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The First Collective Examination of Immunosuppressive Practices Among American Intestinal Transplant Centers

Joshua Weiner, MD,[1] Nathaly Llore, MD,[1] Dylan Ormsby,[1] Masato Fujiki, MD,[2] Maria Cristina Segovia, MD,[3] Mark Obri, MD,[4] Syed-Mohammed Jafri, MD,[4] Jedson Liggett, MD,[5] Alexander H.K. Kroemer, MD, PhD,[5] Cal Matsumoto, MD,[5] Jang Moon, MD,[6] Pierpaolo Di Cocco, MD,[7] Gennaro Selvaggi, MD,[8] Jennifer Garcia, MD,[8] Armando Ganoza, MD,[9] Ajai Khanna, MD,[9] George Mazariegos, MD,[9] Danielle Wendel, MD,[10] and Jorge Reyes, MD[10] for The American Intestinal Transplantation Working Group

Background. Unlike other solid organs, no standardized treatment algorithms exist for intestinal transplantation (ITx). We established a consortium of American ITx centers to evaluate current practices. **Methods.** All American centers performing ITx during the past 3 y were invited to participate. As a consortium, we generated questions to evaluate and collect data from each institution. The data were compiled and analyzed. **Results.** Ten centers participated, performing 211 ITx during the past 3 y (range, 3–46; mean 21.1). Induction regimens varied widely. Thymoglobulin was the most common, used in the plurality of patients (85/211; 40.3%), but there was no consensus regimen. Similarly, regimens for the treatment of acute cellular rejection, antibody-mediated rejection, and graft-versus-host disease varied significantly between centers. We also evaluated differences in maintenance immunosuppression protocols, desensitization regimens, mammalian target of rapamycin use, antimetabolite use, and posttransplantation surveillance practices. Maintenance tacrolimus levels, stoma presence, and scoping frequency were not associated with differences in rejection events. Definitive association between treatments and outcomes, including graft and patient survival, was not the intention of this initial collaboration and is prevented by the lack of patient-level data and the presence of confounders. However, we identified trends regarding rejection episodes after various induction strategies that require further investigation in our subsequent collaborations. **Conclusions.** This initial collaboration reveals the extreme heterogeneity of practices among American ITx centers. Future collaboration will explore patient-level data, stratified by age and transplant type (isolated intestine versus multivisceral), to explore the association between treatment regimens and outcomes.

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The last few decades have witnessed significant technical, pharmacological, and immunologic advances in the field of intestinal transplantation.[1-3] These have improved outcomes and made intestinal transplantation the best option for patients with irreversible intestinal failure who have failed total parenteral nutrition management.[4] However, despite these improvements, intestinal transplantation has the highest rejection rate among solid organ transplants.[5] This has

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[1] Center for Liver Disease and Transplantation, Columbia University Irving Medical Center, New York, NY.

[2] Department of Surgery, Cleveland Clinic, Cleveland, OH.

[3] Department of Medicine, Duke University Medical Center, Durham, NC.

[4] Department of Medicine, Henry Ford Hospital, Detroit, MI.

[5] MedStar Georgetown Transplant Institute, Washington, DC.

[6] Department of Surgery, Mount Sinai Medical Center, New York, NY.

[7] Department of Surgery, University of Illinois Hospital, Chicago, IL.

[8] Miami Transplant Institute, University of Miami Jackson Memorial Hospital, Miami, FL.

[9] Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.

[10] Departments of Surgery and Pediatrics, University of Washington Medical Center/Seattle Children's Hospital, Seattle, WA.

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N.L., D.O., and J.W. are lead authors.

Correspondence: Joshua Weiner, MD, Department of Surgery, Division of Abdominal Organ Transplantation, New York Presbyterian/Columbia University Irving Medical Center, New York, NY 10032. (jiw2106@cumc.columbia.edu).

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required high levels of immunosuppression, predisposing patients to complications, such as infection, malignancy, and graft-versus-host disease (GVHD).[6,7] Complicated posttransplant courses and outcomes relatively inferior to other solid organ transplants, as well as changes in nationwide referral patterns and improvements in parenteral nutrition, have led to decreasing numbers of intestinal transplants.[8] As the practice of intestinal transplantation decreases, fewer physicians and surgeons are regularly exposed to the management of these patients during training, contributing to a further decrease in the number of future intestinal transplants.

The lack of standardized immunosuppression protocols and rejection treatment algorithms limits efforts to achieve better outcomes in intestinal transplantation. Additionally, large studies are not possible due to the small overall number of patients and different types of allografts (±colon, liver, entire foregut, etc) as well as lack of communication, data sharing, and efforts to identify best practices among the American intestinal transplant centers. The few existing exchanges of information indicated that the practices at individual centers are highly variable and continue to diverge. Recognizing the scope of these problems and their importance to the future of intestinal transplantation, we formed a consortium of intestinal transplant centers located in the United States (American Intestinal Transplantation Working Group) to address these concerns.

The goal of our initial collaboration was to present a comprehensive accounting of the pharmacological regimens currently being used by the participating centers for induction and maintenance immunosuppression; treatment algorithms for rejection, GVHD, and posttransplant lymphoproliferative disorder (PTLD); desensitization protocols; and posttransplant surveillance practices. Data stratifying by age and by type of transplant as well as definitive associations between treatments and graft/patient survival are planned for a follow-up study. The data herein reveal patterns in our current practices and identify several emerging trends in management (eg, desensitization protocols, decreased frequency of stoma creation, surveillance endoscopy) so they may be shared and evaluated more widely.

MATERIALS AND METHODS

Center Recruitment

Centers in the United States that performed at least 1 intestinal transplant for patients of any age during the past 3 y were identified using the Scientific Registry of Transplant Recipients database and recruited for the study. We focused on protocols and practices updated during the past 3 y (transplants performed between 2020 and 2022) to analyze our current practices rather than historical protocols. Accepting centers were encouraged to have 1 site director to take ownership of the data from that center and 1 site lead to assist with gathering data.

Compiled Assessment and Data Analysis

We generated a list of questions to address as a group. All centers had the opportunity to review the list of compiled questions and make suggestions before a final list was agreed upon. The collaborators at each center collected and verified their center's data for adult and pediatric case volume, rejection episodes with frequency and grade, and incidence of GVHD and PTLD for all intestinal and multivisceral transplants during the study period. We also collected each center's posttransplant management protocols for ACR, humoral rejection, GVHD, PTLD, induction immunotherapy, maintenance immunotherapy, desensitization, and posttransplant surveillance protocol. Given the aggregate and deidentified nature of the data, no institutional review board approval was necessary. The answers from each center were compiled into a single Excel spreadsheet. Excel was also used to calculate statistics and generate tables and graphs. The article, figures, and tables were shared within the group for editing and approval before submission.

RESULTS

Center Demographics

Of the 15 active American intestinal transplant centers, 13 responded and agreed to participate. Of these 13 centers, 3 subsequently withdrew because of changes in personnel (n = 1) and time constraints (n = 2). The participating centers were located throughout the country, and the vast majority of the intestinal transplants performed during the study period: 211 transplants between 2019 and 2022 (79% out of a total of 268 transplants performed during the study period). The range among the 10 participating centers was 3 to 46 transplants (mean 21.1) (Table 1). However, the average center volume is misleading because the data confirm the idea that, even among the small group of intestinal transplant centers, the majority are performed at an even smaller number of high-volume centers. Although the mean per center is 21.1, the median is 17.5, and half (5/10) of the centers performed ≤10 transplants during the study period.

Patient Demographics

Adult transplants significantly outnumbered pediatric transplants (≤18 y of age). There were 65 pediatric transplants performed compared with 146 adult transplants. The average number of pediatric transplants performed at each center was 6.5 (range, 0–18) compared with a mean of 14.6 adult transplants (range, 0–30; Table 1). Only 1 center performed exclusively pediatric transplants, whereas 2 centers performed exclusively adult transplants. Of the 7 centers that performed both adult and pediatric transplants, adult transplants outnumbered pediatric transplants at all but 2 centers. The median and mode of pediatric transplants among our centers are 4.5 and 5, respectively, versus 9.5 and 30 for adult transplants.

TABLE 1.

Adult and pediatric transplants per center

Center	Total transplants	>18 y	<18 y
1	42	29	13
2	9	8	1
3	35	30	5
4	10	10	0
5	46	30	16
6	6	6	0
7	25	21	4
8	3	0	3
9	8	3	5
10	27	9	18
Total	211	146	65

Induction Regimens by Center

Thymoglobulin is the most commonly used induction agent and is used for some or all patients at all centers, either alone or in combination with other agents. However, there is a large variety of induction regimens used among our consortium, even within individual centers: 5 different regimens were used among the 10 centers. Note that numbers do not add up to 100% because 4 centers (40%) chose from multiple regimens. The regimens and the number of centers using these regimens are as follows: thymoglobulin (n = 9; 90%), thymoglobulin/rituximab (n = 2; 20%), infliximab (n = 1; 10%), basiliximab (n = 1; 10%), and alemtuzumab (n = 1; 10%) (Figure 1). In terms of the choice of induction regimen among the 4 centers with multiple options, thymoglobulin was chosen over alternatives in cases of more extensive transplants (multivisceral rather than isolated intestine), history of malignancy, history of prior transplant, or elevated recipient sensitization. Steroids were used in almost 100% of patients, regardless of the remainder of the induction regimen, and are therefore not included in our analysis.

Induction Regimens by Patient

The number of centers using each regimen differed from the number of patients receiving those regimens because the regimens used at high-volume centers were more commonly used overall. The number (percentage) of patients receiving each regimen was 85 (40.3%) for thymoglobulin, 62 (29.4%) for thymoglobulin/rituximab, 30 (14.2%) for alemtuzumab, 29 (13.8%) for basiliximab, and 1 (0.5%) for infliximab (Figure 2).

Association of Induction Agents With Outcomes

Rejection

The aggregate nature of our data does not allow for a definitive analysis of associations between treatments and outcomes.

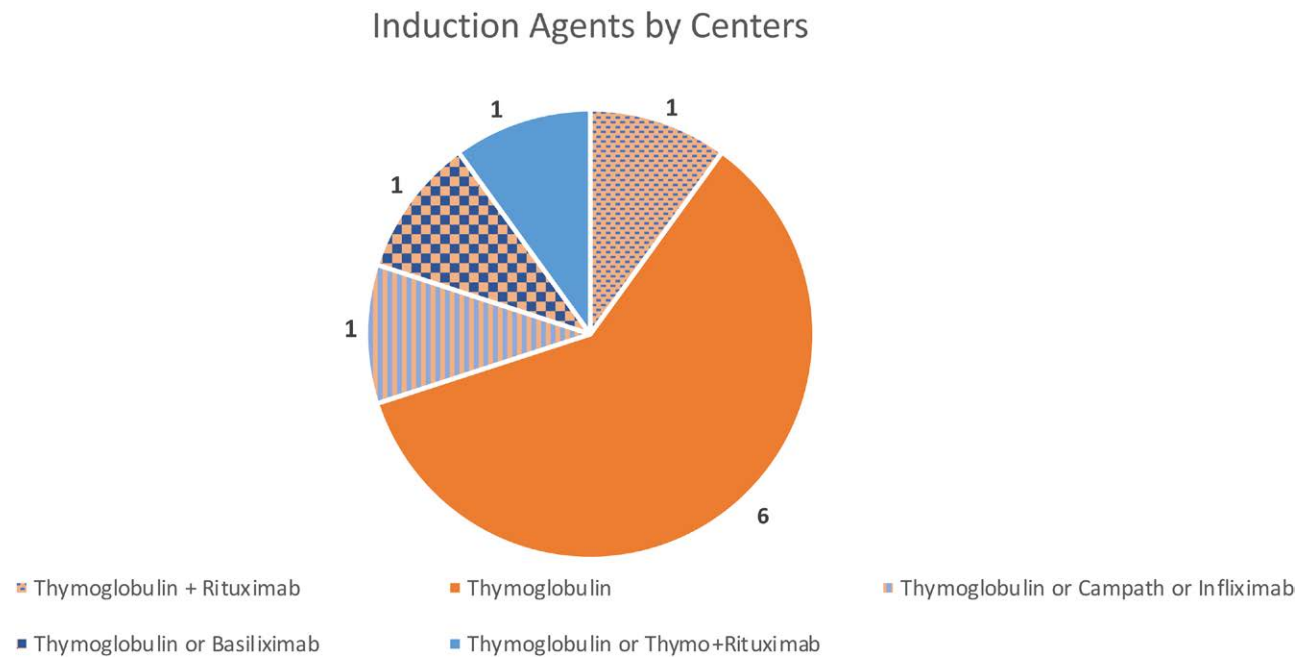

FIGURE 1. Induction agents by centers. Pie chart demonstrating the induction immunosuppression regimens used among the 10 participating centers.

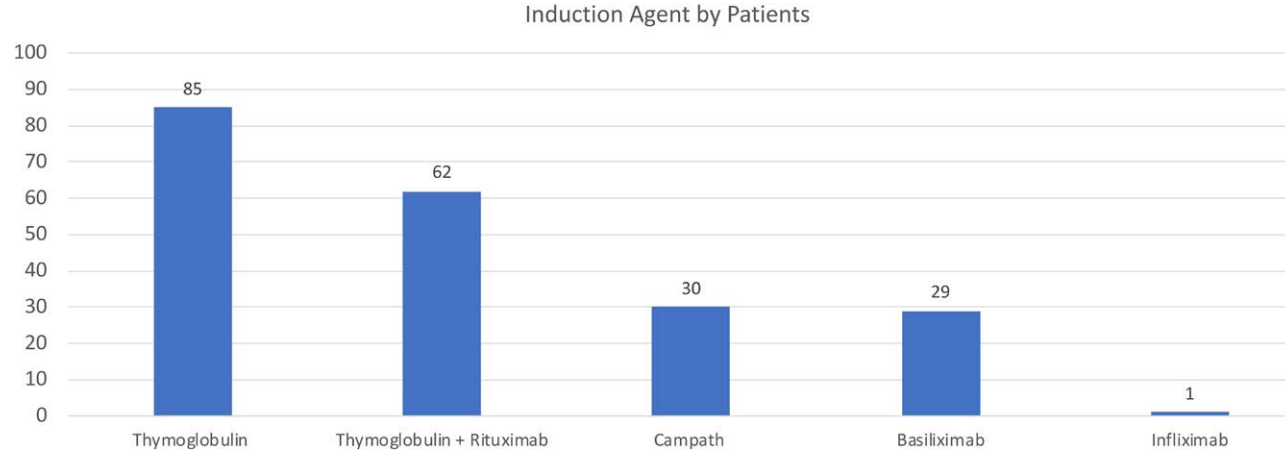

FIGURE 2. Induction agents by patients. Bar graph demonstrating the induction immunosuppression regimen used among the 211 patients.

Although this will be the subject of our future work, we preliminarily examined trends associated with various treatments, which contain multiple confounders (eg, combining adult and pediatrics, isolated intestine, multivisceral transplantation) and are not statistically significant. Figure 3A shows the association of induction regimens with subsequent rejection events on a macroscopic level. Thymoglobulin alone was associated with the highest incidence of subsequent rejection in 40 of 85 patients (47%). However, when rituximab is added, the combination of thymoglobulin/rituximab infusion is associated

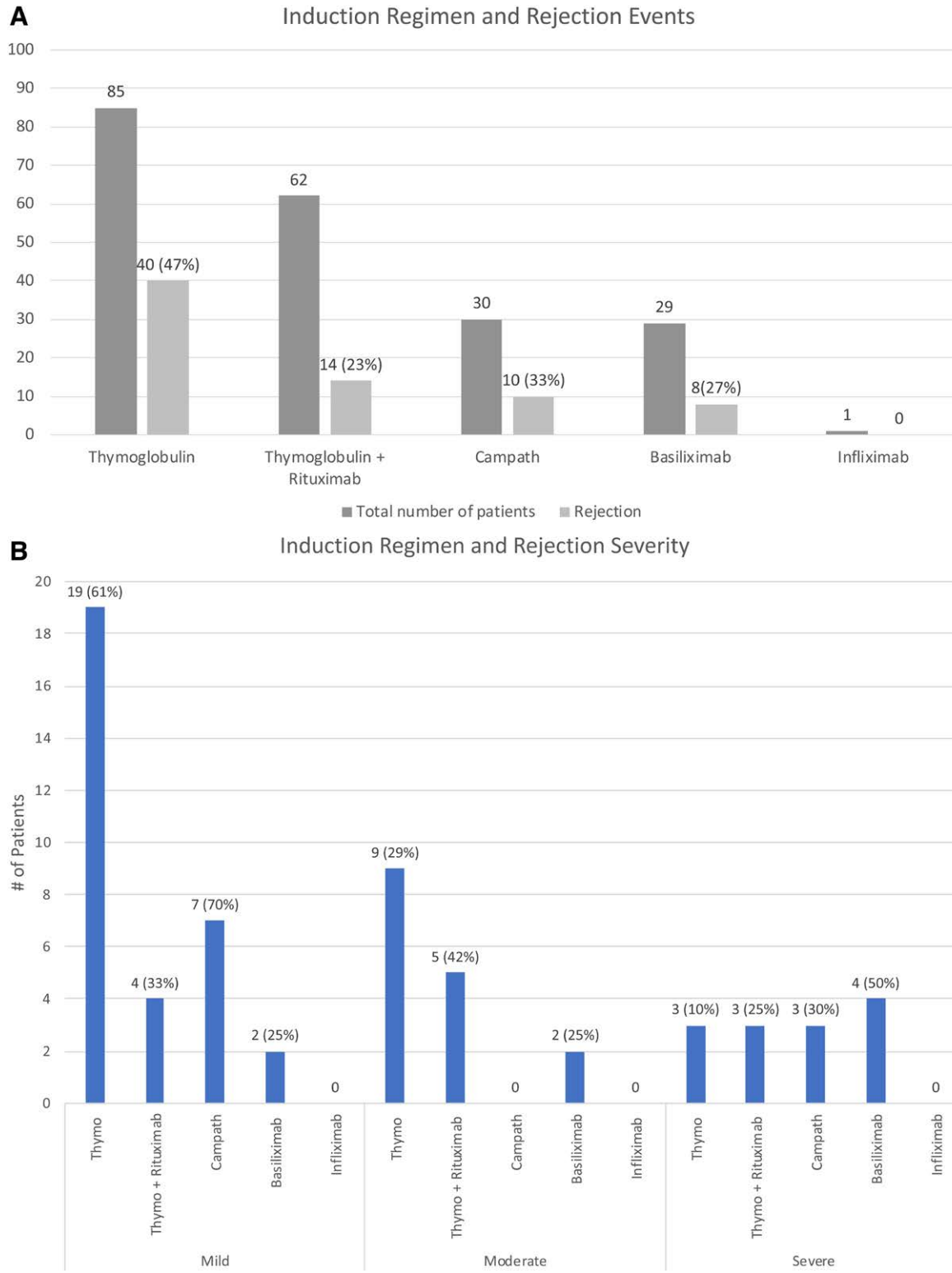

FIGURE 3. Rejection as a function of induction immunosuppression agents. A, Induction regimen and rejection events. Bar graph demonstrating the percentage of patients receiving each induction regimen who subsequently had a rejection event. B, Induction regimen and rejection severity. Bar graph demonstrating the number (and percentage) of patients who had mild, moderate, or severe rejection events subsequent to receiving each induction regimen. Not all patients had data regarding the severity of rejection episodes.

with the lowest rate of subsequent rejection events in 14 of 62 patients (23%). Alemtuzumab was associated with subsequent rejection events in 10 of 30 patients (33%) and basiliximab in 8 of 29 patients (27%). Infliximab alone was used in only a single patient who did not have a subsequent rejection event.

Interestingly, when data for the severity of rejection events were available, the association of induction regimens with subsequent rejection events was different from the association with the severity of the rejection event (Figure 3B). For example, although thymoglobulin induction was associated with the highest rate of subsequent rejection episodes, 61.3% of these episodes were mild, 29% were moderate, and only 9.7% (total 3 episodes) were severe. In contrast, the decreased rate of rejection episodes in patients who received the combination of thymoglobulin/rituximab was mostly due to a decreased rate of the mildest episodes. Only 33.3% of the episodes were mild, but the rates of moderate and severe rejections episodes were 41.7% and 25%, respectively. Thus, thymoglobulin/rituximab was associated with a lower rate of rejection episodes than thymoglobulin alone, but the rate of moderate rejection was approximately 1.3-fold higher, and the rate of severe rejection was approximately 2.5-fold higher, with the difference in the overall rejection episode rates resulting from an almost 2-fold higher rate of mild rejection episodes in the patients receiving thymoglobulin alone. Similarly, basiliximab, with a relatively low 27% rate of rejection episodes, had the highest rate of severe rejection episodes at 50%, with an additional 25% representing moderate rejection episodes. Only 25% of rejection episodes after basiliximab induction were mild. Alemtuzumab, like thymoglobulin alone, was associated with mostly mild rejection (70%) compared with 30% severe and no moderate rejection episodes.

Graft-Versus-Host Disease

The number of patients experiencing GVHD was lower during this period compared with the historical rate of GVHD in the literature.[9] Only 11 patients (5.2%) had GVHD episodes. The rate among centers ranged from 0% to 16.7% (Figure 4). The induction regimens associated with subsequent GVHD were thymoglobulin (n = 7; 8.2%), thymoglobulin/rituximab (n = 3; 4.8%), and basiliximab (n = 1; 3.4%). No GVHD episodes were seen with alemtuzumab or infliximab (Figure 4). There was no obvious association between the induction regimen and subsequent GVHD.

Posttransplant Lymphoproliferative Disorder

Overall, 12 (5.7%) patients developed PTLD. The induction regimens associated with subsequent PTLD were thymoglobulin (n = 6; 7.1%), thymoglobulin/rituximab (n = 2; 3.2%), alemtuzumab (n = 3; 10%), and basiliximab (n = 1; 3.4%). There were no episodes of PTLD seen after infliximab induction (Figure 5). There was no obvious association between induction regimen and subsequent PTLD.

Treatment Algorithms

Treatment algorithms differed markedly between centers and have not previously been widely shared. We herein present the current practices among participating centers for maintenance immunosuppression, ACR, AMR, GVHD, and PTLD.

Maintenance Immunosuppression

Although all centers use tacrolimus, with 1 center substituting sirolimus for pediatric patients, the therapeutic range is highly variable between centers, with some centers having target levels as low as 8 to 10 ng/mL, whereas others target levels as high as 20 to 25 ng/mL (Table 2) in both adult and pediatric patients. Although our data are not powered or controlled for definitive analysis, there is no obvious association between lower levels and increased rejection. Patients at the 2 centers with the highest tacrolimus goals had a 70% and 100% rate of rejection events, whereas the rejection event rate at the 2 centers with the lowest tacrolimus goals was 44% and 0%.

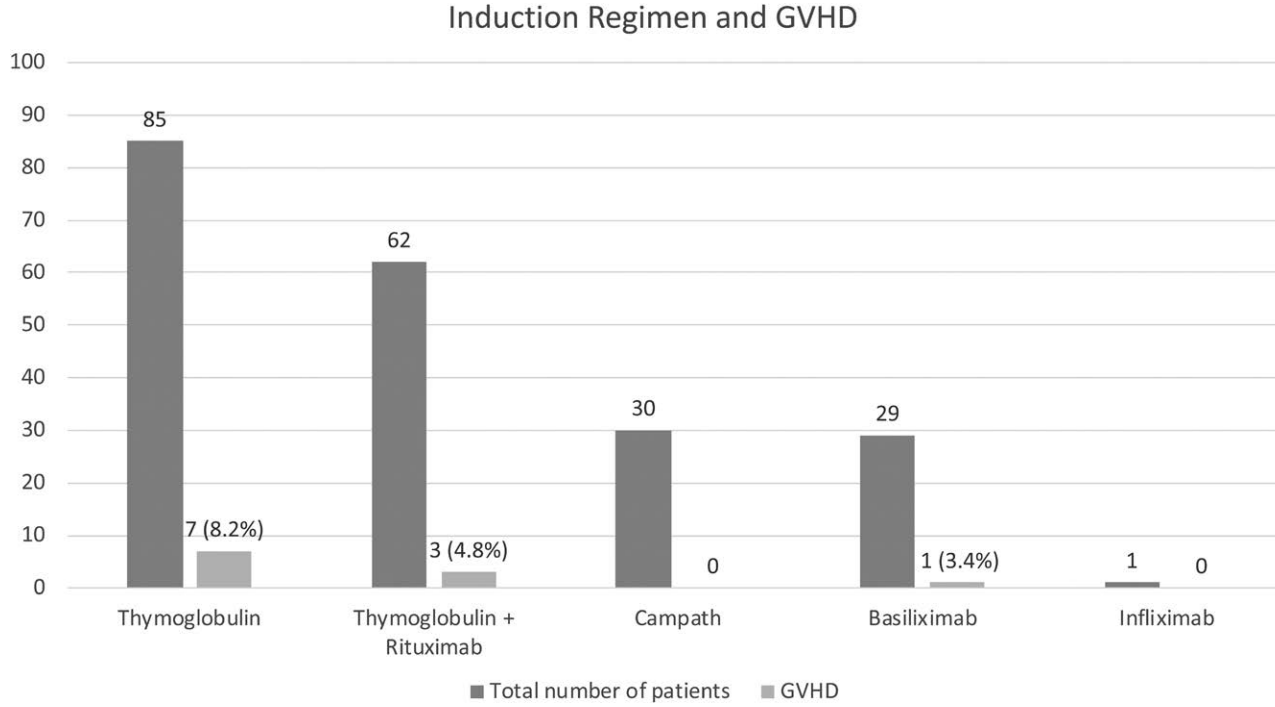

FIGURE 4. Induction regimen and GVHD. Bar graph demonstrating the percentage of patients receiving each induction regimen who subsequently had GVHD. GVHD, graft-versus-host disease

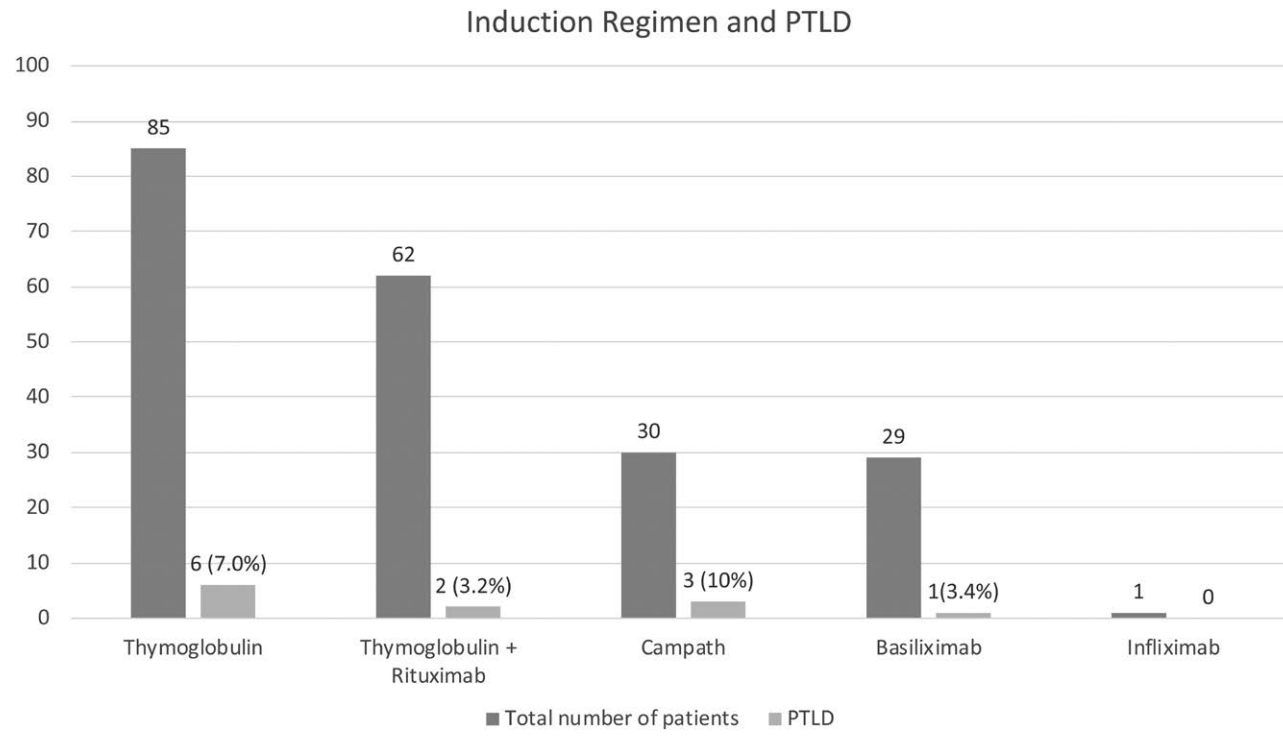

FIGURE 5. Induction regimen and PTLD. Bar graph demonstrating the percentage of patients receiving each induction regimen who subsequently had PTLD. PTLD, posttransplant lymphoproliferative disorder.

TABLE 2.

Tacrolimus weaning protocols by center

Center	0–3 mo	3–6 mo	6–12 mo	>1 y
1	10–15 (liver-inclusive) 12–18 (no liver)	8–10 (liver-inclusive) 10–12 (no liver)	7–8 (liver-inclusive) 8–10 (no liver)	5–6 (liver-inclusive) 7–8 (no liver)
2	10 to 15	8 to 12	8 to 12	8 to 12
3	8 to 10	8 to 10	8 to 10	6 to 9
4	12 to 15	Not answered	Not answered	Not answered
5	20–25 (mo 1), 15–20 (mo 2), 12–15 (mo 3)	8–12	5–8	5–8
6	10–15	10–15	10	10
7	14–16	12–14	10–12	6–10
8	8–10	8–10	8–10	8–10
9	15–20	10–15	10–15	8–10
10	10–11	8–10	7–8	7–8

The algorithms for tapering tacrolimus were also variable between centers (Table 2). Likewise, the use of mTOR inhibitors (timing of use and indications for use) and the inclusion of other agents, such as basiliximab and sirolimus/everolimus, in maintenance immunosuppression protocols varied widely between centers (Table 3). We did not collect data regarding long-term steroid dosing or weaning.

Acute Cellular Rejection

Treatment algorithms for acute cellular rejection (ACR) are highly variable (Table 4). However, the one intervention that is universal is that steroid pulse is the first-line treatment. In addition to steroids, 2 centers additionally increase calcineurin inhibitor (CNI) doses, and 1 center uses vedolizumab. For severe or refractory rejection, the regimens differ by center. Thymoglobulin is the most frequently used agent (5/10 centers), with other centers using infliximab, alemtuzumab, and increased CNI doses.

Antibody-Mediated Rejection

Antibody-mediated rejection (AMR), which participating centers defined on the basis of the combination of donor-specific antibody and C4d staining/capillaritis on histology, also had variable treatment algorithms between centers (Table 5). First-line treatment most often included steroid pulse, often with IVIG (78% of centers) or plasmapheresis (67% of centers). Some centers added alemtuzumab, thymoglobulin, or rituximab. Second-line therapies varied even more widely, with some targeting T cells and some targeting B cells. Agents included thymoglobulin (n = 1 center), alemtuzumab (n = 1), rituximab (n = 3), bortezomib (n = 3), and infliximab (n = 1).

GVHD and PTLD

The first-line treatment in all programs with patients who developed GVHD was methylprednisolone. Thymoglobulin, alemtuzumab, antithymocyte globulin (Atgam), and ruxolitinib were second-line GVHD treatments. All programs

TABLE 3.

Variations on maintenance immunosuppression by center

Center	Timing to start mTOR inhibitor (postop)	Timing to start MMF	Additional maintenance immunosuppression
1	3–6 mo	POD 1	Steroids occasionally
2	1 mo	POD 1	Basiliximab before discharge then monthly for 1 y, bimonthly thereafter
3	1 mo	Not used	No
4	3 mo	Rarely used	Azathioprine, everolimus, and sirolimus for patients with poor renal function Monthly basiliximab × 12 doses for isolated intestine and modified MVT patients only
5	7 d	if not tolerating sirolimus	No
6	6 mo–1 y	POD 1	
7	Only if renal injury	POD 0 if combined with kidney Tx	No
8	Rarely used	Rarely	
9	1 mo	Early postop for DSA issues	No
10	Rarely used	1 wk	

DSA, donor-specific antibody; MMF, mycophenolate mofetil; mTOR, mammalian target of rapamycin; MVT, multivisceral transplantation; POD, postoperative day; postop, postoperative; Tx, transplant.

TABLE 4.

Variations on ACR treatment by center

Center	ACR treatment (first line)	ACR treatment (second line)
1	Methylprednisolone + vedolizumab	Alemtuzumab
2	Methylprednisolone	Infliximab
3	Methylprednisolone	Thymoglobulin
4	Methylprednisolone	
5	Methylprednisolone	Infliximab
6	Increase tacrolimus and prednisone	Tacrolimus
7	Methylprednisolone	Thymoglobulin
8	Methylprednisolone	Thymoglobulin
9	Methylprednisolone + increase tacrolimus/sirolimus by 30%	Thymoglobulin
10	Methylprednisolone	Thymoglobulin

ACR, acute cellular rejection.

TABLE 5.

Variations on AMR treatment by center

Center	AMR treatment (first line)	AMR treatment (second line)
1	Alemtuzumab + IVIG + rituximab ± plasmapheresis	Bortezomib
2	Plasmapheresis + IVIG	
3	Methylprednisolone	Thymoglobulin
4	Plasmapheresis + IVIG ± rituximab	Bortezomib vs alemtuzumab
5	IVIG	Plasmapheresis + IVIG + rituximab
6	Not answered	Not answered
7	Plasmapheresis + IVIG + rituximab	Infliximab
8	Methylprednisolone + thymoglobulin + IVIG	
9	Plasmapheresis + IVIG + methylprednisolone	Rituximab, bortezomib
10	Methylprednisolone	Rituximab

AMR, antibody-mediated rejection.

treated PTLD by decreasing immunosuppression and giving rituximab. Remarkably, only 1 of the 10 patients with PTLD did not recover after treatment.

Desensitization Protocols and Outcomes

Only 4 centers reported having established desensitization protocols, which consisted of (1) plasmapheresis, IVIG, and rituximab; (2) plasmapheresis and IVIG; and (3) rituximab alone. The threshold for the use of these protocols was heterogenous. One center reported no defined threshold, 1 used a PRA >30%, and 1 used positive crossmatch in the presence of donor-specific antibody. The center that used all 3 modalities (plasmapheresis, IVIG, and rituximab) had no rejection in the only patient undergoing this protocol. Both patients receiving plasmapheresis and IVIG without rituximab experienced rejection (Table 6).

Surveillance Practices

As with other practices we have examined, the schedule of surveillance endoscopy/biopsies, and even the choice of whether to create a stoma, is similarly widely divergent among centers (Table 7). Centers that do not create stomas perform endoscopy either at very few set time points or only for cause. Centers that create stomas perform endoscopy on schedules ranging from twice per week to only for cause. Our data are not powered in this study to indicate any clear association between scoping practices and rates or severity of rejection episodes, although this is a goal of future work.

DISCUSSION

This is a landmark collaborative effort among the active American intestinal transplant centers to share and compare current treatment and surveillance protocols. We herein examine our patient demographics, induction regimens,

TABLE 6.

Variations on desensitization protocols by center

Center	Desensitization protocol	Threshold for protocol	Patients w/ rejection episode	Patients w/ protocol
1	Plasmapheresis + rituximab + IVIG	Not defined	0	1
2	Plasmapheresis + IVIG	PRA >30%	2	2
3	Rituximab	Positive CM w/ positive DSA	0	0
4	Plasmaphereis + bortezumab	PRA >70% or multiple positive CM	0	1

CM, crossmatch; DSA, donor-specific antibody; PRA, panel reactive antibody.

TABLE 7.

Variations on surveillance protocols by center

Center	Graft monitoring
1	If stoma: endoscopy weekly × 6 wk then every 2 wk If no stoma: once within the first month and PRN Frequency increased if retransplanted for rejection
2	Endoscopy biweekly × 4 wk Endoscopy weekly: 1 to 4 mo, endoscopy monthly: 4 to 12 mo
3	Endoscopy biweekly × 3 wk Weekly to postop 2 mo Biweekly to postop 4 mo Monthly to postop 6 mo Every 3 mo to postop 1 y, at 1.5 y, at 2 y then annually DSA weekly to 1, 2, 3, and 6 8 mo then every 6 mo
4	Clinic visits may include ileoscopy/zoomscope and biopsy of the intestinal allograft, frequency to be determined by transplant surgeon as needed (clinic visits every 2nd or 3rd week for 1st year)
5	Twice weekly for 1½ mo Weekly from 1½ to 3 mo Biweekly from 3 to 5 mo Monthly from 5 to 12 mo or until ileostomy closure Annually thereafter
6	
7	No surveillance protocol, endoscopic evaluation only when indicated
8	
9	Weekly × 1 mo Every 2 wk × 1 mo, then monthly For cause after 4 mo
10	Enteroscopy (q 3 mo after DC; and annually if no rejection) Annual DSA and pleximune study

DC, discharge; DSA, donor-specific antibody; postop, postoperative; PRN, as needed.

maintenance immunosuppression regimens, treatment algorithms for rejection, GVHD, and PTLD, desensitization protocols, and posttransplant surveillance practices. Overall, we found great variability in practices from center to center, and, for the first time, we shared among our group exactly what those variable practices entail. The presentation of our collective practices in this article clarifies the magnitude of this problem and highlights the importance of our effort to share information about our practices and work together to reach a consensus about best practices. We also identified areas of evolving strategies and possible trends that deserve closer investigation in our follow-up study.

In this first collaborative step, we focused on creating a framework in which our centers could work together to communicate and compare data. For future collaboration, we aim to include centers that have not yet been involved and to associate specific treatment regimens with outcomes, such as graft survival, patient survival, and resolution of immune events being treated (ie, ACR, AMR, GVHD), to identify best practices. This effort is based on a learning system approach in which collaboration and sharing of current practices may lead to more rapid identification of knowledge, outcome gaps, and variances. An example of this is the Starzl Network for Excellence in Pediatric Transplantation (www.starzlnetwork.org).[10]

This initial study cannot (and was not intended to) draw firm conclusions about the risks versus benefits of the various treatment regimens discussed due to a lack patient-level detail, lack of adequate power of study populations, and presence of multiple confounders (eg, combining adult and pediatrics, isolated intestine and multivisceral transplantation). However, several interesting patterns nonetheless emerge. The first is that the use of thymoglobulin alone as the induction regimen appears to be associated with a higher rate of subsequent rejection episodes than other induction regimens. In contrast, the higher rate of rejection episodes after thymoglobulin induction is primarily in the incidence of mild rejection, whereas the incidence of moderate and severe rejection episodes is relatively low. Conversely, the lowest incidence of rejection episodes is associated with thymoglobulin/rituximab induction, but fewer episodes of mild rejection represent the differential but more episodes of moderate and severe rejection. Similarly, basiliximab induction is associated with fewer subsequent rejection episodes than thymoglobulin; however, it tends to be moderate or severe when rejection occurs. Therefore, the incidence of rejection associated with certain induction regimens might be a less important metric than the severity of rejection. This is something that will be addressed in the next part of our collaborative study.

The question of whether certain therapies are associated with mild versus moderate or severe rejection is particularly relevant due to the current change in practice regarding the frequency of surveillance scopes or even whether to create a stoma, as shown in Table 7. As mild ACR is often a histological diagnosis based on apoptotic bodies and often lacks clinical signs or symptoms, it is likely that the incidence of mild rejection is overreported. One study of ileal biopsy findings in healthy adults without transplants found that, based on apoptotic bodies alone, 55% would be read as indeterminate for rejection and 10% would be read as mild rejection.[11] Therefore, it is unclear whether acute rejection episodes diagnosed by histology alone without clinical signs/symptoms or obvious changes in endoscopic appearance represent true rejection, especially because apoptotic bodies can be physiological or result from other types of inflammation, medication effect, or viral infection.[11,12] It remains unknown whether asymptomatic mild rejection is clinically significant if it does not progress. Given the morbidity associated with treatment of rejection, such as steroid pulse or thymoglobulin, this gives urgency to the current debate among intestinal transplant surgeons about how frequently to scope other than for cause and whether a stoma remains necessary for surveillance.[13]

Our collaborative findings raise a few additional questions. One is whether goal tacrolimus levels should be lower. The range in targeted levels (Table 2) is broad but has no obvious correlation with rejection incidence. Therefore, because higher tacrolimus levels are associated with higher morbidity and various tacrolimus-minimizing regimens have shown improved graft and patient survival with a decreased complication related to immunosuppression,[14,15] it is worth evaluating in our future work whether targeting lower tacrolimus levels is beneficial. Similarly, the role of mTOR inhibitors and desensitization protocols, used successfully at some centers (Tables 3 and 6), should be evaluated further in our future work.

Perhaps the most important outcome of this study is that it is the first step in establishing continuing collaboration. Although there are a small number of multicenter collaborations regarding specific questions about intestinal transplant practices,[16,17] there has been no prior effort to disclose and compare practices more broadly or to identify consensus

about best practices. This is partially due to the small number of centers performing intestinal transplantation and the small number of patients at each center, which limits the availability of high-quality outcomes data. Although our collaboration is the first comparison of current intestinal transplantation treatment regimens across American centers and has demonstrated important trends and raised important questions, it also has acknowledged weaknesses. The most obvious weakness is that, despite our recruitment efforts, not every center participated. Therefore, our results and conclusions might be affected by missing data. Second, the current study was not designed to evaluate outcomes definitively. Third, we did not differentiate between intestinal and multivisceral transplants or adult and pediatric patients in analysis of data in this phase. Our aim is that the next phase of this study will include additional centers and will pivot to examining the outcomes of the regimens discussed in this article to identify best practices. In the meantime, we are proud of our collaborative work and the lessons it has already revealed. We hope that it will be as valuable to readers, especially in the intestinal transplant community, as it has been to us, and we look forward to continuing our work together to improve intestinal transplant outcomes.

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