Body weight and mortality in type 2 diabetes: Weighing up the evidence

IMC et mortalité dans le diabète de type 2 : quelles sont les preuves ?

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It is well established that increased body mass is the major risk factor for the development of type 2 diabetes [1]. However, despite the treatment guidelines recommending weight management with the aim of weight loss in type 2 diabetes [2], the benefits of weight loss for cardiovascular disease and mortality once type 2 diabetes is established are unknown.

The relationship between body mass index (BMI) at diagnosis of type 2 diabetes (T2DM) and subsequent mortality has proven to be more complicated than first thought. Recent evidence [3,4] has shown that while the risk of mortality increases at BMI levels above 30 kg/m² at or near the time of T2DM diagnosis, there is also a higher risk of mortality for those diagnosed at a lower BMI. A BMI of around 30 kg/m² at the time of diagnosis is associated with the lowest risk of subsequent mortality in diabetes patients. The reasons for this U-shaped phenomenon are unknown but it may be that BMI at diagnosis (at any given age) reflects the underlying pathophysiology, with those diagnosed at lower BMI having either proportionately greater beta cell failure, or else a greater diabetes predisposition via more rapid ectopic fat storage for a given BMI factors potentially leading to worse outcomes. There is also the possibility of reverse causality whereby the higher risk of mortality in those with lower BMI may be related more to their greater smoking intensity and underlying co-morbid conditions, than their diabetes.

In this edition of Diabetes and Metabolism, Bodegard et al. [5] have been able to explore this association further by looking at weight change within the first year of diagnosis of T2DM and subsequent risk of mortality in 8486 patients from primary care in Sweden. They have shown that increasing BMI by one unit or more within the first year after diagnosis was associated with a 63% higher cardiovascular mortality and a 33% higher all cause mortality compared to maintaining weight stability. There is a number of possible explanations for this other than necessarily a direct effect of obesity itself; these include poor compliance with lifestyle advice or those with poor glycaemic control requiring prescription of higher doses of weight gaining medications such as insulin. Less expected was that a reduction of BMI by one unit in the first year of diagnosis of T2DM was not associated with lower cardiovascular or all cause mortality. However, it should be remembered that this was an observational study and the intentional versus unintentional nature of weight loss cannot be distinguished. Weight loss may stem from very poor glycaemic control or underlying illness, and therefore any beneficial effects of weight loss in those who intentionally lost weight in response to lifestyle advice given on diagnosis of type 2 diabetes are not distinguishable when all weight losers are analysed together.

Given the number of factors that can affect the weight of a patient with type 2 diabetes, these studies do little to either support or refute guidance that weight loss should be recommended in newly diagnosed type 2 diabetes including the important question of whether in some patient groups there would be a detrimental effect of intentional weight loss. What is required are studies of intentional weight loss in type 2 diabetes, ideally randomised to allow testing of this in a variety of patient groups of different ages and duration of diabetes. Studies performed to date have given conflicting results; namely the Swedish Obese subjects (SOS) Study of bariatric surgery and the LookAhead study of intensive lifestyle and dietary therapy, however, there are many fundamental differences between these two studies. The SOS study compared around 2000 patients who had a variety of bariatric surgery procedures to around 2000 who had medical obesity treatment only; not all patients had T2DM, and the cohorts mean age was 46.7 years and mean BMI 42.1 kg/m². The study was not randomised and treatment allocation was on patient preference and there was no set protocol for diabetes care. The study recruited between 1987 and 2001, showed a mean weight loss of 18% of total body weight in the surgery group at 20 years and has published mortality results over a mean of 10.9 years and cardiovascular events over 14.7 years. The data showed a 29% lower risk of mortality in the bariatric surgery group [6], a 33% lower risk for cardiovascular events and a 53% lower risk of cardiovascular deaths [7]. When only those patients with T2DM at baseline were compared, there was a 44% lower risk of myocardial infarction in the bariatric surgery group compared to controls [8].

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The LookAhead study recruited 5145 patients aged between 45 and 76 (mean age 58.9 years) between 2001 and 2004 and randomised them to either an intensive lifestyle intervention (calorie deficit diet plus meal replacements, exercise, behavioural intervention) or a diabetes support and education (DSE) programme as per gold standard care. All the patients’ health care providers were informed of the targets for glycaemia and cardiovascular risk factors and encouraged to actively pursue these. The mean BMI was lower than in SOS at 35.9 kg/m². The intensive lifestyle group achieved a 5.27% weight loss difference at 4 years compared to the DSE controls but given the intensive treatment to glycaemic targets in both groups, this only resulted in a 0.27% (3 mmol/mol) reduction in HbA1c [9]. The trial was stopped prematurely in 2012 for futility with little prospect of achieving the primary outcome of a reduction of cardiovascular events in the intensive lifestyle group despite follow-up of up to 11 years [10].

Care should be taken to not simply interpret these two disparate studies with very different study populations by saying that bariatric surgery reduces mortality in T2DM and intensive lifestyle interventions have little place. These two studies were performed in very different eras of diabetes management; the advent of glycaemic treatment targets and aggressive cardiovascular disease management since the time that the SOS study recruited has resulted in a large reduction in the cardiovascular (and total) mortality associated with T2DM [11]. It may be that the effect of weight loss from intensive lifestyle interventions cannot better the effect of contemporary statins and blood pressure management and better glycaemic control in reducing cardiovascular events; such modalities were not routinely in use in the 1980s when the SOS study recruited. However, what we do see from the LookAhead results is a large reduction in the medications needed to achieve glycaemic and cardiovascular risk factor targets [9], which will have benefits both in terms of costs but also patient quality of life. Bariatric surgery will continue to be an adjunct therapy for the few patients for whom such a procedure is acceptable and affordable but it is not something that could ever be scaled to the large and expanding type 2 diabetes population. Intensive lifestyle interventions should not be dismissed based on the headline cardiovascular end-point results in LookAhead but instead should focus on the potential wider benefits for patients and health care systems. Ways to provide intensive lifestyle interventions in an effective and cost-efficient manner should be explored for the ever-increasing numbers of patients who are likely to benefit.

Disclosure of interests

The authors declare that they have no conflicts of interest concerning this article.

References


J. Logue*

N. Sattar

Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, United Kingdom

*Corresponding author.

E-mail address: Jennifer.logue@glasgow.ac.uk (J. Logue)

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