REVIEW PAPERS

Endovascular treatment of allogeneic kidney transplant artery stenosis

Wewnątrznaczyniowe leczenie zwężeń tętnic przeszczepionej allogenicznej nerki

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KEYWORDS:

- kidney transplantation
- renal artery stenosis
- percutaneous transluminal angioplasty

ABSTRACT

Recent studies have questioned the effectiveness of surgical treatment of renal artery stenosis. However, patients with artery stenosis of the solitary kidney may benefit most from endovascular therapy. Transplant renal artery stenosis is a cause of organ function deterioration, potentially leading to graft loss and increased mortality in the group of patients affected by this complication. However, we do not have data on the optimal treatment of transplant renal artery stenosis. Therapeutic methods includes conservative treatment and possible qualification for surgical treatment. Performing endovascular intervention offers the chance to correct the stenosis and return proper function to the transplanted kidney. Various methods are used during surgery: angioplasty, and stent implantation, including devices that release local antiproliferative drugs. At present, a timely intervention appears to offer the same chances of long-term graft function and survival as in kidney transplant recipients who do not develop TRAS. Data on epidemiology, risk factors and treatment outcomes are sparse, and further studies are needed.

SŁOWA KLUCZOWE:

- przeszczepienie nerki
- zwężenie tętnicy nerkowej
- przezskórna angioplastyka

STRESZCZENIE

Ostatnie badania kwestionują skuteczność chirurgicznego leczenia zwężenia tętnicy nerkowej. Jednak pacjenci ze zwężeniem tętnicy jedynej nerki mogą odnieść największe korzyści z leczenia wewnątrznaczyniowego. Zwężenie tętnicy nerki przeszczepionej jest przyczyną pogorszenia funkcji narządu, potencjalnie mogącą prowadzić do utraty przeszczepu i zwiększenia śmiertelności w grupie chorych dotkniętych tym powikłaniem. Nie dysponujemy jednak danymi dotyczącymi optymalnego leczenia zwężenia tętnicy nerki przeszczepionej. Obejmuje ono leczenie zachowawcze i ewentualną kwalifikację do leczenia zabiegowego. Przeprowadzenie interwencji wewnątrznaczyniowej daje szansę na korekcję zwężenia i powrót właściwej funkcji nerki przeszczepionej. Podczas operacji wykorzystywane są różne metody – angioplastyka, implantacja stentów, w tym również urządzenia uwalniające miejscowo leki antyproliferacyjne. Obecnie wydaje się, że przeprowadzona w porę interwencja daje takie same szanse na długotrwałe funkcjonowanie przeszczepu i przeżycie, jak w grupie biorców przeszczepu nerki nie rozwijających TRAS. Dane dotyczące epidemiologii, czynników ryzyka i wyników leczenia są skąpe, dlatego potrzebne jest przeprowadzenie dalszych badań.

Introduction

A kidney transplant is the most effective method of renal replacement therapy for patients with end-stage renal failure, as it provides the longest mean survival time and the best comfort for the patient. It is also the most commonly performed vascularized organ transplant. Various pathologies limit the functioning of the transplanted allogeneic kidney, often leading to its end-stage failure and the need to convert the patient's therapy to other methods of renal replacement therapy. This is most commonly hemodialysis, less commonly peritoneal dialysis. Transplant renal artery stenosis (TRAS) is the most common long-term vascular complication of a kidney transplant, a major cause of refractory

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hypertension and impaired graft functioning. Most cases of transplant renal artery stenosis are diagnosed within 3 years of the transplant, with a peak in detection between 3-41 months after transplant. The stenosis is most commonly located at the vascular anastomosis site (Fig. 1), but other locations have also been described (Fig. 2).

Figure 1. Tight stenosis located in the anastomosis between the recipient's common iliac artery and the donor's renal artery, visible on arteriography prior to endovascular treatment (A). Control arteriography after successful stenosis correction by the stent implantation (B).

Figure 2. Stenosis located in the artery of the transplanted kidney (A) and successful.

Predisposing factors for stenosis occurrence at a specific site are not known. Transplant renal artery stenosis significantly increases the risk of graft loss and indirectly increases the risk of patient death (1). Transplant renal artery stenosis is often oblique, without significant symptoms. Criteria for diagnosis and screening patterns of kidney transplant recipients for transplant renal artery stenosis vary between centers. Currently, there are no uniform recommendations for this kind of management. The prevalence of transplant renal artery stenosis reported in the literature is in a wide range, from 1% to 23% (2), which is most likely due to a number of factors. Firstly, due to different screening patterns used to image possible pathologies of the transplanted renal artery. Secondly, due to the varying use of marginal organs for transplant, including those with coexisting atherosclerosis, to increase the organ pool used. Thirdly, due to the fact that there are no uniform recommendations for pharmacotherapy of transplant patients to reduce the risk of atherosclerosis. In addition, the influence of genetic factors on the risk of transplant renal artery stenosis is unknown. It should be emphasized that recent publications usually indicate a 1-2% incidence of transplant renal artery stenosis, which may be due to improved organ qualification for transplant surgery, improved post-transplant conservative treatment, including effective prevention of atherosclerosis.

Aetiopathogenesis

Transplant renal artery stenosis most often has atherosclerotic origins and occurs at the recipient and donor vascular anastomosis, but stenosis can be located in any segment, from the recipient's common iliac artery to the interlobar arteries in the transplanted kidney. In the initial post-transplant period, stenosis is thought to result from technical errors in the anastomosis, vascular damage during preparation, torsion or clipping of the recipient's vessels and preoperative changes. At the later stage, stenosis may develop as a result of atherosclerosis. A much rarer cause of transplant renal artery stenosis is compression from outside, for example, by a polycystic kidney.

Risk factors

For many years, research has aimed at detecting risk factors for the development of transplant renal artery stenosis. It may allow for the identification of individuals faced with the greatest risk of developing this complication and for developing preventive methods. Delayed graft function (DGF), the need to dialyze a patient in the first week after the transplant and cytomegalovirus (CMV) infection are most commonly cited as independent risk factors for TRAS (3). It should be emphasized, however, that such a relationship has not been confirmed in all conducted studies. Results from other studies suggest that patients who develop TRAS are older, have higher BMI values, have had previous transplants, and have serum triglyceride levels above 150 mg/dl (4). Anastomosis of the transplanted renal artery to the donor internal iliac artery, rather than typical anastomosis to the side of the common iliac artery, and total ischaemic time appear to be factors that independently increase the risk of TRAS in living donor kidney recipients (5). In the case of patients with TRAS, surgeons were more likely to use the Carell patch for anastomosis during the transplant (6). In addition, single studies have also identified recipient characteristics, such as age over 50 years, coexisting diabetes, the occurrence of an episode of acute rejection, use of induction immunosuppression and those related to a donor: age over 60 years, or to a transplantation procedure: long cold ischaemia time, as risk factors for the development of transplant renal artery stenosis. It should be noted that the results of other studies have not confirmed the influence of these factors on the development of transplant renal artery stenosis.

Diagnostics

Screening of renal transplant recipients includes regular measurement of blood pressure and plasma levels of creatinine, urea and urine output. The frequency of ultrasound examination of the transplanted kidney with an evaluation of intrarenal flows, and the haemodynamics of the transplant renal artery flow, depends on the screening pattern at each center. This examination is also performed when graft failure appears or increases or when hypertension, especially refractory hypertension, occurs. Ultrasound diagnosis of transplant renal artery stenosis comprises evaluation of lumen diameter, vessel morphology and flow parameters, such as peak systolic velocity (PSV) and resistive index (RI). Depending on the definitions used by the authors, TRAS is indicated by a PSV greater than 2-2.5 m/s, and an RI lower than 0.5-0.55. MRI and CT angiography are used to definitively verify the presence of transplant renal artery stenosis when ultrasound findings are inconclusive. The possibility of using both imaging methods is limited in cases of transplant kidney failure. In case of discrepancies between imaging results determining the degree of stenosis, traditional angiography is performed to make a definitive diagnosis. It is usually already performed during the endovascular procedure to dilate transplant renal artery stenosis. The size of transplant renal artery stenosis that should be treated surgically has not yet been determined. It is most commonly accepted that stenosis exceeding 50-75%, especially those with deterioration of renal function or refractory hypertension, is an indication for surgery. Some authors also use the pressure gradient during cardiac systole in qualifying transplant renal artery stenosis for surgical intervention.

Treatment

Widely accepted recommendations for optimal treatment of transplant renal artery stenosis have already been developed. Since the most common cause of transplant renal artery stenosis is atherosclerosis, it is necessary to optimize conservative treatment in case of diagnosis confirmation. A decision regarding surgical treatment is much more important. Many authors emphasize that a significant proportion of patients with TRAS benefit from conservative treatment (7). Publications on the treatment of transplant renal artery stenosis often present poor data quality. There are no randomized trials, and patient populations are usually quite small (8). Therefore, most often, the management of patients with TRAS is based on the findings of native renal artery stenosis. According to the guidelines, surgical treatment of renal artery stenosis is indicated in the case of diagnosing haemodynamically significant stenosis. In patients with native renal artery stenosis, the results of the ASTRAL

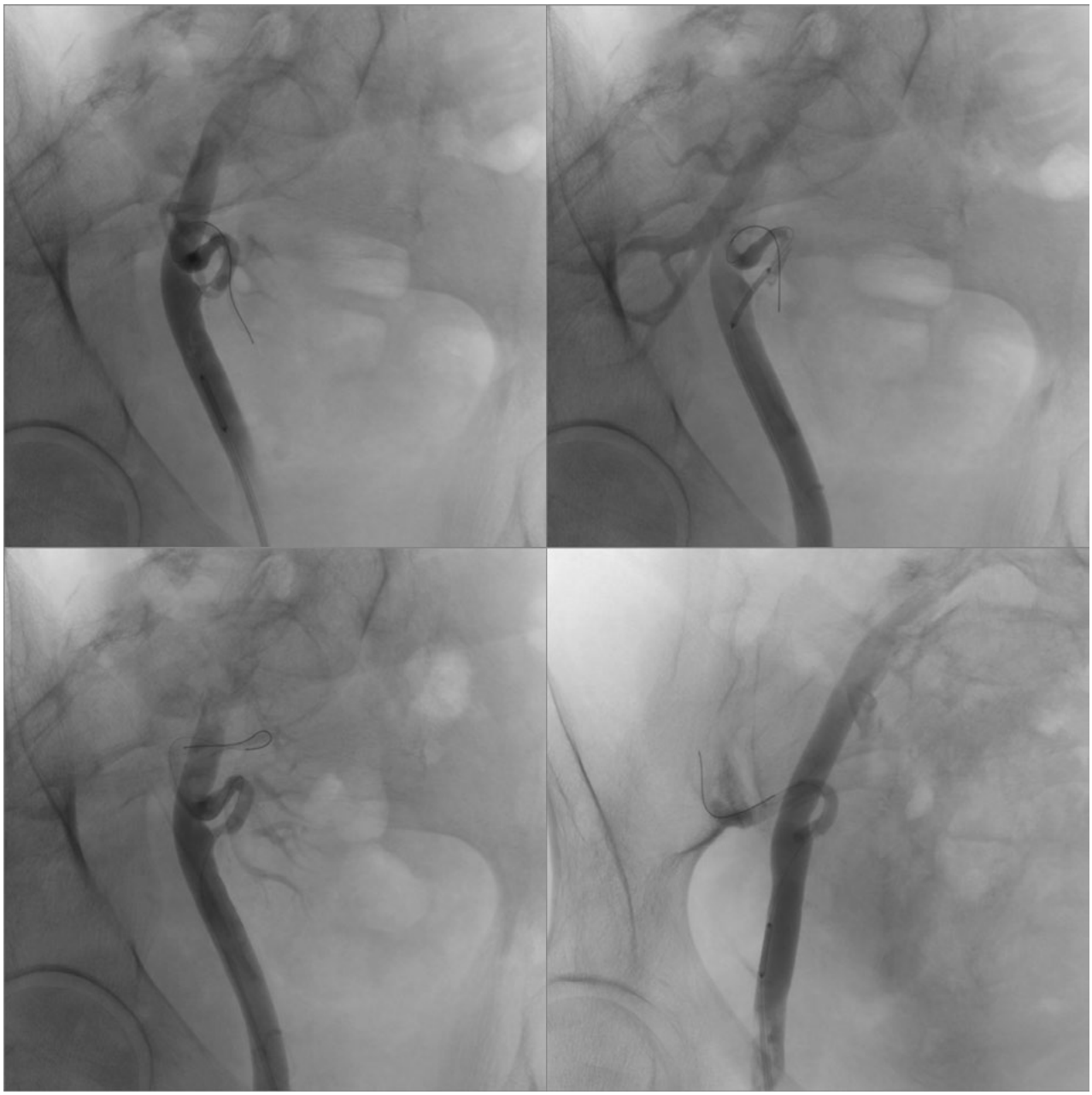

Figure 3. The steps of the percutaneous transluminal angioplasty (PTA) of transplanted kidney renal stenosis. Arteriography shows a hemodynamically significant stenosis located in the anastomosis between the recipient's common iliac artery and the donor's renal artery (A). Balloon introduced into the stenosis before angioplasty (B). Control angiography after angioplasty shows primary PTA ineffectiveness and stenosis persistence (C). Final arteriography after consecutive PTA indicating treatment efficacy – no significant stenosis in the artery of the transplanted. kidney and anastomosis (D).

and CORAL studies indicate equivalent effects of optimal pharmacological treatment to surgical treatment, with no risk of complications with pharmacological treatment (9). The results of several studies indicate that patients with pathology of the only renal artery benefit more from surgical treatment of renal artery stenosis. A similar approach has been proposed for patients with TRAS. At the same time, studies are conducted to identify a subpopulation of patients with TRAS who will benefit from optimized conservative treatment.

Currently, endovascular treatment is the procedure of choice for treating transplant renal artery stenosis. During surgery, balloon angioplasty is performed with both plain balloons (Fig. 3) and drug-eluting/coated balloons (DEB, DCB), bare metal stent (BMS), (Fig. 1) or drug-eluting stents (DES). Qualification for open surgical treatment is now reserved for the very rare cases of multiple renal artery stenosis in the renal hilum, when *ex vivo* reconstruction combined with retransplantation of the transplanted kidney can be used.

Results

Due to the small number of patients included in the studies, it is difficult to define eligibility criteria for surgery. As a result, surgery is performed in patients with varying degrees of transplant kidney failure, making treatment results of published studies inconsistent. The results show that the use of balloon angioplasty alone results in a statistically insignificant decrease in plasma creatinine concentration and mean arterial pressure one month after the intervention, whereas

stent implantation appears to have this effect (10). Stent implantation is associated with a lower incidence of recurrent stenosis and the need for repeat vascular intervention compared to angioplasty alone. The use of a stent is also associated with smaller residual stenosis after the procedure compared to angioplasty (11). When comparing the results of treatment with a bare metal stent (BMS) and a drug-eluting stent (DES), differences in reintervention rates were found (4/11 vs. 0/7), which, however, did not achieve a statistically significant difference due to the small number of patients observed (12). In a paper published in 2018, Li et al. documented the efficacy of correcting transplant renal artery stenosis with drug-coated balloon (DCB) angioplasty. Improvements in blood pressure parameters, creatinine levels and ultrasound features of the stenosis were observed (13).

Endovascular procedures are characterized by their minimally invasive nature and high technical success rates. However, they entail a high risk of recurrent stenosis in the medium- and long-term follow-up. Similarly, recurrent stenosis is observed in some patients after endovascular correction of TRAS. The median time to haemodynamically significant recurrent stenosis is approximately 50 months after endovascular treatment. Risk factors for recurrent transplant renal artery stenosis are not well understood. Results from some studies suggest that they are more common in women. Recurrent transplant renal artery stenosis eligible for surgical reintervention is characterized by a higher PSV and pressure gradient across the stenosis during cardiac systole (14).

Complications

The incidence of complications after endovascular correction of transplant renal artery stenosis is estimated to be approximately 10% (7). The most commonly described complication is arterial dissection (25%). Slightly less common ones include haematomas at the vascular access site, thrombosis of the artery supplying blood to the kidney, displacement or implantation of a stent in the wrong location and pseudoaneurysm formation. Unusual complications include damage to the recipient iliac artery, stent obstruction and loss of graft function. Administration of a contrast medium, especially in patients with impaired function of the transplanted kidney, can cause post-transplant nephropathy. To reduce the risk of this complication, the patient must be optimally hydrated before the endovascular procedure, and the volume of contrast medium administered during the procedure must be limited. Complication rates during angioplasty and stenting of transplant renal artery stenosis appear to be similar.

Initial data indicated an increased mortality and graft loss rate in patients diagnosed with TRAS (15). More recent data seem to suggest that the prognosis of patients with TRAS does not differ from that of the general population of renal transplant recipients (16). This is probably related to the ongoing development of endovascular techniques and the good results of conservative treatment.

Summary

Recent studies have questioned the effectiveness of surgical treatment of renal artery stenosis. However, patients with artery stenosis of the solitary kidney may benefit most from endovascular therapy. Transplant renal artery stenosis is a cause of organ function deterioration, potentially leading to graft loss and increased mortality in the group of patients affected by this complication. However, we do not have data on the optimal treatment of transplant renal artery stenosis. Therapeutic methods includes conservative treatment and possible qualification for surgical treatment. Performing endovascular intervention offers the chance to correct the stenosis and return proper function to the transplanted kidney. Various methods are used during surgery: angioplasty, and stent implantation, including devices that release local antiproliferative drugs. At present, a timely intervention appears to offer the same chances of long-term graft function and survival as in kidney transplant recipients who do not develop TRAS. Data on epidemiology, risk factors and treatment outcomes are sparse, and further studies are needed.

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