influence cancer recurrence and thus survival. Clearly the situation is far more complex than the headline; I do hope when prospective research is undertaken, it takes these wide-ranging aspects of perioperative care into account.

Competing Interests

The author declares no competing interests.

Sarah A. Dawson, M.B.B.S., Northumbria Health NHS Trust, Newcastle upon Tyne, United Kingdom. sarahdawson86@gmail.com

References

1. Wigmore TJ, Mohammed K, Jhanji S: Long-term survival for patients undergoing volatile *versus* IV anesthesia for cancer surgery: A retrospective analysis. Anesthesiology 2016; 124:69–79
2. Hébert PC, Wells G, Blajchman MA, Marshall J, Martin C, Pagliarello G, Tweeddale M, Schweitzer I, Yetisir E: A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med 1999; 340:409–17
3. Goodnough LT, Maggio P, Hadhazy E, Shieh L, Hernandez-Boussard T, Khari P, Shah N: Restrictive blood transfusion practices are associated with improved patient outcomes. Transfusion 2014; 54(10 pt 2):2753–9
4. Miki C, Hiro J, Ojima E, Inoue Y, Mohri Y, Kusunoki M: Perioperative allogeneic blood transfusion, the related cytokine response and long-term survival after potentially curative resection of colorectal cancer. Clin Oncol (R Coll Radiol) 2006; 18:60–6
5. Weber RS, Jabbour N, Martin RC II: Anemia and transfusions in patients undergoing surgery for cancer. Ann Surg Oncol 2008; 15:34–45
6. Cata JP, Wang H, Gottumukkala V, Reuben J, Sessler DI: Inflammatory response, immunosuppression, and cancer recurrence after perioperative blood transfusions. Br J Anaesth 2013; 110:690–701
7. Heaney A, Buggy DJ: Can anaesthetic and analgesic techniques affect cancer recurrence or metastasis? Br J Anaesth 2012; 109(suppl 1):i17–28

(Accepted for publication March 28, 2016.)

Long-term Survival, All-cause Mortality, and Propensity Score Matching

To the Editor:

We read with great interest the article by Wigmore *et al.*[1] The authors have produced one of the largest studies published looking at cancer survival and anesthesia.

In an era where new cancer therapies are becoming ever more expensive to develop, their primary study finding, increase in mortality associated with inhalational anesthesia compared to intravenous anesthesia with an adjusted hazard ratio of 1.46 (1.29 to 1.69) after propensity score matching and multivariate analysis, is one of huge potential significance.

There are three points arising from the study we would like to discuss.

First, we agree with the authors that long-term survival is a key outcome measure in cancer surveillance. However, we noticed this study analyzed patients over a 3-yr period, with a further 18-month follow-up period, giving a maximum total potential follow-up time of 4.5 yr.

Widely accepted measures of long-term cancer survival are 5 and 10 yr.[2,3] We feel that the use of the phrase "long term" in the study title could mislead some readers. Perhaps it would have been more appropriately titled, simply, "survival rates for patients undergoing volatile *versus* intravenous anesthesia for surgery."

Second, we would like to highlight issues around the use of propensity scoring analyses and all-cause mortality data.

All-cause mortality is typically used as an outcome measure in prospective trials. Randomization helps account for unknown confounding factors affecting the outcome, thus facilitating the use of all-cause mortality as a primary outcome.

Usefulness of propensity scoring matching in retrospective studies is limited by the fact that remaining unmeasured confounding may still be present.[4] This makes the all-cause mortality data presented in this study more difficult to evaluate.

Preclinical studies in the literature suggest some form of immunomodulatory effects related to propofol or volatiles[5,6] during the intraoperative period affect the likelihood of recurrence of cancer.

Given this potential for causality combined with the limitations of propensity score matching, we suggest the study could be further refined by looking at cancer-related deaths only as opposed to all-cause mortality.

A possible suggestion would be obtaining mortality data from national cancer registries where cause of death would also be available, as an alternative to the National Health Service demographics service.

Finally, we noticed the Kaplan–Meier survival curves were for unmatched data only. We think that comparing the survival curves for the unmatched groups to those of the groups matched for known variables would add something to the study.

We acknowledge the authors recognized some of the inevitable shortcomings of retrospective studies and support their calls for urgent prospective work to corroborate their findings.

Competing Interests

The authors declare no competing interests.

Usman Ali, M.B.B.S., B.Sc., F.R.C.A., Arshad Ghori, M.B.B.S., M.D., F.R.C.A. Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom (U.A.). u.ali@doctors.org.uk

References

1. Wigmore TJ, Mohammed K, Jhanji S: Long-term survival for patients undergoing volatile *versus* IV anesthesia for

cancer surgery: A retrospective analysis. Anesthesiology 2016; 124:69–79
2. Brenner H: Long-term survival rates of cancer patients achieved by the end of the 20th century: A period analysis. Lancet 2002; 360:1131–5
3. Brenner H, Hakulinen T: Very-long-term survival rates of patients with cancer. J Clin Oncol 2002; 20:4405–9
4. Winkelmayer WC, Kurth T: Propensity scores: help or hype? Nephrol Dial Transplant 2004; 19:1671–3
5. Buckley A, Quaid MS, Johnson P, Buggy D: Serum from women undergoing breast cancer surgery, randomized to propofol-paravertebral anaesthetic technique, maintain natural killer cell anti-tumour activity compared with sevoflurane/opioid technique: ESAPC1-5. Eur J Anaesthesiol 2014; 31:2
6. Melamed R, Bar-Yosef S, Shakhar G, Shakhar K, Ben-Eliyahu S: Suppression of natural killer cell activity and promotion of tumor metastasis by ketamine, thiopental, and halothane, but not by propofol: Mediating mechanisms and prophylactic measures. Anesth Analg 2003; 97:1331–9

(Accepted for publication March 28, 2016.)

In Reply:

Many thanks for your comments on our recent retrospective study.[1]

With regard to the first point posed by Drs. Ali and Ghori, concerning the use of the term "long-term cancer survival," we agree that together with 1-yr survival, 5- and 10-yr survival rates are commonly used when reporting cancer survival. However, contextually, mortality rates for perioperative interventions are commonly reported as either 30 days or length of stay, and as such the reported follow-up of between 18 months and 4.5 yr would qualify as long term.

With regard to the use of the propensity model and all-cause mortality data, we agree that a better approach would have been to consider cancer-attributable mortality. However, these data are not reliably available in the United Kingdom. National cancer registries do not cover the broad span of cancers we considered, and in addition often have incomplete data for the early years covered by the study.

We agree that Kaplan–Meier curves for the propensity-matched groups should have been included in the study. These are now included in figure 1, A–C, and as you can see are very similar to those for the nonmatched groups.

Drs. Doleman, Lun, and Williams raise interesting queries regarding our analysis, much of which we are in agreement with.

There is little doubt that cancer type and stage have a profound effect on outcome, and the lack of accurate data within our study for the latter in particular is a potential major confounder. However, as we state in the discussion, the very lack of availability of staging data to the practitioners administering the anesthesia lessens this fact since it could not have been a deciding factor in the choice of anesthetic.

James C. Eisenach, M.D., served as Editor-in-Chief for this exchange.

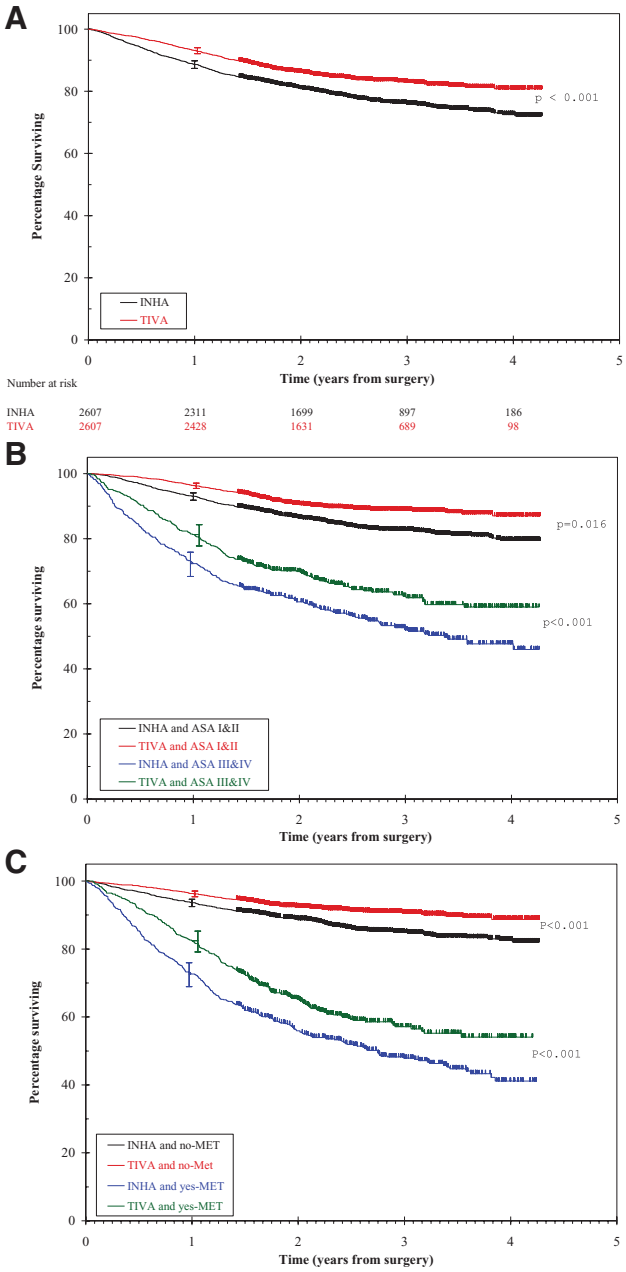

Fig. 1. (*A*) Kaplan–Meier (KM) plot for the propensity-matched patients. (*B*) KM plot for the propensity-matched patients by anesthesia type and American Society of Anesthesiologists (ASA) groups. (*C*) KM plot for the propensity-matched patients by anesthesia type and metastasis status. INHA = volatile inhalational; no-MET = no detected metastases; TIVA = total IV anesthesia; yes-MET = known metastases at the time of surgery.

As far as including cancer types in either the propensity model or the multivariate analysis (beyond the broad groups that have already been included in the analysis, see tables 1 and 2), the major issue is the numbers of different types and subtypes, with consequent substantial implications for outcome. A look through the data reveals more than 20 broad cancer types. Within those types are further subdivisions, for example, triple-negative breast cancer has a very different