

OPTN Pancreas Transplantation Committee Medical Urgency Workgroup

Meeting Summary

December 18, 2020

Conference Call

Antonio Di Carlo, MD, Chair

Introduction

The Pancreas Transplantation Committee Medical Urgency Workgroup (the Workgroup) met via Citrix GoToMeeting teleconference on 12/18/2020 to discuss the following agenda items:

1. Overview of Project
2. Review and Discussion: Medical Urgency Criteria
3. Next Steps

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

1. Overview of Project

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

United Network for Organ Sharing (UNOS) staff reported that, currently, data isn't collected on Type I vs. Type II diabetes, so the Workgroup will need to develop data requests regarding diabetic complications.

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)

Summary of discussion:

A member inquired about factors that increase wait list mortality for pancreas candidates. An endocrinologist subject matter expert (SME) stated that hypoglycemic unawareness is a strong factor because it can cause loss of consciousness and severe seizures. It's estimated that 4-9% of deaths among Type I diabetic are a result of hypoglycemia and this can happen in young patients that are otherwise healthy. The SME explained that there have been patients on the islet list who have had fatal hypoglycemic events while being evaluated for transplant. Islets and pancreas programs immediately address hypoglycemia, by restoring some graft function and endogenous insulin secretion. The SME stated that severe hypoglycemia is something that can kill people quite suddenly, but is immediately addressed in transplant.

The SME also stated that another factor is access to technology. It's hard to see how these closed loop pump systems handle people who have very labile forms of diabetes because they aren't in the clinical trials for those systems. If a candidate was defined as having high medical need for severe hypoglycemia, it probably is severe hypoglycemia that has failed treatment with the continuous glucose monitor (CGM) or inability to wear a CGM due to adhesive allergies.

The SME noted that patients with severe hypoglycemia are often patients that have a longer duration of diabetes, so duration of diabetes might be automatically included in the definition of severe hypoglycemia.

The SME stated that in discussion regarding this project with another endocrinologist noted that cardiac autonomic neuropathy is another reasonable condition to make someone high priority for transplant. DKA could also be on the list; it was pointed out that much of the time episodes with DKA end up being more of a compliance issue, patients have such extreme variability in day-to-day insulin needs that they develop DKA despite attempted adherence.

The SME mentioned that they were unsure how pediatrics would fit into pancreas medical urgency since pediatric pancreas patients don't have renal failure and hypoglycemia that often. However, the SME had witnessed one pediatric patient suffer from a severe insulin allergy, which is not a fatal condition, but does effect the patient's quality of life condition.

The SME shared, from their experience, that they weren't sure Type I vs. Type II diabetes would have different medical urgency.

A member inquired if severe hypoglycemia should be defined as hypoglycemic events or hypoglycemic unawareness. The SME stated that severe hypoglycemic events are more important.

A member inquired about how PDRI relates to medical urgency criteria. The member stated that it could relate to which pancreas are offered to islet candidates versus pancreas candidates. The Workgroup Chair explained that these items were just discussed during the first workgroup meeting and are not definitive.

A member inquired about (1) if the definition of severe hypoglycemia only encompasses the issues of loss of consciousness and seizures, and (2) how many hypoglycemic episodes per year should the Workgroup consider medically urgent. The SME explained that severe hypoglycemia and hypoglycemia unawareness have different definitions; however, most patients who present for pancreas or islet transplant with severe hypoglycemia will also have unawareness. Hypoglycemic unawareness is more of a chronic state in terms of how symptomatic a patient gets with their hypoglycemic episodes. These patients usually don't know they have hypoglycemic unawareness until they are experiencing severe complications. Severe hypoglycemia is defined as any type of mental or physical incapacitation where the patient requires aid from another person. There is a challenge in clinical centers with this definition

of severe hypoglycemia because it is unclear and less concrete. The SME continued by explaining the patients that are really burdened by hypoglycemia are often having more than one episode per year; however, one episode of hypoglycemia could be fatal.

A member inquired about the reversal of cardiac autonomic neuropathy once a patient receives a pancreas transplant. The endocrinologist stated that the reversal of cardiac autonomic neuropathy takes a little bit of time to be reversed, whereas hypoglycemia is almost an instant reversal.

A member inquired whether lack of access to technology should also include those patients that live in a rural area with limited access and those patients whose insurance doesn't cover CGMs. The SME agreed with this point and noted that there are still patients that continue to have hypoglycemic episodes despite having a sensor. The SME also suggested including these patients, whose technology has been tried and failed, under lack of access.

A member noted that issues with gastroparesis can be quite profound and it's a challenge to get these patients through the transplant. Some professionals believe that peripheral neuropathies may get better after two or three years, but the profound challenges with gastric neuropathy may actually be a contraindication to pancreas transplant. The member suggested including gastric neuropathy as a medical urgency criteria.

A member noted that neuropathy is important because, while it's not as well defined, it is still a significant indicator of mortality in diabetics, especially when the cardiac or circulatory systems are involved. Type I diabetics with orthostatic hypotension or cardiac dysregulation have a 50% mortality over 3-5 years. The member expressed that the Workgroup shouldn't worry about what the contraindications are to pancreas transplant because the centers should be able to decide if they can get a patient through a surgical procedure. The member mentioned that there's enough data to suggest that neuropathy will not progress if the patient is in a euglycemic state. A member stated that most of the Type I diabetics had gastroparesis so including this criteria would encompass almost all Type I diabetics on the pancreas list. A member suggested that the criteria should just encompass cardiovascular neuropathy so the criteria is not over-inclusive but the patients that have severe cardiovascular autonomic neuropathy receive priority.

A member inquired about how to quantify glycemic lability because that can be disabling for patients, even if they don't have hypoglycemic unawareness. The endocrinologist explained that there were some old scoring indices that were quite cumbersome, so it may be feasible to define glycemic lability based on CGM. It was also explained that many of the patients who have glycemic lability will also fall into the severe hypoglycemia category.

A member inquired if the transplant community has instruments that can identify cut offs for hypoglycemic unawareness. The endocrinologist stated that, in the U.S., the Clarke score is commonly used and there is a defined cut off of 4 or more, which is considered a reduced or unawareness of hypoglycemia. The endocrinologist also suggested defining severe hypoglycemic episodes instead of hypoglycemic unawareness because most of the patients who have severe hypoglycemia episodes are also hypoglycemia unaware.

A member noted that, in some geographical areas, endocrinologists are not always available. The member inquired if the Workgroup would mandate that a patient with hypoglycemic unawareness be evaluated by an endocrinologist. The SME explained that, even in a more rural setting where that's more difficult, at least seeing an endocrinologist for consult would be wise especially given the advances in technology for Type I diabetes management. A member noted that the standard of care for Type I diabetes management, even in some advanced cases, is not always an endocrinologist – it may be an access issue, geographic practice patterns, or expertise in the internal medicine community. The

member explained that the Workgroup should understand what the current state is of the Type I diabetes community and not put in something that is more burdensome than it currently is. The endocrinologist explained that they were thinking of this criteria in regards to medical urgency. For example, if the patient is going to be labelled medically urgent then they should have an endocrinology consult. A member agreed that an endocrinology consult should be required before a patient is referred for medical urgency, not just a pancreas transplant in general.

A member noted an analogy to requiring an endocrinologist consult for medical urgency, which is a requirement for simultaneous liver-kidney (SLK) patients to see a transplant nephrologist at least once. The member stated that a center with a pancreas program would have an endocrinologist to see those pancreas candidates that want to be labeled as medically urgent.

Members agreed that a single endocrinologist consult would make sense for medically urgent pancreas candidates. A member noted that the endocrinologist should verify that the patient has severe hypoglycemia and, at that point, consult the patient if they need to change care.

A member inquired if this medical urgency criteria only encompasses those patients that need a pancreas alone transplant or if it will also include patients that need a kidney transplant as well. This may complicate the issues because the Kidney Transplantation Committee will need to be involved if the Workgroup is making medical urgency decisions based off of the pancreas. A member noted that this Workgroup is talking about medical urgency for pancreas alone transplant at the moment. In preparation for going to continuous distribution, the goal is to transplant organs based on need and urgency and kidney and pancreas have traditionally based this off of wait time. This Workgroup is working alongside the Kidney Pancreas Continuous Distribution Workgroup to see if there are any reliable data that could be compiled in order to give certain patients who are at higher risk of death on the list some priority for pancreas alone transplant.

A member expressed that if a pancreas alone candidate has a marginal glomerular filtration rate (GFR) and qualifies for medical urgency, but their GFR drops and they become a simultaneous pancreas kidney (SPK) candidate, then they shouldn't lose their medical urgency because they're uremic. However, the candidate shouldn't be able to transfer all of their medical urgency priority to the kidney list, since the kidney is a rare commodity compared to pancreas alone. The member noted that there will be areas that have to be discussed with the Kidney Transplantation Committee, but currently the Workgroup is just discussing medical urgency for pancreas alone transplant.

A member noted that once the Workgroup decides on medical urgency criteria for pancreas alone candidates, then the Workgroup will move on to discuss medical urgency in kidney-pancreas and other combinations.

A member mentioned that they are unsure how Type I vs. Type II diabetes and PDRI would fit into medical urgency. For PDRI, the physiology of the recipient is factored into these other criteria for medical urgency and PDRI is focused solely on the donor. For Type I vs. Type II, again, it seems to be focused on the physiology of the instead of the classification.

A member mentioned that DKA is not life threatening, but it should also have some place in the pancreas continuous distribution model. A member explained that there are two options for medical urgency: (1) candidates are either medically urgent or not, and (2) have gradations of medical urgency. For example, someone that has had DKA and does not have severe hypoglycemia could be Level 1 urgency and a candidate that meets 3-4 of the criteria could be Level 3 urgency. The member noted that the gradations of medical urgency would fit well into the continuous distribution model.

Members agreed to add severe hypoglycemic events and gastroparesis to the list of pancreas medical urgency criteria.

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

- January 29th, 2021 (Teleconference)

Attendance

- **Committee Members**
 - Antonio Di Carlo
 - Anita Patel
 - Earl Lovell
 - Emily Perito
 - Evelyn Hsu
 - Maria Helena Friday
 - Ken Bodziak
 - Reynold Lopez-Soler
 - Peter Stock
 - Rachel Forbes
 - Raja Kandaswamy
 - Silke Niederhaus
 - Todd Pesavento
 - Wayne Tsuang
- **HRSA Representatives**
 - Marilyn Levi
- **SRTR Staff**
 - Bryn Thompson
 - Jonathan Miller
 - Nick Salkowski
- **UNOS Staff**
 - Joann White
 - Rebecca Brookman
 - Ross Walton
 - Kerrie Masten
 - Leah Slife
 - Nang Thu Thu Kyaw
 - Nicole Benjamin
- **Other Attendees**
 - Melena Bellin