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Outcomes of Adult Intestinal Transplant Recipients Requiring Dialysis and Renal Transplantation

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Background. Data on dialysis and renal transplantation (RT) after intestinal transplantation (IT) are sparse. Whether changes in immunosuppression and surgical techniques have modified these outcomes is unknown. **Methods.** Two hundred eighty-eight adult intestinal transplants performed between 1990 and 2014 at the University of Pittsburgh were analyzed for incidence, risk factors and outcomes after dialysis and RT. Cohort was divided into 3 eras based on immunosuppression and surgical technique (1990-1994, 1995-2001, and 2001-2014). Receiving RT, or dialysis for 90 days or longer was considered as end-stage renal disease (ESRD). **Results.** During a median follow-up of 5.7 years, 71 (24.7%) patients required dialysis, 38 (13.2%) required long-term dialysis and 17 (6%) received RT after IT. One-, 3-, and 5-year ESRD risk was 2%, 7%, and 14%, respectively. No significant era-based differences were noted. Higher baseline creatinine (hazard ratio [HR], 3.40 per unit increase, $P < 0.01$) and use of liver containing grafts (HR, 2.01; $P = 0.04$) had an increased ESRD risk. Median patient survival after dialysis initiation was 6 months, with a 3-year survival of 21%. Any dialysis (HR, 12.74; 95% CI 8.46-19.20; $P < 0.01$) and ESRD (HR, 9.53; 95% CI, 5.87-15.49; $P < 0.01$) had higher mortality after adjusting for covariates. For renal after IT, 1- and 3-year kidney and patient survivals were 70% and 49%, respectively. All graft losses were from death with a functioning graft, primarily related to infectious complications (55%). **Conclusions.** In intestinal transplant recipients, renal failure requiring dialysis or RT is high and is associated with increased mortality. Additionally, the outcomes for kidney after IT are suboptimal due to death with a functioning graft.

(*Transplantation Direct* 2018;4:e377; doi: 10.1097/TXD.0000000000000815. Published online 20 July, 2018.)

The evolution of Intestinal transplantation (IT) (isolated and multivisceral) over the last 2 decades is one of the most important breakthroughs in the field of gut failure and rehabilitation. Significant progress has been achieved secondary to increasing clinical experience, improved surgical techniques, and modifications in immunosuppression (IS) protocols over the years.[1-8] Intestinal transplantation is associated with improved quality of life, freedom from dependence on parenteral nutrition (PN), and improved short-term survival in patients with gut failure and complications related to PN.[1,3] This encouraging improvement in short-term survival noted over time has been tempered by results that show improved but suboptimal long-term outcomes over the past 2 decades.[1] Although this is mostly a result of rejections and infectious complications in more than

Received 16 May 2018.

Accepted 2 June 2018.

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The authors declare no funding or conflicts of interest.

C.P. designed the study, participated in data collection and analysis, and wrote the article. A.H. participated in interpretation of data and article editing. S.H. participated in interpretation of data and article editing. R.C. participated in interpretation of data and manuscript editing. A.G. participated in interpretation of data and article editing. Y.P, X.G., and D.L. performed statistical analysis. M.B. participated in data collection and article editing. H.S. conceptualized the study, participated in data interpretation, and co-wrote the article.

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Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantationdirect.com).

ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000000815

50% of the patients, information on other factors which may potentially affect outcome, such as renal dysfunction is limited.[1] Renal impairment is common and associated with worse outcomes in nonrenal solid organ transplantation (SOT), with particularly high rates in patients with IT.[9] This aspect has been explored in detail with large studies for the liver, heart, and lung transplant patients.[9-16] However, similar data in IT patients are limited to small single center studies due to the small number of IT performed at individual centers.[17-23] Additionally, the renal outcomes reported have varied from mild to moderate renal dysfunction to need for dialysis. Furthermore, very little is known about patients who undergo a renal transplantation (RT) after a previous IT, with the only available literature on this, per our knowledge, pertains to a series of 8 patients previously described from our center.[24]

University of Pittsburgh Medical Center has been one of the largest centers of IT since the beginning of the IT era. More than 600 intestinal transplants have been performed since 1990s, including both pediatric and adult patients.[7] We used the prospectively collected data on the adult patients in this cohort to analyze the details of renal dysfunction after IT. Our aim was to describe the epidemiology and outcomes of patients requiring dialysis and RT after IT.

MATERIALS AND METHODS

Study Design and Patient Selection

Retrospective cohort study of 307 adult patients (age, ≥ 18 years), who underwent IT at the Thomas E. Starzl Transplantation Institute of the University of Pittsburgh Medical Center, between January 1990 and March 2014.

Inclusion and Exclusion Criteria

We included patients with all combination of IT: isolated small bowel (SB), liver-SB and multivisceral (full and modified) transplant (MVT). We excluded patients with retransplants, simultaneous intestinal and RT, and those that had dialysis or RT before IT.

Indications for IT and IS Management

This has been described in detail in a previous article that described the first 500 combined adult and pediatric transplants performed at our center.[7,25] Briefly, the most common indications for IT was irreversible intestinal failure with PN-related complications, such as central venous catheter infection, losing central venous access, or intestinal failure associated liver disease. The number of transplanted organs was dictated by the extent of the disease and the presence of intestinal failure-associated liver disease. All organs were from deceased donors and were ABO-identical.

Immunosuppression has varied over the 20 years of follow-up except for the use of tacrolimus, which was a common factor from the very first transplant in this cohort in 1990. Immunosuppression from 1990 to 1994 consisted of tacrolimus and steroid based regimens with 12-hour tacrolimus trough goals of 20 to 30 ng/mL for the first 3 months. Azathioprine was used in selective cases. Immunosuppression between 1995 and 2001 consisted of bone marrow augmentation protocol with donor-derived hematopoietic cells and induction therapy with cyclophosphamide (until 1998) or daclizumab (1998-2001) along with use of either azathioprine, mycophenolate mofetil, or sirolimus as an additional immunosuppressive agent. From July 2001, preconditioning regimens using T cell–depleting agents were used, with rabbit antithymocyte globulin (thymoglobulin) being the T cell–depleting agent until 2003 followed by alemtuzumab from 2003 onward. Maintenance IS in these patients was with tacrolimus monotherapy with, subsequent addition of steroids, mycophenolate mofetil, sirolimus or azathioprine restricted to patients with rejections or other complications, such as renal insufficiency. Twelve-hour tacrolimus trough goals for the first 3 months were reduced to 15 to 20 ng/mL for the transplants performed between 1995 and 2001 and then to 10 to 15 ng/mL for transplants performed after July 2001. For selected patients with IT performed after 2001, attempts were made to reduce the dose and frequency of tacrolimus on an individual basis, based on rejection risks (clinical, endoscopic, and immunological). Treatment of rejections also evolved over time but essentially consisted of steroids and/or T cell–depleting agents (OKT3, alemtuzumab, thymoglobulin) for cellular rejections, and IVIG and plasmapheresis for antibody-mediated rejections.

Outcomes and Variables

Renal outcomes studied were need for any dialysis after IT, and end-stage renal disease (ESRD) defined as a composite of long-term dialysis and RT. We considered patients as requiring long-term dialysis if they remained dialysis dependent for 90 days or more. Patients that died during follow-up were censored for the outcomes of interest. We also measured patient survival after initiation of dialysis. For all patients that had dialysis post-IT, presence or absence of acute kidney injury (AKI) immediately preceding dialysis requirement was assessed using AKI definitions as per the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) classification.[26]

Data for analysis were obtained from the University of Pittsburgh Medical Center's transplant database, corroborated and supplemented with individual chart reviews. Information was collected for baseline demographics, renal functions, IT characteristics (type of IT, induction agent used, rejection episodes, and graft survival) and presence of traditional risk factors for renal disease, such as body mass index (BMI), hypertension (HTN) and diabetes mellitus (DM). We divided the study period into 3 eras: era 1 (May 1990-Dec 1994), era 2 (January 1995-June 2001), and era 3 (July 2001-July 2014) based on the IS protocol. For the 17 patients who received a renal transplant after IT, we collected additional information about the type of donor (living vs deceased), dialysis duration before RT, time to RT from IT, induction agent used and estimated patient as well as renal graft survival rates.

Ethical Guidelines and Privacy Protection

Patient information was obtained from transplant database through institutionally designated individuals at our transplant center as regulated by the institutional review board guidelines at the University of Pittsburgh. Our institution maintains a prospectively collected electronic database of all patients with IT. For statistical analysis, research data was coded to prevent identification of subjects directly or through linked identifiers. The study was conducted under the institutional review board number PRO-13060220.

Statistical Analysis

Baseline characteristics are summarized as mean (SD) or median (range) for continuous variables, and counts and percentages for categorical variables. Kaplan Meier survival

curves were used to analyze time to death, time to renal outcome after IT, survival after initiating dialysis and renal graft survival for renal after IT. Univariate and multivariate Cox proportional hazards model was fit separately for each of the renal outcomes of interest: any dialysis and ESRD, and results are reported as hazard ratios (HR) with 95% confidence intervals (CI). Variables found to be significantly associated with a *P* value less than 0.05 on univariate analysis were included in the multivariate analysis. Association of AKI (KDIGO stage 2 or above) and need for long-term dialysis was tested using χ^2 test. Cox proportional hazards model was used to assess the mortality risk in IT patients from dialysis or ESRD. For variables with multiple categories, that is, type of transplant, and induction medication, the likelihood ratio test was used to evaluate significance of the overall variable. Variables were treated as time-dependent where appropriate. All analyses were performed with STATA version 14.

RESULTS

Baseline Characteristics

A total of 343 intestinal transplants were performed in 307 patients between 1990 and 2014. After excluding retransplants, simultaneous renal and intestinal transplants and patients needing dialysis or RT before IT, there were 288 patients in the study cohort (Figure 1). The median duration of follow-up was 5.7 years. Table 1 shows the baseline characteristics. Median age 43 years and 93% of the patients were white. Diabetes and HTN before IT were present in 21 (7.3%) and 14 (4.9%), respectively. Mean baseline serum creatinine at the time of IT was 0.9 mg/dL (range, 0.3-2.3 mg/dL).

Intestinal Transplantation

Seventy-six percent (221/ 288) of the ITs were performed in the latest era of 2001 to 2014, whereas 6% (17/ 288) and 18% (52/288) were performed between 1990-1994 and 1995-2001, respectively (Table 1). Isolated IT was the most common type of IT and was performed in 148 (52%) of the cases. Indications for IT were short gut syndrome (65.6%), portal vein thrombosis (13%), tumors (10%), and dysmotility syndromes (11%). Two hundred eighteen (76%) patients received induction therapy, alemtuzumab in 135 (47%) thymoglobulin in 44 (15%), and daclizumab in 39 (14%) patients. Acute cellular rejection (ACR) of the IT was documented in 214 (75%) patient. 1-, 5-, and 10-year probabilities of patient survival after IT were 88%, 63%, and 44%, respectively (**Figure S1,** http://links.lww.com/TXD/A118). Death-censored IT graft survival at 1, 5, and 10 years were 84%, 56% and 45% respectively.

Renal Outcomes

Seventy-one (25%) of 288 patients required dialysis at some point after IT during a follow-up period of 1609 person-years, yielding a rate of 46.6 per 1000 person-years. Of these, 38 (13%) progressed to requiring long-term dialysis. Cumulative probabilities of receiving dialysis at 3 and 5 years were 16% and 22% respectively, while the probabilities of long-term dialysis were 6% and 11%, respectively

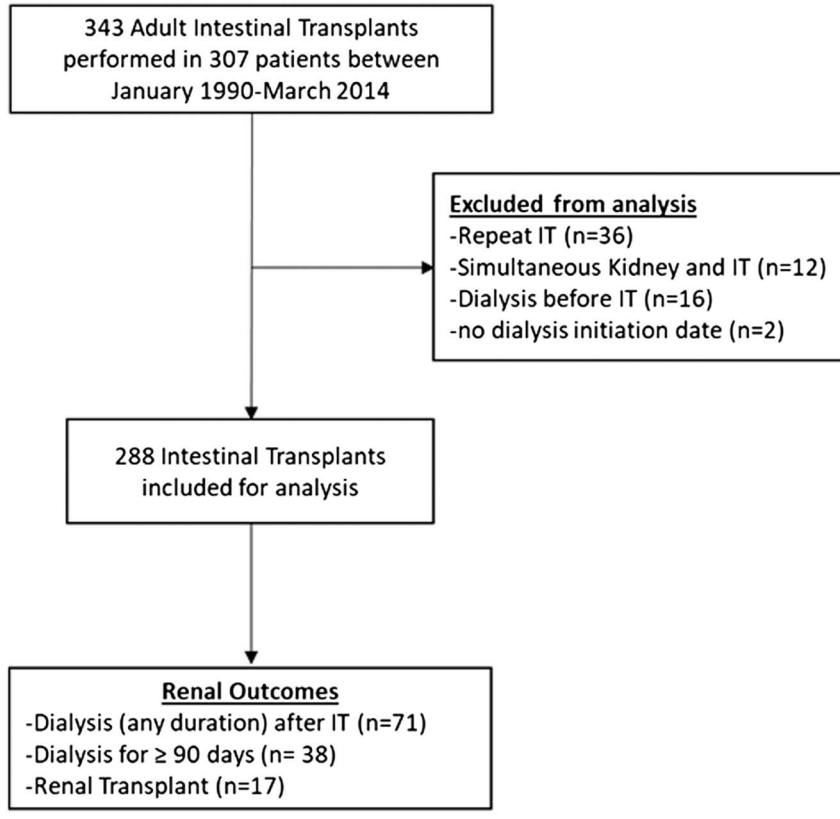

FIGURE 1. Study cohort, excluded groups, and renal events after IT.

TABLE 1.

Patient characteristics and details of IT

Variables	N = 288
Era-based number of transplants, n (%)	
Era 1: May 1, 1990 to December 31, 1994	17 (5.9)
Era 2: January 1, 1995 to June 20, 2001	52 (18.1)
Era 3: July 1, 2001 to July 30, 2014	219 (76.0)
Indications for IT, n (%)	
Short gut syndrome	189 (65.6)
Portal vein thrombosis	37 (12.9)
Neoplastic disorders	30 (10.4)
Dysmotility	32(11.1)
Age: median (min, max), y	43 (18, 71)
Female, n (%)	167 (57)
Race, n (%)	
American Indian	1 (0.4)
Black	19 (6.7)
White	262 (92.9)
Unknown	6 (2.1)
BMI: mean (SD), kg/m^2	23.58 (5.4)
Baseline serum creatinine: mean (SD), mg/dL	0.93 (0.4)
Pretransplant DM, n (%)	21 (7.3)
Pretransplant HTN, n (%)	14 (4.9)
Type of intestinal transplant, n (%)	
Isolated SB	148 (51.4)
Liver/SB/pancreas	44 (15.3)
Full MVT	55 (19.1)
Modified MVT	34 (11.8)
Intestine/pancreas	7 (2.4)
Liver-containing graft, n (%)	99 (34.4)
Induction therapy, n (%) med	
None	70 (24.3)
Thymoglobulin	44 (15.3)
Alemtuzumab	135 (46.9)
Daclizumab	39 (13.5)
Intestinal graft failure, n (%)	147(51.0)
Acute rejection, n (%)	214 (74.3)

(Table 2 and Figure 2). Seventeen (6%) of 288 patients received RT after IT.

Risk Factors for Renal Outcomes

On univariate analysis (Table 3), baseline serum creatinine (HR, 2.46; 95% CI, 1.27-4.78; $P < 0.01$), pretransplant DM (HR, 2.4; 95% CI, 1.18- 4.88; $P = 0.02$), HTN (HR, 4.63; 95% CI 2.29-9.36; $P < 0.01$), and use of liver-containing IT (HR, 3.31; 95% CI, 2.06-5.31; $P < 0.01$) had statistically significant increased risk of requiring dialysis after IT. Factors associated with risk of ESRD were baseline serum creatinine (HR, 3.69; 95% CI 1.63-8.34; $P < 0.01$), the era of transplantation (recent era associated with lower risk of ESRD, HR, 0.32; 95% CI 0.13-0.77; $P = 0.03$), pretransplant HTN (HR, 3.65; 95% CI 1.3-10.31, $P = 0.01$), use of liver containing grafts (HR, 2.31; 95% CI, 1.39-4.12; $P < 0.01$), and type of induction therapy (thymoglobulin showing a lower risk; HR 0.2; 95% CI, 0.04-0.92; $P < 0.01$). There was no significant association of acute rejections and IT graft loss with renal outcomes.

On multivariate analysis (Table 4), pretransplant DM, HTN, and use of liver containing IT remained with higher risk of needing dialysis. Risk of ESRD was significantly elevated with higher baseline creatinine and use of liver containing IT. Era of transplantation and type of induction agent were not statistically significant on multivariate analysis.

The KDIGO stage ≥2 AKI was present in 73% of patients at the time of starting dialysis. This was associated with a lower likelihood of progressing to long-term dialysis compared to those that had no AKI preceding dialysis initiation (relative risk, 0.45; 95% CI: 0.24-0.66, $P = <0.001$).

Effect of Renal Outcomes on Survival After IT

Requiring dialysis was associated with increased risk of mortality after IT (Table 5). Hazard ratio for death after IT for patients needing any dialysis was 12.74 (95% CI, 8.46-19.20, $P < 0.01$) and for ESRD was 9.53 (95% CI, 5.87-15.49, $P < 0.01$). Patients who required renal after IT also had an increased risk of death (HR, 3.28; 95% CI, 1.63-6.61). Median survival after dialysis initiation was 6 months, with a 1- and 3-year survivals of 35% and 21%, respectively (Figure 3). For patients requiring long-term dialysis, 1- and 3-year survivals were 48% and 20%, respectively.

RT After IT

Seventeen patients in the study cohort had RT after an IT. Median time to RT 84 months after IT (range, 7-178 months). Six (35%) were living donor transplants and 8 (47%) were performed preemptively (Table 6). Induction agent was used in 7 (41%). 1 and 3-year graft and patient survivals were 70% and 49% respectively with median survival being 3.2 years after RT. All the graft losses were secondary to death with a functioning graft with infections accounting for 6 of the 11 patient

TABLE 2.

Renal events after IT

Renal event	N (%)	Freedom from renal event
Any dialysis	71 (24.7%)	1 y = 0.91
		3 y = 0.84
		5 y = 0.78
		10 y = 0.69
Long-term dialysis (ie, dialysis dependent for ≥90 d)	38 (13.2%)	1 y = 0.98
		3 y = 0.94
		5 y = 0.89
		10 y = 0.80
Renal transplant	17 (5.9%)	1 y = 1
		3 y = 0.98
		5 y = 0.97
		10 y = 0.93
ESRD (long-term dialysis + renal transplant)	46 (15.9%)	1 y = 0.98
		3 y = 0.93
		5 y = 0.86
		10 y = 0.76

Freedom from renal event noted in the last column indicates the proportion of patients at 1, 3, 5, and 10 years that had not developed the outcome of interest (ie, dialysis, renal transplant, ESRD).

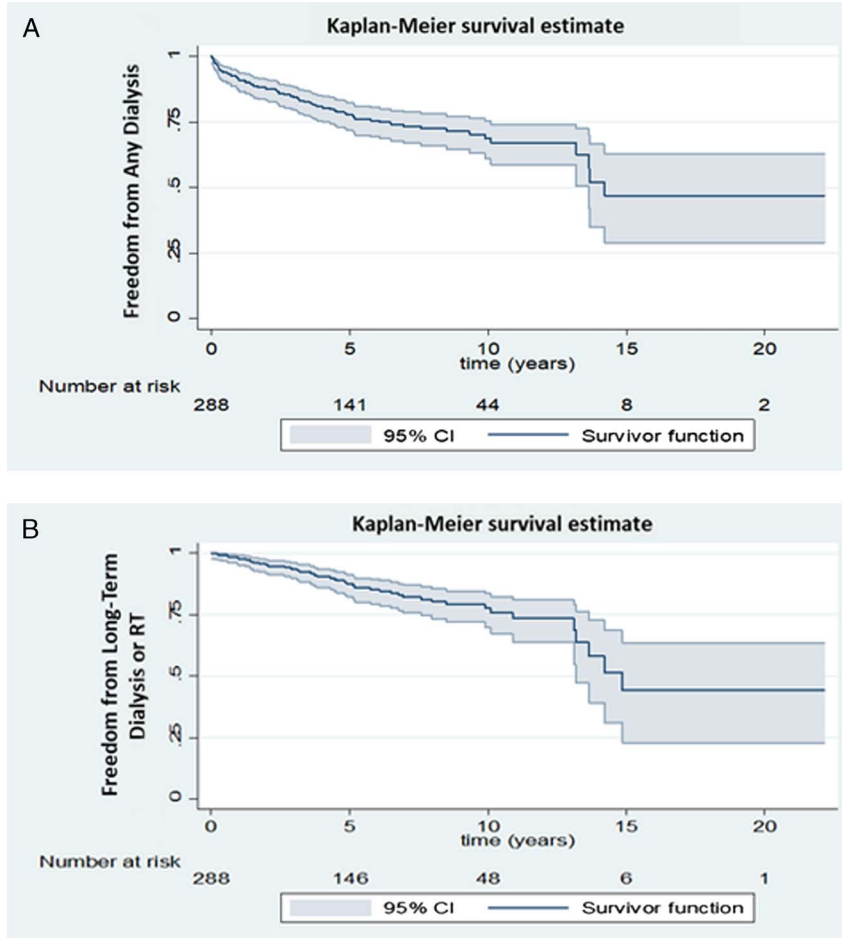

FIGURE 2. Time to renal outcomes (dialysis, ESRD) after IT. A, Survival curve for freedom from any form dialysis after IT. Dialysis free probability at 1, 3, 5, and 10 years were 0.91, 0.84, 0.78, and 0.69, respectively. B, Survival curve for freedom from ESRD (either long-term dialysis and/or renal transplant) after IT. ESRD-free probability at 1, 3, 5, and 10 years were 0.98, 0.93, 0.86, and 0.76, respectively.

deaths. There were no differences in patient and graft survival with or without the use of T cell–depleting induction therapy (data not shown).

DISCUSSION

Intestinal transplantation is one of the most remarkable advances in transplantation, and with steady rise over the years, the current number of patients with a functional IT in the United States has reached more than 1000.[1,7,27] Despite the higher incidence of renal dysfunction after IT, there are limited data on hard renal endpoints such as dialysis and RT, unlike in other nonrenal SOT.[9-12,28-30] In this analysis of a large cohort of adult intestinal transplant recipients, we have described the epidemiology of severe renal dysfunction over a long follow-up period. Although baseline prevalence of renal impairment was low, up to a fourth of patients developed renal dysfunction severe enough to warrant dialysis or transplantation. Survival after dialysis initiation was extremely low, even for those patients that survived beyond 90 days. Although it is well known that renal failure is associated with inferior outcomes in heart, lung and liver transplantation, studies in intestinal transplant patients have been limited by small sample sizes. The only large multicenter center study to examine renal outcomes after IT was limited to patients transplanted before 2001.[9] It however excluded renal events immediately after transplantation, did not report IT specific mortality risk with dialysis, and did not report outcomes for RT after IT. To our knowledge, this is the largest single-center study on IT patients to report these renal outcomes.

Our study identified several key aspects pertaining to renal dysfunction after IT. We did not observe any significant association of the different eras on renal outcomes. Although a suggestion of increased dialysis was noted in the recent era, this did not translate to higher ESRD risk, possibly from the competing risk of death before reaching chronic dialysis status. A significantly large proportion of patients had moderate AKI preceding onset of dialysis requirement, suggesting that need for dialysis was precipitated by a sudden deterioration of patient's clinical status. We hypothesize that this may be related to episodes of sepsis in majority of the patients, which likely explains the high mortality rates after initiation of dialysis in these patients. Calcineurin inhibitor toxicity has been considered the predominant risk factor for long-term renal impairment after nonrenal SOT[11,28-32]; our data suggest that AKI is an additional major risk factor for dialysis requirement in IT patients. Though the baseline prevalence of traditional risk factors, such as DM and HTN, was low, they did contribute to the overall risk of renal failure post-IT, and

TABLE 3.

Univariate Cox models for time to renal events (any dialysis and ESRD)

Predictor	Any dialysis (N = 71) HR (95% CI)	P	ESRD (long-term dialysis + renal transplant) (N = 46) HR (95% CI)	P
Era of IT[a]		0.66		0.03
Era 1: 1990-1994	—		—	
Era 2: 1995-2001	1.13 (0.37-3.48)		0.66 (0.27-1.62)	
Era 3: 2001-2014	1.44 (0.50-4.16)		0.32 (0.14-0.77)	
Age	1.02 (1.01-1.05) (p)	<0.01	1.02 (0.99-1.04)	0.12
Pretransplant DM	2.40 (1.18-4.88)	0.02	2.04 (0.72-5.80)	0.18
Pretransplant HTN	4.63 (2.29-9.36)	<0.01	3.65 (1.30-10.31)	0.01
Type of IT[a]		<0.01		0.01
Isolated SB	—		—	
Liver/SB/pancreas	2.17 (1.11-4.24)		1.48 (0.67-3.27)	
Full MVT	4.16 (2.40-7.23)		2.38 (1.22-4.66)	
Modified MVT	0.89 (0.24-2.35)		0.21 (0.03-1.54)	
Intestine/pancreas	0.73 (0.10-5.43)		0.78 (0.10-5.81)	
Liver-containing graft	3.31 (2.06-5.31)	<0.01	2.31 (1.29-4.12)	<0.01
Induction therapy[a]		0.3		<0.01
None	—		—	
Thymoglobulin	0.62 (0.29-1.34)		0.20 (0.04-0.92)	
Alemtuzumab	0.59 (0.33-1.05)		0.91 (0.42-1.95)	
Daclizumab	0.89 (0.44-1.80)		1.80 (0.82-3.95)	
IT failure[b]	0.89 (0.38-2.08)	0.79	1.10 (0.46-2.64)	0.82
Acute rejection[b]	1.49 (0.86-2.58)	0.16	1.02 (0.52-2.00)	0.96
Baseline BMI	1.02 (0.99-1.05)	0.05	1.02 (0.99-1.05)	0.27
Baseline creatinine[c]	2.46 (1.27,4.78)	<0.01	3.69 (1.63-8.34)	<0.01

[a] Overall Wald test *P* values are presented for categorical variables with >2 categories.

[b] Denotes a variable specified as a time-dependent in the Cox model.

[c] HR per unit increase.

hence require close monitoring and management just as in the general population. Not surprisingly, baseline creatinine before IT was a strong predictor of renal events. Strategies to minimize secondary insults, such as AKI, nephrotoxic antimicrobials, and supratherapeutic calcineurin inhibitor levels might limit additive nephrotoxicity.

Reasons for our finding of positive correlation between renal dysfunction and use of liver containing IT are unclear. It is

TABLE 4.

Multivariable Cox models for time to renal events (any dialysis and ESRD)

Predictors	Any dialysis (N = 71) HR (95% CI)	P	ESRD (long-term dialysis + renal transplant) (N = 46) HR (95% CI)	P
Era of IT[a]		0.10		0.07
Era 1: 1990-1994	—		—	
Era 2: 1995-2001	1.01		0.35	
Era 3: 2001-2014	3.28		0.16	
Age	1.01 (0.99-1.03)	0.36	1.02 (0.99-1.06)	0.19
Pretransplant DM	1.98 (0.83-4.73)	0.12	1.59 (0.50-5.08)	0.43
Pretransplant HTN	3.90 (1.72-8.82) ($P < 0.01$)	<0.01	2.14 (0.72-9.03)	0.19
Liver containing graft	2.43 (1.39-4.26)	<0.01	2.01 (1.69-6.58)	0.04
Induction therapy[a]		0.08		0.25
None	—		—	
Thymoglobulin	0.65		0.30	
Alemtuzumab	0.43		1.97	
Daclizumab	1.57		1.60	
Baseline BMI	1.01 (0.98-1.04)	0.41	1.02 (0.99-1.06)	0.24
Baseline serum creatinine[b]	1.72 (0.86-3.43)	0.12	3.40 (1.39-8.30)	<0.01

[a] Overall Wald test p values are presented for categorical variables with >2 categories.

[b] HR per unit increase.

TABLE 5.

Multivariable Cox models for effect of any dialysis and ESRD on time to mortality after IT

	Mortality after IT			
Predictor	**Any dialysis (N = 71) HR (95% CI)**	***P***	**ESRD (long-term dialysis + renal transplant) (N = 46) HR (95% CI)**	***P***
Renal event	12.74 (8.46-19.20)	<0.01	9.53 (5.87-15.49)	<0.01
Era of IT[a]		0.57		0.29
Era 1: 1990-1994	—		—	
Era 2: 1995-2001	1.66		2.06	
Era 3: 2001-2014	1.19		2.09	
Age	1.00 (0.99-1.02) ($P = 0.75$)	0.75	1.00 (0.99-1.02) ($P = 0.57$)	0.57
Pretransplant DM	0.87 (0.39-1.93)	0.74	1.15 (0.54-2.43)	0.71
Pretransplant HTN	2.07 (1.03-4.17)	0.04	2.20 (1.11-4.35)	0.02
Liver containing graft	0.90 (0.59, 1.36)	0.62	1.22 (0.83-1.81)	0.31
Induction therapy[a]		0.05		<0.01
0 = none	—		—	
1 = thymoglobulin	0.55		0.79	
2 = alemtuzumab	0.44		0.38	
3 = daclizumab	0.79		0.92	
Baseline BMI	1.01 (0.99-1.03)	0.15	1.01 (0.99-1.03)	0.23
Baseline serum creatinine	1.36 (0.80-2.32)	0.26	1.29 (0.76-2.18)	0.35

[a] Overall Wald test *P* values have been presented for categorical variables with more than 2 categories.

Mortality for any dialysis column (column 2) provides the HR for death for the those that needed any dialysis and provides corresponding HR for other variables used in the multivariate analysis. Similarly, column 4 provides the HR for death for those that developed ESRD and the corresponding HR for other variables used in the multivariate analysis.

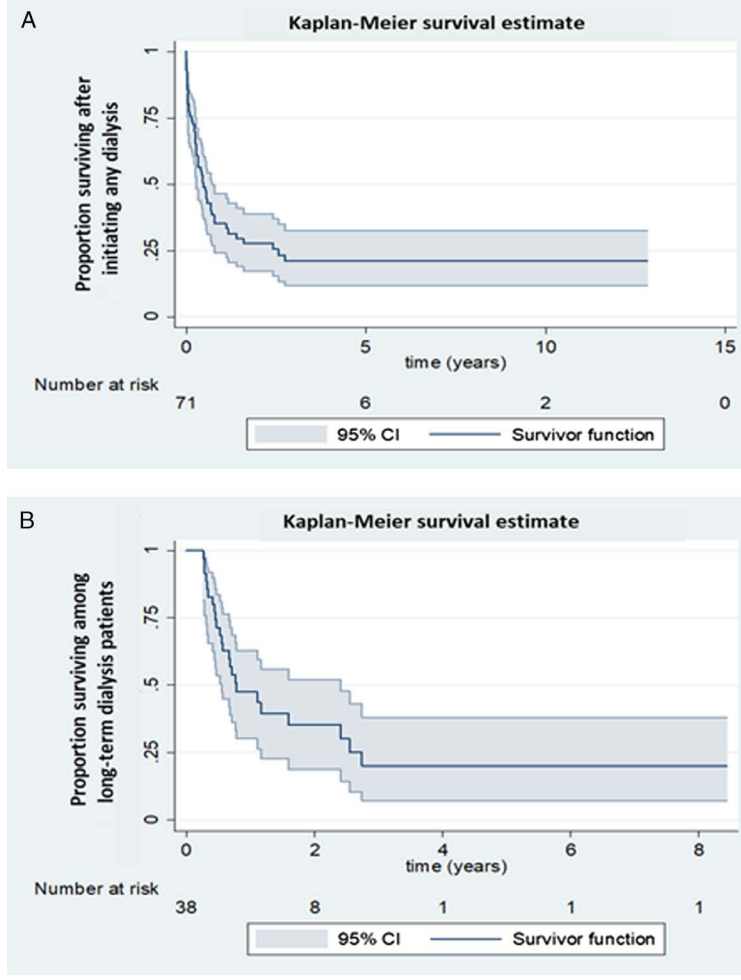

FIGURE 3. Kaplan-Meier estimate of patient survival after dialysis initiation. A, Patient survival after initiating any form of dialysis. Survival probability at 1 and 3 years were 0.35 and 0.21 respectively, with a median survival of 6 months. B, Patient survival with long-term (≥90 days) dialysis. Survival probability at 1 and 3 years were 0.48 and 0.2, respectively, with a median survival of 9 months.

TABLE 6.

Demographics and transplant characteristics of patients undergoing RT after IT

Predictors	N = 17
Age, median (min, max)	45 (19-67)
Female, n (%)	7 (41)
Race, n (%)	
Black	2 (11)
White	15 (88)
Preemptive transplant (no dialysis before RT), n (%)	8 (47)
Living donor transplants, n (%)	6 (35)
Pretransplant DM, n (%)	1 (6)
Pretransplant HTN, n (%)	1 (6)
Type of intestinal transplant, n (%)	
Isolated SB	10 (59)
Liver/SB/pancreas	5 (30)
Full MVT	1 (6)
Modified MVT	1 (6)
Liver containing intestinal graft, n (%)	6 (36)
Induction therapy for RT, n (%)	
None	10 (59)
Thymoglobulin	0 (0)
Alemtuzumab	6 (35)
Basiliximab	1 (6)
Acute rejection of RT, n (%)	5 (29)

known that patients receiving liver intestine transplants have a favorable outcome in the long run, with lower rejection rate and better survival when compared with other types of IT.[6,7] However, patients awaiting a liver-intestine transplant have higher mortality on the waitlist, and in the first year after transplantation compared with intestine without liver transplant recipients.[6,27] Hence, this effect on worse renal outcomes may be related to the early posttransplant events and warrants further study.

Our study highlights the significantly increased mortality risk associated with starting dialysis in IT recipients with only one fourth of the patients surviving to 1 year. Future studies should look for potentially modifiable risk factors among clinical events surrounding dialysis initiation.

Finally, patients that received a RT after IT had suboptimal graft survival at 1 and 3 years, which were predominantly related to patient deaths from infectious complications. This RT survival is lower than observed for RT after liver, heart, or lung transplantation.[33-35] Reasons for this are unclear but is probably related to the overall survival of IT recipients. The sample size was insufficient to draw any conclusions with regard to the use of induction therapy, living donor transplants or preemptive RT. Although these results temper expectations for RT after IT, additional studies are needed to confirm our findings. Still, we believe these results will aid transplant teams in counseling of IT patients with renal failure, and their prospective living donor candidates. Our study was not designed to look at the survival benefit of transplantation over dialysis in IT patients developing renal failure. Although RT fared better than dialysis, this might be related to a selection bias, with only relatively less sick patients making it to RT. However, given the benefits of RT in general, carefully selected patients should continue to be offered the option of RT. Additionally, we have observed in our practice intestinal ischemia that was temporally related to dialysis related hypotension, which is known to occur in the dialysis population.[36]

Our study had limitations. Though the overall study cohort was large, the number of patients in the earlier 2 eras was small. Although our era-specific analysis accounted for the major modifications in the IS protocols and surgical techniques, it did not account for the specific modifications that occurred during the study period. We were unable to study the etiology of AKI preceding dialysis initiation. Data regarding sepsis events, volume depletion, and use of nephrotoxic medications, such as aminoglycosides, amphotericin, and vancomycin, were not available for analysis. Inability to account for sepsis likely overestimates the association of renal failure with mortality. The number of patients with kidney after intestinal transplant was small, thus limiting assessment of risk factors for poor outcomes. We only included adult IT recipients and thus our study findings may not be applicable to the pediatric patients who account for 40% of the annual intestinal transplant recipients.[27] Finally, though large, this is still a single-center study, and findings should be interpreted with that limitation.

There are several strengths to our study. Loss to follow-up was minimal despite long duration of follow-up. We used clear definitions for dialysis and ESRD while assessing renal outcomes. Additionally, these outcomes were patient oriented unlike intermediate outcomes, such as change in creatinine or glomerular filtration rate. Lastly, this is the first large study in intestinal transplant patients to report the effect of these renal outcomes on patient survival. We believe our study provides healthcare providers with useful data that can be used while discussing dialysis-related prognosis with IT patients and family members.

In summary, we have shown that renal failure requiring dialysis or RT is strongly associated with poor patient outcomes after IT. Baseline creatinine and the use of liver containing grafts had higher risk for needing dialysis or RT after IT. Acute kidney injury episodes preceded dialysis initiation in a significant proportion of patients suggesting maximal care should be taken to preserve native renal function whenever possible. We also show that renal allograft survival after IT is suboptimal, largely from death with a functioning renal allograft which needs further exploration.

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