EDITORIAL COMMENT

The AUTAX (Austrian Multivessel TAXUS-Stent) Registry

Another Useful Registry on Stented Angioplasty for Multivessel Disease?*

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At the exact time when the 2-year results of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) trial (1) are about to be reported, one wonders what can be learned from the AUTAX (Austrian Multivessel TAXUS-Stent) registry, a 441-patient prospective, multicenter registry performed in Austria in the years 2004 to 2005 and reported in this issue of JACC: Cardiovascular Interventions (2).

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What did the authors consider as the key messages of their study? In the abstract, they state: “With the aim of complete revascularization, Taxus stent implantations can be safe for patients with multivessel disease. The AUTAX registry, including patients with post-PCI lesions, provides additional information to the SYNTAX study.”

Thus, key features of the AUTAX registry are the inclusion of real-life patients, the aim for complete revascularization, and the use of Taxus stents. Findings pertain to favorable safety metrics (low mortality, myocardial infarction, and stent thrombosis rates at 2 years), and the strong positive impact of complete revascularization on outcome.

Since no comparator group is available, understanding the relevance of these findings requires a comprehensive description of the study design and patient population.

Questions Related to Study Design, Conduct, and Analysis

The registry was designed to include “all incoming patients with possible complete revascularization with PCI.” Presumably this prerequisite for complete revascularization disqualified a large number of patients with multivessel disease presenting at the participating centers. Cardiology in Austria is very well developed, and the total burden of patients with multivessel disease presenting at the 9 high volume centers participating in the registry must be higher than 1,000 over 2 years. If not, each center would perform on average no more than 30 multivessel coronary artery bypass graft (CABG) and 35 multivessel percutaneous coronary intervention (PCI) procedures per year, which obviously cannot be the case.

Of 1,012 patients screened on these premises, the preferred option was selected by a multidisciplinary team. “The multidisciplinary team, which also included noninvasive cardiologists, ensured that the most balanced and appropriate advice was consistently offered regarding the choice of revascularization strategy.” In a way, this scenario is similar to the preferred option registries in the SYNTAX trial, whereby CABG was the choice of the team over PCI in a 4:1 ratio. Much like in the SYNTAX study, PCI was preferred in the presence of comorbidities while CABG was preferred with increasing complexity of the coronary anatomy. Unlike was the case in the SYNTAX study, the preferred option ratio between CABG and PCI was surprisingly 1:1. Surprisingly because in the AUTAX registry the more complex cases that were still included in the randomized arms of the SYNTAX study (the upper tertile of SYNTAX scores) were sent to surgery, perhaps because of the prerequisite of high chance of complete revascularization with PCI. As a result, the SYNTAX scores of the patients reported here correspond to the lower and intermediate complexity subsets from the SYNTAX study. Which are all those patients then, in whom PCI was the preferred option? First, nearly one-third of the patients undergoing PCI had refused CABG. Second, 42% of patients in the PCI group had undergone prior revascularization procedures, mostly PCI in 39%, and presented with at least 1 restenosis in 27% of cases. The latter group is excluded from most trials, perhaps inappropriately. The AUTAX registry shows, indeed, that they are many. While contemporary trial design aims at inclusion of “real-life” patients, exclusion of patients with prior percutaneous revascularization restricts the ability to generalize trial results, yet trial relevance. This is a significant lesson from the AUTAX registry.

The issues related to patient’s preference are complex. It appears that despite the involvement of a multidisciplinary team, despite the failure of prior PCI in a significant number of instances, many patients in Austria seem to refuse to undergo surgery. One would like to understand better the process that led to this decision: which type of information was provided to the patient, how were the options discussed and with whom? Depending on cultural diversity, there are many areas in the world where patients...
prefer not to be involved in the balancing act of medical decision. In my own experience, it is very unusual that patients presented with a consensus recommendation on behalf of interventional and surgical colleagues will actually decline that proposition, even if it were CABG. Today, patients and physicians are torn between the (too) many options available to them. After decades of explosive technological innovation, we have reached a stage where nearly every condition can be treated in more than one way, leaving the choice between several different options for each strategy. This places extra demands on the information and the consent processes that should be driven by high ethical standards.

Comparison of Outcomes

Outcome in the present study was good, but the authors wisely refrain from emphasizing comparisons of outcomes between the AUTAX registry and previously reported registries (3, 4) or randomized trials on multivessel disease revascularization. One could indeed argue about differences in patient baseline characteristics (less severe than in the SYNTAX study), differences in end point definitions (myocardial infarction, use of target lesion revascularization instead of target vessel revascularization), differences in calculation of event rates (based on time to first event analysis rather than on hierarchical ranking), lack of central adjudication of critical end points such as myocardial infarction and stent thrombosis (there is no tabulation of definite, probable, and possible thrombosis events). However, in the absence of a comparator group, results can only be accepted “as is” and the study scrutinized in an attempt to identify predictors of good outcome. When successful, this exercise will provide useful information, to be added to the wealth of data that matter and should be considered, when trying to identify “what is best for this individual patient?” (5). From this perspective, 2 key lessons of this registry require our attention.

Key Lessons From the AUTAX Registry

Good results with stented angioplasty using Taxus stents for multivessel disease patients including a large proportion of cases with prior PCI were dependent on a number of requirements: careful patient selection, exclusion of the more complex coronary anatomy, achievement of complete revascularization, dual antiplatelet therapy up to 2 years, repeat angiography in 78% of cases followed by additional or repeat PCI as required.

The threshold for repeat angiography used to be very low in the early days of angioplasty. Today, systematic angiography is no longer common practice since the introduction of stents, let alone drug-eluting stents. The question arises whether such attitude should not be reintroduced in patients with multiple stent implantation or high-risk features. Silent restenosis and disease progression can be pro-actively detected and treated, perhaps preventing later events, potentially more severe than repeat PCI. Increased mortality and infarction rates, especially during hospital stay, were significantly associated with failure to achieve complete revascularization. The authors do not specify how stenosis significance was evaluated, but it would seem that decisions were taken purely on the basis of angiographic stenosis severity. These results are difficult to reconcile with the results of the FAME (Fractional flow reserve versus Angiography for Multivessel Evaluation) trial (6), which support the use of a combined anatomic and functional standard (using pressure-derived fractional flow reserve) as the appropriate decision maker for multivessel revascularization by PCI. Indeed, the FAME study showed that revascularization decisions based on angiographic guidance result in stenting of nonhemodynamically significant stenoses in a significant proportion of cases. Interestingly, the SYNTAX score did not predict outcome in the AUTAX registry, and the authors offer several explanations for this observation. In addition to those, one could hypothesize that patient outcome relates primarily to the reduction in SYNTAX score after PCI, an objective angiographic marker of completeness of revascularization, and that chances to achieve a larger delta decrease with increasing pre-procedural complexity, reflected by higher pre-procedural scores. Given the high rate of complete revascularization in the AUTAX registry, pre-procedural SYNTAX score would be expected to lose its predictive power. This intriguing observation calls for a post-hoc analysis of the original SYNTAX dataset in order to evaluate the predictive value of changes in SYNTAX score achieved by the PCI procedure, as compared with the predictive power of the baseline score.

Conclusions

The authors should be commended for the results of this prospective registry, in particular for their ability to select patient and lesion subsets that are well suited for multivessel angioplasty using Taxus. Unlike the case in the SYNTAX study and most other trials, patients with prior PCI were not excluded from this registry. More than the actual outcome results, the AUTAX registry usefully draws the attention to the importance of completeness of revascularization and tight follow-up (including angiography as felt desirable) in patients with multivessel disease of low-to-moderate complexity. No conclusions can be drawn regarding equivalence or superiority of the preferred approach versus bypass surgery. With all due respect for our excellent Austrian colleagues, the level of evidence provided by the AUTAX registry is not beyond, but rather behind, the SYNTAX study.
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REFERENCES


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