Fluoroquinolones and the Risk of Aortic Aneurysm or Aortic Dissection: Evidence From a Nationwide Nested Case-Control Study Paralleled With Matched Experimental Models

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INTRODUCTION

Fluoroquinolones (FQ) are among the most commonly used antibiotic classes worldwide owing to their broadspectrum antimicrobial activity. However, FQ have been associated with aortic aneurysm and aortic dissection (AA/AD) resulting in an official FDA warning. Yet, recently large-scale epidemiological studies have failed to confirm this association.

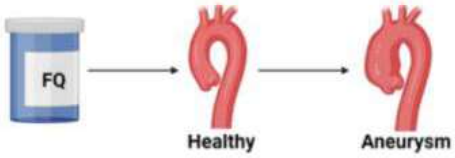

Figure 1. Hypothesis. FQ administration will lead to aneurysm formation. FQ, fluoroquinolones

AIMS

The current study aimed to scrutinize the FQ-AA/AD association through a retrospective nested case cohort analysis supplemented with matched animal experimentation.

METHODS

Danish nationwide registers were used to conduct a nested case-control study. For analyses, three separate cohorts were identified: i) A main cohort, ii) a high-risk cohort, and iii) a cohort with known aortic disease. Experimentally, ciprofloxacin was evaluated in three different mouse models: i) Wild type mice, ii) hypertensive mice, and iii) an experimental model of Marfan disease.

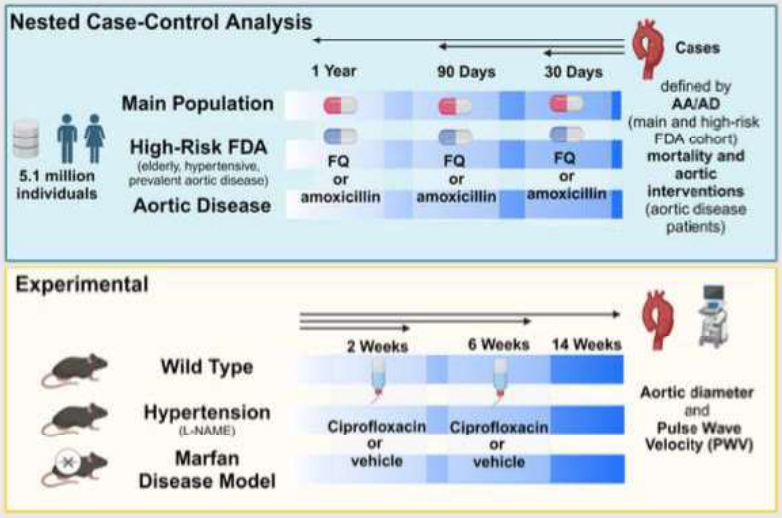

Figure 2. Overview of clinical and experimental investigations. FQ, fluoroquinolone; AA/AD, aortic aneurysms or aortic dissections; L-NAME, Nω-Nitro-L-arginine methyl ester hydrochloride.

RESULTS

FQ exposure was not associated with increased AA/AD hazard ratios in main and high-risk (elderly ≥65 years, hypertensive, and prevalent aortic disease) populations. Additionally, FQ did not cause increased mortality or aortic interventions in aortic disease patients. Moreover, in animal experimentation ciprofloxacin did not enlarge aortic diameters nor increase arterial stiffness.

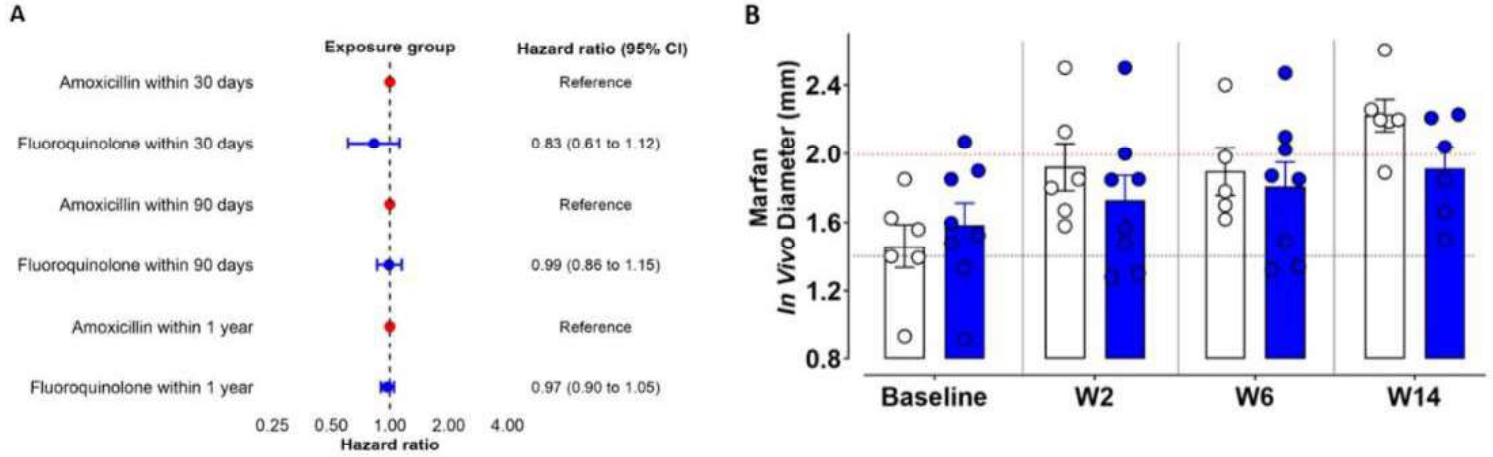

Figure 3.(A) Risk of first-time aortic aneurysm/aortic dissection (AA/AD) by antibiotic use in high-risk nested patients.(B) Aortic dilation or aneurysm formation following ciprofloxacin treatment in genetic (Fbn1$^{C1039G/+}$) Marfan model mice.

CONCLUSION

The current study, which employed a large nationwide cohort of patients, as well as experimental mouse models, was unable to replicate FQ-AA/AD findings. Collectively our study offers a reasonable degree of confidence that FQ usage should not be discouraged due to primary concerns of aortic disease when clinically indicated.

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