Dimorphic Mortality in Alzheimer's Disease Patients using Antipsychotics: A Real-World Study

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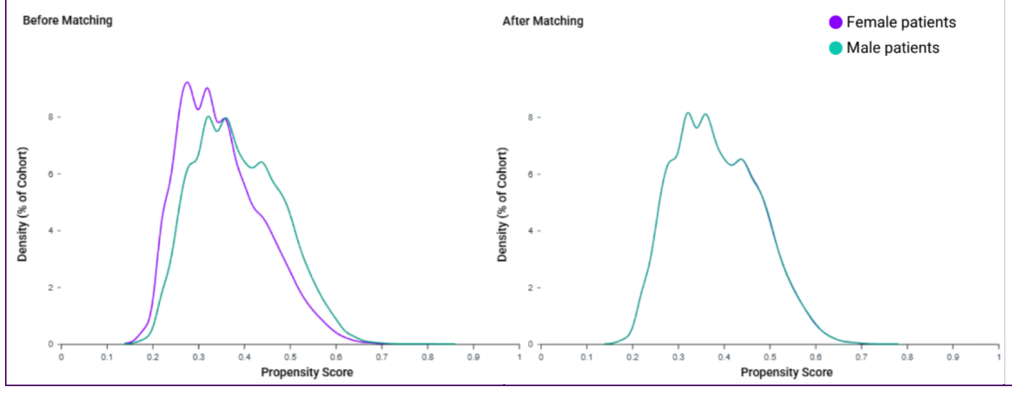
Male patients with Alzheimer's disease receiving antipsychotic therapy exhibited significantly higher all-cause mortality than female patients over a 3-year follow-up (30.4% vs. 24.5%). Female sex was associated with a 19.6% lower relative risk of death and a 25.9% lower hazard of mortality, highlighting biological sex as an important factor in risk stratification, shared decision-making, and the optimization of antipsychotic prescribing in Alzheimer's disease.

INTRODUCTION

Introduction: Antipsychotic (AP) use in patients with Alzheimer's disease (AD) is associated with increased mortality. However, potential sex differences in outcomes among AP users with AD remain underexplored. This study aimed to evaluate mortality risk and survival differences between male and female AD patients using APs.

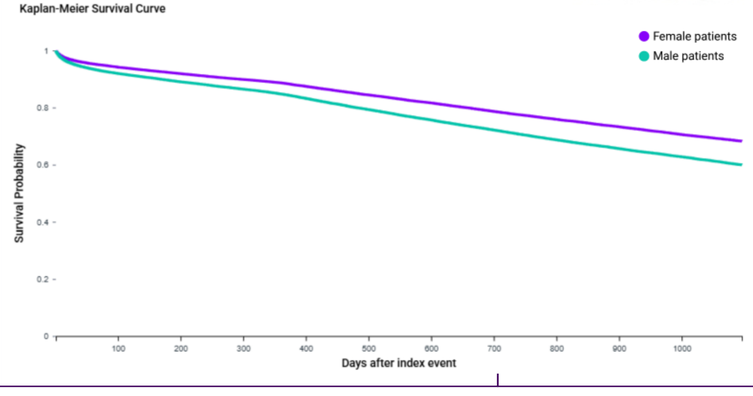
METHODS

Methods:We conducted a retrospective cohort analysis using TriNetX, a global health research network with real-world data. Patients diagnosed with Alzheimer's disease and prescribed antipsychotics were stratified by sex. Mortality risk, odds ratios (OR), risk ratios (RR), and hazard ratios (HR) were calculated. Kaplan-Meier survival analysis and log-rank tests were performed to assess survival probability over time.



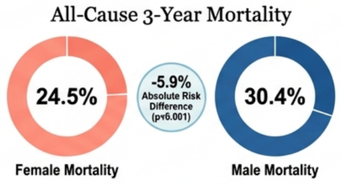
RESULTS

Results: : The female AP user cohort (n=112,566) had a lower mortality risk (25.2%) compared to male AP users (n=74,251; risk: 27.6%). The risk difference was -0.024 (95% CI: -0.028 to -0.020, p<0.001), with a risk ratio of 0.913 and OR of 0.883. Median survival was longer in females (3,018 days) versus males (2,372 days), with a survival probability of 19.1% vs. 26.3% at the end of the time window. The hazard ratio was 0.823 (95% CI: 0.809–0.838, p<0.001). In an additional analysis, stratifying by patients with longer follow-up, the mortality risk remained significantly lower in females (17.2%) than males (27.2%), with a risk difference of -0.10 and HR of 0.544 (95% CI: 0.533–0.554, p<0.001). Median survival for females was 6,770 days versus 3,383 for males.



CONCLUSIONS

Conclusions: Among Alzheimer's patients using antipsychotics, females consistently demonstrated lower mortality and longer survival than males. These findings underscore the importance of considering sex as a biological variable in treatment decisions and mortality risk assessments for AP use in AD.



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