Assessing the association between hormone therapy use in female breast cancer and subsequent risk of cardiovascular disease: a cohort study in the UK Clinical Practice Research Datalink

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Background: Tamoxifen is known to be associated with an increased risk of thromboembolic events, but the long-term cardiovascular consequences of aromatase inhibitors are unclear, and trials have not been powered for cardiovascular outcomes. We aimed to examine the association between AIs in comparison to tamoxifen, and a range of cardiovascular outcomes in a cohort of post-menopausal breast cancer survivors in the UK.

Methods: Using primary care data from the UK CPRD, we assembled a cohort of women over the age of 54, who had survived for 1 year following a breast cancer diagnosis, and were prescribed either tamoxifen or an AI between 2002 and 2015. The outcomes were incident cardiovascular events. Associations between hormone therapy (AI vs tamoxifen) and outcomes were analysed using Cox regression, adjusted for potential confounders.

Results: 15,116 women were included, of whom 6,524 were originally prescribed tamoxifen, and 8,592 were originally prescribed AIs. There was strong evidence of an increased risk of heart failure in those ever prescribed an AI, compared with those only ever prescribed tamoxifen (adjusted HR: 1.78, 95% CI: 1.29-2.46), but this was not maintained once patients stopped their AI therapy (HR: 1.11, 95% CI: 0.65-1.88). There was strong evidence that ever-AI users were at decreased risk of venous thromboembolism (VTE) compared with those prescribed tamoxifen only (HR: 0.72, 95% CI: 0.55-0.94). There was also weak evidence of an increased risk of stroke in ever-AI users, in comparison with those prescribed tamoxifen only (HR: 1.32, 95% CI: 0.95-1.84), which was maintained once women stopped their AI therapy (HR: 1.81, 95% CI: 1.06-3.11).

Conclusion: We found a lower risk of VTE among AI users compared to tamoxifen users, consistent with the established increased risk of VTE associated with tamoxifen use. We also provide new evidence of an increased risk of heart failure during AI use in comparison to tamoxifen use. There was some evidence of a higher risk of stroke in AI users compared to tamoxifen users, but the pattern of risks suggested that this may be driven by a protective effect of tamoxifen on stroke.

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