Anesthesiology 2009; 111:203

Retrospective but Not Rigorous

To the Editor:—We read with much interest the article by Biki *et al.*[1] regarding the effect of anesthetic technique and postoperative analgesia on the cancer recurrence rate after open radical prostatectomy. The results suggesting that epidural anesthesia/analgesia lowers the rate of recurrence are certainly intriguing; however, we are concerned with the lack of detailed information presented in various parts of this retrospective study. Not only does this diminish the quality of the publication, but it also raises questions about the validity of the results.

Most areas where detailed information is omitted are located within the Materials and Methods section. The primary rationale for presenting methodology in any scientific publication is to allow the reader to determine the applicability of the study conditions to their own circumstances/practice and/or to replicate the study if desired. As such, meticulous and accurate reporting of details is essential. This may be particularly relevant for retrospective studies, as the most appropriate use of such studies is to generate hypotheses for the development of future clinical trials, the design of which will depend to a large extent on the methods used in the retrospective study.

The most important example of incomplete information relates to the epidural anesthetic/analgesic. There is an almost complete lack of information regarding the intraoperative and postoperative epidural management, and, most significantly, the type and quantity of local anesthetic are mentioned nowhere. Certainly, "not all epidurals are created equal," and knowing the type and quantity of medication administered *via* this route is of major relevance from both a research and clinical perspective. The authors also fail to provide data regarding the quantity of potent inhalational anesthetics or opioids actually administered in the perioperative period. Both types of agents inhibit natural killer cell activity,[2,3] and may thus potentially increase the risk of cancer recurrence after surgery. Although the authors state in the Discussion section that "it is *highly plausible* that patients in the epidural group . . . required *considerably less* volatile anesthetic" and those receiving epidural anesthesia/analgesia "*presumably* required *little* opioid, whereas those given general anesthesia alone *surely* required *considerable* amounts of opioid," they present no data to support these statements. Indeed, when the authors describe the general anesthetic as "*most typically*" consisting of a list of drugs, volatile anesthetics are not even included. Slightly more information is presented for opioids (fentanyl 1–2 μg/kg is included in the list of "*most typically*" used intraoperative drugs; morphine 0.1–0.15 mg/kg is merely reported as having been "given for postoperative pain;" and the postoperative morphine patient-controlled anesthesia settings are stated for the general anesthesia–postoperative opioids group), but the quantity actually received by patients in the two groups is not reported. One further example of incomplete methodological information is not only deficient, but also inaccurate. The term "*sizable minority*" is used to describe the percentage of patients who received general anesthesia–postoperative opioids; however, this contradicts the actual numbers of patients in each group: 123 patients received general anesthesia–postoperative opioids whereas 102 received epidural anesthesia/analgesia. No explanation is given for this discrepancy.

The above discussion leads to a more general issue: The standard of reporting expected for retrospective studies. Although some information may not be available, every attempt must be made to achieve the same standard of rigorous reporting as for clinical trials and laboratory investigations. Indeed, with the inherent drawbacks of retrospective studies, one could argue that the presentation of the information that *is* available should reach an even higher standard than that used for other types of scientific articles. Furthermore, if important data are not available, this calls into question whether the study should even be performed, as its validity may be suspect. As computerized record-keeping and databases are increasingly used, it is quite possible that retrospective studies will become more and more common. To provide meaningful information, these studies should strive to achieve the same high standards expected of other scientific publications.

M. Denise Daley, M.D., Peter H. Norman, M.D.* *University of Texas M. D. Anderson Cancer Center, Houston, Texas. phnorman@mdanderson.org

References

1. Biki B, Mascha E, Moriarty DC, Fitzpatrick JM, Sessler DI, Buggy DJ: Anesthetic technique for radical prostatectomy surgery affects cancer recurrence: A retrospective analysis. Anesthesiology 2008; 109:180–7

2. Markovic SN, Knight PR, Murasko DM: Inhibition of interferon stimulation of natural killer cell activity in mice anesthetized with halothane or isoflurane. Anesthesiology 1993; 78:700–6

3. Vallejo R, de Leon-Casasola O, Benjamin R: Opioid therapy and immunosuppression: A review. Am J Ther 2004; 11:354–65

(Accepted for publication December 3, 2008.)

Anesthesiology 2009; 111:203–4

In Reply:—We are proponents of prospective research and between us have published more than 400 randomized trials. Randomized trials are considered the gold standard for clinical evidence because they minimize the risks of selection bias, measurement bias, confounding, and reverse causation. There are nonetheless occasions when retrospective studies are helpful. For example, retrospective studies can provide initial evidence to support a novel hypothesis and estimate the potential treatment effect.

The theory that regional analgesia may reduce the risk of cancer recurrence is both novel and recent. It is likely that a randomized trial testing this hypothesis will take 5 yr or longer, given that it will be necessary not only to enroll patients, but to wait for cancer recurrences. However, agencies are unlikely to fund such a large effort without at least some human data. Furthermore, an estimate of treatment effect is necessary to properly develop *a priori* sample-size estimate and interim analysis plans. It was in this spirit that we published our current observations in men having prostate cancer surgery,[1] and previous ones in women having breast cancer surgery.[2]

We also wish that more details about anesthetic management were available. It is because these details would so obviously have been interesting that we commented about them in the manuscript. However, a limitation of retrospective studies is that much interesting information is often unavailable—as in our patients.

We were explicit in our recent paper, and our previous one, that small retrospective studies are no basis for changing clinical practice—and we reiterate that here. But our current[1] and previous[2] results, to say nothing of overwhelming animal evidence,[3,4] do provide considerable basis for large randomized trials.[5] The Outcomes Research Consortium has already started randomized trials of paravertebral an-