Small bowel transplantation – the latest developments

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Abstract

The UK has played a pivotal role in the development of intestinal transplantation to a procedure that is routinely offered to patients with complex intestinal failure and other life-threatening conditions. In the international Intestinal Transplant Registry's latest report, the overall survival figures were inferior to those expected for patients on parenteral nutrition (PN). However, in the better performing centres, survival figures for isolated intestinal transplantation are approaching those of PN, and good candidates for surgery might be offered the procedure as an alternative to PN if this trend continues. The more complex procedure to transplant multiple abdominal viscera including liver – multivisceral transplantation – is reserved for patients with an expected survival of less than a year without this procedure. Careful patient selection is important and has been enhanced by the National Adult Small Intestinal Transplant forum, which provides a national multidisciplinary review of patients considered as potential transplant candidates. The development of systems to estimate patient survival would enhance patient selection and allow more timely transplantation. This might also reduce late referral, which continues to contribute to mortality. Clinicians should consider referral of patients at an early stage to allow timely consideration of transplantation is also discussed.

Keywords Infections; intestinal; MRCP; multivisceral; nutrition; transplantation

Key points

- The possibility of future intestinal transplantation should be considered in the management of all intestinal failure (IF) patients and those with extensive benign intra-abdominal disease. Combined grafts including the intestine should be considered for patients with cirrhosis and extensive porto-mesenteric venous thrombosis precluding isolated liver transplant, or patients with short bowel and end-stage renal disease
- IF patients with significant complications of parenteral nutrition should be referred for transplantation assessment or at least discussed with a centre
- Ultrashort small bowel (<20 cm) should be considered for early transplantation.
- Post-transplant patients presenting acutely to hospital must be treated without delay and advice should be sought as soon as possible from their transplantation centre.
- Quality of life on 'home parenteral nutrition' can be improved by transplantation in about one-third of patients.

A brief history of intestinal transplantation

The innovations in surgical techniques developed in the canine model by Richard Lillehei the 1950s and 1960s, and the vascular anastomotic methods of Carrel, are of fundamental importance in the development of intestinal transplantation. Together with the introduction of a series of powerful anti-rejection agents in the late 1980s,[1] they promoted attempts in humans, leading to a cluster of reports describing transplantation of part or all the intestine, in combination with other organs or as isolated grafts.[2]

Survival, however, remained poor[3] until the introduction of lymphocyte-depleting induction therapy with agents such as alemtuzumab in the 1990s, and the appreciation that preoperative preparation, patient selection and postoperative management bring a series of unique challenges often without precedent. In addition, most treatment has little or no evidence base to guide practice.[4] This demands a fastidious, multidisciplinary approach to all aspects of management. Today, intestinal transplantation can be considered a routine component of the management of adult and paediatric patients with intestinal failure (IF) and is beginning to replace parenteral nutrition (PN) in long-term management for many of them.

Intestinal transplantation has progressed from the implantation of isolated small bowel to the inclusion of additional organs as a multivisceral transplant (where liver and other organs are transplanted as a composite cluster of organs) or a modified multivisceral transplant, in which the small intestine and pancreas are transplanted along with a variety of other organs (which can include stomach, kidney, colon, spleen and occasionally abdominal wall) depending on requirements, but excludes the liver. Transplantation of the colon is now more common and has been introduced as a means of improving fluid balance and quality of life (QOL). Over the last 20 years, indications for transplant have broadened to include patients with more complex conditions such as portomesenteric venous thrombosis, and the development of new techniques such as

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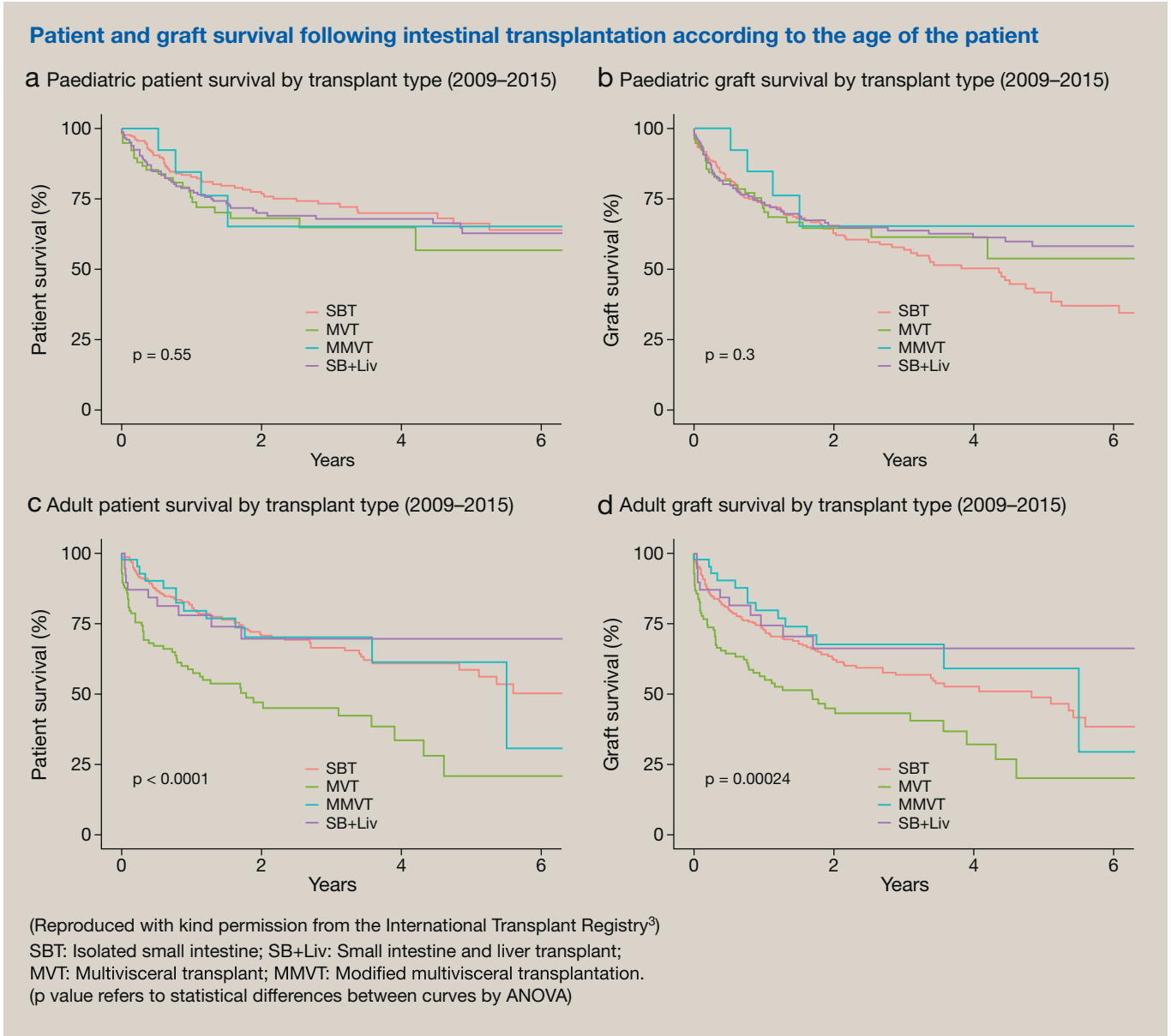
preoperative embolization of the superior mesenteric artery to reduce peroperative bleeding.

The current role of transplantation in the management of intestinal failure

The survival rates of patients requiring home parenteral nutrition (HPN) are 86–97% at 1 year, 57–83% at 5 years and 43–71% at 10 years. Survival after intestinal transplantation (any combination of organs including small intestine), as reported by the international registry,[3] (Figure 1) is lower than for HPN (Table 1), but this survival gap has closed over the last decade.

As the survival gap between HPN and transplantation decreases, the importance of improved QOL increases. Where there is little to choose between the two techniques regarding survival, patients whose QOL can be enhanced by transplantation should logically be given this opportunity. The limited QOL data published suggest that considerable improvements can be seen in individual patients after transplantation; however, overall about half the patients do not improve, and around 20% experience a deterioration in QOL after transplantation. Psychiatric health can also deteriorate after transplantation, as can nutritional status, with some patients losing up to 25% of their body weight during the first postoperative year. Nevertheless, recent advances in practice, such as the inclusion of a colonic segment, can improve both independence from PN and graft survival. This and the appreciation that preoperative co-morbidity greatly influences survival,[4] might lead to better patient selection and define a cohort of patients for earlier transplantation.

The current indications for intestinal transplantation can be conceptualized around the premise that survival is better on HPN. Transplantation should be considered before patients lose the opportunity owing to disease progression and progressive co-



(Reproduced with kind permission from the International Transplant Registry[3])
SBT: Isolated small intestine; SB+Liv: Small intestine and liver transplant;
MVT: Multivisceral transplant; MMVT: Modified multivisceral transplantation.
(p value refers to statistical differences between curves by ANOVA)

Figure 1

Patient survival after transplantation compared with HPN

	1 year (%)	5 years (%)
Home parenteral nutrition (HPN)	83–97	49–79
Adult patients (2008–2014)		
Data from international registry[3]		
Isolated intestinal transplantation	80	59
Modified multivisceral transplantation	72	50
Multivisceral transplantation	66	22
2008–2018 data from Cambridge		
Isolated intestinal transplantation	85.6	75
Liver-containing graft (multivisceral)	75.5	28
Paediatric patients (2008–2012)		
Data from international registry[3]		
Intestinal transplantation	86	70
Modified multivisceral transplantation	67	67 (3 years)
Multivisceral transplantation	75	48

Table 1

morbidity, in particular loss of adequate venous access and IF-associated liver disease (Table 2).

What does intestinal transplantation involve?

In the UK, candidates are formally assessed at an intestinal transplantation centre. There are currently four of these: two adult centres — Cambridge (Addenbrooke's Hospital) and Oxford (Churchill Hospital); and two paediatric centres — Birmingham (Birmingham Children's Hospital) and London (King's College Hospital, London). Assessment is usually conducted during an inpatient stay, when a comprehensive review of the patient's physical and psychological status is conducted. Co-morbidity is investigated and resolved as far as possible. After formal

Selection criteria for intestinal transplantation in the UK

Conditions that are considered for transplantation

There is a high mortality on intestinal transplant lists both in adults and in children, mostly due to end-stage intestinal failure-associated liver disease. The timing of referral for intestinal transplantation must be decided on a case-by-case basis. It is, however, recommended that adults and children with irreversible intestinal failure who develop complications should be discussed with an intestinal transplant centre before life-threatening complications develop. Pre-operative co-morbidity has a profound influence on postoperative survival.

1.1 Irreversible intestinal failure, plus

1. Life-threatening complications of parenteral nutrition

a) Progressive intestinal failure-associated liver disease (IFALD) or non-IFALD despite all remedial actions

- Objective evidence of liver disease judged by biochemistry and biopsy
- Combined intestinal and liver transplant (rather than isolated intestinal transplantation) is best considered in the presence of advanced liver disease (portal hypertension or advanced fibrosis)

b) Severe sepsis

- More than one life-threatening episode of catheter-related sepsis for which no remediable cause can be identified by a recognised intestinal failure centre
- Endocarditis or other metastatic infection

c) Limited central venous access

- Venous access limited to three major conventional sites in adults (above and below the diaphragm) and two major conventional sites above the diaphragm in children
- Conventional central venous sites are defined as internal jugular, subclavian and femoral veins

2. Very poor quality of life thought likely to be correctable by transplantation

1.2 Patients with indications for extensive surgery involving partial or complete evisceration

1. Surgery to remove a large proportion of the abdominal viscera which is considered untenable without associated multi-visceral transplantation/isolated small bowel transplantation (e.g. extensive desmoid disease, extensive severe mesenteric arterial disease requiring intervention)
2. Localized malignancy considered amenable to curative resection which would necessitate extensive evisceration (e.g. localized neuroendocrine tumours). Particular caution should be exercised in this group and patients should be discussed in a multidisciplinary multicentre forum before any planning is commenced. (e.g. National Adult Small Intestinal Transplant, NASIT).

1.3 Patients requiring transplantation of other organs where exclusion of simultaneous intestinal transplantation would adversely affect patient survival

1. Where the transplantation procedure is expected to preclude the possibility of future intestinal transplantation (e.g. loss of venous access or further human leukocyte antigen sensitization)
2. Where the need for subsequent intestinal transplantation is considered likely and the risk of death is increased by excluding the intestine from the graft. Examples include predictable problems related to administering immunosuppression (e.g. line sepsis), or continuing severe intestinal disease such as diabetic visceral neuropathy, or ultrashort bowel syndrome, which may cause fluid, electrolyte and acid base balance problems that would damage an existing or planned renal graft

1.4 Inclusion of a renal graft at the time of intestinal or multi-visceral transplantation

Deterioration in renal function is expected following intestinal transplantation and studies suggest a fall to 43% of preoperative glomerular filtration rate (GFR) can be expected 2 years after transplantation, and this is greater in those with cumulative tacrolimus levels >4500 ng/day/ml, at 34% of pre-transplant GFR. Therefore, patients with moderately impaired renal function can be expected to develop significant dysfunction over the first 2 years. This can seriously affect their survival as many have very poor venous access which will not support renal replacement therapy. Adults are particularly prone to renal deterioration whereas children are less affected. It is recommended that adults with corrected GFR of <45 ml/minute/m^2 are evaluated for the possibility of simultaneous renal transplantation. This should also be considered for children with impaired renal function although as the expected deterioration is less, the nGFR threshold for transplantation may be lower.

Table 2

Common Infections after intestinal transplantation in the UK

	Most common pathogens	Location	Prophylaxis	Clinical features	Diagnosis	Treatment
Bacterial	*Escherichia coli*	Bowel translocation	Two weeks' piperacillin-tazobactam	Generalized sepsis ± organ-specific features (respiratory, urinary, intra-abdominal)	Blood/urine/sputum/wound/drain cultures	Initially broad-spectrum antibiotics, adjusting according to sensitivities of cultured organisms
	Klebsiella pneumoniae	Wound	Meropenem if penicillin-allergic or prior ESBL		Cross-sectional imaging, occasionally PET-CT	
		Pneumonia				
		Abdominal collection/peritonitis				
		Urinary tract				
	Pseudomonas aeruginosa	Pneumonia				
	Stenotrophomonas maltophilia	Pneumonia				
		Central line related				
	Staphylococcus aureus (including MRSA)	Central line related	Add vancomycin if prior MRSA			
		Wound				
	Enterococcus (including VRE)	Bowel translocation				
		Abdominal collection/peritonitis				
	Mycobacteria/Nocardia	Anywhere				
Fungal	*Candida* spp.	Bowel translocation	Two weeks' caspofungin, then fluconazole for 6 months	Generalized sepsis ± organ-specific features (respiratory, urinary, intra-abdominal)	Blood/urine/sputum/wound/drain cultures	Anidulafungin, adjusting according to sensitivities
		Central line related				
		Mucocutaneous (oropharyngeal, genito-urinary)				
		Disseminated (intra-abdominal, endocarditis, endophthalmitis				

	Aspergillus spp.	Pulmonary	Two weeks' amphotericin B, then discuss with microbiology		Cross-sectional imaging	Voriconazole, amphotericin B or caspofungin
		Disseminated			BAL and trans-bronchial biopsy	
		Cerebral Sinusitis			Galactomannan (BAL/serum)	
	Mucoraceous moulds	Pulmonary	Two weeks' amphotericin B, then discuss with microbiology			Amphotericin B, discuss with microbiology
		Disseminated Cerebral Sinusitis				
	PCP	Pneumonia	Co-trimoxazole	Pneumonia	BAL with PCR	Co-trimoxazole
Viral	CMV	CMV colitis, retinitis and hepatitis	One year prophylactic ganciclovir/valganciclovir if donor or recipient is CMV-positive	Non-specific flu-like symptoms	Viraemia detected on regular bloods screening	CMV: initially treatment dose ganciclovir
	EBV	EBV-PTLD late >1 year	1 year prophylacic aciclovir if donor and recipient are CMV-negative	CMV often targets mucosal surfaces-colitis, retinitis	Viral inclusions/positive immunohistochemistry seen in bowel biopsies	Foscarnet/cidofovir depending on resistance
				EBV viraemia may precipitate PTLD	Cross sectional imaging, PET-CT and targeted biopsy for suspected PTLD	PTLD: rituximab ± CHOP chemotherapy
Parasites	*Toxoplasma*	Disseminated	Co-trimoxazole	Non-specific flu-like symptoms	PCR	Pyrimethamine-sulfadiazine
	Strongyloides			Pneumonia		

BAL, bronchiolar lavage; CMW, cytomegalovirus; EBV, Epstein—Barr virus; PCP, Pneumocystis carinii (jirovecii) pneumonia; PET-CT, positron emission tomography-computed tomography; PTLD, post-transplant lymphoproliferative disorder.

Table 3

assessment, adult patients in the UK are presented to a national forum (National Adult Small Intestinal Transplantation (NASIT)) at which their details are considered by a multidisciplinary group including specialists who are not from transplant centres. Expert opinion from the major intestinal failure (IF) centres is available. This forum is designed to provide a balanced view of the potential benefit of transplantation for each patient. If NASIT approval is given, patients are listed. Because of the constraints of donor selection, they may, however, wait a year or more for surgery, particularly if they have been sensitized to antigens in the human leukocyte antigen (HLA) group.

The surgical procedure is often protracted, and the recipient procedure may extend over 16 hours or more. The intestine is transplanted as an isolated graft or in combination with other organs as a so-called 'cluster graft'. Most transplants, however, fall into one of four categories:

- isolated intestine
- liver and intestine
- multivisceral (liver, intestine, stomach, pancreas)
- modified multivisceral (intestine, stomach, pancreas).

In addition, patients usually undergo colonic and sometimes renal transplantation. Patients invariably have an ileostomy, at least initially, to provide access for ileoscopic surveillance biopsies to detect rejection.

After surgery, it is common to remain in an intensive therapy unit for 2–3 days, followed by a high-dependency unit for 2 or 3 weeks. Finally, there is usually a less intensive ward stay for a further 4–6 weeks to establish full enteral nutrition, satisfactory immunosuppression and resolution of any postoperative problems such as infection.

Infection is the most common postoperative complication (Table 3). Rejection remains a frequent problem despite the advent of lymphocyte-depleting agents. However, early detection and treatment remain a pivotal part of the process, and surveillance biopsies are taken via the stoma weekly in the first month. Fluid and electrolyte balance is also challenging but of critical importance to prevent the downward spiral triggered by a confluence of salt and water imbalance, impaired renal function and sepsis, which can result in multiorgan failure. At this point, other pre-existing comorbidities and the lack of venous access for treatments, such as haemodialysis, can result in inexorable deterioration.

The postoperative management of these patients is complex and requires a fully integrated team of consultants from a broad range of specialties who are well motivated and able to provide prompt, combined, consultant-led multidisciplinary management. The combination of inducing profound immunosuppression and transplanting an organ with very high antigenicity that also contains a host of potential pathogens produces a unique clinical setting.

Which patients should be referred to a transplant centre for consideration?

All patients with IF should be managed by a multidisciplinary intestinal rehabilitation team. The aims are to maximize enteral function to achieve partial or full weaning from PN, improve QOL and reduce complications. Patients who meet established criteria for transplantation (Table 2) or have special circumstances suggesting that they may soon meet the criteria (Table 4) should be referred. It can be difficult to decide the right time to list a patient for transplantation, but it is preferable to refer them to a transplant centre early so that they can be observed. The window for transplantation can otherwise be missed, particularly if patients have rapidly progressive liver disease, insufficient vascular access to facilitate transplantation or the development of a contraindication. Patients who are well enough to be transplanted from home have been found to have better postoperative survival (Figure 2).

Patients with complications of extensive portomesenteric venous thrombosis, whether this occurs in the setting of cirrhosis or develops as a result of a prothrombotic disorder, benefit from referral and discussion in a multiprofessional setting. Special consideration should also be given to PN-dependent patients who require transplantation of other organs (e.g. with short bowel syndrome or end-stage renal failure). They may benefit from a cluster graft including intestine rather than undergoing sequential transplants, which carries risks of tissue sensitization and increased immunosuppression. An emerging indication is that of the abdominal catastrophe, which can be caused by widespread acute arterial or venous disease, abdominal penetrating injury or compartment syndrome. For cases with no 'standard' surgical options, urgent discussion with a transplant centre is needed.

What is the likely future demand for intestinal transplantation?

There is a process of evolution for organ transplant operations, which often originate as last-hope, largely emergency procedures (which are predictably very likely to fail in such circumstances). As outcomes improve, the indications change to becoming routine life-*saving* procedures, and then life-*prolonging* when it is possible to predict likely outcomes without transplantation. Finally, they may become life-*enhancing* when the organ failure or its supportive therapy carries unacceptable morbidity. Intestinal transplantation is currently largely reserved for those patients who have significant problems with HPN or other conditions necessitating transplantation (Table 2), and transplantation is not employed as an alternative to uncomplicated HPN. However, indications are evolving, and for those with ultrashort bowel (<20 cm) syndrome, transplantation may offer a survival advantage. A particular problem in this group is the risk of rapidly developing liver cirrhosis; these patients are now often considered as candidates for early transplantation as an alternative to HPN.

The cost of intestinal transplantation and follow-up is equivalent to about 3 years of HPN, and the procedure is cost-effective in the long run. Furthermore, there is currently no significant donor shortage for intestines given the small number of operations performed. It is therefore likely that informed patient choice will be increasingly taken into account in decision-making for intestinal transplantation. The number of procedures undertaken will therefore probably increase as a result of balancing the marginal benefit in terms of life expectancy from HPN against the potential improvement of QOL after transplantation.

Approximately 2500 adult patients in the UK are given HPN support. Of these approximately a third have short bowel syndrome (around 140 new registrations a year for this indication) and could be future candidates for intestinal transplantation. A

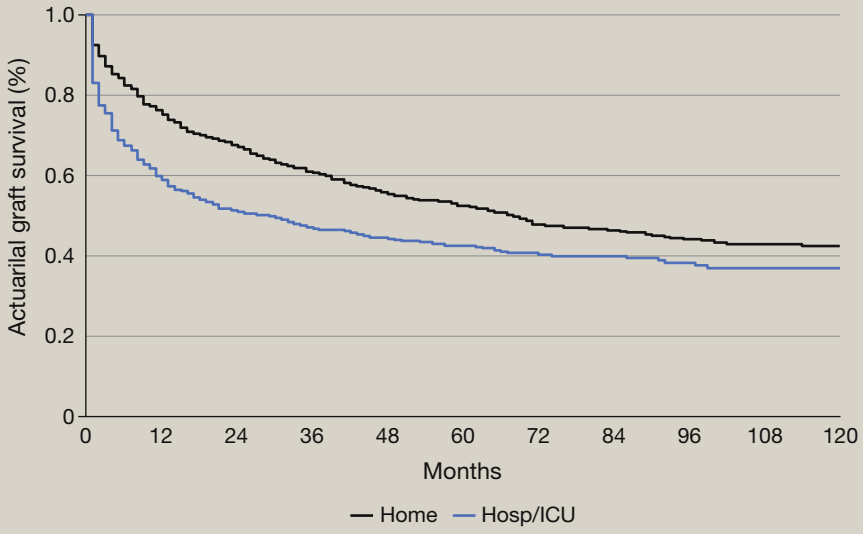
Circumstances where consideration of intestinal or multivisceral transplantation may be appropriate (in addition to the standard indications for transplantation in Table 2)

Patients with IF and one or more of the following		
• Liver disease	IF-associated liver fibrosis is potentially reversible by early intestinal transplantation Outcomes for isolated intestine transplantation are better than for combined liver and intestine, so it is best to identify liver disease early and refer before liver transplantation is required	Significant IF-associated liver disease can be difficult to detect as liver blood tests are often abnormal on long-term PN but can also be normal in the presence of advanced fibrosis FibroScan® results are unreliable, and signs of portal hypertension may be absent because of reduced portal inflow in short bowel syndrome Liver biopsy is currently the only reliable diagnostic test in this setting
• Frequent line sepsis	Patients with three or more episodes of line sepsis in a year or one episode of life-threatening sepsis may be candidates for transplantation, particularly if there are other relative indications	Evaluate aseptic technique Reduce additional intravenous medications and access Consider use of taurolidine lock Discuss with regional/national IF centre
• Ultrashort bowel syndrome	Less than 20 cm of jejunum to a stoma is associated with rapid-onset liver disease. These patients should be referred early for the reasons given above	Refer to or discuss with an IF or transplant centre
• Coexisting diabetes mellitus with complication	Pancreatic transplantation is increasingly being considered in type 1 diabetes mellitus, particularly in combination with kidney transplantation Gastrointestinal neuropathy may make intestinal transplantation a consideration in this setting	Refer to transplantation centre for consideration of combined pancreas and small bowel transplantation
• Pseudo-obstruction. Complicated by severe abdominal pain	Patients with intractable abdominal pain from distended small and large intestine who are PN-dependent are a relatively high-risk group for PN complications and may be assessed for transplantation at an earlier stage	Refer patient to transplant centre
• High-output stoma	Patients with a very high stoma output, often from a proximal jejunostomy, are at risk of renal impairment and may have a significant impairment of QOL as a result of leaking stoma bags and fluid balance dynamics	Discuss with transplant centre
Patients without IF		
• Desmoid disease	Consider for extensive disease threatening or damaging other important structures Early surgical intervention may be preferable before the tumour becomes unresectable or requires resection of the abdominal wall or major vascular structures	Refer to transplantation centre for assessment or to the national desmoid centre[a]
• Mesenteric vascular disease	For extensive mesenteric arterial or venous disease involving the intestine and other essential intra-abdominal organs — thrombosis may occur acutely in otherwise asymptomatic individuals An acute presentation is not a contraindication	Refer to transplantation centre for assessment For urgent cases, emergency transfer and transplantation may need to be considered

[a] UK National Desmoid Centre, St Mark's Hospital, Harrow, Middlesex.

Table 4

Effect of pre-transplant status on graft survival (transplants between 2001 and 2012)



(Reproduced with kind permission from the International Transplant Registry[3])
Home, patient transplanted from home; hospital/ICU, patient transplanted from hospital, including intensive care unit.

Figure 2

survey in 2011 of >800 patients in European centres[5] who had been given HPN showed that around 20% met current indications for intestinal transplantation with no existing contraindications. Interestingly, only 1 in 10 of these were actually transplanted during a 5-year follow-up period. Therefore, as the option of transplantation becomes more widely appreciated, a 5–10-fold increase in procedures might be predicted. Furthermore, as outcomes improve, the indications for transplantation will broaden. Recently, indications have extended and a number of patients have been given multivisceral grafts before requiring HPN (for indications such as portomesenteric thrombosis and acute widespread mesenteric vascular occlusion), although this situation greatly increases the risk associated with transplantation, it offers the patient a reasonable chance of survival in an otherwise hopeless situation.

Why do gastroenterologists need to know about intestinal transplantation?

Transplantation will become an increasing part of gastroenterological practice as more patients are transplanted and require follow-up at a local level in collaboration with the main centres. Within the next 10 years, it is likely that intestinal transplantation will become an integral part of most gastrointestinal specialty registrar training programmes, in a similar manner to liver transplantation in hepatology training today.

Patients are also becoming increasingly aware of the option of intestinal transplant and may have an expectation of being considered for this. The referring gastroenterologist should have an awareness of the indications (Table 2), processes and risks

Advice for management of sick intestinal transplantation patients admitted to a non-transplantation hospital

1. Contact the appropriate transplant centre without delay for advice and possible transfer
2. Undertake a full infection screen, including culture (and microscopy) of blood, urine, sputum and stoma effluent/stool, cytomegalovirus polymerase chain reaction, chest X-ray, abdominal X-ray (computed tomography scan of the abdomen and chest as required)
3. If infection is suspected (usual), commence broad-spectrum antimicrobial therapy without delay. This usually includes meropenem, vancomycin, AmBisome® and ganciclovir. If there is evidence of pulmonary infection, consider high-dose co-trimoxazole, which is active against *Pneumocystis jirovecii*. Advice should be sought from the transplant centre
4. Be aware of the possibility of tacrolimus nephrotoxicity and neutropenia associated with valganciclovir and co-trimoxazole (patients may already be taking these)
5. Patients will be prone to salt and water depletion. They should be aware of their normal body weight. Assess sodium and water balance with spot urinary sodium and osmolarity, respectively (urine dipstick for specific gravity is a helpful initial guide)
6. Graft rejection is difficult to diagnose so patients should be transferred to an appropriate transplantation centre as soon as possible

Table 5

involved in transplantation. In particular, the trajectory of disease should be considered to ensure that patients are referred before it is too late (Table 4). They must also be physically and psychologically robust enough to undergo transplant. If the referring team is uncertain about a patient's fitness or indication for transplant, an informal discussion with the transplant team can take place first.

At present, the most likely interaction with a local centre will be an urgent admission of a sick transplant patient (Table 5). It is important to consider the high level of immunosuppression and to be familiar with the adverse effects of the commonly used drugs. The most common presentation is with sepsis. In this scenario, broad-spectrum antibiotics and antifungal treatment should be started promptly after cultures have been taken and the transplant centre contacted. Viral infections are also common and should be considered, depending on the clinical presentation. Many of the drugs used (azathioprine, mycophenolate mofetil, valganciclovir, co-trimoxazole) can cause leucopenia, and this may need to be supported with granulocyte–macrophage colony-stimulating factor (GM-CSF) if the patient has sepsis. Complex problems involving coagulopathy and bleeding are also very common, and the transplant unit must be involved in any decisions regarding starting or stopping anticoagulation. In certain scenarios, particularly if the patient shows rejection of the transplant, it is more appropriate for them to be transferred to the transplant unit. ◆

KEY REFERENCES

1 Calne RY. Cyclosporine and liver transplantation. *Mt Sinai J Med* 1987; **54:** 465–6.
2 Grant D, Wall W, Mimeault R, et al. Successful small-bowel/liver transplantation. *Lancet* 1990; **335:** 181–4.
3 Intestinal transplant registry, 2013 report. http://www.intestinaltransplant.org/itr/.
4 Middleton SJ, Nishida S, Tzakis A, et al. Cambridge-Miami score for intestinal transplantation preoperative risk assessment: initial development and validation. *Transplant Proc* 2010; **42:** 19–21.
5 Pironi L, Joly F, Forbes A, et al. Long term follow-up of patients on home parenteral nutrition in Europe: implications for intestinal transplantation. *Gut* 2011; **60:** 17–25.

FURTHER READING

Calne RY, White DJ, Thiru S, et al. Cyclosporin A in patients receiving renal allografts from cadaver donors. *Lancet* 1978; **2:** 1323–7.
Middleton SJ, Pither C, Gao R, et al. Adult small intestinal and multivisceral transplantation: lessons through the "Retrospecto-scope" at a single UK centre from 1991 to 2013. *Transplant Proc* 2014; **46:** 2114–8. https://doi.org/10.1016/j.transproceed.2014.06.035.
NHSBT annual report on intestinal transplantation 2017/2018, https://www.odt.nhs.uk/statistics-and-reports/statistics-and-reports-summary/.
Pither C, Duncan S, Gao R, et al. Quality of life and performance status before and after small intestinal transplantation. *Transplant Proc* 2014; **46:** 2109–13.
POLICY POL194/4.1. 2018, https://www.odt.nhs.uk/transplantation/tools-policies-and-guidance/policies-and-guidance/#intestinal.

TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A 41-year-old woman has chronic intestinal pseudo-obstruction causing intestinal failure and had been having parenteral nutrition for 3 years. She had experienced three episodes of intravenous feeding line infection and had recently recovered from bacterial endocarditis.

What is the most appropriate management?

A Maintain her on a long-term prophylactic antibiotic
B Change her intravenous feeding access lines and sites every 4 months
C Continue current management but provide her with intensive training for line management
D Refer her to an intestinal transplant centre for consideration of transplantation
E Remove the dilated small and large bowel to reduce the risk of bacterial translocation

Question 2

A 50-year-old man presented with small bowel infarction resulting from severe mesenteric atherosclerotic disease. He underwent emergency surgery to remove the necrotic section of small intestine and was left with 50 cm of small bowel leading to a stoma. His large bowel remained intact but was not in continuity.

What is the most appropriate management of this patient?

A List for small bowel transplantation
B Continue parenteral nutrition long term as the only form of nutrition
C Undertake immediate surgery to re-establish continuity to improve fluid balance
D Undertake surgery to lengthen his remaining small intestine
E Continue parenteral nutrition, and introduce oral feeding as tolerated.

Question 3

A 26-year-old woman presented for review. She had been established on parenteral nutrition for short bowel syndrome after a road traffic accident 5 years previously. This had resulted in severe abdominal trauma and the loss of most of her large and small intestine, leaving only 40 cm of small bowel to a jejunostomy.

Investigations

- Bilirubin 18 micromol/litre (1–22)
- Alanine aminotransferase 43 U/litre (5–35)
- Alkaline phosphatase 120 U/litre (45–105)
- Ultrasonography showed evidence of a fatty liver

What is the next most appropriate investigation?

A CT scan of abdomen and pelvis
B FibroScan® (ultrasound elastography)
C Repeat liver function tests in 6 months
D Measure the serum lipid profile
E Undertake a liver biopsy