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Renal scintigraphy of the transplanted kidney: Innovative approaches to monitoring and prognostic value

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Abstract. *The preferred treatment for severe chronic kidney disease (CKD) is kidney transplantation. However, delayed graft function and acute graft dysfunction resulting from acute tubular necrosis, rejection, cyclosporine toxicity, urine leak, hematoma, blockage, lymphocele, and renal artery stenosis are frequent post-transplant complications. Renal biopsy remains the gold standard for diagnosis, but it is invasive and associated with complications and sampling errors, underscoring the need for accurate non-invasive alternatives.*

Renal scintigraphy (RS) is a non-invasive nuclear imaging technique that uses radiopharmaceuticals to evaluate renal structure and function. It has demonstrated value in diagnosing complications such as acute tubular necrosis, acute allograft rejection, urine leakage, urinoma formation, and vesicoureteral reflux. Importantly, baseline RS performed in the early postoperative period may also provide prognostic information on long-term graft survival.

Although several reviews have addressed the diagnostic role of RS in transplantation, less attention has been given to its prognostic applications, its integration with emerging techniques such as radiolabeled antibodies and hybrid imaging, and its potential to reduce reliance on invasive biopsies. This review, therefore, aims to synthesize current evidence on both the diagnostic and prognostic value of RS in kidney transplantation, with emphasis on recent innovations and future perspectives that distinguish it from earlier literature.

Key words: *renal scintigraphy, implications, kidney transplant, diagnostic values.*

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Сцинтиграфія трансплантованої нирки: інноваційні підходи до моніторингу та прогностичне значення

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Резюме. *Оптимальним методом лікування термінальної стадії хронічної хвороби нирок (ХХН) є трансплантація. Затримки функції трансплантата та гостра дисфункція трансплантата внаслідок гострого тубулярного некрозу, відторгнення, токсичності циклоспорину, витоку сечі, гематоми, закупорки сечових шляхів, лімфоцеле, стенозу ниркової артерії тощо є найчастішими проблемами, які виникають під час та після трансплантації*

Сцинтиграфія нирок (СН) — це неінвазивна ядерна методика візуалізації, яка використовує радіофармацевтичні препарати для оцінки структури та функції нирок. Вона довела свою цінність у діагностиці ускладнень, таких як гострий тубулярний некроз, гостре відторгнення трансплантата, витік сечі, формування уріномами та рефлюкс сечоводу. Важливо, що базова СС, виконана у ранньому післяопераційному періоді, також може надавати прогностичну інформацію щодо тривалості функції трансплантата

Незважаючи на те, що певна кількість оглядів літератури присвячено діагностичній ролі СН у трансплантації нирки, менше уваги приділено її прогностичним можливостям, інтеграції з новими технологіями, такими як радіомічені антитіла та гібридна візуалізація, а також потенціалу зменшення потреби в інвазивних біопсіях. Тому цей огляд має на меті узагальнити сучасні дані щодо діагностичної та прогностичної цінності СН у трансплантації нирки, з особливим акцентом на новітні інновації та перспективи, які відрізняють його від попередньої літератури.

Ключові слова: *сцинтиграфія нирки, клінічне значення, трансплантація нирки, діагностика*

Introduction. Renal scintigraphy (RS) refers to a list of methods using radiopharmaceuticals to assess the structure and function of the kidneys [1]. RS is a non-invasive diagnostic procedure that uses radioactive isotopes; it was originally used in 1965 for post-transplant evaluation. The most popular method for RS is a dynamic planar process that creates two-dimensional images by imaging a radioactive isotope using a gamma camera. Magnetic resonance imaging (MRI), computed tomography (CT), ultrasound, and biopsy with subsequent immunostaining methods can also be employed. Still, all of them have specific restrictions.

A radiopharmaceutical or radiotracer that produces a small amount of radioactivity is injected into the patient during each of the various types of renal scans, which are used to investigate distinct functional features of the kidneys. The radiotracer can assist doctors in determining whether the kidneys are functioning regularly or if there is a problem with them because it interacts differently in different types of tissue. A kidney transplant can also be assessed using renal scintigraphy [1, 2].

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Clinicians can use a variety of diagnostic techniques to identify post-transplant problems, including vascular and urologic issues, acute tubular necrosis (ATN), acute rejection (AR), etc. The optimal procedural method for assessing post-transplant renal impairment is still up for debate. It is frequently necessary to do a renal needle biopsy, which is usually regarded as the gold standard for diagnosing complications of kidney transplantation. The majority of medical professionals favor non-invasive techniques, including RS [3-5].

RS is a reasonably priced, noninvasive, and non-nephrotoxic diagnostic technique. The RS results, however, are challenging to interpret [4-6]. At the same time, CT has limits because of the nephrotoxic drugs utilized, but it offers precise views of the architecture of the kidney transplant and the surrounding tissue. MRI is primarily referred to as a second-line diagnostic modality. However, its application for both anatomical and functional evaluation has grown in recent years [5-7].

Although several reviews have summarized the role of RS in kidney transplantation, they have predominantly focused on its diagnostic utility in differentiating ATN from rejection or in detecting surgical complications. Far less attention has been paid to the prognostic role of RS in predicting delayed graft function and long-term allograft survival, or to recent innovations such as radiolabeled antibodies, hybrid imaging, and quantitative approaches that can increase the accuracy of interpretation. Moreover, the clinical impact of RS

in reducing the need for invasive biopsies and guiding individualized treatment strategies has not been comprehensively addressed.

The aim of this paper is therefore to review and synthesize current literature on the main diagnostic and prognostic aspects of RS in kidney transplantation, with particular emphasis on innovative approaches and future perspectives that distinguish this review from previous ones.

Material and methods. A review of scientific publications indexed in international scientometric databases was conducted. The databases searched included PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The search covered articles published between January 2000 and June 2025. The following keywords and their combinations were used: "renal scintigraphy," "kidney transplantation," and "allograft rejection. Inclusion criteria were original research articles, systematic reviews, and clinical guidelines addressing the use of renal scintigraphy in kidney transplantation, both in diagnostic and prognostic contexts. Exclusion criteria were case reports, conference abstracts without full text, studies not involving human kidney transplantation, and non-English publications. Additional references were identified through cross-checking citations in relevant articles.

Renal scintigraphy. Basic principles. With advancements in other modalities, renal scintigraphy's use and indications have evolved, especially in relation to each modality's capacity to clarify kidney anatomy and assess the kidneys for illness. Scintigraphy continues to play a crucial role in assessing renal function, even if advancements in anatomic resolution by other modalities have reduced its use for anatomic evaluation. It contributes to the assessment of bladder, ureteral, pylocalyceal, and renal anatomy [**1, 8**].

Renal graft structure, blood flow, and function are evaluated by RS, which enables imaging of decreased flow, blockages, or leakage. The three successive stages of renal function are described by the different interpretation methodologies, which include visual, qualitative, and quantitative analysis: The radiotracer's passage through the blood vessels is depicted in the vascular phase, also known as the flow study; the nephrons' extraction of the tracer from the blood occurs during the parenchymal or function phase.

Renovascular hypertension, obstructive uropathy, renal abnormalities, renal transplant, renal parenchymal infections, including pyelonephritis and postinfectious scarring, as well as renal and ureteric trauma, are among the conditions that can be clinically evaluated with nuclear medicine agents.

RS requires gamma scintillation camera systems for RS. These devices create display images from photons released by the radiopharmaceuticals' radiotracer. A collimator, scintillation crystal, photomultiplier tubes (PMTs), and a processing computer make up the gamma camera system [**8, 9**]. Depending on the distribution of the radiopharmaceutical, the computer of the gamma camera system transforms the output signal into an image. On Figure 1 we present our RS equipment established in National specialized children's hospital «Okhmatdyt" (Kyiv, Ukraine) (Fig. 1).

Fig. 1. Basic scheme of the RS block in the National specialized children's hospital «Okhmatdyt" (Kyiv, Ukraine).

The type of renal scan has an impact on the radiopharmaceutical selection. Renal scintigraphy uses a variety of radiotracer agents. The most often utilized ones are:

Diethylene triamine penta-acetic acid (Tc-99m DTPA) helps measure GFR because it can be mainly eliminated by glomerular filtration.

Tc-99m dimercaptosuccinic acid, sometimes known as technetium-99m DMSA. Technetium-99m DMSA allows cortical imaging by primarily binding to renal tubular cells in the renal cortex. It is mostly utilized for cortical anatomy and the evaluation of diseases such as renal ectopia or renal scarring because of its prolonged binding to the cortex.

Tc-99m MAG3, or technetium-99m mercaptoacetyl triglycine. The proximal renal tubules release the majority of Tc-99m MAG3, with the glomeruli filtering a small portion (about 5%). More effective extraction of Tc-99m MAG3 from plasma results in preserved parenchymal activity, enabling assessment of the renal parenchyma. Compared to Tc-99m DTPA, it has 40% more plasma clearance, which enhances imaging [9, 10].

RS is the precise method, dependent on serial static or dynamic image acquisitions set up at various points during the investigation. It usually takes one second for a radioactive bolus inserted into an antecubital vein to go from the aorta to the renal arteries. Serial dynamic pictures are obtained every one to two seconds for a maximum of one minute in order to assess renal blood flow. In healthy patients, the kidneys often become visible in 5 or 6 seconds after injection and reach their peak activity 30 to 60 seconds later [3-5, 8].

After one minute of the renal perfusion phase, a sequence of pictures is taken in order to assess renal parenchymal function. With 99mTc-DTPA, images are taken every 15–60 seconds for 3–5 minutes, and with 99mTc-MAG3, images are taken every 20–30 minutes. The best imaging of renal architecture by parenchymal uptake is possible at this phase. By minutes 4 to 8, radiotracer activity typically begins to show up in the collecting system or bladder. After taking a diuretic (the dosage of Lasix depends on age and renal function) or walking to encourage pyelocalyceal system drainage, the system is evaluated. Since a full bladder restricts or delays upper urinary tract emptying, patients with urinary bladder non-compliance or difficulties urinating must have an indwelling open bladder catheter [8].

The images obtained are used to visually evaluate renal structure and function (Fig. 2).

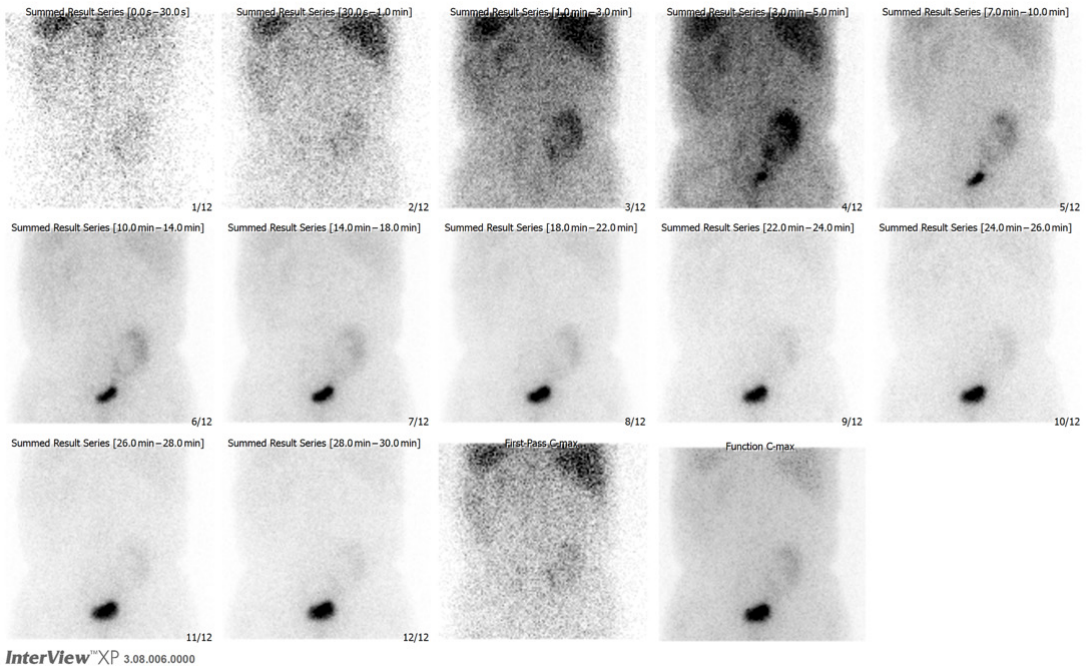

Fig. 2. Dynamic images from a normal functional RS.

Furthermore, the set of pictures is used to construct a time-activity curve, which is then used to quantify renal function in procedures like Tc-99m MAG3 in RS. The computer creates time activity curves by evaluating radionuclide activity over a region of interest (ROI).

Data is shown visually for 20 to 30 minutes following the injection of the radiotracer. There are three phases in a normal renogram. The radiotracer entering the kidneys is represented by phase one, which is referred to as the vascular transit phase. Typically, it lasts between 30 and 60 seconds. When the radiotracer enters the tubules, phase two, sometimes referred to as the tubular concentration phase or parenchymal transit phase, typically lasts for 1 to 5 min. A peak in the renogram serves as its representation. A downslope in the renogram is a sign that the radiotracer's excretion from the kidneys and removal from the collecting system is indicative of phase three. Usually, it begins 4 to 8 minutes after the radiotracer injection [9-11] (see Fig. 2).

Because the retained radiotracers in the renal pelvis complicate the renal cortical assessment, the ROI should be limited to the renal cortex and exclude renal pelvic activity when assessing renal cortical function. The renogram can be used to obtain a variety of semiquantitative statistics, including half-time excretion (T1/2), relative uptake ratios, time to peak activity (Tmax), and 20-minute time to peak count ratios (20-min/max count ratio) [9, 12].

Renal scintigraphy of the transplanted kidney. 99mTc-MAG3 for RS is used to assess kidney transplant function, complications, and treatment monitoring [13, 14]. For baseline function analysis, scintigra-

phy is done soon after surgery. If there are any concerns about the transplant, such as worsening function or postsurgical complications, follow-up renal scintigraphy imaging is done. Renal cadaveric transplant survival is predicted by measuring the time to peak in 99mTc-MAG3 clearance early after surgery. The graft exhibits radiotracer activity when perfusion is normal. It is evaluated in connection with the iliac vessels that supply the normal graft [11-14].

Acute tubular necrosis (ATN) and acute allograft rejection (AR) are the most frequent complications of kidney transplantation. ATN typically manifests in the first three to four days following transplantation [15]. ATN typically arises as a result of transplant ischemia following harvesting but prior to transplantation. The most common instance of this is in cadaveric transplants. Reduced renal function and cerebral retention are visible on 99mTc-MAG3 scintigraphy. The characteristic scintigraphic findings of ATN include gradual accumulation of the radiotracer in the renal cortex, delayed uptake and excretion of tubular secretion agents, such as Tc-99m MAG3, and preserved or very slightly diminished perfusion. Since perfusion is less impacted in grafts affected by ATN than those affected by AR, scintigraphic perfusion criteria have been promoted to help with the differential diagnosis between ATN and AR. Also, on serial studies, progressive decline in function and poor perfusion are thought to favour AR [15, 16].

Similar observations of normal uptake and enhanced cortical retention with little to no excretion due to impaired tubular activity are seen in renal transplant damage from the antirejection medications [17]. Likewise, medication poisoning does not have a particular imaging pattern. Although cyclosporine nephrotoxicity can be differentiated from ATN by its correlation with cyclosporine levels and its time of presentation, which typically occurs several weeks after renal transplant, by which time acute tubular necrosis should have resolved, the scan findings seen in this condition have been reported to mimic both ATN and AR [15-17].

Urine leakage and the formation of urinoma are frequently observed as post-operative problems. Usually detected on ultrasonography, a post-transplant fluid collection could be a hematoma, lymphocele, seroma, abscess, or urinoma. Fever and elevated inflammatory markers are common symptoms of an abscess; hematoma, seroma, and urinoma are frequently observed in the initial days after surgery, although a lymphocele usually appears months later. On scintigraphy, a post-transplant fluid collection shows up as a peri-renal photopenic region. Despite a slight degree of filling-in on delayed imaging, a lymphocele appears as a persistent photopenic region (Fig. 3).

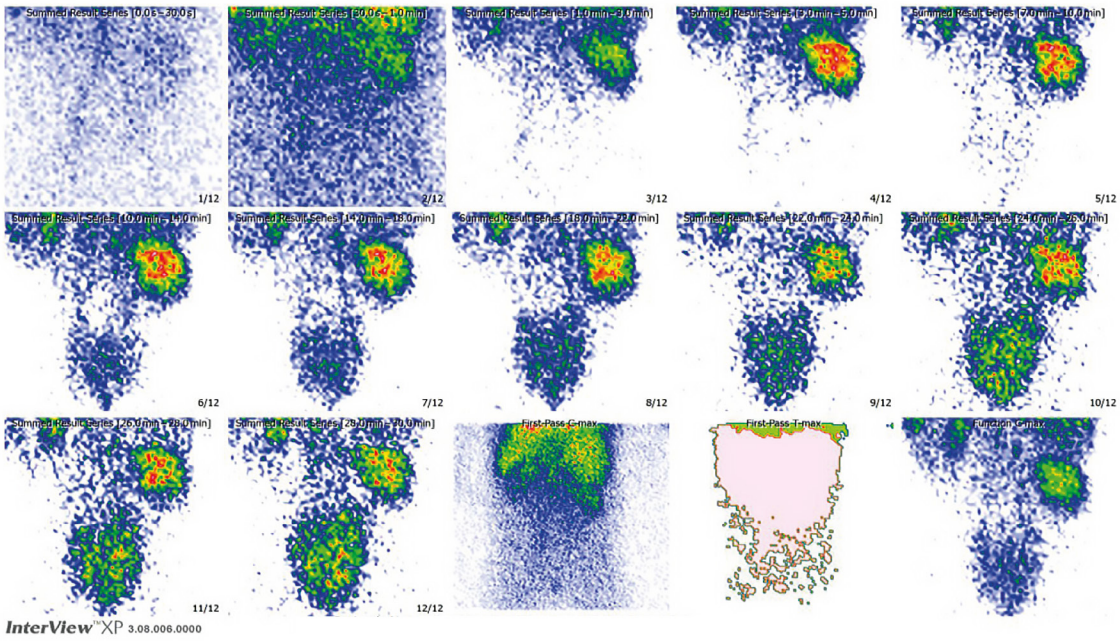

Fig. 3. Sequential Imaging of Renal Perfusion and Function in the case of ureter obstruction.

Urinary leaks are strongly suggested by a photopenic region that gradually fills in with powerful radiotracer during the scan or by discharged activity outside the urinary system. On the other hand, a small leak can make it impossible to differentiate a urinoma from other fluid collections using scintigraphy [18].

Finally, renal transplant rejection may be observed after the transplantation. Depending on when it first appears, renal transplant rejection is typically categorized as hyperacute, acute, or chronic, with each type being caused by a distinct mechanism. RS usually reveals delayed excretion, reduced absorption, and impaired perfusion in rejection (Fig. 4).

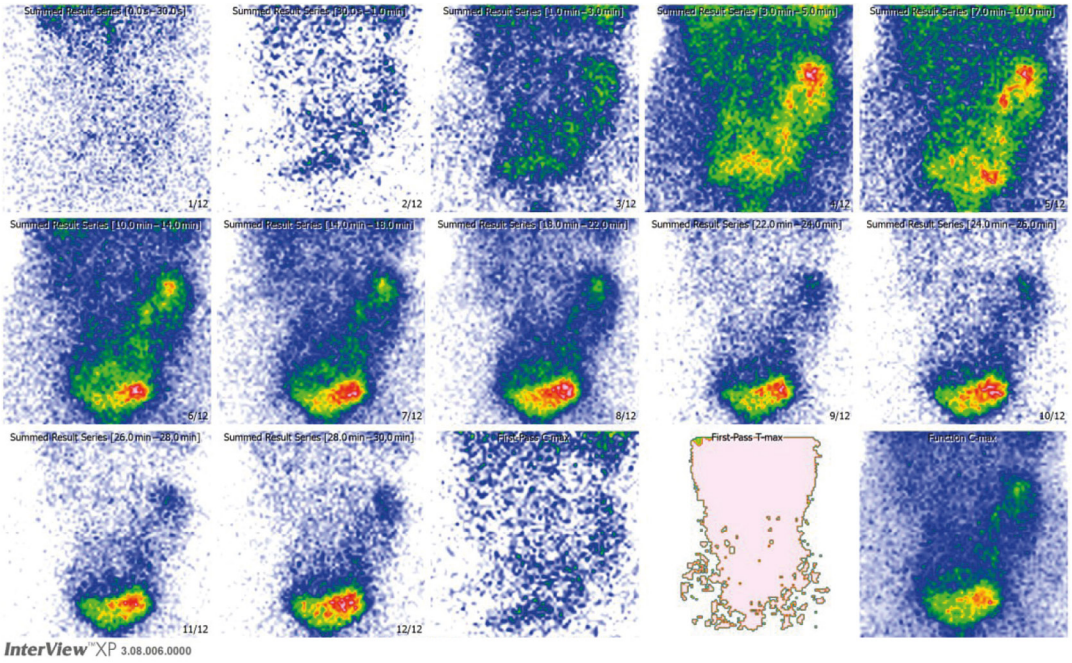

Fig. 4. Sequential Imaging of Renal Perfusion and Function of the rejected kidney after the transplantation.

RS shows no renal perfusion or function within 0–24 hours of surgery in cases of hyperacute transplant rejection. The recipient's pre-existing antibodies to a foreign body, in this case, cause the development of venous thrombosis. Cell-mediated lymphocytic infiltration typically results in acute rejection within two to three months. Reduced renal perfusion, as well as radioactive uptake and excretion, are revealed by RS. An antibody-mediated process that lasts longer than three months to years following surgery is known as chronic rejection. In these situations, nuclear scanning reveals a progressive decline in transplant performance and perfusion [15-19].

It is important to confirm urologic problems as a distinct category of kidney transplant issues. One typical complication that may occur soon after transplant surgery is vesicoureteral reflux [20]. Due to its non-specific symptoms, reflux is often accidentally discovered on Tc-99m MAG3 RS while searching for a cause of graft failure. When reflux occurs, RS typically shows a "double peak" on the time-activity curve. The first peak indicates the beginning of the regular excretory phase, whereas the second peak results from radiotracer reentrance into the kidney due to bladder reflux. From a visual standpoint, the radiotracer is first removed from the collecting system and expelled from the renal parenchyma [19, 20].

Additionally, the prediction of long-term allograft function may be influenced by baseline scintigraphy done in the early post-operative phase. Graft survival has been found to correlate with a number of quantitative measures of perfusion and/or uptake obtained from Tc-99m DTPA and Tc-99m MAG3 RS conducted one to four days following transplantation. According to a recent study, quantitative evaluation of Tc-99m DTPA perfusion scintigraphy conducted within two days of transplantation was better than Doppler ultrasonography in measuring the intra-renal resistance index; it was helpful in predicting long-term graft performance for up to five years [21].

In order to identify post-transplant problems including vascular or urological issues, ATN, or rejection, it is essential to monitor renal function following kidney transplantation. Consequently, a more individualized and patient-specific treatment plan and potential decrease in early graft failure could be the outcome of an imaging technique with a high predictive value for post-transplantation problems [3-5].

Depending on the kidney graft type, - donation after circulatory death (DCD), donation after brain death (DBD), or after living donation, and delayed graft function (DGF), this common complication following kidney transplantation can range from 2% to 50%. The definitions of DGF that are most frequently used include [22]:

Dialysis-based DGF, which requires postoperative dialysis within seven days of KTX;

Functional DGF, which is indicated by a blood creatinine level that does not drop by 10% for three days in a row after kidney transplantation.

RS was first used in earlier research as a technique for DGF evaluation and/or prediction. However, because there are numerous quantitative indices and radiopharmaceuticals accessible, accurate acquisition and interpretation are challenging [18, 22].

According to studies, RS results can predict the duration of recovery following DGF and could offer valuable insights into identifying patients who have further allograft pathology. This could make it easier to take image-guided therapy decisions, which would reduce the need for diagnostic biopsies and speed up treatment.

Discussion. Nuclear medicine is a fast-developing science, and the continued development of new imaging and radiotracer techniques. This is promising for improving the sensitivity and specificity of nuclear medicine investigations in identifying problems associated with kidney transplants. Renal perfusion, function, and anatomy are all assessed with renal scintigraphy. At the same time, ultrasound, CT scans, and MRIs are the main methods used to evaluate anatomy [1-3].

In terms of anatomy, renal scintigraphy is now utilized in cases where a patient is allergic to the contrast substance used in CT or MRI scans [1, 2]. When renal function is impaired and GFR is altered, IV contrast is not used in CT or MR scans. In these situations, nuclear scanning agents may be employed. For claustrophobic patients who are unable to have CT or MRI scans, renal scintigraphy is also recommended.

A great technique for both qualitative and quantitative evaluation of kidney transplant performance is RS. It helps detect complications after transplantation. Early detection of kidney transplant function enables prompt management choices, such as transplant removal when irreversible. A patient can avoid needless immunosuppression by having a defective transplanted kidney removed as soon as possible [3-5]. In Table 1, a comparison of the main imaging tools is presented.

Table 1

Comparison of Imaging Modalities for Renal and Transplant Evaluation

Feature	RS	Ultrasound (US)	CT	MRI
Functional assessment	Excellent (perfusion, GFR, excretion)	Limited	Poor	Limited (dynamic contrast studies required)
Anatomical resolution	Low	Moderate	High	High
Radiation exposure	Moderate	None	High	Low (contrast-dependent)
Cost	Moderate	Low	High	High
Contrast requirement	Usually none	None	Iodinated	Gadolinium (risk in CKD)
Use in transplant	Highly sensitive to early functional changes	Useful for hydronephrosis, fluid collections	Detects anatomy, complications	Detects anatomy, perfusion with contrast
Limitations	Limited anatomy; small lesions may be missed	Operator-dependent; limited functional info	Radiation; nephrotoxic contrast	Expensive, motion artifacts; limited availability

Compared to a CT scan, renal scintigraphy continues to be used in the assessment of pediatric renal anatomy, whether it is normal, abnormal, or diseased, due to its extremely minimal radiation dose. To offer high quality investigations, renal scintigraphy requires a coordination and multi-team communication between radiologists, nuclear medicine physicians, nuclear medicine technologists, and the treating physicians and/or surgeons [3-5, 19].

In conclusion, we offer a strategy outlining the primary risks, limitations and benefits of the RS on the kidney transplant (Fig. 5).

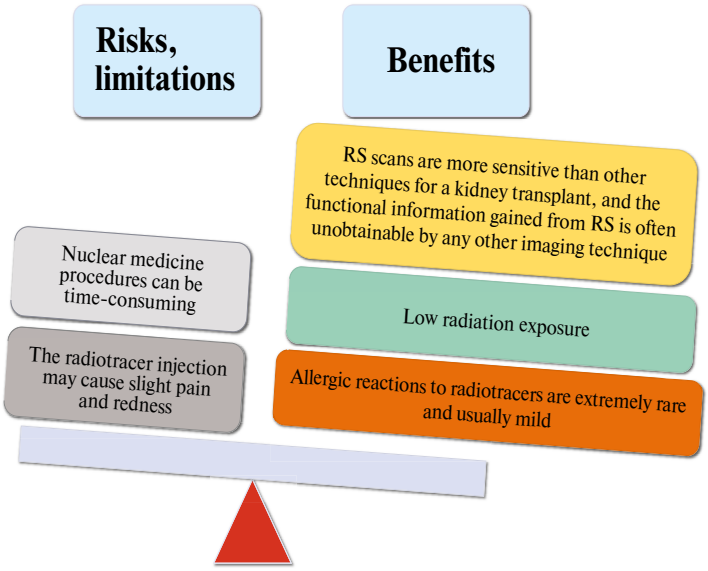

Fig. 5. Comparative analysis of the limitations and benefits of RS.

In summary, RS uses a variety of radioactive tracers to evaluate the kidneys and collecting systems. Perfusion to the kidneys, tracer extraction from the blood, and tracer excretion through the collecting system can all be evaluated with dynamic renal investigations. Perfusional anomalies, assessment of kidney transplants, computation of differential renal function, study of deteriorating renal function, and examination of mechanical renal tract blockage (including pelviureteric and vesicoureteric junction obstruction) are among the indications.

Advanced combined methodologies will be used in the field of kidney transplantation and RS in the future. Acute renal rejection was shown recently to be treated with anti-CD3 monoclonal antibodies. For the purpose of visualizing and detecting acute renal rejection, research teams have labeled anti-CD3 monoclonal antibodies with technetium-99m in several trials. Tc-99m SHNH-visilizumab, a more biocompatible radiolabelled CD3 antibody, is undergoing testing [**23**].

Conclusions:

RS is a significant supplementary technique in the assessment of potential issues after kidney transplantation since it is a non-invasive study that offers useful information on the functional condition and structure of an allograft.

It is necessary to combine the interpretation of the scintigraphic results with the clinical presentation and other imaging modalities that are available.

Radiotracer and imaging techniques are still being developed, with the goal of accurately and early detection of kidney transplant-related complications for prompt intervention.

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