## The cardio-protective effects of anti-diabetic agents Hung-Yuan Li

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Diabetes results in increased risk of cardiovascular diseases. Intensive glycemic control can reduced the risk of cardiovascular events, as shown in EDIC study for subjects with type 1 diabetes and UKPDS 10-year follow up study for subjects with type 2 diabetes. However, it takes a long period of time to observe this beneficial effect.

Among the anti-diabetic agents, several drugs have been shown to have cardio-protective effects. Use of metformin is associated with a reduction in cardiovascular events and mortality in subjects with type 2 diabetes, as shown in UKPDS 34 study, two cohort studies, and a meta-analysis. In recent decades, several cardiovascular safety trials have demonstrated cardiovascular benefit on top of glycemic control. Sodium glucose co-transporters 2 (SGLT2) inhibitors, including empagliflozin, dapagliflozin, and canagliflozin, could reduce cardiovascular events or even cardiovascular mortality, as shown in EMPA-REG, CANVAS, and DECLARE studies. The cardio-protective effect develops early after the use of SGLT2 inhibitors and is mainly effective in subjects with a history of atherosclerotic cardiovascular diseases, ie. as secondary prevention. Besides, these drugs could also reduce the risk of hospitalization for heart failure. On the other hand, glucagon-like peptide-1 (GLP-1) receptor agonists are also cardio-protective. Liraglutide, dulaglutide, and semaglutide could reduce cardiovascular events, as shown in the LEADER, REWIND, and SUSTAIN-6 studies. In addition, thiozolidinedione is another class of anti-diabetic drug with cardio-protective effect. In PROACTIVE study, use of pioglitazone resulted in reduced cardiovascular events. However, this drug increased the risk of edema and heart failure. Therefore, in patients with NYHA functional class III and IV heart failure, this drug is contra-indicated. The details of these anti-diabetic agents with cardio-protective effects will be addressed in this talk.