Aortic aneurysm: Fluoroquinolones, genetic counseling

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TO THE EDITOR: We read with interest the article by Cikach et al on thoracic aortic aneurysm.[1] For medical management of this condition, the authors emphasized controlling blood pressure and heart rate and also avoiding isometric exercises and heavy lifting. In addition to their recommendations, we believe there is plausible evidence to advise caution if fluoroquinolone antibiotics are used in this setting.

Three large population-based studies, from Canada,[2] Taiwan,[3] and Sweden,[4] collectively demonstrated a significant 2-fold increase in the incidence of aortic aneurysm and dissection presenting within 60 days of fluoroquinolone use compared with other antibiotic exposure. Moreover, a longer duration of fluoroquinolone use was associated with a significantly higher incidence of aortic aneurysm and dissection.[3]

Mechanistically, fluoroquinolones have been shown to up-regulate production of several matrix metalloproteinases, including metalloproteinase 2, leading to degradation of type I collagen.[2,5] Type I and type III are the dominant collagens in the aortic wall, and collagen degradation is implicated in aortic aneurysm formation and expansion.

Fluoroquinolones are widely prescribed in both outpatient and inpatient settings and are sometimes used for long durations in the geriatric population.[2] It is possible that these drugs have a propensity to increase aortic aneurysm expansion and dissection in older patients who already have aortic aneurysm. Accordingly, this might make the risk-benefit ratio unfavorable for using these drugs in these situations, and other antibiotics should be used, if indicated.

Furthermore, if fluoroquinolones are used in patients with aortic aneurysm, perhaps imaging studies of the aneurysm should be done more frequently than once a year to detect accelerated aneurysm growth. Finally, physicians should be aware of the possibility of increased aortic aneurysm expansion and dissection with fluoroquinolone use.

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REFERENCES

1. **Cikach F, Desai MY, Roselli EE, Kalahasti V**. Thoracic aortic aneurysm: how to counsel, when to refer. Cleve Clin J Med 2018; 85(6):481–492. doi:10.3949/ccjm.85a.17039
2. **Daneman N, Lu H, Redelmeier DA**. Fluoroquinolones and collagen associated severe adverse events: a longitudinal cohort study. BMJ Open 2015; 5:e010077. doi:10.1136/bmjopen-2015-010077
3. **Lee C-C, Lee MG, Chen Y-S, et al**. Risk of aortic dissection and aortic aneurysm in patients taking oral fluoroquinolone. JAMA Intern Med 2015; 175:1839–1847. doi: 10.1001/jamainternmed.2015.5389
4. **Pasternak B, Inghammar M, Svanström H**. Fluoroquinolone use and risk of aortic aneurysm and dissection: nationwide cohort study. BMJ Open 2018; 360:k678. doi:10.1136/bmj.k678
5. **Tsai W-C, Hsu C-C, Chen CPC, et al**. Ciprofloxacin up-regulates tendon cells to express matrix metalloproteinase-2 with degradation of type I collagen. J Orthop Res 2011; 29(1):67–73. doi: 10.1002/jor.21196

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TO THE EDITOR: The review of thoracic aortic aneurysm by Cikach et al[1] was excellent. However, we noted that referral for clinical genetic counseling and testing is suggested only if 1 or more first-degree relatives have aneurysmal disease.

Absence of a family history does not rule out syndromic aortopathy, which can occur de novo. In addition, a clinical diagnosis of syndromic aortopathy can be made on the basis of physical features that can be very subtle, such as pectus deformities, scoliosis, dolichostenomelia, joint hypermobility or contractures, craniofacial features, or skin fragility.[2]

Genetic counseling is paramount even if molecular testing is negative or inconclusive,

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which can occur in more than 50% of patients referred.[3] Clinical genetic evaluation would also facilitate testing for other family members who may be affected, and would help to coordinate care for nonvascular conditions that may be associated with the syndrome.

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REFERENCES

1. **Cikach F, Desai MY, Roselli EE, Kalahasti V**. Thoracic aortic aneurysm: how to counsel, when to refer. Cleve Clin J Med 2018; 85(6):481–492. doi:10.3949/ccjm.85a.17039
2. **McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University**. OMIM. Online mendelian inheritance in man, https://omim.org/. Accessed July 31, 2018.
3. **Mazine A, Moryousef-Abitbol JH, Faghfoury H, Meza JM, Morel C, Ouzounian M**. Yield of genetic testing in patients with thoracic aortic disease. J Am Coll Cardiol 2017; 69(11):2005. doi:10.1016/S0735-1097(17)35394-9

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IN REPLY: We thank Drs. Goldstein and Mascitelli for their comments regarding fluoroquinolones and thoracic aortic aneurysms. We acknowledge that fluoroquinolones (particularly ciprofloxacin) have been associated with a risk of aortic aneurysm and dissection based on large observational studies from Taiwan, Canada, and Sweden. Although all of the studies have shown an association between ciprofloxacin and aortic aneurysm, the causative role is not well established. In addition, the numbers of events were very small in these large cohorts of patients. In our large tertiary care practice at Cleveland Clinic, we have very few patients with aortic aneurysm or dissection who have used fluoroquinolones.

We recognize the association; however, our paper was intended to emphasize the more common causes and treatment options that primary care physicians are likely to encounter in routine practice.

We also thank Drs. Ayoubieh and MacCarrick for their comments about genetic counseling. We agree that genetic counseling is important, as is a detailed physical examination for subtle features of genetically mediated aortic aneurysm. In fact, we incorporate the physical examination when patients are seen at our aortic center so as to recognize the physical features. We do routinely recommend screening of first-degree relatives even without significant family history on an individual basis and make appropriate referrals for other conditions that can be seen in these patients. Our article, however, is primarily intended to emphasize the importance of referring these patients for more-focused care at a specialized center, where we incorporate all of the suggestions that were made.

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