

Long-term Survival for Patients Undergoing Volatile Versus IV Anesthesia for Cancer Surgery: A Retrospective Analysis

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Volatile inhalational anesthetic (INHA) gases and total IV anesthesia (TIVA) are 2 main classes of drugs used to maintain general anesthesia. In addition, there are a number of retrospective studies suggesting that the use of regional anesthesia during cancer surgery is beneficial, although the reason is uncertain. Consequently, in the current review, the authors evaluate whether patients who receive volatile inhalational agents for anesthesia maintenance experience worsened outcomes. This was a retrospective, 3-year-long, cohort study at a comprehensive cancer center and compared long-term survival of patients who underwent elective surgery using either INHA or TIVA with continuous propofol infusion and short-acting opioid.

Data were collected on anesthetic technique, age/height/weight at time of surgery, sex, severity of surgery, procedure, tumor site and group, presence of metastasis, intraoperative blood transfusion, use of epidural analgesia, and use of opioids. Cox proportional hazard regression models, univariate and multivariate regression models adjusted for significant confounders, and subgroup analyses were used for statistical analysis.

Data of a total of 7030 patients (3316 INHA patients and 3714 TIVA patients) were reviewed. Patients in the INHA group were more likely to be male, have American Society of Anesthesiologists physical status score of III or IV, and have more complex surgery, blood transfusion, epidural, and metastatic cancers. No other differences between groups were found. Overall mortality was 18.5% and was higher in the INHA group than in the TIVA groups (24% vs 13.6%). One-year survival for all patients was 91.2%, and lower in the INHA group than the TIVA group (87.9% vs 94.1%). The INHA group had a hazard ratio (HR) of 1.59 for univariate analysis and 1.46 for multivariate and propensity-score analyses. There was a substantially worsened outcome for the INHA group for all severities of surgery except 3, for patients with American Society of Anesthesiologists physical status I to III, and for patients with or without metastasis at the time of surgery. After multivariable analysis, a statistically significant association was found in patients with gastrointestinal cancer.

A limitation of this study is that the baseline characteristics of the 2 groups differ. Staging data were also not included. Nevertheless, this large, retrospective analysis demonstrates an HR of 1.46 (1.29–1.66) for death for patients receiving INHA compared with patients receiving TIVA. As there are thousands of patients with cancer diagnosis, further studies are urgently needed to evaluate these findings.

COMMENT

Despite impressive advances in oncology, cancer remains a feared cause of morbidity and mortality. Approximately 14.1 million new cases of cancer were diagnosed worldwide in 2012, and it is estimated that 1500 individuals succumb to cancer every day in the United States. Metastasis is a complicated biological process, the outcome of which depends on several complex interactions between the proclivity of the particular tumor to metastasize and the robustness of the host's immune system. The major defense against invading tumor cells is cell-mediated immunity, and the immunosuppression caused by surgery, stress, and anxiety creates a window of opportunity for tumor cells to evade immune destruction. Another factor that has been proposed to be associated with increased risk of cancer recurrence is allogenic blood transfusion, which is associated with immunomodulation. Moreover, it has been suggested that volatile anesthetics up-regulate hypoxia-inducible factor 1a in neoplastic cells, thereby enhancing angiogenesis.

The current study by Wigmore and colleagues is an interesting retrospective analysis comparing mortality after cancer surgery in more than 7000 patients given either INHA or TIVA. Mortality was approximately 50% greater with INHA than with TIVA, with an adjusted HR of 1.46. The authors were candid, however, about the limitations of their investigation, the most notable of which was the disparity in baseline characteristics of the 2 groups. The INHA group included more patients who were male, had a physical status score of III or IV, had metastatic cancer, and were having higher-grade surgery. Although the authors performed propensity matching to correct for these factors as well as other potential confounders, the noninclusion of staging data was also a potential confounder. Furthermore, the investigators concluded that it was not possible to establish the reason for the difference in outcomes. The results might be owing to a negative effect of INHA or a beneficial effect of TIVA, a combination of both, or owing to unaccounted-for confounding factors.

What is the take-home message? Perioperative immune competence is impaired by several factors, including surgery and anesthesia. Most of the studies involving the role of anesthetic technique and/or agents are retrospective analyses flawed by major confounding and selection issues, and the available data are so conflicting that they prevent clinicians from extracting meaningful and relevant conclusions to apply to the care of their cancer patients. Nonetheless, several important prospective, blinded, randomized trials are in progress, and their results are eagerly anticipated. In the interim, applying the same best practices currently recommended for noncancer patients to our patients with cancer seems a reasonable and meritorious approach. The focus should be on adequate analgesia, blunting of the stress response, avoidance of allogenic transfusion if feasible, and mitigation of inflammation.

*Comment by Kathryn E. McGoldrick, MD, FCAI(Hon)
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