SEE Summaries of Emerging Evidence

# SEE Question

**A 45-year-old woman is scheduled to undergo a bilateral mastectomy for metastatic breast cancer. According to a recent study of patients undergoing breast cancer surgery with general anesthesia maintained with propofol or volatile agents, which of the following MOST likely describes overall survival with use of propofol compared to volatile agents?**

☐ (A) Higher ☐ (B) Lower ☐ (C) No difference

Retrospective evidence suggests that the choice of sevoflurane or propofol for maintenance of general anesthesia in patients undergoing cancer surgery can have an approximately 5 percentage-point difference in long-term survival. However, when studying breast cancer alone, these retrospective studies have differing results concerning long-term survival. Maintenance of general anesthesia with sevoflurane is the globally dominant technique; thus, if the costs of switching to a propofol-based anesthetic are to be considered, there needs to be substantial evidence to switch. The Cancer and Anesthesia (CAN) study is an ongoing prospective randomized controlled trial that shows no difference in survival between sevoflurane and propofol groups with a minimum of one-year follow-up. Because of this short time frame, large retrospective studies may be able to supply complementary evidence while prospective studies are under way.

A recent large retrospective cohort study that used national Swedish registry data was conducted to analyze survival in breast cancer patients based on anesthetic technique. All breast cancer patients who underwent surgery between 2013 and 2019 were identified in the National Quality Registry for Breast Cancer, and data were sent to Uppsala Clinical Research Center, where they were added to data from the Swedish PeriOperative Registry. The independent variable was the drug used for anesthesia maintenance (propofol or inhaled volatile agent). Age at surgery, ASA Physical Status, and body mass index were dependent variables that were considered true confounders. Hospitals were divided into three groups based on surgical volume (<100 surgeries, 100-500 surgeries, and >500 surgeries) to minimize the confounding effect of annual surgical volume on outcomes. Two propensity score-matched cohorts were created, and scores were calculated through logistic regression models. In the first cohort, scores were calculated using all collected characteristics except body mass index and blood loss (because of missing values). In the second cohort, scores were calculated using only the variables that had a standardized mean difference greater than 0.1. The primary outcome was overall survival between patients who had propofol- or volatile-maintained anesthesia. *Overall survival* was defined as from the date of surgery to death from any cause or the end of follow-up, whichever occurred first. As an additional analysis, overall survival and mortality were explored in a subgroup of triple-negative breast cancer patients. Triple-negative breast cancer is an aggressive form of cancer lacking receptors for $ERBB_2$ (formerly $HER_2$), estrogen, and progesterone, which is associated with worse prognosis.

The final study cohort included 18,674 patients, of whom 13,873 (74.3%) were anesthetized with propofol during anesthesia maintenance. The propofol group was younger, had lower ASA Physical Status, and had lower tumor grading than the volatile group. Triple-negative cancer proportions did not differ between the groups.

In the unmatched cohort, higher overall survival was found in the propofol group (97.2%) than in the volatile group (84.1%) (hazard ratio [HR], 0.80; 95% CI, 0.70-0.90). After propensity score matching (Figure), no difference in overall survival was found between propofol (92.0%) and volatile agents (92.1%) (HR, 0.98; 95% CI, 0.85-1.13). The second propensity score-matched cohort (standardized mean difference > 0.1) also showed no difference between groups. No survival benefit was found with propofol in propensity score-matched, triple-negative breast cancer patients (HR, 1.17; 95% CI, 0.79-1.72).

In summary, the authors of this study found no difference in long-term overall survival in postsurgical breast cancer patients who received general anesthesia maintained with propofol versus inhaled volatile agent. These findings are not consistent with those of biomarker studies (whose findings support that inhaled agents would increase the risk of metastasis or local recurrence, while propofol could be protective). It should be noted that propofol was used for induction in all patients; however, it is unlikely that this would modify the outcome in the volatile group. ■

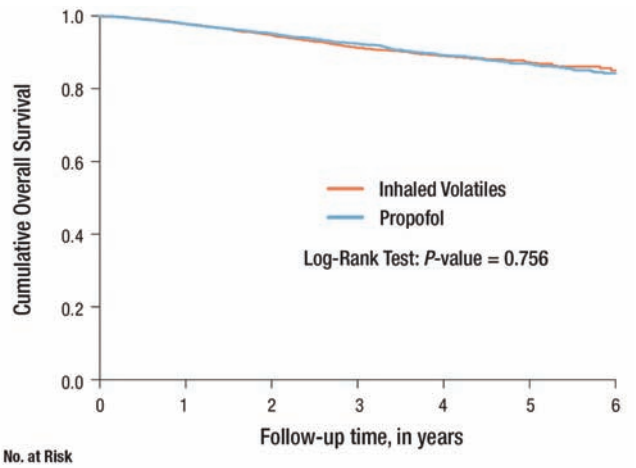


**Figure:** Overall survival by type of anesthesia for 4,658 pairs from a full propensity score match of patients given an inhaled volatile anesthetic or propofol for anesthesia maintenance for breast cancer surgery. Used with permission, from Enlund M, Berglund A, Enlund A, Bergkvist L. Volatile versus propofol general anesthesia and long-term survival after breast cancer surgery: a national registry retrospective cohort study. *Anesthesiology.* 2022;137(3):315-326. doi:10.1097/ALN.0000000000004309

**References:**

1. Enlund M, Berglund A, Enlund A, Bergkvist L. Volatile versus propofol general anesthesia and long-term survival after breast cancer surgery: a national registry retrospective cohort study. *Anesthesiology.* 2022;137(3):315-326. doi:10.1097/ALN.0000000000004309
2. Enlund M, Enlund A, Berglund A, Bergkvist L. Rationale and design of the CAN study: an RCT of survival after propofol- or sevoflurane-based anesthesia for cancer surgery. *Curr Pharm Des.* 2019;25(28):3028-3033. doi:10.2174/1381612825666190705184218

Answer: C

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