Evidence-Based Medicine: Are We on the Right Track?

A summary of key presentations by the Antonio Colombo Alumni Association at the 1st Annual Innovation in Interventional Cardiovascular Therapy (IICT) meeting.

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Evidence-based medicine has emerged in response to empiric clinical decision making. Yet, as evidence-based medicine has evolved as a dominant paradigm within medicine, its more formulaic approach has led to an emphasis away from a critical approach to data interpretation, clinical reasoning and, by extension, away from individualized patient care. Often, data from prospective randomized clinical trials are presented and perceived with unquestionable certainty. Yet, as Einstein once said, "As far as the laws of mathematics refer to reality, they are not certain; and as far as they are certain, they do not refer to reality."[1] Hence, the trend to portray evidence-based medicine as the "ultimate and unquestionable truth" that should supersede all other components of clinical decision making at the individual patient level needs to be re-examined.

Two contributions have enabled tremendous progress in interventional cardiovascular medicine: first, innovative efforts by individual pioneers who advanced concepts, techniques, or devices that brought about a leap of progress in the field; and second, the application of prospective randomized clinical trials that put new concepts/devices to scientific validation. Although these two currents should be complementary in their contribution to progress, there has been a trend to overemphasize the importance of findings from clinical trials over that of individual judgment and critical thinking in formulating clinical decision making. Ongoing efforts continue to structure hierarchies of evidence that demote and devalue evidence derived from anything other than prospective randomized clinical trials. Individual judgment and critical analysis have been increasingly discouraged if they do not mirror the "accepted evidence" at the time.

This trend is compounded by the fact that the debate on the value of evidence-based medicine in mainstream medical literature and conferences has been one-sided, with the predominance of pro evidence-based medicine viewpoints and the increasingly marginalized nature of any criticism of evidence-based medicine, including unofficial censor of investigators who attempt to articulate fundamental criticisms of its methodologies.[2] In brief, evidence-based medicine has become the dominant ideology of medical discourse.[3,4] Although this approach may seem "scientific" to some interventionists, there is mounting legitimate dissent because accepted clinical evidence at a given point in time may be subsequently proved incorrect. There are numerous examples in the medical literature illustrating this fact, the latest of which are findings from the HORIZON trial.[5] In this study of treatment options for patients with acute myocardial infarction, glycoprotein IIb/IIIa receptor antagonists appeared to increase mortality, whereas a few years ago, a flood of evidence-based medicine literature made it unethical not to use them in these patients, despite the overt clinical observation that they increase bleeding.

One of the major challenges in evidence-based medicine for the practicing clinician is trying to match individual patient needs with the collective patient data that evidence-based medicine generates. The complexity and inherent inequity in the relationship between patients and clinicians means that it is impossible to neatly categorize into goals and values all of the important factors and characteristics of a particular patient seeking care.

Present-day outcomes-based research deals less with patients as individuals than as populations. Evidence-based medicine struggles to apply the fruits of population-based research to individuals who are often not as predictable as linear quantitative research would like them to be. The present evidence-based medicine literature neglects a lot of events it does not deem statistically significant, and it assumes that because associations are showed between interventions and outcomes in RCTs/meta-analysis, these associations are linear and causal in the real world. Although they may be demonstrated repeatedly in highly controlled environments, in the real "uncontrolled" world of clinical practice with real people, their validity may break down. Evidence-based medicine should represent a bottom-up approach that integrates the best external evidence with individual clinical expertise and patient choice; it cannot result in cookbook approaches to patient care. External clinical evidence should inform, not replace, individual clinical expertise, and it is this expertise that decides whether the external evidence applies to the individual patient at all and, if so, how it should be integrated into a clinical decision.

There is a need to initiate a serious debate within the interventional cardiovascular community—a debate that is already underway in other academic circles, as to the importance of recalibrating the relative value of the various components of clinical decision making for an individual patient. On the current path, there is a real danger of depleting valuable resources in search of *P* values rather than answers to urgent clinical needs. Although this is most certainly a demanding task under the current conditions for debate, it is not only worthwhile, but it is essential in working toward the optimal practice of interventional cardiovascular medicine.

In this spirit, the Antonio Colombo Alumni Association held the 1st Annual Innovation in Interventional Cardiovascular Therapy meeting, with an objective of contributing to such a platform.

THE 1ST ANNUAL INNOVATION IN INTERVENTIONAL CARDIOVASCULAR THERAPY MEETING PROCEEDINGS

The conference began by honoring Antonio Colombo, MD, for his contributions to the field of interventional cardiovascular medicine as a clinician, mentor, innovator, and researcher. The conference was an inauguration meeting for the alumni association and its first scientific meeting.

Key Conference Presentations

The first session was structured as a debate entitled, "The Role of Evidence-Based Medicine in Shaping the Future of Interventional Cardiology: Are We on the Right Track?" Dr. Colombo presented the perspective, "What Is Wrong About the Way Evidence-Based Medicine Is Being Integrated Into Interventional Cardiovascular Practice?" Dr. Colombo made the case that although well-designed, large randomized clinical trials continue to provide the best evidence of the balance of safety and efficacy of new treatments, these trials are marred with limitations that would require the individual physician to use judgment and critical thinking before applying these findings in clinical practice. He made the following points:

- Interventional devices are not pills, and their performance is intimately linked to operator experience, which often is not accounted for.
- The interaction among patient/device/operator becomes more important with increasing lesion and device complexity.
- Several devices that have real clinical value have almost become extinct because of poorly designed clinical trials (ie, rotational atherectomy, directional atherectomy).
- The *on-label/off-label* terms that are regulatory terms are now pervasive among clinicians in practice and, in many cases, limit patients' access to potentially effective treatment.
- Generalizing results from clinical trials to practice is not hard science and therefore requires experience and common sense.

On the other side of the debate, Martin B. Leon, MD, presented the perspective, "What Is Right About the Way Evidence-Based Medicine Is Being Integrated Into Interventional Cardiovascular Practice?" Dr. Leon took the position that without evidence-based medicine, interventional cardiovascular medicine would be little more than a pseudosurgical subspecialty struggling to survive. He went on to state that in the future, evidence-based medicine outcomes will determine not only the regulatory approval of new devices but also reimbursement policies and, ultimately, physician use patterns. However, he also agrees that there are several problems in the current evidence-based medicine environment, and he listed these problems in the "watch-out-for" list:

- "Spin" artists (in scientific presentations, clinical trials design, etc.)
- Generalizing results of randomized trials to the real world
- The short-term follow-up: 6 months is not forever
- Masquerading meta-analyses
- Inappropriate study designs, endpoints, subgroup

analyses, statistical methodology, or interpretations
- Political agendas

This debate addressed important issues that are well recognized by the larger medical community, regulatory agencies, and the medical device industry. However, merely recognizing these limitations and then turning around to incorporate the constantly changing and occasionally conflicting new data into clinical guidelines that affect practice patterns constitute a "rush to judgment," to say the least. The debate should continue, but it should be a means to an end and not an end by itself.

Subsequent Sessions

The subsequent sessions focused on the unmet needs in coronary, structural, and peripheral vascular interventions. Each of these sessions proceeded with a taped case presentation that was followed by a panel discussion on how evidence-based medicine generated data, as well as other components of decision making, are incorporated on the individual patient level. The didactic presentations focused on critically reviewing the most recent data and defining their relevance to clinical practice.

Coronary Interventions

Dr. Colombo opened the coronary session with a presentation entitled, "LM Interventions: Successes, Failures, and What the Future Holds." Dr. Colombo critically reviewed the current state of knowledge and suggested that there are reasonable data supporting the utility of drug-eluting stents in ostial and body left main artery lesions despite the absence of randomized trials. However, he stressed that recurrence remains a problem with distal left main bifurcation stenting. Jeffrey W. Moses, MD, discussed the current state of recanalization of coronary CTOs. He reviewed the various dedicated CTO wires, the antegrade and retrograde approaches, and suggested various tips and tricks for dealing with common procedural obstacles. Issam Moussa, MD, discussed the current trends of treating coronary bifurcation lesions, with a focus on the disconnect between clinical trials and clinical practice. Dr. Moussa adopted the position that the published randomized clinical trials evaluating provisional stenting versus double stenting for the treatment of coronary bifurcations do not provide adequate answers

to the questions faced in clinical practice for the following reasons:

- Coronary bifurcations in randomized trials represent a lower scale of complexity compared to those encountered in clinical practice.
- Unlike nonbifurcation lesions, bifurcations are significantly more heterogeneous and cannot be simply grouped based on vessel size and lesion length.
- In clinical practice, patients undergoing double stenting are different from those undergoing provisional stenting.

Dr. Moussa suggested that the double stenting versus provisional stenting technique debate should be reframed to address how clinicians can better match the technique to the patient's anatomy. Joseph De Gregorio., MD, discussed the problem of diffuse coronary disease and whether drug-eluting stents have improved the outcome of these patients. He stressed the lack of studies addressing patients with truly diffuse coronary disease as opposed to long lesions. The preponderance of available data indicates a restenosis rate in the double digits, with a higher incidence of periprocedural non–Q-wave myocardial infarction. These data suggest the need for improvements in drug-eluting stent platforms and deployment technique.

Structural Heart Disease Intervention

Dr. Moses opened the Valvular Catheter-Based Interventions session with a presentation entitled, "The Advantages and Limitations of the Edwards Sapien Valve." Dr. Moses stated that after a long and difficult gestation period, transfemoral aortic valve replacement seems to have arrived as a relatively consistent procedure. However, technical challenges, such as vascular access and valve crossing concerns, remain and will hopefully be alleviated with next-generation, lower-profile, and sheath-based catheter systems. Maurice Buchbinder, MD, followed by reviewing the CoreValve program, its technical properties, device evolution to an 18-F platform, as well as the ongoing clinical trials and plans for introduction of the device to the US market.

Jonathan Tobis, MD, opened the Structural Heart Disease Interventions session with discussion of the status of patent foramen ovale (PFO) closure in the US. He pointed out the lack of approved clinical indications for PFO closure outside the frame of the ongoing clinical trials. He also reviewed the pathophysiology of migraine and its relationship to PFO. This presentation was followed by a discussion of proper case selection for atrial septal defect and ventricular septal defect closure by Dr. Ziyad Hijazi.

Peripheral Interventions

On the second day of the meeting, Dr. Bernard Reimers opened the session with a comprehensive review of carotid artery stenting with a special focus on the value of proper patient selection and the utility of proximal versus distal protection devices. Dr. Moussa followed with a discussion of techniques and outcomes of recanalizing chronic occlusions of the iliofemoral vessels with a special focus on the role of reentry devices. Robert M. Bersin, MD, concluded the session with a presentation that addressed the role of the interventional cardiologist in caring for patients with abdominal aortic aneurysms.

SUMMARY

The impetus to form this association and its annual meeting is to build on Antonio Colombo's contributions to the field of interventional cardiovascular medicine and preserve and propagate the spirit of critical analysis, technical innovation, and patient-centered decision making. The small size of the meeting and the superb quality of the faculty afforded everyone the opportunity for intimate and meaningful interaction on a full range of topics facing the interventional cardiologist today.

We are planning to continue this forum in the upcoming years and open it for general attendance. The primary focus would be to provide a platform for open debate regarding the proper integration of external clinical evidence (what is called *evidence-based medicine*) into individualized patient-centered decision making using actual case reviews across the spectrum of interventional cardiovascular medicine. ■

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