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APOE genotypes predict cardiometabolic outcomes in individuals with metformin and metformin-sulfonylurea combination therapy

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Recent evidence suggests improved clinical outcomes with metformin in patients with type 2 diabetes (T2D) and heart failure. However, the role of anti-diabetic medications in response to APOE genotypes is less understood. The objectives of this investigations were: 1) to evaluate the distribution of APOE polymorphisms in a large diabetic cohort of the Asian Indian Diabetic Heart Study, 2) to evaluate the impact of APOE variants on quantitative risk factors of T2D and heart disease, and 3) to examine the role of APOE genotypes in response to anti-diabetic therapy. A total of 4,769 individuals (2,690 T2D cases and 2,079 controls) were included in this study. No significant difference in the distribution of APOε4 was observed among T2D cases and controls. However, APOε4 carriers had higher fasting glucose ($p=0.021$), higher diastolic blood pressure (DBP), higher LDL cholesterol (LDL-C) and lower HDL-C ($p=0.031$) compared to non-APOε4 carriers. Further stratification of data from diabetic patients by APOE genotypes and anti-diabetic treatments revealed a significant decrease in fasting glucose ($p<0.0001$), 2 h glucose ($p<0.0001$), systolic blood pressure (SBP) ($p=0.007$), DSP, and LDL-C ($p<0.0001$) among the APOε4 carriers compared to non-APOε4 carriers on metformin monotherapy. Similar improved clinical outcomes were observed in patients with metformin-sulfonylurea combination therapy ($n=618$). Our study suggests APOε4 to be a potential risk factor for cardiometabolic susceptibility in patients with T2D. Our findings also report significantly improved cardiometabolic outcomes among APOε4 carriers in response to metformin and metformin-sulfonylurea combination therapy. These findings warrant confirmation in a large independent datasets.

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