EDITORIAL COMMENT

Physician Judgment in Cardiology

The Art of Medicine Lives On*
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The randomized clinical trial has become the apotheosis of our endeavor to determine the efficacy of different therapies. Probably no other field in medicine has embraced clinical trials as has cardiovascular medicine, the home of the megal trial. The overall success of the modern clinical trial has led to a great emphasis on what has been termed evidence-based medicine. Certainly, when it comes to whether a particular medication has benefit, the comparison with a placebo can give scientifically reliable evidence (although even here whether the benefit extends to all can be obscured by broad inclusion criteria and the limitations of subgroup analyses [1]).

Randomized clinical trial design has also been applied to complex decisions in medicine, including the appropriate choice of invasive procedures. In cardiovascular medicine there is now a rich history of such trials, and they have impacted our daily decision-making process for a myriad of cardiac conditions from revascularization strategies to timing of valve replacement to implantation of a cardioverter-defibrillator.

Randomized clinical trials, whether of a pharmacologic or a mechanical intervention, are based on the assumption that patients in the different arms being compared have similar baseline characteristics. In the case of the comparison of coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI), the assumption is that both treatments would be of equal a priori appropriateness. But the physician as well as patient preference may include a host of factors beyond those included in clinical trial criteria and that may have biologic significance. Some of these may simply reflect the overly simplistic assessment of coronary anatomy inherent in clinical trial criteria compared with the individualized reading of angiograms, more fully reflective of each patient’s unique anatomy. Moreover, our decisions are often guided by our overall experience and the “gestalt” of the patient’s suitability for the procedure. Is there room, therefore, in this evidence-based era for individual physician and patient judgment? Are outcomes incorporating such judgment better than the reliance on evidence-based clinical trial data?

Some insight into the possible role of physician (and patient) judgment in the process of choosing between revascularization procedures has been gained from the accompanying registries of trials such as the EAST (Emory Angioplasty versus Surgery Trial) (2), BARI (Bypass Angioplasty Revascularization Investigation) (3), and the AWESOME (Veterans Affairs’ Angina With Extremely Serious Operative Mortality Evaluation) trial (4). In these three trials comparing PCI and CABG, patients who had similar inclusion criteria but were not randomized in the clinical trials were enrolled in the accompanying registries. The randomized EAST study (2) showed equivalency between angioplasty and CABG in 3-year survival, myocardial infarction, and major myocardial ischemia. Baseline characteristics seemed to be similar between the patients in the registry and the randomized trial, yet patients in the registry (5) seemed to do somewhat better than patients randomized in the trial, with 3-year survival being 96.4% versus 93.4%. It was suggested that physician judgment may have guided patients to better decisions in the registry. In the BARI trial (3), of 4,039 patients with multivessel coronary artery disease, only 1,829 consented to randomization. The remaining patients were followed in a registry (6). The main study showed overall equivalency between CABG and angioplasty, but also showed that diabetic patients had a significant survival advantage with CABG (5-year mortality of 19% vs. 35%). Interestingly, within the registry this striking advantage of CABG in diabetic patients was not apparent, with an all-cause mortality of 14.9% for angioplasty versus 14.9% for CABG (6), although there was some increase in risk with angioplasty after adjusting for baseline differences (risk ratio for mortality of 1.29) (7).

In the difficult decision between PCI and CABG, not only physician judgment but also patient judgment plays an important role. Both the BARI and the EAST registry publications emphasized physician judgment in the registry results. Although patients tend to choose PCI over CABG more often, the AWESOME registry also included a group of patients who were deemed equally eligible for either PCI or CABG but refused randomization. These patients (n = 327) constituted a patient-choice registry (8). They were compared with 1,650 patients in whom the physicians themselves did not agree on the appropriateness of randomization (physician-directed registry) as well as the 454 patients who consented to randomization. All 3 groups had similar survival, with a trend for best outcome in the patient-choice PCI patients (8).

Although the aforementioned registries and their comparison with the randomized trials provided insights into the role of physician and patient judgment, they are limited by possible confounders and selection bias. Indeed there may be significant differences between patients who consent to be randomized and those who do not. How can one test...
for physician (and patient) judgment while maintaining the randomization in a clinical trial? The answer to this seeming non-sequitur is published in this issue of the Journal. Pereira et al. (9) used a most ingenious method. Within the context of the MASS II (Medicine, Angioplasty, or Surgery Study) (10), a randomized trial comparing medical, percutaneous, and surgical treatment of stable multivessel coronary artery disease, they recorded the consensus preference of two cardiologists before the patient's randomization. They then examined the outcome in patients who happened to be randomized to the treatment modality that the two consultant cardiologists preferred (concordant group) compared with those randomized to a treatment modality that differed from the physicians’ choice (discordant group). Interestingly, there was an increased event rate in the discordant group, with a higher incidence of patients requiring revascularization for refractory angina. The main difference was explained by an increased event rate in the patients who underwent PCI but were in the discordant group (i.e., their physicians would not have chosen PCI for those patients). Angiographic characteristics identified by the physicians but not captured in the criteria for inclusion in the trial were identified as significantly different between the concordant and discordant group. The presence of three-vessel disease was a clear predictor of discordance, but nearly half of concordant PCI patients also had three-vessel disease, suggesting that more complex physician assessment of PCI feasibility was involved.

The MASS II trial showed an advantage to the medical therapy group when the entire randomized population is examined (10). Interestingly, in the concordant subgroup, all three modalities had a similar outcome, suggesting that physician judgment was helpful in correctly identifying the appropriate treatment modality, particularly those patients who should not have PCI.

The interesting report from the MASS II study is limited by a relatively small overall sample size of 611 patients and the lack of drug-eluting stents. The possible role of patient judgment was not evaluated (conceivably patients could be asked to report what their choice is before randomization as well). Still, this intriguing report is noteworthy both for its demonstration of the importance of clinical judgment as well as for its unique and creative methodology. As we continue to embrace evidence-based medicine as well as evaluate randomized clinical trials, the important lessons from this report of the MASS II study should also be kept in mind. It is indeed reassuring that there is still a role for the art of medicine.

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