Renal stenting: still alive after ASTRAL and STAR publications?

Renal stent uygulaması: ASTRAL ve STAR yayınlarından sonra hala canlı mı?

Renal artery stenosis may cause systemic hypertension and renal failure (1, 2) and is associated with increased cardiovascular morbidity and mortality (3, 4). Renal obstruction is a relatively frequent finding in patients with diffuse atherosclerosis. Indeed, among patients undergoing coronary angiography, the prevalence of renal stenosis is reported to be between 11% and 23% (7). Renal stenting has been associated with improved blood pressure control and stabilized or improved renal function (5, 6), thus it represents an accepted treatment for patients with renal artery stenosis and severe hypertension and/or renal insufficiency (8).

In the retrospective study published in the current issue of the journal, Dervişoğlu et al. (9) report the effects of renal stenting on both renal function and blood pressure control in 36 patients treated on 43 arteries at 9.3+8.6 months follow-up. Despite the adoption of a relatively outdated technique (7 Fr guiding catheters, 0.018" hand-crimped stents), the authors achieved excellent immediate results with no major procedural complications. They found a significant improvement in blood pressure control with a reduction of both the mean arterial blood pressure (MABP) (from 123±22 mmHg pre-procedure to 101±14 mmHg at follow-up ($p<0.001$)) and the number of antihypertensive medications (from 2.1±1.0 (range, 0-4) pre-procedure to 1.3±1.0 (range, 0-4) at follow-up ($p<.001$)). Moreover, regarding renal function, although no significant change in estimated glomerular filtration rate (EGFR) from pre-procedure to follow-up (71.4±40.2 mL/min vs.73.3±39.0 mL/min; $p=0.483$) was documented, in the group of patients with renal impairment (EGFR ≤ 59 mL/min), 41% showed improvement, 29% showed no change and 29% demonstrated deterioration in EGFR.

The results of this study, although not completely innovative, contribute to the discussion on the safety and the efficacy of renal stenting. However, there are some specific points that need to be discussed. First of all, the number of patients included (n=36) is rather small and the inclusion of patients with both atherosclerotic disease and fibromuscular dysplasia may be confounding. The observational design of the study does not allow conclusions about the incremental value of renal stenting over optimal medical therapy on blood pressure control, renal function and clinical outcome. No data about the occurrence of adverse events (death, MI, stroke, end-stage renal failure) during follow-up is reported making hard to understand the risk profile of the studied population. The statement "PTRA/S preserves and even improves renal function..." is inaccurate since control group is lacking and in 29% of the patients EGFR indeed deteriorated. Finally, the assumption "...this beneficial effect was accompanied by renal function preservation...particularly in patients with impaired renal function.." is equivocal. Indeed, the authors found a deterioration of EGFR in 29% of patients with reduced baseline EGFR compared to 10% of patients with EGFR>60 ml/min.

The scientific data supporting stenting versus conservative management in renovascular disease are so far inconsistent. In the DRASTIC, one of the largest prospective randomized studies (10) published to date, renal angioplasty, compared to medical therapy, was associated to an early reduction of blood pressure which was no longer significant after 9 months. However, these findings are difficult to interpret as, in this study, the cross-over rate in the medical group was as high as 44%, angioplasty was performed almost exclusively by balloon (resulting in 48% restenosis rate) and 106 patients only were enrolled across 26 centers during the 5-year recruitment period (less than 1 patient per year per centre) (10). The more recently published STAR trial (11), which randomized to stent or medical therapy 140 patients with atherosclerotic renal stenosis and impaired renal function (eGFR less than 80 ml/min/1.73m2), similarly failed to demonstrate any difference in 2-year blood pressure control in stented compared to medically treated patients. Conversely, in the large "Multicenter Palmaz Stent renal artery stenosis revascularization registry" an improvement of blood pressure control was documented in the 1058 enrolled patients, during a 4-year follow up period (12). This is in agreement with the recently published data of the ASTRAL trial (13) in which the number of antihypertensive drugs at 1-year follow-up was significantly lower in the revascularization group compared to the medically treated group (2.77 vs 2.97, $p=0.03$).

With regard to renal function, the results of previous studies are also inconsistent. Although Arthurs et al. (14) found that

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stenting slows the rate of renal function decline and other studies reported a significant and prolonged decrease of creatinine levels after stenting (15-17), in the majority of the studies creatinine remained stable after angioplasty (12, 18-32). In the recently published data from the large ASTRAL (13) trial, in which 806 patients were randomized to stenting versus medical therapy based on uncertainty whether to revascularize or not, renal stenting failed to demonstrate significant benefits over medical therapy at up to 5 years. However, it must be noted that in the ASTRAL trial, although the patients enrolled were sicker than those usually included in the studies (mean baseline serum creatinine around 2 mg/dl), were not taking antiplatelet therapy at the time of stenting in a significant proportion (up to 24%) and exhibited a mild renal stenosis (<70%) in up to 40%, there was a strong trend toward a decreased rate of renal impairment in the revascularization group compared to the medically treated group (difference in the slope of the reciprocal of the serum creatinine level 0.06x10-3 liters per micromole per year, p=0.06).

Distal embolization has been advocated as the main cause of renal function deterioration after stenting. In a recent study, (33) ultrasound evaluation of intrarenal flow demonstrated that distal embolization may occur at any time during angioplasty, mostly during stent implantation and postdilation. Henry et al (34-35) showed that distal protection, with either distal occlusive balloons or filters, allows to retrieve embolized material in more than 80% of stenting procedures. They also recently reported a very low rate of postprocedural worsening of renal function in protected stenting procedures (1% immediate, 5% at 6 months). Finally, Cooper et al. (36) recently demonstrated in a randomized trial a beneficial interaction between glycoprotein IIb/IIIa inhibitors and filters on the glomerular filtration rate, suggesting a potential role of embolic protection in the prevention of renal function decline after stenting.

In conclusion, as frequently occurring in medicine, results coming from real life observational studies performed in experienced centers are sometimes conflicting with those derived from large randomized controlled trials (RCTs). This could be due to self- referral and underreporting of adverse events in non controlled studies, but could also reflect the unbalance of the trials. Indeed, in order to achieve the required patient population, trials often include low-volume centers with limited experience and these results in poor outcome and increased major complications undermining the results of the study. Although the evidence -based medicine must stay as the cornerstone of our practice, we should not exclusively rely on RCTs results, but we need to critically evaluate them in comparison with well conducted real life observational registries.

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