risk surgery in the two groups. An appropriate non-parametric test of statistical significance could have been used to compare the two groups of ordinal data.[2]

Another factor that may have affected the results is the fact that group II patients received highly variable treatments. I consider 50 μg/kg fentanyl anesthesia radically different from "balanced" anesthesia. Yet, all patients in group I received essentially the same treatment. Perhaps the increased morbidity and mortality in group II had some relationship to high-dose narcotic anesthesia.

The conclusion that "some aspect of the anesthetic management of the patients who received EAA acted to improve their overall outcome" may not be valid.[1]

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67:1026–1028, 1987

In Reply:—We appreciate the opportunity to respond to the letters from Drs. Clark, Day, Frumin, Jenkins, and Kehlet. They raise several interesting and important questions.

The first question relates to the design of the study. Dr. Kehlet asks why we included different operative procedures, and why the type of anesthesia given to control patients was not defined by protocol. When we initiated this study, we chose to include different surgical procedures and to allow the anesthesiologist some latitude in deciding how best to care for each patient. This, we believed, would make the control group more representative of current anesthesia practice and the results of the study of greater value to other practitioners.

Were the two treatment groups identical to each other in all relevant regards, so that any observed difference in outcome can be attributed causally to only the difference in treatment? For each possible factor that we thought might be relevant *a priori*, we compared the distributions of the data for each treatment group, and we used randomization to control for all other factors that we did not think were relevant but, in fact, might be. *A posteriori*, the actual data show that comparability was achieved. We included the ASA Physical Status Classification because it is commonly used as a predictor of outcome, despite the fact that it is not applied consistently from one observer to the next,[1] large variability in outcome is observed for any given class, and it was never intended to predict outcome.[2] With regard to the Goldman Index, which was intended to predict cardiovascular morbidity, we have enclosed the distribution data of the two groups (table 1).

TABLE 1. Distribution of Goldman Index

	Group I		Group II	
Value	n	%	n	%
3	7	25	9	36
6	2	7	0	0
8	11	39	10	40
10	1	4	1	4
11	2	7	2	8
14	0	0	1	4
15	3	11	2	8
25	1	4	0	0
33	1	4	0	0
Total	28	100	25	100

Regarding the conduct of the study, study protocol stated that patients with epidural catheters should receive local anesthetic injections to maintain sensory analgesia to the fourth thoracic dermatome until the end of the operation. The epidural narcotic used was morphine. The dose of epidural morphine was dictated by clinical response and not by rigid dosing schedules, which we find to have a high likelihood of undesirable effects, especially incomplete pain relief.

Cause of death in all patients can only be described as multisystem failure. In three of the four patients who died, the decision was finally made to withdraw intensive care support. In one patient, the terminal event was a myocardial infarction with the patient dying in cardiogenic shock. Although we were primarily interested in postoperative morbidity, we included the mortality statistics in the published results simply because the only alternative was to not include them. We pointedly avoided suggesting that the use of epidural anesthesia

and analgesia can decrease mortality, because we believe that this would be, at best, a tenuous conclusion from the results of this study. We do agree with Dr. Clark that morbidity in the control group may have been related in some way to the use of high-dose narcotic anesthesia. Perhaps we should have stated that ". . . some aspect of the anesthetic management of the patients who received EAA acted to improve their overall outcome" *when compared to control patients.* We examined all of the data to search for actual confounding of the causal relationship under study, and we found no confounding that was uncontrolled.

Dr. Jenkins' letter regrettably adds no new information to the results of the study. It is well known that the confidence intervals that he writes about are related in a one-to-one manner with the significance tests, as used in our paper.[3] Thus, our giving *P* values and his giving confidence intervals for the study are two sides of the same coin. We think the reader is well guided by considering the *P* value, because he or she will want to know about the chance of committing a Type I error (calling a difference significant when, in fact, no difference exists). We have given these *P* values as exactly as possible, leaving it to the reader to judge whether the Type I error is sufficiently under control. For the parameters studied, there do indeed seem to be some statistically significant treatment differences, even with the relatively small size of our study.

The confidence interval pertains to a related statistical inference: if we do an infinite number of randomized, controlled clinical trials of the size we used, under the same conditions, and construct a confidence interval for each, then 95% (or 99%) of the confidence intervals will contain the true difference between the treatments. Dr. Jenkins has decided to use 99% confidence intervals, although the 95% confidence interval is more commonly used, just as the conventional 5% value is used for the usual declaration of statistical significance. In table 2, we give both 95% and 99% confidence intervals. The reader can see that, at 95%, all intervals for the true treatment difference avoid zero, and, at 99%, half of the parameters avoid zero. Thus, our disagreement is only partial.

Dr. Jenkins and Dr. Day recall for us the classical dilemma in performing a randomized, controlled clinical trial; namely, when to stop the trial. Because this study could not use double blinding of either treatments or most end-points (mortality and morbidity), or even single blinding of most of the end-points, the anesthesiologists and surgeons who cared for the patients in this study were very concerned about the results that were achieved—they, too, could do the statistical tests. When it became clear for several of the parameters that the treatments were different, we could not continue to randomize new patients based on ethical grounds. We had to stop the trial.

TABLE 2.

Parameter	Difference	Confidence Intervals 95%	Confidence Intervals 99%
Mortality	16.0%	1.3, 30.7	−3.7, 35.7
Cardiovascular failure	37.7%	13.6, 61.8	5.6, 69.8
Major infection	32.9%	10.9, 54.8	3.5, 62.2
Cortisol—mean (1st 24 h)	36.6 μg/h	1.4, 71.8	−10.9, 84.1

Finally, and most importantly, it is worth pointing out that our results are *not* unique. The effects of epidural anesthesia and analgesia which we observed on the occurrence of perioperative congestive heart failure,[4,5,*] pneumonia,[6] duration of mechanical ventilation,[5,7] cost and duration of hospitalization,[7,8] and the adrenocortical response to surgical trauma[9] have all been observed by other investigators. These results have been observed almost exclusively in groups of patients who have a high incidence of significant perioperative morbidity. The patients in our study groups are different from those in the study of Hjortso *et al.*[10] in which the operative procedures were much shorter and the patients did not require postoperative intensive care. The decision to utilize complication rate and intensity as a measure of postoperative morbidity was not based on previously published reports. It was based on our own clinical experience in a post-surgical intensive care unit. To the extent that this is a novel approach to morbidity analysis, the data warrant particularly close scrutiny.

* Reiz S, Balfors E, Sorensen MB, et al: Coronary hemodynamic effects of general anesthesia and surgery: Modification by epidural analgesia in patients with ischemic heart disease. Regional Anesth 7:S8, 1982

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Erratum

In ANESTHESIOLOGY volume 67, number 3, in the Review Article by Beatrice L. Selvin titled "Electroconvulsive Therapy—1987," table 3 was printed incorrectly. The table should correctly be as follows:

TABLE 3. Comparison of Type and Relative Frequency of Cardiac Arrhythmias in the Cardiac and Non-cardiac Patients Using Various Intravenous Anesthetic Agents*

	Non-cardiac		Cardiac	
	Vagal	Sympathetic	Vagal	Sympathetic
Methohexital[39,116–119]	10%	20%	10%	20%
Thiopental[116–119]	20%	40%	40%	80%
Thiamylal[39]	60%	40%	**	**
Diazepam[39,117,122]	40%	60%	80%	80%

All percentages in the columns are approximate.
* All patients received prophylactic atropine and were oxygenated and ventilated.
** No data available.