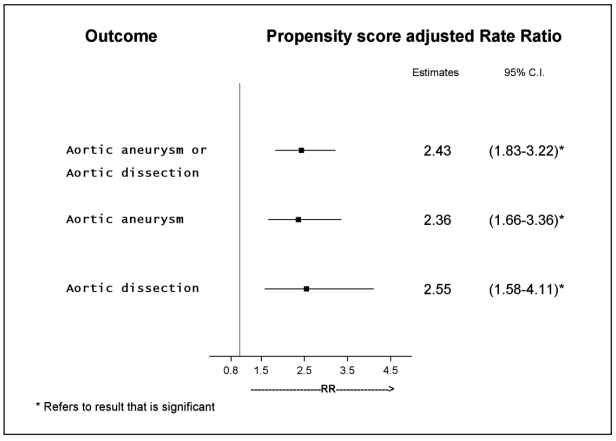
Risk of aortic dissection and aortic aneurysm in patients taking oral fluoroquinolone

NTU College of Medicine uncovers new global drug safety insights by using big data from the National Health Insurance Database

A research team at the National Taiwan College of Medicine has uncovered new insights into global drug safety. The team discovered a nearly 3-fold increase in the risk of aortic aneurysm and dissection in users of fluoroquinolone, a widely used antibiotic. Fluoroquinolones are widely used for the treatment of bacterial infections in the respiratory tract, intra-abdominal organs, eyes, skin and skin structure, and genitourinary tract. The global prescription of fluoroquinolone antibiotics increased from 4.75 billion pills to 7.81 billion pills between 2000 and 2010. In Taiwan, the number of people taking fluoroquinolones within 1 year increased nearly 1.8 times from 0.5 million to 0.9 million.

With the increasing number of people taking fluoroquinolone antibiotics, once-rare adverse drug events have now become a growing public health problem. Recently, fluoroquinolone has been associated with a series of collagen-related disorders, such as Achilles tendon rupture, tendinopathy in multiple muscle groups, and retinal detachment. As fluoroquinolones may induce the degradation of collagen and cause tendinopathy, this raises the concern of whether fluoroquinolones may cause or aggravate aortic aneurysm and dissection through a similar mechanism. Aortic dissection is defined as a separation of the layers within the aortic wall, while aortic aneurysm is defined as a localized or diffuse dilation of the aorta. Ruptured aortic aneurysms and dissections are associated with high morbidity and mortality rates.

Unfortunately, because aortic aneurysm and dissection are both relatively rare, with only hundreds of new cases per million people, testing the association between fluoroquinolone therapy and aortic aneurysm and dissection by traditional clinical trials is infeasible. Thus, the team decided to use the large Taiwanese National Health Insurance



Research database to test the association between fluoroquinolone therapy and aortic aneurysm and dissection. However, this is not a simple clinical question—it requires input from statisticians and specialists in both infectious diseases and cardiology. Prof. Shan-Chwen Chang and Dr. Chien-Chang Lee assembled a 7-person team to investigate cases of aortic aneurysm or dissection in a Taiwanese population of one million for over 12 years. A total of 1,477 individuals who experienced aortic aneurysm or dissection were identified and matched to 147,700 controls. After propensity score adjustment, the current use of fluoroquinolones was associated with an increased risk of aortic aneurysm or dissection (rate ratio [RR]=2.43, 95% CI, 1.83-3.22). The risk for this serious yet rare adverse

event should be considered in benefit-risk calculations for fluoroquinolone use, and further research must explore how these important antibiotics affect collagen.

Reference

Chien-Chang Lee, Meng-tse Gabriel Lee, Yueh-Sheng Chen, Shih-Hao Lee, Yih-Sharng Chen, Shyr-Chyr Chen, Shan-Chwen Chang. (2015). Risk of Aortic Dissection and Aortic Aneurysm in Patients Taking Oral Fluoroquinolone. *JAMA Internal Medicine*, 175(11):1839-1847. DOI: 10.1001/jamainternmed.2015.5389

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A simple, powerful, and widely applicable 3-microRNA scoring system for prognostication in de novo acute myeloid leukemia patients

Acute myeloid leukemia (AML) is a heterogeneous disease with various pathogenesis, treatment responses and clinical outcomes. Personalized treatment according to individual patient risk could both improve patient survival and reduce treatment side effects.

MicroRNAs are a class of small, non-coding RNAs that are derived from precursor RNAs processed by a protein complex containing Dicer and Drosha. They regulate gene expression post-transcriptionally through either mRNA degradation or translation inhibition. In AML, microRNAs are involved in hematopoietic cell differentiation, proliferation, and survival and can affect treatment responses and outcomes.

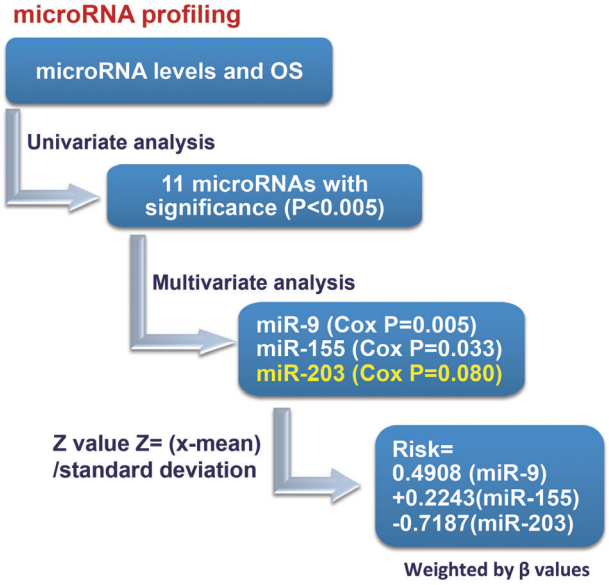

Figure 1. Analysis of miRNA array data, selection of microRNAs whose expressions are associated with survival, and construction of a microRNA scoring system

Using univariate Cox analysis , eleven microRNAs are selected from the microRNA array data whose expressions are significantly associated with overall survival (OS). By multivariate Cox model, expressions of three microRNA are identified as independent prognostic factors. High expression of miR-9 and miR-155 were independently associated with poor OS, while that of miR-203 had a trend of association with favorable OS. By focusing these 3 microRNAs, a risk scoring system is constructed:

Risk = 0.4908 [hsa-miR-9-5p] + 0.2243 [hsa-miR-155-5p] - 0.7187 [hsa-miR-203], where the weights of microRNAs are beta values from multivariate Cox analysis and the expression levels of microRNAs are z-transformed (ie. subtracting the mean and then divided by the standard deviation) across patients so that each microRNA has zero mean and unit standard deviation.