The truth about sugar

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In September 2011, the United Nations announced that, for the first time in human history, chronic, noncommunicable diseases, such as heart disease, cancer, and diabetes, pose a greater health burden worldwide than do infectious diseases, contributing to 35 million deaths annually. Over the past 50 years, consumption of sugar has tripled worldwide, contributing to the rise of metabolic syndrome: diabetes, hypertension, lipid problems, cardiovascular disease, and nonalcoholic fatty liver disease. The truth about sugar is that it is now considered to be an addictive and toxic drug, to the same degree as tobacco and alcohol.¹

Although patients with the diseases mentioned above may develop diabetes mellitus (DM) type 2, owing to increasing insulin resistance, cystic fibrosis (CF) patients are at risk of developing DM with increasing age, as a result of insulin deficiency. In contrast to DM type 1 patients, insulin deficiency in CF is not caused by an autoimmune process, but rather is the result of destruction of pancreatic islets, during the natural course of the disease, which leads to fibrosis and beta-cell dysfunction. Early stages of insulin deficiency may be contributing to catabolism and deteriorating lung function in these patients.

According to the latest report on the registry of the International Society for Heart and Lung Transplantation, nearly 7000 CF patients (16%) underwent transplantation for respiratory failure resulting from chronic respiratory infections and bronchiectasis.² Cystic fibrosis is the third most common primary indication for lung transplantation (LTx), following chronic obstructive pulmonary disease (33%) and interstitial lung disease (24%). Five-year survival is highest in patients who have CF (60%), compared with those who have chronic obstructive pulmonary disease (55%) or interstitial lung disease (50%).²

The impact of DM as a risk factor for survival in LTx candidates and recipients with CF remains largely unclear. This article by Hayes and colleagues³ represents the largest reported series so far investigating the influence of DM in CF on survival before and after LTx separately. The authors

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Central Message

Cystic fibrosis patients with diabetes who are on the list for lung transplantation need better management strategies to reduce their mortality risk.

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queried the United Network for Organ Sharing database for all CF patients who were listed for the first time or underwent LTx between 2005, the year of implementation of the lung allocation score, and 2013.

Outcome was analyzed in a total of 2781 CF patients with known data on DM status, while they were on the LTx waiting list. The presence of DM in LTx candidates was associated with a significant reduction in survival ($P < .01$). The risk for death associated with DM was about 40% higher compared with the risk for non-DM candidates, as shown in an adjusted multivariate Cox model (hazard ratio [HR] [95% confidence interval {CI}]: 1.410 [1.206-1.648]; $P < .001$) and confirmed with propensity-score matching (HR [95% CI]: 1.395 [1.097-1.774]; $P < .01$). Candidates with DM had a significantly lower forced expiratory volume (FEV₁) and forced vital capacity (FVC), reflecting poorer pulmonary functional status. Higher body mass index, higher FEV₁, higher FVC, and higher 6-minute walk distance were covariates associated with reduced risk of death in univariate analysis, with body mass index the only remaining significant covariate in a multivariate model. Improving nutritional, and thus respiratory status in patients with low body mass index, by using an enteral tube feeding while waiting for LTx, should therefore be considered.⁴

In comparison, the outcome in 3638 lung recipients with CF was not affected by the presence of DM ($P = .95$), with no significantly increased risk for death (HR [95% CI]: 1.083 [0.961-1.219]; $P = .191$; and HR [95% CI]: 1.190 [0.999-1.417]; $P = .051$), respectively.³

This report represents the largest comparative clinical LTx series on CF candidates and recipients, with or without DM, ever reported. It clearly confirms that the presence of DM is not a contraindication for LTx. Moreover, the study revealed that CF candidates with DM have a higher risk for dying while they await a suitable lung offer. Better treatment strategies are therefore needed to bridge these patients safely to transplantation. This finding also calls into question the current system of lung allocation, suggesting that higher priority for receipt of a lung offer should be given to CF candidates with DM. However, in the current lung allocation score, DM is already included as a parameter to prioritize these candidates for lung offers by assigning them a higher score.⁵

Obviously, the analysis suffers from its retrospective design, with missing data points and potential entry errors. Data were collected from a large database, possibly including unknown confounding variables in the analysis. In addition, data on the severity of DM at the time of listing were not available, thereby limiting the study from describing the progression of DM. Nevertheless, the authors are to be acknowledged for their analysis of

the largest series so far on outcomes in CF patients before and after LTx.

What we should remember from this article is that better management strategies should be considered for CF patients on the waiting list for LTx, so they can be in better condition to receive the transplant. Clinical care concentrated in accredited CF centers may lead to a dramatic increase in their life expectancy.⁶ The truth about sugar in CF is that glucose levels should be monitored continuously with real-life glycemic control to improve survival in patients with CF-related diabetes.⁷

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