Long-Term Outcomes of Intestinal and Multivisceral Transplantation at a Single Center in Argentina

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ABSTRACT

Background. Intestinal failure (IF) patients received parenteral nutrition (PN) as the only available therapy until intestinal transplantation (ITx) evolved as an accepted treatment. The aim of this article is to report the long-term outcomes of a series of ITx performed in pediatric and adult patients at a single center 9 years after its creation.

Patients and Methods. This is a retrospective analysis of the ITx performed between May 2006 and January 2015. Diagnoses, pre-ITx mean time on PN, indications for ITx, time on the waiting list for types of ITx, mean total ischemia time, and warm ischemia time, time until PN discontinuation, incidence of acute and chronic rejection, and 5-year actuarial patient survival are reported.

Results. A total of 42 patients received ITx; 80% had short gut syndrome (SG); the mean time on PN was 1620 days. The main indication for ITx was lack of central venous access followed by intestinal failure–associated liver disease (IFALD) and catheter-related infectious complications. The mean time on the waiting list was 188 days (standard deviation, ±183 days). ITx were performed in 26 children and 14 adults. In all, 32 procedures were isolated ITx (IITX); 10 were multiorgan Tx (MOT; 3 combined, 7 multivisceral Tx (MVTx), 1 modified MVTx and 2 with kidney); 2 (4.7 %) were retransplantations: 1 IITx, 1 MVTx, and 5 including the right colon. Thirteen patients (31%) received abdominal rectus fascia. All procedures were performed by the same surgical team. Total ischemia time was 7:53 ± 2:04 hours, and warm ischemia time was 40.2 ± 10.5 minutes. The mean length of implanted intestine was 325 ± 63 cm. Bishop–Koop ileostomy was performed in 67% of cases. In all, 16 of 42 Tx required early reoperations. The overall mean follow-up time was 41 ± 35.6 months. The mean time to PN discontinuation after Tx was 68 days ($P = .001$). The total number of acute cellular rejection (ACR) episodes until the last follow-up was 83; the total number of grafts lost due to ACR was 4; and the total graft lost due to chronic rejection was 3. At the time of writing, the overall 5-year patient survival is 55% (65% for IITx vs 22% for MOT; $P = .0001$); 60% for pediatric recipients vs 47% for adults (P = NS); 64% when the indication for ITx was SG vs 25% for non-SG ($P = .002$).

Conclusions. At this center, candidates with SG, in the absence of IFALD requiring IITx, showed the best long-term outcomes, independent of recipient age. A multidisciplinary approach is mandatory for the care of intestinal failure patients, to sustain a rehabilitation and transplantation program over time.

SEVERAL years have passed since the first intestinal transplantation (ITx), combined liver–intestinal transplantation (LITx), and multivisceral transplantation (MVTx) were performed. Indications, surgical techniques, protocols for immunosuppression, and patient care before

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and after transplantation have evolved in the last decades; the results of that evolution are reflected by improved short and long term results [1,2]. Nevertheless, in many developing countries, parenteral nutrition (PN) is the only and final option for patients with intestinal failure, because the development of intestinal transplantation has been limited by dismal results and lack of muldisiciplinary intestinal failure programs. In this article, we report the long-term outcomes of a series of intestinal transplantations performed in pediatric and adult patients at a single center in Argentina.

PATIENTS AND METHODS

We report a retrospective database analysis of all transplants containing an intestinal graft performed between May 2006 and January 2015 at Hospital Universitario–Fundación Favaloro, Buenos Aires, Argentina. Diagnoses, mean time on PN before intestinal transplantation (ITx), indication for ITx, time on waiting list (WL), types of ITx, mean total ischemia time (TIT), warm ischemia time (WIT), surgical technical details, post-ITx time until PN discontinuation, use of a pretransplantation immunological risk–based protocol for immunosuppression, incidence of acute and chronic rejection, freedom-from-rejection survival, graft and patient survival, and long-term nutritional status are analyzed and reported.

During the pre-Tx evaluation, the patients were prospectively divided into 2 immunological risk categories: a low-risk (LR) group, which included candidates for isolated ITx receiving a primary procedure, with ABO-compatible match, or patients with low PRA titer (below 30%); and a high-risk (HR) group, which included candidates requiring a multiorgan graft (LITx or MVTx) or retransplantations, patients with ABO-compatible mismatch, patients with high PRA titer (>30%), and patients with B-cell–positive crossmatch; in the last 2 cases, a desensitization protocol was used [3]. The primary immunosuppressive protocol was defined according to patient category as follows. The LR group received induction with interleukin-2 (IL-2) antibodies 10 mg/IV in patients <30 kg, and 20 mg/IV in >30 kg, on post-ITx days 0 and 4, combined with steroids, tacrolimus, and mycophenolate mofetil. The HR group received induction with thymoglobulin (1.5 mg/kg) combined with steroids, tacrolimus, and sirolimus. Statistical analyses were performed using IBM SPSS Statistics 20.0, with P values of less than .05 considered significant.

RESULTS

Between May 2006 and January 2015, a total of 42 transplants (Tx) were performed in 40 patients. The primary diagnoses at pre ITx evaluation were as follows: volvulus (25.8%), Hirschsprung disease (18.1%), ischemia (9.7%), gastroschisis (9.7%), trauma (6.5%), atresia (6.5%), necrotizing enterocolitis (3.2%), chronic intestinal pseudo-obstruction (3.2%), thrombosis (3.2), microvillus inclusion disease (3.2%), tumors (3.2%), surgical complications (3.2%), chronic rejection (3.2%), and others (3.2%). Of the patients, 80% had short gut syndrome (Fig 1). The mean time on PN at the time of the pretransplantation evaluation was 1620 days. The indications for ITx were lack of central vascular access (36.8%), intestinal failure–associated liver disease (IFALD; 25%), catheter-related sepsis (13.6%), and

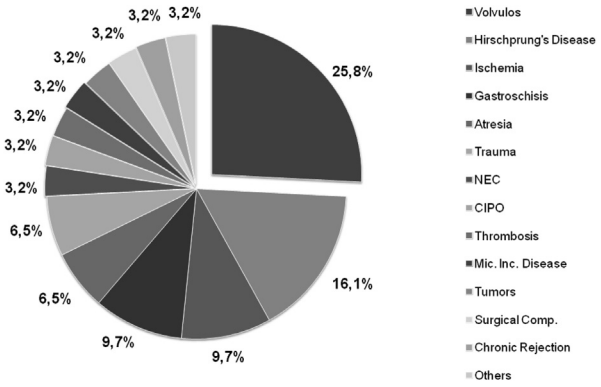

Fig 1. Primary diagnosis at evaluation. NEC, necrotizing enterocolitis; CIPO, chronic intestinal pseudo-obstruction; Mic. Inc. Disease, microvillous inclusion disease.

others representing less than 5% each (Fig 2). The mean time on the WL for all the patients was 188 ± 183 days (53.1 ± 43.3 days for adults and 225.7 ± 176.4 days for pediatric patients; $P = .006$). The overall WL mortality was 9% and the drop-out from the WL was 17.2%; however, mortality reached 33% for pediatric candidates waiting for liver-containing grafts. A total of 14 ITx were performed in 14 adults (33%), and 26 pediatric patients received 28 ITx (67%). The adults received 10 ITx, 3 MVTx, and 1 spleen-preserving modified MVTx (mMVTx) for Peutz–Jeghers syndrome, with adenomatous polyps along the whole gastrointestinal track but carrying severe dysplasia in the duodenum. The pediatric patients received 22 ITx, 3 ILTx, and 3 MVTx. Two patients underwent retransplantation, 1 received a MVTx with kidney, and the other received an isolated ITx (Fig 3). The mean TIT was 7.53 ± 2.04 hours and WIT was 40.2 ± 10.5 minutes. In all cases, the intestinal

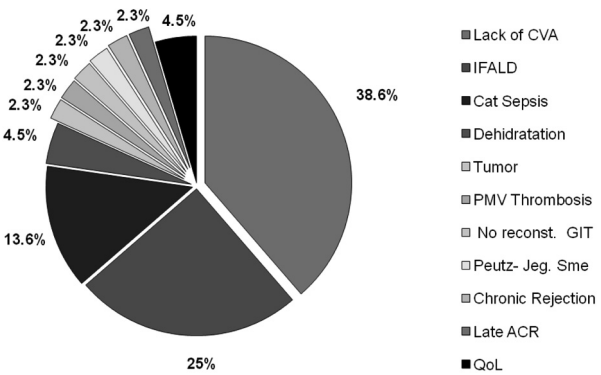

Fig 2. Indications for transplantation. IFALD, intestinal failure–associated liver disease; Cat, catheter-related; Peutz-Jeg sme, Peutz–Jeghers syndrome; ACR, acute cellular rejection; QoL, quality of life; CVA, central venous access; IFALD, intestinal failure associated liver disease; No reconst. GIT, no reconstructable gastrointestinal tract; PMV, porto mesenteric vein thrombosis; Peutz-Jeg. Sme, Peutz-Jeghers Syndrome; ACR, late acute cellular rejection.

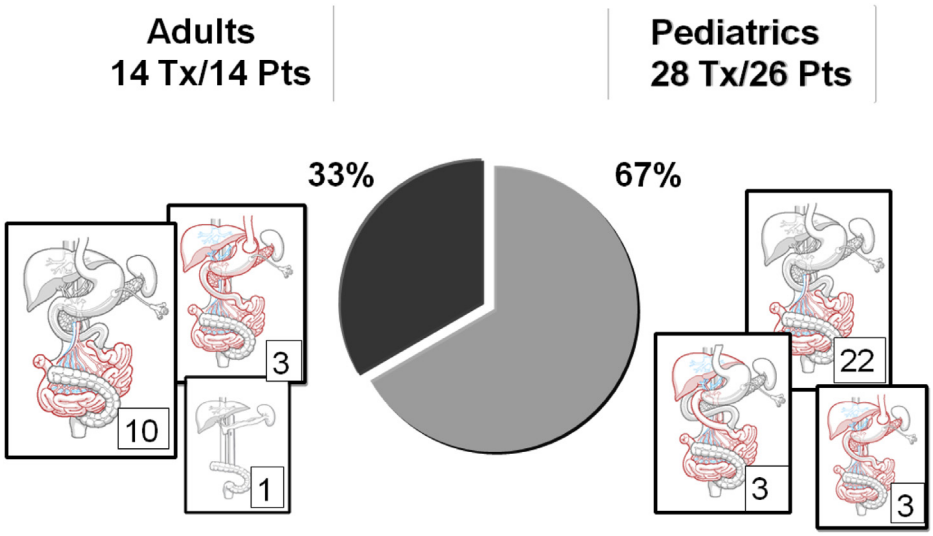

Fig 3. Type of transplants performed, by recipient age, including 2 retransplantations (1 isolated, 1 multivisceral + kidney). Pts, patients; Tx, transplantation.

length of the graft was measured and the mean length was 325 ± 63 cm. A Bishop–Koop ileostomy was performed in 28 of 42 cases (67%); a loop ileostomy was performed in 2 of 42 cases (9.5%); and a terminal ostomy (colostomy or ileostomy) was created in the other 12 cases (28.6 %). In 5 ITx (12 %), the right colon was included in the graft. In 13 ITx (31%), the abdominal rectus fascia was used to enlarge the abdominal domain. No synthetic or bio-meshes were used for the abdominal wall closure. Sixteen ITx patients (38%) required early reoperation in all cases. The main indications for early reoperation were postoperative intra-abdominal bleeding or abdominal collections. No percutaneous approach was used in those cases. No gut injuries were observed. The mean time for PN discontinuation after ITx was 68.7 ± 43 days. Three Tx were excluded from the immunological analysis due to early deaths (during the first postoperative week; 1 LITx and 2 MVTx). All of the rejection episodes were identified through protocol or clinically indicated biopsies according to the accepted pathology criteria [4]. The rejection episodes were considered as different events when there were at least 2 normal biopsy results in between. In all, 26 patients were categorized as LR, and 13 as HR. The total number of acute cellular rejection (ACR) episodes until the last follow-up was 83. A total of 53 episodes were classified as mild rejection (43 in LR vs 10 in HR; $P = .5$), 12 episodes were moderate (10 in LR vs 2 in HR; $P = .3$), and 18 were severe (15 in LR vs 3 in HR; $P = .5$). Nine patients (34%) in the LR group and 5 (38%) in the HR group had ACR less than 30 days after ITx ($P = .83$); 2 patients (7.6%) in LR group and 1 patient (7.6%) in the HR group had a first rejection episode in less than 90 days ($P = .81$). The long-term freedom-from-rejection survival by group is shown in Fig 4. The total number of grafts lost due to ACR was 4, comprising 2 in the LR group and 2 in the HR group ($P = .7$). Two of the grafts that were lost due to ACR were explanted (1 at time of the retransplantation and 1 during the ACR episode), and the other 2 grafts went on to post-Tx intestinal failure and the patients were listed for retransplantation. The total number of grafts lost due to chronic rejection was 3, comprising 1 in the LR group and 2 in the HR group. Those 2 patients in the HR group were highly sensitized before ITx; they had been successfully desensitized with intravenous immunoglobulin (IVIG), and underwent transplantation with negative crossmatch.

The long-term nutritional status of the patients is shown in Table 1. The overall 5-year actuarial survival was 55% (60% for pediatric transplant recipients vs 47% for adults,

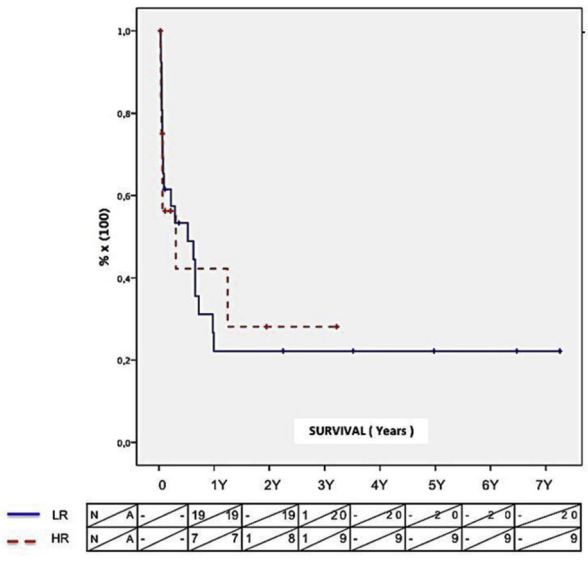

Fig 4. Long-term freedom from ACR survival by risk group. (P = NS). N, new Pts with rejection; A, cumulative number of Pts with rejection.

Table 1. Nutritional Outcome

	Pediatrics		Adults
	BMI Z-score	H/A Z-score	BMI
Pre Tx	−0.71 ± 1.21	−1.99 ± 1.73	19.5 ± 2.7
Post Tx	−0.88 ± 1.43	1.4 ± 1.32	20.4 ± 4.0

P = NS). Isolated ITx was associated with better patient survival than MVTx/LITx (65% vs 22%, P = .0001). The long-term 5-year patient and graft survival based on the pre-Tx immunological risk was 59% and 51% for the LR group and 52% and 50% for the HR group, respectively (log-rank = NS). Patients with short gut syndrome as primary diagnosis had better survival than patients without short gut syndrome (64% vs 25%, P = .002).

DISCUSSION

Several experiences reported worldwide have emphasized that the inclusion of intestinal failure patients into multidisciplinary intestinal rehabilitation and intestinal transplantation programs improves patients' long-term prognoses and survival [1,5–8]. In Latin America, the first ITx was performed at Hospital Das Clinicas do Sao Pablo, Brazil, in 1968. Almost 30 years later, in 1999, 2 centers, 1 in Mexico and 1 in Argentina, attempted to start their ITx programs, with dismal results. Five years later, in Chile, the transplant group Clinica Das Condes reported an ITx case with 1-year post-Tx survival, and in 2006, Hospital Pablo Tobón Uribe of Colombia and the reporting institution, Hospital Universitario Fundacion Favaloro of Argentina, simultaneously created intestinal rehabilitation and transplantation units. To date, the Colombian group has performed 26 ITx and Fundacion Favaloro performed has 42 Tx operations [9–12]. Short gut syndrome was reported to be the primary diagnosis of patients referred for ITx evaluation (80%) in our series, as it is seen in larger centers worldwide. Lack of central vascular access has become the first indication for ITx in our center over the last 2 years, followed by IFALD and catheter-related sepsis (2 episodes per year for bacterial infections or 1 episode of fungal infection). At the beginning of our program, IFALD was the major indication, because there was an inactive transplantation program before. Therefore, as it has been recently reported by the Scientific Registry of Transplant Recipients (SRTR), now in our country the number of patients developing liver failure and requiring LITx has been decreasing since 2009 as consequence of a better management while patients require PN [13]. Other indications for ITx evaluation that account for 30% to 40%, are severe recurrent dehydration episodes, electrolytes imbalance, poor quality of life, unresectable low-grade tumors, diffuse porto-mesenteric thrombosis, visceral myopathy, and the need for retransplantation [14–18].

The waiting list mortality is greater for patients with IFALD and for young patients with congenital diseases. However, this mortality has decreased in recent years, because the management of the home PN has been optimized, and patients are given additional PELD/MELD scores for priority [19–25].

Previously, some authors reported that the inclusion of a segment of colon could worsen early outcome; however, recent reports have shown that the inclusion of the colon does not affect the morbidity and graft survival [25], and could enhance gut function, especially with respect to fluid absorption and free fatty acid uptake [26,27]. In the small group of patients receiving the colon as part of the graft reported in this article, the same phenomenon was observed.

In all, 31% of our patients did not have an adequate amount or a good quality of tissue for performing complete abdominal wall closure. After considering the available options, our group decided to to enlarge the domain with a tension-free abdominal closure using the abdominal rectus a fascia; the short- and long-term results of these techniques have been reported elsewhere [28–30].

Nearly 80% of the immune cells of the human body reside in the gut. After the ITx, the graft is repopulated with recipient cells; this is the main reason for the complexity of the immunological management of the intestinal graft compared to other organs. The immunotherapy must be targeted to each patient [31–33].

Data from the International Transplant Registry, as well as reported single-program results, have proved the importance of using induction therapies that include monoclonal or polyclonal antibodies against leukocytes [13,14]. Not only has the use of tacrolimus allowed better survival, but also the implementation of different immunosuppressive agents, such as sirolimus, has had a positive impact [13,33]. The gold standards for graft monitoring and rejection diagnosis are the histological findings, using either protocol biopsies or biopsies performed because of clinical suspicion. The improvements in immunosuppressive regimens and graft monitoring have raised the 5-year freedom from rejection survival to greater than 20% [13,19].

Chronic rejection is the next challenge; it is the main cause of late graft dysfunction, with an incidence of 10% to 15% in isolated ITx and 5% in LITx. This process leads to fibrosis generation and intestinal villi damage [19,34–39]. Mazariegos et al reported that 8.1% of the pediatric ITx in their program are retransplantations due to chronic rejection, with lower survival. Retransplantations are expected to increase with time and with increasing experience and graft survival. However, organ shortage is still an unsolved problem, and therefore we need to work on extending the survival of the primary grafts, to avoid the need for retransplantation [40].

Nutritional autonomy, provided by adequate graft function, is quickly accomplished in the early post-ITx period, and it is achieved by 93% of patients in the first month post-ITx. Dietary tolerance usually starts at day 5 post-Tx following resolution of the postsurgical ileus; once 50% of the caloric requirements are achieved by enteral feedings, PN is discontinued [39,41]. During the rejection episodes, it is sometimes necessary to restart the PN [14,35]. Pediatric

patients often have distorted eating habits, oral aversion, or lack of sucking and swallowing coordination, requiring tube feedings until these problems are treated and solved. Up to 30% of patients have moderate anorexia in the post-Tx period, which makes the supplementation with tube feedings mandatory [32,42,43]. The goal of a specialized follow up in ITx is the early detection and prompt treatment of rejection and infections; this results in a decrease in morbidity and an improvement in patient and graft survival. To date, there is no standardized laboratory or marker to monitor for graft rejection; this is why it is still advisable to perform protocol biopsies in the early post-Tx period [27,44]. The Intestinal Transplant Registry Report in 2013 showed an actuarial patient survival rate at 1 and 5 years of 77% and 58%. These results are equivalent to those observed in our center [26].

Finally, a multidisciplinary team approach is mandatory to care for intestinal failure patients. This is the approach needed to improve patient health status, to perform early and correct diagnoses for proper treatment of complications, to increase intestinal rehabilitation, to recognize indications for transplantation in a timely manner, to improve patient survival and quality of life, and to sustain the program over time [45,46].

REFERENCES

[1] Fishbein TM. Intestinal transplantation. Current concepts review article. N Engl J Med 2009;361:998–1008.

[2] Abu-Elmagd K. Intestinal transplantation: indications and patients selection. In: Langnas A, Goulet O, Quigley M, Tappenden K, editors. Intestinal failure, diagnosis, management and transplantation. 1st ed. Malden, Mass: Blackwell Publishing; 2008. pp. 245–53.

[3] Gondolesi G, Blondeau B, Maurette R, Hoppenhauer L, Rodriguez-Laiz G, Schiano T, et al. Pretransplant immunomodulation of highly sensitized small bowel transplant candidates with intravenous immune globulin. Transplantation 2006;81:1743–6.

[4] Ruiz P, Bagni A, Brown R, Cortina G, Harpaz N, Magid M, et al. Histological criteria for the identification of acute cellular rejection in human small bowel allografts: results of the Pathology Workshop at the VIII International Small Bowel Transplant Symposium. Transplant Proc 2004;36:335–7.

[5] Reyes JD. Intestinal transplantation: an unexpected journey. J Pediatr Surg 2014;49:13–8.

[6] Starzl TE, Kaupp HA, Brock DR, Butz GW, Linman JW. Homotransplantation of multiple organs visceral. Am J Surg 1962;103:219–29.

[7] Gondolesi GE, Almau HM. Intestinal transplantation outcomes. Mt Sinai J Med 2012;246–55.

[8] Kirkman R. Small bowel transplantation. Transplantation 1984;37:429–33.

[9] Langnas A. The history of intestinal failure and transplantation. In: Langnas A, Goulet O, Quigley M, Tappenden K, editors. Intestinal failure, diagnosis, management and transplantation. 1st ed. Malden, Mass: Blackwell Publishing; 2008. pp. 245–53.

[10] da Silva R, de Paula A, Arroyo Jr P, Gonzales A, Marchini J, Duca W, et al. Report of initial experience in small bowel transplantation at São José do Rio Preto Medical School Hospital. Transplant Proc 2008;40:827–9.

[11] Trentadue J, Rumbo C, García Hervás MD, Saá G, Martínez MI, Orce G, et al. Intestinal transplantation in pediatrics. Analysis of the first recipient series in Argentina. Arch Argent Pediatr 2011;109:135–41.

[12] Gondolesi GE, Rumbo C, Fernández A, Mauriño E, Ruf A. Intestinal transplant. Review and description of its evolution in Latin America. Acta Gastroenterol Latinoam 2009;39:63–80.

[13] Smith JM, Skeans MA, Thompson B, Horslen SP, Edwards EB, Harper AM, et al. OPTN/SRTR 2011 Annual Data Report: Intestine 2013. Am J Transplant 2013;13(Suppl. 1): 103–18.

[14] Abu-Elmagd KM, Costa G, Bond GJ, Soltys K, Sindhi R, Wu T, et al. Five hundred intestinal and multivisceral transplantations at a single center. Ann Surg 2009;250:567–81.

[15] Mazariegos GV, Steffick ED, Horlsen S, Farmer D, Frier J, Grant D, et al. Intestine transplantation in United States, 1999–2008. Am J Transplant 2010;10(Part 2):1020–34.

[16] Vianna RM, Mangus RS. Present prospects and future perspectives of intestinal and multivisceral transplantation. Curr Opin Clin Nutr Metab Care 2009;12:281–6.

[17] Kaufman SS, Atkinson JB, Bianchi A, Goulet OJ, Grant D, Langnas AN, et al. Indications for pediatric intestinal transplantation: a position paper of the American Society of Transplantation. Pediatr Transplant 2001;5:80–7.

[18] Ruiz P. Updates on acute and chronic rejection in small bowel and multivisceral allografts. Curr Opin Organ Transplant 2014;19:293–302.

[19] Cheng E, Kaneku H, Farmer D. The role of donor specific antibodies in intestinal transplantation; long term outcome with special reference to the liver. Am J Transplant 2012;12: 3047–60.

[20] Criterios de inclusión em lista de espera para Tx de intestino, INCUCAI. Available at: http://cresi.incucai.gov.ar/cresi/.

[21] Freeman Jr RB, Steffick DE, Guidinger MK, Farmer DG, Berg CL, Merion RM. Liver and intestine transplantation in the United States, 1997–2006. Am J Transplant 2008;8:958–76.

[22] Horslen S. Organ allocation for liver-intestine candidates. Liver Transpl 2004;10:S86–9.

[23] Fryer J, Pellar S, Ormond D, Koffron A, Abecassis M. Mortality in candidates waiting for combined liver-intestine transplants exceeds that for other candidates waiting for liver transplants. Liver Transpl 2003;9:748–53.

[24] Desschans B, Van Gelder F, Van Hees D, de Rocy J, Monbaliu D, Aerts R, et al. Evolution in allocation rules for renal, hepatic, pancreatic and intestinal grafts. Acta Chir Belg 2008;108: 31–4.

[25] Kato T, Selvaggi G, Gaynor JJ, Takahashi H, Nishida S, Moon J, et al. Inclusion of donor colon and ileocecal valve in intestinal transplantation. Transplantation 2008;86:293–7.

[26] Grant D, Abu-Elmagd K, Mazariegos G, Vianna R, Langnas A, Magnus R, et al. Intestinal transplant registry report: global activity and trends. Am J Transplant 2015;15:210–9.

[27] Fishbein T, Gondolesi G, Kaufman S. Intestinal trasplantation for gut failure. Gastroenterology 2003;124:1615–28.

[28] Levi DM, Tzakis AG, Kato T, Madariaga J, Mittal NK, Nery J, et al. Transplantation of the abdominal wall. Lancet 2003;361:2173–6.

[29] Gondolesi G, Selvaggi G, Tzakis A, Rodríguez-Laiz G, González-Campaña A, Fauda M, et al. Use of the abdominal rectus fascia as a nonvascularized allograft for abdominal wall closure after liver, intestinal, and multivisceral transplantation. Transplantation 2009;27(87):1884–8.

[30] Gondolesi G, Farinelli P, Ramisch D, Romero P, Rumbo C, Trentaude J, et al. Use of abdominal rectus fascia after intestinal and multiorgan transplantation in a single center, long-term follow-up [World Transplant Congress abstract]. Am J Transplant 2014;(Suppl.):217.

[31] Kaufman SS. Small bowel transplantation: selection criteria, operative techniques, advances in specific immunosuppression, prognosis. Curr Opin Pediatr 2001;13:425–8.

[32] Fishbein TM, Florman S, Gondolesi G, Schiano T, LeLeiko N, Tschernia A, et al. Intestinal transplantation before and after the introduction of sirolimus. Transplantation 2002;73: 1538–42.

[33] Abu-Elmagd KM, Costa G, Bond GJ, Wu T, Murase N, Zeevi A, et al. Evolution of the immunosuppressive strategies for the intestinal and multivisceral recipients with special reference to allograft immunity and achievement of partial tolerance. Transpl Int 2009;22:96–109.

[34] Minneci PC. Intestinal transplantation: an overview. Pathophysiology 2014;21:119–22.

[35] Avitzur Y, Grant D. Intestine transplantation in children update 2010. Pediatr Clin North Am 2010;57:415–31.

[36] Zanfi C, Lauro A, Cescon M, Dazzi A, Ercolani G, Grazi GL, et al. Clizumab and alemtuzumab as induction agents in adult intestinal and multivisceral transplantation: rejection and infection rates in 40 recipients during the early postoperative period. Transplant Proc 2010;42:35–8.

[37] Gondolesi G, Blondeau B, Maurette R, Hoppenhauer L, Rodriguez-Laiz G, Schiano T, et al. Pretransplant immunomodulation of highly sensitized small bowel transplant candidates with intravenous immune globulin. Transplantation 2006;81: 1743–6.

[38] Iyer KR, Srinath C, Horslen S, Fox IJ, Shaw BW, Sudan DL, et al. Late graft loss and long-term outcome after isolated intestinal transplantation in children. J Pediatr Surg 2002;37:151–4.

[39] Shiffman ML, Saab S, Feng S, Abecassis MI, Tzakis AG, Goodrich NP, et al. Liver and intestine transplantation in the United States, 1995–2004. Am J Transplant 2006;6:1170–87.

[40] Mazariegos GV, Soltys K, Bond G, Girnita A, Machaidze Z, Jaffe R, et al. Pediatric intestinal retransplantation: techniques, management, and outcomes. Transplantation 2008;86: 1777–82.

[41] Mazariegos GV, Squires RH, Sindhi RK. Current perspectives on pediatric intestinal transplantation. Curr Gastroenterol Rep 2009;11:226–33.

[42] Matarese LE, Costa G, Bond G, Stamos J, Koritsky D, O'Keefe SJ, et al. Therapeutic efficacy of intestinal and multivisceral transplantation: survival and nutrition outcome. Nutr Clin Pract 2007;22:474–81.

[43] O'Keefe SJ, Emerling M, Koritsky D, Martin D, Stamos J, Kandil H, et al. Nutrition and quality of life following small intestinal transplantation. Am J Gastroenterol 2007;102:1093–100.

[44] Gondolesi G, Ghirardo S, Raymond K, Hoppenhauer L, Surillo D, Rumbo C, et al. The value of plasma citrulline to predict mucosal injury in intestinal allografts. Am J Transplant 2006;6:2786–90.

[45] Mangus RS, Tector AJ, Kubal CA, Fridell JA, Vianna RM. Multivisceral transplantation: expanding indications and improving outcomes. J Gastrointest Surg 2013;17:179–86.

[46] Abu-Elmagd KM, Kosmach-Park B, Costa G, Zenati M, Martin L, Koritsky DA, et al. Long-term survival, nutritional autonomy, and quality of life after intestinal and multivisceral transplantation. Ann Surg 2012;256:494–508.