



talization for heart failure.”

The intent of my article was to provide a critical review of the literature in order to address the question, “Do TZDs cause heart failure?” This is an important scientific question, since the development of heart failure in patients with diabetes has been associated with poorer long-term survival.<sup>2</sup> It was my intention to point out that people who take TZDs clearly have a risk of developing fluid retention, but the risk of developing heart failure is less clear.

In fact, all glucose-lowering drugs have been implicated to some degree with regard to their heart failure risks, with insulin being the most prominent.<sup>3</sup> However, the clinical diagnosis of heart failure is often subjective and nonadjudicated, and therefore definitive clinical evidence is limited.

Nevertheless, placebo-controlled echocardiographic studies have not directly linked fluid retention caused by TZDs with worsening cardiac performance.<sup>4</sup> Careful analysis from the Kaiser Permanente Northern California Diabetes Registry of 23,440 patients with type 2 diabetes also did not find evidence that short-term TZD use was associated with an elevated risk of hospitalization from heart failure compared with other standard, first-line diabetes therapies.<sup>5</sup> It is also reassuring that rates of death from heart failure in the PROactive study were similar between the TZD and the placebo groups (25/2605 vs 22/2633,  $P = .634$ ), despite the aforementioned increase in reported rates of edema and hospitalizations for heart failure.<sup>6</sup>

In a recent analysis of 16,417 elderly diabetic patients discharged after hospitalization for heart failure, the use of insulin sensitizers (TZDs and metformin, both contraindicated in heart failure) was associated with a lower death rate compared with drugs other than insulin sensitizers.<sup>7</sup> The discrepancy between the development of heart failure reported in patients with diabetes treated with TZDs and the potential benefit of fewer deaths is interesting and will require further insights from upcoming large clinical trials.

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#### REFERENCES

1. Tang WHW. Do thiazolidinediones cause heart failure? A critical review. *Clev Clin J Med* 2006; 73:390–397.
2. Bertoni AG, Hundley WG, Massing MW, Bonds DE, Burke GL, Goff DC Jr. Heart failure prevalence, incidence, and mortality in the elderly with diabetes. *Diabetes Care* 2004; 27:699–703.
3. Nichols GA, Koro CE, Guillion CM, Ephross SA, Brown JB. The incidence of congestive heart failure associated with antidiabetic therapies. *Diabetes Metab Res Rev* 2005; 21:51–57.
4. St John Sutton M, Rendell M, Dandona P, et al. A comparison of the effects of rosiglitazone and glyburide on cardiovascular function and glycemic control in patients with type 2 diabetes. *Diabetes Care* 2002; 25:2058–2064.
5. Karter AJ, Ahmed AT, Liu J, Moffet HH, Parker MM. Pioglitazone initiation and subsequent hospitalization for congestive heart failure. *Diabet Med* 2005; 22:986–993.
6. Dormandy JA, Charbonnel B, Eckland DJ, et al. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial in macroVascular Events): a randomised controlled trial. *Lancet* 2005; 366:1279–1289.
7. Masoudi FA, Inzucchi SE, Wang Y, Havranek EP, Foody JM, Krumholz HM. Thiazolidinediones, metformin, and outcomes in older patients with diabetes and heart failure: an observational study. *Circulation* 2005; 111:583–590.

#### CORRECTION

## Thiazolidinediones and heart failure

(APRIL 2006)

The article “Do thiazolidinediones cause heart failure? A critical review?” by Dr. Wilson Tang in the April 2006 issue (*Cleve Clin J Med* 2006; 73:390–397) contained several errors regarding the interpretation of the PROactive study (*Lancet* 2005; 366:1279–1289). The

CCJM article incorrectly stated that the differences between the pioglitazone and placebo groups were not statistically significant for any report of heart failure, for heart failure needing hospital admission, or for the occurrence of edema without heart failure. In fact, the pioglitazone group showed significantly higher rates of any report of heart failure and of heart failure needing hospital admission. The errors occurred as the article was being revised in the galley stage.