Clinical and Experimental Nephrology (2021) 25:325–364
https://doi.org/10.1007/s10157-020-01986-6

SPECIAL REPORT

Kidney biopsy guidebook 2020 in Japan

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Published online: 19 February 2021

Keywords Kidney biopsy · Indication of kidney biopsy in adults · Indication of kidney biopsy in children · Percutaneous native kidney biopsy under the ultrasonic guidance · Open (surgical) kidney biopsy and laparoscopic kidney biopsy · Relative contraindication for percutaneous native kidney biopsy · Bleeding complications after kidney biopsy

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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GPA	Granulomatosis with polyangiitis
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HUS	Hemolytic-uremic syndrome
HIV	Human immunodeficiency virus
IF	Immunofluorescence microscopy
ISH	In situ hybridization
LM	Light microscopy
MRI	Magnetic resonance imaging
MPA	Microscopic polyangiitis
MN	Membranous nephropathy
MCNS	Minimal change nephrotic syndrome
NAG	*N*-Acetyl-β-D-glucosaminidase
PT	Prothrombin time
PCR	Polymerase chain reaction
RNP	Anti ribonucleoprotein antibody
SI	Selectivity index
SM	Anti-Smith (anti-Sm) antibody
SLE	Systemic lupus erythematosus
TMA	Thrombotic microangiopathy
TTP	Thrombotic thrombocytopenic purpura
TAFRO	Thrombocytopenia, anasarca, myelofibrosis, renal dysfunction, and organomegaly
US	Ultrasonography
α1MG	α1-Microglobulin
β2MG	β2-Microglobulin

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 tubulointerstitial 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 biopsied 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].

Table 3 Clinical condition of the high risk (equaling relative contraindication) for percutaneous native kidney biopsy under ultrasonic guidance

1. Solitary native kidney
2. Contracted kidneys, small hyperechoic kidneys or end-stage kidneys
3. Kidneys of anatomic abnormalities including horseshoe kidney, malrotation kidney and renal arterial aneurysm
4. Polycystic kidney disease
5. Hydronephrosis
6. Malignant nephrosclerosis related to hypertensive emergency and scleroderma renal crisis
7. Uncontrolled bleeding diathesis or severe thrombocytopenia
8. Pregnancy
9. Severe obesity
10. Renal mass including malignant neoplasma
11. Chronic anticoagulant therapy while taking antiplatelet or anticoagulant medication
12. Active renal or perirenal infection, or skin infection over the biopsy site
13. Inability to provide informed consent
14. Uncooperative patient or inability to follow instructions during biopsy

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

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
Dipyridamole	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

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.

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.

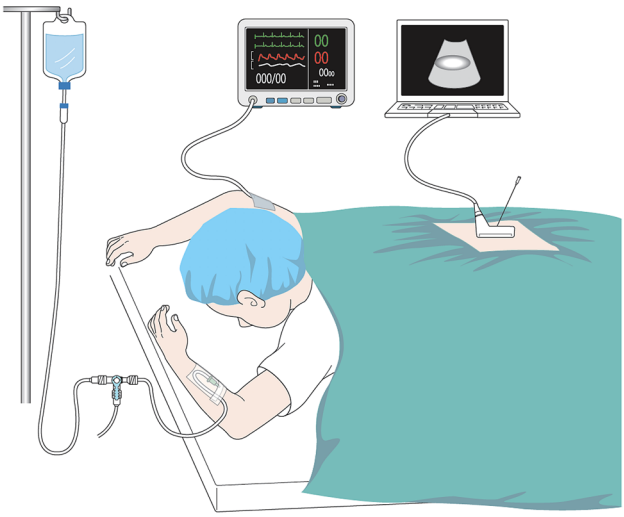

Fig. 1 How to do a kidney biopsy

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 overdoing 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.

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.

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.

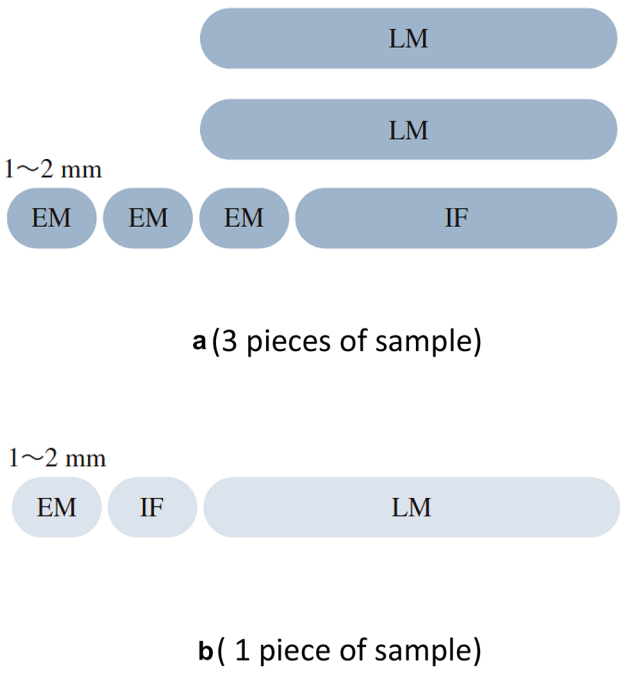

Fig. 2 How to divide a sample of the kidney biopsy

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. Radioisotope 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.

Q2: 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).

Chapter 5. Method of kidney biopsy (technique)

Q1: 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.

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 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 occludes 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 Adult	Percutaneous native kidney biopsy Children	Open biopsy	Transplanted kidney biopsy
Total number of biopsies	15,657	1685	1156	3808
Macroscopic hematuria with no treatment	431 (2.8%)	105 (6.2%)	9 (0.78%)	12 (0.31%)
Erythrocyte transfusion	121 (0.8%)	0 (0%)	4 (0.35%)	2 (0.05%)
Transcatheter arterial embolization	31 (0.2%)	1 (0.06%)	2 (0.17%)	4 (0.1%)
Bladder lavage	56 (0.4%)	9 (0.5%)	0 (0%)	0 (0%)
Nephrectomy	0 (0%)	0 (0%)	0	1 (0.03%)

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. Proteinuria and glomerular hematuria
2. Nephrotic syndrome	1. Steroid-resistant nephrotic syndrome
	2. Coexistence of hematuria, hypertension, renal dysfunction, and hypocomplementemia
	3. Congenital nephrotic syndrome
3. Systemic disease with a urinalysis abnormality	1. Systemic lupus erythematosus
	2. IgA vasculitis (Purpura nephritis)
	3. Microscopic polyangiitis
	4. Others
4. Intrinsic acute kidney injury	
5. Others	1. Drug-related disease
	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 (SpO_2), 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].

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 hematoma 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].

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].

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 asymptomatically and may progress.

Q1: Please tell me about transplant kidney biopsy

A1

Kidney biopsy that is performed at renal dysfunction such as rejection is named episode biopsy, and premeditated kidney biopsy that is also performed just after renal transplant and at constant time even for the time when renal function is stable is named protocol biopsy.

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.

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].

Acknowledgements The study was supported by the Japanese Society of Nephrology. The authors would like to thank Naoki Kashihara (President of the Japanese Society of Nephrology), and the members of the Japanese Society of Nephrology.

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.

References

1. Japanese Society of Nephrology. Guidebook of the kidney biopsy. Tokyo: Tokyo-Igakusha; 2004. (**In Japanese**).
2. Salama AD, Cook HT. The kidney biopsy. In: Skorecki K, Chertow GM, Marsden PA, Taal MW, Yu AS, editors. Brenner & Rector's The Kidney. 10th ed. New York: Elsevier; 2016.
3. Dhaun N, Bellamy CO, Cattran DC, Kluth DC. Utility of kidney biopsy in the clinical management of renal disease. Kidney Int. 2014;85:1039–48.
4. Kawaguchi T, Nagasawsa T, Tsuruya K, Miura K, Katsuno T, Morikawa T, Ishikawa E, Ogura M, Matsumura H, Kurayama R, Matsumoto S, Marui Y, Hara S, Maruyama S, Narita I, Okada H, Ubara Y, Committee of Practical Guide for Kidney Biopsy 2019. Correction to: A nationwide survey on clinical practice patterns and bleeding complications of percutaneous native kidney biopsy in Japan. Clin Exp Nephrol. 2020a;24(5):389–401.
5. Kawaguchi T, Nagasawsa T, Tsuruya K, Miura K, Katsuno T, Morikawa T, Ishikawa E, Ogura M, Matsumura H, Kurayama R, Matsumoto S, Marui Y, Hara S, Maruyama S, Narita I, Okada H, Ubara Y, Committee of Practical Guide for Kidney Biopsy 2019. A nationwide survey on clinical practice patterns and bleeding complications of percutaneous native kidney biopsy in Japan. Clin Exp Nephrol. 2020b;24(5):402–3.
6. Yamagata K, Takahashi H, Tomida C, Yamagata Y, Koyama A. Prognosis of asymptomatic hematuria and/or proteinuria in men. High prevalence of IgA nephropathy among proteinuric patients found in mass screening. Nephron. 2002;91:34–42.
7. Kawamura T, Ohta T, Ohno Y, Wakai K, Aoki R, Tamakoshi A, Maeda K, Mizuno Y. Significance of urinalysis for subsequent kidney and urinary tract disorders in mass screening of adults. Intern Med. 1995;34:475–80.
8. Nieuwhof C, Doorenbos C, Grave W, de Heer F, de Leeuw P, Zeppenfeldt E, van Breda Vriesman PJ. A prospective study of the natural history of idiopathic non-proteinuric hematuria. Kidney Int. 1996;49:222–5.
9. Vivante A, Afek A, Frenkel-Nir Y, Tzur D, Farfel A, Golan E, Chaiter Y, Shohat T, Skorecki K, Calderon-Margalit R. Persistent asymptomatic isolated microscopic hematuria in Israeli adolescents and young adults and risk for end-stage renal disease. JAMA. 2011;306:729–36.
10. Richards NT, Darby S, Howie AJ, Adu D, Michael J. Knowledge of renal histology alters patient management in over 40% of cases. Nephrol Dial Transplant. 1994;9:1255–9.
11. Iseki K, Ikemiya Y, Iseki C, Takishita S. Proteinuria and the risk of developing end-stage renal disease. Kidney Int. 2003a;63:1468–74.
12. Iseki K, Ikemiya Y, Iseki C, Takishita S. The okinawa screening program. J Am Soc Nephrol. 2003b;14(7 Suppl 2):S127-130.
13. Berden AE, Ferrario F, Hagen EC, Jayne DR, Jennette JC, Joh K, Neumann I, Noël LH, Pusey CD, Waldherr R, Bruijn JA, Bajema IM. Histopathologic classification of ANCA-associated glomerulonephritis. J Am Soc Nephrol. 2010;21:1628–36.
14. Muso E, Endo T, Itabashi M, Kakita H, Iwasaki Y, Tateishi Y, Komiya T, Ihara T, Yumura W, Sugiyama T, Joh K, Suzuki K. Evaluation of the newly proposed simplified histological classification in Japanese cohorts of myelo-peroxidase-anti-neutrophil cytoplasmic antibody-associated glomerulonephritis in comparison with other Asian and European cohorts. Clin Exp Nephrol. 2013;17:659–62.
15. Berden AE, Jones RB, Erasmus DD, Walsh M, Noël LH, Ferrario F, Waldherr R, Bruijn JA, Jayne DR, Bajema IM, European Vasculitis Society. Tubular lesions predict renal outcome in anti-neutrophil cytoplasmic antibody-associated glomerulo-nephritis after rituximab therapy. J Am Soc Nephrol. 2012;23:313–21.
16. Merkel F, Pullig O, Marx M, Netzer KO, Weber M. Course and prognosis of anti-basement membrane antibody (anti-BM-Ab)-mediated disease: report of 35 cases. Nephrol Dial Transplant. 1994;9:372–6.
17. Levy JB, Turner AN, Rees AJ, Pusey CD. Long-term outcome of anti-glomerular basement membrane antibody disease treated with plasma exchange and immunosuppression. Ann Intern Med. 2001;134:1033–42.
18. Alchi B, Griffiths M, Sivalingam M, Jayne D, Farrington K. Predictors of renal and patient outcomes in anti-GBM disease: clinicopathologic analysis of a two-centre cohort. Nephrol Dial Transplant. 2015;30:814–21.
19. Kellum JA, Lameire N, KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care. 2013;17:204.
20. Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, Choudhury D, Finkel K, Kellum JA, Paganini E, Schein RM, Smith MW, Swanson KM, Thompson BT, Vijayan A, Watnick S, Star RA, Peduzzi P. Intensity of renal support in critically ill patients with acute kidney injury". N Engl J Med. 2008;359:7–20.
21. Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, Balow JE, Bruijn JA, Cook T, Ferrario F, Fogo AB, Ginzler EM, Hebert L, Hill G, Hill P, Jennette JC, Kong NC, Lesavre P, Lockshin M, Looi LM, Makino H, Moura LA, Nagata M, International Society of Nephrology Working Group on the Classification of Lupus Nephritis. The classification of glomerulonephritis in systemic lupus erythematosus revisited. J Am Soc Nephrol. 2004;15:241–50.
22. Parikh SV, Rovin BH. Current and emerging therapies for lupus nephritis. J Am Soc Nephrol. 2016;27:2929–39.

23. Almaani S, Meara A, Rovin BH. Update on lupus nephritis. Clin J Am Soc Nephrol. 2017;12:825–35.
24. Toriu N, Sawa N, Oguro M, Mizuno H, Oshima Y, Hasegawa E, Sumida K, Suwabe T, Kawada M, Ueno T, Hayami N, Sekine A, Hiramatsu R, Yamanouchi M, Hoshino J, Takaichi K, Ohashi K, Fujii T, Yanagita M, Ubara Y. Renal-limited cryoglobulinemic vasculitis: two case reports. Intern Med. 2018;57(13):1879–86.
25. Endo A, Hoshino J, Suwabe T, Sumida K, Mise K, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Sawa N, Takaichi K, Ohashi K, Fujii T, Ubara Y. Significance of small renal artery lesions in patients with antineutrophil cytoplasmic antibody-associated glomerulonephritis. J Rheumatol. 2014;41(6):1140–6.
26. Mahajan SK, Ordóñez NG, Feitelson PJ, Lim VS, Spargo BH, Katz AI. Lupus nephropathy without clinical renal involvement. Medicine (Baltimore). 1977;56:493–501.
27. Wada Y, Ito S, Ueno M, Nakano M, Arakawa M, Gejyo F. Renal outcome and predictors of clinical renal involvement in patients with silent lupus nephritis. Nephron Clin Pract. 2004;98:c105-111.
28. Wakasugi D, Gono T, Kawaguchi Y, Hara M, Koseki Y, Katsumata Y, Hanaoka M, Yamanaka H. Frequency of class III and IV nephritis in systemic lupus erythematosus without clinical renal involvement: an analysis of predictive measures. J Rheumatol. 2012;39:79–85.
29. Hasegawa J, Hoshino J, Sekine A, Hayami N, Suwabe T, Sumida K, Mise K, Ueno T, Yamanouchi M, Hazue R, Sawa N, Ohashi K, Fujii T, Takaichi K, Ubara Y. Clinical and pathological features of anti-neutrophil cytoplasmic antibody-associated vasculitis in patients with minor urinary abnormalities. Nephrology (Carlton). 2018;23:1007–12.
30. Hoshino J, Furuichi K, Yamanouchi M, Mise K, Sekine A, Kawada M, Sumida K, Hiramatsu R, Hasegawa E, Hayami N, Suwabe T, Sawa N, Hara S, Fujii T, Ohashi K, Kitagawa K, Toyama T, Shimizu M, Takaichi K, Ubara Y, Wada T. A new pathological scoring system by the Japanese classification to predict renal outcome in diabetic nephropathy. PLoS ONE. 2018;13:e0190923.
31. Toriu N, Yamanouchi M, Hiramatsu R, Hayami N, Hoshino J, Sekine A, Kawada M, Hasegawa E, Suwabe T, Sumida K, Ueno T, Sawa N, Ohashi K, Fujii T, Takaichi K, Yanagita M, Kobayasi T, Ubara Y. Preservation of renal function by intensive glycemic control. Endocrinol Diabetes Metab Case Rep. 2018;2018:17–0136.
32. Yamanouchi M, Hoshino J, Ubara Y, Takaichi K, Kinowaki K, Fujii T, Ohashi K, Mise K, Toyama T, Hara A, Kitagawa K, Shimizu M, Furuichi K, Wada T. Value of adding the renal pathological score to the kidney failure risk equation in advanced diabetic nephropathy. PLoS ONE. 2018;13:e0190930.
33. Furuichi K, Shimizu M, Yuzawa Y, Hara A, Toyama T, Kitamura H, Suzuki Y, Sato H, Uesugi N, Ubara Y, Hohino J, Hisano S, Ueda Y, Nishi S, Yokoyama H, Nishino T, Kohagura K, Ogawa D, Mise K, Shibagaki Y, Makino H, Matsuo S, Wada T, Research Group of Diabetic Nephropathy, Ministry of Health, Labour and Welfare of Japan, and Japan Agency for Medical Research and Development. Clinicopathological analysis of biopsy-proven diabetic nephropathy based on the Japanese classification of diabetic nephropathy. Clin Exp Nephrol. 2018;22:570–82.
34. Mise K, Ueno T, Hoshino J, Hazue R, Sumida K, Yamanouchi M, Hayami N, Suwabe T, Hiramatsu R, Hasegawa E, Sawa N, Fujii T, Hara S, Wada J, Makino H, Takaichi K, Ohashi K, Ubara Y. Nodular lesions in diabetic nephropathy: collagen staining and renal prognosis. Diabetes Res Clin Pract. 2017;127:187–97.
35. Furuichi K, Yuzawa Y, Shimizu M, Hara A, Toyama T, Kitamura H, Suzuki Y, Sato H, Uesugi N, Ubara Y, Hisano S, Ueda Y, Nishi S, Yokoyama H, Nishino T, Kohagura K, Ogawa D, Mise K, Shibagaki Y, Kimura K, Haneda M, Makino H, Matsuo S, Wada T. Nationwide multicentre kidney biopsy study of Japanese patients with type 2 diabetes. Nephrol Dial Transplant. 2018;33:138–48.
36. Hoshino J, Mise K, Ueno T, Imafuku A, Kawada M, Sumida K, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Suwabe T, Sawa N, Hara S, Fujii T, Ohashi K, Ubara Y, Takaichi K. A pathological scoring system to predict renal outcome in diabetic nephropathy. Am J Nephrol. 2015;41:337–44.
37. Mise K, Hoshino J, Ueno T, Sumida K, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Suwabe T, Sawa N, Fujii T, Hara S, Ohashi K, Takaichi K, Ubara Y. Clinical implications of linear immunofluorescent staining for immunoglobulin G in patients with diabetic nephropathy. Diabetes Res Clin Pract. 2014;106:522–30.
38. Mise K, Hoshino J, Ubara Y, Sumida K, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Suwabe T, Sawa N, Fujii T, Ohashi K, Hara S, Takaichi K. Renal prognosis a long time after kidney biopsy on patients with diabetic nephropathy. Nephrol Dial Transplant. 2014;29:109–18.
39. Mise K, Yamaguchi Y, Hoshino J, Ueno T, Sekine A, Sumida K, Yamanouchi M, Hayami N, Suwabe T, Hiramatsu R, Hasegawa E, Sawa N, Fujii T, Hara S, Sugiyama H, Makino H, Wada J, Ohashi K, Takaichi K, Ubara Y. Paratubular basement membrane insudative lesions predict renal prognosis in patients with type 2 diabetes and biopsy-proven diabetic nephropathy. PLoS ONE. 2017;12:e0183190.
40. Mise K, Hoshino J, Ueno T, Hazue R, Hasegawa J, Sekine A, Sumida K, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Suwabe T, Sawa N, Fujii T, Hara S, Ohashi K, Takaichi K, Ubara Y. Prognostic value of tubulointerstitial lesions, urinary *N*-acetyl-β-D-glucosaminidase, and urinary β2-microglobulin in patients with type 2 diabetes and biopsy-proven diabetic nephropathy. Clin J Am Soc Nephrol. 2016;11:593–601.
41. Mise K, Hoshino J, Ueno T, Imafuku A, Kawada M, Sumida K, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Suwabe T, Sawa N, Fujii T, Hara S, Ohashi K, Takaichi K, Ubara Y. Impact of tubulointerstitial lesions on anaemia in patients with biopsy-proven diabetic nephropathy. Diabet Med. 2015;32:546–55.
42. Moriya T, Omura K, Matsubara M, Yoshida Y, Hayama K, Ouchi M. Arteriolar hyalinosis predicts increase in albuminuria and GFR Decline in Normo- and micro-albuminuric japanese patients with type 2 diabetes. Diabetes Care. 2017;40:1373–8.
43. Mazzucco G, Bertani T, Fortunato M, Bernardi M, Leutner M, Boldorini R, Monga G. Different patterns of renal damage in type 2 diabetes mellitus: a multicentric study on 393 biopsies. Am J Kidney Dis. 2002;39:713–20.
44. Sharma SG, Bomback AS, Radhakrishnan J, Herlitz LC, Stokes MB, Markowitz GS, D'Agati VD. The modern spectrum of kidney biopsy findings in patients with diabetes. Clin J Am Soc Nephrol. 2013;8:1718–24.
45. Nair R, Bell JM, Walker PD. Kidney biopsy in patients aged 80 years and older. Am J Kidney Dis. 2004;44:618–26.
46. Omokawa A, Komatsuda A, Nara M, Fujiwara T, Sato R, Togashi M, Okuyama S, Sawada K, Wakui H. Kidney biopsy in patients aged 80 years and older: a single-center experience in Japan. Clin Nephrol. 2012;77:461–7.
47. Moutzouris DA, Herlitz L, Appel GB, Markowitz GS, Freudenthal B, Radhakrishnan J, D'Agati VD. Kidney biopsy in the very elderly. Clin J Am Soc Nephrol. 2009;4:1073–82.
48. Bomback AS, Appel GB, Radhakrishnan J, Shirazian S, Herlitz LC, Stokes B, D'Agati VD, Markowitz GS. ANCA-associated glomerulonephritis in the very elderly. Kidney Int. 2011;79:757–64.
49. Savige J, Gregory M, Gross O, Kashtan C, Ding J, Flinter F. Expert guidelines for the management of Alport syndrome

and thin basement membrane nephropathy. J Am Soc Nephrol. 2013;24(3):364–75.
50. Imafuku A, Nozu K, Sawa N, Hasegawa E, Hiramatsu R, Kawada M, Hoshino J, Tanaka K, Ishii Y, Takaichi K, Fujii T, Ohashi K, Iijima K, Ubara Y. Autosomal dominant form of type IV collagen nephropathy exists among patients with hereditary nephritis difficult to diagnose clinicopathologically. Nephrology (Carlton). 2018;23:940–7.
51. Imafuku A, Nozu K, Sawa N, Nakanishi K, Ubara Y. How to resolve confusion in the clinical setting for the diagnosis of heterozygous COL4A3 or COL4A4 gene variants? Discussion and suggestions from nephrologists. Clin Exp Nephrol. 2020;24:651–6.
52. Nachman PH. Repeat kidney biopsy for lupus nephritis: an important step forward. Kidney Int. 2018;94:659–61.
53. De Rosa M, Azzato F, Toblli JE, De Rosa G, Fuentes F, Nagaraja HN, Nash R, Rovin BH. A prospective observational cohort study highlights kidney biopsy findings of lupus nephritis patients in remission who flare following withdrawal of maintenance therapy. Kidney Int. 2018;94:788–94.
54. Pakozdi A, Pyne D, Sheaff M, Rajakariar R. Utility of a repeat kidney biopsy in lupus nephritis: a single centre experience. Nephrol Dial Transplant. 2018;33:507–13.
55. Hruskova Z, Honsova E, Berden AE, Rychlik I, Lanska V, Zabka J, Bajema IM, Tesar V. Repeat protocol kidney biopsy in ANCA-associated renal vasculitis. Nephrol Dial Transplant. 2014;29:1728–32.
56. Shima Y, Nakanishi K, Kamei K, Togawa H, Nozu K, Tanaka R, Sasaki S, Iijima K, Yoshikawa N. Disappearance of glomerular IgA deposits in childhood IgA nephropathy showing diffuse mesangial proliferation after 2 years of combination/prednisolone therapy. Nephrol Dial Transplant. 2011;26:163–9.
57. Shen XH, Liang SS, Chen HM, Le WB, Jiang S, Zeng CH, Zhou ML, Zhang HT, Liu ZH. Reversal of active glomerular lesions after immunosuppressive therapy in patients with IgA nephropathy: a repeat-biopsy based observation. J Nephrol. 2015;28:441–9.
58. Ahmad H, Tejani A. Predictive value of repeat renal biopsies in children with nephrotic syndrome. Nephron. 2000;84:342–6.
59. Zhong Y, Xu F, Li X, Chen H, Liang S, Zhu X, Liu Z, Zeng C. The evolution of morphological variants of focal segmental glomerulosclerosis: a repeat biopsy-based observation. Nephrol Dial Transplant. 2016;31:87–95.
60. Ubara Y, Hara S, Katori H, Tagami T, Kitamura A, Yokota M, Matsushita Y, Takemoto F, Yamada A, Nagahama K, Hara M, Chayama K. Splenectomy may improve the glomerulopathy of type II mixed cryoglobulinemia. Am J Kidney Dis. 2000;35:1186–92.
61. Iwadate D, Hasegawa E, Hoshino J, Hayami N, Sumida K, Yamanouchi M, Sekine A, Kawada M, Hiramatsu R, Suwabe T, Sawa N, Yuasa M, Wake A, Fujii T, Ohashi K, Takaichi K, Ubara Y. The long-term outcomes after VAD plus SCT therapy in a patient with AL amyloidosis and severe factor X deficiency. Intern Med. 2018;57:701–6.
62. Ueno T, Kikuchi K, Hazue R, Mise K, Sumida K, Hayami N, Suwabe T, Hoshino J, Sawa N, Arizono K, Hara S, Takaichi K, Fujii T, Ohashi K, Ubara Y. Five sequential evaluations of renal histology in a patient with light chain deposition disease. Intern Med. 2016;55:2993–9.
63. Toriu N, Sawa N, Hiramatsu R, Mizuno H, Ikuma D, Sekine A, Hayami N, Sumida K, Yamanouchi M, Hasegawa E, Hoshino J, Takaichi K, Wake A, Ohashi K, Fujii T, Ubara Y. Regression of renal amyloid deposits by VAD therapy plus autologous stem cell transplantation in a patient with primary AL amyloidosis. CEN Case Rep. 2020;9(1):6–10.
64. Health and Public Policy Committee. American College of Physicians. Clinical competence in percutaneous kidney biopsy. Ann Intern Med. 1988;108:301–3.
65. Doyle AJ, Gregory MC, Terreros DA. Percutaneous native kidney biopsy: comparison of a 1.2-mm spring-driven system with a traditional 2-mm hand-driven system. Am J Kidney Dis. 1994;23:498–503.
66. Hogan JJ, Mocanu M, Berns JS. The native kidney biopsy: update and evidence for best practice. Clin J Am Soc Nephrol. 2016;11:354–62.
67. Fine DM, Arepally A, Hofmann LV, Mankowitz SG, Atta MG. Diagnostic utility and safety of transjugular kidney biopsy in the obese patient. Nephrol Dial Transplant. 2004;19:1798–802.
68. Margaryan A, Perazella MA, Mahnensmith RL, Abu-Alfa AK. Experience with outpatient computed tomographic-guided kidney biopsy. Clin Nephrol. 2010;74:440–5.
69. Mukhtar KN, Mahmood SN, Umair SF. CT guided percutaneous kidney biopsy versus ultrasound guided for obtaining adequate tissue. J Pak Med Assoc. 2012;62:880–2.
70. McDougal WS, Tolkoff-Rubin NE, Michaelson MD, Mueller PR, Braaten K. Case records of the Massachusetts General Hospital. Case 28-2006. A 59-year-old man with masses in both kidneys. N Engl J Med. 2006;355:1161–7.
71. Mizunoe S, Yamasaki T, Tokimatsu I, Kushima H, Matsunaga N, Hashinaga K, Miyazaki Y, Komatsu E, Kadota J. Sarcoidosis associated with renal masses on computed tomography. Intern Med. 2006;45:279–82.
72. Ubara Y, Hara S, Katori H, Yamada A, Morii H. Renovascular hypertension may cause nephrotic range proteinuria and focal glomerulosclerosis in contralateral kidney. Clin Nephrol. 1997;48:220–3.
73. Bandari J, Fuller TW, Turner Ii RM, D'Agostino LA. kidney biopsy for medical renal disease: indications and contraindications. Can J Urol. 2016a;23:8121–6.
74. Corapi KM, Chen JL, Balk EM, Gordon CE. Bleeding complications of native kidney biopsy: a systematic review and meta-analysis. Am J Kidney Dis. 2012;60:62–73.
75. Schow DA, Vinson RK, Morrisseau PM. Percutaneous kidney biopsy of the solitary kidney: a contraindication? J Urol. 1992;147:1235–7.
76. Wilczek HE. Percutaneous needle biopsy of the renal allograft. A clinical safety evaluation of 1129 biopsies. Transplantation. 1990;50:790–7.
77. Tøndel C, Vikse BE, Bostad L, Svarstad E. Safety and complications of percutaneous kidney biopsies in 715 children and 8573 adults in Norway 1988–2010. Clin J Am Soc Nephrol. 2012;7:1591–7.
78. Mejía-Vilet JM, Márquez-Martínez MA, Cordova-Sanchez BM, Ibargüengoitia MC, Correa-Rotter R, Morales-Buenrostro LE. Simple risk score for prediction of haemorrhagic complications after a percutaneous kidney biopsy. Nephrology (Carlton). 2018a;23:523–9.
79. Sumida K, Ubara Y, Marui Y, Nakamura M, Takaichi K, Tomikawa S, Fujii T, Ohashi K. Recurrent proliferative glomerulonephritis with monoclonal IgG deposits of IgG2λ subtype in a trans-planted kidney: a case report. Am J Kidney Dis. 2013;62:587–90.
80. Matsunami M, Ubara Y, Sumida K, Oshima Y, Oguro M, Kinoshita K, Tanaka K, Nakamura Y, Kinowaki K, Ohashi K, Fujii T, Igawa T, Sato Y, Ishii Y. The efficacy and safety of anti-interleukin-6 receptor monoclonal blockade in a renal transplant patient with Castleman disease: early post-transplant outcome. BMC Nephrol. 2018;19(1):263.
81. Glenn JF. Analysis of 51 patients with horseshoe kidney. N Engl J Med. 1959;261:684–7.

82. Satav V, Sabale V, Pramanik P, Kanklia SP, Mhaske S. Percutaneous nephrolithotomy of horseshoe kidney: our institutional experience. Urol Ann. 2018;10:258–62.
83. Glodny B, Petersen J, Hofmann KJ, Schenk C, Herwig R, Trieb T, Koppelstaetter C, Steingruber I, Rehder P. Kidney fusion anomalies revisited: clinical and radiological analysis of 209 cases of crossed fused ectopia and horseshoe kidney. BJU Int. 2009;103:224–35.
84. Hu P, Jin M, Xie Y, Chen P, Zhang X, Yin Z, Cai G, Chen X. Immunoglobulin A nephropathy in horseshoe kidney: case reports and literature review. Nephrology (Carlton). 2014;19:605–9.
85. Chaabouni Y, Guesmi R, Hentati Y, Kammoun K, Hmida MB, Mnif Z, Boudawara T, Hachicha J. Minimal change disease in horseshoe kidney. Pan Afr Med J. 2017;26:243.
86. Sumida K, Ubara Y, Hoshino J, Hayami N, Suwabe T, Hiramatsu R, Hasegawa E, Yamanouchi M, Sawa N, Takaichi K, Ohashi K. Myeloperoxidase-antineutrophil cytoplasmic antibody-associated crescentic glomerulonephritis in autosomal dominant polycystic kidney disease. BMC Nephrol. 2013;14:94.
87. Ito Y, Sekine A, Takada D, Yabuuchi J, Kogure Y, Ueno T, Sumida K, Yamanouchi M, Hayami N, Suwabe T, Hoshino J, Sawa N, Takaichi K, Kinowaki K, Fujii T, Ohashi K, Kikuchi H, Mandai S, Chiga M, Mori T, Sohara E, Uchida S, Ubara Y. Renal histology and MRI findings in a 37-year-old Japanese patient with autosomal recessive polycystic kidney disease. Clin Nephrol. 2017;88:292–7.
88. Takada D, Sekine A, Yabuuchi J, Kogure Y, Ueno T, Yamanouchi M, Sumida K, Suwabe T, Hayami N, Hoshino J, Takaichi K, Kinowaki K, Fujii T, Ohashi K, Mori T, Sohara E, Uchida S, Ubara Y. Renal histology and MRI in a 25-year-old Japanese man with nephronophthisis 4. Clin Nephrol. 2018;89:223–8.
89. Hirabayashi Y, Ishikawa E, Ito M. Bilateral renal hilar tumors in IgG4-related disease. Clin Exp Nephrol. 2017;21:1131–2.
90. Senekjian HO, Stinebaugh BJ, Mattioli CA, Suki WN. Irreversible renal failure following vesicoureteral reflux. JAMA. 1979;241:160–2.
91. Imai T, Yumura W, Takemoto F, Kotoda A, Imai R, Inoue M, Hironaka M, Muto S, Kusano E. A case of IgG4-related tubulointerstitial nephritis with left hydronephrosis after a remission of urinary tract tuberculosis. Rheumatol Int. 2013;33:2141–4.
92. Obayashi M, Uzu T, Harada T, Yamato M, Takahara K, Yamauchi A. Two cases of lupus cystitis complicated by lupus nephritis treated successfully with steroid therapy. Nihon Jinzo Gakkai Shi. 2003;45:765–70 (**In Japanese**).
93. Takeuchi Y, Takeuchi E, Kamata K. A possible clue for the production of anti-glomerular basement membrane antibody associated with ureteral obstruction and hydronephrosis. Case Rep Nephrol Dial. 2015;5:87–95.
94. Shibata S, Ubara Y, Sawa N, Tagami T, Hosino J, Yokota M, Katori H, Takemoto F, Hara S, Takaichi K, Fujii A, Murata H, Nishi T. Severe interstitial cystitis associated with Sjögren's syndrome. Intern Med. 2004;43(3):248–52.
95. Nonaka K, Ubara Y, Sumida K, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Suwabe T, Hoshino J, Sawa N, Takaichi K, Kuroda Y, Oohashi K. Clinical and pathological evaluation of hypertensive emergency-related nephropathy. Intern Med. 2013;52:45–53.
96. Takada D, Hoshino J, Kikuchi K, Yabuuchi J, Kogure Y, Ueno T, Sekine A, Yamanouchi M, Sumida K, Mise K, Suwabe T, Hayami N, Sawa N, Takaichi K, Hayasi N, Fujii T, Ohashi K, Ubara Y. Anti-RNA polymerase III antibody-associated scleroderma renal crisis in a patient with limited cutaneous systemic sclerosis: a case report. Mod Rheumatol. 2018;28:369–72.
97. Yamanouchi M, Ubara Y, Imafuku A, Kawada M, Koki M, Sumida K, Hiramatsu R, Hasegawa E, Hayami N, Suwabe T, Hoshino J, Sawa N, Ohashi K, Fujii T, Matsuda M, Takaichi K. Malignant nephrosclerosis in a patient with familial Mediterranean fever. Intern Med. 2015;54:2643–6.
98. Shidham GB, Siddiqi N, Beres JA, Logan B, Nagaraja HN, Shidham SG, Piering WF. Clinical risk factors associated with bleeding after native kidney biopsy. Nephrology (Carlton). 2005;10:305–10.
99. Shima N, Sumida K, Kawada M, Sekine A, Yamanouchi M, Hiramatsu R, Hayami N, Hasegawa E, Suwabe T, Hoshino J, Sawa N, Takaichi K, Ohashi K, Fujii T, Ubara Y. Eltrombopag improves refractory thrombocytopenia in a patient with systemic lupus erythematosus. Case Rep Rheumatol. 2018;2018:6305356.
100. Mise K, Ubara Y, Matsumoto M, Sumida K, Hiramatsu R, Hasegawa E, Yamanouchi M, Hayami N, Suwabe T, Hoshino J, Sawa N, Ohashi K, Kokame K, Miyata T, Fujimura Y, Takaichi K. Long term follow up of congenital thrombotic thrombocytopenic purpura (Upshaw–Schulman syndrome) on hemodialysis for 19 years: a case report. BMC Nephrol. 2013;14:156.
101. Sekine A, Hasegawa E, Hiramatsu R, Mise K, Sumida K, Ueno T, Yamanouchi M, Hayami N, Suwabe T, Hoshino J, Sawa N, Takaichi K, Ohashi K, Fujii T, Ubara Y. Two types of renovascular lesions in lupus nephritis with clinical thrombotic thrombocytopenic purpura. Case Rep Nephrol Dial. 2015;5:192–9.
102. Noda-Narita S, Sumida K, Sekine A, Hoshino J, Mise K, Suwabe T, Hayami N, Yamanouchi M, Ueno T, Mizuno H, Kawada M, Hiramatsu R, Hasegawa E, Sawa N, Takaichi K, Ohashi K, Fujii T, Ubara Y. TAFRO syndrome with refractory thrombocytopenia responding to tocilizumab and romiplostim: a case report. CEN Case Rep. 2018;7:162–8.
103. Mizuno H, Sawa N, Watanabe S, Ikuma D, Sekine A, Kawada M, Yamanouchi M, Hasegawa E, Suwabe T, Hoshino J, Takaichi K, Kinowaki K, Fujii T, Ohashi K, Nagata M, Yamaguchi Y, Ubara Y. The clinical and histopathological feature of renal manifestation of TAFRO syndrome. Kidney Int Rep. 2020;5(8):1172–9.
104. Simard-Meilleur MC, Troyanov S, Roy L, Dalaire E, Brachemi S. Risk factors and timing of native kidney biopsy complications. Nephron Extra. 2014;4:42–9.
105. Piccoli GB, Daidola G, Attini R, Parisi S, Fassio F, Naretto C, Deagostini MC, Castelluccia N, Ferraresi M, Roccatello D, Todros T. Kidney biopsy in pregnancy: evidence for counselling? A systematic narrative review. BJOG. 2013;120:412–27.
106. Blom K, Odutayo A, Bramham K, Hladunewich MA. Pregnancy and glomerular disease: a systematic review of the literature with management guidelines. Clin J Am Soc Nephrol. 2017;12:1862–72.
107. Davison JM, Dunlop W. Renal hemodynamics and tubular function normal human pregnancy. Kidney Int. 1980;18:152–61.
108. Higby K, Suiter CR, Phelps JY, Siler-Khodr T, Langer O. Normal values of urinary albumin and total protein excretion during pregnancy. Am J Obstet Gynecol. 1994;171:984–9.
109. Li Y, Wang W, Wang Y, Chen Q. Fetal risks and maternal renal complications in pregnancy with preexisting chronic glomerulonephritis. Med Sci Monit. 2018;24:1008–16.
110. Piccoli GB, Cabiddu G, Attini R, Vigotti FN, Maxia S, Lepori N, Tuveri M, Massidda M, Marchi C, Mura S, Coscia A, Biolcati M, Gaglioti P, Nichelatti M, Pibiri L, Chessa G, Pani A, Todros T. Risk of adverse pregnancy outcomes in women with CKD. J Am Soc Nephrol. 2015;26:2011–22.
111. Limardo M, Imbasciati E, Ravani P, Surian M, Torres D, Gregorini G, Magistroni R, Casellato D, Gammaro L, Pozzi C, Rene e Gravidanza Collaborative Group of the Italian Society of Nephrology. Pregnancy and progression of IgA nephropathy: results of an Italian multicenter study. Am J Kidney Dis. 2010;56:506–12.
112. Caritis S, Sibai B, Hauth J, Lindheimer MD, Klebanoff M, Thom E, VanDorsten P, Landon M, Paul R, Miodovnik M, Meis P, Thurnau G. Low-dose aspirin to prevent preeclampsia in women

at high risk. National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. N Engl J Med. 1998;338:701–5.
113. Bujold E, Roberge S, Lacasse Y, Bureau M, Audibert F, Marcoux S, Forest JC, Giguère Y. Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis. Obstet Gynecol. 2010;116(2 Pt 1):402–14.
114. Lindheimer MD, Spargo BH, Katz AI. Kidney biopsy in pregnancy-induced hypertension. J Reprod Med. 1975;15:189–94.
115. Ochsenbein-Kölble N, Roos M, Gasser T, Huch R, Huch A, Zimmermann R. Cross sectional study of automated blood pressure measurements throughout pregnancy. BJOG. 2004;111:319–25.
116. Radisic MV, Feldman D, Diaz C, Froment RO. Unexplained hematuria during pregnancy: right-sided nutcracker phenomenon. Int Urol Nephrol. 2007;39:709–11.
117. Motha MB, Palihawadana TS, Dias TD, Wijesinghe PS. Nutcracker syndrome in pregnancy: a worrying presentation of a benign condition. Ceylon Med J. 2017;62:238–9.
118. Silverman SG, Gan YU, Mortele KJ, Tuncali K, Cibas ES. Renal masses in the adult patient: the role of percutaneous biopsy. Radiology. 2006;240:6–22.
119. Smith EH. Complications of percutaneous abdominal fine-needle biopsy. Rev Radiol. 1991;178:253–8.
120. Gordetsky J, Eich ML, Garapati M, Del Pena MCR, Rais-Bahrami S. Active surveillance of small renal masses. Urology. 2019;123:157–66.
121. Sawa N, Ubara Y, Katori H, Hoshino J, Suwabe T, Tagami T, Takemoto F, Miyakoshi S, Taniguchi S, Ohashi K, Takaichi K. Renal intravascular large B-cell lymphoma localized only within peritubular capillaries. Report of a case. Intern Med. 2007;46:657–62.
122. Hasegawa J, Hoshino J, Suwabe T, Hayami N, Sumida K, Mise K, Ueno T, Sawa N, Wake A, Ohashi K, Fujii T, Honda K, Takaichi K, Ubara Y. Characteristics of intravascular large B-cell lymphoma limited to the glomerular capillaries: a case report. Case Rep Nephrol Dial. 2015;5:173–9.
123. Biondi-Zoccai GG, Lotrionte M, Agostoni P, Abbate A, Fusaro M, Burzotta F, Testa L, Sheiban I, Sangiorgi G. A systematic review and meta-analysis on the hazards of discontinuing or not adhering to aspirin among 50,279 patients at risk for coronary artery disease. Eur Heart J. 2006;27:2667–74.
124. Lees JS, McQuarrie EP, Mordi N, Geddes CC, Fox JG, Mackinnon B. Risk factors for bleeding complications after nephrologist-performed native kidney biopsy. Clin Kidney J. 2017;10:573–7.
125. Fujimoto K, Fujishiro M, Kato M, Higuchi K, Iwakiri R, Sakamoto C, Uchiyama S, Kashiwagi A, Ogawa H, Murakami K, Mine T, Yoshino J, Kinoshita Y, Ichinose M, Matsui T, Japan Gastroenterological Endoscopy Society. Guidelines for gastroenterological endoscopy in patients undergoing antithrombotic treatment. Dig Endosc. 2014;26(1):1–14.
126. Fernandez Lynch H, Joffe S, Feldman EA. Informed consent and the role of the treating physician. N Engl J Med. 2018;378:2433–8.
127. Whittier WL, Korbet SM. Timing of complications in percutaneous kidney biopsy. J Am Soc Nephrol. 2004;15:142–7.
128. Lin WC, Yang Y, Wen YK, Chang CC. Outpatient versus inpatient kidney biopsy: a retrospective study. Clin Nephrol. 2006;66:17–24.
129. Bairy M, Beleed K, Webb AT, Bhandari S. Safety of outpatient kidney biopsy: one center's experience with 178 native kidney biopsies. Am J Kidney Dis. 2008;52:631–2.
130. Roccatello D, Sciascia S, Rossi D, Naretto C, Bazzan M, Solfietti L, Baldovino S, Menegatti E. Outpatient percutaneous native kidney biopsy: safety profile in a large monocentric cohort. BMJ Open. 2017;7:e015243.
131. Šimunov B, Gunjača M, Čingel B, Škegro D, Knotek M. Safety of outpatient kidney biopsies. Nephron. 2018;138:275–9.
132. Kajawo S, Moloi MW, Noubiap JJ, Ekrikpo U, Kengne AP, Okpechi IG. Incidence of major complications after percutaneous native renal biopsies in adults from low-income to middle-income countries: a protocol for systematic review and meta-analysis. BMJ Open. 2018;8(4):e020891.
133. Iversen P, Brun C. Aspiration biopsy of the kidney, 1951. J Am Soc Nephrol. 1997;8(11):1778–87 (**discussion 1778-86**).
134. Schorr M, Roshanov PS, Weir MA, House AA. Frequency, timing, and prediction of major bleeding complications from percutaneous kidney biopsy. Can J Kidney Health Dis. 2020;25(7):2054358120923527.
135. Korbet SM. Nephrology and the percutaneous kidney biopsy: a procedure in jeopardy of being lost along the way. Clin J Am Soc Nephrol. 2012;7:1545–7.
136. Kark RM, Muehrcke RC. Biopsy of kidney in prone position. Lancet. 1954;266:1047–9.
137. Kark RM, Muehrcke RC, Pollak VE, Kiefer JH. An analysis of five hundred percutaneous renal biopsies. AMA Arch Intern Med. 1958;101:439–51.
138. Madaio MP. kidney biopsy. Kidney Int. 1990;38:529–43.
139. Donovan KL, Thomas DM, Wheeler DC, Macdougall IC, Williams JD. Experience with a new method for percutaneous kidney biopsy. Nephrol Dial Transplant. 1991;6:731–3.
140. Bataille S, Jourde N, Daniel L, Mondain JR, Faure M, Gobert P, Alcheikh-Hassan Z, Lankester M, Giaime P, Gaudart J, Dussol B, Berland Y, Burtey S. Comparative safety and efficiency of five percutaneous kidney biopsy approaches of native kidneys: a multicenter study. Am J Nephrol. 2012;35:387–93.
141. Tuladhar AS, Shrestha A, Pradhan S, Manandhar DN, Chhetri Poudyal PK, Rijal A, Poudel P, Maskey A, Bhoomi KK. USG assisted and USG guided percutaneous kidney biopsy at Nepal Medical College Teaching Hospital: a three and half years study. Nepal Med Coll J. 2014;16:26–9.
142. Rao NS, Chandra A. Needle guides enhance tissue adequacy and safety of ultrasound-guided renal biopsies. Kidney Res Clin Pract. 2018;37:41–8.
143. Shamshirgar F, Bagheri SM. Percutaneous ultrasound-guided kidney biopsy; a comparison of axial vs. sagittal probe location. Rom J Intern Med. 2017;55:96–102.
144. Bandari J, Fuller TW, Turner Ii RM, D'Agostino LA. Kidney biopsy for medical renal disease: indications and contraindications. Can J Urol. 2016b;23(1):8121–6.
145. Stec AA, Stratton KL, Kaufman MR, Chang SS, Milam DF, Herrell SD, Dmochowski RR, Smith JA Jr, Clark PE, Cookson MS. Open Kidney biopsy: comorbidities and complications in a contemporary series. BJU Int. 2010;106(1):102–6.
146. Shetye KR, Kavoussi LR, Ramakumar S, Fugita OE, Jarrett TW. Laparoscopic Kidney biopsy: a 9-year experience. BJU Int. 2003;91(9):817–20.
147. Furness PN, Philpott CM, Chorbadjian MT, Nicholson ML, Bosmans JL, Corthouts BL, Bogers JJ, Schwarz A, Gwinner W, Haller H, Mengel M, Seron D, Moreso F, Cañas C. Protocol biopsy of the stable renal transplant: a multicenter study of methods and complication. Transplantation. 2003;76:969–73.
148. Schwarz A, Gwinner W, Hiss M, Radermacher J, Mengel M, Haller H. Safety and adequacy of renal transplant protocol biopsies. Am J Transplant. 2005;5:1992–6.
149. Danovitch GM, editor. Handbook of kidney transplantation. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2010.
150. Korbet SM. Percutaneous Kidney biopsy. Semin Nephrol. 2002;22:254–67.
151. Burstein DM, Schwartz MM, Korbet SM. Percutaneous Kidney biopsy with the use of real-time ultrasound. Am J Nephrol. 1991;11:195–200.

152. Marwah DS, Korbet SM. Timing of complications in percutaneous Kidney biopsy: what is the optimal period of observation? Am J Kidney Dis. 1996;28:47–52.
153. Mendelssohn DC, Cole EH. Outcomes of percutaneous kidney biopsy, including those of solitary native kidneys. Am J Kidney Dis. 1995;26:580–5.
154. Kim D, Kim H, Shin G, Ku S, Ma K, Shin S, Gi H, Lee E, Yim H. A randomized, prospective, comparative study of manual and automated renal biopsies. Am J Kidney Dis. 1998;32:426–31.
155. Nass K, O'Neill WC. Bedside Kidney biopsy: ultrasound guidance by the nephrologist. Am J Kidney Dis. 1999;34:955–9.
156. Eiro M, Katoh T, Watanabe T. Risk factors for bleeding complications in percutaneous Kidney biopsy. Clin Exp Nephrol. 2005;9:40–5.
157. Manno C, Strippoli GF, Arnesano L, Bonifati C, Campobasso N, Gesualdo L, Schena FP. Predictors of bleeding complications in percutaneous ultrasound-guided Kidney biopsy. Kidney Int. 2004;66:1570–7.
158. Fraser IR, Fairley KF. Kidney biopsy as an outpatient procedure. Am J Kidney Dis. 1995;25:876–8.
159. Jones B, Puvaneswary M, Nanra R, Trevillian P, Carney S, Gillies A. Reduced duration of bed rest after percutaneous Kidney biopsy. Clin Nephrol. 1991;35:44–5.
160. Simckes AM, Blowey DL, Gyves KM, Alon US. Success and safety of same-day kidney biopsy in children and adolescents. Pediatr Nephrol. 2000;14:946–52.
161. Takeuchi Y, Ojima Y, Kagaya S, Aoki S, Nagasawa T. Manual compression and reflex syncope in native Kidney biopsy. Clin Exp Nephrol. 2018;22:1100–7.
162. Ishikawa E, Nomura S, Obe T, Katayama K, Oosugi K, Murata T, Tanoue A, Fujimoto M, Matsuo H, Ito M. How long is strict bed rest necessary after Kidney biopsy? Clin Exp Nephrol. 2009;13:594–7.
163. Manno C, Bonifati C, Torres DD, Campobasso N, Schena FP. Desmopressin acetate in percutaneous ultrasound-guided kidney biopsy: a randomized controlled trial. Am J Kidney Dis. 2011;57:850–5.
164. Khajehdehi P, Junaid SM, Salinas-Madrigal L, Schmitz PG, Bastani B. Percutaneous Kidney biopsy in the 1990s: safety, value, and implications for early hospital discharge. Am J Kidney Dis. 1999;34:92–7.
165. Rasmussen LR, Loft M, Nielsen TK, Bjødstrup Jensen M, Høyer S, Hørlyck A, Graumann O. Short-term complications for percutaneous ultrasound-guided biopsy of renal masses in adult outpatients. Acta Radiol. 2018;59(4):491–6.
166. Renal Physicians Association. RPA position on optimal length of observation after percutaneous Kidney biopsy. Clin Nephrol. 2001;56:179–80.
167. Waldo BD, Grabau ZJ, Mengistu TM, Crow WT. The value of post-biopsy ultrasound in predicting complications after percutaneous Kidney biopsy of native kidneys. Nephrol Dial Transplant. 2009;24:2433–9.
168. Ishikawa E, Nomura S, Hamaguchi T, Obe T, Inoue-Kiyohara M, Oosugi K, Katayama K, Ito M. Ultrasonography as a predictor of overt bleeding after Kidney biopsy. Clin Exp Nephrol. 2009;13:325–31.
169. Brachemi S, Bollée G. Kidney biopsy practice: what is the gold standard? World J Nephrol. 2014;3:287–94.
170. Franke M, Kramarczyk A, Taylan C, Maintz D, Hoppe B, Koerber F. Ultrasound-guided percutaneous Kidney biopsy in 295 children and adolescents: role of ultrasound and analysis of complications. PLoS ONE. 2014;9(12):e114737.
171. Xu DM, Chen M, Zhou FD, Zhao MH. Risk factors for severe bleeding complications in percutaneous Kidney biopsy. Am J Med Sci. 2017;353(3):230–5.
172. Yamamoto H, Hashimoto H, Nakamura M, Horiguchi H, Yasunaga H. Relationship between hospital volume and hemorrhagic complication after percutaneous Kidney biopsy: results from the Japanese diagnosis procedure combination database. Clin Exp Nephrol. 2015;19:271–7.
173. Tanaka K, Kitagawa M, Onishi A, Yamanari T, Ogawa-Akiyama A, Mise K, Inoue T, Morinaga H, Uchida HA, Sugiyama H, Wada J. Arterial stiffness is an independent risk factor for anemia after percutaneous native kidney biopsy. Kidney Blood Press Res. 2017;42:284–93.
174. Chikamatsu Y, Matsuda K, Takeuchi Y, Kagaya S, Ojima Y, Fukami H, Sato H, Saito A, Iwakura Y, Nagasawa T. Quantification of bleeding volume using computed tomography and clinical complications after percutaneous Kidney biopsy. Clin Kidney J. 2017;10:9–15.
175. Mejía-Vilet JM, Márquez-Martínez MA, Cordova-Sanchez BM, Ibargüengoitia MC, Correa-Rotter R, Morales-Buenrostro LE. Simple risk score for prediction of hemorrhagic complications after a percutaneous Kidney biopsy. Nephrology (Carlton). 2018b;23:523–9.
176. Palsson R, Short SAP, Kibbelaar ZA, Amodu A, Stillman IE, Rennke HG, McMahon GM, Waikar SS. Bleeding complications after percutaneous native kidney biopsy: results from the Boston kidney biopsy cohort. Kidney Int Rep. 2020;5(4):511–8.
177. Chen TK, Estrella MM, Fine DM. Predictors of kidney biopsy complication among patients with systemic lupus erythematosus. Lupus. 2012;21:848–54.
178. Fish R, Pinney J, Jain P, Addison C, Jones C, Jayawardene S, Booth J, Howie AJ, Ghonemy T, Rajabali S, Roberts D, White L, Khan S, Morgan M, Cockwell P, Hutchison CA. The incidence of major hemorrhagic complications after renal biopsies in patients with monoclonal gammopathies. Clin J Am Soc Nephrol. 2010;5:1977–80.
179. Altindal M, Yildirim T, Turkmen E, Unal M, Boga I, Yilmaz R, Arici M, Altun B, Erdem Y. Safety of percutaneous ultrasound-guided kidney biopsy in patients with AA amyloidosis. Nephron. 2015;131:17–22.
180. Ali H, Murtaza A, Anderton J, Ahmed A. Post Kidney biopsy complication rate and diagnostic yield comparing hands free (ultrasound-assisted) and ultrasound-guided biopsy techniques of renal allografts and native kidneys. Springerplus. 2015;4:491.
181. Mai J, Yong J, Dixson H, Makris A, Aravindan A, Suranyi MG, Wong J. Is bigger better? A retrospective analysis of native renal biopsies with 16 Gauge versus 18 Gauge automatic needles. Nephrology (Carlton). 2013;18:525–30.
182. Antunes PRB, Prado FFM, de Souza FTA, de Siqueira EC, de Campos MÁ, Álvares MCB, Neto RB. Clinical complications in Kidney biopsy using two different needle gauges: the impact of large hematomas, a random clinical trial study. Int J Urol. 2018;25:544–8.
183. Prasad N, Kumar S, Manjunath R, Bhadauria D, Kaul A, Sharma RK, Gupta A, Lal H, Jain M, Agrawal V. Real-time ultrasound-guided percutaneous Kidney biopsy with needle guide by nephrologists decreases post-biopsy complications. Clin Kidney J. 2015;8:151–6.
184. Torres Muñoz A, Valdez-Ortiz R, González-Parra C, Espinoza-Dávila E, Morales-Buenrostro LE, Correa-Rotter R. Percutaneous Kidney biopsy of native kidneys: efficiency, safety and risk factors associated with major complications. Arch Med Sci. 2011;7:823–31.
185. Lubas A, Wojtecka A, Smoszna J, Koziński P, Frankowska E, Niemczyk S. Hemodynamic characteristics and the occurrence of Kidney biopsy-related arteriovenous fistulas in native kidneys. Int Urol Nephrol. 2016;48:1667–73.

186. Meng CH, Elkin M. Immediate angiographic manifestations of iatrogenic renal injury due to percutaneous needle biopsy. Radiology. 1971;100:335–41.
187. Stiles KP, Yuan CM, Chung EM, Lyon RD, Lane JD, Abbott KC. Kidney biopsy in high-risk patients with medical diseases of the kidney. Am J Kidney Dis. 2000;36:419–33.
188. Gülcü A, Göktay Y, Soylu A, Türkmen M, Kavukçu S, Seçil M, Karabay N. Doppler US evaluation of Kidney biopsy complications in children. Diagn Interv Radiol. 2013;19:15–9.
189. Buczek M, Popiela TJ, Urbanik A. Pseudoaneurysma as iatrogenic complication of Kidney biopsy: management by transcatheter embolization. Przegl Lek. 2012;69:357–9.
190. Ito T, Ishikawa E, Ito M. Lumbar artery injury following Kidney biopsy. Clin Exp Nephrol. 2016;20:145–6.
191. Krejčí K, Černá M, Žamboch K, Orság J, Klíčová A, Zadražil J. Late rupture of lumbar artery as an unusual complication after Kidney biopsy: case report. Urol Int. 2017;98:112–4.
192. Ono A, Inoue T, Tomori K, Okada H. Page kidney following Kidney biopsy. Intern Med. 2017;56:875.
193. Ham YR, Moon KR, Bae HJ, Ju HJ, Jang WI, Choi DE, Na KR, Lee KW, Shin YT. A case of urine leakage: an unusual complication after Kidney biopsy. Chonnam Med J. 2011;47:181–4.
194. Whittier WL, Sayeed K, Korbet SM. Clinical factors influencing the decision to transfuse after percutaneous native kidney biopsy. Clin Kidney J. 2016;9:102–7.
195. Alotaibi M, Shrouder-Henry J, Amaral J, Parra D, Temple M, John P, Connolly B. The positive color Doppler sign post biopsy: effectiveness of US-directed compression in achieving hemostasis. Pediatr Radiol. 2011;41:362–8.
196. Hu T, Liu Q, Xu Q, Liu H, Feng Y, Qiu W, Huang F, Lv Y. Absorption fever characteristics due to percutaneous Kidney biopsy-related hematoma. Medicine. 2016;95:e4754.
197. Shima N, Hayami N, Mizuno H, Kawada M, Sekine A, Sumida K, Hiramatsu R, Yamanouchi M, Hasegawa E, Suwabe T, Hoshino J, Sawa N, Takaichi K, Ohashi K, Fujii T, Minota S, Ubara Y. Arteriovenous fistula-related renal bleeding 5 days after percutaneous Kidney biopsy. CEN Case Rep. 2019;8(4):280–4.
198. Solez K, Axelsen RA, Benediktsson H, Burdick JF, Cohen AH, Colvin RB, Croker BP, Droz D, Dunnill MS, Halloran PF, et al. International standardization of criteria for the histologic diagnosis of renal allograft rejection: the Banff working classification of kidney transplant pathology. Kidney Int. 1993;44:411–22.
199. Corwin HL, Schwartz MM, Lewis EJ. The importance of sample size in the interpretation of the Kidney biopsy. Am J Nephrol. 1988;8:85–9.
200. Wang HJ, Kjellstrand CM, Cockfield SM, Solez K. On the influence of sample size on the prognostic accuracy and reproducibility of renal transplant biopsy. Nephrol Dial Transplant. 1998;13:165–72.
201. Luciano RL, Moeckel GW. Update on the native kidney biopsy: core curriculum 2019. Am J Kidney Dis. 2019;73:404–15.
202. Nasr SH, Galgano SJ, Markowitz GS, Stokes MB, D'Agati VD. Immunofluorescence on pronase-digested paraffin sections: a valuable salvage technique for renal biopsies. Kidney Int. 2006;70:2148–51.
203. Deshpande V, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T, Klöppel G, Heathcote JG, Khosroshahi A, Ferry JA, Aalberse RC, Bloch DB, Brugge WR, Bateman AC, Carruthers MN, Chari ST, Cheuk W, Cornell LD, Fernandez-Del Castillo C, Forcione DG, Hamilos DL, Kamisawa T, Kasashima S, Kawa S, Kawano M, Lauwers GY, Masaki Y, Nakanuma Y, Notohara K, Okazaki K, Ryu JK, Saeki T, Sahani DV, Smyrk TC, Stone JR, Takahira M, Webster GJ, Yamamoto M, Zamboni G, Umehara H, Stone JH. Consensus statement on the pathology of IgG4-related disease. Mod Pathol. 2012;25:1181–92.
204. Vernier RL, Farquhar MG, Brunson JG, Good RA. Chronic renal disease in children; correlation of clinical findings with morphologic characteristics seen by light and electron microscopy. AMA J Dis Child. 1958;96:306–43.
205. Vehaskari VM, Rapola J, Koskimies O, Savilahti E, Vilska J, Hallman N. Microscopic hematuria in school children: epidemiology and clinicopathologic evaluation. J Pediatr. 1979;95:676–84.
206. Takei S, Maeno N, Shigemori M, Imanaka H, Mori H, Nerome Y, Kanekura S, Takezaki T, Hokonohara M, Miyata K, Fujikawa S. Clinical features of Japanese children and adolescents with systemic lupus erythematosus: results of 1980–1994 survey. Acta Pediatr Jpn. 1997;39:250–6.
207. Wakiguchi H, Takei S, Kubota T, Miyazono A, Kawano Y. Treatable renal disease in children with silent lupus nephritis detected by baseline biopsy: association with serum C3 levels. Clin Rheumatol. 2017;36:433–7.
208. Ito S, Ogura M, Kamei K, Matsuoka K, Warnock DG. Significant improvement in Fabry disease podocytopathy after 3 years of treatment with agalsidase beta. Pediatr Nephrol. 2016;31:1369–73.
209. Najafian B, Mauer M, Hopkin RJ, Svarstad E. Renal complications of Fabry disease in children. Pediatr Nephrol. 2013;28:679–87.
210. Emma F, Bertini E, Salviati L, Montini G. Renal involvement in mitochondrial cytopathies. Pediatr Nephrol. 2012;27:539–50.
211. Nozu K, Nakanishi K, Abe Y, Udagawa T, Okada S, Okamoto T, Kaito H, Kanemoto K, Kobayashi A, Tanaka E, Tanaka K, Hama T, Fujimaru R, Miwa S, Yamamura T, Yamamura N, Horinouchi T, Minamikawa S, Nagata M, Iijima K. A review of clinical characteristics and genetic backgrounds in Alport syndrome. Clin Exp Nephrol. 2019;23(2):158–68.
212. Kamiyoshi N, Nozu K, Fu XJ, Morisada N, Nozu Y, Ye MJ, Imafuku A, Miura K, Yamamura T, Minamikawa S, Shono A, Ninchoji T, Morioka I, Nakanishi K, Yoshikawa N, Kaito H, Iijima K. Genetic, clinical, and pathologic backgrounds of patients with autosomal dominant Alport syndrome. Clin J Am Soc Nephrol. 2016;11(8):1441–9.
213. Horinouchi T, Nozu K, Yamamura T, Minamikawa S, Omori T, Nakanishi K, Fujimura J, Ashida A, Kitamura M, Kawano M, Shimabukuro W, Kitabayashi C, Imafuku A, Tamagaki K, Kamei K, Okamoto K, Fujinaga S, Oka M, Igarashi T, Miyazono A, Sawanobori E, Fujimaru R, Nakanishi K, Shima Y, Matsuo M, Ye MJ, Nozu Y, Morisada N, Kaito H, Iijima K. Detection of splicing abnormalities and genotype-phenotype correlation in X-linked Alport syndrome. J Am Soc Nephrol. 2018;29(8):2244–54.
214. Greenbaum LA, Simckes AM, McKenney D, Kainer G, Nagaraj SK, Trachtman H, Alon US. Pediatric biopsy of a single native kidney. Pediatr Nephrol. 2000;15:66–9.
215. Kang S, Yoon HS, Lee EH. Should healthy children who will undergo minor surgery be screened for coagulation disorder? Pediatr Hematol Oncol. 2016;33:233–8.
216. Guay J, Faraoni D, Bonhomme F, Borel Derlon A, Lasne D. Ability of hemostatic assessment to detect bleeding disorders and to predict abnormal surgical blood loss in children: a systematic review and meta-analysis. Paediatr Anaesth. 2015;25:1216–26.
217. Bhasin N, Parker RI. Diagnostic outcome of preoperative coagulation testing in children. Pediatr Hematol Oncol. 2014;31:458–66.
218. Samková A, Blatný J, Fiamoli V, Dulíček P, Pařízková E. Significance and causes of abnormal preoperative coagulation test results in children. Haemophilia. 2012;18:e297-301.
219. Estcourt LJ, Malouf R, Doree C, Trivella M, Hopewell S, Birchall J. Prophylactic platelet transfusions prior to surgery for

people with a low platelet count. Cochrane Database Syst Rev. 2018;9:CD012779.
220. Varnell CD Jr, Stone HK, Welge JA. Bleeding complications after pediatric kidney biopsy: a systematic review and meta-analysis. Clin J Am Soc Nephrol. 2019;14:57–65.
221. Zhu MS, Chen JZ, Xu AP. Factors that can minimize bleeding compli-cations after Kidney biopsy. Int Urol Nephrol. 2014;46:1969–75.
222. Rianthavorn P, Kerr SJ, Chiengthong K. Safety of paediatric percutaneous native kidney biopsy and factors predicting bleeding complications. Nephrology (Carlton). 2014;19:143–8.
223. Vidhun J, Masciandro J, Varich L, Salvatierra O Jr, Sarwal M. Safety and risk stratification of percutaneous biopsies of adult-sized renal allografts in infant and older pediatric recipients. Transplantation. 2003;76(3):552–7.
224. Kark RM. The development of percutaneous Kidney biopsy in man. Am J Kidney Dis. 1990;16:585–9.
225. Pokhrel A, Agrawal RK, Baral A, Rajbhandari A, Hada R. Percutaneous Kidney biopsy: comparison of blind and real-time ultrasound-guided technique. J Nepal Health Res Counc. 2018;16(1):66–72.
226. Lindgren PG. Ultrasonically guided punctures. A modified technique. Radiology. 1980;137:235–7.
227. Chunduri S, Whittier WL, Korbet SM. Adequacy and complication rates with 14- vs. 16-gauge automated needles in percutaneous Kidney biopsy of native kidneys. Semin Dial. 2015;28:E11-14.
228. Øvrehus MA, Oldereid TS, Dadfar A, Bjørneklett R, Aasarød KI, Fogo AB, Ix JH, Hallan SI. Clinical phenotypes and long-term prognosis in white patients with biopsy-verified hypertensive nephrosclerosis. Kidney Int Rep. 2019;5(3):339–47.
229. Sethi I, Brier M, Dwyer A. Predicting post Kidney biopsy complications. Semin Dial. 2013;26(5):633–5.
230. White RH, Poole C. Day care Kidney biopsy. Pediatr Nephrol. 1996;10:408–11.
231. Davis ID, Oehlenschlager W, O'Riordan MA, Avner ED. Pediatric Kidney biopsy: should this procedure be performed in an outpatient setting? Pediatr Nephrol. 1998;12:96–100.
232. Sinha MD, Lewis MA, Bradbury MG, Webb NJ. Percutaneous real-time ultrasound-guided Kidney biopsy by automated biopsy gun in children: safety and complications. J Nephrol. 2006;19(1):41–4.
233. Hussain F, Watson AR, Hayes J, Evans J. Standards for renal biopsies: comparison of inpatient and day care procedures. Pediatr Nephrol. 2003;18:53–6.
234. Murphy MS. Sedation for invasive procedures in pediatrics. Arch Dis Child. 1997;77:281–4.
235. Reich DL, Silvay G. Ketamine: an update on the first twenty-five years of clinical experience. Can J Anaesth. 1989;36:186–97.
236. Green SM, Johnson NE. Ketamine sedation for pediatric procedures: part 2, review and implications. Ann Emerg Med. 1990;19:1033–46.
237. Mikhael MS, Wray S, Robb ND. Intravenous conscious sedation in children for outpatient dentistry. Br Dent J. 2007;203:323–31.
238. Di Liddo L, D'Angelo A, Nguyen B, Bailey B, Amre D, Stanciu C. Etomidate versus midazolam for procedural sedation in pediatric outpatients: a randomized controlled trial. Ann Emerg Med. 2006;48:433–40.
239. Cravero JP, Beach ML, Blike GT, Gallagher SM, Hertzog JH, Pediatric Sedation Research Consortium. The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: a report from the Pediatric Sedation Research Consortium. Anesth Analg. 2009;108:795–804.
240. Kamat PP, McCracken CE, Gillespie SE, Fortenberry JD, Stockwell JA, Cravero JP, Hebbar KB. Pediatric critical care physician-administered procedural sedation using propofol: a report from the Pediatric Sedation Research Consortium Database. Pediatr Crit Care Med. 2015;16:11–20.
241. Mallory MD, Baxter AL, Yanosky DJ, Cravero JP, Pediatric Sedation Research Consortium. Emergency physician-administered propofol sedation: a report on 25,433 sedations from the pediatric sedation research consortium. Ann Emerg Med. 2011;57:462–8 (**e1**).
242. Mourani CC, Antakly MC, Haddad-Zebouni S. Pediatric Kidney biopsy: ambulatory versus overnight hospitalization. J Med Liban. 2001;49(6):316–8.
243. Hussain F, Mallik M, Marks SD, Watson AR, British Association of Paediatric Nephrology. Renal biopsies in children: current practice and audit of outcomes. Nephrol Dial Transplant. 2010;25:485–9.
244. Gupta A, Campion-Smith J, Hayes W, Deal JE, Gilbert RD, Inward C, Judd BA, Krishnan RG, Marks SD, O'Brien C, Shenoy M, Sinha MD, Tse Y, Tyerman K, Mallik M, Hussain F, British Association for Paediatric Nephrology. Positive trends in paediatric Kidney biopsy service provision in the UK: a national survey and re-audit of paediatric Kidney biopsy practice. Pediatr Nephrol. 2016;31:613–21.
245. Muthusami P, Sunder S, Gallibois C, Kitamura E, Parra D, Amaral J, John P, Noone D, Connolly B. Measuring hemoglobin prior to early discharge without routine surveillance ultrasound after percutaneous native Kidney biopsy in children. Pediatr Nephrol. 2017;32:1927–34.
246. Gagnon MH, Lin MF, Lancia S, Salter A, Yano M. A color flow tract in ultrasound-guided random renal core biopsy predicts complications. J Ultrasound Med. 2020;39(7):1335–42.
247. Ding JJ, Lin SH, Huang JL, Wu TW, Hsia SH, Lin JJ, Chou YC, Tseng MH. Risk factors for complications of percutaneous ultrasound-guided Kidney biopsy in children. Pediatr Nephrol. 2020;35(2):271–8.
248. Isiyel E, Fidan K, Buyukkaragoz B, Akcaboy M, Kandur Y, Gonul II, Buyan N, Bakkaloglu S, Soylemezoglu O. Results of native and transplant kidney biopsies of children in a single center over a 15 years period. Ren Fail. 2017;39(1):702–6.
249. Hunsicker LG, Bennett LE. Design of trials of methods to reduce late renal allograft loss: the price of success. Kidney Int (Suppl). 1995;52:S120-123.
250. Wilkinson A. Protocol transplant biopsies: are they really needed? Clin J Am Soc Nephrol. 2006;1(1):130–7.
251. Birk PE, Blydt-Hansen TD, Dart AB, Kaita LM, Proulx C, Taylor G. Low incidence of adverse events in outpatient pediatric renal allograft biopsies. Pediatr Transplant. 2007;11(2):196–200.