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Commentary

Meta-Analysis on the Potential Co-Relations of Cardiovascular Diseases and Impotence in Males

Miaoyong Ye[1], Fan Zhao[2*], Lan Ma[3*]

[1]Department of Urology, The First People's Hospital of Wenling, Wenling, Zhejiang Province, China; [2]Department of Urology, Affiliated Hospital of Nantong University, Nantong, Jiangsu Province, China; [3]Department of Cardiology, Affiliated Hospital of Nantong University, Nantong, Jiangsu Province, China

DESCRIPTION

The relationship between Cardio Vascular Disease (CVD) and Erectile Dysfunction (ED) is a topic of great interest among clinical cardiologists and urologists [1]. With the accidental discovery that cardiovascular drugs (sildenafil) used to treat angina can also improve ED, there has been a sudden increase in research on the relationship between ED, cardiovascular health, and related treatments. According to the latest clinical guidelines for CVD prevention, ED is considered as a tool for assessing CVD risk. This is because CVD and ED share common risk factors and pathophysiology such as endothelial dysfunction, inflammation, and low plasma testosterone levels [2]. In fact, the prevalence of ED is very high in patients with CVD. ED affects more than 70% of CVD patients, and its incidence increases with the duration and severity of CVD [3]. Therefore, ED is considered as a valuable tool for assessing CVD risk and can be an opportunity for preventing and treating CVD events. Simultaneously, treating CVD may also help to improve ED. While previous approaches to investigating the correlation between the two disorders involved prospective and retrospective cohort designs, and a meta-analysis based on traditional controlled studies offers a higher degree of clinical evidence [4].

The Mendelian Randomization (MR) study is a method for conducting human medical and biological research that capitalizes on randomization. The volume of MR-related publications has increased each year, with 1,699 papers published last year alone. As per the number of publications utilizing MR research techniques as of April 1st this year, this trend looks set to continue, possibly leading to a new record for related papers by the conclusion of the present year. The MR method can reveal the random correlation between exposure and outcome diseases, as opposed to traditional randomized controlled studies, which can reduce bias caused by confounding factors in epidemiological research, as well as the reverse causality between the two. Secondly, MR studies are typically conducted using large-scale genome-wide association studies, which can provide stronger statistical power than conventional clinical trials. MR studies use single nucleotide polymorphisms as genetic Instrumental Variables (IVs), which are randomly assigned according to Mendel's law during gamete formation and fertilization, so there is no association between IVs and potential confounding factors after expanding the sample size [5].

To conduct MR studies, three fundamental assumptions must be met: (1) genetic IVs are related to the exposure factor; (2) genetic IVs are not associated with confounding factors; and (3) genetic IVs only affect the outcome through the exposure factor. The most classic basic research designs include two-sample MR studies and bidirectional two-sample MR studies. In addition, multivariate MR studies extended from two-sample MR studies are also commonly used. Furthermore, there are more advanced MR study strategies available, such as linear, nonlinear, network, stratified, and factorial MR studies, which are currently hot research methods. It should be emphasized that while MR studies, also known as "natural randomized studies," have significant advantages over traditional clinical randomized studies, they cannot replace clinical trials due to limitations in the availability of suitable genetic instruments and the need for large sample sizes [6]. Instead, MR studies can offer supplementary insights to randomized trials that aim to address the same research question.

Traditional clinical research and meta-analysis have demonstrated a strong association between ED and CVD [7]. Utilized a basic bidirectional MR approach to investigate the causal correlation between CVD and ED. The outcomes suggested that ischemic stroke (odds ratios [OR] = 1.34, 95% confidence interval [CI]: 1.08–1.21, P=0.007), heart failure (OR=1.36, 95% CI 1.07–1.74, P=0.013), and coronary artery disease (OR = 1.15, 95% CI 1.09–1.18, P = 0.022) possess a genetic susceptibility for causing ED, while myocardial infarction (OR 1.07, 95% CI 0.99-1.17, P=0.099) is not genetically susceptible to ED. Moreover, reverse MR studies indicated that there is no causal genetic susceptibility of ED to any type of CVD. By providing an additional perspective to the conventional

Correspondence to: Lan Ma, Department of Cardiology, Affiliated Hospital of Nantong University, Nantong, Jiangsu Province, China, E-mail: malan@ntu.edu.cn; Fan Zhao, Department of Urology, Affiliated Hospital of Nantong University, Nantong, Jiangsu Province, China, E-mail: zhaofan@ntu.edu.cn

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observational studies, this research underscores the importance of giving greater clinical consideration to the emergence of ED in individuals afflicted with CVD [8].

CONCLUSION

MR research methods have the potential to become a pivotal force in the realm of andrology, not only by providing more precise estimations of causal effects and statistical power but also by revealing genetic variants related to male diseases that indicate potential drug targets and accelerate the development of drugs for men's health issues. Thus, MR can optimize the efficiency and design of clinical trials in men's medicine by providing more accurate evaluations of causal effects and aiding researchers in identifying potential drug targets.

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