Diagnostic imaging of transplanted kidney

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Kidney transplantation plays currently basic role in treatment of chronic kidney disease. To enable graft functioning close clinical, laboratory and imaging supervision is needed to early detect and combat complications. In selected cases histopathological examination of biopsy material is indispensable. Diagnostic imaging currently offers multimodal, modern, both structural and functional examinations enabling non-invasive diagnosis of most complications. We present a brief review of actually available imaging methods in patients with transplant kidneys and candidates for graft donors or recipients.

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Diagnostyka obrazowa nerki przeszczepionej

Przeszczep nerki odgrywa obecnie podstawową rolę w terapii przewlekłej niewydolności nerek. By zapewnić funkcjonowanie przeszczepu konieczny jest ścisły nadzór kliniczny, laboratoryjny oraz metodami diagnostyki obrazowej, co umożliwia szybkie wykrycie komplikacji. W części przypadków konieczne jest badanie histopatologiczne materiału biopsyjnego. Współczesna diagnostyka obrazowa oferuje wielomodalne, nowoczesne badania zarówno morfologiczne jak i czynnościowe, pozwalając na nieinwazyjną diagnozę większości powikłań przeszczepu nerek. W naszym artykule prezentujemy krótki przegląd metod diagnostyki obrazowej wykorzystywanych u pacjentów po transplantacji nerki oraz w grupie potencjalnych dawców i biorców.

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Introduction

The prevalence of chronic kidney disease (CKD) is estimated for 11-16.8 percent [1-6]. Prevalence of end stage renal disease (ESRD) is about 0.22-0.4 percent [2,7]. Most patients with ESRD require renal replacement therapy in a form of either hemodialysis / peritoneal dialysis or renal transplantation. Renal transplantation is optimal choice for most patients offering longest survival time. Effectiveness of renal transplantation was grossly improved due to better immunosuppressive medication, more precise antigen matching, progress in surgical techniques and creation of dedicated to transplantation specialized organizations in the national health systems. A success of renal transplantation is highly dependent on a proper pre- and post operation diagnostic imaging. From the radiologist's point of view post-transplant complications can be divided in four main categories: perinephric, parenchymal, concerning collecting system and vascular. Separate category of complications is associated with renal biopsy. Renal graft is usually located in the right iliac fossa, but the opposite side can be chosen in a case of favorable vascular system conditions on the left side of the body. Donor's grafts are typically excised with a part of aorta, what makes easier the creation of end-to-side anastomosis to patient's external iliac artery. In grafts from familial donors, the artery is linked end-to-end to patient's internal iliac artery or end-to-side to external iliac artery. Renal vein is typically anastomozed end-to-side to external iliac vein. Urinary tract continuity is typically restored by implantation of ureter into urinary bladder wall (ureteroneocystostomy), rarely ureter-ureter or patient ureter-graft pelvis anastomosis is applied. Increasing number of renal transplantations make imaging of renal graft complications actual and important topic.

Perinephric fluid accumulation

Perinephric fluid accumulation is quite frequent after renal transplantation and occurs in up to 50% of cases [8]. This includes hematomas, seromas, lymphoceles, urinomas and abscesses. Importance of perinephric fluid collection depends on its dimensions, growth rate and the site of occurrence. The role of scintigraphy in diagnosing these complications is limited with exception of urinoma. The ultrasound studies, which are typically used for the transplant follow-up, cannot differentiate between types of fluid with high reliability. Hematomas and abscesses in ultrasound examination tend to be echogenic in contrast to urinomas and lymphoceles, which are typically anechoic or have occasionally moderate amount of echogenic fragmentations (some lymphoceles). Old hematomas may however be completely anechoic. In CT hematoma in acute phase is hyperdense and decreases its density with time or divides into portions of different densities, lymphocele or urinoma presents however near water density. Acute hematoma typically shows the high intensity in T1W and low in T2W MR imaging [9]. The time of appearance and growth rate is helpful in differentiating of perinephric fluid collection. Hematomas and seromas are very common and they appear early after transplantation in contrast to lymphoceles, which typically appear 4-8 weeks post-operation and are the consequence of iatrogenic lymphatic drain's damage. Urinomas tend to appear during the first two weeks following trans-

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plantation and can grow quite rapidly. Fast growth of fluid collection is characteristic for hematoma, urinoma and infection. Specific location of the fluid gives some suggestion – hematomas and seromas are typically crescentic around the kidney, urinomas are typically localized between the kidney and urinary bladder. Every fluid collection around the kidney can turn to be infected and to form an abscess (especially in immunosuppressed post-transplant patients). It is typically echogenic with characteristic gas bubbles seen in ultrasound or CT, in early phase abscess demonstrates increase of density in fluid lesion or contrast enhancement of the wall. In MRI abscess demonstrates diffusion restriction in DWI sequence. Biochemical analysis of aspirated fluid can help to elucidate its character – urinomas have higher creatinine levels and lower glucose levels in comparison to serum [10], lymphoceles have the creatinine and protein levels similar to serum [11]. Biochemical characterization of perinephric fluid in patients with poorly functioning graft can be sometimes misleading, because they may produce urine with low creatinine concentration. Cellular composition of aspirate can confirm abscess or suggest lymphocele (some leucocytes with negative culture). In general population the modality of choice for demonstrating of urine leak is contrast-enhanced CT with delayed registration of 5-20 minutes post injection of contrast phase. Intravenous pyelography has the low sensitivity in detection of ureteral urinary leak [12]. Antegrade or retrograde pyelography demonstrate high sensitivity in detection of ureteral urinary leak [12], but they are quite invasive procedures. When intravenous iodinated contrast media studies are relatively contraindicated (in case of increased creatinine, allergy, after receiving renal transplant) dynamic radionuclide scintigraphy plays an important role in detecting and confirmation of urine leak [10]. Planar scintigraphy (non-tomographic and without adjunct of co-registered CT) has limited ability to assess the exact location and extent of extravasated urine and these limitations can be minimized with usage of bimodal SPECT-CT image registration [13]. Scintigraphic image of hematoma, seroma or lymphocele is not characteristic – they present typically as unspecific area of diminished radiotracer activity (photopenic focus).

Parenchymal complications

Pathological process in transplanted kidney can be focal or diffuse. Diffuse processes encompass acute tubular necrosis (ATN), rejection and drug nephrotoxicity. Diagnostic imaging cannot differentiate with high confidence between these conditions and final confirmation by biopsy usually is needed [11]. Scintigraphic studies of renal transplant typically are performed with radiotracer either passively filtrated or actively excreted in tubule such e.g. 99mTc-DTPA or 99mTc-MAG3. Image registration is performed in a dynamic manner with initial short-frame images depicting early perfusion and the following long-frame images showing radiotracer's uptake and excretion. Scintigraphic differentiation between ATN and acute rejection (AR) is typically based on observation that in ATN, in opposition to AR, perfusion is preserved. Scintigraphy when compared with biopsy as a "gold standard" in acute rejection had the sensitivity 30-96% and specificity 60-100%. In acute tubular necrosis sensitivity was 50-95% and specificity 50-92% [14-25]. Regretfully scintigraphic findings in cyclosporine A (CyA) nephrotoxicity and AR are similar and scintigraphic differentiation between these two entities is problematic [20,26,27]. Chronic rejection on scintigraphy usually presents as a gradual decrease in parenchymal radiotracer's uptake and flattening of renographic curve (proportionally to renal fibrosis) with preservation of particular renogram phases [28]. In grayscale ultrasound parenchymal complications like acute rejection or acute tubular necrosis can be seen as a kidney enlargement, effacement of central echo complex, changes in echogenicity pattern (increase or decrease of echogenicity, loss of corticomedullary differentiation, the pyramidal enlargement), thickening of collecting system walls, but frequently the image is normal. All these signs in grayscale ultrasound are highly observer-dependent and unspecific [29-32]. In chronic rejection grayscale ultrasound can show an increased parenchymal echogenicity, poorer corticomedullary differentiation, size decrease, cortical thinning and mild hydronephrosis, but frequently image is normal. In drug toxicity grayscale ultrasound image typically is normal. In Doppler ultrasound parenchymal complication can increase arteriolar resistive (RI) index above 0.75, but this finding is unspecific and is not useful in differentiation between types of parenchymal complications [32-36]. Similarly, MR findings in parenchymal complications are not specific enough to substitute renal biopsy [9]. Until now biopsy remains "gold standard" in differentiating parenchymal complications and gives final diagnosis in most cases. Diagnostic imaging accuracy (including scintigraphy) in parenchymal complications is not sufficient to obviate biopsy procedure.

Vascular complications

Vascular complications are present in 1.9-12.5% of posttransplant patients [37-39]. They are associated with relatively high risk of graft's loss and in many cases can be treated with good effect, so early and accurate diagnosis is of utmost importance. Most frequent vascular complication is renal artery stenosis (RAS). Most cases of RAS develop disease during the first year after transplantation. It is present in up to 10% of graft recipients [40-43]. RAS can be located in anastomosis (typically) and in both anastomozed arteries before and after anastomosis. RAS results from improper surgical technique, damage, kinking or compression of artery, atherosclerosis, and immunologic reaction to suture. Especially end-to-end arterial anastomoses are prone to stenosis. Basic imaging modality in detection of RAS is Doppler ultrasound. Superficial location of renal transplant makes ultrasound assessment of transplant and its vessels easier than in case of native kidneys. Doubtful cases can be elucidated by magnetic resonance angiography (MRA). Best results yield MRA with gadolinium-contrast obtaining sensitivity and specificity 100% and 98% respectively using digital subtractional angiography (DSA) as reference [44]. DSA enables performing of transluminal angioplastic procedures and restoring normal perfusion in most stenotic cases. Similarly good results are present using CT angiography [45], but nephrotoxicity of iodine contrast media and ionizing radiation dose are relevant disadvantage and CT angiography is not routinely considered as a first-line diagnostic modality [46]. Scintigraphic captopril test basing on comparison of baseline and post-captopril dynamic scan is less accurate than MR, CT and US [45]. Renal artery thrombosis is a rare complication leading typically to graft loss. It may develop in both renal artery and smaller arteries level selectively resulting in small focal infarctions. Renal artery thrombosis in most cases is sequel of acute rejection (AR), kinking, compression and intima injury. In Doppler ultrasound the absence of flow distal to thrombus, including the renal vein is seen. In segmental infarcts Doppler presents perfusion deficits in shape of a wedge, which have to be differentiated with heavy acute rejection, where the blood flow is sometimes minimal [47] and with the other pathologies as heavy pyelonephritis or transplant's mechanical injury. In case of thrombosis of main trunk of renal artery grayscale ultrasound shows enlarged hypoechoic kidney, in segmental infarcts hypoechoic lesion are limited to area supplied by infracted artery. On scintigraphy kidney with renal artery thrombosis present as uncharacteristic photopenic defect [48], but segmental infarctions can be easily detected. Contrast enhanced CT easily demonstrates perfusion defects but is relatively contraindicated in renal failure patients. Therefore in cases of unclear Doppler image the MR angiography should be employed. Renal vein thrombosis is present in 2-7 % of patients [49].Typical findings are present in Doppler ultrasound. It shows absence of flow in main renal vein and reversal of diastolic flow in renal artery. Sometimes ultrasound detects echogenic material in renal vein. In scintigraphy kidney with fully thrombosed renal vein presents as uncharacteristic photopenic defect [48]. In partial thrombosis Doppler ultrasound may show some flow in renal vein (sometimes with acceleration) and increased resistive index in renal artery. In chronic cases creation of collateral vein outflow is possible. In cases of partial thrombosis scintigraphy may show uncharacteristic pattern of decreased blood flow and prolonged uptake of radiotracer. Final confirmation of renal vein thrombosis can be performed with MR angiography, CT angiography or DSA. Segmental infarctions can be the result of segmental artery thrombosis or may occur in course of acute rejection. Ultrasound demonstrates them as wedge shaped areas of increased or decreased echogenicity with absent perfusion (40). Scintigraphy demonstrates wedge-shaped deficits of radiotracer uptake that have to be differentiated with focal infection [50,51].

Arteriovenous fistulas and pseudoaneurysms

Intrarenal arteriovenous fistulas (AVF) and pseudoaneurysms usually are com-

plication of renal biopsy. Usually they are small, self-limiting processes and may resolve without intervention. Larger fistulas can lead to kidney hypoperfusion or bleeding into pelvocalyceal system and have to be treated interventionally by angiography and coiling. Pseudoaneurysms are symptomatic when they rupture and bleed into perinephric space or pelvocalyceal system. Basic modality for noninvasive demonstration of AV fistula or pseudoaneurysm in kidney is color Doppler ultrasound. B-mode, grayscale ultrasound in AVFs is typically normal, in pseudoaneurysms present the uncharacteristic cystic lesion. Color Doppler in fistula demonstrates focus of turbulent, low-impedance flow with an increased velocity in comparison to normal vessels and arterialization of flow spectrum in draining vein. In pseudoaneurysms are seen cystic structure with swirling, turbulent perfusion pattern and characteristic bidirectional, to-and-fro flow in the neck of pseudoaneurysm is detected. Angiography is the most sensitive technique in diagnosing of AVFs or pseudoaneurysms and additionally can guide the minimally invasive interventional curative procedures, which are successful in the majority of cases. Typically AVFs produce the premature appearance of contrast in renal vein due to shunting. Grade of this early opacification of renal vein is proportional to fistula's size. Pseudoaneurysms typically present as the pooling of contrast media, most notably visible in arterial phase. Intensity of pseudoaneurysm opacification is proportional to size of its neck and inversely proportional to amount of thrombus inside the pseudoaneurysm. Extrarenal AVFs and pseudoaneurysms are infrequent and in most cases asymptomatic. Typically they are the consequence of improper surgical technique or paranephric infection, rarely are sequelae of biopsy procedure. The symptoms usually appear when a shunt volume is high or when they compress blood vessels. Pseudoaneurysms are potentially life threatening because they sometimes break and cause the rapid death. Contrast enhanced CT is not helpful in AVFs diagnosis, in pseudoaneurysms round low-attenuation paranephric lesion with high contrast enhancement is seen.

Collecting system (urologic) abnormalities

Three main categories of urologic complications can be defined: urinary leak (discussed above), obstruction of urinary outflow and vesico-ureteral reflux. The most common complication is urine leakage (discussed above) which occurs in 6.2-6.5 percent of patients and occurs typically in first two weeks after transplantation [52,53]. Obstruction of urinary tract occurs in 1.4-5.8 percent of patients and appears in first six months after transplantation [52,54,55]. It is the result of ischemia, technical error during surgery, edema, external compression, kinking of ureter, infection, blocking by blood clots, necrotic tissue in papillary necrosis and fungal colonies. Most frequent cause of urinary outflow obstruction is a stricture in distal part of ureter due to ischemia [54]. Denervation of graft kidney causes the patient has not pain complaints in a case of obstruction as in the case of native kidney. Enlargement of the collecting system can be easily visualized with ultrasound and in case of longer persistence or size's increase it strongly suggests an obstruction of urinary tract. The diagnostic problem is the fact that some dilatation of collecting system is frequently present in transplanted kidneys and in most cases is not associated with obstruction or another pathology [56]. As graft pelvocalyceal system is denervated it is easily distended and enlargement may persist longer time after normalization of pressure in PCS system. Additionally, late enlargement of pelvocalyceal system (PCS) is sometimes seen in non-obstructed grafts among patients with chronic rejection [41,57]. Dynamic renal scintigraphy performed with furosemide helps to differentiate obstructed and non-obstructed grafts [28,58] and reaches high specificity and sensitivity in a range 80-90 % depending on variation of the study used [58]. Excretory urography is typically unsuccessful in demonstration of obstruction site and antegrade pyelography is necessary. Imaging as ultrasound and fluoroscopic imaging is additionally useful in guiding of interventional procedures as percutaneous nephrostomy, JJ stent placement or balloon ureteroplasty which are commonly used in urologic complications.

Infection

Patients receiving renal transplants are particularly susceptible to infection as they are surgically operated, immunosuppressed, sometimes carrying indwelling catheters or stents. The process may be localized in surgical wound, in any perinephric fluid collection with perinephric abscess formation, or in the kidney and PCS sometimes leading do renal abscess formation. The role of diagnostics including imaging is particularly important because immunosuppressed patients may present only mild symptoms [8,59]. In case of pyelonephritis ultrasound findings show an increase or decrease of echogenicity and blood flow reduction. Unfortunately these ultrasound findings are not characteristic and appear also in infarction or rejection too. Abscess typically presents as inhomogeneous, cystic, septated area [60]. Presence of gas bubbles in lesion (intra- or extrarenal) increases the study specificity and strongly suggest an abscess. Gas content is easily demonstrated in CT imaging or ultrasound as reverberation artifact [8]. In case of pelvocalyceal system infection ultrasound demonstrate echogenicity change in normally anechoic PCS lumen: pyonephrosis gives some diffuse subtle echoes, fungus ball shows as weakly shadowing mass, also separated necrotic renal papillae may be detected. Infection may be demonstrated with radionuclide studies with use of 67-Gallium or 111-In-leucocytes [61,62], but false positive results may occur in case of rejection [62] or without confirmed pathology [63]. CT or ultrasound additionally can guide catheter placement in abscess.

Nephrolithiasis

In population of renal graft recipients the risk of nephrolithiasis is about 1 percent [64,65]. It especially affects patients with persistent hyperparathyroidism after end-stage renal disease cure. Because of denervation of transplanted kidney patients for a long time may present only the mild colic complaints or to be asymptomatic [64,65]. Ultrasound, CT or antegrade pyelography is useful in calculus detection and characterization. Unenhanced CT serves as reference "gold standard" method reaching sensitivity and specificity 98 % [66]. In majority of cases the low-invasive therapy techniques (endoscopic, lithotripsy) are employed and usually successful [65,67]. In some individuals the temporal percutaneous nephrostomy has to be applied to decompress and protect the kidney until stone removal [65].

Kidney donors evaluation

In living donor kidney transplant evaluation minimally invasive procedures gain popularity. Before graft kidney harvesting the anatomy of renal vasculature must be defined. Variations in renal vasculature are very common and present in 27-50 % of kidneys [68]. Advances in magnetic resonance angiography (MRA) in last years made it an alternative for X-ray methods: primarily angiography and in last decades angio-CT [68]. Concordance of angio-CT in delineation of renal vessels is very high using the surgery as reference and reaches 98 % [69], making it "gold standard" in imaging of graft vessel variations. MRA assessment of arterial part yields sensitivities between 85 and 97 % [70-75] and is comparable to angio–CT offering the sensitivity of 93 % and concordance with surgery findings in 98 % [76,77]. MRA is even better than CT in diagnosing of venous part reaching sensitivities between 90 and 100 % [68,76,77]. Renal dynamic scintigraphy allows easy and exact detection of functional asymmetries between kidneys of donor and prevents excision of dominating kidney [78]. Separate, rare problem is the risk of neoplasm transmission with graft kidney, most frequently transmitted are melanoma, lung cancer and renal cancer [79,80].

Conclusions

Progress in medical imaging that has been made during the last decades allows earlier detection and more accurate differential diagnosis in cases of renal transplant complications. In the current era of multimodality and strong development of functional imaging radiology delivers rich information about condition of graft kidneys. In many cases however the renal biopsy is still needed to establish the final diagnosis. We hope, in some time diagnostic imaging will reach level of accuracy needed to substitute invasive histopathologic studies.

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