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## Finding the Sweet Spot Between Cardiovascular and Diabetes Care



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Today in healthcare, more emphasis is being placed on treating the patient rather than a particular disease. In this sense, it is not unusual that the line between cardiology and diabetes care has become more blurred. As more cardiologists are finding themselves prescribing diabetes treatments, the need for interdisciplinary knowledge has become even more urgent.

At the American College of Cardiology's (ACC) 68th Annual Scientific Session & Expo 2019, the session 'Changing Paradigm in Cardiovascular Risk Reduction in Diabetes' explored this further. Ran by James L. Januzzi Jr., M.D., F.A.C.C. and Laurence S. Sperling, M.D., F.A.C.C., the session looked at bridging the gap in knowledge to help cardiologists venturing into the field of diabetes care.

The main cause of mortality and morbidity amongst individuals with Type 2 Diabetes (T2D) is cardiovascular disease (CVD). Metformin and changes in one's lifestyle are currently the main treatments for T2D. Microvascular outcomes can be improved by intensive glucose control, but no benefits have been seen which reduce the risk of cardiovascular events.

It is only through the recent popularity of sodium-glucose co-transporter-2 inhibitors (SGLT-2i) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs), that diabetes drugs have been shown to reduce the risk of CVD independent of reducing glucose levels.

### SGLT-2 Inhibitors

SGLT-2i works in the nephron by inhibiting sodium-glucose transporters, ultimately slowing urinary glucose reabsorption, leading to reduced serum glucose levels and glucosuria (depending on blood glucose levels).

This inhibitor improves cardiovascular outcomes through its natriuretic and diuretic properties, as well as its ability to reduce blood pressure and stimulate weight loss. It is also thought to have positive effects on myocardial metabolism, the sympathetic nervous system and also cardiac remodelling.

Canagliflozin, empagliflozin and dapagliflozin are part of the SGLT-2i drug class, all of which are administered orally. Even though benefits for SGLT-2i drugs have been demonstrated whilst in combination with other diabetes treatments (such as metformin), they can also be used individually for treatment.

SGLT-2 inhibitors have been shown to reduce hospitalisations from heart failure and also kidney disease progression. Whilst effects, even though less significant, have also been recorded for CVD, strokes, non-fatal myocardial infarction (MI), major adverse cardiovascular events (MACE) and generally any cause of death.

However, SGLT-2i drugs have also been found to increase the risk of genital mycotic infections. Other side effects, for example with canagliflozin, can include increased risk of amputation for patients with peripheral arterial disease, however, this does not seem to affect the whole class of SGLT-2 inhibitors. Also, caution should be taken for patients with renal impairment or acute kidney injury, as SGLT-2i can cause volume depletion/hypotension in patients on diuretics.

### GLP-1 RAs

When patients with T2D are given glucose orally, the physiologic response is reduced. This means the GLP-1 effect is reduced, increasing insulin resistance by decreasing GLP-1 expression and ultimately its effects downstream. By using a GLP-1 agonist, which interacts with the receptors, the downstream response is stimulated. This results in increased satiety and insulin secretion/sensitivity and also weight loss and reduced HbA1C.

Exenatide was the first GLP-1 RA to be approved in the USA, which happened over 10 years ago. Since then, there are now many other GLP-1 RAs, with different durations of action but all to be administered subcutaneously.

Liraglutide and semaglutide are the only GLP-RAs known to improve cardiovascular outcomes, except in the case of heart failure. Benefits of this treatment include weight loss and also renal benefits (most likely by increasing natriuresis and diuresis).

Although, GLP-RAs can induce vomiting and nausea because of its ability to slow gastric emptying. Caution should, therefore, be taken with

diabetic patients with gastroparesis. There have also been questions regarding GLP-RAs influence on pancreatitis and pancreatic cancer, however, findings from the FDA have not confirmed this. It is also possible that treatment with GLP-RAs could increase the risk of retinopathy, however, the notes on the FDA database are not consistent with this.

## Mind the [Knowledge] Gap

In light of these new findings, the following challenges remain:

1. Frequency of new studies means a constant wealth of new information
2. Different recommendations from professional societies
3. Keeping the patient as the main focus – due to the copious side effects

The ACC Expert Consensus Document has been guiding the way for cardiologist professionals tackling interdisciplinary challenges and has recommended that T2D patients that have, or have a risk of, ASCVD should be screened; cardiovascular risk factors should be treated aggressively; data for the latest antihyperglycaemic agents should be incorporated into routine practice. This has already started to be embraced by the cardiology field as the '2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease' recommended the use of SGLT-2i or GLP-1 RAs for patients with T2D as a second-line of therapy.

The take-home message of the session at ACC 19 demonstrated that for patient centricity, cardiologists need to engage with different specialists. However future questions remain on the specifics of treatments with this newly popular class of drugs.

Source: [American College of Cardiology](#)

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Published on : Thu, 1 Aug 2019