Kidney biopsy guidebook 2020 in Japan

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Abbreviations
APTT Activated partial thromboplastin time
ANCA Antineutrophil cytoplasmic antibody
BP Blood pressure
CKD Chronic kidney disease
CT Computed tomography
DKD Diabetic kidney disease
ds-DNA Double-stranded DNA antibodies
DM Diabetes mellitus
EM Electron microscopy
EGPA Eosinophilic granulomatosis with polyangiitis
EB virus Epstein–Barr virus
EBER Epstein–Barr virus-encoded small RNA
FDP Fibrin/fibrinogen degradation products
FSGS Focal segmental glomerulosclerosis
GBM Glomerular basement membrane

In 2020, Japanese Society of Nephrology established Committee of Practical Guide for Kidney Biopsy 2020, which published in (Jinseiken guidebook, 2020, vol. 2, page 1–180). This is the English version of that report.

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Overview

A kidney biopsy is performed for a treatment strategy of renal disease by pathologically diagnosing renal disease. Kidney biopsy is a reliable gold standard technique, but various complications are common when obtaining tissue from an abundant vascular kidney. During a biopsy, vasovagal reflexes, including cold sweat, discomfort, nausea, vomiting, hypotension, and bradycardia, can occur. Hemorrhagic complications after a biopsy are important; 89% of hemorrhagic complications have been reported to occur within 24 h. Therefore, a cooperation system including nurses and physicians by performing intravenous feeding and medication, while performing electrocardiogram monitoring and oxygen saturation monitoring, is necessary.

Therefore, it is necessary to always take the benefits and risks of kidney biopsy into consideration and decide if there is an indication for kidney biopsy.

The conventional criteria for the indication of kidney biopsy for adults are shown in Table 1, according to previous reports [1–3]. However, there is an opinion that it is necessary to extend these indications [3]. The following opinions were sent by a member of the Japanese Society of Nephrology.

- There is an indication for kidney biopsy beyond the above indication. The indication must be considered in every case. It is important that it does not limit the experience-rich institutional practice.
- Nephrologists, including young doctors with little experience in kidney biopsy, should recognize the safety procedures that are necessary to prevent the threshold to high-risk clinical conditions from lowering.
- Cases of serious complications such as bleeding can happen, and the appropriate security guidelines for treatment should be prepared before a kidney biopsy.

The clinical treatment of renal disease is possible without performing a kidney biopsy. However, many nephrologists should note that a higher-quality clinical treatment is enabled by performing kidney biopsy.

The final decision of whether you perform kidney biopsy should be decided based on each institution’s guidelines and should be judged for every individual patient carefully. With respect to the decision, it is necessary to be performed based on the concept of “shared decision making: SDM,”

### Table 1 The conventional criteria for the indication of the kidney biopsy for adults

1. Glomerular hematuria with any degree of proteinuria
2. Isolated proteinuria > 1 g/day (or g/gCr)
3. Unexplained renal disease or intrinsic acute kidney injury
4. Renal manifestation related to systemic disease

### Table 2 Indication of kidney biopsy in adults

1. Isolated glomerular hematuria
2. Isolated proteinuria
3. Proteinuria and glomerular hematuria
4. Rapidly progressive glomerulonephritis
5. Intrinsic acute kidney injury
6. Systemic disease with a urinalysis abnormality
7. Systemic disease with renal dysfunction, and/or without urinalysis abnormality
8. Diabetes mellitus
9. Elderly renal disease
10. Hereditary renal disease
11. Repeated kidney biopsy
after each attending physician explains the need and the risk of kidney biopsy to each patient thoroughly. We have provided explanations in the ‘Kidney biopsy guidebook 2020 in Japan’ along with questions and answers based on the results of a questionnaire survey for kidney biopsy that was performed in Japan from 2015 through 2017 by the Committee of Practical Guide for Kidney biopsy [4, 5], while adding the outline of the first edition of 2004 [1].

Chapter 1: Indication for kidney biopsy (Table 2)

Q1: Please tell me about kidney biopsy for patients with isolated glomerular hematuria

A1
- Cares is needed for kidney biopsy in cases with isolated glomerular hematuria showing dysmorphic erythrocytes.
- Careful observation should be conducted for isolated glomerular hematuria, and when proteinuria begins to be detected, kidney biopsy is performed.
- For cases with gross hematuria at the time of cold, and a family history of renal disease, IgA nephropathy, or Alport syndrome is assumed, kidney biopsy is performed [6–9].

Q2: Please tell me about kidney biopsy for patients with isolated proteinuria

A2
- For patients with nephrotic syndrome with nephrotic-range proteinuria more than 3.5 g/day, kidney biopsy is indicated.
- For patients with proteinuria of 3.5–1.0 g/day, a kidney biopsy is indicated, to the same extent as cases with nephrotic syndrome.
- For patients with proteinuria of less than 1.0 g, the final decision of whether you perform kidney biopsy should be judged based on each institutional forum and should be judged for every individual patient carefully. Orthostatic proteinuria characterized by elevated levels of urinary protein excretion while in the upright position and normal protein excretion when in the supine or recumbent position should be excluded. Kidney biopsy in these cases has been reported to show focal segmental glomerulosclerosis (FSGS), IgA nephropathy, or membranous nephropathy (MN) which does not require immunosuppressive therapy for a good prognosis. However, when proteinuria is increased more than 1.0 g daily, a kidney biopsy can be performed [10].
Q3: Please tell me about kidney biopsy of patients with both proteinuria and glomerular hematuria

A3
For patients presenting with both proteinuria and glomerular hematuria, kidney biopsy is indicated. Proteinuria is a risk factor of end-stage renal failure. The risk to end-stage renal failure increases according to urine protein excretion amount and increases in proportion to the degree of microhematuria. Care is necessary while performing kidney biopsy for cases of chronic kidney disease (CKD) G 4-5 [11, 12].

Q4: Please tell me about kidney biopsy of patients with rapidly progressive glomerulonephritis

A4
Kidney biopsy is a diagnostic method to judge treatment and to expect a better prognosis. The measurements of the anti-glomerular basement membrane (GBM) antibody level and antineutrophil cytoplasmic antibody (ANCA) level are important. When renal failure usually progresses within several months, ANCA-related nephritis is predicted, and when renal failure usually progresses within several weeks, anti-GBM antibody type nephritis is predicted. If a higher frequency of cellular crescents is detected by kidney biopsy, intensive immunosuppressive therapy can be provided considering the risk of the side effects of drugs. However, if such lesions cannot be detected, and a higher frequency of sclerotic glomeruli is detected, immunosuppressive therapy is avoided or minimized. Kidney biopsy provides valuable information for these judgments. Acute tubulointerstitial nephritis including myeloma cast nephropathy and sarcoidosis, lupus nephritis with hemolytic-uremic syndrome (HUS) or thrombotic microangiopathy (TMA), scleroderma kidney, and malignant nephrosclerosis are the differential diagnoses [13–18].

Q5: Please tell me about kidney biopsy of patients with acute kidney injury (AKI)

A5
Acute kidney injury (AKI), previously called acute renal failure, is a sudden episode of kidney failure or kidney damage that occurs within a few hours or a few days. AKI can be caused by the following: prerenal type, by decreased blood flow; intrinsic or renal type, by direct damage to the kidneys; and postrenal type, by blockage of the urinary tract. Although prerenal and postrenal AKI are usually not indicated for kidney biopsy, intrinsic or renal AKI is indicated for kidney biopsy because acute glomerulonephritis, acute tubular necrosis, or acute interstitial nephritis are assumed. Ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) provide vital information in the evaluation of the acute changes in the kidney. An increase in cortical echogenicity and kidney size by US suggests intrinsic AKI in patients with definite primary disease and even in patients with unknown primary disease and is indicated for kidney biopsy. However, small-sized kidney by US suggests the existence of long-standing chronic renal disease [19–20].

Q6: Please tell me about kidney biopsy of patients with systemic disease with a urinalysis abnormality

A6
Systemic disease with urinalysis abnormalities includes systemic lupus erythematosus (SLE), systemic vasculitis such as microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis, Goodpasture's syndrome, IgA vasculitis (formerly known as Henoch Schoenlein purpura), cryoglobulinemia, dysproteinemia such as amyloidosis, multiple myeloma, light or heavy chain deposition disease, and diabetic mellitus. For these patients, kidney biopsy provides essential information [21–25].
Q7: Please tell me about kidney biopsy for systemic disease with renal dysfunction, and/or without urinalysis abnormality

A7
For these cases, kidney biopsy is reported to provide significant information to aid diagnostic decisions.

- Systemic disease with renal dysfunction, but without a urinalysis abnormality, includes acute or chronic tubulo-interstitial nephritis secondary to sarcoidosis, drug-related disease such as tyrosine kinase inhibitors and checkpoint inhibitors. IgG4-related nephritis, or hypercalcemic nephropathy by activated cholecalciferol. A high value of tubular impairment markers such as β2-microglobulin (β2MG), α1-microglobulin (α1MG), or N-acetyl-β-D-glucosaminidase (NAG) is characteristic.

- Systemic lupus erythematosus without urinary abnormality is called silent lupus nephritis. Light microscopy of kidney biopsy is reported to show mild glomerular change with class I or class II on 74% of silent lupus nephritis according to ISN-RPS lupus nephritis classification, but immunofluorescent microscopy shows IgG and C1q stain, and electron microscopy shows electron-dense deposits in the mesangium or subepithelium, which are characteristic to lupus nephritis.

- Systemic vasculitis, including MPA, GPA and EGPA, can be diagnosed by extrarenal complications such as fever, upper respiratory tract disease, lung disease, neuropathy, and positivity for ANCA, even though urinary abnormality is negative. For these patients, kidney biopsy is reported to show crescent formation or vasculitis of small arteries with a frequency of 69%, although extrarenal organ biopsy may not show any vasculitis [26–29].

Q8: Please tell me about kidney biopsy of patients with diabetes mellitus (DM)

A8
DM patients with renal complications have been considered to show typical diabetic nephropathy and have not been indicated for kidney biopsy. However, it has recently been reported that kidney biopsy gives vital information for the diagnosis and treatment of DM patients. Renal disease in DM patients is named diabetic kidney disease (DKD) because kidney biopsy examination clarified various histological findings.

For DM patients with renal complications, a kidney biopsy can provide the following information: (1) existence of typical diabetic glomerulopathy including thickening of the GBM, mesangial expansion or nodular glomerulosclerosis (Kimmelstiel-Wilson lesions), (2) existence of arteriolar hyalinosis without typical diabetic glomerulopathy, (3) existence of glomerular lesion except diabetic glomerulopathy, and (4) (1 or 2) + (3). Even for patients with clinical information suggesting typical diabetic glomerulopathy accompanied by nephrotic-range proteinuria, retinopathy, and neuropathy, kidney biopsy is reported to provide pathological information for treatment strategies to improve renal prognosis. In kidney biopsy for DM patients with renal complications, it has been reported that 40% of cases showed typical DM glomerulopathy and 45% showed glomerular lesions, except for diabetic glomerulopathy.

In Japan, DM patients are reported to be the first place out of primary renal diseases to require dialysis, but statistical analysis for the requirement of dialysis by using kidney biopsy remains unknown. Accurate histological diagnosis of DM patients is also expected to be important for renal disease treatment [1, 3, 30–44].
Q9: Please tell me about kidney biopsy for elderly patients

A9
For elderly patients over 80 years, kidney biopsy is considered to provide important information concerning histological diagnosis and renal prognostic treatment, although arteriolosclerosis and arteriolar sclerosis, as well as tubulointerstitial damage due to aging, are accompanied at high frequency [45–48].

Q10: Please tell me about kidney biopsy for hereditary renal disease

A10
For patients with a family history of renal disease, kidney biopsy is considered to provide important information concerning histological diagnosis, although characteristic clinical information and gene analysis clarified hereditary renal diseases such as Alport syndrome, Fabry disease, mitochondria disease, and polycystic kidney disease [49–51].

Q11: Please tell me about repeated kidney biopsy

A11
Repeated kidney biopsy is indicated in the following situations: (1) When a diagnosis is difficult with the specimen being obtained in initial kidney biopsy, because of a very small amount of specimen or the absence of the required amount of specimens necessary for an appropriate diagnosis; (2) To evaluate an appropriate immunosuppressive drug or to avoid excessive treatment, to examine additional treatment, and for the reexamination of the therapy; (3) to re-examine initial histological diagnosis.

Repeated kidney biopsy is reported for patients with refractory nephrotic syndrome and recurrent lupus nephritis [52–63].

Chapter 2: Kidney biopsy for patients with a clinical condition of high risk for percutaneous native kidney biopsy

Overview

The following renal disease was contraindicated for percutaneous native kidney biopsy under the ultrasonic guidance...
in the previous edition of the guidebook because the risk of hemorrhagic complications after a kidney biopsy is very high, and renal tissue sampling necessary for diagnosis is not obtained [1] (Table 3). However, as biopsy techniques, by using a newer US device and automatic biopsy needle, improved safety, there have been several reported case series that required or enabled histological diagnosis by kidney biopsy [4]. Therefore, when the benefit is judged to exceed a risk, kidney biopsy is indicated for patients with a clinical condition of high risk. A kidney biopsy should be performed in institutions that can treat hemorrhagic complications. The following diseases are not absolute contraindicated anymore but are described as a renal disease with high risk by a question and answer method.

| Table 4 Chronic anticoagulation and drug holiday before kidney biopsy including two types of options in Japan |
| Drug | Drug holiday |
|------|--------------|
| Antiplatelet medication |  |
| Ticlopidine | ① 5–7 days, ② 10–14 days |
| Clopidogrel | ① 5–7 days, ② 14 days |
| Cilostazol | ① 1 day, ② 2–4 days |
| Icosapentaenoic acid | 7–10 days |
| Beraprost | 2–3 days |
| Sarpogrelate | 1–2 days |
| Aspirin | ① 3 days, ② 7–10 days |
| Dipryidamole | 1–2 days |
| Prasugrel | ① 5–7 days, ② 14 days |
| Anticoagulant medication |  |
| Heparin | 1 day |
| Dalteparin | 1 day |
| Warfarin | 3–5 days (intravenous heparin) |
| Dabigatran | 1–4 days |
| Edoxaban | 1 day |
| Rivaroxaban | 1 day |
| Apixaban | 1–2 days (intravenous heparin) |
| Vasodilator |  |
| Limaprost | 1 day |
| Coronary vasodilator |  |
| Dilazep hydrochloride | 1 day |

Q1: Please tell me about the previous report for contraindication of kidney biopsy

A1

Absolute contraindications for the performance of a percutaneous native kidney biopsy were defined in a position paper by the Health and Public Policy Committee of the American College of Physicians in 1988 [64]. These include severe uncontrolled hypertension, uncontrollable bleeding diathesis, uncooperative patients, and a solitary native kidney. However, recently, these renal diseases are not ‘absolute’ contraindications due to the improved safety associated with newer imaging and biopsy techniques but have been named ‘relative’ contraindications for kidney biopsy because of the high risk for complications of kidney biopsy.

Q2: Please tell me about biopsy techniques for kidney disease with high risk

A2

When an US-guided percutaneous kidney biopsy has been paused, open kidney biopsy, laparoscopic kidney biopsy, and CT-guided kidney biopsy may become the next option. An open biopsy is performed under general anesthesia. The surgeon looks at the surface of the kidneys and determines the area from which the tissue samples should be taken. Hospitalization has become relatively long. There is the risk that the wound becomes big. CT-guided kidney biopsy is considered safe for severe obesity patients and renal mass lesions [65–71].
Q3: Please tell me about kidney biopsy of solitary native kidneys

A3
When hemorrhagic complications occur, renal function decreases, and dialysis may be required. Therefore, kidney biopsy should be performed in an institution with the facilities for emergency treatment after an indication of kidney biopsy is examined closely. A solitary native kidney includes a contralateral kidney as one kidney was resected for renal carcinoma, contralateral kidney with one kidney of atrophy or hypoplasia, as well as born with a solitary kidney. A solitary kidney with nephrotic-range proteinuria and rapidly progressive renal disease is indicated for kidney biopsy. Although the US-guided method has been considered contraindicated for kidney biopsy of a solitary kidney, recently, there are several reports of using the US-guided method [72–76].

Q4: Please tell me about kidney biopsy of patients with contracted kidneys, small hyperechoic kidneys, or end-stage kidneys

A4
For contracted kidneys or small hyperechoic kidneys, nephrologists will find that sclerotic glomerular ratio rises, and there are only a few preserved glomeruli necessary for a diagnosis. Kidneys with a small renal size or end-stage kidneys are known to be risk factors for hemorrhagic complications. However, there are reports that beneficial information about recurrent nephritis after a renal transplant was obtained from the kidney biopsy of end-stage kidneys after dialysis was started [77–80].

Q5: Please tell me about kidney biopsy of patients with kidneys of anatomic abnormalities, including horseshoe kidney, malrotation kidney, and renal arterial aneurysm

A5
When such kidneys are accompanied by nephrotic range proteinuria or rapidly progressive renal dysfunction, we confirm renal blood flow and an abnormal vascular position by using color-doppler US and 3D-CT angiography. When an US-guided percutaneous kidney biopsy is hesitated, open kidney biopsy becomes the choice. Horseshoe kidney is characterized by the bilateral renal union at a lower renal position. Kidneys usually exist at a lower position, and the nephric hilar region is located in the high rank going outward. Because the renal artery is concentrated towards an inferior pole, kidney biopsy in the upper renal pole is desirable [81–85].

Q6: Please tell me about kidney biopsy of patients with polycystic disease

A6
When such kidneys are accompanied by nephrotic range proteinuria or rapidly progressive renal dysfunction, and normal renal parenchyma was confirmed between cysts by using CT or US, kidney biopsy is indicated. Renal biopsy of polycystic disease including autosomal dominant polycystic kidney disease, autosomal recessive polycystic kidney disease, nephronophthisis, and medullary cystic kidney disease has been reported [86–88].

Q7: Please tell me about kidney biopsy of patients with hydronephrosis

A7
When relatively mild hydronephrosis is accompanied by nephrotic range proteinuria or rapidly progressive renal dysfunction, and normal renal parenchyma that we can obtain safely was confirmed by using CT or US, kidney biopsy is indicated. Reflux nephropathy secondary to vesicoureteral reflux, IgG4-related tubulointerstitial nephritis accompanied by retroperitoneal fibrosis and lupus cystitis with ureteral obstruction is included in this setting [89–94].
Q8: Please tell me about kidney biopsy of patients with malignant nephrosclerosis related to hypertensive emergency (malignant hypertension) and scleroderma renal crisis

A8

For patients with malignant nephrosclerosis related to hypertensive emergency (was called malignant hypertension) and scleroderma renal crisis (including severe hypertension that cannot be controlled with antihypertensive medications), when blood pressure (BP) is managed appropriately (less than 140/90 mmHg) even for an acute phase, a kidney biopsy is indicated. The term ‘malignant hypertension’ has been used to describe a syndrome characterized by elevated BP accompanied by encephalopathy, pulmonary edema, retinal hemorrhage, or acute nephropathy. Malignant hypertension was used because the prognosis of this disease was poor, the same as that of malignant tumors. However, strict control of the BP by antihypertensive therapy has improved the prognosis of this condition, and this term has been removed. Hypertensive emergency has come to be used for this disease. The chief structural change of the kidneys associated with hypertensive emergency is severe onion skin pattern with luminal narrowing or fibrinoid necrosis of the small arteries and arterioles, which is called malignant nephrosclerosis. Because the change of the renal tissue is not a phenomenon that would disappear in the short term, kidney biopsy should be indicated after a whole-body control was performed [95–98].

Q9: Please tell me about kidney biopsy of patients with uncontrolled bleeding diathesis

A9

For such clinical condition, when it is judged that there is a benefit of the kidney biopsy, although hemorrhagic complications are risky, kidney biopsy is performed. However, kidney biopsy should be performed in an institution with the facilities for emergency treatment such as renal arterial embolization or surgery, after an indication of kidney biopsy is examined closely. Thrombocytopenia accompanied by rapidly progressive renal failure includes HUS/TTP /TMA, thrombocytopenia, anasarca, myelofibrosis, renal dysfunction, and organomegaly (TAFRO) syndrome, lupus nephritis with vasculitis, and antiphospholipid syndrome [99–104].

Q10: Please tell me about kidney biopsy of patients with pregnancy

A10

Several series have shown complication rates of the percutaneous approach in the prone position similar to those reported in nonpregnant patients. However, as there is always the potential for maternal–fetal morbidity, consideration should be given to avoid performing the procedure until the postpartum period, unless change management is performed before delivery and kidney biopsy is performed after delivery. When renal disease, except pregnancy-induced hypertension nephropathy, is suspected before mid-pregnancy (16–27 weeks), a biopsy is considered for the case that treatment strategy except emergent parturition is thought about [105–117].
Q11: Please tell me about kidney biopsy of patients with severe obesity

A11
We consider whether a kidney biopsy is technically possible. When it is thought that US-guided percutaneous kidney biopsy is difficult, choices include CT-guided kidney biopsy [67, 73].

Q12: Please tell me about kidney biopsy of renal mass, including malignant neoplasm

A12
When renal carcinoma is diagnosed on an image, surgical therapy is usually chosen, but a renal tumor biopsy is considered by a urologist for a case to hesitate about a diagnosis, or for the inoperable case in consideration of chemotherapy when the benefit is thought to be high. The occurrence of serious hemorrhagic complications or cancer cell dissemination after the biopsy is considered very low. There are reports of case series that led to a diagnosis of intravascular lymphoma by kidney biopsy that was performed for the further examination of fever of unknown origin or rapidly progressive renal failure [118–122].

Q13: Please tell me about kidney biopsy of patients on chronic anticoagulation

A13
Several issues must be considered in patients on chronic anticoagulation when judged that a tissue diagnosis by kidney biopsy is necessary (Table 4).

- For patients on chronic anticoagulation, kidney biopsy usually cannot be selected.
- Whether kidney biopsy is essential or necessary for diagnosis, prognosis, and/or management must be discussed in the conference conducted at the institute.
- If anticoagulation is temporarily stopped (e.g., mechanical heart valves), the risk of thrombosis must be judged in consideration of an individual situation, often in consultation with hematology and cardiology.
- If anticoagulation is continued, the risk for bleeding after kidney biopsy must be evaluated in consideration of an individual situation. Kidney biopsy should be performed in an institution with the facilities for emergency treatment [123–125] (Table 4).

Q13-1: Please tell me about kidney biopsy in patients on antiplatelet medication

A13-1
After having considered the likelihood of a thrombotic vascular event when a drug is discontinued, a drug holiday (period when the patient stops taking medication): (1) criteria following minor operation and (2) criteria following major operation [e.g., Aspirin: (1) 3–5 days, (2) 7–10 days] [125]. Many institutes in Japan agree to criteria following a major operation. It is desirable to cope according to each institution’s guidelines, in every case. Many institutes agree to an option “since the time when hemostasis was confirmed” as the restarting time of the antiplatelet drug after kidney biopsy.

Q13-2: Please tell me about kidney biopsy in patients on anticoagulant medication

A13-2
When it is judged that a tissue diagnosis by kidney biopsy is necessary, the drug holiday before kidney biopsy is as follows; warfarin (3–5 days), dabigatran (1–4 days), edoxaban (1 day), rivaroxaban (1 day), apixaban (1–2 days). For cases with a high risk of thromboembolism who require intravenous heparin, it should be stopped for at least 5 h pre-biopsy to allow the activated partial thromboplastin time (APTT) to normalize. Although most clinically significant bleeding is recognized in the first 12–24 h post-biopsy, bleeding may occur up to several days after the procedure. Oral anticoagulation is resumed 7 days post-biopsy, or the day when hemostasis was confirmed.
Q14: Please tell me about kidney biopsy in patients with active renal or perirenal infection or skin infection over the biopsy site

A14
For times with active infectious disease, kidney biopsy is not to be indicated. However, kidney biopsy is considered at the stage when the infectious disease healed, if a clinical condition suggestive of the indication of kidney biopsy exists.

Q15: Please tell me about kidney biopsy of patients that informed consent is not obtained

A15
For such patients, a kidney biopsy is not indicated. However, for pediatrics, the agreement of parents is given priority over the agreement of the patient.

Q16: Please tell me about kidney biopsies of patients whose cooperation is not obtained or who cannot obey testing instructions

A16
For patients who cannot keep rest or cannot hold their breath in the prone position or whose BP falls down for tension, when US-guided percutaneous kidney biopsy has hesitated, open kidney biopsy or laparoscopic kidney biopsy may become the next option. Perioperative postoperative rest is not often maintained in the pediatric population. After calming patients by intravenous anesthesia, US-guided percutaneous kidney biopsy or open biopsy is performed.

Chapter 3: Informed consent and explanation document to the patients

Informed consent in kidney biopsy

Overview
Kidney biopsy is a gold standard for renal disease diagnosis and is the testing that we cannot miss in renal disease practice. However, it is invasive testing, and adequate informed consent is necessary. With respect to the nephrologist, it is necessary to explain the possible complications by the testing procedures, including hemorrhagic complications, in addition to the benefits of kidney biopsy to the patients. With respect to the patients, it is important to consent to kidney biopsy based on their own intention after having understood the benefits (merits) and disadvantages (demerits) of kidney biopsy explained by a physician [126].

In Japan, informed consent is obtained before kidney biopsy, and kidney biopsy is performed after, as a general rule, having acquired an agreement by letter. In this issue, the informed consent is commented by a question and answer method.
**Q1:** What is the point that is important about informed consent of kidney biopsy?

**A1**
The chief physician explains the need, complications, and testing procedure of kidney biopsy in plain terms. It is important that the patients agree after having understood the explanation provided by the doctor. When we explain kidney biopsy, as for the physician, it is necessary to always recognize that there is a major difference in medical knowledge and understanding, from the beginning, between patients and doctors. We avoid the use of technical terms. It is explained by terms as easy as possible to understand; why is kidney biopsy necessary? How is kidney biopsy performed? What can result from kidney biopsy? What is the length of the hospital stay? How is lifestyle or attention affected after discharge? The procedure of the testing is easy to become the punctum cecum of the explanation. Because the procedure of the testing is daily as doctors, it is often omitted. However, it is the first experience for the patients and should be explained. We confirm whether the patients and a family can understand the contents during explanation. It is important that we make an atmosphere where patients can ask a question anytime. An explanation will be necessary about the instances when we do not perform a biopsy. It is a point that the patients agree based on their own intention after having understood the contents adequately. It cannot be said that we performed appropriate informed consent by handing only an explanation paper of a kidney biopsy to the patients without adequate explanation and only by getting a signature on the consent form. The work of leaving documentary evidence is not just to prevent you from being brought into question legally.

**Q2:** Where should the informed consent of kidney biopsy be carried out?

**A2**
The interview should be performed at the calm place that privacy can be preserved as much as possible, including the interview room. Informed consent should be obtained at a place where explanations can be provided in a calm manner in a sitting position. The consideration of privacy is necessary. Explanations at the bedside of large rooms should be avoided as much as possible. A kidney biopsy is a team approach in medical care. An extraneous medical attendant performs a simple plain explanation in the outpatient, and after hospitalization, a hospitalization medical attendant should explain slowly and carefully again at the place that the privacy, including the interview room, can be preserved [126].

**Q3:** Please tell me about the utility of the clinical path in the case of kidney biopsy hospitalization

**A3**
The use of the clinical path helps provide high-quality medical care and nursing care premeditatedly. It becomes useful in helping patients consent to undergoing kidney biopsy.

**Q4:** How much is the length of hospital stay after undergoing kidney biopsy?

**A4**
Many institutions assume the option of 6 days and five nights to 4 days and three nights in Japan. It has been reported that the rate of occurrence of hemorrhagic complications after kidney biopsy is 89% within 24 h, and it is desirable to place the patients under the observation of medical care for 24 h. Kidney biopsy reports are generally given in a single day in America. In the case of increased risk, the wait at the possible place of prompt hospital visiting is desired. Hospitalization of approximately 1 week has been traditionally recommended in many institutions in Japan [127–131].
Q5: After hospitalization, when do you perform kidney biopsy?

A5
Many institutions perform kidney biopsy on the next day of hospitalization. On the first day of the hospitalization, explanations of kidney biopsy and the final confirmation of laboratory findings and the anticoagulant are conducted. Because bleeding after kidney biopsy often occurs within 6 h, kidney biopsy should be performed in the morning when postoperative management is easy to be performed during the daily service zone.

Q6: In the case of an explanation of kidney biopsy, should you acquire the consent form for transfusion?

A6
It is necessary to explain the likelihood of the transfusion before kidney biopsy, and as for the acquisition of the transfusion consent form, it is the judgment of each institution.

Explanation document to the patients

Q1: What kind of testing is kidney biopsy?

A1
There are various causes for renal disease to induce proteinuria, hematuria, and a decrease in renal function. There are many cases that it is difficult to diagnose the cause only by blood, urinalysis, and imaging study.

We take some kidney tissue by using the needle with the core size of the ball-point pen, observe it with a microscope, and clarify a cause of renal disease occurring in kidney. If a cause of the illness is understood, we can suggest an optimal therapy. A procedure or an operation to take out kidney tissue is named kidney biopsy.

Q2: Please tell me the purpose of kidney biopsy

A2
The purpose of a kidney biopsy is three.
1. We find renal cause and severity of illness.
2. We can predict a prospect of illness.
3. We can suggest an optimal therapy.

Q3: When is kidney biopsy required?

A3
Kidney biopsy is required in the following case.
1. Hematuria persisted, and renal function worsens.
2. Proteinuria over 1.0 g a day persists. Nephrotic range proteinuria is included.
3. Hematuria and proteinuria are detected at the same time.
4. Proteinuria and hematuria are mild or absent, but renal function worsens.
5. A decrease in renal function progresses rapidly.
6. Renal disease is suspected in patients with systemic lupus erythematosus, vasculitis, and DM.
7. For unidentified renal failure, the kidney is still normal size.
Q4: Are there patients requiring scrupulous attention for a kidney biopsy?

A4
The patients with the following disease require scrupulous attention for the complication.
1. There is only one kidney. Only one kidney functions. → Renal function worsens on renal hemorrhage after kidney biopsy.
2. The renal form is different from that of the normal kidney; for example, it is atrophic kidney, horseshoe kidney, hydronephrosis. → Kidney biopsy is difficult to perform.
3. The kidney has many cysts (bag-formed structure). → Kidney biopsy is difficult to perform.
4. Blood pressure is very high. → It is easy to bleed
5. Platelet counts are less than 100,000/μL; coagulation ability decreases, and patients take medicines that help prevent blood clots. → It is easy to bleed.
6. Pregnant → Kidney biopsy is difficult to perform.
7. High percentage of fat → Kidney biopsy is difficult to perform.

Q5: In what cases is kidney biopsy not indicated?

A5
Kidney biopsy is not indicated as follows.
1. A consent to undergo kidney biopsy is not obtained from the patients or a family.
2. There is an infectious disease in the kidney and the urinary tract, and skin infection is observed over the biopsy site.
3. You cannot keep rest in the prone position, holding your breath is difficult, BP falls when tense, and you cannot obey the instructions of the doctor. For these patients, an US-guided kidney biopsy is not indicated, but open biopsy and laparoscopic biopsy are indicated under general anesthesia.

Q6: Please tell me, in specifics, how kidney biopsy is performed

A6
Kidney biopsy is usually carried out using an automatic biopsy needle under the ultrasonic guidance (Fig 1).

1. We put an indwelling needle for intravenous feeding in the blood vessel of the arm before testing. An antimicrobial agent and/or hemostatic are usually given before testing. When BP falls or you came to feel sick during testing, a drug is given through an indwelling needle.
2. We cancel your diet before the testing. This is because you come to feel sick, and you may vomit by the pressure from a back hemostasis.
3. There is the kidney at the position near a back. You lie on your face and the stomach. A renal place is confirmed by US. From the skin of the back surface to the renal surface, a local anesthetic is injected in place to prick with a needle. We cut about a 2–3 mm opening in the skin surface. This section may remain as a minimal wound subsequently.
4. The thickness of the needle taking the renal tissue is a core size of the ball-point pen, and the length is around 2 cm. When a needle is inserted, there is no pain, but there is the sense that the back is pushed. When the needle reaches the kidney, we signal you. Please hold your breath for 5-10 s. We take the renal tissue at that moment. You hear a clicking sound at the moment that we take the renal tissue. Because there is no pain, do not worry. We conduct this operation 2–4 times.
5. When kidney biopsy is completed, we exert pressure from the back for 10–15 min to stop bleeding.
6. The testing is completed in approximately 30 min. After testing, you turn over on your back. Rest is required in a bed for 6–24 h. Eating and drinking after the testing is performed lying down. Urination and the defecation are carried out on the bed, too. When urination is difficult, we may use a tube called a urethral catheter. After testing, fever may occur. The cause is considered absorption fever occurring when the hematoma that occurred after a biopsy is absorbed.
7. For 4 weeks from the next morning, walking is possible, but please avoid running up the stairs, and please avoid intense, laborious work to avoid exerting stress on the area that was affected by the procedure.
8. With respect to the method of kidney biopsy performed in Japan, an automatic biopsy needle is now used under the ultrasonic guidance in almost all institutions. Kid-
ney biopsy is considerably safer than when performed blindly, and it may be said that it is an established testing method. However, when it may be hard to obtain renal tissue, we may cancel testing on the way without doing it. When we cannot obtain renal tissue, or when glomeruli necessary for a diagnosis are not included, we may make a testing plan again.

Q7: Other than the percutaneous kidney biopsy under the ultrasonic guidance, is there another method of kidney biopsy?

A7
There is an "open kidney biopsy" to gather renal tissue under general anesthesia in an operating room. We cut the skin open and confirm the kidney directly and take the renal tissue. Renal tissue is obtained surely. There is an advantage with a little risk of hemorrhagic complications to the nephric surface, surely because we can stop bleeding. However, a wound of approximately 3 cm is left in the back. There is a risk of bleeding complications to the urinary tract.

Q8: How is the tissue which we obtained by kidney biopsy examined?

A8
We observe the specimen, which we obtained by three methods; light microscopy, fluorescent microscopy, and electron microscopy.

By light microscopy, we can observe the whole, including glomeruli, renal tubules, and the blood vessels, and can obtain basic information.

By fluorescent microscopy, we observe the presence or absence of deposition and a deposition place of immunoglobulin, including IgG, IgA, and IgM, and complements, such as C3 and C1q.

By electron microscopy, we confirm the cellular internal structure, including glomerular and tubular structure, and a deposit causing nephritis, which spreads approximately 15,000 times.

After performing three tests, a diagnosis of renal disease is made.

There is a "laparoscopic kidney biopsy," which takes the renal tissue while confirming the kidney using laparoscopy as other methods directly (Fig. 1).

When there is the high-risk clinical condition and hemorrhagic complications by percutaneous kidney biopsy, when renal tissue is not gained by percutaneous kidney biopsy, "opening kidney biopsy" or "laparoscopic kidney biopsy" is chosen.

Fig. 2 How to divide a sample of the kidney biopsy
Q9: Are there complications from kidney biopsy?

A9

- There are the following possible complications.
- Bleeding to the renal surface: Approximately 1/4 of total blood volume, which has been sent from the heart flows into the kidney. Because the nephric surface is damaged by kidney biopsy, hematoma is present around the kidney in most cases. Hematoma is small and is absorbed in one month, and it does not usually become the problem. It may be associated with febricula at the absorption of the hematoma.
- Bleeding to the urinary tract: The gross hematuria is found in around 2–3%, but usually disappears within a few days. It is a rare complication, but a large amount of blood flows rarely into the bladder through a urinary tract from kidney. The outlet of the bladder may be occluded by hematoma, which is called bladder tamponade. In this case, we detain urethral catheters and perform intravesical sustained irrigation. When there is a great deal of bleeding, transfusion is required, and we examine the cause of bleeding on computed tomography and angiography testing when bleeding is difficult to stop. And we treat it by the renal artery embolization using the embolus material called the micro coil, when we detect the renal arteriovenous fistula in which blood flow of the intrarenal arteries is connected to a vein.
- We may produce a vasovagal reflex symptom including nausea, vomiting, hypotension, and bradycardia from excessive tension during kidney biopsy, and lumbago by bed rest after testing. Furthermore, renal function worsens temporarily, and serum creatinine may rise.

- When there is the drug allergy for an anesthetic agent, an analgesic, and the antimicrobial agent, please report to an attending physician before testing because these drugs cause an allergic reaction.
- Although it is very rare, a needle injures other organs except the kidney, such as the liver, spleen, or intestinal tract.
- It is very rare, but with the situation that coagulation ability enhances in patients with nephrotic syndrome, patients may be complicated with venous thrombosis and pulmonary thromboembolism after kidney biopsy. In addition, you may present with a serious thrombotic complication including cerebral infarction and myocardial infarction and pulmonary embolism when you discontinue anticoagulant and an antiplatelet drug for kidney biopsy temporarily.
According to questionnaire survey by the Japanese Society of Nephrology for kidney biopsy that was performed in Japan from 2015 through 2017, out of 15,657 adult patients who underwent kidney biopsy by a nephrologist, transfusion was required in 121 cases (0.8%), hemostasis treatment by renal artery embolization in 31 cases (0.2%), gross hematuria with no treatment in 431 cases (2.8%), vesicoclysis in 56 cases (0.4%), death in one (0.006%). Close evaluation of the death cases clarified that bleeding after kidney biopsy is not a direct cause, but the overall status of these cases was poor before kidney biopsy and worsened after kidney biopsy.

Chapter 4: Pre-biopsy evaluation

Q1: Please tell me about the necessary check item before kidney biopsy

A1
Kidney biopsy is extremely useful for diagnosing and treating renal diseases. However, bleeding complications can occur because it is an invasive study. It is necessary to evaluate a patient risk of the complication so that kidney biopsy can be performed safely. Moreover, clinical information, including laboratory and imaging tests, is crucially important for relevant differential diagnosis and clinical management, as well as pathological information obtained by kidney biopsy. The items for pre-biopsy evaluation are as follows [74, 104, 132].

1. Medical history
   ① Detailed history of present illness.
   ② Family history of renal diseases.
   ③ Past medical and social history.
   ④ History of patient medication.

2. Physical examination

3. Blood test
   ① Complete blood cell count
      Erythrocyte transfusion is considered for severe anemia before kidney biopsy. The cutoff value of Hb is 7–8 g/dL. Platelet transfusion is considered for severe thrombocytopenia with platelet count less than 50,000/μL.
   ② Coagulation study
      Tests for prothrombin time (PT), APTT, fibrinogen, and fibrin/fibrinogen degradation products (FDP) (or D-dimer) are recommended for pre-operative screening. When a coagulation abnormality is found, close examination and adequate treatment are required before kidney biopsy. When a thrombotic tendency is pointed out, especially in high-risk patients with nephrotic syndrome, screening tests for deep vein thrombosis and pulmonary embolism are also considered.
   ③ Biochemistry
      Serum tests include total protein, albumin, urea nitrogen, creatinine, uric acid, AST, ALT, LDH, and electrolytes (Na, K, Cl, Ca, P, and Mg). Estimated GFR by using serum creatinine or cysteine C values are important to evaluate renal function. Arterial blood gas analysis (including anion gap) is also helpful for the differential diagnosis of kidney diseases with acid–base abnormality.
   ④ Blood sugar (glucose) test
      As well as fasting plasma glucose (sugar), HbA1C and glycoalbumin are useful for evaluation of hyperglycemic conditions.
   ⑤ Immunology
      Immunological tests include immunoglobulin (IgG, IgA, IgM, IgG4), complement (CH50, C3, C4), autoantibody (antinuclear antibody, ds-DNA, SM, RNP, ANCA, GBM, anticardiolipin, lupus anticoagulant), serum monoclonal protein.
   ⑥ Endocrinology
      Endocrinological examinations include renin, aldosterone, and BNP.
   ⑦ Tests for infection
HBV, HCV, syphilis (RPR/TPHA), and HIV are screened.

4. Urinalysis

① Urinary qualitative test (dipstick test).
② Urinary sediment.
   Dysmorphic erythrocytes suggest hematuria with glomerular diseases.
③ Urinary quantitative test.
   Urinary protein is measured by using spot urine or 24-h collected urine. NAG, β2MG, and α1MG are useful markers for tubular dysfunction. Selectivity index (SI) is also helpful in the differential diagnosis of nephrotic proteinuria.

5. Imaging test

Diagnostic imaging includes US, CT, and MRI. Radiisotope examinations are also useful for understanding renal pathophysiology. 99mTc-MAG3, an isotope secreting from proximal tubules, is utilized for evaluating effective renal plasma flow (ERPF) of right and left kidneys. 99mTc-DTPA, an isotope filtrating from glomeruli, is used for the measurement of glomerular filtration rate (GFR) of right and left kidneys.

Q1: Please tell me about utility of bleeding time

A2

Bleeding time has been used as a screening test to evaluate the platelet function. However, the reliability of bleeding time is now considered low. In fact, bleeding time is not measured for preoperative evaluation in many facilities. The Duke method for bleeding time seems unreliable because of low precision. The Ivy method has not been used since the measurement device was unavailable. The platelet function is usually evaluated using platelet count and APTT. If a patient has past history or family history of bleeding tendency, platelet agglutinating capacity and platelet adhesion ability should be directly measured. Minimum set of pre-biopsy measurement for bleeding tendency includes a platelet count, PT, APTT, fibrinogen, and FDP (or D-dimer).

Q2: Please tell me about a history of the percutaneous kidney biopsy

A1

• The percutaneous kidney biopsy had been started for renal disease from the 1940s and was reported by Danish Iversen and Brun for the first time in the world in 1951 [73, 133–135].
• In Japan, Kinoshita et al. of Niigata University succeeded in establishing the clinical application of kidney biopsy for the first time in 1954, and the posture of the patients was loci at first, and an aspiration needle was used as a puncture needle.
• The method using the Silverman needle in a prone position was reported by America Kark and Muehrcke, and the quantity of collected specimen increased, and the rate of complication decreased.
• Tru-Cut needle was used subsequently in the 1980s.
• Automatic biopsy needles (biopsy gun) came to be used widely in Japan from the 1990s.
• Because confirmation method of the renal place was blind at first and was performed on palpitation, there was an increased risk for puncturing big arteries and other organs.
• Then drip infusion pyelography (intravenous pyelography) method was used.
• Then the method of taking renal tissue while visualizing kidney using US was started in the 1980s.
• Currently, kidney biopsy under the ultrasonic guidance using the automatic biopsy needle is widely performed in a prone position [136–139].
**Q2:** Please tell me about fact-finding result (questionnaire survey) in 2018 for the method of kidney biopsy in Japan

| A2: | Usually, percutaneous kidney biopsy under the ultrasonic guidance is performed in 99% of institutions in Japan. In cases with high-risk clinical conditions, according to a questionnaire survey (2018) for kidney biopsy, percutaneous kidney biopsy under the ultrasonic guidance is performed in 74% of cases; open biopsy in 19%; laparoscopic biopsy in 5% [4–5]. |

**Q3:** Please tell me about the method of percutaneous kidney biopsy in Japan

| A3: | - Patients lie on the face and on the stomach.  
- A renal place is confirmed by US.  
- From the skin of back surface to the renal surface, local anesthetic is injected in the place to be pricked with a needle.  
- Physicians cut around 2–3 mm open on the skin surface to facilitate passage.  
- Real-time US (method to puncture while observing kidney by US) is most commonly used to guide the biopsy needle directly into the lower pole of the kidney (at which the risk of puncturing a major vessel is minimized).  
- After kidney biopsy is completed, physicians exert pressure on the patients from the back for 10–15 min to stop bleeding.  
- Patients turn over onto back. Rest is required in bed for 6–24 h. Eating and drinking after the testing requires the posture of lying down but are possible.  
- Urination and defecation are performed on the bed too. When urination is difficult, the physician may use a urethral catheter.  
- Automatic 14-/16-/18-gauge biopsy needles are used, but 16-/18-gauge biopsy needles are most commonly used in Japan.  
- As an enforcement place of the percutaneous kidney biopsy, ward treatment rooms and hospital rooms are often used.  
- It is important that we maintain infection prophylaxis including the use of a cap and mask, sterile gown, sterile gloves, and sterile drapes for the whole body.  
- Antimicrobial agents are used in 59% of institutions, atropine in 19%, carbazochrome sodium sulfonate hydrate (Adona) in 71%, and tranexamic acid (Transamin) in 54% as routine drugs [4, 5, 140–143]. |
Q4: Please tell me about the method of open (surgical) kidney biopsy in Japan

A4: Usually under general anesthesia, the open biopsy is performed.

- Setting the patient in lateral jack-knife position, through 3 cm of horizontal incision from 12 rib tip the muscles are divided in each layer to reach the inferior pole of the kidney covered by adipose tissue. Confirming not to damage the peritoneum, the circumrenal fat and Gerota fascia are cut to reach the surface of kidney. The biopsy gun for needle biopsy on the kidney or the wedge incision for block type specimen is used to take a piece of the kidney. After biopsy, hemostasis is securely performed by pressure with the forefinger for 10–15 min. The muscles and skin are closed in layers to finish the procedure. [144, 145].

Q5: Please tell me about the method of laparoscopic kidney biopsy in Japan

A5

- Under general anesthesia, we put a skin incision of approximately 12 mm at the 12th rib tip with the patient in the side-lying jack-knife position which assumed the biopsy side the upper part and arrive at the retroperitoneum by splitting of muscle.
- After inserting a forefinger, and having abraded, we insert a PDB balloon (an orbicular type or kidney type) and extend retroperitoneum. We insert a 12 mm trocar and start pneumoperitoneum at 8–12 mmHg for the first port (camera port).
- We place a 5-mm trocar on the dorsolumbar group of muscles circumference of the 20 mm head side than the first port at the speculum and assume it the second port (operator left hand).
- We put a 5 mm or 12 mm trocar on the middle point between the anterior armpit line and the rectus abdominis muscle circumference of 20 mm head side than the first port, and we assume it the third port (the operator right hand).
- We confirm the inferior pole of the kidney covered by adipose tissue. We cut the lateral conic fascia open towards the inferior pole of the kidney to avoid damaging the peritoneum. We abrade the circumrenal fat and Gerota fascia and reach the nephric surface.
- We insert a biopsy needle from the second port (the operator right hand) and the third port (operator left hand) and obtain renal tissue at an angle of 60°–90° on the nephric surface.
- The operation using the biopsy needle is simpler and easier as a procedure for laparoscopic approach.
- The hemostasis is carried out using bipolar and soft coagulation, and we perform certain hemostasis using tissue adhesion seats when hemostasis is difficult. The suture hemostasis becomes the choice.
- Finally, we remove each port and put pneumoperitoneum away and sew up the fascia and skin with absorption thread [144, 146].
Q6: Please tell me about the method of transplant kidney biopsy

A6

The percutaneous transplant kidney biopsy is usually performed under the ultrasonic guidance with local anesthesia.

- Because hemostasis pressure can be provided surely as compared with a native kidney biopsy, it is not necessary to discontinue the anticoagulant therapy. However, it is desirable to conduct an examination for coagulation system in advance.
- Under local anesthesia the biopsy needle is put into the kidney to take a piece of the kidney. This may be performed 2–3 times to obtain an adequate specimen.
- Just after the procedure, the physician presses the puncture area for 10–15 min for hemostasis. After that, a 1 kg sandbag is put on the puncture area to maintain pressure for an hour. A small pillow is fixed with elastic tape on the area. Thereafter the patient must lie in bed for 6 h or until seen by the doctor. The patient must pay attention for blood in their urine after the biopsy.
- The fixing elastic tape will be removed on next morning. Before discharge a blood count, biochemistry test, and urinalysis are examined. The discharge is permitted after having confirmed that there is no hematoma and hydronephrosis around the renal graft by US [147–149].

Chapter 6: After care of the biopsy and post procedure observation

Aftercare of the biopsy and postprocedure observation are essential to prevent hemorrhagic complications. After biopsy, bed rest for 6–8 h in an extraneous dressing room is mandated in Europe and America. In Japan, kidney biopsy is performed during hospitalization. Just after the biopsy is performed, pressure is exerted on the back by using both hands and a sandbag for hemostasis. Subsequently, bed rest in the dorsal (supine) position is common [98, 150–160].

Q1: Please tell me about the pressure method using both hands and a sandbag for hemostasis after kidney biopsy

A1

Just after the puncture, we suppress the puncture area with both hands while using our weight in a prone position for 10–15 min, and sequentially for 2–6 h there is a sandbag used while the patient is in prone position in 61.5 % of institutions. Hypotension via the vasovagal reflex by manual pressure should be considered [161, 162].

Q2: Please tell me about the use of a hemostatic agent after kidney biopsy

A2

The use of a hemostatic agent, including carbazochrome sodium sulfonate hydrate (Adona) and tranexamic acid (Transamin), after kidney biopsy has been conducted as a routine method in Japan, but clear evidence of its utility has not been reported. The use of dDAVP is reported as an option for cases with high risk of bleeding [163].

Q3: Please tell me about supine position, rest time (time before changing position including the lateral position) after kidney biopsy, and time during bed rest (time before taking an erect position and walking)

A3

Dorsal (supine) position rest time after kidney biopsy is 4–6 h, and the remaining time for bed rest is 16–24 h, or until the next morning. Hemorrhagic complications after kidney biopsy are high risk within the first 5 h; <4 h (38%), 4–8 h (29%), 8–12 h (22%), 12–24 h (2%) [127, 164–166].

Q4: Please tell me about an examination of drawing blood after kidney biopsy

A4

Drawing blood the next morning is normative [164].

Q5: Please tell me about US after kidney biopsy

A5

US just after kidney biopsy is normative. If hematoma is detected, an observation that is more elaborate is necessary [167, 168].
**Q6:** Please tell me about the resumption time of anticoagulant and the antiplatelet drug after kidney biopsy

**A6**
Resumption at 1–2 days after biopsy is normative, or resumption at the time when hemostasis was confirmed is normative. It is determined in consideration of the underlying disease, drug type, dose, and amount bleeding after the biopsy. There is a report of discontinuation of anticoagulant for 7 days in cases that are not of high thrombotic risk [4, 5].

**Q7:** Please tell me about the days of physical limitation after kidney biopsy

**A7:** It is reported that bleeding after kidney biopsy occurs for 5–7 days after the procedure. As for physical limitation after kidney biopsy, normal exercise and light work are permitted after 1-2 weeks, and strong exercise including loading is permitted after four weeks [4, 5].

**Q8:** Please tell me about the period of hospital stay for kidney biopsy

**A8**
In Japan, kidney biopsy and recovery are undergone in a hospital. Four days and three nights to 6 days and five nights of hospital stay are normative [4, 5]. In Europe and America, there are two types of options including overnight hospitalization and the outpatient department. Complete bed rest of 4-h is required after kidney biopsy, and subsequently for 12–24 h, bed rest is also required. Moreover, in these cases, recovering near the hospital, including at a hotel, is required.

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**Chapter 7: Complications**

According to the questionnaire survey results that were performed for the publication of this book, among 21,648 kidney biopsy cases that were performed in Japan, gross hematuria after kidney biopsy was found in 511 patients (2.4%), bladder wash was in 79 cases (0.36%), red blood cell transfusion was in 161 cases (0.74%), renal arterial embolization was in 44 cases (0.22%), and death occurred in one case (0.005%). The underlying cause of death in this case was not due to bleeding after kidney biopsy, but the overall status of this case was confirmed poor before kidney biopsy and worsened after kidney biopsy (Table 5) [1, 4, 5, 66, 74, 156, 169–174].

**Q1:** Please tell me about complications of kidney biopsy

**A1**
Because the kidney has abundant blood vessels, bleeding complications after kidney biopsy are an issue. Before testing and during testing, vasovagal reflex symptoms, including nausea, vomiting, hypotension and bradycardia from excessive tension, are common, and lumbago due to lying in the bed after undergoing kidney biopsy is also common, but it is transient. Bleeding complications after kidney biopsy are of high concern and can occur at four sites: (1) bleeding into the urinary tract, leading to microscopic or gross hematuria and possible ureteral obstruction; (2) bleeding into the subcapsular space, leading to pain via pressure tamponade; (3) bleeding into the perinephric space, leading to hematoma formation and a possibly a large fall in hematocrit; (4) intrarenal bleeding. The bleeding subsides and is absorbed within a few days or within 1 month.

**Q2:** Please tell me about clinical conditions that are easy to cause bleeding complications

**A2**
According to the questionnaire survey, out of 44 patients who presented with serious renal bleeding that required renal artery embolization, patients with an underlying disease that is considered as a risk factor are small. This indicates that we should recognize that serious renal bleeding may occur in cases that are not at high risk [4, 5, 77, 175–179].
Q3: Please tell me about the relation between the diameter of the needle in kidney biopsy and bleeding complications

A3
Three kinds of needles of 14 G, 16 G and 18 G are used in Japan, and 16 G is most often used. There is no reported relation between the diameter of the needle and bleeding complications. While, 18 G has few bleeding complications, there are reports of retrieving too few glomerular numbers [4, 5, 104, 180–182].

Q4: Please tell me about the relationship between puncture number and renal bleeding

A4: No report that renal bleeding was common in cases with many numbers of punctures was obtained [4, 5, 130, 183].

Q5: Please tell me about appropriate blood pressure management during kidney biopsy

A5
It is suggested that we avoid extreme hypertension during kidney biopsy, but absolute restriction on BP is not described. Many institutions in Japan aim for systolic BP that is lower than 160 mmHg, and diastolic BP that is lower than 100 mmHg. For patients receiving antihypertensive medications, these drugs are administered on the morning before biopsy and are adjusted while examining the status of the BP, after kidney biopsy enforcement [184].

Q6: Please tell me about other bleeding complications.

A6
Pain lasting more than 12 h is observed and is considered due to ureteral obstruction from a blood clot in patients with gross hematuria, or due to stretching of the renal capsule by a subcapsular hematoma. Arteriovenous fistulas formation due to damage to the walls of an adjacent artery and vein is important but resolves spontaneously over 1–2 years. The "page kidney" related to a large subcapsular hematoma can lead to chronic hypertension due to persistent activation of renin angiotensin. Puncture of the liver, pancreas, spleen, or intestine may occur. Urinoma formation from puncture of the urinary tract occurs rarely. Injury of the lumbar artery running through the back has been reported [185–193].

Q7: Please tell me about the treatment for subcapsular bleeding, perinephric bleeding, and intrarenal bleeding after kidney biopsy

A7: These types of bleeding subside within a few days or within 1 month, but there are serious cases requiring renal transarterial embolization (TAE). According to the questionnaire survey that was performed for the publication of this book, renal TAE for these serious bleedings was performed in 32 cases (0.17%) [4, 5, 194–196].
Q8: Please tell me about the treatment for gross hematuria due to bleeding into a urinary tract

A8
This bleeding also subsides spontaneously within a few days or within 1 month, but when gross hematuria due to massive bleeding into the urinary tract persists, hematoma occcludes exit parts of the bladder, resulting in bladder tamponade. A urethral catheter is inserted, and the hematoma is removed while performing a bladder wash. However, for serious cases, renal TAE is required. According to the questionnaire survey that was performed for the publication of this book, renal TAE for this type of serious bleeding was performed in five cases (0.02%) [4, 5, 167,197].

Chapter 8: Histological evaluation of kidney biopsy specimen

Kidney biopsy remains the gold standard to diagnose renal disease and evaluate acute and chronic renal damages. Specimens are processed for the diagnostic approach of light microscopy (LM), immunostaining by immunofluorescence (IF) or immunohistochemistry, and electron microscopy (EM). To minimize the bleeding risk, less passes to obtain tissue is desirable; on the other hand, sufficient quantity of tissue is required for definite diagnosis. When small sample size of renal tissues was obtained, dividing samples appropriately into LM, IF, and EM studies should be carefully considered (Fig. 2).

Q1: Please tell me appropriate sample dividing of the kidney biopsy

A1
In most of the institutions, 1 to 3 kidney biopsy cores are obtained. Ideally, biopsy cores should contain predominantly cortical tissue. The core should be divided in a manner to maximize glomeruli in each of the samples for LM, IF and EM. It is necessary to secure two or three small tissue fragments of more than 1.5 mm for IF and EM (Fig 2). Regarding LM examination, it is estimated that glomerular number of 20-25 is necessary to evaluate glomerular lesion appropriately [198–201].

Q2: Please tell me the tissue processing of light microscope specimens

A2
For the adequate tissue quality, specimens must be fixed, and the most commonly used fixative is 10% neutral buffered formalin (formaldehyde). Some laboratories prefer alcoholic Duboscq-Brasil fixatives that provide better preservation of certain morphological structures. On daily practice, standard thickness of the sectioning is approximately 1-2 μm. Routine staining consists of hematoxylin and eosin, PAS, PAM, Masson trichrome, and Elastica- or PAM-Masson trichrome that permit the diagnosis in most cases. According to the microscopic findings, other staining will be added such as Congo Red and phosphotungstic acid hematoxylin (PTAH). In case of rapid diagnosis, samples can be processed within 8 to 24 h after the biopsy [4, 5].
Q3: Please tell me the practical applications of IF studies

A3
A frozen section (cryosection) is a pathological laboratory technique used for rapid microscopic examinations. In the renal pathology, frozen sections are also utilized for IF studies and plays a pivotal role in the pathological diagnosis. Samples are frozen immediately after tissue obtaining, and a fresh frozen sections are prepared using cryostat with 2-3um thickness. A routine antibody panel for IF on native kidney biopsy consists of IgG, IgA, IgM, C1q, and C3; C4 staining is performed in approximately 60% of institutions. Immunostaining of fibrinogen and albumin are not commonly used in Japan. In transplant kidney biopsy, C4d staining is required to evaluate antibody-mediated rejection. IgG subclass staining (IgG1, IgG2, IgG3, IgG4) has been shown to be of great diagnostic utility in glomerular diseases that includes IgG-containing immune-type deposits. IgA subclass staining (IgA1, IgA2) may be also added for a diagnosis of IgA-containing immune type glomerulonephritis [202].

Q4: Please tell me the practical applications of immunohistochemical studies

A4
Immunohistochemistry is an extraordinarily powerful tool in the routine diagnostic workflow of the surgical pathology, applied to numerous diseases such as cancer, inflammatory disorders, and degenerative diseases. Immunohistochemistry is also an important tool to diagnose various renal diseases; the increased ratio of IgG4/IgG-positive plasma cells (>40%) provides critical diagnostic criteria for IgG4-related renal disease. Immunostaining of Amyloid A, Amyloid light chain (κ and λ), β2-microglobulin, and transthyretin is essential to classify subtypes of renal amyloidosis. The anti-SV40 and anti-adenovirus antibodies are required to diagnose BK virus and adenovirus nephropathy in the renal allograft [203].

Q5: Please tell me the concise method of sample preparation for the electron microscopic studies

A5
The samples are fixed with glutaraldehyde and osmium tetraoxide, followed by epoxy resin embedding and ultra-thin sectioning. Specimens are stained with heavy metals including lead and uranium to scatter electrons and thereby give contrast between different biological structures. In the diagnostic process of renal biopsy, approximately 60% of cases can be diagnosed based on the findings of light microscopy and immunostaining. Remaining 40% requires the findings revealed by the electron microscopy.
Q6: Please tell me about the current applications of special techniques

A6
In some challenging cases that require further evaluations, special techniques such as in situ hybridization (ISH), polymerase chain reaction (PCR), and laser microdissection followed by mass spectrometry analysis can be applied. In the case of post transplantation lymphoproliferative disorders, ISH (κ and λ) can be used to evaluate light chain restriction. ISH targeting Epstein-Barr virus-encoded small RNA (EBER) is extremely useful to examine the involvement of EB virus. For the suspicious cases of malignant lymphoma, PCR is applicable from the paraffin sections to detect immunoglobulin and T cell receptor gene rearrangement. The robust utility of the proteomics analysis using a mass spectrometry device has been reported in the diseases such as amyloidosis where immunohistochemical studies were unsuccessful due to non-specific staining. Identifying the subcomponents of monoclonal light chain or heavy chain defines the diagnosis of AL or AH amyloidosis. With respect to the renal transplant rejection, accumulating evidence compiled through gene expression profiles provides the mechanistic insights and molecular classification of specific rejection type; antibody versus T cell mediated rejection.

Q7: Please tell me the rules regarding the handling of personal information

A7
Regarding the tissue samples, histological images as well as genomic sequence data obtained from kidney biopsy paraffin or frozen sections, it is important to ensure that the individual’s privacy is respected. Samples and obtained data including DNA sequences should be handled according to the Act on the Protection of Personal Information (Act No. 57 of 2003).

Chapter 9: Kidney biopsy in children

Kidney biopsy in the pediatric population was reported for the first time in 1958 and has a history of more than 60 years [204]. The procedure has become relatively safe in children as well as in adults owing to technical advances and improvement of medical devices. However, the indication for kidney biopsy must be carefully determined based on benefits and potential risks for serious bleeding complications.

Indication of kidney biopsy (Table 6)

Q1: Please tell me about the indication of kidney biopsy for patients with isolated glomerular hematuria

A1
Isolated glomerular hematuria showing dysmorphic erythrocytes does not commonly become an indication for kidney biopsy, because renal function is less likely to decrease. However, for patients with gross hematuria at the time of cold or a family history of renal failure, kidney biopsy may be useful, because there is a possibility of hereditary nephritis and IgA nephritis resulting in a decrease of renal function [4, 205].
Q2: Please tell me about the indication of kidney biopsy for patients with isolated proteinuria

A2
When morning urine protein/creatinine ratio (U-TP/Cr) ≥ 0.5 g/gCr persists for more than 3 months and renal function decreases, kidney biopsy often presents renal histology except for the minimal change nephrotic syndrome (MCNS). In the pediatric population, for patients with nephrotic syndrome with severe proteinuria, treatment including steroids often precedes without kidney biopsy, because the histopathology shows MCNS in more than 90% of patients with childhood idiopathic nephrotic syndrome. For steroid-resistant nephrotic syndrome where remission is not obtained by steroid therapy, kidney biopsy is indicated. When coexistence of hematuria, hypertension, renal dysfunction, and hypocomplementemia is present, kidney biopsy is also indicated.

Q3: Please tell me about the kidney biopsy of patients with both proteinuria and glomerular hematuria

A3
For patients presenting with both proteinuria and glomerular hematuria, kidney biopsy is indicated because chronic glomerulonephritis including IgA nephropathy, membranoproliferative glomerulonephritis, etc., is diagnosed histologically [4, 5].

Q4: Please tell me about kidney biopsy of patients with rapidly progressive glomerulonephritis or acute kidney injury (AKI)

A4
Kidney biopsy is indicated according to adult criteria [4, 5].

Table 5: Bleeding complications after kidney biopsy

|                      | Percutaneous native kidney biopsy | Open biopsy | Transplanted kidney biopsy |
|----------------------|----------------------------------|-------------|---------------------------|
| Total number of biopsies | Adult 15,657                     | 1,085       | 3,898                     |
|                      | Children 431 (2.8%)               | 105 (6.2%)  | 12 (0.31%)                |
| Macroscopic hematuria with no treatment | Adult 1,065 (6.2%)                | 4 (0.35%)   | 2 (0.05%)                 |
| Erythrocyte transfusion | Adult 121 (0.8%)                  | 1 (0.06%)   | 0 (0.05%)                 |
| Transcatheter arterial embolization | Adult 31 (0.2%)                   | 9 (0.5%)    | 0 (0.05%)                 |
| Bladder lavage        | Adult 56 (0.4%)                   | 9 (0.5%)    | 0 (0.05%)                 |
| Nephrectomy           | Adult 0 (0%)                      | 1 (0.03%)   | 0 (0.05%)                 |

Results from questionnaire survey for kidney biopsy that was performed in Japan from 2015 through 2017
Table 6  Indication of kidney biopsy in children

| 1. Abnormal urinalysis | 1. Isolated proteinuria 0.5 g/gCr or more |
|------------------------|------------------------------------------|
| 2. Nephrotic syndrome  | 2. Proteinuria and glomerular hematuria    |
| 2. Steroid-resistant nephrotic syndrome | 1. Steroid-resistant nephrotic syndrome |
| 2. Coexistence of hematuria, hypertension, renal dysfunction, and hypocomplementemia | 2. Coexistence of hematuria, hypertension, renal dysfunction, and hypocomplementemia |
| 3. Systemic disease with a urinalysis abnormality | 3. Congenital nephrotic syndrome |
| 1. Systemic lupus erythematosus | 1. Systemic lupus erythematosus |
| 2. IgA vasculitis (Purpura nephritis) | 2. IgA vasculitis (Purpura nephritis) |
| 3. Microscopic polyangiitis | 3. Microscopic polyangiitis |
| 4. Others | 4. Others |
| 4. Intrinsic acute kidney injury | 1. Drug-related disease |
| 5. Others | 2. Transplanted kidney |

Q5: Please tell me about the utility of kidney biopsy for renal disease secondary to systemic disease including autoimmune disease

A5
Kidney biopsy is indicated according to adult criteria [4, 5, 206–209].

Q6: Please tell me about kidney biopsy for hereditary renal disease such as Alport syndrome, Fabry disease, mitochondria disease, polycystic kidney disease

A6
Kidney biopsy is not essential in the current medical care that genetic screening developed but is useful for diagnosis or differential diagnosis [210–213].

Kidney biopsy for clinical condition with high risk

Kidney biopsy is indicated according to adult criteria [214].

Pre-biopsy evaluation

We may need sedation or general anesthesia in children. Therefore, it is necessary to evaluate the airway and the overall status (underlying disease) beforehand.

Q1: Please tell me about the evaluation of bleeding tendency before kidney biopsy

A1
In addition to a platelet count, PT, and APTT by blood test, we should identify the patient history and family history of previous bleeding [215–218].

Q2: Please tell me about kidney biopsy for patients with thrombocytopenia

A2
For patients with thrombocytopenia <50,000/μL or <100,000/μL, the final decision of whether you perform kidney biopsy should be based on each institutional forum [219].

Q3: Please tell me about kidney biopsy for patients with renal dysfunction or hypertension

A3
The final decision whether you perform kidney biopsy or not should be judged based on each institutional forum [220–222].
### Informed consent for kidney biopsy, explanation about kidney biopsy

#### Q1: What point is important in informed consent of kidney biopsy?

**A1**

The basic way of obtaining informed consent is similar to that for an adult case. However, in children, the methods and complications of sedation should be explained as needed [4].

#### Q2: Is it necessary to obtain consent for blood transfusion before kidney biopsy?

**A2**

Acquisition of the transfusion's consent should be judged based on each institutional forum [220, 223].

#### Q3: Please tell me about the explanation document to patients

**A3**

An explanation document to the patients follows the adult case, but the agreement of parents is important [4].

### Method of kidney biopsy (technique)

#### Q1: Please tell me about the method of kidney biopsy in the pediatric population

**A1**

Percutaneous needle kidney biopsy was performed in the pediatric population in 96% of institutions [183, 224, 225].

#### Q2: Please tell me about the indication of open kidney biopsy

**A2**

Open biopsy is chosen for high risk cases and infants [4].

#### Q3: Please tell me about the diameter of the needle

**A3**

Two kinds of needles of 16 G and 18 G are used in Japanese children. The 16 G is used in 65% of institutes, and 18 G is used in 35% of institutes [77, 157, 220, 226–229].

### Sedation

#### Q1: Please tell me about sedation of children

**A1**

Patients cannot often sleep perioperatively and postoperatively because of anxiety or a sense of fear. It is necessary to try to relax in such cases. Kidney biopsy is performed primarily in a ward or an operating room.
Q2: Please tell me about the method of sedation

A2
The safety of sedatives in children is not fully established, and most of sedatives are used off-label. Moreover, it is necessary to set a dose while considering age, renal function, liver function of the patients. Generally, for sedation by intravenous anesthesia of children, complications such as a decrease of oxygen saturation related to laryngospasm and bronchospasm due to increased airway hypersensitivity, and hypotension or bradycardia by the vasovagal impulse are common. It is important to monitor the electrocardiogram, oxygen saturation (SpO2), and BP in sedation [160, 230–233].

Q3: Please tell me about fasting before induction of anesthesia

A3
For preoperative eating and drinking, light meal, artificial milk, and milk are possible until 6 h before biopsy. Mother's milk can be fed until 4 h. Clear water can be fed until 2–3 h.

Q4: Please tell me about premedication

A4
Hydroxyzine (Atarax P) (1 mg/kg) and diazepam (0.2–0.4 mg/kg), pethidine (weak Pethilorfan) (1 mg/kg) are often administered for relieving preoperative anxiety. Atropine sulfate (0.01–0.02 mg/kg) is used to inhibit the sudden bradycardia, hypotension, salivation, and airway secretion due to the parasympathetic reflex.

Q5: Please tell me about intravenous anesthetic

A5
Intravenous anesthetics are used off-label for sedation of children. It is important to obtain informed consent from caregivers of the patients. Because intravenous anesthetics often cause respiratory depression and BP fluctuation, careful monitoring is required [234–241].

1. Ketamine (Ketalar) (initial dose, 1–2 mg/kg): duration of action is 5–10 min.
2. Midazolam (Dormicum) (initial dose, 0.05–0.1 mg/kg): half-life in blood is 0.8–1.8 h.
3. Pentazocine (Sosegon) (initial dose, 0.5–1.5 mg/kg): half-life in blood is 3–4 h
4. Thiopental (Ravonal), Thiamylal (Isozol) (initial dose, 4–6 mg/kg): duration of action is ten minutes.
5. Propofol (Diprivan) (initial dose, infants 3–5 mg/kg, older children 2.5–3 mg/kg): duration of action is 5–15 min.

After care of the biopsy and post procedure observation

Q1: Please tell me about the pressure method of using both hands

A1
Just after the puncture, we suppress the puncture department with both hands while using our weight in prone position for 10–15 min. This follows from adult cases [195].

Q2: Please tell me about supine position rest time (time before changing position including the lateral position)

A2
Supine position rest time after kidney biopsy is 4–8 h [4, 233, 242–244].
**Chapter 10: Biopsy of transplanted kidney**

For the long-term engraftment after the renal transplant, early detection and early treatment for rejection or early detection of the side effect with the immunosuppressive drug are important. Because treatment totally varies according to clinical condition, the pathological evaluation of the renal graft tissue is important in treatment strategy decision. These clinical conditions occur asymptptomatically and may progress.

1. **Episode biopsy:** Transplant kidney biopsy is generally performed when an acute renal allograft rejection is suspected within a year after operation. The main clinical indicator is an increase in serum creatinine levels of 20% above a baseline value. Furthermore, a year after operation, for patients with renal dysfunction or proteinuria, the following diseases are clarified by kidney biopsy: chronic allograft nephropathy (CAN), chronic rejection (antibody-mediated rejection and T cell-mediated rejection), recurrence of underlying disease and calcineurin inhibitors nephrotoxicity [76, 149, 249].

2. **Protocol biopsy:** kidney biopsy is performed at the renal transplant surgery for 0 h (just after perfusion of the isolated kidney), an hour (after renal graft blood flow resumption), at post transplantation 2–3 months, and at a year after. Whether immunosuppressive therapy is appropriate, asymptomatic acute rejection occurs, or underlying disease recurs can be determined.

**Complications**

**Q1:** Please tell me about complications of kidney biopsy

**A1**
Bleeding complications after kidney biopsy are important, but the occurrence of serious cases is rare. According to the questionnaire results that obtained for the publication of this book, among 1685 pediatric kidney biopsy cases that were performed in Japan, gross hematuria after kidney biopsy was found in 105 patients (6.2%) and bladder wash in 9 cases (0.5%). Renal arterial embolization occurred in one case (0.03%) (Table 5) [4, 77, 176, 222, 248].

**Q3:** Please tell me about the examination of drawing blood after kidney biopsy

**A3**
The next morning is normative. This follows adult cases [4, 245].

**Q4:** Please tell me about US after kidney biopsy

**A5**
After 16–24 h are normative. The observation that is more elaborate when hematomas is detected is necessary [4, 188, 246].

**Q5:** Please tell me about the period of hospital stay for kidney biopsy

**A5**
In Japan, kidney biopsy is undergone at the hospital. More than 5 days and five nights of hospital stay is normative [4, 5, 127, 247].
Q2: Please tell me about complication of renal graft biopsy

A2
Because hemostasis after renal graft biopsy can be performed more surely by pressure, rest after testing is less strict than native kidney biopsy. However, for bleeding complication, attention is necessary. According to the questionnaire survey that was performed for the publication of this book, among 3,868 kidney biopsy cases that were performed in Japan, gross hematuria after kidney biopsy was found in 12 patients (0.31%), renal TAE for this serious bleeding was performed in four cases (0.1%), and nephrectomy of renal graft was performed in one case (0.03%) (Table 5) [74, 147, 148, 250, 251].

Q3: Please tell me about the period of hospital stay for kidney biopsy

A3
In Japan, almost of kidney biopsy are undergone as inpatient. Two days and one night (47%) or 3 days and two nights (29%) of hospital stay are more frequent. The rate of occurrence of hospital stay for more than 4 days and three nights is 24% [4].

Chapter 11: Open (surgical) kidney biopsy and laparoscopic kidney biopsy

Q1: Who needs open (surgical) kidney biopsy in Japan?

A1
The following situation is included; (1) when there is an uncorrectable bleeding diathesis; (2) when there is a solitary kidney; and (3) after failed attempts at percutaneous biopsy.

Surgeons directly look at the surface of the kidneys and determine the area from which the tissue samples should be taken. There are two type of methods including a needle biopsy and wedge biopsy. The incidence of severe bleeding of renal surface is very low, and mortality is rare, but the risk of hemorrhage into the urinary tract exists. Attention is necessary for the development of renal arteriovenous fistula (arteriovenous fistula: AVF) causing bleeding to the urinary tract. Other relatively minor postoperative complications including fever, atelectasis, and ileus can occur. In addition, an open biopsy under general anesthesia is associated with a longer hospital stay and a larger surgical scar. On wedge biopsy, the specimens may increase the proportion of shallow layer of the cortex resulting in less information of the cortex deep part and medulla [4].

Q2: Please tell me about complication of open (surgical) kidney biopsy

A2
According to the questionnaire survey that was performed for the publication of this book, among 1,156 kidney biopsy cases that were performed in Japan, gross hematuria after kidney biopsy was found in 9 patients (0.78%), renal TAE for this serious bleeding was performed in 2 cases (0.17%) (Table 5).

Q3: Please tell me about laparoscopic kidney biopsy in Japan

A3
Laparoscopic kidney biopsy is advocated by some surgeons as an alternative method to open kidney biopsy for patients unable or unwilling to undergo percutaneous kidney biopsy.

- As for the complications peculiar to laparoscopic kidney biopsy, nephric subcapsular hematoma, subcutaneous emphysema, peritoneal injury, and injury of the circumference organ are reported.
- An advantage of laparoscopic kidney biopsy in comparison with the percutaneous kidney biopsy includes certain sampling of renal tissue as well as confirmation and hemostasis of a bleeding point.
• An advantage of laparoscopic kidney biopsy in comparison to open kidney biopsy includes shortening of the hospital stay, pain reduction, and compatibility of the incised wound [4].

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Compliance with ethical standards

Conflict of interest No authors have declared any competing interest about the contribution of this article. All the authors have declared no conflict of interest exists.

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