Renal transplant artery stenosis

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Abstract

Renal transplant artery stenosis is a relatively frequent complication after transplantation, with an incidence of up to 23% being reported. The gold standard for the diagnosis still remains renal arteriography. Several imaging techniques are available to confirm the diagnosis (duplex-Doppler, nuclear magnetic resonance, spiral computerized tomography), and their use depends, in part, on the centre’s experience. The treatment can either be conservative (providing graft perfusion is not jeopardized) or by revascularization (surgical or percutaneous transluminal angioplasty). There are several unresolved questions concerning revascularization of the graft: whether and when to intervene? Is the stenosis progressive in the long term? Is hypertension alone an indication for angioplasty? How do we assess the haemodynamic significance of the stenosis? What is a significant stenosis—50, 60, 80 or 90%? Is stenosis ‘good’ for something? In Slovenia, since 1990, all renal transplant recipients are screened regularly for the presence of stenosis by duplex-Doppler (performed by nephrologists), and also in cases of deterioration of graft function or hypertension. In the majority of patients with a diagnosed stenosis, the latter was found to be stable over time (assessed by regular Doppler, graft function and hypertension control). In some patients, spontaneous regression of the stenosis was observed. Frequent Doppler assessment of these patients helps to be more conservative with angioplasty and angiography. Deterioration of graft function (with stenosis diagnosed by Doppler) is the main indication for angiography (and angioplasty). Better definition of significant stenosis and randomized studies comparing conservative treatment vs angioplasty are warranted.

Duplex-Doppler seems to be the ideal screening and follow-up test.

Keywords: kidney allograft; percutaneous angioplasty; renal artery stenosis; transplant

Introduction

Renal transplant artery stenosis is a relatively frequent complication after renal transplantation, with a reported incidence of up to 23%, depending on definition and taking into account that renal angiography is not performed in all patients [1]. In a report where all patients were screened by Doppler examination immediately after the operation, monthly during the first year and then annually, the incidence was reported to be 12.4% [2]. Stenosis can cause hypertension, deterioration of renal function and/or graft failure because of artery occlusion. It usually occurs during the first 2 years after transplantation. Renal angiography still remains the gold standard for diagnosis. Duplex-Doppler studies, introduced in the late 1980s, offered some advantages of being non-invasive, performed if needed at the bedside or intensive care unit, having high specificity and sensitivity (although significant discrepancies between centres are reported), with the capability of assessing haemodynamic significance and being an ideal test for follow-up and assessment of the success of revascularization [3,4].

Aetiology

There are three main types of renal transplant artery stenosis: (i) stenosis at the anastomosis; (ii) localized stenosis, proximal or distal to the anastomosis; and (iii) diffuse or multiple stenoses.

The most common causes of stenosis are ‘technical’ where the stenosis occurs due to surgical technique,
usually located at the anastomosis and especially at the end-to-end anastomosis. The other ‘technical’ causes reported were vessel lesions during preservation or due to vascular clamps and torsion, kinking or angulation of the artery. Stenosis can also occur due to donor or recipient atherosclerosis. Immunological injury is also proposed as the possible cause [2], especially in diffuse and multiple stenoses. A haemodynamic mechanism has been suggested in end-to-side anastomosis, with angulation between donor renal artery and the recipient iliac artery, or because of the presence of a turbulent flow in a redundant renal artery with kinking [1].

Clinical manifestation

Stenosis is usually manifested as difficult-to-treat hypertension, with deterioration of renal function, especially after the use of angiotensin-converting enzyme (ACE) inhibitors. Some authors found erythrocytosis to be associated with stenosis. A vascular murmur in the iliac fossa can often be present but is not specific for significant stenosis. It can be a consequence of turbulent flow in the iliac or femoral arteries. On the other hand, significant stenosis can also occur in the absence of the audible bruit [1].

There are few data regarding the natural course of stenosis and its progressiveness, if treated conservatively. Spontaneous regression has been described [5]. Duplex-Doppler examinations enabled us to follow the grade of stenosis precisely and accurately in the long term [6,7]. There are reports of favourable long-term follow-up of stenosis treated by percutaneous angioplasty [8,9].

Hypothetically, a certain degree of stenosis could even be beneficial, similar to reports of unilateral native renal artery stenosis which protected the kidney from the development of focal segmental glomerular sclerosis [10] or diabetic nephropathy.

Diagnosis

The gold standard for diagnosing stenosis still remains renal angiography [1].

Captopril scintigraphy can be of value in assessing the stenosis of a segmental artery [11]. There is a report of losartan scintigraphy that revealed stenosis that was overlooked by captopril scintigraphy [12]. However, today, in general, scintigraphy does not play a major role in diagnosing renal transplant artery stenosis.

Duplex-Doppler examination, performed by an experienced operator, is an invaluable tool for the diagnosis and follow-up of a stenosis [3,4,13]. The main advantages are its non-invasiveness, high sensitivity and specificity, the possibility that it can be performed at the bedside (e.g. in an intensive care unit) [14], the ability to assess the haemodynamic significance, the grading and localization of the stenosis, and the result of revascularization. In addition, Doppler study is ideal for the follow-up of an already diagnosed and/or treated stenosis. The main disadvantages are its operator dependency and its time-consuming examination.

There are basically two different approaches for diagnosing a stenosis in both the native and the transplanted kidney [13]. The first approach (so-called extravascular Doppler) includes duplex scanning of the renal artery from the anastomosis to the hilus. The peak systolic velocity is measured along the course of the renal artery. At the stenosis site, there is an increase in peak systolic velocity of >2 m/s. The advantages of this approach are the high accuracy of diagnosing the severity of the stenosis (diagnosis of non-significant, relative stenosis is also possible) and the possibility of its localization. The main disadvantage is the high operator dependency. The second approach (so-called intravascular Doppler) is based on an analysis of a Doppler signal at the intrarenal vessels, distal from the stenosis. This so-called ‘parvus–tardus’ pattern of intrarenal signal includes a decrease of the peak systolic velocity, loss of the early systolic peak and prolongation of the acceleration time to systolic peak. The ‘parvus–tardus’ pattern can be amplified by use of captopril [15].

This type of Doppler examination is not so operator dependent, but can only diagnose high grade stenoses (>75–80%), with no possibility of localizing the stenosis along the renal artery.

The preferred approach is to combine both the extra- and intravascular Doppler examination, as is suggested for native renal artery stenosis [13].

Magnetic resonance imaging (MRI) can be considered a safe and non-invasive alternative to angiography in cases where assessment of intrarenal vessels in native renal arteries is not required [16]. In transplant renal arteries, where stenosis on intrarenal vessels can occur and be of clinical importance, the usefulness of MRI is still to be defined.

Spiral computed tomography can provide a satisfactory three-dimensional reconstruction of vessels and avoids arterial puncture, but still requires administration of intravenous contrast. Fervenza et al. believe that carbon dioxide angiography is the preferred imaging technique as it avoids nephrotoxicity and hypersensitivity reactions [1].

Treatment

A stenosis could be treated conservatively or by revascularization. Not all stenoses require intervention. Stenosis can be treated successfully pharmacologically provided that allograft perfusion is not jeopardized. The first problem to be solved in treating stenosis by intervention is to define significant stenosis. Some studies considered stenosis as
significant if there was > 50% reduction of the lumen on angiography [2]. Fervenza et al. consider > 70% stenosis and a pressure gradient > 15 mmHg as haemodynamically significant [1]. The study from Schoenberg et al. where stenoses were created experimentally, gradually increased and evaluated by MRI in a canine model revealed that stenosis of 30–80% minimally affected blood flow in the kidney. Only the stenosis of > 90% significantly depressed blood flow by > 50% [17].

Revascularization can be surgical or by percutaneous transluminal renal angioplasty (PTRA) [1,8,18]. PTRA is the preferred initial mode of therapy [1,8]. Arguments in favour of revascularization are the presence of one kidney (if stenosis progresses, or renal function is lost), and the possible improvement of hypertension and renal function. On the other hand, there are arguments against revascularization such as technical difficulties and complications, uncertain influence on hypertension, non-progressive nature of the stenosis or the possibility of spontaneous regression. Randomized studies comparing revascularization vs conservative treatment are not available.

**Our experience**

Since 1990, all our renal transplant recipients in Slovenia are screened regularly for the presence of stenosis by duplex-Doppler (performed by nephrologists experienced in the technique), as are cases of deterioration of graft function or hypertension. In the majority of patients, stenosis was stable over time, assessed by regular Doppler. Therefore, nowadays, we are more reluctant to perform angiography (and angioplasty) than 10 years ago, and the main indication for angiography (and angioplasty) is deterioration of renal function in the presence of stenosis already proved by Doppler. Frequent Doppler assessment of these patients helps us to be more conservative regarding angioplasty.

In the last decade, we have observed three patients with high grade stenosis (> 80%), who after suboptimal angioplasty (because of technical problems) remained stable over 7–12 years of follow-up, with good graft function. Since that observation, we have performed a retrospective clinical study in which we have analysed 3 years of follow-up of 34 renal transplant recipients with stenosis of the renal artery (> 50%) and compared them with 34 renal transplant recipients without stenosis, matched in terms of age, sex, type of graft (living related vs cadaveric, the first vs the second graft) and duration of graft function. In the stenotic group, a gradually decreasing maximum systolic velocity at the stenotic site has been found (which can be used as a measure of the severity of the stenosis). There were no significant differences in graft function (assessed by serum creatinine, haemoglobin level, blood pressure and number of antihypertensive drugs between the stenotic and non-stenotic group. In 7/34 (20.6%) patients with stenosis, spontaneous regression to a non-significant level occurred [19].

**Conclusions**

According to our experience, renal transplant artery stenosis seems to remain stable over time in the majority of patients and can be treated medically, provided that graft perfusion is not jeopardized (assessed by good graft function). Spontaneous regression is possible. Duplex-Doppler examination is the ideal test for screening and follow-up of the stenosis. Hypertension alone, being multifactorial in renal transplant recipients, is not a major indication for revascularization, but deterioration of graft function in PTRA is the preferred initial form of intervention. A better definition of significant stenosis (a cut off of > 50% of lumen reduction at angiography seems to be too low) and randomized studies of conservative treatment vs angioplasty are warranted.

**References**

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