Is Postoperative Pain a Mediator of Cancerous Mortality?

Xiaofeng Shen, *[1] Shiqin Xu, *[1] Rong Shen, † Xirong Guo, † Fuzhou Wang *‡Δ

SUMMARY: Postoperative pain is considered as a risk factor for the mortality of cancerous patients. Are there convincing evidence demonstrating the causality between them? It is hard to draw a conclusion from the currently available data. Pain itself is an immune suppressor and functions as a tumor-promoting mediator, but it is strongly associated with the pain intensity. The mild-to-moderate pain is a favorable factor to the recovery for patients from surgeries. Everything possesses dual facets: *yin* and *yang* balance system. What we need to do is how to take advantage of the favorable from both sides rather than debate which is superior to the other. Yes, even overbalance there, the key necessary for it is to taking measures to keep them on balance.■

*: Department of Anesthesiology and Critical Care Medicine, Nanjing Maternity and Child Health Care Hospital, Nanjing Medical University, Nanjing 210004, China
†: Institute of Pediatrics, Nanjing Maternity and Child Health Care Hospital, Nanjing Medical University, Nanjing 210004, China
‡: Division of Neuroscience, The Bonoi Academy of Science and Education, Winston-Salem, NC 27157, USA
Δ: Correspondence to: Dr. Fuzhou Wang, No. 123, Tianfei Xiang, Mochou Rd., Nanjing 210004, China. Tel: +86-25-5222-6112; Fax: +86-25-8420-0723
E-mail: zfwang50@njmu.edu.cn
1: These authors contributed equally to this work
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WE READ the paper published in the *British Journal of Medicine* with great interest on the effect of perioperative epidural analgesia on long-term cancer-free survival (1). This multicentral follow-up study compared the cancer recurrence-associated mortality in patients undergone epidural postoperative analgesia with those without epidural analgesia, and found epidural analgesia early after the cancer surgeries will not increase the long-term mortality. This was an intriguing trial and added information for the understanding upon the safety of early epidural analgesia after cancer excision, whereas imprecise data were reported.

The authors described the background information of the study through underlining the impact of analgesia with or without opioids on immune functions that may be associated with the tumor matastasis. From the study protocol appeared in the present and previously published reports (1-3), the patients were randomized into one of the two groups: group epidural, intraoperative general anesthesia plus intraoperative epidural anesthesia and postoperative epidural analgesia; group control, intraoperative general anesthesia plus postoperative intravenous opioids based analgesia. Such a design would undoubtedly result in a big difference in the consumption of anesthetics and analgesics because of the role of combined epidural and general anesthesia in reducing intraoperative drugs usage compared with general anesthesia alone (4, 5), and these changed drugs might produce undetected role in affecting immune cells function (6). Therefore, as the data presented in the study did not include the intraoperative drugs consumption, which consequently makes us want to know whether or not a difference in drugs usage exists, and if yes, was there any positive or negative influence of this difference on

Table 1. Example of skewed pain data with same mean but different median.

	Group I (n = 8)	Group II (n = 8)	P value
Original values of pain	0, 0, 0, 0, 0, 0, 1, 10	1, 1, 1, 1, 1, 2, 2, 2	–
Mean (SD/SEM)	1.4 (3.5/1.2)	1.4 (0.5/0.2)	1.0 *
Median (IQR)	0.0 (0.0 – 0.5)	1.0 (1.0 – 2.0)	0.02 †

* Denotes tested with student's t test under the assumption that the data were normally distributed.
† Denotes tested with Mann-Whitney test for the data's skewed property.
SD: standard deviation; SEM: standard error of means; IQR: interquartile range.

the study outcome?

Second, pain, specifically the postoperative pain itself is an immune suppressor (7), and even a tumor-promoting mediator (8). Although the authors presented pain intensity measured with visual analogue scale (VAS), they did not performed in-depth analyses of the effect of pain changes on the cancer survival. The pain intensity in the present study was at the mild-to-moderate level, though, the study found a significant difference in pain at day 1 after surgeries (both at rest and with coughing) and at days 1 to 3 with coughing, thus it was still possible that the pain affected the function of immune cells which finally influences the recurrence of the cancer. So it would be better to do a subgroup analysis of the potential effect of postoperative pain on the long term cancerous survival.

Third, the authors reported their observations of pain with mean and standard deviation (SD). This may be an issue needs to be corrected. Theoretically and practically, pain scorings are skewed data that need to be converted to logarithmic values if presented with means and SDs (9, 10). If without such a conversion, the median and interquartile range (IQR) of the pain scorings would be far more precise in predicting the overall effect of analgesia. Given the difference of statistical methods used in analyzing normally and non-normally distributed data, it might be lead to different statistical results (Table 1). Therefore, the pain intensity scores in this study should be corrected to median and corresponding IQR or converted to logarithmic values.■

CONFLICT OF INTERESTS

None

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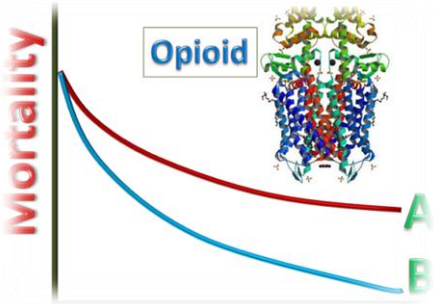

REFERENCES

1. Myles PS, Peyton P, Silbert B, Hunt J, Rigg JR, Sessler DI, ANZCA Trials Group Investigators. Perioperative epidural analgesia for major abdominal surgery for cancer and recurrence-free survival: randomised trial. BMJ 2011; 342: d1491.
2. Peyton PJ, Myles PS, Silbert BS, Rigg JA, Jamrozik K, Parsons R. Perioperative epidural analgesia and outcome after major abdominal surgery in high-risk patients. Anesth Analg 2003; 96: 548-54.
3. Rigg JR, Jamrozik K, Myles PS, Silbert B, Peyton P, Parsons RW, Collins K. Design of the multicenter Australian study of epidural anesthesia and analgesia in major surgery: the MASTER trial. Control Clin Trials 2000; 21: 244-56.
4. Lu CH, Borel CO, Wu CT, Yeh CC, Jao SW, Chao PC, Wong CS. Combined general-epidural anesthesia decreases the desflurane requirement for equivalent A-line ARX index in colorectal surgery. Acta Anaesthesiol Scand 2005; 49: 1063-7.
5. Li Y, Zhu S, Yan M. Combined general/epidural anesthesia (ropivacaine 0.375%) versus general anesthesia for upper abdominal surgery. Anesth Analg 2008; 106: 1562-5.
6. Welden B, Gates G, Mallari R, Garrett N. Effects of anesthetics and analgesics on natural killer cell activity. AANA J 2009; 77: 287-92.
7. Page GG, Ben-Eliyahu S. The immune-suppressive nature of pain. Semin Oncol Nurs 1997; 13: 10-5.
8. Page GG, Blakely WP, Ben-Eliyahu S. Evidence that postoperative pain is a mediator of the tumor-promoting effects of surgery in rats. Pain 2001; 90: 191-9.
9. Bowalekar SK. Statistics in medical research-II. Measures of central tendency. J Postgrad Med 1993; 39: 166-73.
10. McCluskey A, Lalkhen AG. Statistics II: Central tendency and spread of data. Continuing Education in Anaesthesia, Critical Care & Pain. Brit J Anaesth 2007; 7: 127-30.■