Composite confusion

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ejection function, and that impaired contractile function may not be irreversible in all these patients. As Essop mentions, Wisenbaugh (7) reported that, among patients with mitral regurgitation, 10 of 14 with ejection fraction <0.60 and 4 of 13 with ejection fraction >0.60 had muscular dysfunction and that others did not. His results and ours clearly show that LV dysfunction cannot be predicted with ejection fraction alone. It may be important to us to acknowledge that ejection fraction decreases after surgery in general, but that in some patients it can increase owing to improved contractility.

Finally, among 171 patients in our analysis of LV dysfunction, 65 patients had moderate mitral regurgitation, and 106 patients had severe mitral regurgitation.

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Composite Confusion

In their retrospective post hoc analysis of the CADILLAC study, Dr. Cox et al. (1) state that the one-year composite adverse event rate (death, reinfarction, disabling stroke, or target vessel revascularization [TVR]) was greater after optimal percutaneous transluminal coronary angioplasty (PTCA) than routine stenting (21.9% vs. 13.8%, $p = 0.001$) and that this was driven largely by increased rates of ischemic TVR (19.1% vs. 9.1%, $p = 0.001$). As a result, they conclude that early and late outcomes can be further improved with routine stent implantation.

The conclusion seems excessive given results glossed over as simply nonsignificant. Perhaps what the investigators might have stated was that the difference in the composite outcome was driven *entirely* by the least clinically relevant and softest outcome event, namely TVR. Indeed, as shown in Table 3 of their study, the risks of death, recurrent myocardial infarction (MI), and disabling stroke were all higher (but not statistically significantly so) with stenting at 30 days. Moreover, at one year the relative increase in the risk of death with stenting was 31.3% and the absolute increase was 1.0%; this is about the same as the benefit of tissue plasminogen activator over streptokinase and far larger than any putative benefit of glycoprotein IIb/IIIa inhibitors in acute coronary syndromes. I cannot help but believe that had the estimates for the individual outcome events been reversed (that is, favoring stenting) readers would have seen phrases such as "strong trends" or "lack of statistical power" as an explanation. This worrisome increase in clinically important outcome events, also seen in other studies of stents in MI, should not be dismissed as just play of chance or as not significant. I would have thought it might merit a line or two in the discussion.

Could the investigators please provide readers with the differences between stent and optimal PTCA groups for: 1) death and disabling stroke, and 2) death, disabling stroke, and recurrent MI at 30 days and at 1 year?

Finally, should we not discard this silly notion of composite end points that equate a death and a disabling stroke as equivalent to a recurrent revascularization procedure? Is that how our patients view these events? Interpretive difficulties are sure to arise in problematic reports, such as the study by Cox et al. (1), where elements of the composite go in opposite directions (the treatment reduces TVR, but death, disabling stroke, and recurrent MI may be increased) (2). Careful wordsmithing often gives the illusion that all elements of the composite end point are favorably affected (3).

In the absence of a consensus-weighting scheme for elements of a composite, perhaps we need a hierarchical nomenclature for composites that make the results more transparent, particularly in the published abstract. For example, one could state that the composite was significantly lower among patients randomized to stenting (21.9% vs. 13.8%, $p = 0.001$, death [inc-ns], disabling stroke [inc-ns], re-MI [nd-ns], TVR [dec-sig]). All elements of the composite are reported, and they are ranked starting with death and followed by those of lesser clinical importance. Those elements deemed to be hard and objective are capitalized, whereas those that are more subjective or clinician-driven are given in lowercase. It is specified whether the point estimate is in keeping with an increase (inc), decrease (dec), or no difference (nd); and whether there is conventional statistical significance (sig) or not (ns).

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REPLY

We thank Dr. Massel for his interest in our study (1), and though we agree with some of his points, there is one major flaw with his reasoning: The optimal percutaneous transluminal coronary angioplasty (PTCA) group was defined in the study as having near perfect angiographic results, whereas the routine stent group as defined included all patients, whether or not an optimal (or even successful!) result was obtained. Most pertinently, 100% of patients in the optimal PTCA group achieved Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 (by definition), compared to only 95.7% of patients in the routine stent group ($p < 0.0001$), clearly explaining the weak trends toward increased mortality Massel notes. In light of this unfair playing field, it is particularly noteworthy that the benefits of stents in reducing restenosis and infarct artery reocclusion are still strongly apparent. As we stated in the Limitations section of our report, our data are hypothesis generating only; an adequately powered randomized trial of stenting versus no stenting in patients achieving optimal PTCA results is required to definitely address this issue. Such a study, the Florence Randomized Elective Stenting in Acute Coronary Occlusions (FRESCO) trial, was performed in a relatively small number of patients ($n = 150$) undergoing primary angioplasty using now obsolete first-generation stents, demonstrating not only marked reductions in clinical and angiographic restenosis, but also nonsignificant reductions toward *reduced* rates of mortality and reinfarction (2).

Where we do agree with Massel is in our disdain for composite end points. Although at times a necessary evil to allow realistic sample sizes in randomized trials, they may obscure the forest for the trees. Hierarchical rankings, unfortunately, introduce as many new problems and vagaries as they solve. A balanced perspective can usually be obtained through careful consideration of the patient populations and methods, and by judicious examination of all component end points. Finally, as important as it is to understand beta error (realizing that real differences between groups may not become statistically apparent with small sample sizes), it is equally vital to recognize that small sample sizes can also by chance suggest possible differences (or even large treatment effects) where none exist.

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Characteristics of a Great Review

I found myself reacting to the Editor's Page describing the characteristics of an excellent manuscript peer review in a recent issue of the *Journal* (1) with great surprise—surprise that these characteristics had not previously been so carefully considered and clearly communicated.

Dr. DeMaria states that "an excellent review is one that is objective and constructive, one that avoids antagonism and points out areas in which the article can be improved." I would suggest that this might be rephrased as, "One should write reviews one would be happy to receive." Far too many reviews are caustic and derisive. They serve the medical literature poorly and can be especially destructive to young researchers. It is not too much to expect that a review be as dispassionately scientific as the work that is being reviewed. The suggestions made by the editors of *JACC* deserve widespread adoption.

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