

# The challenge of treating elderly coronary artery disease patients

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Most of the clinical trials that have compared coronary artery bypass graft (CABG) surgery with percutaneous coronary interventions (PCI) have reported similar results in terms of overall and cardiac mortality between these two options for the treatment of stable coronary artery disease (CAD) (1-4). They have also shown similar results in terms of freedom from acute myocardial infarction. However, the major difference between these strategies is the superiority of CABG regarding freedom from new coronary interventions. Because of the similarities in terms of death and myocardial infarction, both interventions are believed to have similar effectiveness. However, CABG protects patients from having to undergo new interventions, but it is a more aggressive procedure and PCI although a less aggressive intervention, results in a greater need of future revascularizations.

However, when patients with diabetes and patients with triple-vessel disease were specifically studied in important clinical trials (FREEDOM and SYNTAX trials) of drug-eluting stents, these studies reported a novel and interesting finding: lower mortality and myocardial infarction rates in the groups that underwent CABG compared with PCI (5,6).

Considering the fact that PCI has been expanding its indications during recent decades and even encompassing patients with multi-vessel disease who have always been treated thus far with bypass surgery or medical therapy alone, the results of these studies bring important new insights into daily medical practice regarding CAD patients. PCI is an important intervention for the treatment of CAD, but some specific groups of CAD patients may benefit from CABG. Actually, based on the results of these trials, patients with multi-vessel disease, especially those with diabetes mellitus and those with moderate and high SYNTAX scores (SYNTAX  $\geq 23$ ) would benefit in terms of mortality, myocardial infarction, and new coronary interventions if

they were treated with CABG.

As has been shown by an interesting post-hoc study from the MASS trial, judicious clinical judgment can result in the correct choice for the initial treatment strategy for CAD patients that may be associated with fewer coronary events (7). Moreover, even in a group of enrolled patients suitable for any of the three possible CAD treatments (medical therapy, angioplasty, or bypass surgery) by the careful analysis of a clinical physician, an interventional cardiologist, and a cardiac surgeon, this study showed that clinical judgment better identified the best treatment for CAD patients, because the option of the clinical cardiologist before randomization had an impact in clinical outcomes. Remarkably, the authors found that the group with the worst cardiovascular outcomes was those not indicated to receive PCI treatment but who underwent PCI according to the choice of randomization. On the other hand, and also reinforcing the importance of clinical judgment, the patients in whom PCI was indicated and accomplished by the choice of randomization had good clinical evolution comparable to that of the other groups in terms of cardiovascular events.

Thus, studies that bring new insights in terms of specific groups of patients and their prognosis when they undergo particular treatments for CAD are highly important. In such groups, there might be important differences between these two strategies of coronary revascularization that could help cardiologists specifically individualize the treatment for each group.

Special attention should be paid to the patient's age and sex in daily practice when prescribing coronary interventions. It is assumed that age and sex have an impact on outcomes, but the nature of that impact is not completely understood. Moreover, few studies in the literature have delved deeply into the study of these groups in terms of their outcomes after coronary interventions. Of

note, most of the trials have limited the number of elderly patients and women that participate in these studies.

With the aging process that has occurred in recent decades (8), the number of elderly patients with CAD has substantially increased. Moreover, due to the greater severity of coronary damage and the higher global risk profile, CAD treatment in these patients may be challenging. Thus, the comparative study of treatments in these populations is of utmost importance. Most of the studies that have addressed these questions are subanalyses of main trials or retrospective studies (9,10).

A subanalysis of the MASS II trial from the older group of patients ( $\geq 65$  years at the time of randomization) studied patients with multivessel CAD randomized to medical therapy, PCI, or CABG. This study showed similar rates of overall death and myocardial infarction between the two interventional procedures; however, the need for new interventions in the CABG group was significantly lower (11). Interestingly, in the medical therapy and CABG arms, there was no difference in terms of acute myocardial infarction between younger and older patients, but the group of elderly PCI patients had higher rates of myocardial infarction compared with the younger patients.

In an analysis of collaborative trials that included over 7,000 patients, age had an influence on the comparative results of CABG versus PCI on mortality (12). Thus, in this analysis, older patients had better outcomes when they underwent CABG compared with PCI, while younger patients tended to have more favorable outcomes with PCI. However, the studies included in this analysis often excluded very elderly patients and also considered the cutoff level of 65 years as the definition of older patients, which may not be the cutoff currently being used to define this population.

The influence of sex on clinical outcomes after coronary interventions has also rarely been evaluated in clinical trials, but the few studies that addressed this question did not reveal any differences in clinical events between men and women groups (13). And such differences may be relevant in the clinical setting.

Recently, Yamaji *et al.* addressed these questions in the multicenter CREDO-Kyoto registry (14). In this retrospective, observational, “real world” study of more than 25,000 patients, the authors selected 5,651 patients with triple-vessel coronary artery disease who underwent PCI with bare metal or drug-eluting stents or CABG. The authors showed that the adjusted mortality for PCI patients were higher than that for CABG patients when the overall

groups were compared, but this result was mainly driven by the higher mortality in the PCI group of patients older than 74 years of age. In the other two groups of younger patients, the results were similar between PCI and CABG. PCI compared with CABG was also associated with a significantly higher risk for cardiac death, myocardial infarction, heart failure hospitalization, and new coronary interventions, but with similar risk for sudden death, and significantly lower risk for stroke.

Considering sex, the PCI mortality was still significant in men and trended toward being significant in women, but no interaction was observed between sex and the risk of mortality in PCI relative to CABG.

Because the diabetic state might have influenced the comparative results of these two treatment strategies and the coronary complexity might likewise have caused technical difficulties in the revascularization treatments, especially the PCI intervention, the authors also evaluated the results of this study in terms of diabetic status and the SYNTAX score. Of note, the patients who underwent CABG had higher rates of diabetes and higher SYNTAX scores. Interestingly, the authors found that diabetes did not change the higher mortality rates for PCI in the elderly patients. Moreover, regardless of the inclusion of SYNTAX score in the statistical analysis, the higher risks associated with PCI compared to CABG did not change. These results suggest that other variables might have influenced the differences in outcomes when the two coronary revascularization strategies were compared.

However, the results from retrospective studies should be interpreted very cautiously. Despite all the adjusted analysis performed, the reasons why the patients from this study underwent one or another therapy cannot be adjusted, and thus other variables might have influenced the physician’s judgment in favor of one of the possible strategies over another. On the other hand, it is important to emphasize that this study had more than 5,000 patients, and of these, more than 1,800 were greater than 74 years of age. Currently, even in the era of multinational studies, it would be very challenging to enroll such a great number of very elderly patients in a prospective randomized study.

Finally, the results from this large “real world” study reinforce the fact that PCI must be carefully considered in the treatment of elderly CAD patients. Individualization is essential, but as suggested by the results of the last contemporary trials and observational studies, patients with CAD and diabetes, triple-vessel disease, and elderly patients might benefit in terms of overall mortality if they

were treated using CABG. Yet, the increasing knowledge of the pathophysiology of the disease, the indications and limitations of the distinct therapies, and judicious clinical judgment are essential tools for the treatment of this disease in many challenging clinical settings.

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