Comment on: Robertson (2010) Islet Transplantation a Decade Later and Strategies for Filling a Half-Full Glass. Diabetes;59:1285–1291

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In his *Perspectives in Diabetes* (1), Robertson asked whether islet transplantation achievements should be considered a partial failure or a partial success. This question, which would sound naïve for bone marrow, skin, or organ transplantation, is actually more than germane for islet transplantation. So far, no study has formally compared the outcomes of patients with type 1 diabetes receiving islet transplantation or continued medical therapy; hence, whether this expansive procedure is actually more effective than insulin treatment in preventing diabetic complications, improving health quality, or reducing morbidity or mortality is still a matter of debate (2). In other words, whether achieving transient insulin independence with islet transplantation justifies chronic exposure to immunosuppressive drugs and their related side-effects still has to be established. Therefore, Robertson is right in stating that the answer to whether islet transplantation is a half-full or half-empty glass "is in the eye of the beholder" (1).

This, however, places islet transplantation outside the common paths of evidence-based medicine, where new treatments are first tested for safety (phase I studies) and thereafter are compared in terms of efficacy with the best available ones (phase II and III trials). If properly designed, such studies can provide enough evidence to assess whether newer treatments are more effective or safer than therapies previously used. Yet, after more than two decades since the first islet transplantations in humans, this information has still not been provided.

Pancreas transplantation provides much higher rates of insulin independence compared with islet transplantation. Nonetheless, comparative analyses versus patients on the waiting list showed that this procedure improved patients' survival only when combined with kidney transplantation, and that pancreas transplant alone may actually increase mortality over continued insulin therapy (3). Without control subjects, this crucial information would have been missed, and successful insulin independence might have possibly led to a worrisome underestimation of mortality risk related to surgery complications and toxicity of immunosuppressive drugs.

The American Diabetes Association (ADA) recommends performing islet transplantation only in the context of controlled research studies (4). This advice has been largely disregarded so far, and the search for strategies to improve outcomes of the procedure has distracted attention from designing a properly controlled trial comparing islet transplantation with medical therapy in type 1 diabetes. Until the results of this study become available, islet transplantation should be considered just an experimental procedure (5). As a result of the poor methodological approach toward islet transplantation, 40 years after the seminal experience of islet transplantation in diabetic rats by Paul Lacy (6), we still do not know whether islet transplant achievements should be interpreted as half failure or as half success.

Physicians, patients, and health care providers deserve to know the relative cost/efficacy profile of islet transplantation over insulin therapy in type 1 diabetes. Only when this information is be provided will it be reasonable to try to identify strategies to fill the glass and whether the next studies should be performed in the lab or in the clinical setting.

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