EDITORIAL

From Monitoring to Predicting Outcome

It is the desire of all who take care of surgical patients to do it better. Certainly this is true for the modern surgeon and anesthesiologist who, working together in the operative period, have access to a great amount of physiologic data *via* current monitoring modalities. It is now routine to measure the patient's blood pressure, heart rate, cardiac rhythm, arterial hemoglobin saturation, expired CO_2, and temperature. In high-risk patients more data are usually available, such as pulmonary artery pressure, cardiac output, pulmonary artery mixed venous saturation, ST segment analysis, and transesophageal echocardiographic visualization of the heart. Finally computers are available to help in the recording, organization, analysis, and reporting of this wealth of physiologic information.

Because so much data now is available in a potentially useful way, it is important to identify those variables most important in predicting an adverse outcome. In this issue Charlson and coworkers report the patterns of intraoperative mean arterial pressure (MAP) that predict postoperative complications. They find that sustained (more than 60 minutes) decreases in MAP of ≥20 mmHg are associated with cardiac and renal complications in hypertensive and diabetic noncardiac surgical patients.

The authors are to be commended for their search for meaningful predictors of bad outcome, and the report has several significant strengths and limitations that should be discussed. First the patient population is a group of patients prone to postoperative complications. Hypertensive and diabetic patients have coronary and renal disease and are, therefore, a subgroup of the general surgical population in whom it would be useful to know predictors of morbidity and mortality. Hypertensive patients[1] and diabetics[2] have abnormal cerebral blood flow autoregulation. If this is true for the heart and kidney, then sustained hypotension could lead to hypoperfusion and possible ischemic damage. Diabetic and hypertensive patients, however, do not represent the majority of general surgical patients and generalization of the results of the Charlson study to that larger group of patients is problematic.

Second the authors have examined a single physiologic variable, MAP. Unfortunately blood pressure was obtained in a nonstandardized manner (three different methods used) and only at 5-minute intervals, thus possibly missing potentially important increases and decreases. Probably it is a valid observation that there is no difference in predictive value between the use of a 20-mmHg decrease and a 20% decrease from baseline because normal MAP for the patients under study ranges from about 70 to 110 and a 20% change would range from 14 to 22 mmHg—close to 20 mmHg. Also certainly it is not surprising that overall mean blood pressure is not a predictor of outcome because during most cases the blood pressure is kept as close to normal as possible by the anesthesiologist.

One perplexing finding regarding blood pressure is that although time at ≥20 mmHg mean arterial decrease is predictive of adverse outcome, greater decreases (*e.g.,* ≥40 mmHg) are not predictive. It is troubling that there seems to be no 'dose-effect' relationship of blood pressure to outcome, *i.e.,* the greater the decrease the worse the outcome. This suggests that MAP is not the only, or even the major, contributor to cardiac and renal morbidity in these patients. This conclusion is almost predictable because MAP is the product of systemic vascular resistance and cardiac output. A low MAP could reflect low resistance and/or low cardiac output. Low cardiac output is a product of reduced heart rate and/or reduced stroke volume. Stroke volume is influenced by preload and contractile function of the heart. Thus there are many possibilities for a reduced MAP, some of which are easily altered (or caused) by the anesthesiologist (*e.g.,* systemic vascular resistance and loading condition) and others might not be. The fact that so many variables affect this one measurement suggest that a simple cause-and-effect relationship between blood pressure and adverse outcome (20% reduced blood pressure causes bad outcome) may not hold in many settings.

A third consideration is use of observational analysis and logistic regression to predict outcome. The advantages and disadvantages of this form of analysis for predicting adverse postoperative outcome recently have been critiqued.[3] The investigators explored various patterns of MAP response, correctly using a logistic regression model. It is not clear if their model contained only the MAP pattern or the MAP pattern plus other significant covariates, such as diabetes, cardiac disease, and saline infusion. Appropriate use of logistic regression should provide information on the relative contribution of the multiple covariates. There are many other covariates available to the investigators that may predispose patients to adverse outcomes, but in logistic regression there is a limit to the number of variables that can be analyzed reliably. Harrell and colleagues[4] have suggested that no more than one covariate can be adequately analyzed for every 10 patients with the least frequent category of adverse outcome variable. Charlson and colleagues had 54 patients (21% of the study population) with an adverse outcome and 200 patients with no adverse outcome. Applying Harrell's 10-to-1 ratio would indicate that, at most, five covariates were analyzed reliably by Charlson and coworkers with their sample size of 200 patients. In an observational study, in which there are many pertinent uncontrolled factors, the number of covariates (age, blood pressure abnormality, HR changes, sex, surgery type, length of surgery, pre-existing comorbid conditions, and so on) to be analyzed may be large indeed and thus require a very large number of patients for the study to identify the important predictors of outcome. In short the sample size used by Charlson et al. is inadequate to accurately assess the relative importance of the several potentially important covariates.

Examples of two potentially important covariates are the length of surgery and heart rate changes. The length of surgery may be important not only because of its effect on outcome but also because it may impart a bias to the data. A patient with a short length of surgery is less likely to have a 60-minute episode of hypotension observed than a person with a long surgery simply because the short surgery might terminate before observing the full 60-minute episode. With regard to heart rate, it has been proved in patients with coronary artery disease, for example, that tachycardia is associated with ST evidence of ischemia.[5,6] In fact, in patients undergoing coronary artery bypass surgery, increase in heart rate is associated more with cardiac morbidity than with changes in blood pressure. Presumably this is so because tachycardia reduces oxygen supply not only by reducing the diastolic interval of cardiac perfusion but also by increasing myocardial oxygen demand at the same time.

Charlson and colleagues have implicitly recognized these problems when they state that the study should be done at multiple institutions. We would like to reinforce that sentiment with some added caveats. First the study should be done in a single-surgery type, or in multiple institutions across several specified surgery types with standardized surgery and anesthesia techniques. Second if MAP is a variable of interest, its measurement should be measured in a standardized way in all patients with sufficient time resolution to accurately measure the time course of events. Third the numbers of patients should be sufficiently large both to develop and test the logistic model. Fourth the analysis must extend beyond the few hours in the operating room to that greater amount of time after operation in recovery and/or intensive care. It is unlikely that hemodynamic events in the operating room are any more important than those during the entire perioperative period.

With the wealth of physiologic data and the electronic and computing capacity to meaningfully capture these data, it is important to use the appropriate statistical methods now available to us to predict deviations from acceptable values that lead to adverse outcome. With this knowledge surgery should be safer for our patients. Factors found during and after operation that affect outcome must be identified and thoroughly tested so the increasingly elderly and medically complicated patients we now care for can benefit from the type of important clinical research attempted by Charlson and coworkers. Monitoring in the perioperative period then will be more important in assuring optimal patient outcome.

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