The Lesson from the CORAL Trial: Choose Better your Target

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EDITORIAL

Atherosclerotic renal artery stenosis (RAS) affect 5% of hypertensive patients, thus considering the wide diffusion of high blood pressure (BP), it represents a huge and increasing problem. Only in USA, from 2 to 4 millions of individuals have to face it [1].

Reno-vascular hypertension has been considered a revertible disease and, for over 30 years, endovascular intervention has been accounted as excellent therapeutic option for its accepted ability to correct intra-renal hemodynamic disorders leading to high CV risk and kidney function impairment [2,3].

Today over 40,000 of these operations were performed each year until publication of Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trial, which unleashed a storm of discussions.

CORAL promised to be successful where many other trials had failed (ASTRA, STAR) weighting Percutaneous transluminal renal angioplasty (PTRA) against optimal medical therapy [4].

Considering as primary end point prevention of major CV and renal events, it proved that angioplasty isn’t the best strategy in patients with RAS, hypertension and/or chronic kidney disease (CKD), when added to comprehensive multifactorial medical therapy [4].

Only a “little reduction” of systolic blood pressure (SBP) was seen in PTRA arm (~2.3 mm Hg), while in the same group some patients experienced various adverse event like arterial dissection, branch vessel occlusion and angiographic distal embolization [4].

Therefore, on the basis of this result, authors suggested to don’t choose stenting as first step in patient with RAS, but to prefer medical intervention.

However, before to give up to PTRA, a correct data analysis and interpretation is mandatory.

CORAL enrolling a large cohort (947 participants) of patients promised to be successful where many other trials had failed (ASTRA, STAR) weighting Percutaneous transluminal renal angioplasty (PTRA) against optimal medical therapy [4].

Adopted inclusion criteria allow to enclose patient with stenosis between 60%-100%, but really enrolled subjects displayed only a “mild renal-artery stenosis” (in the experimental arm, average angiographically proven stenosis of 67.3%) meaning that critical and severe hemodynamic stenosis weren’t really considered in randomization [4].

Hemodynamic studies reveal that renal blood flow changes only when obstruction involves over 70%-80% of the vascular lumen (a so called “critical stenosis”), because only these condition can trigger pathway leading to ischemic tissue remodeling [5].

As we can see from published data [4], CORAL study had a strong chance to recruit subjects who weren’t affected by reno-vascular hypertension and therefore that can’t benefit from PTRA.

Afterwards a key point is diagnostic tools; identify hemodynamically significant vascular obstruction is essential for a correct selection of PTRA suitable subjects, because the degree of flow limitation influence reversibility-irreversibility of parenchyma injury [6].

We know that, in order to verify the true influence of arterial stenosis to renal circulation, both Computed Tomography angiography (angio-CT) and angiography may not be the best mean [6].

In CORAL trial authors used angio-CT as decision making tool in the most part of cases (68% in both arms), and this may have partly influenced a proper patients selection.

Current used guideline by American College of Cardiology and American Heart Association guidelines recommend to offer renal artery stenting to patients with atherosclerotic severe RAS (>70% angiographic diameter renal artery stenosis or 50% to 70% stenosis with hemodynamic confirmation of lesion severity) associated with resistant hypertension and failure of 3 drugs, 1 of which have to be a diuretic, or patients with hypertension and intolerance to medication [7].

Indeed, as disclosed by a recent analysis performed by Ritchie J et al, some clinical parameters like flash pulmonary edema and rapidly declining kidney function may also suggest the use of an interventional approach (something that didn’t taken into account in CORAL) [8].

Therefore, after CORAL what is changed for us?

Managing RAS patients still remains a challenge for clinicians.

Now is out of question that PTRA isn’t superior to optimal medical therapy in patients who have not-obstructive stenosis, but certainly this doesn’t mean that we have to deny stent in all cases.

Beyond the CORAL, before to completely change our practice, we need to know the best therapeutic approach in subjects showing rapid disease progression or lack of response to “optimal” medical therapy.

We are also waiting for new evidence about when and in which interventional treatment should be the first choice and what is the best strategy to plan revascularization.

Some of these questions could be explained by METRAS study that is still in progress. This trial will recruit stenosis “either >70% or, if <70, with post-stenotic dilatation”. Indeed this protocol’s strengths could be the use of sequential renal scintiscan to assess kidney function [9].

Indeed, doubts raised by recently published trials about revascularization maybe will shift research attention to new pharmacological approaches aimed at the achievement of both pressure target and renoprotection.

For this purpose is necessary to undertake complex therapies acting to all systems physiologically involved in renal perfusion’s controls which are too hyper-activated by arterial obstruction and that start tissue damage and fibrogenesis.

Pathophysiological and pharmacological evidences suggest to exploit the synergistic effect of multiple drugs on RAAS, intra-renal sympathetic system and mechanisms of tubular reabsorption with, in addition, many pleiotropic effects against inflammatory and pro-fibrotic pathways [10].

Thus, new studies, improving the currently use of available drug’s classes, could more tip the balance in favor of conservative RAS management.

In conclusion we hope that future new well-planned trials will include patients with high-grade RAS, specifying criteria for inclusion suited for daily clinical practice and will reconsider the use of functional diagnostic tools to better identify patients in which an interventional endovascular approach is justified.

REFERENCES