The controversial indications for ACE-Inhibitors in valvular heart disease

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Probably the most important decision in patients with significant valvular heart disease is aimed at the optimal timing of valve surgery. However, as long as these patients are followed conservatively, apparently minor decisions with regard to the initiation or continuation of ACE-Inhibitors, which are among the most commonly prescribed drugs, can nevertheless be very controversial. Their use is particularly controversial in patients with aortic stenosis and in the settings of both aortic and mitral regurgitation.

Valvular Heart Disease

1 - ACE-Inhibitors in patients with aortic stenosis

a) Epidemiology

Calcific aortic valve disease is diagnosed increasingly often in the older age populations. The presence of aortic stenosis or even aortic sclerosis is not only associated with a high incidence of cardiovascular risk factors, but it is also a marker of increased general and cardiovascular morbidity and mortality.

Summarizing the published studies, it appears that around 40% of patients with aortic stenosis have concomitant hypertension (1, 2). Patients with aortic stenosis are a population at high risk for cardiovascular events (2), thus requiring a thorough adjustment of their risk factors, one of them being arterial hypertension. However, treatment of hypertension in patients with aortic stenosis is problematic since most antihypertensive agents are contraindicated in aortic stenosis.

b) Guidelines

There is particular concern that vasodilators may lead to a reduction of the coronary perfusion pressure. In fact, the use of ACE-Inhibitors in aortic stenosis is classically

considered to be contraindicated (3). The guidelines only mention and justify the use of ACE-Inhibitors in patients with significant aortic stenosis who have depressed left ventricular function and who are not candidates for aortic valve surgery (4) – with no mention being made of patients with normal left ventricular function and those who are potential candidates for surgery.

c) Current practice and data

In this context, the observation that the prescription rates for ACE-Inhibitors among patients with aortic stenosis may be as high as 50%, may appear surprising.

Although not designed to assess the safety of ACE-Inhibitor use in patients with aortic stenosis, the findings of a retrospective study indicate that a significant number of patients with aortic stenosis seen in daily clinical practice receive treatment with ACE-Inhibitors because of concomitant arterial hypertension (102 of 211 patients) (5). The observation that a high proportion of patients with documented aortic stenosis already receives ACE-inhibitors is also shared by O'Brien and colleagues. In their series, 30% received an ACE-Inhibitor (6). There are also data suggesting that their use may be safe in aortic stenosis. O'Brien and colleagues have recently demonstrated that the initiation of ACE-Inhibitors was safe and well tolerated in a group of 13 patients with mild-to-moderate aortic stenosis with preserved left ventricular function (6).

In the SCOPE-AS trial, symptomatic patients with severe aortic stenosis and normal left ventricular function who were no candidates for surgery, were randomized to treatment with enalapril or placebo7. ACE-inhibitors were well tolerated in these patients, however patients, having reduced left ventricular functions, were prone to develop hypotension.

Finally, Jimenez-Candil and colleagues designed an elegant drug withdrawal study. 20 patients with moderate-to-severe aortic stenosis already receiving and ACE-Inhibitor were included (8). Both the withdrawal and the careful reintroduction of the drug were well tolerated. While taking the ACE-Inhibitor, patients had a lower blood pressure, higher transvalvular gradients but kept an unchanged exercise capacity and symptomatic status.

These data suggest that there might be a role for ACE-Inhibitors therapy in patients with aortic stenosis in the future. Nevertheless, prospective, randomized trials are required before initiating ACE-Inhibitor therapy can generally be recommended in these patients. In the frequent cases of clinically stable patient with aortic stenosis already receiving an ACE-Inhibitor, it might be preferable not to discontinue the treatment. However it has to be considered that with an increasing severity of AS, reducing the dosage of ACE-Inhibitors might be necessary, since hypertension may become less accentuated and even hypotension may develop as a result of further narrowing of the aortic valve.

2- ACE-Inhibitors in patients with aortic regurgitation

In contrast to aortic stenosis, the use of an ACE-Inhibitor in aortic regurgitation is

definitely not harmful. The rationale for prescribing vasodilator therapy in patients with chronic aortic regurgitation is that vasodilation leads to a reduction in the peripheral resistance, in the regurgitant volume, thus increasing the effective stroke volume. But are these hemodynamic effects translated into an improved outcome? Sconamiglio and colleagues have reported that patients with chronic aortic regurgitation who were randomized to a vasodilator treatment with nifedipine were less likely to require valve replacement within the following years than patients who were randomized to digitalis therapy (9).

However, recently, Evangelista and colleagues have observed no significant differences in outcomes between patients with severe aortic regurgitation randomized to placebo, nifedipine or ACE-inhibitors (9, 10). While the two studies are limited by their relatively small size, it is very unlikely that larger studies giving a definite answer will be performed in the near future. In the meantime, it is certainly neither an obligation nor a mistake to initiate vasodilator therapy in patients with significant aortic regurgitation.

3 - ACE-Inhibitors in patients with aortic regurgitation mitral regurgitation

In mitral regurgitation however, ACE-inhibitor therapy is clearly controversial. ACE-inhibitors have been found to reduce left ventricular volumes and also to reduce the regurgitant volume (11). A great concern yet, is that ACE-inhibitors may mask a beginning ventricular impairment and consequently endanger the optimal timing for surgery. Until the long-term outcome of ACE-inhibitors in patients with mitral regurgitation is studied, they should be used very carefully. Nevertheless, their use is accepted for long-term therapy of symptomatic patients or in patients with a reduced left ventricular function, who are no candidates for surgery. Furthermore, ACE-inhibitors might be beneficial as short-term therapy in patients with mitral regurgitation and significantly reduced left ventricular function before mitral valve surgery.

The content of this article reflects the personal opinion of the author/s and is not necessarily the official position of the European Society of Cardiology.

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Notes to editor

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