

Mendelian Randomization Study in Cardiovascular Disease

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Epidemiological studies not only identified most major risk factors for cardiovascular disease, but also contributed to improvement in clinical practice by evaluating the effectiveness of disease screening, diagnosis and treatment modalities. More recently, epidemiological research has discovered a huge number of biomarkers which are associated with or predict the risk of cardiovascular disease. If a newly identified biomarker is causally related to the development of a disease, the biomarker can be a potential target for prevention and treatment of the disease. Thus, a causal biomarker has an important advantage compared to simply diagnostic biomarkers. However, it is extremely difficult to determine whether a biomarker is casually related to a disease or it simply reflects the risk of a disease. Randomized controlled trial is a best way to evaluate the causal relationship between a risk factor and disease. However, randomized controlled trial is usually not feasible for evaluating the relationship between a biomarker and disease, because we cannot determine or assign the biomarker levels for research purpose.

Mendelian randomization study is a new alternative to assess the causal relationship between a risk factor (or biomarker) and a disease. Mendelian randomization studies evaluate the relationship between genetically-determined biomarker levels and the risk of target disease. If the genetic determination of biomarker level is random and independent of non-genetic confounders, we can assume that the observed biomarker-disease relationship is similar to the relationship between randomly assigned biomarker levels and the disease risk. Increasing number of Mendelian randomization studies are evaluating biomarkers, including low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, fibrinogen and C-reactive protein, in their causal relationship with cardiovascular disease. However, Mendelian randomization studies also have several inherent limitations and need to be carefully designed and interpreted. Mendelian randomization studies cannot replace the randomized trials and other epidemiological studies, but they will improve our understanding of the roles of biomarkers in the development of cardiovascular disease.