

At-a-Glance

Proposal for the Definition of Pancreas Graft Failure

Affected/Proposed Policy:

Policy 1.2 Definitions, Policy 3.6.B.ii Non-function of a Transplanted Pancreas, Tiedi Help Documentation, Pancreas and Kidney-Pancreas OPTN Data Collection Forms

Pancreas Transplantation Committee

Currently, there is no nationally and consistently utilized definition specifically for how to identify and document pancreas allograft failure. Pancreas transplant programs reporting when a pancreas graft failed varies due to no standard definition, and thereby, limits the ability to analyze and compare pancreas programs' outcomes.

The proposal's purpose is to draft policy that assists transplant professionals to identify when pancreas allograft failure occurs and how to document the pancreas graft failure event. The proposal achieves this purpose by drafting policy for when a pancreas graft failed, updating Tiedi help documentation surrounding how to document pancreas graft failure, and updating the graft status section in the pediatric and adult pancreas and kidney-pancreas OPTN Recipient Registration and Recipient Follow-Up forms. (Unless otherwise noted, "OPTN pancreas forms" refers to the adult and pediatric pancreas and kidney-pancreas Transplant Recipient Registration Form (TRR) and Transplant Recipient Follow-up Form (TRF) throughout the proposal.)

The Pancreas Transplantation Committee (the Committee) understands the essential and urgent need to measure, and thereby manage outcomes. Although the proposed changes are a significant step forward in the effort for transplant professionals to consistently identify and document pancreas graft failure on a national basis, the Pancreas Transplantation Committee acknowledges the proposed language has room for growth. Currently, the OPTN policy requirements for reporting pancreas graft failure do not consistently coincide with all current, clinical definitions of pancreas graft failure. Nor does OPTN policy identify all potential scenarios for when pancreas graft failure may occur. As such, the Committee decided to respond to the imminent need with this proposal and believes this proposal is a significant first step in achieving consistent identification and documentation of pancreas graft failure throughout the U.S. In turn, creating a foundation for which transplant programs may be monitored.

Affected Groups

Directors of Organ Procurement
Lab Directors/Supervisors
OPO Executive Directors
OPO Medical Directors
OPO Coordinators
Transplant Administrators
Transplant Data Coordinators
Transplant Physicians/Surgeons
Transplant Program Directors

Organ Recipients

Number of Potential Candidates Affected

The number of potential transplant recipients affected includes all patients who have or will have received a pancreas transplant. As of September 2, 2014 there are 1,175 pancreas candidates and 2,048 kidney-pancreas candidates on the waiting list. Over the last five years there have been an average of 302 pancreas transplants and 867 kidney-pancreas transplants per year. After implementation of this policy proposal all pancreas recipients will be a part of the affected population and all pancreas recipients who have already received a pancreas transplant and the pancreas graft has not been reported, on OPTN pancreas forms as a failure, will be an affected population as well.

Compliance with OPTN Strategic Goals and Final Rule

Pancreas transplant programs' graft outcomes cannot be accurately and fairly analyzed and compared to a national standard since varying definitions of pancreas graft failure is used throughout the network. A consistent definition will allow for uniformly reported allograft failure, which will allow for improved estimates of expected graft failure using national data. This change will promote transplant patient safety, members' abilities to self-assess their performance, and members' abilities to strive for improvements.

Specific Requests for Comment

We welcome comments on the entire proposal. In addition, the Committee seeks feedback on the following specific additional questions:

- Please provide any recommended changes to the general definition of graft failure. Should there be one general definition for graft failure? Alternatively, should there be organ specific definitions of graft failure?
- Do you support including recipient deaths in the definition of pancreas graft failure? Should all recipient deaths count as graft failure?
- Should programming the proposed additional fields on the OPTN pancreas forms be implemented simultaneously as the proposed policy language? If programming the additional fields will take approximately three years, should the proposed policy language be implemented in three years?

Proposal for the Definition of Pancreas Graft Failure

Affected/Proposed Policy:

Policy 1.2 Definitions, Policy 3.6.B.ii Non-function of a Transplanted Pancreas, Tiedi Help Documentation, Pancreas and Kidney-Pancreas OPTN Data Collection Forms

Pancreas Transplantation Committee

Public comment response period: September 29 – December 5, 2014

Summary and Goals of the Proposal:

The proposal's purpose is to draft policy that help transplant professionals identify when pancreas allograft failure has occurred and how to document the pancreas graft failure event. The proposal achieves this purpose by drafting policy for when a pancreas graft failed, updating Tiedi help documentation surrounding how to document pancreas graft failure, and updating the graft status section in the OPTN pancreas forms.

Background and Significance of the Proposal:

There has been concern that transplant centers report graft failures at different clinical endpoints. For example, some programs report a graft as failed if there is any return to insulin therapy whereas other programs only report failure if insulin use rises above a certain threshold. Dosage of insulin, duration of insulin therapy, c-peptide levels, and Hba1c are some parameters that can vary widely in patients who have been determined to have graft failure at their respective institutions. As the MPSC implements use of statistical models to assess pancreas program performance, this difference in reporting could impact whether a pancreas program is identified for outcome review under *Appendix D.10 A. Transplant Program Survival Rates*. Therefore, the Committee drafted a definition for pancreas allograft failure in order to set a measurable standard for what constitutes pancreas graft failure.

As background, the Tiedi help documentation includes guidance on how to categorize a functioning, partial functioning, and failed pancreas graft. In pertinent part, the current Tiedi help documentation reads:

- **Functioning:** The graft has sufficient function so that the recipient is **NOT** receiving any insulin or oral medication for blood sugar control
- **Partial Function:** The patient is taking some insulin, but \leq 50% of the usual amount taken before transplant, or C-Peptide is present
- **Failed:** The graft has totally failed and the patient is completely dependent upon insulin or oral medication for blood sugar control

While reviewing the Tiedi help documentation, the Committee noted several deficiencies. These deficiencies of the pertinent section of the Tiedi guidance are that the help documentation:

- Conflicts with the definition of graft failure in policies not in the forefront of transplant professionals' minds since it is not located in policy
- Is unclear regarding amount or duration of insulin use
- Does not specify a c-peptide threshold nor does it address Type 1 vs. Type 2 diabetics

- Does not address the scenario where a patient taking oral medications only to support their glucose control is declared a failure, but is very uncommon that this scenario would be deemed a failure by the transplant center.

Further, since few centers utilize the “Partial Function” category on the OPTN pancreas forms, this suggests that the “Partial Function” category is either underutilized or unnecessary.

During the course of the project, the Committee also looked to other areas of policy for guidance on graft failure definitions. The Tiedi glossary defines graft failure as, “When organ removal, death, or replacement on chronic allograft support system has occurred.” In addition, the current general definition for graft failure, as located in OPTN Policy, is, “Occurs when an organ is removed, a recipient dies, or a recipient is placed on a chronic allograft support system.” However, neither definition encompasses all situations for when a pancreas graft has failed. The Committee noted that the definition of graft failure for other organs is a terminal event, and in contrast, the Committee had to include gradual failure (i.e. the insulin category), in addition to complete failure.

During the project’s development, the Committee noted that the general definition of graft failure, which is currently located in Policy 1.2 Definitions, needs an update. As part of this proposal, the Committee will gather suggestions for updates to the general definition of graft failure. Specifically, should there be a general definition of graft failure for all organs except for pancreas? Should there be a general definition of graft failure for some of the organs, and some of the organs have an organ-specific definition of graft failure? Should there be a separate organ-specific definition for graft failure for each organ? Feedback on these questions may be used for a separate proposal to update the general definition of graft failure in Policy 1.2.

The current general definition of graft failure is located in Policy 1.2 Definitions, and reads:

Graft Failure

Occurs when an organ is removed, a recipient dies, or a recipient is placed on a chronic allograft support system.

In addition to drafting the definition of pancreas graft failure, the Committee cleaned up language in Policy 3.6.B.ii Non-function of a Transplanted Pancreas, to omit references to pancreas graft failure so that Policy 3.6.B.ii and the proposed definition of pancreas graft failure do not conflict. While redacting references to pancreas graft failure in the current Policy 3.6.B.ii language, the Committee discussed further potential policy language changes to Policy 3.6.B.ii. The Committee decided to table the discussion of potential, extensive, language changes to Policy 3.6.B.ii for a future date. The Committee made this decision because it did not want to expand the scope of definition for pancreas graft failure project. However, the Committee welcomes feedback from the pancreas transplant community as to whether Policy 3.6.B.ii Non-function of a Transplanted Pancreas needs extensive language changes and whether Policy 3.6.B.ii needs substantive changes to the meaning of the policy section.

• **Collaboration:**

Although the definition of pancreas graft failure project was not a combined project with the MPSC, because the project directly effects MPSC’s program assessments, the Committee has routinely kept the MPSC updated on the projects progress.

Two aspects of the proposed definition have caused significant discussion. The first aspect that has caused discussion is the insulin category within the proposed definition of pancreas graft

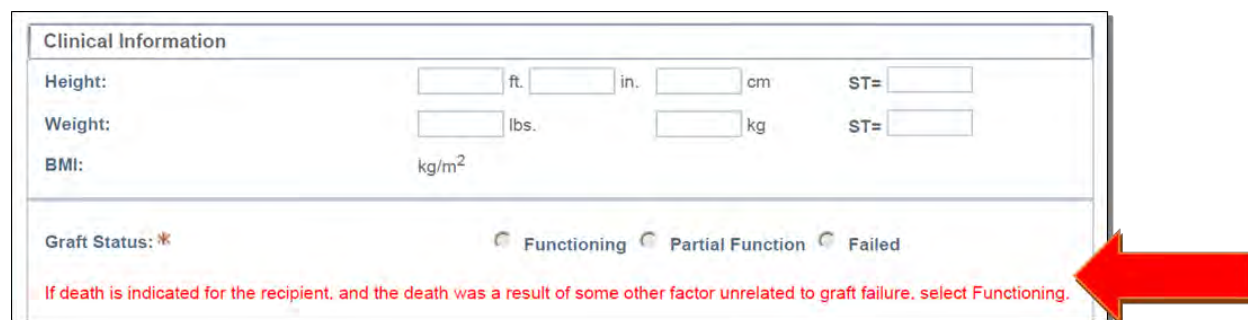
failure. The second aspect of the definition that has caused discussion is the recipient death category.

The proposed definition of pancreas graft failure states that a pancreas graft failure occurs when “A recipient’s insulin use is greater than or equal to 0.5 units/kg/day for a consecutive 90 days”. The insulin category of graft failure identifies situations where graft failure occurs gradually over time. Gradual pancreas graft failure caused a lot of discussion and negotiation amongst Committee members and interested parties (interested parties being pancreas transplant professionals who are not currently Committee members). Specifically, Committee members and interested parties debated over the amount of insulin that indicates pancreas graft failure. In the end, all parties agreed that 0.5 units/kg/day, over a consecutive, three-month time period indicates the graft failed. This is a conservative measure that the medical expertise agreed on as being an indicator that the graft has failed.

Recipient deaths also caused a lot of discussion. The proposed definition states that pancreas graft failure occurs when “[a] recipient dies”. The Committee intends for the recipient death category to mean that a recipient died with a functioning pancreas allograft because a patient that dies with a failed pancreas allograft should already have been reported when the graft failed.

The discussion surrounding the recipient death category stems from instructional language that is currently located on the OPTN pancreas forms. Underneath the graft status section of the OPTN pancreas forms, instructional language, in red font, states: “If death is indicated for the recipient, and the death was a result of some other factor unrelated to the graft failure, select Functioning.”

A screen shot of the pertinent section of the OPTN pancreas form is below. This screen shot is taken specifically from the adult pancreas Transplant Recipient Follow Up form (TRF) but the information in the screen shot is located in all the OPTN pancreas forms:



The screenshot shows a form titled "Clinical Information" with fields for Height (ft., in., cm), Weight (lbs., kg), and BMI (kg/m²). Below these fields is the "Graft Status" section with three radio button options: "Functioning", "Partial Function", and "Failed". A red arrow points to the "Functioning" option. Below the radio buttons, there is a red instruction: "If death is indicated for the recipient, and the death was a result of some other factor unrelated to graft failure, select Functioning."

The OPTN pancreas forms retrospectively qualify the state of the pancreas at the time of death. This has been interpreted by some to mean death with a functioning graft does not constitute graft failure. The Committee supports collecting the status of the pancreas graft at the time of death, which is in conjunction with how the graft status data is currently reported on follow-up forms. At the same time, the Committee feels that the pancreas graft failure definition should include recipient death of all causes. As part of this proposal, the Committee recommends to make the following updates to the OPTN pancreas forms:

- Remove “Partial Function” graft status category
- Updating the instructional language, in red font
- Create additional fields for specific data collection that will allow for future enhancement to the pancreas graft failure definition

Regarding the instructional language in red, the Committee proposes to change the sentence to either:

- “If the recipient does not fall within one of the OPTN policy definition categories of pancreas graft failure, at the time of death, then report the graft as “Functioning”, or
- If death is indicated for the recipient, report graft status up until the instance of death.”

Further, the Committee proposes to update the Tiedi help documentation to also include instructional directions for when to select “Functioning” versus “Failed” for graft status.

- ***Alternatives considered:***

The Committee’s first draft of the definition for pancreas graft failure was as follows.

Pancreas graft failure has occurred if a Type 1 diabetic pancreas recipient has:

- a stimulated c-peptide less than 0.4 and is insulin dependent,
- undergone a pancreatectomy,
- been retransplanted, or
- died

One aspect of the first draft includes a c-peptide threshold that indicates pancreas allograft failure. However, Committee members questioned the validity of the c-peptide value, 0.4. As such, the Committee members performed a literature review to determine if current medical literature speaks to a c-peptide value that corresponds with pancreas allograft failure. The results of the literature review were inconclusive. In addition, the OPTN does not collect c-peptide values for pancreas transplant recipients either before transplant or at graft failure.

Therefore, the Committee decided to perform a C-peptide Data Collection Study in order to determine a c-peptide value that corresponds with pancreas allograft failure. (See Supporting Evidence and/or Modeling section for further discussion on the C-peptide Data Collection Study.)

- ***Strengths and weaknesses:***

The proposal’s strength is that it creates a solution to a project that has been in existence and discussed for numerous years. The solution addresses a topic that is understandably unpopular in the community, yet necessary for the medical advancement of pancreas transplantation. Another strength is that the proposed solution creates a simple definition of pancreas graft failure that creates a straightforward evaluation of a transplant recipient’s graft status where pancreas graft failure encompasses the fluctuating disease of diabetes - a disease that can morph from Type 1 diabetes to Type 2 diabetes in a single transplant and varies drastically depending upon patient compliance – the proposed definition attempts to create a uniform benchmark. At this time, there is not sufficient information and OPTN data available to draft a specific definition of pancreas graft failure, which addresses every situation in which a graft may fail for a Type 1 or Type 2 diabetic.

However, the proposed definition creates a strong infrastructure in which the Committee may expand upon, in the future, as information becomes available. From a different perspective, the benchmark definition creates an incomplete definition for pancreas graft failure. The proposed definition does not encompass all scenarios in which a transplanted pancreas may fail. However, the Committee acknowledges this point. The Committee chose to produce a benchmark definition at this time for two reasons:

- (1) Timing: The Committee's proposal creates a pancreas graft failure definition that the MPSC may use to begin monitoring pancreas transplant centers in the relatively near future. This will allow the MPSC to monitor pancreas transplant outcomes.
- (2) Need: The pancreas community needs a definition that can be applied consistently throughout the country. The Committee's proposed definition applies to all diabetes types and removes vagueness of partial function (as a currently available reporting field on the OPTN pancreas forms). One of the challenges of identifying and reporting pancreas graft failure is that a pancreas graft may gradually fail over time. The current guidance on how to document pancreas graft failure is unclear as to when to report graft failure when the graft gradually loses function.

- ***Description of intended and unintended consequences:***

The intended consequences of this proposal are to produce a pancreas graft failure definition that the MPSC may use to collect data to monitor outcomes, as well as to educate and communicate to members what constitutes graft failure and how to document graft failure. The latter intended consequence will also allow members to consistently and uniformly document pancreas graft failure. In turn, such a consistent and uniform practice will produce accurate and reliable nationally reported data that ideally will allow the Committee, and pancreas community, to make the definition more specific in the future as well as gain more insight as to when graft failure occurs. Ultimately, a more detailed understanding of pancreas graft failure will lead to better graft management.

An unintended consequence is that the proposed definition will capture false graft failures or under report graft failures. The Committee plans to manage this unintended consequence by monitoring the graft failure outcomes data and to utilize the data, collected from the new fields on the OPTN pancreas forms, to draft a more specific definition of pancreas graft failure, in the future.

Supporting Evidence and/or Modeling:

As mentioned above, the first draft of the definition for pancreas graft failure included a c-peptide threshold. The Committee questioned the appropriateness of the c-peptide threshold, and when a literature review did not speak to what c-peptide threshold indicates pancreas allograft failure, the Committee performed its own c-peptide study.

The Committee performed a C-peptide Data Collection Study in order to determine a c-peptide value that corresponds with pancreas allograft failure. This data collection project consisted of collecting pancreas transplant recipients' c-peptide values at pre transplant, at return to insulin, and at graft failure. This purpose of the study was to allow members to determine the c-peptide value and methodology that indicates pancreas allograft failure.

The research plan was for each participating center to collect the past decade of pancreas transplant recipients' c-peptide values pre transplant and at graft failure. Then, the centers compiled the data and analyzed the results to determine if a c-peptide threshold was consistently used to indicate graft failure or if c-peptide at graft failure could be predicated with pre transplant c-peptide. The study was limited by the only available indicator of graft function being graft status as reported on OPTN pancreas and kidney-pancreas registration and follow-up forms.

Study Structure

Seven centers submitted data for the C-peptide Data Collection Study. The data spanned over the last ten years of reported pancreas graft failures for pancreas or kidney-pancreas transplants since 2002 reported in OPTN database. The data were collected at the following points: pre-transplant, return to insulin, and graft failure. The data collected were c-peptide value, c-peptide type (fasting or stimulated), creatinine value, and corresponding measurement dates.

C-peptide Data Collection Study Results

The table below shows data compiled as voluntarily submitted by participating centers in the OPTN/UNOS Pancreas Transplantation Committee's Definition for Pancreas Allograft Failure Project. C-peptide data on pancreas recipients are not currently required by the OPTN.

Table 1. Empirical distribution of C-Peptide values pre-transplant, at insulin resumption, and at graft failure for data submitted through the Outcomes Subcommittee data collection project.

	N	Mean	SD	Min	25th Percentile	Median	75th Percentile	Max
Pre-Transplant C-Peptide	149	2.03	6.1	0	0.1	0.2	0.5	33
C-Peptide at Return to Insulin	94	2.28	2.2	0.1	0.6	1.46	3.4	12.1
C-Peptide at Graft Failure	233	2.11	3.3	0	0.4	0.9	2.7	33

Table 1 shows the empirical distribution of all c-peptide values submitted at each time point for this data collection project. Note that there is a large range from minimum to maximum, which speaks to insulin resistance. The table doesn't show results separated between Type 1 and Type 2 diabetics so any recipient with c-peptide less than or equal to one was considered a Type 1 diabetic by the Committee. This separation was understood when examining graphical representations of the data.

Table 2. Number of C-Peptide values pre-transplant, at insulin resumption, and at graft failure by encrypted transplant center for data submitted through the Outcomes Subcommittee data collection project.

Encrypted Center ID	Pre-Transplant C-Peptide	At Return to Insulin C-Peptide	At Graft Failure C-Peptide	N With Both Pre-Transplant and at Graft-Failure C-Peptide	N With C-Peptide at all 3 points
	N Available	N Available	N Available	N Available	N Available
23250	5	0	3	2	0
3410	2	3	4	0	0
6820	40	6	39	29	3
24800	22	22	17	2	2
7347	1	0	94	1	0
16957	21	7	19	19	7
7905	58	56	57	24	24
Total	149	94	233	77	36

Table 2 shows the volume of data queried and submitted by each center. Note the inconsistency on when transplant centers collect the c-peptide values.

Figure 1. Distribution of C-Peptide values pre-transplant for data submitted through the Outcomes Subcommittee data collection project.

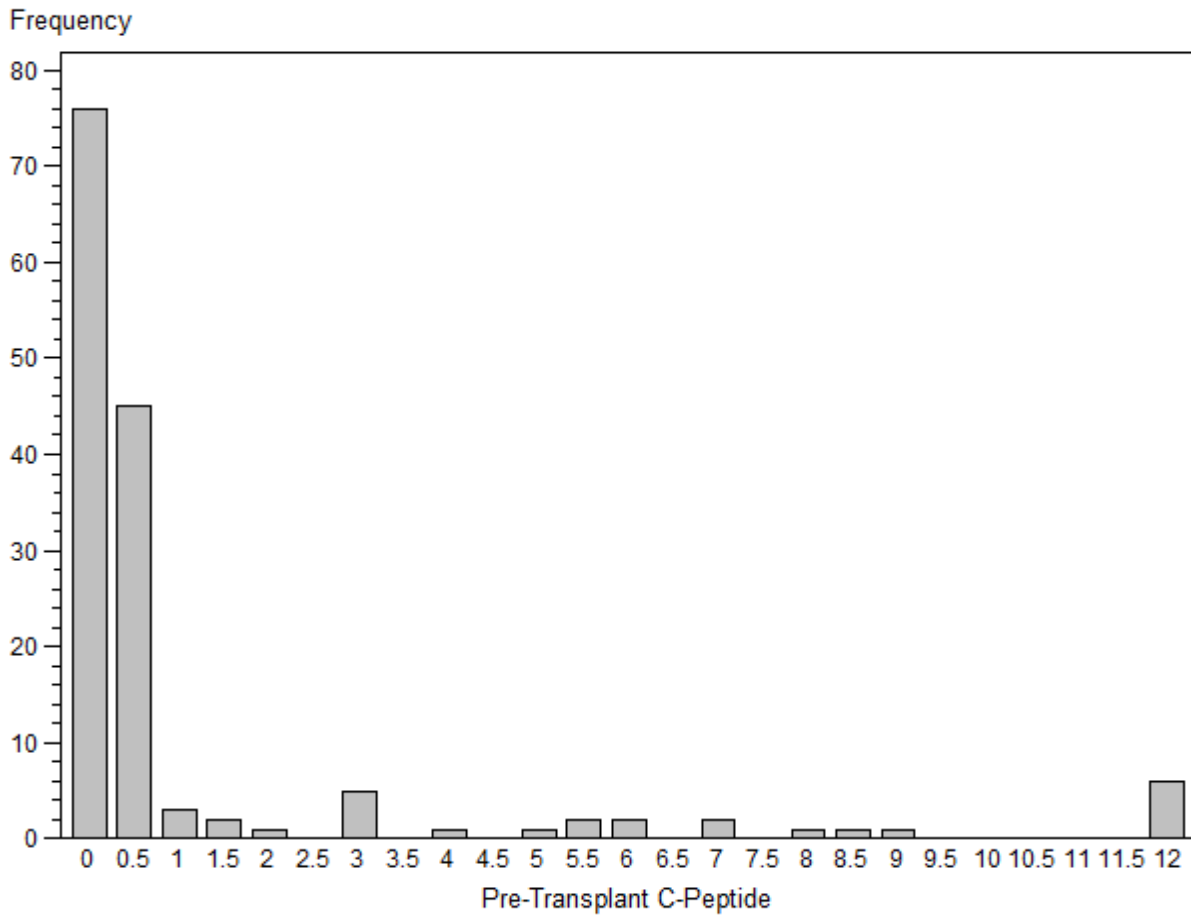


Figure 1 graphically shows the distribution of all pre-transplant c-peptide values submitted in this study. The majority of recipients had c-peptide less than 1 pre-transplant.

Figure 2. Distribution of C-Peptide values at insulin resumption (n=94) for data submitted through the Outcomes Subcommittee data collection project.

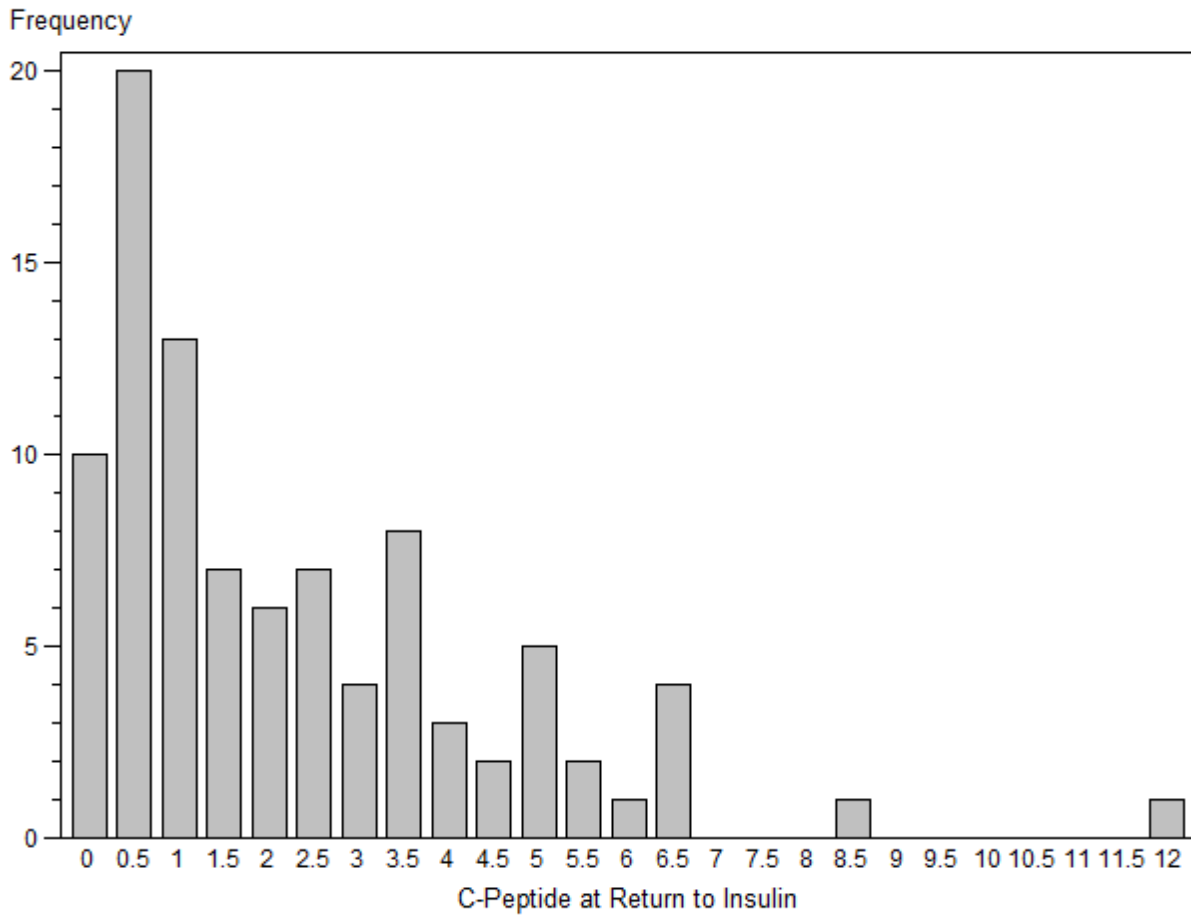


Figure 2 shows the distribution of all c-peptide values at return to insulin for this project. What this shows is that physicians are returning their patients to insulin at varying levels of pancreas function.

Figure 3. Distribution of c-peptide values at graft failure (n=233) for data submitted through the Outcomes Subcommittee data collection project.

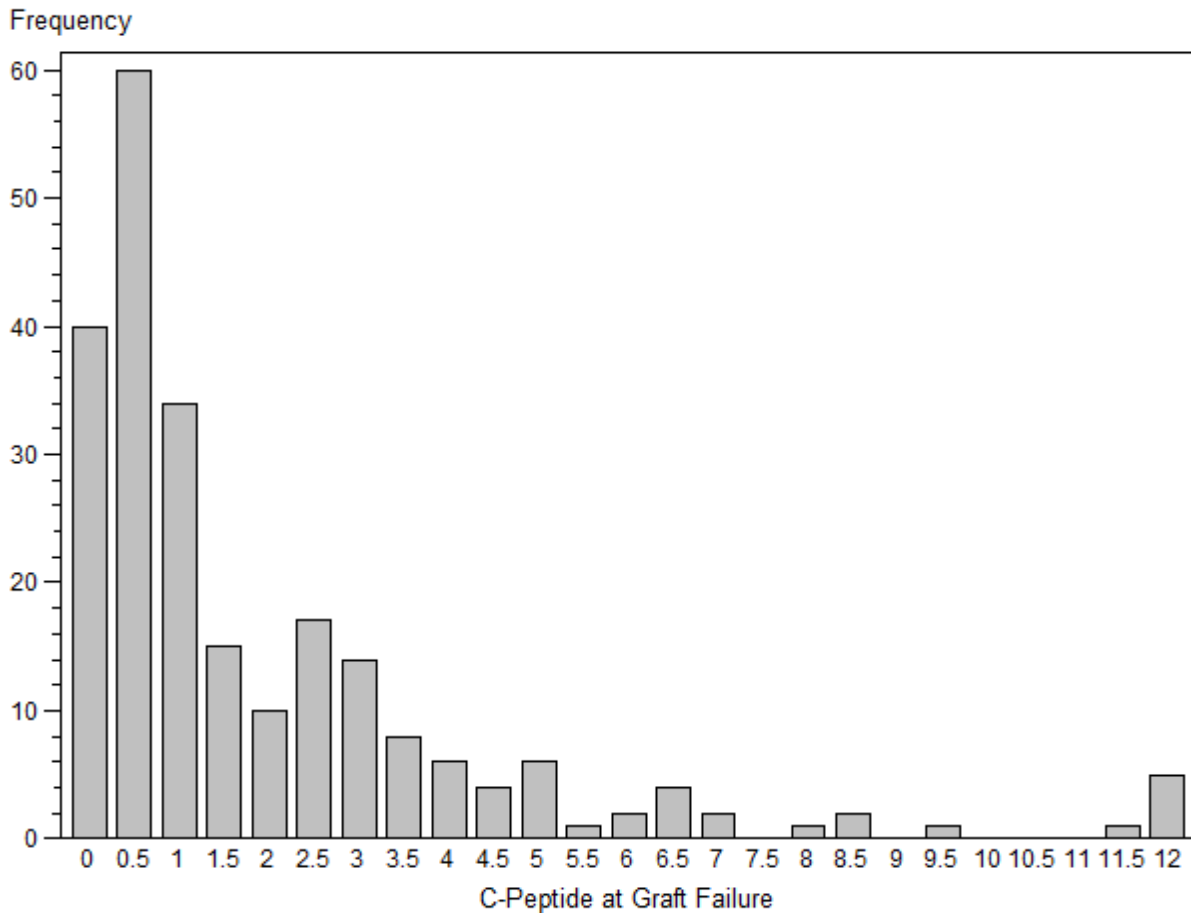


Figure 3 shows the distribution of all c-peptide values at graft failure submitted in this project. This distribution shows that transplant centers are calling a graft failed at varying levels of recipient c-peptide. However, this distribution is more right skewed, favoring smaller values, than the distribution at return to insulin.

Figure 4. Bivariate Distribution of c-peptide values pre-transplant and at graft failure (n=77) for data submitted through the Outcomes Subcommittee data collection project.

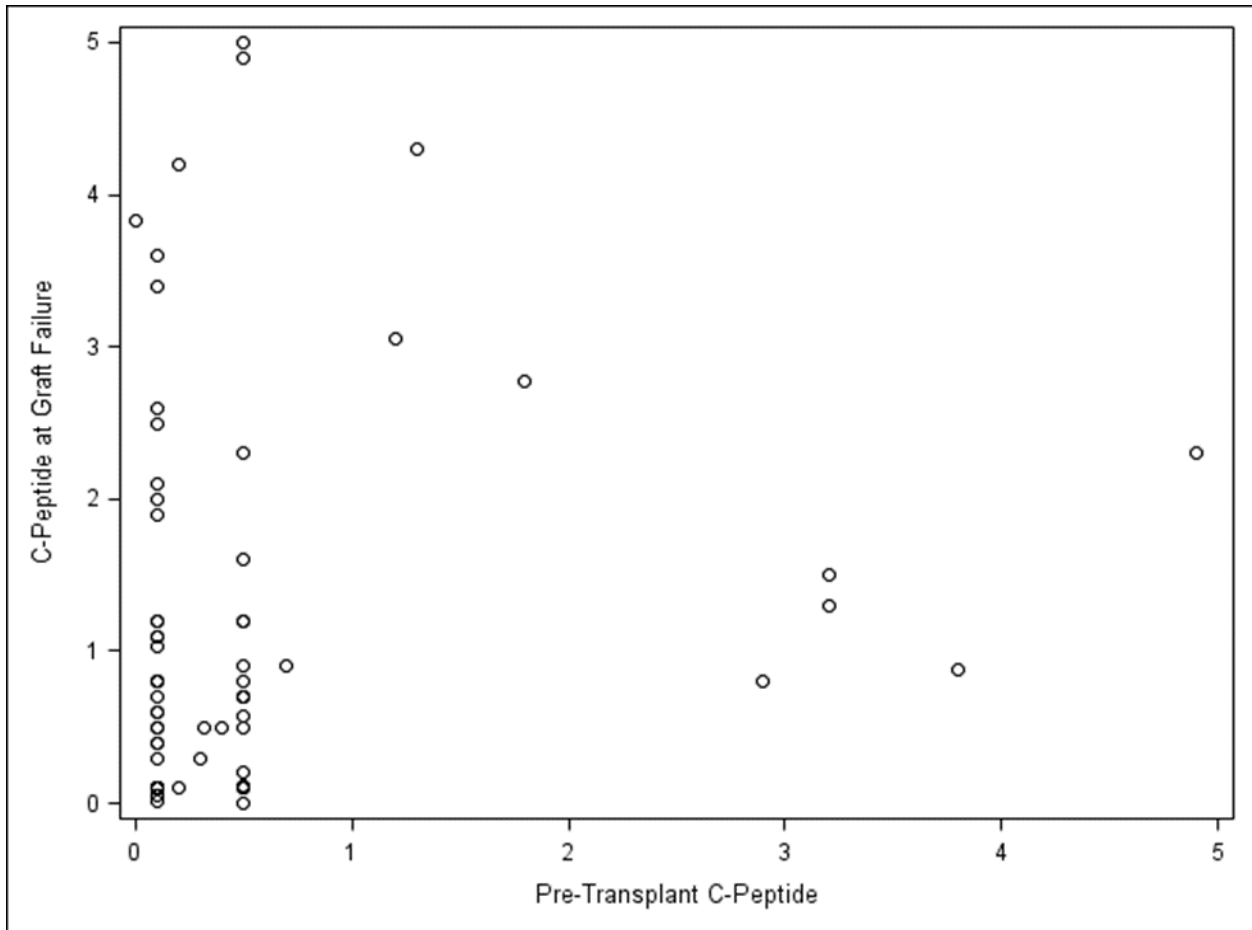


Figure 4 shows the bivariate distribution of all 77 pairs of pre-transplant and at graft failure c-peptide values. It is seen here that although most recipients had c-peptide less than 1 pre-transplant, their graft failure was claimed at varying levels of c-peptide.

Table 3. Number of c-peptide values pre-transplant, at insulin resumption, and at graft failure by encrypted transplant center for data submitted through the Outcomes Subcommittee’s C-peptide Data Collection Project.

Encrypted Center ID	N Total Graft Failures	N With Both Pre-transplant and at Graft Failure C-Peptide	N With C-Peptide at All 3 Points	N with Pre-Transplant 0.75 or less and at Graft Failure Value Available
3410	14	0	0	0
6820	66	29	3	28
7347	94	1	0	1
7905	139	24	24	22
16957	21	19	7	7
23250	6	2	0	2
24800	75	2	2	1
Total	415	77	36	61

Table 3 shows the total number of graft failures that were voluntarily submitted for this study, the number with c-peptide values at pre-transplant and graft failure, as well as the number with measurements at all three points (pre-transplant, return to insulin, and at graft failure). Additionally, the last column shows the number of graft failures that were voluntarily submitted to this study with pre-transplant c-peptide less than or equal to 0.75 (likely the Type 1 diabetics) and with a graft failure c-peptide value available. There were 36 recipients with c-peptide collected at all three time points (pre-transplant, return to insulin, and at graft failure). Of these 36 recipients, 30 recipients returned to insulin at graft failure.

Figure 5. Distribution of c-peptide values of 1 or less at pre-transplant (n=77) for data submitted through the Outcomes Subcommittee’s C-peptide Data Collection Project. Horizontal axis labels are midpoints.

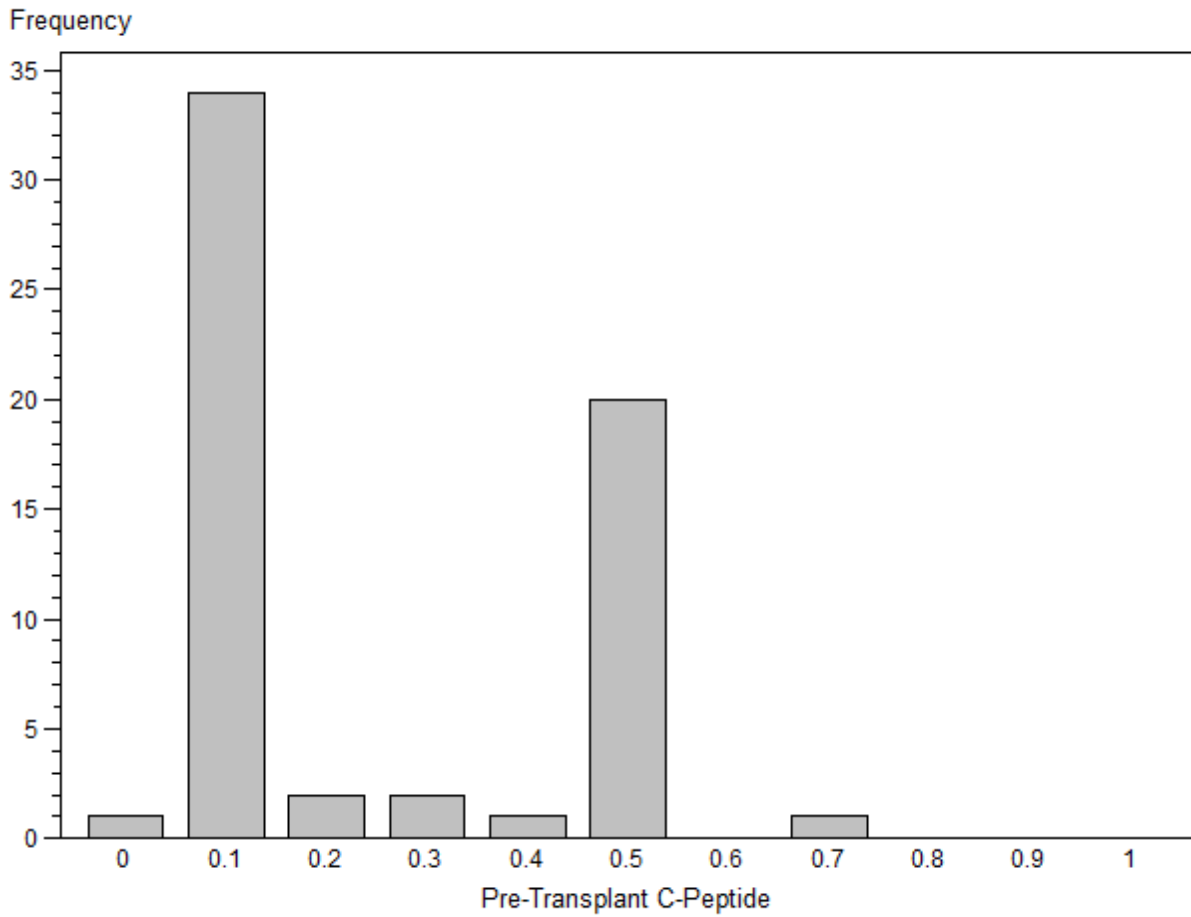


Figure 5 displays all pre-transplant c-peptide values submitted that are less than or equal to 1. The frequency in the bins containing 0.1 and 0.5 are due to the many submissions of values “<0.1” and “<0.5”. Currently, some labs report c-peptide values at two values: <0.1” and “<0.5”. This reporting practice should be considered when collecting c-peptide values on the OPTN pancreas forms.

Figure 6. Distribution of c-peptide values at graft failure for data submitted through the Outcomes Subcommittee's C-peptide Data Collection Project where both graft failure and pre-transplant c-peptide values were submitted (n=77). Horizontal axis labels are midpoints.

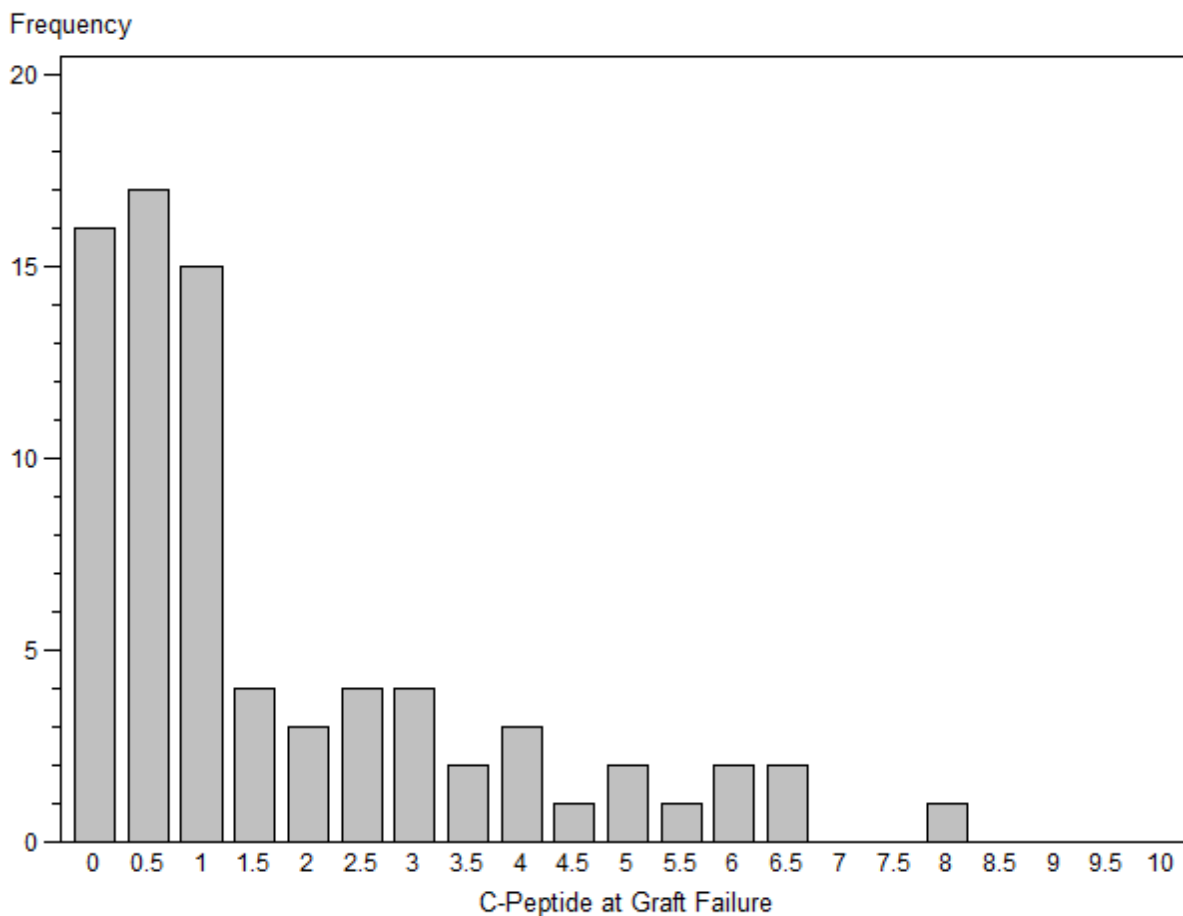


Figure 6 displays the distribution of c-peptide values at Graft Failure for all 77 graft failures that were submitted with both pre-transplant and graft failure c-peptide values.

Figure 7. Distribution of c-peptide values at graft failure for data submitted through the Outcomes Subcommittee’s C-peptide Data Collection Project where both graft failure and pre-transplant c-peptide values were submitted and the pre-transplant value was 0.75 or less (n=61). Horizontal axis labels are midpoints.

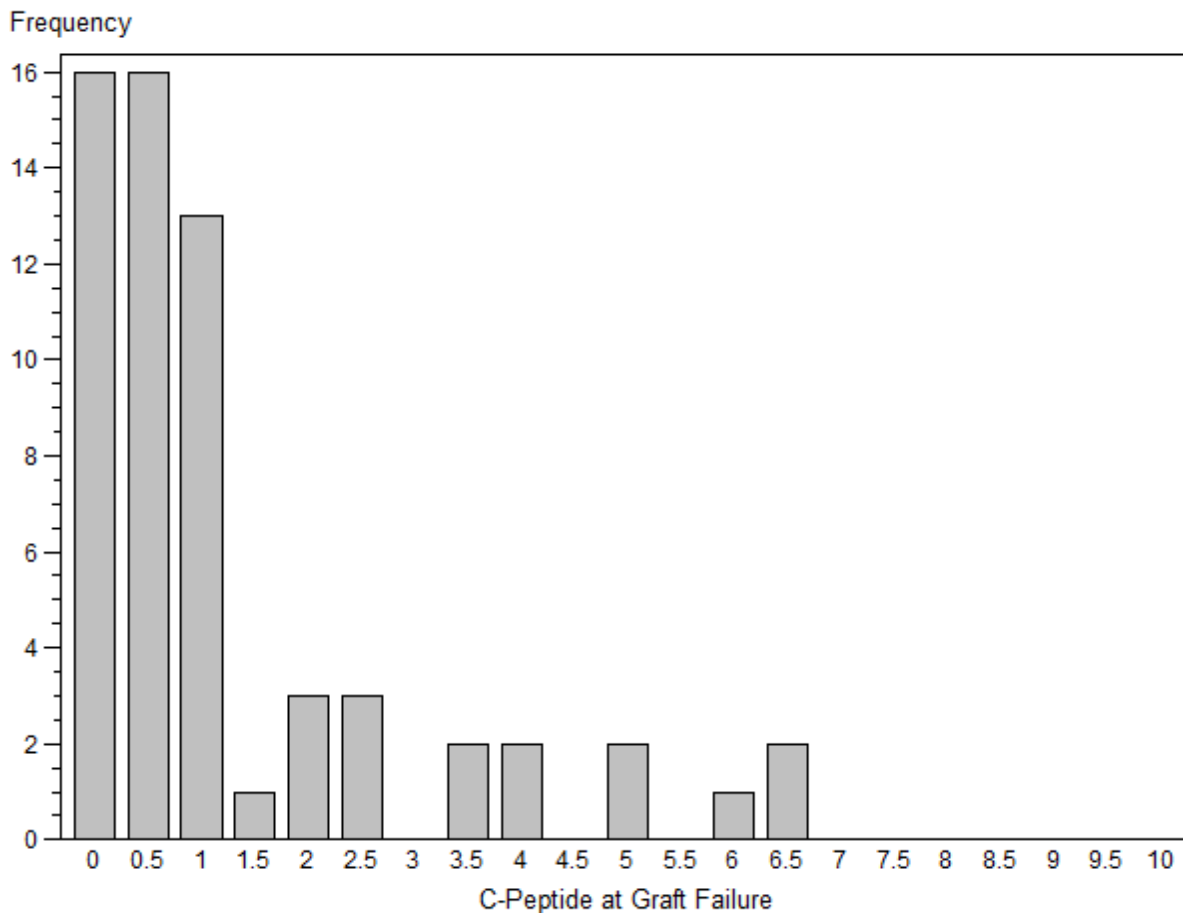


Figure 7 displays the distribution of c-peptide values at Graft Failure for all 61 graft failures that were submitted with both pre-transplant and graft failure c-peptide values where the pre-transplant c-peptide value was 0.75 or less. This distribution tends towards smaller values at graft failure in comparison to Figure 2 which contains all pairs of values. It is likely that those who had pre-transplant c-peptide of 0.75 or less are Type 1 diabetics, and the recipients with pre-transplant c-peptide values greater than 0.75 are predominantly Type 2 diabetics.

Figure 8. Bivariate Distribution of c-peptide values pre-transplant (0.75 or less) and available c-peptide value at graft failure (n=61) by whether the graft failure c-peptide was taken fasting for stimulated for data submitted through the Outcomes Subcommittee’s C-peptide Data Collection project.

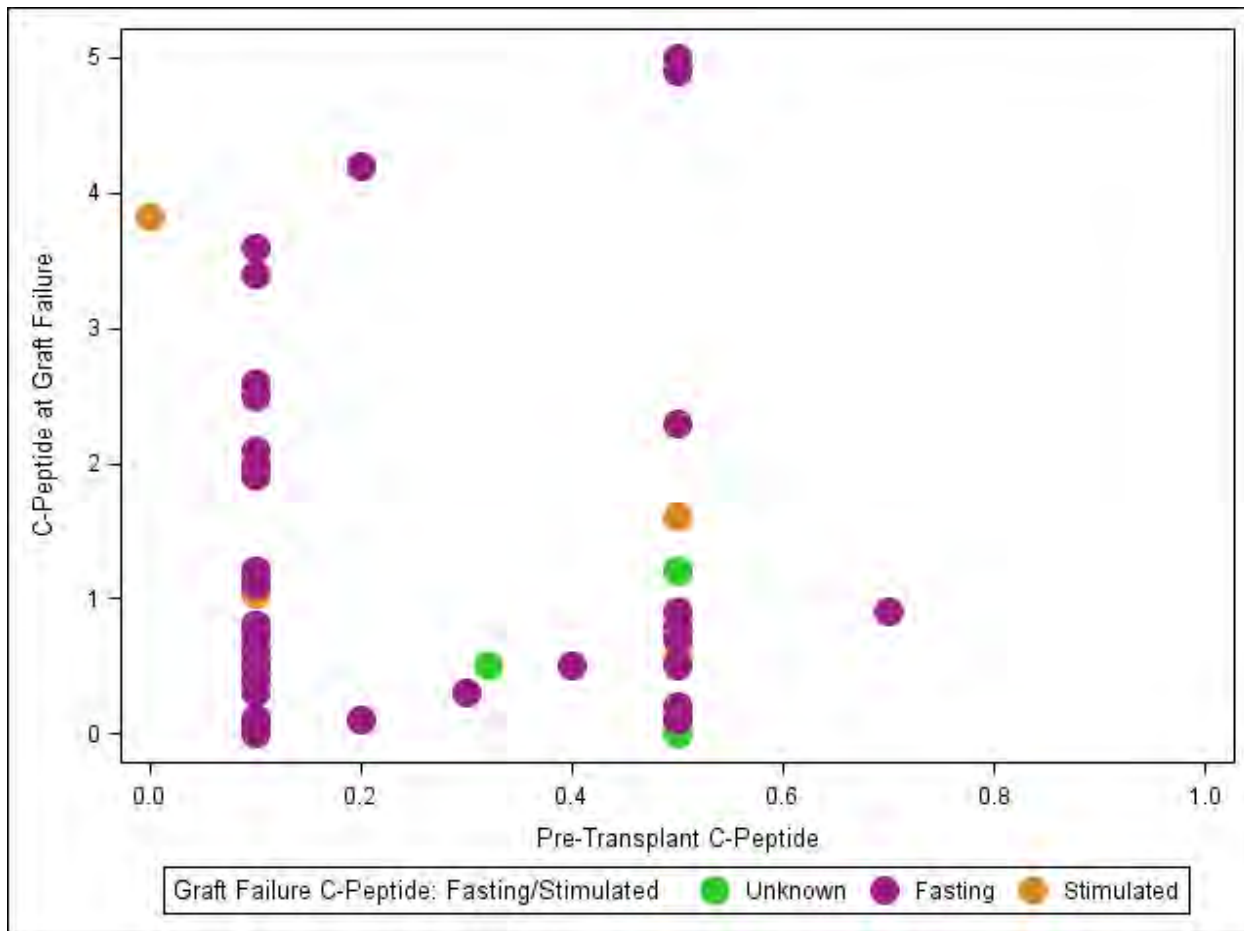


Figure 8 shows the bivariate distribution for the graft failures represented in this study with both pre-transplant and graft failure measurements with c-peptide at pre-transplant 0.75 or less by whether or not the value was taken fasting or stimulated. Of the 61 pairs, 3 graft failure values did not indicate whether they were fasting or stimulated, 4 were taken stimulated, and the other 54 were fasting. Even though there are small sample sizes, the fact that the higher values of c-peptide at graft failure were not biased by stimulated testing indicates that graft failure is not uniformly reported at any specific level of c-peptide.

Figure 9. Bivariate Distribution of c-peptide values pre-transplant (0.75 or less) and available c-peptide value at graft failure (n=61) by encrypted center for data submitted through the Outcomes Subcommittee’s C-peptide Data Collection Project.

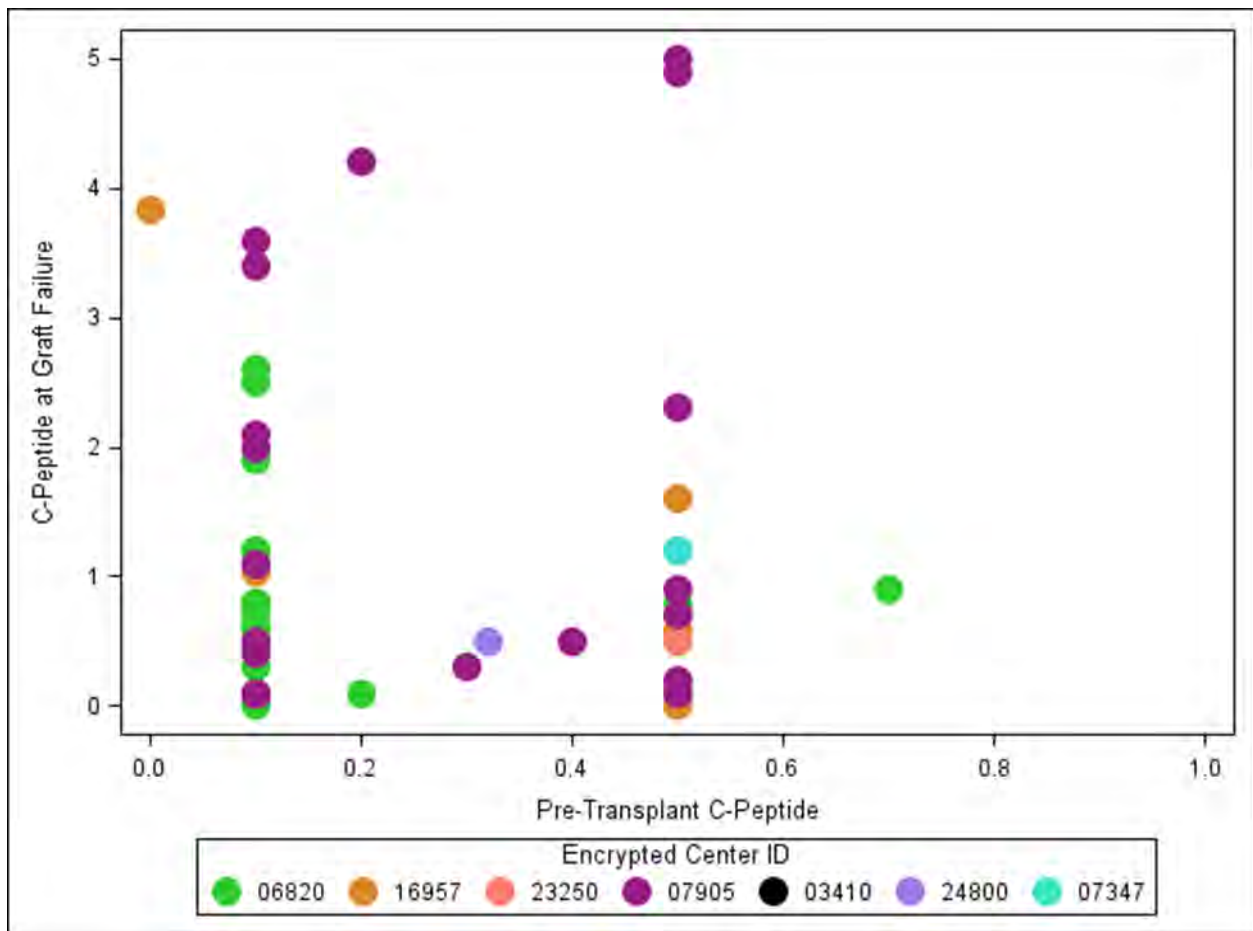


Figure 9 represents the bivariate distribution of all pairs of pre-transplant c-peptide values and c-peptide values at graft failure and the marker colors represent the centers that voluntarily submitted data as part of this project. It does not look like certain centers were reporting graft failures are higher levels than other centers.

The C-peptide Data Collection Study data presented here is compiled as voluntarily submitted by participating centers in the OPTN/UNOS Pancreas Transplantation Committee’s Definition for Pancreas Allograft Failure Project. C-peptide data on pancreas recipients are not currently required by the OPTN.

C-peptide Data Collection Study Conclusions

The study results show that pancreas graft failure is reported at various levels of pancreas functioning. There is variation between centers in how they report graft failure as well as a variation from patient-to-patient.

It appears that there is not a consistent c-peptide threshold that surgeons use to determine when a pancreas failed. The data suggests the practice is more of a case-by-case situation used to determine when the graft failed.

The c-peptide levels show a large fluctuation, which implies differing levels of pancreas function at graft failure. Graft failure is being reported at all levels of c-peptide values and patients are being returned to insulin at all levels of c-peptide values. There is variation in what surgeons constitute pancreas graft failure, and suspected variation in what surgeons call return to insulin. Notably, the reason that the return to insulin endpoint is variable could in part account for some variability of the c-peptide at return to insulin. However, this last point is merely suspect at this time.

The SRTR notified the Committee that the SRTR has performed a separate research project on oral agent use, insulin use, and pancreas graft failure. This separate research project is an analysis of merged OPTN and IMS data that shows:

- Many patients are on insulin after transplant. Some of these are reported as graft failures, while others are not.
- There is not sufficient evidence for a dose-response relationship between insulin and kidney graft failure or patient death.

Furthermore, similar to the results of the C-peptide Data Collection Study that the Committee performed, SRTR's analysis supports the need for a uniform definition of graft failure. The Committee did not request nor review the results of SRTR's study. The Committee is aware of this separate research project, and based on general background of the project, decided it did not need to review the data in detail, on the separate SRTR project in conjunction with this proposal.

Expected Impact on Living Donors or Living Donation:

Not applicable.

Expected Impact on Specific Patient Populations:

The specific patient populations impacted by this proposal are those patients who have received or will receive a pancreas, pancreas after kidney, or simultaneous kidney-pancreas transplant. The expected impact on these specific patient populations is how their graft status, regarding graft failure, is documented may change. The documentation may change depending upon how the surgeon currently documents pancreas graft failure. Specifically, modifications to the OPTN pancreas forms may effect a patient depending on when a surgeon declares a patients' pancreas graft has failed.

Expected Impact on Program Goals, Strategic Plan, and Adherence to OPTN Final Rule:

Pancreas transplant programs' graft outcomes cannot be accurately and fairly analyzed and compared against national expectations with the use of varying definitions for pancreas graft failure. A consistent definition will allow for graft outcome comparisons to a nationally derived expectation, which will promote transplant patient safety and improve post-transplant patient survival. Specifically, consistently and nationally reported pancreas graft failure data will strengthen the validity of future outcomes studies because the study results will be based on uniformly reported data.

Plan for Evaluating the Proposal:

After the proposal goes into effect and there is a sufficient follow-up time period the Committee will evaluate submitted data and center reporting every six months during the first year and

potentially annually for several years thereafter. The Committee will be looking at the parameters reported on the OPTN pancreas forms as well as the graft outcomes as reported by centers. The Committee will ask questions when analyzing and determining reporting trends. These questions will include but are not limited to:

- How is the pancreas graft failure definition fairing in practice?
- Are centers' graft survival data dramatically changing?
- Evaluate the values of c-peptide, HbA1c, and insulin use reported on OPTN adult and pediatric pancreas and kidney-pancreas Transplant Recipient Registration Form and Transplant Recipient Follow-up Form in conjunction with which follow-up form is being report (i.e. at graft failure, death, or routine follow-up) Are the OPTN pancreas forms being submitted incompletely?
- Does reporting of graft failure vary by center based on pancreas and kidney-pancreas recipient characteristics (i.e. BMI, c-peptide, insulin use, HbA1c)
- Does graft failure reporting vary by individual patient categories, such as age, gender, ethnicity, highly sensitized, geographic location.

Notably the Committee will be simultaneously evaluating impacts from changes to the pancreas allocation system as well as impacts from this proposal.

Additional Data Collection:

Additional data collection will be required because of the proposal's policy change. There will be additional fields added to the adult and pediatric pancreas and kidney-pancreas OPTN Data Collection Forms. Specifically, the following fields will be added to the Transplant Candidate Registration Form (TCR), Transplant Recipient Registration Form (TRR), and Transplant Recipient Follow-up Form (TRF) for pediatric and adult pancreas and kidney-pancreas candidates/recipients:

- Fasting C-peptide serum level (ng/ml)
- HbA1c (%)
- Insulin use – amount per kg/day and duration of use

These additional fields will be required on the pancreas and kidney-pancreas registration or follow-up forms solely when a patient is alive with a functioning pancreas graft.

The additional fields support the Principles of Data Collection in that the additional fields will allow further development of transplant policies. As acknowledged, the proposed definition of pancreas graft failure is a starting point. Due to the lack of national and consistent information available about what constitutes pancreas graft failure, the Pancreas Transplantation Committee chose to propose a basic definition at this time. The intent is that in the future, the definition may evolve and become more specific. Therefore, the additional data fields will provide the Pancreas Transplantation Committee the information it needs to develop a more specific definition of pancreas graft failure, in the future.

Expected Implementation Plan:

If public comment on this proposal is favorable, this proposal will be submitted to the OPTN Board of Directors in June 2015. If passed, the proposal would go into effect September 1, 2015.

In order to comply with the policy change a transplant center will need to be aware that a definition for pancreas graft failure exists in policy, be aware of the changes to the pancreas OPTN Data Collection Forms, and how the two changes interact. A transplant center will need to understand what constitutes pancreas graft failure, and how to fill out the graft status section of the pancreas OPTN Data Collection Forms.

Further, the transplant center should be aware there would be additional fields in the pancreas OPTN Data Collection Forms and the transplant center will be required to provide information in the additional fields when filling out the forms.

Communication and Education Plan:

This proposal will require a policy modification and changes to Tiedi forms. This proposal will be monitored for specific instructional needs. A small instructional program may likely be needed prior to the implementation of changes to Tiedi forms.

The specific Communication and Education efforts associated with the proposal are listed below.

Communication & Education Activities

- Policy notice
- System notice
- E-newsletter/member archive article
- Presentation at Regional Meetings
- Formal training (e-modules, Live Meetings, Webinars, etc.)
- Articles/Guidance Documents on the Web and Member Archive

Compliance Monitoring:

Based upon the proposed language, members will be expected to accurately report graft failure. However, the proposed language will not be added to the current routine monitoring of pancreas programs. Any data entered in UNetSM may be subject to OPTN review, and members are required to provide documentation as requested.

This proposal will improve the quality of the data available to the SRTR for analysis of program graft survival and production of the reports used by the Membership and Professional Standards Committee in its post-transplant performance reviews.

Policy or Bylaw Proposal:

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~).

1.2 Definitions

The definitions that follow are used to define terms specific to the OPTN Policies.

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Graft failure

For all organs except pancreas, graft failure occurs when any of the following occurs:

- ~~a~~ A recipient's transplanted organ is removed;
- ~~a~~ A recipient dies;
- ~~or a~~ A recipient is placed on a chronic allograft support system.

Pancreas graft failure occurs when any of the following occurs:

- A recipient's transplanted pancreas is removed
- A recipient re-registers for a pancreas
- A recipient registers for an islet transplant after receiving a pancreas transplant
- A recipient's insulin use is greater than or equal to 0.5 units/kg/day for a consecutive 90 days
- A recipient dies

3.6 Waiting Time

3.6.B.ii Non-function of a Transplanted Pancreas

Immediate and permanent non-function of a transplanted pancreas is defined as ~~pancreas graft failure requiring the removal of the transplanted pancreas within the first 14 days of~~ after transplant.

Pancreas waiting time will be reinstated when the OPTN Contractor receives a completed *Pancreas Waiting Time Reinstatement Form* and *either* of the following:

- An operative report of the removal of the pancreas.
- A statement of intent from the transplant hospital to remove the transplanted pancreas, and a statement that there is documented, radiographic evidence indicating that the transplanted pancreas has failed.

The transplant hospital must maintain this documentation. The OPTN Contractor will send a notice of waiting time reinstatement to the transplant hospital involved.