

## **OPTN Pancreas Transplantation Committee Medical Urgency Workgroup**

### **Meeting Summary**

**January 29, 2021**

**Conference Call**

**Antonio Di Carlo, MD, Chair**

### **Introduction**

The Pancreas Transplantation Committee Medical Urgency Workgroup (the Workgroup) met via Citrix GoToMeeting teleconference on 1/29/2021 to discuss the following agenda items:

1. Overview of Project & Recap of 12/18 Meeting
2. Review and Discussion: Medical Urgency Criteria
3. Next Steps

The following is a summary of the Workgroup's discussions.

#### **1. Overview of Project & Recap of 12/18 Meeting**

The Workgroup reviewed the goal of the Medical Urgency project, which is to evaluate and discuss criteria that should be considered medically urgent as it pertains to pancreas candidates. The following is the definition and goal of the medical urgency attribute in the pancreas continuous distribution model:

*Medical Urgency:* Amount of risk to a candidate's life or long term health without receiving an organ transplant

*Goal of Medical Urgency:* Prioritize sickest candidates first to reduce waiting list mortality

#### Summary of discussion:

There were no comments or questions.

#### **2. Review and Discussion: Medical Urgency Criteria**

The Workgroup reviewed the potential medical urgency criteria discussed during the Workgroup's previous call. The following were the suggested criteria:

- Hypoglycemic Unawareness
- Type I vs. Type II diabetics
- Pancreas Donor Risk Index (PDRI)
- Cardiac Autonomic Neuropathy
- Total duration of diabetes
- Pediatrics
- Accessibility to technology
- Diabetes ketoacidosis (DKA)
- Severe Hypoglycemic events
- Gastroparesis

The Workgroup continued discussions with an endocrinology subject matter expert (SME) to gather more information on the following topics:

- Impaired awareness vs. Hypoglycemic unawareness
- Type I vs Type II diabetics

#### Summary of discussion:

The SME emphasized the importance of using the correct term of impaired awareness of hypoglycemia (IAH), which is the inability to sense symptoms of severe hypoglycemia. The SME explained that patients with Type I diabetes lose the ability to sense hypoglycemia, which leads to an increase in impaired awareness of hypoglycemia, and creates a vicious cycle where patients with Type I diabetes lose the ability to compensate and recover from hypoglycemia. Impaired awareness is a precursor of hypoglycemia and severe hypoglycemia. The SME stated that hypoglycemia, by itself, doesn't have to be severe; however, patients with Type I diabetes don't have the ability to defend themselves from hypoglycemia and are not aware until their glucose levels reach the 40s or 30s and they are risk of losing consciousness.. The SME mentioned that episodes of severe hypoglycemia make impaired awareness worse. One episode of severe hypoglycemia can result in the patient becoming impaired and if these episodes continue, their impairment can worsen. The SME emphasized that the concern is that impaired awareness is a precursor of severe hypoglycemia and severe hypoglycemia can lead to death and will increase the morbidity in some patients because they can have an accident or hurt themselves. Severe hypoglycemia and impaired awareness affect about 70,000-100,000 Type I diabetics.

The SME stated that patients who need a pancreas or islet transplantation are those patients with severe hypoglycemia or impaired awareness. If the patient is a Type I diabetic and needs a pancreas alone or islet alone transplant, that means that they have impaired awareness of hypoglycemia that is so severe it's putting them at risk. If the patient is a Type II diabetic, it's rare that the patient would get to the level of insulin deficiency where they would require a pancreas or islet transplant alone. If the patient has Type I diabetes and needs a kidney transplant, then there's no question that they should receive a kidney and pancreas together. If the patient isn't able to receive the kidney and pancreas together, then it would be acceptable for them to receive pancreas or islet transplant later on since the kidney will help control their insulin. The SME emphasized that Type II diabetics will usually only receive a kidney-pancreas (KP) because of a medical decision and not a clear indication of hypoglycemia. The SME stated that Type II diabetes is a minority of the diabetic population, so it's a small number of patients that would need a pancreas or islet transplant and the decision should be made on an individual basis. In terms of the condition of impaired awareness of hypoglycemia, Type I diabetics will require endocrine replacement through an islet or pancreas transplant.

The SME also noted that islet transplantation is becoming a standard of care in Europe and they do both pancreas and islet transplants, depending on the candidate's situation. In the US, islet transplants are not an approved entity though they have been proven to work. The indication for islet transplantation will be impaired awareness of hypoglycemia and severe hypoglycemia, so those candidates selected for islet or pancreas transplantation alone have similar conditions. The SME stated that, currently, many patients with Type I diabetes are using continuous glucose monitors (CGM) in order to prevent severe hypoglycemia, but these patients still have impaired awareness. With more patients using CGM devices, there's an ability to monitor the time a patient spent with a glucose below 70 and their duration of time spent in hypoglycemia, instead of waiting for them to have severe hypoglycemia. The SME emphasized, though, that there needs to be new criteria to define patients with impaired awareness who have a very high risk of death due to hypoglycemia, but have failed to improve with normal management of Type I diabetes.

The Workgroup Chair inquired if a CGM is needed to diagnose impaired awareness of hypoglycemia or if the diagnosis is based on patient related factors. The SME stated that, normally, the diagnosis is based

on medical history of the patient and by application of questionnaires, such as the Clarke or Gold score. These questionnaires have been validated in order to help label a patient unaware, but most of the questions are clinical, such as asking the patient when they start feeling that their glucose is low, which normally the patient has learned over time. The SME mentioned that complicated formulas could be used to create a hypoglycemic score; however, the formulas are more for research purposes.

A Health Resources and Services Administration (HRSA) representative inquired if the CGM devices are able to provide an alert to the patient of lower glucose levels and impending hypoglycemia. The SME mentioned that alarms can be set up using the CGM; however, many patients will sleep through the alarm and they will still have hypoglycemia. If the patient is living with someone, then the other person will hear the alarm and the severe hypoglycemia event will be prevented; however, if the patient is alone, they may sleep through the alarm, so night time is a big risk. The SME stated that it has been clearly shown that if severe hypoglycemia is prevented, then it improves the patient's awareness.

A HRSA representative inquired if there is any indication for when a patient should receive an islet transplant versus a pancreas transplant. The SME stated that pancreas and islet transplants are not competing approaches and there are patients that would prefer one over the other. Pancreas transplants are a surgical procedure and more aggressive than islet transplantation, but they are both viable options. The SME mentioned that it depends on what the patient wants and that there are some patients that can't have the pancreas transplant, due to the aggressiveness of the procedure, therefore the alternative would be the islet transplant. The SME pointed out that it also depends on the center, whether the center is more versed on islet or pancreas transplant; however, there are centers that can do both.

A member inquired if the SME has a sense of the accuracy for the assessment of how urgent it is to offer transplant to a patient who has multiple hypoglycemic episodes or impaired awareness. The SME stated that Type I diabetics with severe hypoglycemia or impaired awareness can be successful in the majority of cases with effective management. The real problem is that many patients are not seen by endocrinologists and many endocrinologists don't know how to manage Type I diabetes. The SME emphasized that there is still a significant number of patients, despite their management, who cannot control the rise and fall of their glucose levels and these would be the candidates that have the urgency for having a pancreas or an islet transplant. The SME mentioned that, in Europe, they have hypoglycemic centers that deal solely with severe hypoglycemia and these centers found that, of the patients referred to them, only one third will need an islet transplant. The SME suggested that the criteria for candidates listed for pancreas or islet transplants would be that they have gone through medical care or endocrinologist care and, despite state of the art management, they have failed treatment.

A member inquired about the access to the state of the art management in rural and remote areas and whether the SME has an estimate of the number of in rural areas that have this access. The member also inquired about how monitoring and management would work if it was remote. The SME stated that patients coming from these rural areas either have general physicians managing their diabetes or are doing it themselves. Sometimes these patients come with pumps or CGMs, but many of the patients don't know how to use these tools. Usually these patients have severe hypoglycemia due to poor management or lack of education; however, they will improve with better management. The SME stated that patients with Type I diabetes should be seen by a Type I diabetes specialist at least once a year and shouldn't be managed by their general physician. The SME stated that, in their experience, they send these patients back to instruction or to an endocrinologist to manage them and, if they continue with the treatment, then they usually get better.

A member inquired if the SME knows the ratio of the remote/rural patients to endocrinologists in the United States. The SME was not aware of this information, but pointed out that it's also important to consider the access to academic transplant centers versus the broader transplant community, because the diabetes management is not the same.

A member stated that there seems to be multiple layers that have to be considered when discussing hypoglycemia unawareness. The first layer would be that patients either have or don't have hypoglycemic unawareness based on objective and subjective criteria. Then, the next layer would be that not all patients with hypoglycemic unawareness will have severe hypoglycemic episodes, depending on the severity of the unawareness or effective management. So, if patients are able to avoid hypoglycemia, then they don't meet the second threshold of severe hypoglycemic events; however, if the patient does have severe hypoglycemia despite treatment, then what is considered the standard of good care? The member stated that the majority of diabetics are managed by non-endocrinologists and that they aren't sure if there's reliable data on who is taking care of those patients with Type I diabetes and severe hypoglycemia, although it would vary depending on where the patient lives and their access to care. A member stated that at least 50% of diabetic patients referred to them are being managed by an internist or a family doctor, so the pattern of good care is variable.

A member stated that it's difficult to designate what care should have been completed prior to being able to qualify medical urgency and that, instead, there should be a threshold that recognizes the variations in terms of access and social situations.

A member inquired if the Workgroup is going to have a scale for each of these criterion. The Workgroup Chair mentioned that this is an interesting idea and suggested that the Workgroup should do research to see if, currently, scales are being used or if the criteria should be a binary scale.

A member inquired about how pancreas donor risk index (PDRI) impacts the medical urgency of the recipient. The Workgroup Chair mentioned that the criteria the Workgroup has developed has not been finalized, so the Workgroup can still eliminate criteria if they see fit. A member suggested that Type II diabetics may not be fitting for the Workgroup's medical urgency criteria either, since the main concern centers around Type I diabetics. The Workgroup Chair stated that they would be interested to hear what a professional with experience in Type II diabetes would have to say, but wouldn't be opposed to eliminating that criteria as well.

A member inquired if Staff could reach out to the companies that sell CGMs to see if they could provide information on the number of devices used or functioning in the United States and the geographic distribution of where the units are functioning.

The Workgroup Chair suggested adding impaired hypoglycemic awareness. Members agreed adding this to the suggested medical urgency criteria. The Workgroup Chair also prompted members to invite diabetologists or other experts to the Workgroup meetings.

There was no further discussion.

### **3. Next Steps**

UNOS staff stated that they will create a spreadsheet that includes the criterion along with their official definitions and share it with the Workgroup for feedback. The Workgroup will continue discussing the medical urgency criteria and will begin developing data requests.

There were no additional comments or questions. The meeting was adjourned.

## **Upcoming Meetings**

- February 19<sup>th</sup> , 2021 (Teleconference)

## Attendance

- **Committee Members**
  - Antonio Di Carlo
  - Anita Patel
  - Earl Lovell
  - Emily Perito
  - Evelyn Hsu
  - Ken Bodziak
  - Rachel Forbes
  - Reynold Lopez-Soler
  - Silke Niederhaus
  - Todd Pesavento
  - Wayne Tsuang
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
  - Raelene Skerda
- **SRTR Staff**
  - Bryn Thompson
  - Jon Miller
  - Nick Salkowski
  - Raja Kandaswamy
- **UNOS Staff**
  - Joann White
  - Rebecca Brookman
  - Ross Walton
  - Kerrie Masten
  - Leah Slife
  - Nang Thu Thu Kyaw
  - Nicole Benjamin
- **Other Attendees**
  - Alejandro Rodolfo