## Diabetes and premature death



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After overcoming, in the last century, the obstacle of a short life expectancy of about third years, humanity was faced with an amplitude of challenges associated to the several genetic vulnerabilities linked to lifestyle changes and aging. At the center of these dis-adjustments, is the type II diabetes mellitus (DM II). Despite the persistence of the unbalance in the calorie intake and lack of physical activity, according to estimates by the International Diabetes Foundation (IDF), the expansion curve for the incidence of DM2 shows a slight deceleration, at a ratio of 0.5%. However, the condition has already affected 7% of the world population of adults and is the cause of around 10% of all deaths<sup>1-8</sup>. Thus, a diagnosis of DM2 means a decrease of up to two decades in life expectancy, according to the type and prematurity of the DM2 found9. Besides, morbidities such as amaurosis, dementia, neuropathies, and chronic kidney disease make this condition a topic of absolute urgency and relevancy.

Since it started being recorded, cardiovascular disease (CV) has been responsible for 80% of deaths of individuals with DM2<sup>10</sup>. Thus, several observational and interventional studies sought to identify the primary mediators for CV risk in individuals with

DM2 in order to improve the risk estimate and intervene slowing down the high mortality. Blood glucose control was the most significant intervention for reducing mortality. However, the intensive control of blood glucose levels to values close to those of healthy individuals did not present any benefits<sup>11</sup> and, in one of the studies, was even associated with an increase in mortality (+2.9 deaths for every 1,000 patients/ year<sup>12</sup>. Likewise, the control of the arterial pressure (-3.2 deaths for every 1,000 patients/year per 10 mm Hg)13 and the LDL cholesterol (-2.1 deaths for every 1,000 patients/year per 39 mg/dL)14 were critical elements in this strategy for risk control. Similarly to the blood glucose control, the intensification of these interventions did not present any benefits regarding survival<sup>15,16</sup>. In addition, anti-diabetes therapies were associated with an increase in the incidence of cardiovascular diseases<sup>17</sup>.

The high residual mortality and the uncertainty of the CV effects of the therapies led to a demand for new treatments systematically tested by cardiovascular safety studies. Despite having been outlined to asses safety, two classes of anti-diabetic medication have shown a reduction in mortality regardless of the effect on glucose: sodium-glucose cotransport-

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er-2 (SGLT-2i) inhibitors (-9 deaths for every 1,000 patients/year)<sup>18</sup> and Glucagon-like peptide-1 (GLP-1) agonists (-4 deaths for every 1,000 patients/year)<sup>19</sup>. Thus, over the last five years, not only the reduction of the possibility of prolonging the life of DM2 patients was demonstrated, but it was done as an addi-

tional effect to the control of traditional risk factors.

In this edition, we bring a selection of original studies and reviews dedicated to DM2 grouped with the purpose of emphasizing the enormous mortality of this disease, but also to the substantial advancements achieved for its control.

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