Title: Impact of Preoperative Varenicline compared to Nicotine Replacement Therapy in Cardiac Surgery

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Objectives

Nicotine dependence increases the risk of adverse outcomes after cardiac surgery, yet no established studies directly compare smoking cessation medications in this setting. This study evaluated postoperative outcomes among these patients undergoing cardiac surgery, comparing preoperative varenicline use with nicotine replacement therapy (NRT).

Methods

We performed a retrospective cohort study using the TriNetX Research Network, including adults with documented nicotine dependence who underwent cardiac surgery between 2005 and 2025. We compared preoperative varenicline use vs preoperative NRT use and preoperative varenicline use vs active smokers who did not receive pharmacologic cessation therapy. Varenicline and NRT exposure were defined by nicotine dependence with prescription records within 3 months prior to cardiac surgery. We used independent 1:1 propensity score matching to create matched cohorts. Primary outcomes were all-cause mortality, MACE, and ED admission. Secondary outcomes included MI, arrhythmias,

pneumonia, acute respiratory failure or ARDS, mechanical ventilation, postoperative infection, and antipsychotic use. All outcomes were measured 6 months post-op.

Results

After propensity score matching, 316 patients were included in each cohort. At 6 months, there was no significant difference in all-cause mortality. Varenicline use was associated with significantly lower risks of MACE (18.0% vs 33.2%; RR 0.54, 95% CI 0.41-0.72; p<0.01) and ED admission (13.3% vs 19.6%; RR 0.68, 95% CI 0.47-0.97; p=0.032). Among secondary outcomes, varenicline was associated with a significantly lower risk of MI (12.3% vs 26.9%; RR 0.46, 95% CI 0.33-0.65; p<0.01) and postoperative infection (4.7% vs 9.2%; RR 0.52, 95% CI 0.28-0.95; p=0.029). No differences in other secondary outcomes.

Conclusions

In our study, varenicline use was associated with significantly lower risks of MACE, MI, postoperative infection, and ED admission compared to NRT.