DRUG-ELUTING STENT SOLUTIONS

Evidence-Based Medicine with Drug-Eluting Stents

This monthly column in Cath Lab Digest *reviews important points of distinction in drug-eluting stents, from characteristics to techniques, to provide valuable and relevant information about this technology.*

This article, the second of a two-part series on clinical data, focuses on evidence-based medicine and its role with drug-eluting stents.

By Dr. Sigmund Silber

Sigmund Silber, MD, FACC, FESC, is Professor of Medicine at Cardiology Practice and Hospital in Munich, Germany.

Q **What is evidence-based medicine?**

A In my opinion, evidence-based medicine is the treatment of patients according to current knowledge, that is, evidence from major studies. Due to the large number of exclusion criteria in most of these studies, you will probably not be able to treat the majority of your patients according to evidence-based medicine. Evidence-based medicine can only be applied if your patient is similar to those who have been studied in these trials.

Q **How do you assess evidence?**

A The first question you have to answer when applying evidence-based medicine is, what is the primary goal? Do I want to make the patient feel better, or do I want to treat a surrogate parameter? A surrogate parameter substitutes for a clinical endpoint. In other words, it provides an indication of how well a treatment may affect clinical endpoints such as mortality. Most studies use surrogate parameters, not primary clinical endpoints, because surrogate endpoint studies are smaller and more cost-effective. But with a small, underpowered study, you have a higher likelihood of arriving at the wrong conclusion. For example, in Europe, many drug-eluting stent (DES) trials are small, with only 20 to 25 patients. A stent may be approved based on these trials. However, larger, randomized clinical trials later show that the stent does not work, or even worse, is harmful.

A study that has a primary clinical endpoint is powered to evaluate whether a patient feels better or not. For these larger trials, important points to note are whether the study is double-blinded and the timeframe of the primary endpoint. Effects of DES also occur after nine months, so longer observation periods are needed. Studies like TAXUS, SIRIUS and ENDEAVOR are examples of good trials.

Q **What happens if you have too little data?**

A You have a higher chance of being wrong. Meta-analyses attempt to compensate for this, but if you have many small, underpowered studies that lead to wrong conclusions, putting them together does not make them better. I think meta-analyses are good for generating a hypothesis, but then the hypothesis must be proven in a large, randomized clinical trial.

Q **What is the Silber score and why did you develop it?**

A The Silber score (Figure 1) is my suggestion for a better evidence-based medicine scoring system. It's not perfect, but it's a very nice tool to stimulate the discussion. I developed the Silber score because I feel that the traditional levels of evidence used by American College of Cardiology (ACC)/American Heart Association (AHA)/European Society of Cardiology

continued from previous page

Figure 1. The Silber score.

(ESC) — A (evidence from two or more multiple randomized clinical trials or meta-analyses), B (evidence from a single trial or meta-analysis) and C (expert opinion) – are not sufficient, particularly for percutaneous interventions.

Q **What are the major limitations of the ACC/AHA/ESC scoring system in assessing evidence?**

A The major limitation of this scoring system is that it does not differentiate between clinical and surrogate endpoints. It does not address whether the size of a trial is adequate for the hypothesis. The ACC/AHA/ESC scoring system states that two randomized clinical trials are sufficient as evidence, but it does not outline the number of patients and follow-up period. Furthermore, there is subjective influence possible in this scoring system, so it can be arbitrary.

Q **What are the major differences between the Silber and the ACC/AHA/ESC scoring systems?**

A The Silber score takes into account the power of a trial, which should be a least 80 percent. My scoring system also requires a minimum number of patients to be followed depending on the primary endpoint. In the Silber system, you should have a follow-up of at least 95 percent of patients for evidence to be sufficient. Finally, the Silber score is highly reproducible, so each investigator or group should result in the same level of evidence.

In the Silber system, multi-center studies with at least three centers get one point, whereas studies with less than three centers get zero points. This is important because the more centers that participate, the better picture you get. Single-center studies are usually smaller so they are often not sufficient and underpowered. In other scoring systems, the number of centers is not reflected at all.

Sponsored by Boston Scientific Corporation

For more information on the Silber score, visit the Evidence Based Medicine Center (EBMC) on www.tctmd.com, which is made possible by support from Boston Scientific Corporation. EBMC was developed to help physicians evaluate the strength of evidence from the currently available clinical studies and initiate discussion about how to interpret such evidence.