.

Introduction of the microtome for cutting paraffin blocks led to further progress of histopathological investigations. In 1939 K. Rohlm and in 1943 P. Iversen used thick needle biopsy to investigate hepatic tumors. Such a method was initially applied in adults only to obtain kidney specimens. In children, because of smaller dimensions of the internal structures, surgical biopsies were generally performed. Only after the advent of ultrasound in the 1980's and development of US-guided kidney biopsy methodology for adults allowed to apply this technique in children [1,4,5]. However, because of potential complications, there are still too few centers in Poland using this method in children in everyday clinical practice. The method, acknowledged and commonly used in clinical nephrology, allows to determine the type of inflammatory lesions, their extent and severity, and, by repeated biopsies, the dynamics of the pathologic process in the kidneys. Oligobiopsy is now the leading method of obtaining material for histopathology, which is indispensable in nephrology for the diagnosis and assessment of the results of treatment. Providing exclusion of contraindications such as anticoagulant treatment and use of appropriate methodology (including general anesthesia in children), the procedure is safe, although it carries some risk. The following potential complications are distinguished:

- macroscopic hematuria persisting for over 72 hours;
- colic pains caused by the passage of thrombi through the ureters;
- ureteral obstruction by a thrombus;
- perirenal hematoma;
- arteriovenous shunt;
- renal infarction;
- damage to the ureter or the renal pelvic with urinary fistula;
- local or systemic infection;
- damage to the adjacent organs;
- paralytic ileus;
- pneumothorax.

According to various authors, macroscopic hematuria occurs in ca. 7% of cases and requires blood transfusions in 1.7% patients [3,5–7]. The reported biochemical abnormalities such as hyperuricemia, hypernatremia and hypokaliemia are usually transient and do not affect the prognosis. Surgical interventions, usually due to a perirenal hematoma or arteriovenous shunts, take place in 0.5% patients undergoing the biopsy. It is most frequently the result of material collection from the borderline between the cortex and medulla, or from the region of the renal capsule. The reports concerning complications indicate the necessity to abandon the so-called "freehand" biopsy practice and to replace it with US-guided procedures using an automatic needle. This method is much more precise and free of the described complications. It requires not only familiarity with ultrasound, but also expertise in the biopsy technique. Many authors emphasize that the procedure should be performed by one person [3,8–10].

The aim of the study was to estimate the diagnostic value of ultrasound in percutaneous diagnostic biopsy in children on the basis of analyses of histopathology results, number and type of complications and the learning curve assessed with relation to procedure (anesthesia) duration, number of effective biopsies (presence of diagnostic material) number of obtained renal glomeruli and complication rate.

Material and Method

Percutaneous diargnostic renal biopsies were performed in the Department of Medical Radiology and Radiodiagnostics in Zabrze in 174 children from the Pediatric Department. The distribution according to gender was practically equal, i.e. 88 girls and 86 boys. The patients' age ranged from 4 to 19 years, 12 on the average. The procedures were performed under short-lasting general anesthesia in prone position, with a bolster placed under the abdomen

Table 1. The final clinical diagnosis in 174 children who underwent renal biopsy.

Diagnosis	Percentage (%)	Number of biopsies (n=174)
MCD	48.9%	85
FSGS	25.9%	45
DMP	18.4%	32
Others	3.4%	6
Less than 6 glomeruli	12.6% including 3.4% non-diagnostic	22 including 6 non-diagnostic

MCD – minimal change disease; FSGS – focal segmental glomerulosclerosis; DMP – diffuse mesangial proliferation.

to straighten the lumbar region. No local anesthesia was applied. Procedure time (two punctures in most cases) was measured from the moment of making a cutaneous incision with a skalpel to obtaining the second specimen for macroscopic assessment. At that moment, the anesthesiologist started „waking up" of the patient. Automatic Tru-Cut type 16G (sporadically 18G) needles in an automatic BARD "biopsy gun" were used. The needles were 20 cm long with 18 mm notch length. The right kidney was usually punctured, with sporadic biopsies of the left one, as it is located lower than the right one and US guidance allows to avoid accidental damage to the inferior vena cava. After pronation of the child, during induction of the anesthesia, the lumbar region was washed with 75% alcochol solution, and then detailed visualization of the right kidney with ultrasound was started. A portable ultrasound unit with a 5 or 3.5 MHz linear probe, depending on the child's age, was used in most cases. Sometimes a stationary USG unit with a convex type probe was applied. No significant differences in kidney evaluation between both unit types were observed at that stage of the procedure. The easy availability of the portable unit was an advantage. In control ultrasound scans performed 24 and 72 hours after the procedure, the best USG equipment available in the Department was used. The level of the lower kidney pole was drawn on the skin with a marker and the surgical area was washed again under sterile conditions. After making a cutaneous incision with a scalpel, the biopsy needle was introduced under the guidance of ultrasound operated by the assisting doctor (usually a resident-radiologist) in the region of the lower kidney pole after capsule "depression" was detected. At the moment of the patient's inspiration, the blockade of the biopsy needle in the automatic „gun" was released. It was intended to introduce the needle only into the renal cortex, tangentially to the surface. After withdrawal of the needle, the collected material was assessed macroscopically; the correct cylindrical speciment in formaldehyde was paced, (for optical microscopy) and the second biopsy was initiated. The second specimen was fixed in a test tube (for electron microscopy). If no or insufficient amount of material was obtained, the next biopsy was performed. The maximum number of punctures was 5 (in a single case), and in 59 more than two punctures were performed. After the procedure, USG was performed to assess the kidney immediately after the biopsy, and then an ice compress was applied. The child stayed in bed for approximately 24 hours. Table 1 presents the biopsy results.

Results

The biopsy effectiveness was assessed after the diagnostic material was obtained. Only in two children (1.1%), no renal tissue was obtained. At least 10 glomeruli per bioptate is the number considered sufficient to establish histopathological diagnosis. As reported by other authors, close cooperation between a pediatric nephrologist and a histopathologist allows to make diagnostic conclusions in case of a lower number of glomeruli in the bioptate, having the diagnostic results from electron microscopy. In our material, only in 6 (3.5%, including 2 where no diagnostic material was available) out of 22 bioptates with less than 6 glomeruli in each (12.6%) the ultimate diagnosis could not be established. The numbers of glomeruli for optic microscopy assessment are presented in Table 2.

The postbiopsy complications, occurring with similar rates to those reported by other authors, were divided into mild (including transient erythrocyturia, pain in the lumbar area) and severe (macroscopic hematuria of over 5 days' duration, subcapsular hematomas >2 cm). Mild complications occurred after 65.5% of all biopsies, and severe ones after 3.4%. It should be emphasized that in our material the complications did not require intervention, but only a prolonged period of observation of the patients in hospital (Table 3).

The search for correlation between the time needed to perform the procedure and the date when it was performed can be treated as testing association between two variables, one of which is systematic in character (biopsy date, limited by definition to the month and year), and the other purely quantitative (duration of the procedure at that time).

The so-called **Spearman's rank correlation coefficient** was calculated. It allowed to detect the presence of negative correlation – the „higher" the date of the procedure, the shorter its duration (Figure 1).

Similar statistical analysis was carried out to correlate the number of renal glomeruli per bioptate with the date of biopsy (year and month). In this case, no statistical association between these data was found. It is closely related to the clinical data, because the number of glomeruli per bioptate depends on the advancement of the disease rather than on the investigator's experience. As observed, the highest numbers of glomeruli were obtained in the cases of early-stage disease, i.e. MCD.

Except for two cases, in which no tissue material was obtained, it was present in the remaining 172 biopsies. It was regarded as a measure of accuracy of the method, calculated according to the following formula:

$$A=(EB/n) \times 100\%$$

where A – accuracy, EB – effective biopsy, n – number of bioptates, and amounting to

$$A=98.8\%$$

Table 2. The number of glomeruli per tissue specimen (n=174).

The number of glomeruli per tissue specimen in 174 examined children					
None	**2–5**	**6–10**	**11–20**	**>20**	**Mean**
2	20	64	74	14	12
1.1%	11.5%	36.8%	42.6%	8%	

Table 3. The complications after kidney biopsy (n=174).

L.p.	Complication type	Number of cases	% (n=174)
1	Macroscopic hematuria (without baseline microscopic hematuria)	31	17.8%
2	Macroscopic hematuria >5 days	3	1.7%
3	Subcapsular hematoma up to 2 cm	8	4.6%
4	Subcapsular hematoma >2 cm	2	1.1%
5	Increased microscopic hematuria > 5 days (n=122)	75	61.47%
6	Anesthesia-related complications	1	0.5%

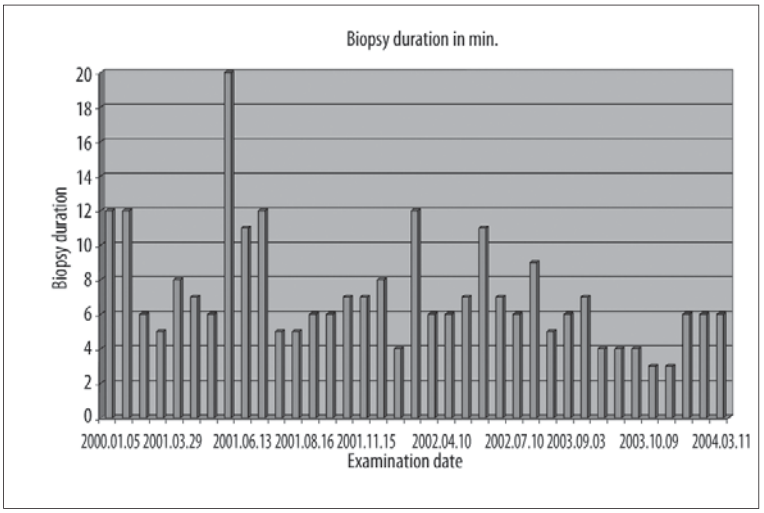

Figure 1. The graph of biopsy duration and the date of procedure.

Discussion

Irrespectively of the cause of referral for renal biopsy, MCD was the most frequent finding (48.9%). Similar results were obtained in the study by B.R.Nammalwara et al. (MCD 52.1%). The result obtained and reported by Kumar et al. was different – 38% FSGS and 32% MCD in 290 children [4,8,10]. This finding does not influence the effectiveness of renal biopsy procedure. The percentage of procedures in which no material allowing histopathological diagnosis is important. Such "failed" biopsies are understood as the lack of ultimate diagnosis. Obtaining fewer than 6–10 glomeruli per bioptate makes histological diagnosis more difficult. In our material, 12.6% specimens contained less than 6 glomeruli, but only 3.4% of the collected material was non-diagnostic. These rates are similar to those obtained by other authors [5,10–12]. The complications were divided into mild and severe. The „mild" ones included transient microscopic hematuria and subjective sensations of „pain in the lumbar region". Macroscopic hematuria of over 5 days' duration, subcapsular hematomas more than 2 cm in diameter and complications associated with general anesthesia were classifired as „severe" complications. The complication rates in our material were as follows: mild 65.5% and severe 3.4%. The data reported by other authors are varied. Nammalwara et al. observed a total of 32.8% mild complications, which correlates with the studies by Feneberg et al. and Doyle et al. [9,11–13]. Cozen et al. had only 15% of mild and 1% of severe complications. The percentage of severe complications seems to be similar in all studies, whereas the percentages of mild ones, classified in different ways, vary. As they subside spontaneously (e.g. lumbar pain), without intervention or longer hospitalization time, it can be presumed that their rates are dependent on classification [3,4,8,11,12]. In our material, no nephrectomy was necessary, and blood transfusions were given only in two cases of subcapsular hematomas, which correlates with the results of other studies [2,4,13,14]. The introduction of ultrasound as an important part of the procedure improves the safety, which is emphasized by other authors. Owing

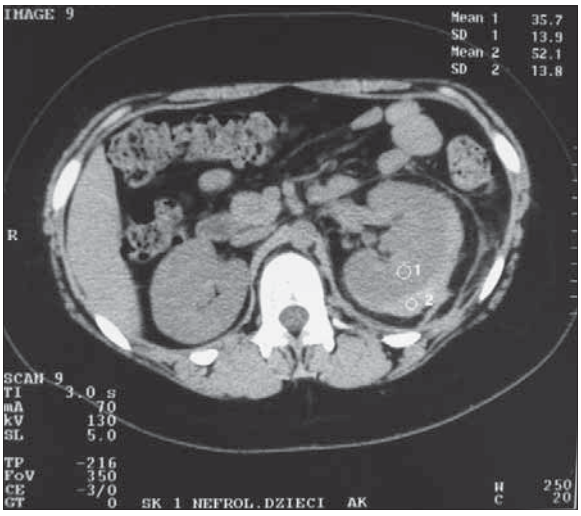

Figure 2. CT of the abdomen – a subcapsular hematoma in the lower pole of the left kidney.

to the possibility to observe the position of the needle in ultrasound, the effectiveness of the procedure understood as obtaining the material for histological investigations has improved significantly (Figure 2) [2,3,8,10].

Conclusions

Ultrasound examination in percutaneous renal biopsy in children is of great value. MCD is the most frequent clinical diagnosis, and the percentage of complications is low, which makes the procedure safe despite its invasive character. The biopsy duration depends on the examiner's experience (learning curve), and the number of glomeruli on the degree of renal disease advancement.

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