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# Concerns and hopes of patients with type 1 diabetes prior to islet cell transplantation: A content analysis☆,☆☆

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ABSTRACT

*Aims:* Islet cell transplantation can functionally cure type 1 diabetes complicated by hypoglycemia unawareness (HU), but requires immunosuppression. This study identified the lived experiences and risk/benefit considerations of patients pre-transplant.
*Methods:* Content analysis identified themes from four open-ended questions pre-transplant in an islet transplant clinical trial. The sample included 23 (19 female) patients, with a mean age = 48.3 and diabetes duration = 29.3 years.
*Results:* Lack of control due to diabetes and HU was the overarching theme pre-transplant. Four sub-themes were also identified: fear of hypoglycemia, diabetes-related complications, hopes/expectations after transplant, and transplant outcomes. Patients expressed fear of HU and long-term complications pre-transplant, and hoped islet transplant would improve diabetes management. Patients further emphasized anxiety over burdening others, and hopes of advancing research. In addition, other patients emphasized frustrations regarding the impact of HU on themselves, such as the inability to perform activities of daily living. Many patients were primarily worried about immunosuppressive side effects rather than islet transplant success.
*Conclusions:* Patients viewed islet transplantation as a means to gain autonomy and control over their lives. They desired reduced anxiety associated with HU, despite concerns over immunosuppressive side-effects. These findings need confirmation, but may help to further improve patient education and patient-provider communication.



## 1. Introduction

Hypoglycemia (blood glucose ≤70 mg/dL) unawareness (HU) is a debilitating condition that affects up to 25%[1] of 1.25 million Americans with type 1 diabetes.[2] The impaired counterregulatory hormonal and autonomic responses in type 1 diabetes cause diminished physiological symptoms, including tremors, palpitations, and HU.[1,3] Risk factors include prior episodes of hypoglycemia,[4] longer duration of type 1 diabetes,[5,6] and increasing age.[1,6] Prolonged and/or severe hypoglycemic episodes due to HU can cause debilitating neuroglycopenic sequelae, including mood disturbances, cognitive impairment, seizures, and coma, increasing risk for injury and death.[4,6,7] During hypoglycemic episodes, individuals with HU often require assistance from family members or emergency services.[8–11] This dependency impacts individuals' sense of autonomy and can be a source of conflict in both social relationships and diabetes management.[8,12] Studies show that HU negatively impacts psychosocial functioning, leading to depression and anxiety,[13,14] and stress within relationships.[8,15] HU can also severely compromise quality of life (QoL).[12,13]

Islet cell transplantation is currently an experimental, minimally invasive procedure for patients with HU that provides a potential functional cure for type 1 diabetes.[16] A five-year follow-up study of a Phase 1/2 islet cell transplantation clinical trial at the University of Illinois at Chicago (UIC) showed that patients experienced long-term islet graft function, insulin independence, and improved glycemic stability (i.e., lower HbA1c) with fewer episodes of severe hypoglycemia compared to pre-transplant.[17] Islet cell transplantation has also been shown to essentially eliminate HU with the restoration of near normal glycemic control.[18,19] While accumulating evidence supports islet cell transplantation as a clinical treatment for HU in type 1 diabetes,[18,20,21] few qualitative studies have investigated patients' psychosocial

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experiences prior to, or their rationale for choosing to receive islet transplantation.[22,23]

To the best of our knowledge, Speight et al.'s cross-sectional study in the United Kingdom and Canada is the most current research that analyzes the experiences of islet transplant patients. The study used semi-structured interviews to identify patients' transplantation expectations, and experiences while on the waitlist and after transplantation. The sample size for the pre-transplant interview was limited to eight, however, researchers found that participants had realistic expectations for physiological and psychological improvements.[23]

Other QoL studies on islet transplantation have utilized standard psychosocial measurements, for example the Health-Related or Diabetes Specific Quality of Life (DQoL), to assess worry, health perception, and social functioning pre- and post-transplant.[22,24] Although findings show an improvement in the QoL pre- to post-transplant,[22,24–27] standardized psychometric questionnaires do not measure specific factors that may contribute to patients' psychosocial risk-benefit analysis prior to islet transplantation, such as anxiety due to potential side effects. As islet transplantation may soon gain FDA approval, and is not without risk due to long-term immunosuppression, it is vital to understand patients' deeper, more complex personal experiences and perceptions regarding this experimental treatment. Currently, there is a gap in knowledge regarding expectations and concerns for patients considering islet cell transplantation. To begin to address this, we used content analysis to identify the concerns, fears, and hopes of patients with type 1 diabetes and HU prior to islet transplantation.

Additionally, we examined patients' reasons for choosing to undergo islet transplantation. To our knowledge, this is one of the first qualitative studies in the United States addressing this gap. The resulting narrative themes may help illuminate some of the specific experiences of individuals considering islet transplantation and potentially facilitate and improve patient-provider communication and decisional processing prior to transplant.

## 2. Subjects, materials and methods

### 2.1. Participants

Potential participants for the current study were patients enrolled in UIC's Phase 1/2 (n = 10) and Phase 3 (n = 20) islet transplantation clinical trials (NCT00679042) from 2005 to 2016. As of the end of 2017, 16 patients were still participating with functioning islet grafts. Patients eligible for the clinical trials included those 18–70 years old who had type 1 diabetes for more than five years. They had to have severe hypoglycemic episodes complicated by HU despite optimal insulin therapy.[20] Exclusion criteria included: comorbid cardiac, kidney, and/or psychiatric disease; a history of non-adherence; BMI >26 kg/m$^2$ (Phase 1/2) or >27 kg/m$^2$ (Phase 3); persistent insulin requirement >0.7 units/kg/day; HbA1c >12%; smoking; or excess alcohol consumption.[20] Each patient received 1–3 islet transplants in an attempt to achieve insulin independence. The first four recipients in Phase 1/2 were placed on immunosuppression per the Edmonton protocol.[21] The subsequent recipients received the Edmonton protocol plus etanercept and exenatide (i.e., the UIC protocol).[20] The clinical trials were approved by the UIC Institutional Review Board and the patients provided written informed consent.

Patients were included in the current content analysis if they completed any of four open-ended response questions during screening prior to first islet transplant as of the end of 2016. Of the 30 patients, seven (one in Phase 1/2 and six in Phase 3) were offered but declined to complete any of the four questions. Patients who did not complete the questionnaire were younger and less likely to be taking concomitant medications than patients who completed the questionnaire (Table 1).

### 2.2. Approach/data analysis

This study was a secondary analysis of self-reported data, from four open-ended questions administered prior to their initial islet transplant, about patients' concerns, hopes, and fears about/concerning islet transplantation. Specifically, a content analysis was conducted, which is a method of uncovering and analyzing specific lived experiences,[28,29] and is a recommended approach when there is limited information regarding relevant themes and life-experiences of a group.[28–30] The four open-ended questions answered by patients during screening prior to transplant were:

- What is your biggest concern regarding your diabetes?
- What in your life do you expect to change by having an islet cell transplant?
- What is your biggest concern regarding having an islet cell transplant?
- What would you hope to gain by having an islet cell transplant?

Content analysis was used to assess major and sub-themes embedded within participants' responses to the four questions. Two trained coders (Q.F.L. and C.J.V.) independently reviewed the data. The data were then reviewed iteratively by both coders together until all potential themes had been exhausted. The themes were coded by manually highlighting each line of text and attaching labels to relevant quotes from each patient.[31] The direct quotes were clustered into broad themes. Under each broad theme, sub-themes identified specific patterns and relationships based on the frequency of the concept appearing in the data.[29] Consensus of the findings was supported twice by the two coders. Additionally, other authors supported the labeling and sorting of data to reach a final consensus. This established that relevant data and themes were not inadvertently omitted.

**Table 1**
Pre-transplant characteristics of the UIC islet transplant cohort, stratified by patients who completed (n = 23) or did not do (n = 7) the questionnaire.

| Characteristics at visit with questionnaire | UIC cohort (n = 30) | Completed questionnaire (n = 23) | Did not do questionnaire (n = 7) | *p*-Value |
|---|---|---|---|---|
| Age (years), mean (SD) | 46.7 (11.5) | 48.3 (10.8) | 41.6 (13.3) | 0.19 |
| Female sex, n (%) | 24 (80) | 19 (82.6) | 5 (71.4) | 0.60 |
| Race (white), n (%) | 30 (100) | 23 (100) | 7 (100) | 1.0 |
| Ethnicity (non-Hispanic), n (%) | 29 (96.7) | 22 (95.7) | 7 (100) | 1.0 |
| BMI, mean (SD) | 23.3 (2.0) | 23.4 (1.9) | 23.0 (2.5) | 0.72 |
| HbA1c (%), mean (SD) | 7.3[a] (0.9) | 7.3[b] (0.9) | 7.5 (0.8) | 0.64 |
| Antihypertensive medication, n (%) | 15 (50) | 13 (56.5) | 2 (28.6) | 0.40 |
| Statin medication, n (%) | 16 (53.3) | 15 (65.2) | 1 (14.3) | 0.03 |
| Depression/anxiety medication, n (%) | 11 (36.7) | 9 (39.1) | 2 (28.6) | 1.0 |
| Age at diagnosis (years), mean (SD) | 18.1 (12.9) | 19.0 (13.0) | 14.9 (13.1) | 0.46 |
| Duration of diabetes (years), mean (SD) | 28.7 (11.9) | 29.3 (12.1) | 26.7 (12.0) | 0.64 |

Completed vs. did not do questionnaire compared using Student's *t*-test or Fisher's Exact test.
[a] n = 29.
[b] n = 22.

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