

Cardiovascular Outcomes Trials of Glucose-Lowering Drugs or Strategies in Type 2 Diabetes



Hertzel C. Gerstein, MD, MSc*, Reema Shah, MD

KEYWORDS

- Type 2 diabetes • Cardiovascular complications • Glucose-lowering drugs • Cardioprotective agents

KEY POINTS

- Diabetes affects approximately 1 in 10 adults worldwide, most with type 2 diabetes, which is characterized by an inability to make sufficient insulin to prevent glucose levels from increasing.
- Type 2 diabetes arises from various factors including genetic predisposition, aging, obesity, diet, family history, ethnicity, culture, economics, and lifestyle.
- As recently as 20 years ago there were essentially no randomized controlled trials of potentially cardiovascular protective therapies in people with type 2 diabetes.
- More than 120,000 people to date have been recruited into the trials studying diabetes and cardiovascular disease.
- The discovery of at least 4 agents with cardioprotective properties, represents a remarkable addition to the evidence for cardiovascular protection in people with type 2 diabetes.

Diabetes is a metabolic disease characterized by persistently elevated fasting and/or postprandial glucose levels that are at or above carefully defined diagnostic thresholds. In addition to suffering from the symptoms of hyperglycemia, including fatigue, changes in weight, nocturia, polyuria, polyphagia, and polydipsia, people with diabetes are at high risk of developing a wide variety of serious health outcomes. These

Disclosure: Dr H.C. Gerstein is supported by the McMaster-Sanofi Population Health Institute Chair in Diabetes Research and Care. Dr Gerstein has received research grant support from Sanofi, Lilly, AstraZeneca, and Merck, honoraria for speaking from Sanofi, Novo Nordisk, and AstraZeneca, and consulting fees from Sanofi, Lilly, AstraZeneca, Merck, Novo Nordisk, Abbot, Amgen, Janssen, and Boehringer Ingelheim. Dr R. Shah has nothing to disclose.

Department of Medicine, Population Health Research Institute, McMaster University, Hamilton Health Sciences, HSC 3V38, 1280 Main Street West, Hamilton, Ontario L8S 4K1, Canada

* Corresponding author.

E-mail address: gerstein@mcmaster.ca

Endocrinol Metab Clin N Am 47 (2018) 97–116

<https://doi.org/10.1016/j.ecl.2017.10.003>

0889-8529/18/© 2017 Elsevier Inc. All rights reserved.

endo.theclinics.com

include retinal disease and vision loss, renal failure, nerve damage and neuropathic pain, cardiovascular diseases (ischemic heart disease, heart failure, and cardiovascular death), cerebrovascular disease, peripheral vascular disease, cancers, cirrhosis, cognitive decline, erectile dysfunction, and premature mortality. Some of these health problems, such as retinopathy, are highly specific to diabetes, whereas others occur earlier in people with diabetes than in people without diabetes. The fact that the retinal changes associated with diabetic retinopathy only occur with hyperglycemia was used as the basis for establishing the diagnostic thresholds for diabetes (ie, fasting and 2 hour post oral glucose load plasma glucose levels of 7 and 11.1 mmol/L respectively or a hemoglobin A1c [HbA1c] of $\geq 6.5\%$).¹ These diagnostic thresholds, therefore, represent glucose levels above which the risk of retinopathy increases exponentially, and below which the relationship is fairly flat. Notably, they are much higher than the fasting, 2 hour postglucose load, and HbA1c levels of 5.59 mmol/L, 7.79 mmol/L and 5.6%, respectively, that characterize normal glucose physiology.¹

Diabetes affects approximately 1 in 10 adults worldwide. The vast majority (>90%) of affected individuals have type 2 diabetes, which is characterized by an inability to make sufficient insulin to prevent glucose levels from rising. Type 2 diabetes arises from various combinations of factors including aging, obesity, diet, family history, ethnicity, culture, economics, and lifestyle, factors that have contributed to its rapid increase in prevalence over the last 20 years.

CARDIOVASCULAR DISEASES PROMOTED BY DIABETES

Diabetes is an independent risk factor for cardiovascular diseases. Compared with people without diabetes, the incidence of myocardial infarctions, strokes, coronary death, peripheral vascular disease, and heart failure are all increased by approximately 100%.^{2,3} Not surprisingly, diabetes also doubles the risk of cardiovascular death⁴ and reduces life expectancy. In a recent metaanalysis of data from 689,300 participants from 91 cohorts followed for a median of 12.8 years, during which 128,843 deaths occurred, the incidence of death in people with diabetes was similar to that of people without prior diabetes who had a prior myocardial infarction or a prior stroke (about double the incidence of death in people with none of these risk factors). In the same study, people with both prior diabetes and either a prior myocardial infarction or stroke had about a 4-fold greater incidence of death than people with none of these risk factors.⁵ Moreover, in an international registry of people aged 45 years or older with prior cardiovascular disease or related risk factors, the risk for heart failure hospitalization was 33% greater in people with diabetes versus those without diabetes, and 470% higher in people with both prior heart failure and diabetes versus prior heart failure alone.⁶ These relationships reduce life expectancy by 5.7 years for a 60-year-old man and 6.7 years for a 60-year-old woman with diabetes alone, and 12 and 13 years for a 60-year-old man or woman, respectively, in the setting of diabetes plus either a prior myocardial infarction or stroke, with 59% of the excess deaths owing to cardiovascular diseases.⁵ Finally, despite evidence of decreasing incidence rates of myocardial infarction and stroke over the last 20 years in the United States, a large gap between people with diabetes and the general population persists for these outcomes.⁷

LINK BETWEEN DYSGLYCEMIA AND CARDIOVASCULAR DISEASE

Compared with retinal disease, the link between dysglycemia and incident cardiovascular (CV) disease (ischemic heart disease, cerebrovascular disease, cardiovascular death, and heart failure) starts well below the diabetes threshold (ie, at

Download English Version:

<https://daneshyari.com/en/article/8722640>

Download Persian Version:

<https://daneshyari.com/article/8722640>

[Daneshyari.com](https://daneshyari.com)