Intestinal transplantation: surgical techniques and rejection

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By

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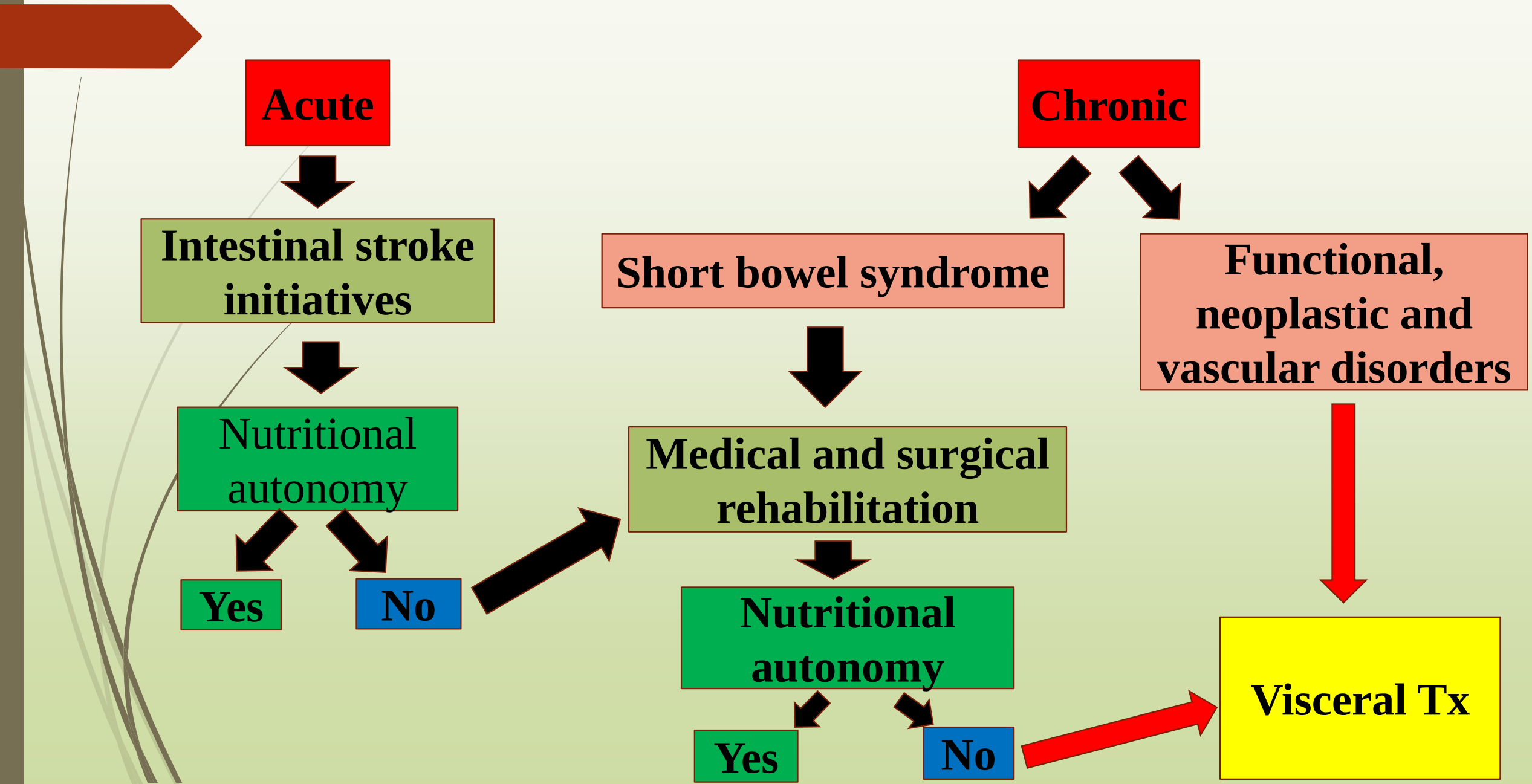
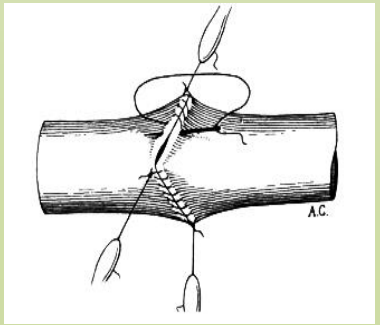
Management of IF



History of Visceral Tx

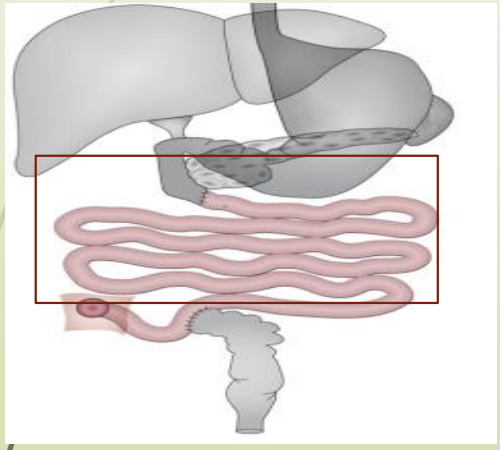
- **2000** → Center for Medicare and Medicaid Services → **Visceral Tx** → **Approved therapeutic modality for chronic IF with insurance coverage**
- **1995**
  - → **n=162, visceral Tx.** | **Tacrolimus; improved patient and graft survival.**
  - → **n=18, visceral Tx.** | **Cyclosporine; refractory rejection and sepsis.**
- **1985**
- **1970** → **Worldwide n=8, ISB Tx.** | **Azathioprine; disappointing results**
- **1967** → Lillehei → **1st Reported ISB Tx in Human.**
- **1960** → Starzl → **1st MV Tx in dogs.**
- **1959** → Lillehei → **1st ISB Tx in dogs.**
- **1902** → Alexis Carrel → **Triangulation method**



Visceral (intestinal) Transplantation (Tx)

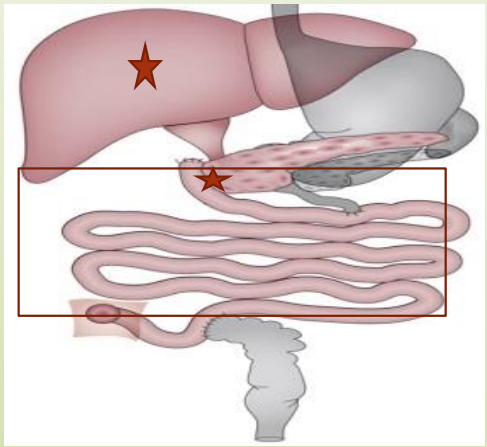
Types

Isolated small bowel (ISB) Tx



Intestine

Liver-intestine (LI) Tx

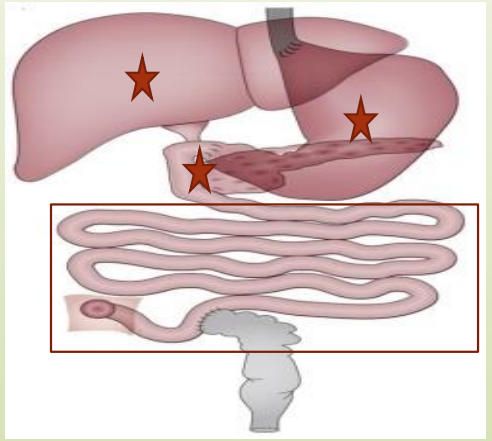


Intestine

Liver

Multivisceral (MV) Tx

Full MV Tx



Intestine

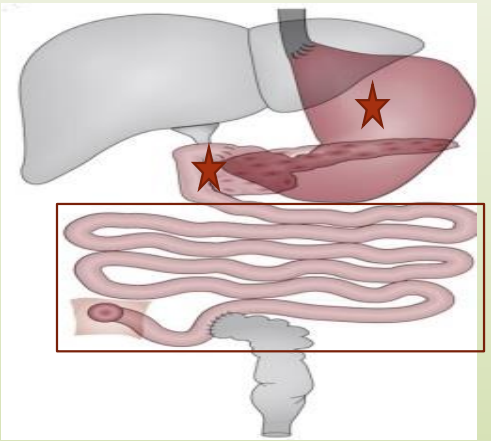
Liver

Stomach

Duodenum

Pancreas

Modified MV Tx



Intestine

Stomach

Duodenum

Pancreas

Visceral Tx

Protocols of immunosuppression

	Induction agent (s)	Maintenance agent (s)
Protocol 1	• **Daclizumab.**	• **Tacrolimus.** • **Steroids.**
Protocol 2	• **rATG (rabbit antithymocyte globulin).** • **Rituximab.**	• **Tacrolimus.**
Protocol 3	• **Alemtuzumab.**	• **Tacrolimus.**

PATIENTS AND METHODS

Setting of the study

GI Transplant Division, Miami Transplant Institute/Jackson Memorial Hospital, University of Miami Miller School of Medicine, Miami, Florida, USA

Subjects

Criteria of the recipients

Inclusion criteria

Failure of TPN

- **Liver failure.**
- **Thrombosis of central veins.**
- **Central line-related systemic sepsis.**
- **Dehydration.**

Conditions associated with early death

- **Desmoid tumor.**
- **Ultra-SBS.**
- **Congenital mucosal disorders.**
- **IF with high morbidity.**

Exclusion criteria

- **Significant cardiopulmonary insufficiency**
- **Incurable malignancy**
- **Intraabdominal or systemic infections**
- **Severe immune deficiency syndromes**

PATIENTS AND METHODS

TECHNICAL DESIGN

Subjects

Criteria for the donors

Inclusion criteria

- **Cadaveric (Brain dead, heart beating).**
- **Younger than 50 years old.**
- **Identical and compatible ABO-blood grouping.**
- **BMI is less than 28 kg/m^2.**
- **ICU stay is ≤5 days.**
- **CIT is no longer than 9 hours.**
- **Good liver function, if MV allograft is being procured.**
- **Serum sodium level is not higher than 155 mEq/L.**
- **CMV and EBV positive or negative donors.**

Exclusion Criteria

- **Extended criteria donors.**

PATIENTS AND METHODS

TECHNICAL DESIGN

Tools of the study

49 Patients

13 Patients

Group (I)

ISB transplant recipients

- **SBS.**
- **Congenital motility disorders.**
- **Enterocyte absorptive capacity deficiency.**
- **Gardner's syndrome.**

36 Patients

Group (II)

Full MV transplant recipients

PN associated liver failure

+

- **SBS.**
- **Complex abdominal pathology.**

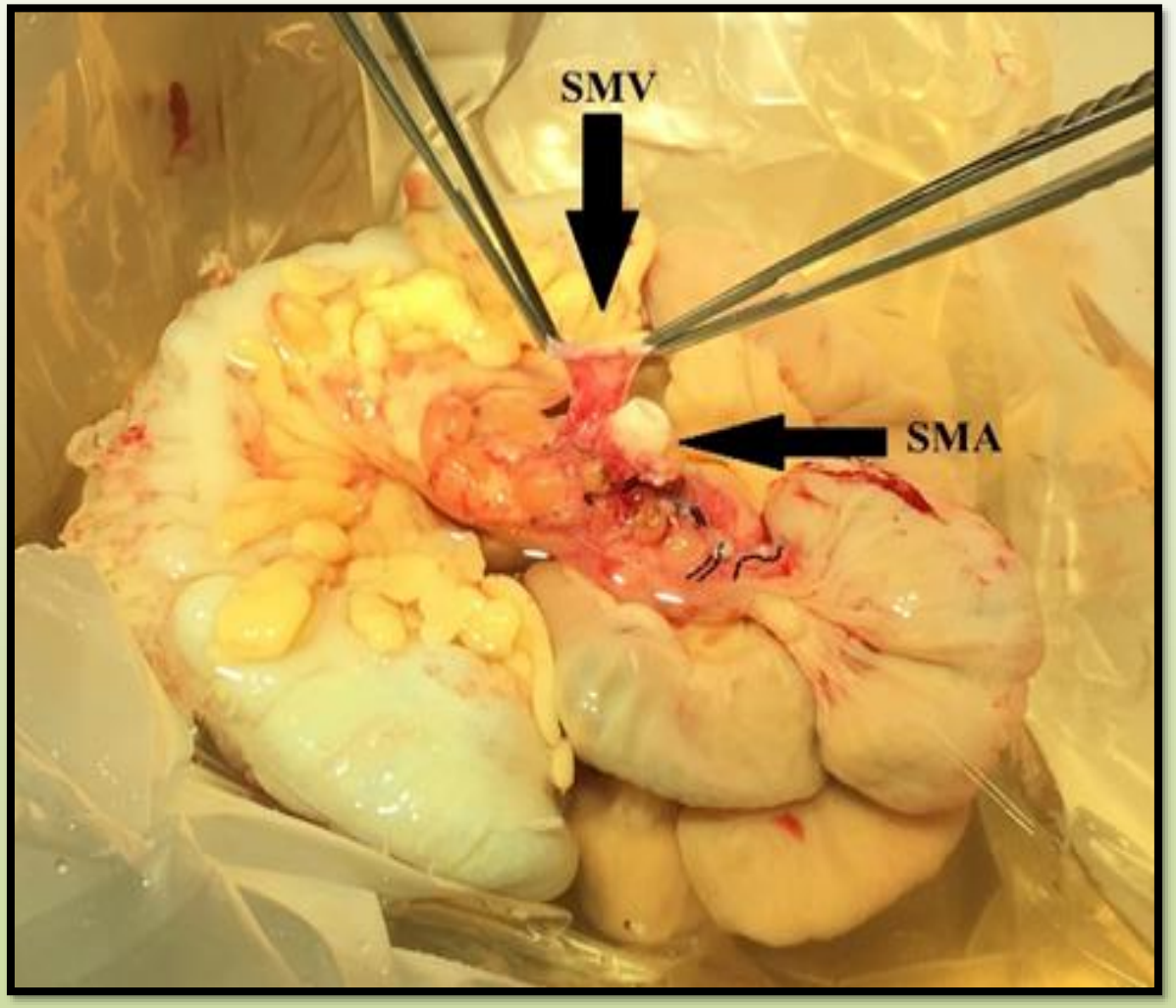
PATIENTS AND METHODS

OPERATIONAL DESIGN

Surgical techniques

ISB Tx (n=13)

Back-table preparation



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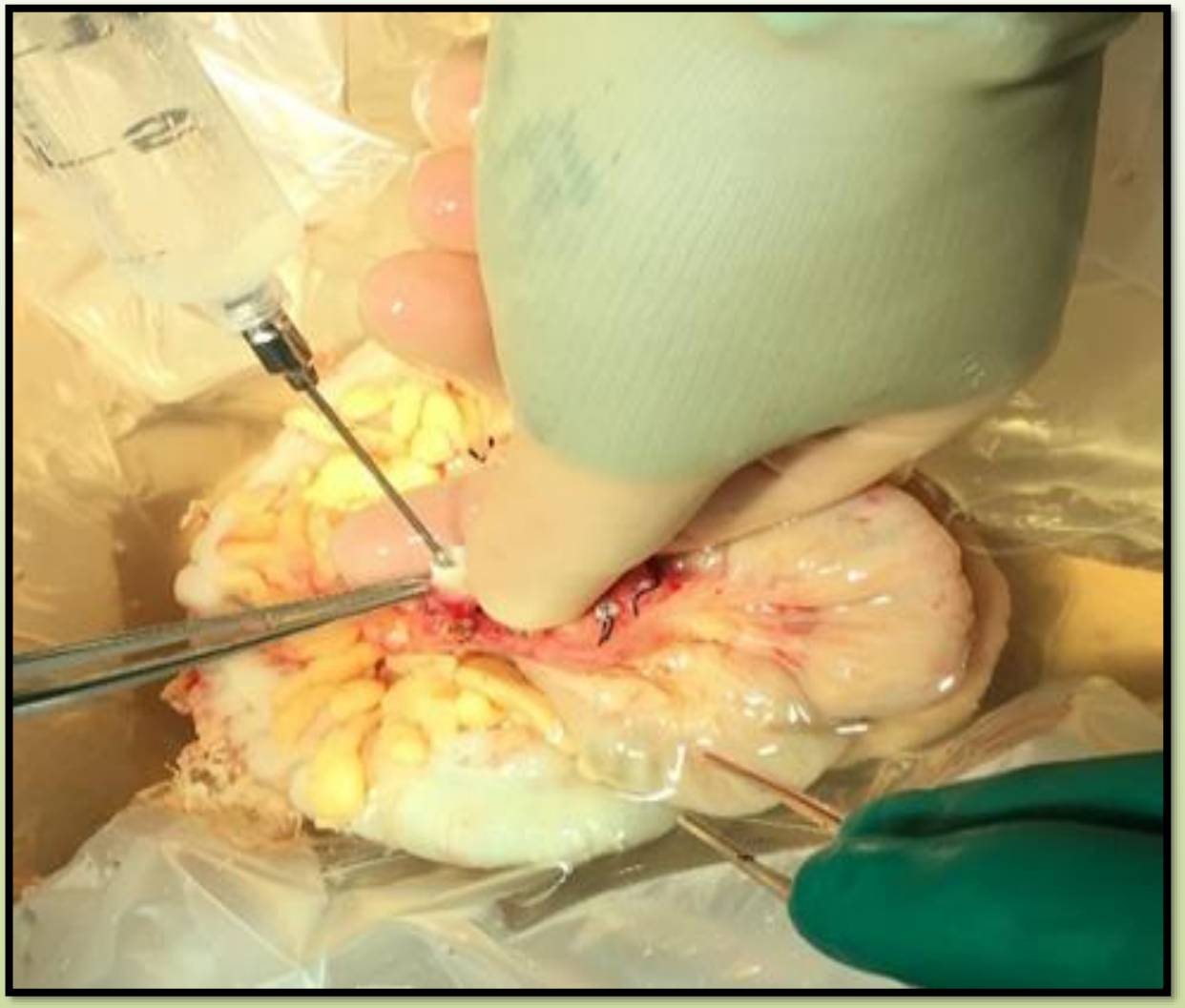

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ISB Tx (n=13)

Recipient procedure

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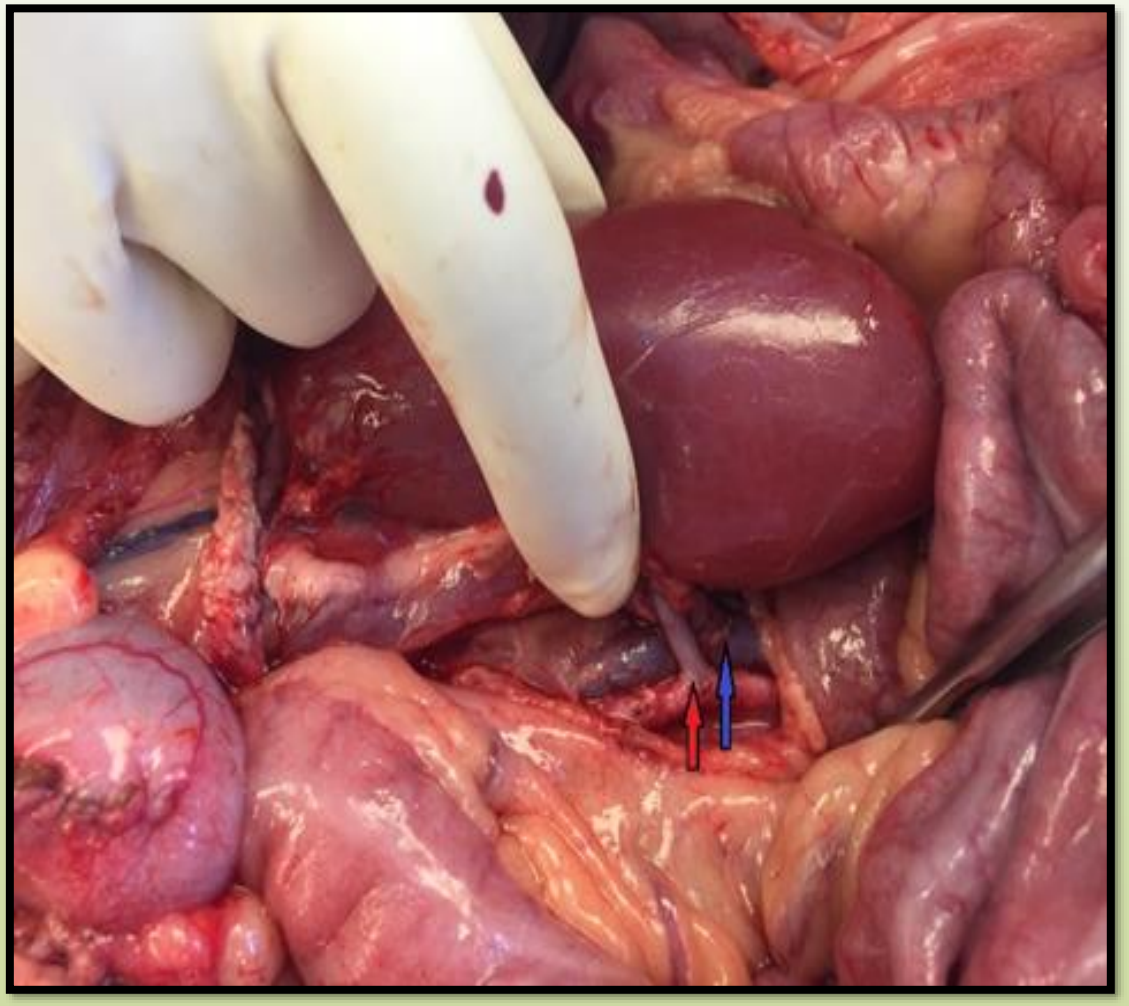

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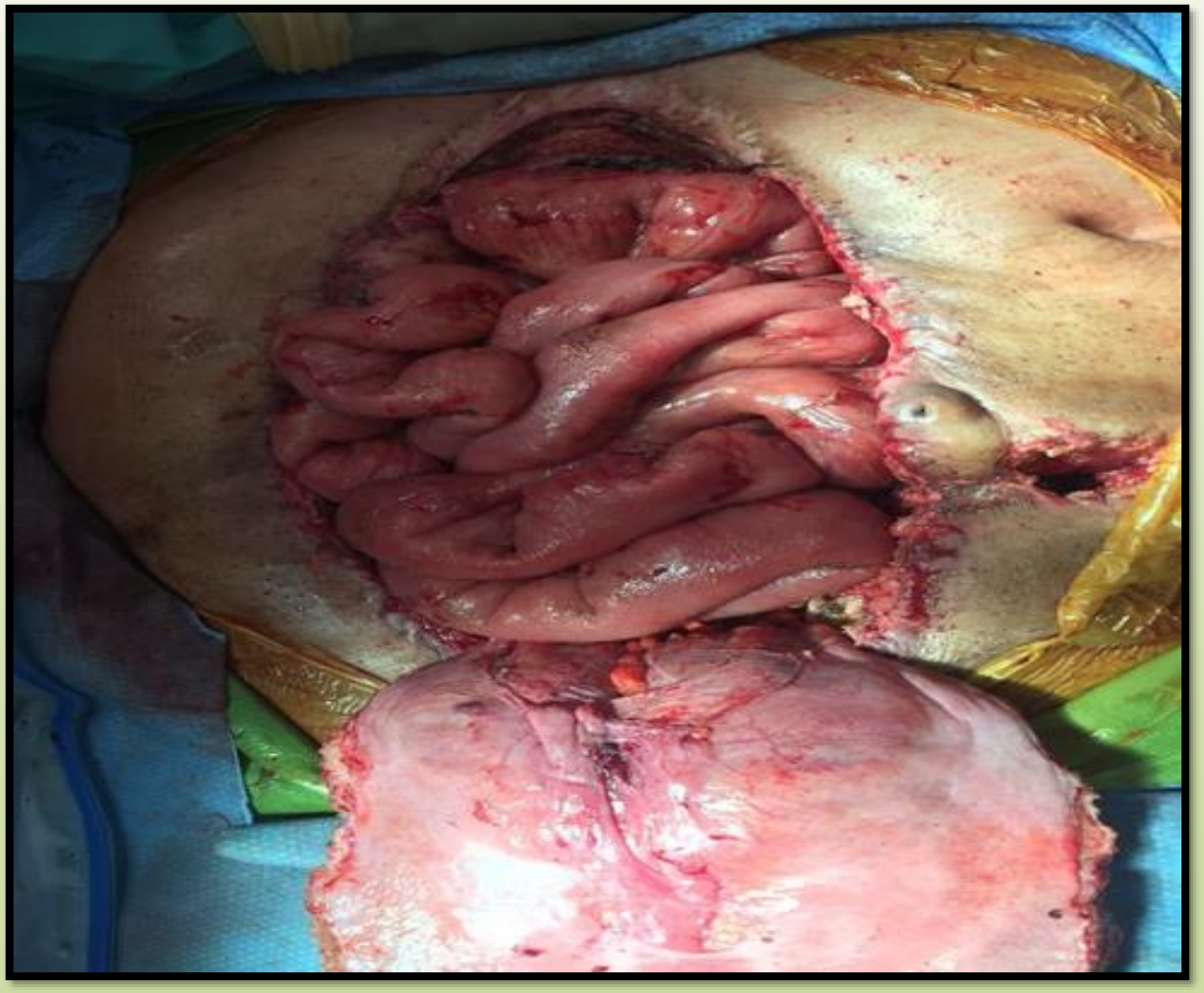

PATIENTS AND METHODS

OPERATIONAL DESIGN

Surgical techniques

ISB Tx (n=13)

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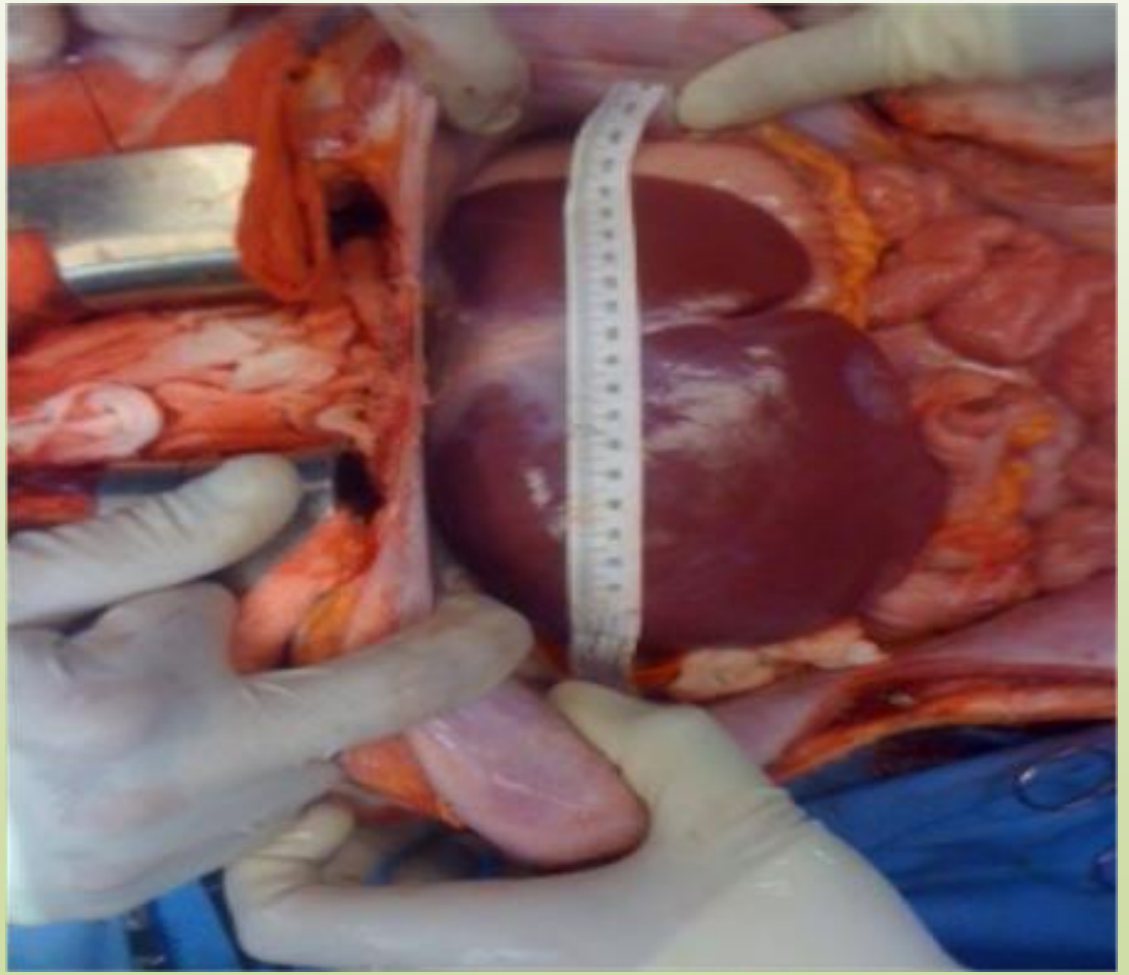
PATIENTS AND METHODS

OPERATIONAL DESIGN

Surgical techniques

Full MV Tx (n=36)

Donor procedure



PATIENTS AND METHODS

OPERATIONAL DESIGN

Surgical techniques

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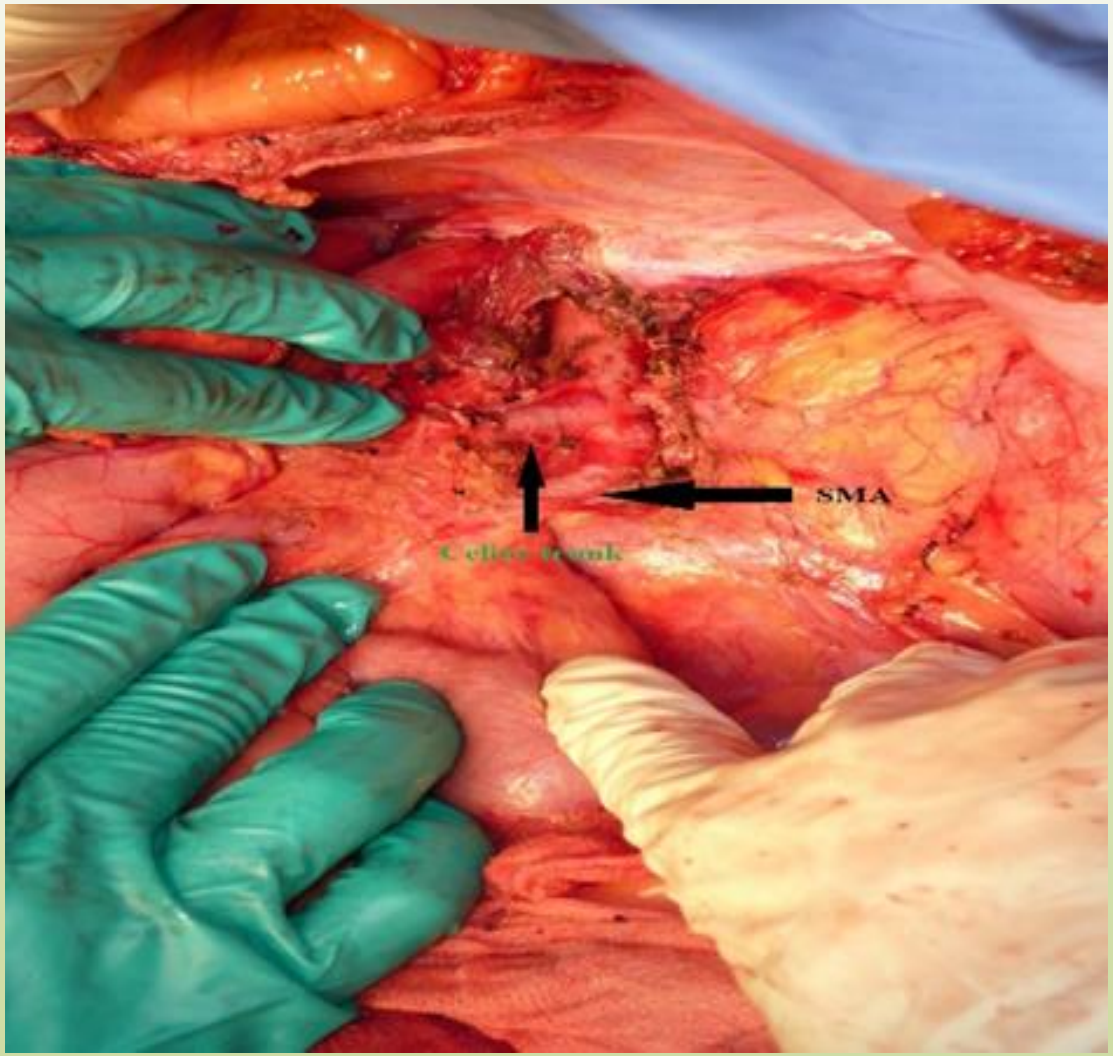

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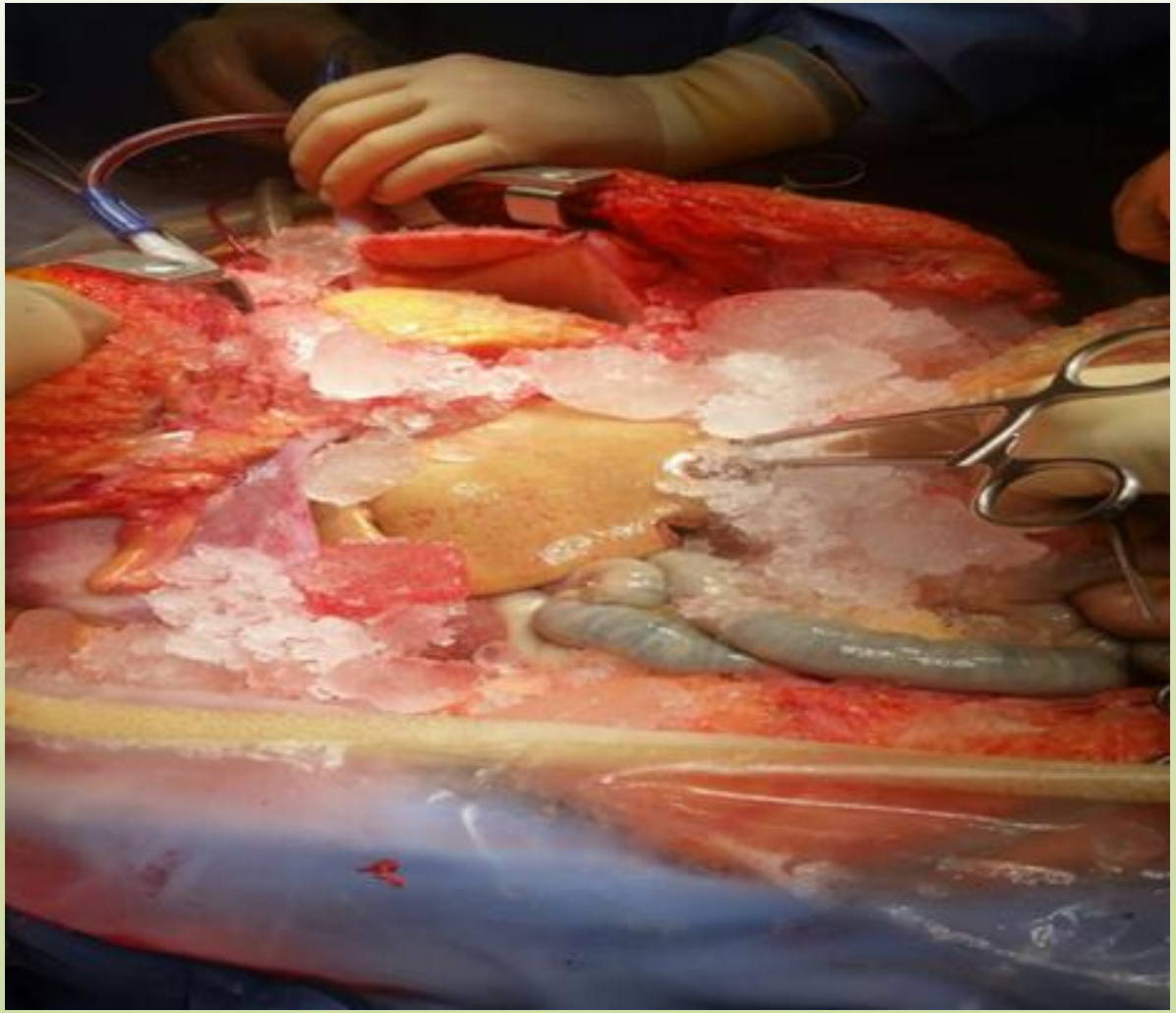

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Donor procedure

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Full MV Tx (n=36)

Back-table preparation

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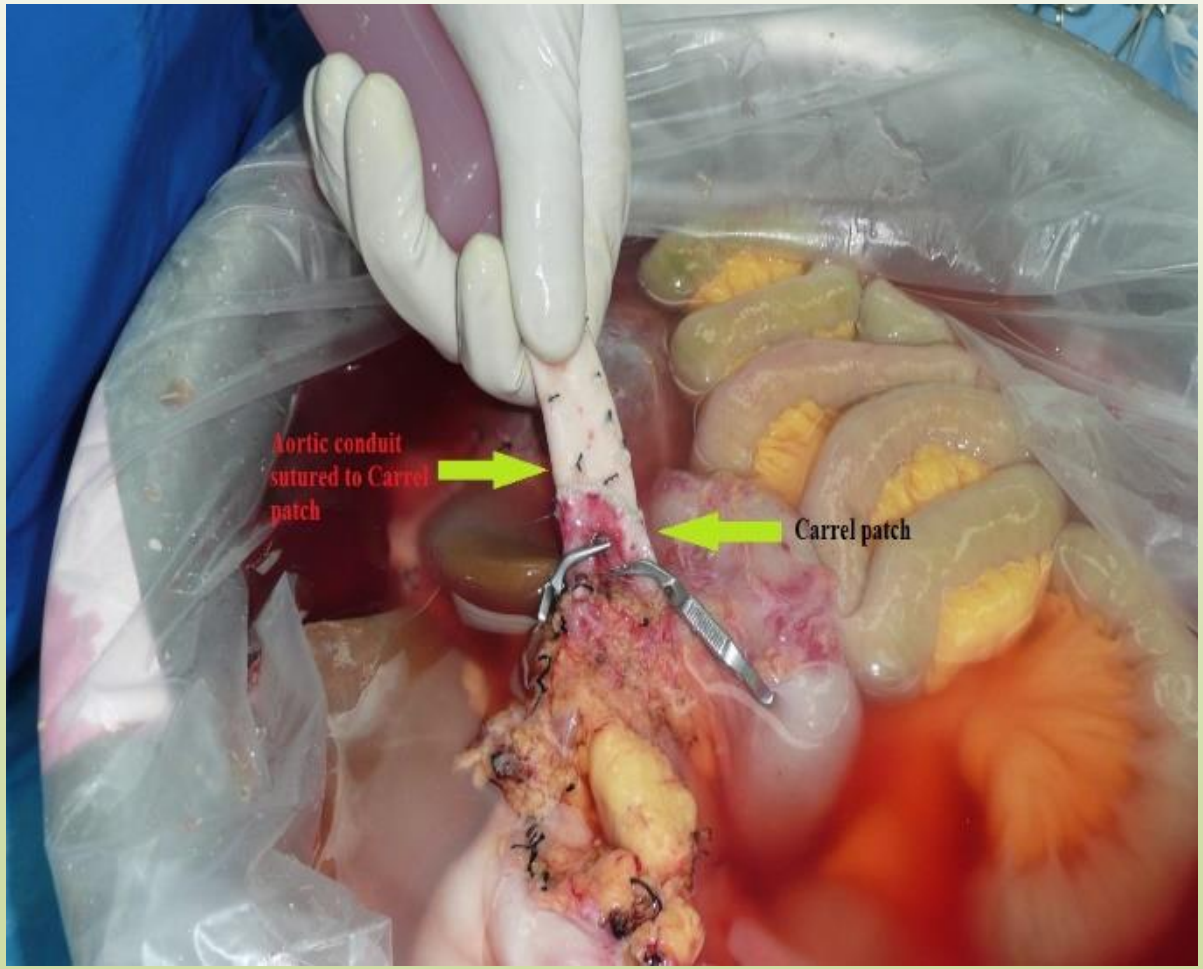

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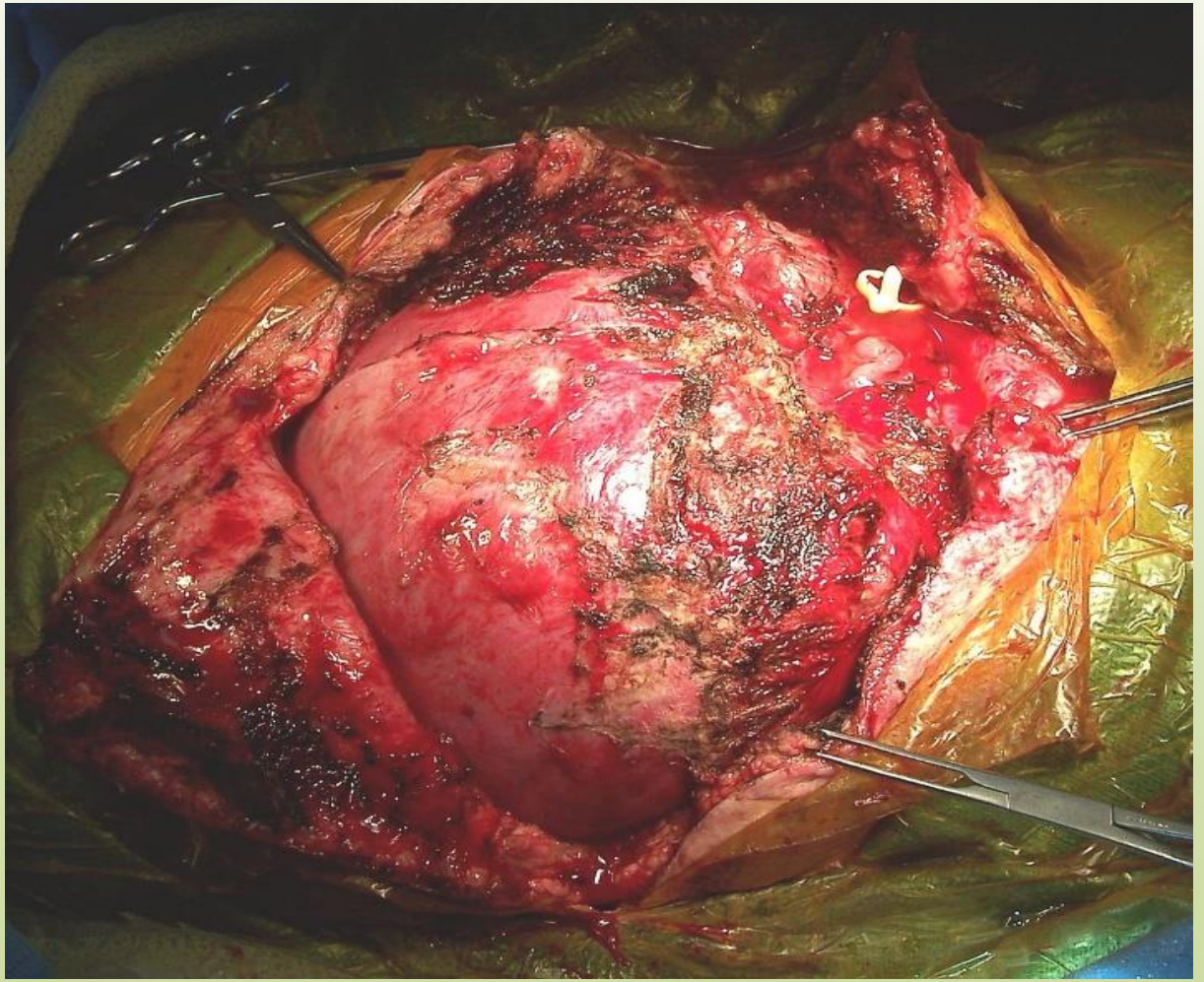

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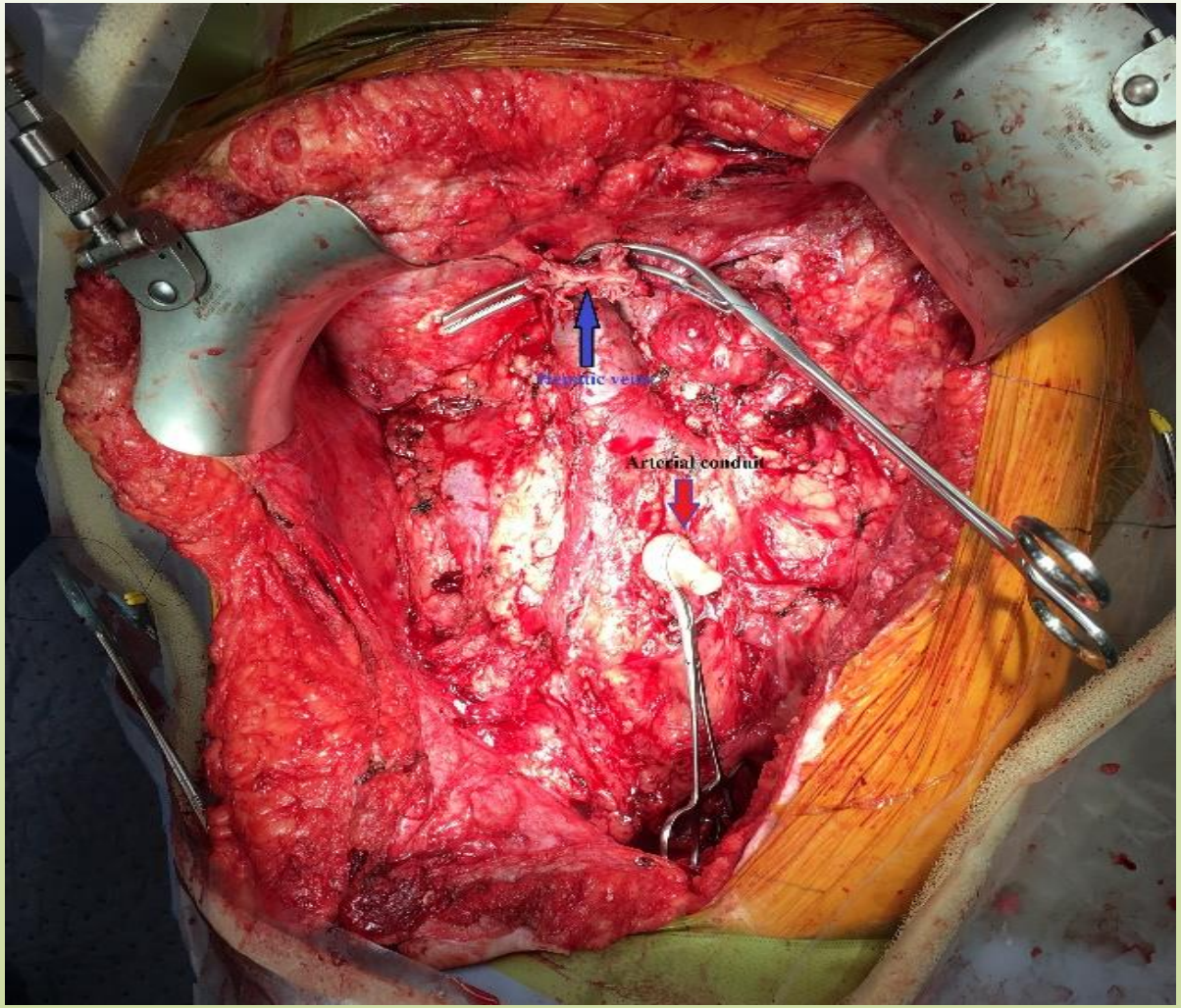

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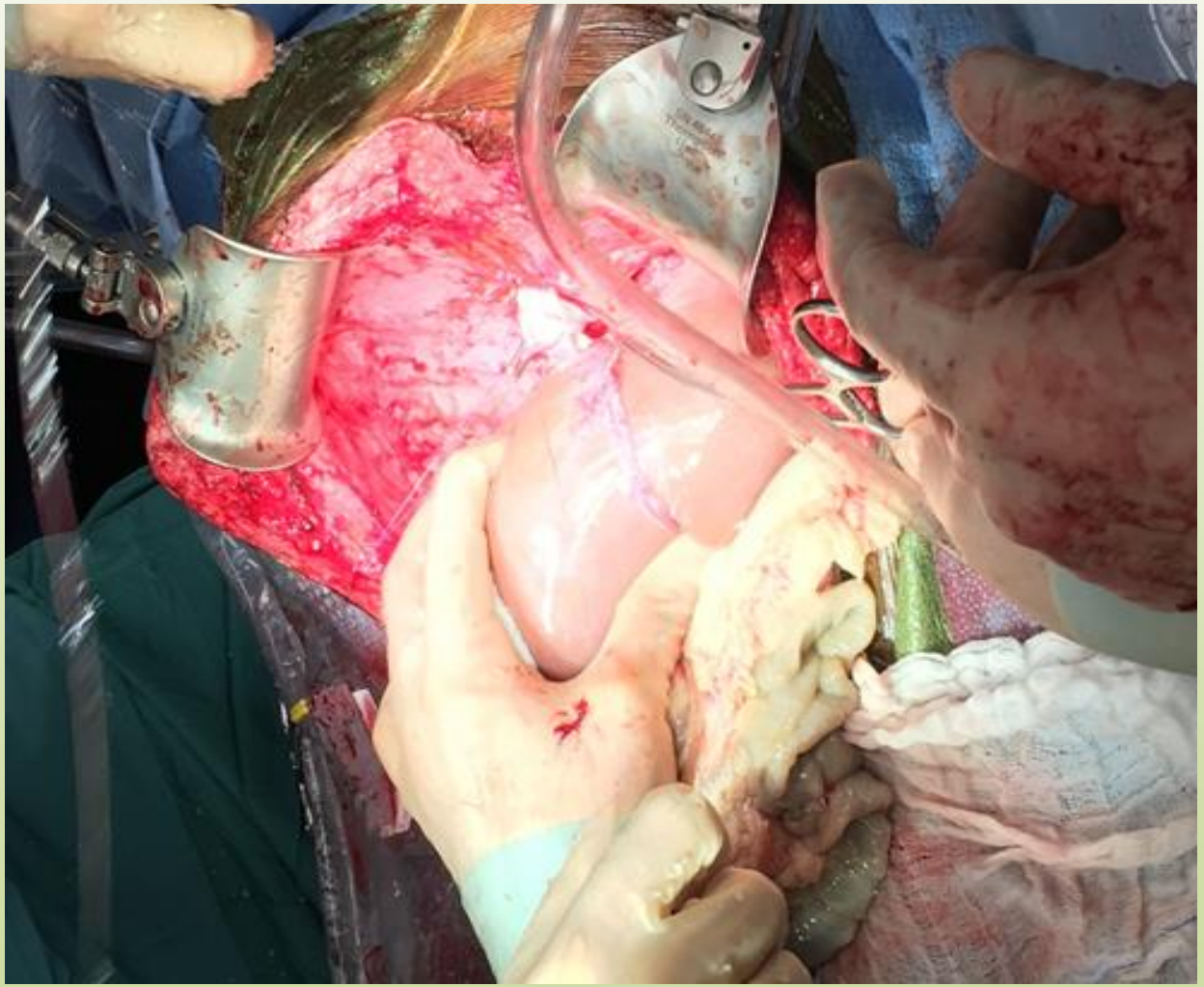

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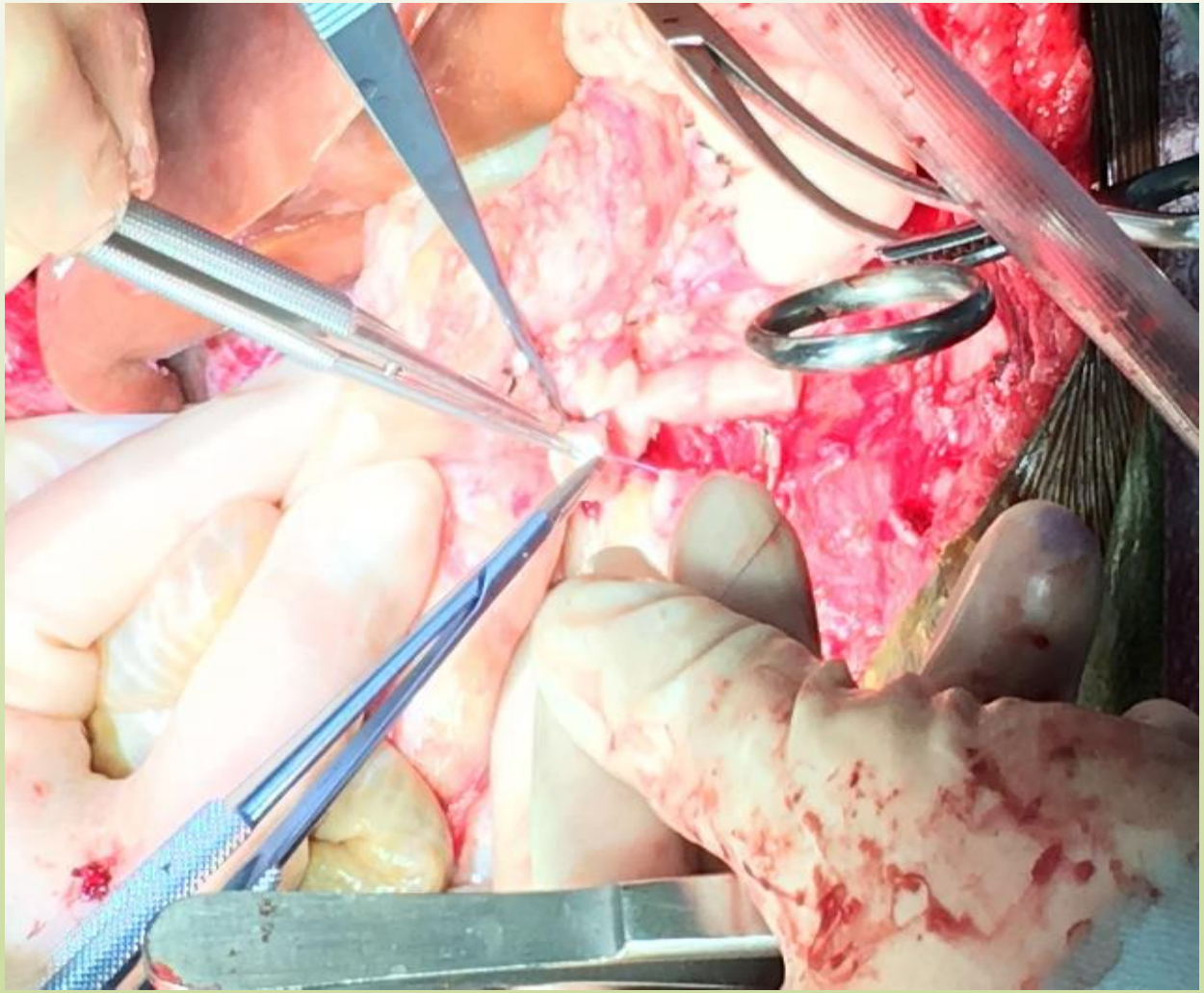

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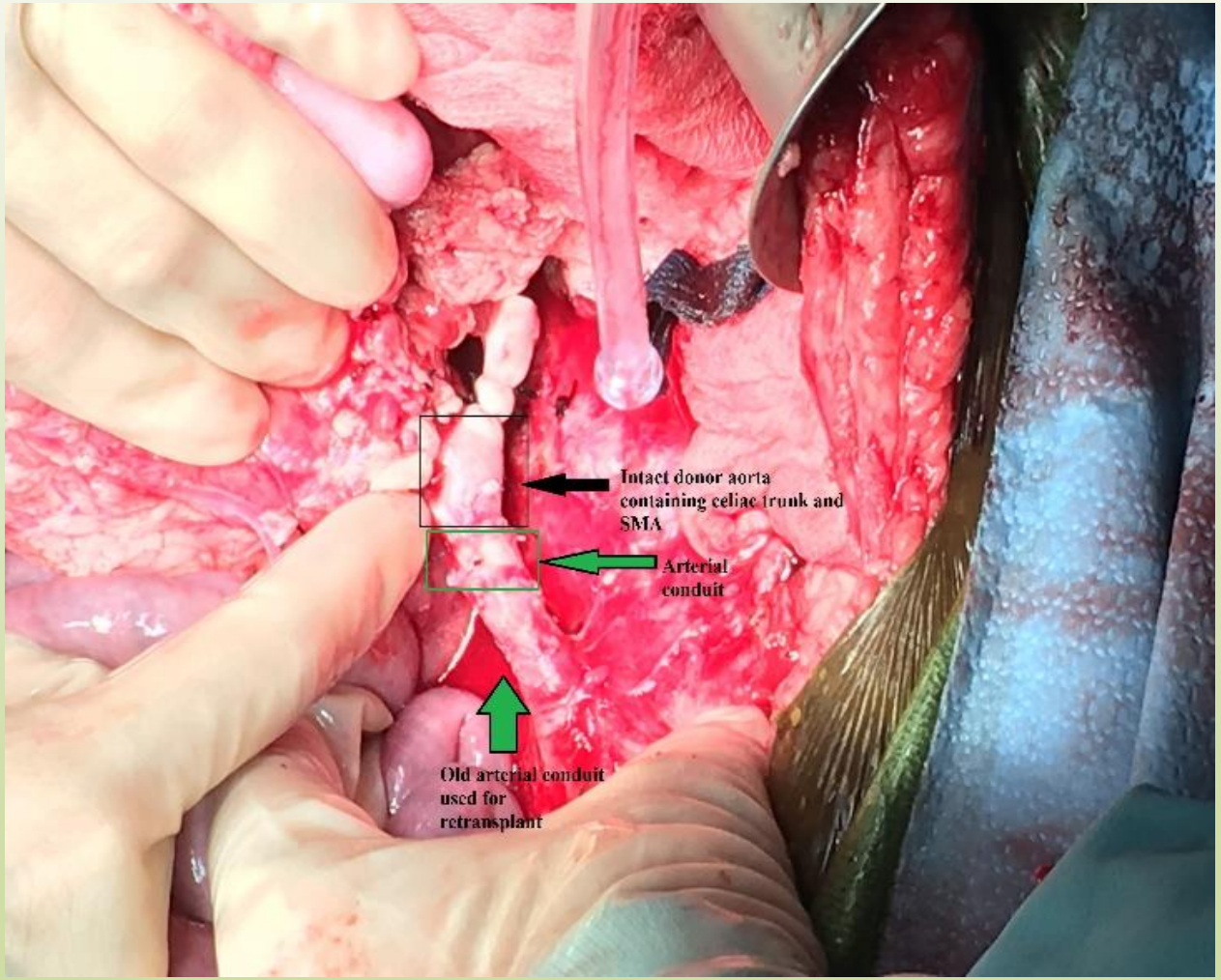

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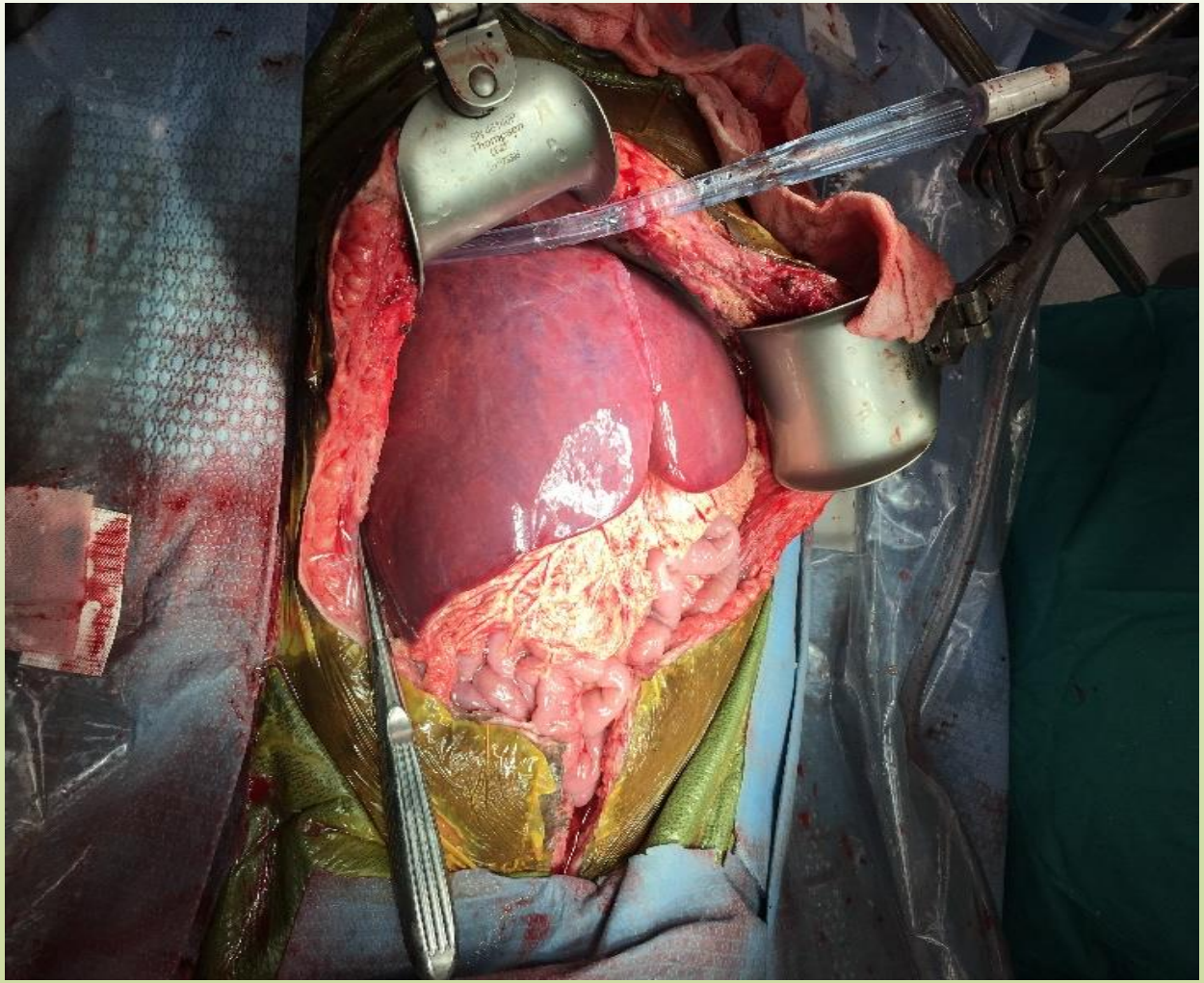

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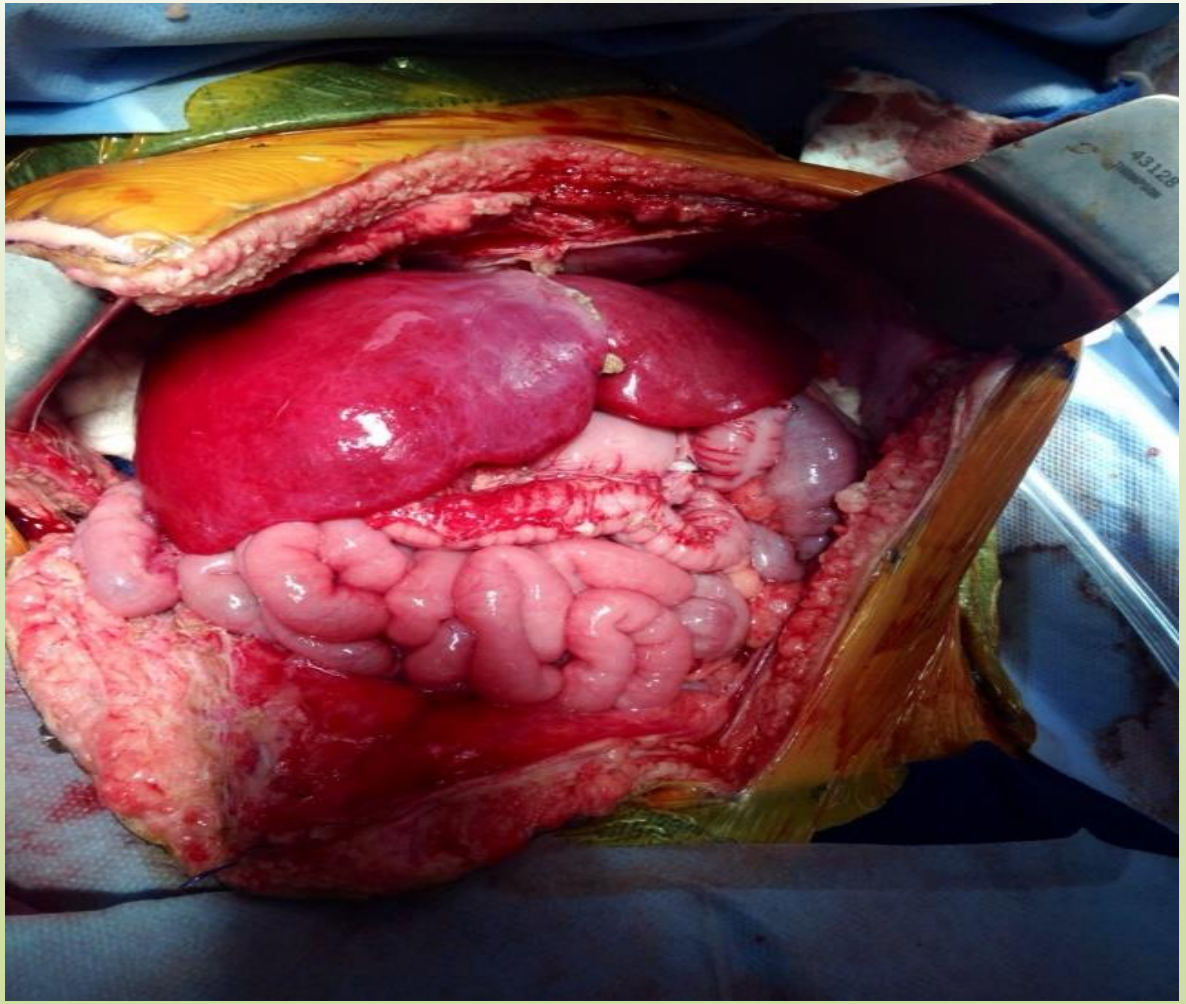

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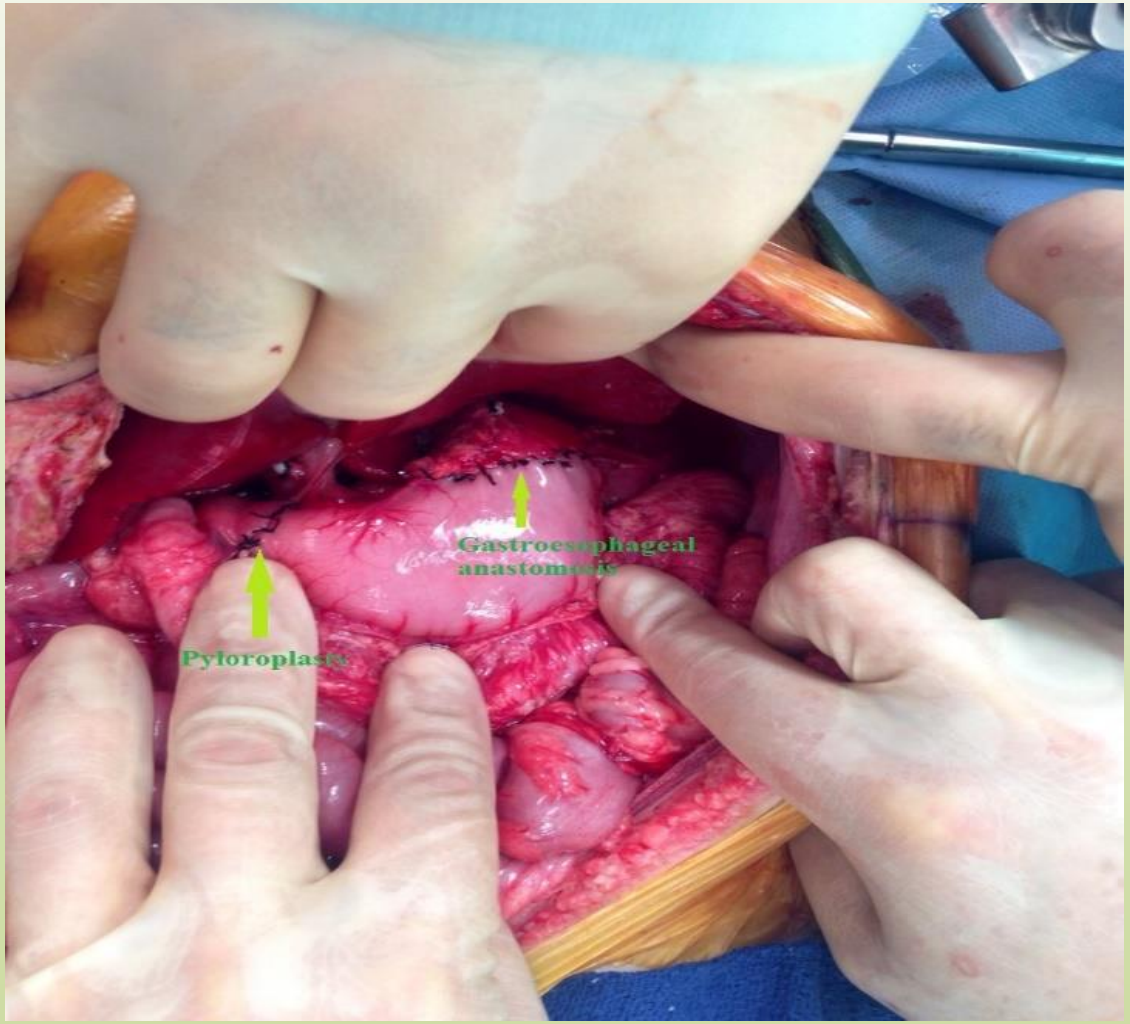

PATIENTS AND METHODS

OPERATIONAL DESIGN

Surgical techniques

Full MV Tx (n=36)

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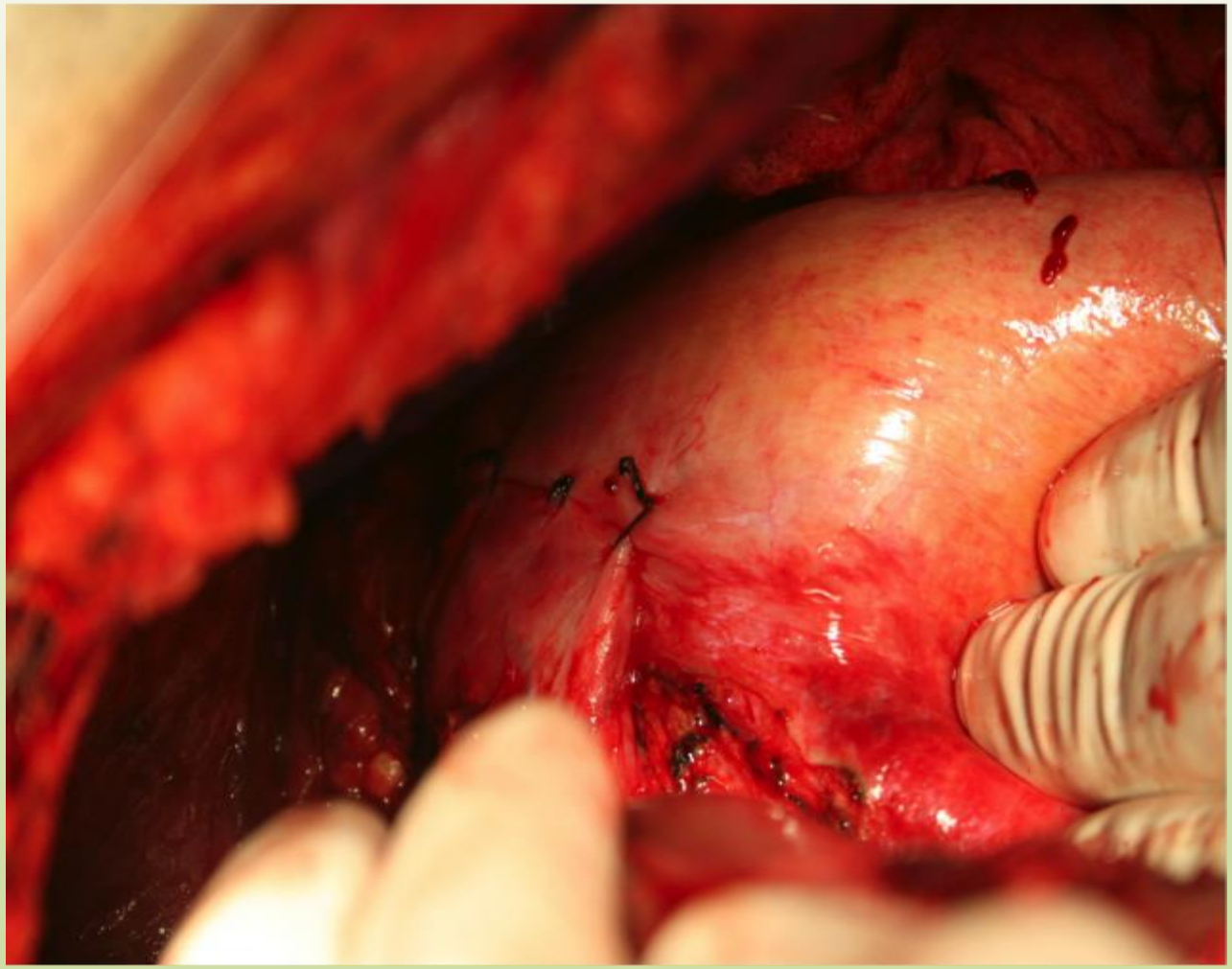


PATIENTS AND METHODS

OPERATIONAL DESIGN

Surgical techniques

Full MV Tx (n=36)

Recipient procedure

PATIENTS AND METHODS

OPERATIONAL DESIGN

Immunosuppression protocol

Induction immunosuppression

- **rATG: 2 mg/kg X5.**
- **Steroids (Solu-Medrol) in a tapering mode.**
- **Rituximab.**
- **Basiliximab.**

Maintenance immunosuppression

- **Tacrolimus.**
- **Everolimus.**

PATIENTS AND METHODS

OPERATIONAL DESIGN

Graft monitoring

- Frequent endoscopies.
- Serum level of citrulline.
- Clinical examination and hand-held Doppler US.

RESULTS

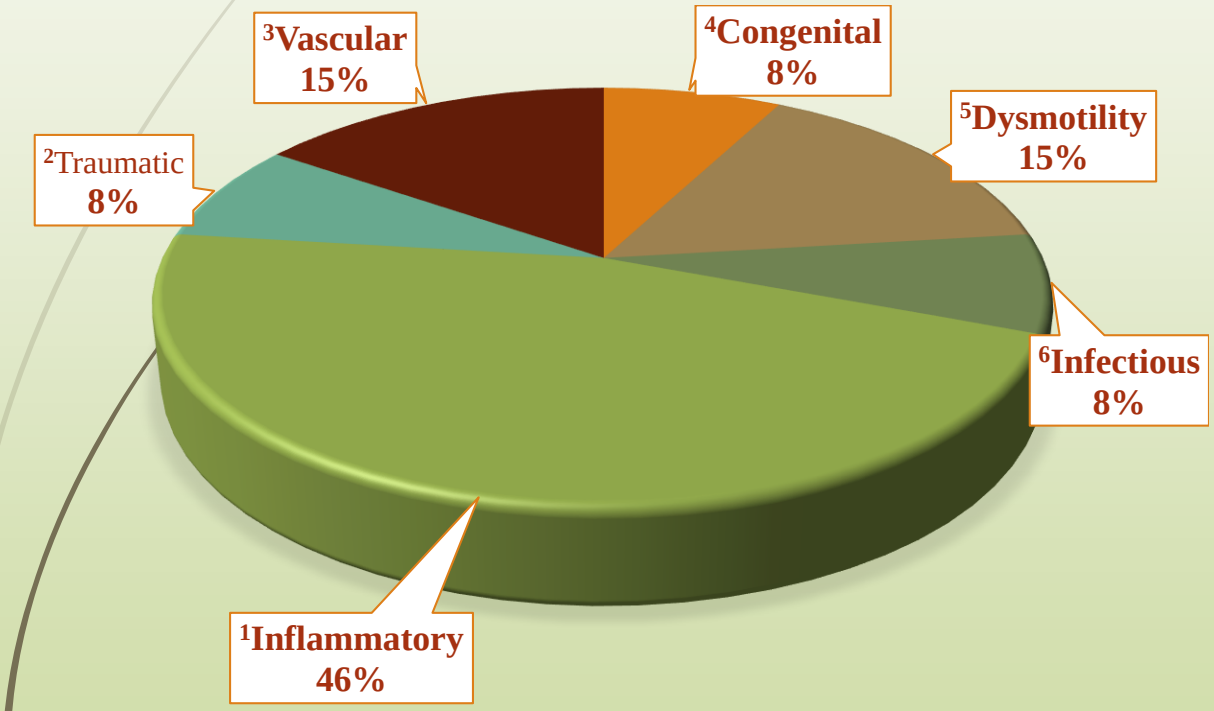
Recipient Baseline Variables	ISB Tx (n=13) Mean ± SE	Full MV Tx (n=36) Mean ± SE	P-value
A. Age (year)	31.9 ± 5.3	26.9 ± 4.1	0.50
1. Adult (≥18 year)	69.2% (n=9/13)	50.0% (n=18/36)	0.23
B. Gender			0.23
1. Female	46.2% (n=6/13)	50.0% (n=18/36)	
2. Male	53.8% (n=7/13)	50.0% (n=18/36)	
C. Race/Ethnicity			0.82
1. White (non-Hispanic)	53.8% (n=7/13)	52.8% (n=19/36)	
2. Black (non-Hispanic)	23.1% (n=3/13)	16.7% (n=16/36)	
3. Hispanic	23.1% (n=3/13)	30.6% (n=11/36)	
D. Pre-transplant BMI	21.2 ± 1.1	21.8 ± 1.0	0.69
E. ABO-Blood Group			0.25
1. A	15.4% (n=2/13)	33.3% (n=12/36)	
2. B	23.1% (n=3/13)	8.3% (n=3/36)	
3. O	61.5% (n=8/13)	58.3% (n=21/36)	
F. Type of Transplant			
1. Primary Transplant	84.6% (n=11/13)	91.7% (n=33/36)	0.47
2. Secondary Transplant	15.4% (n=2/13)	8.3% (n=3/36)	

RESULTS

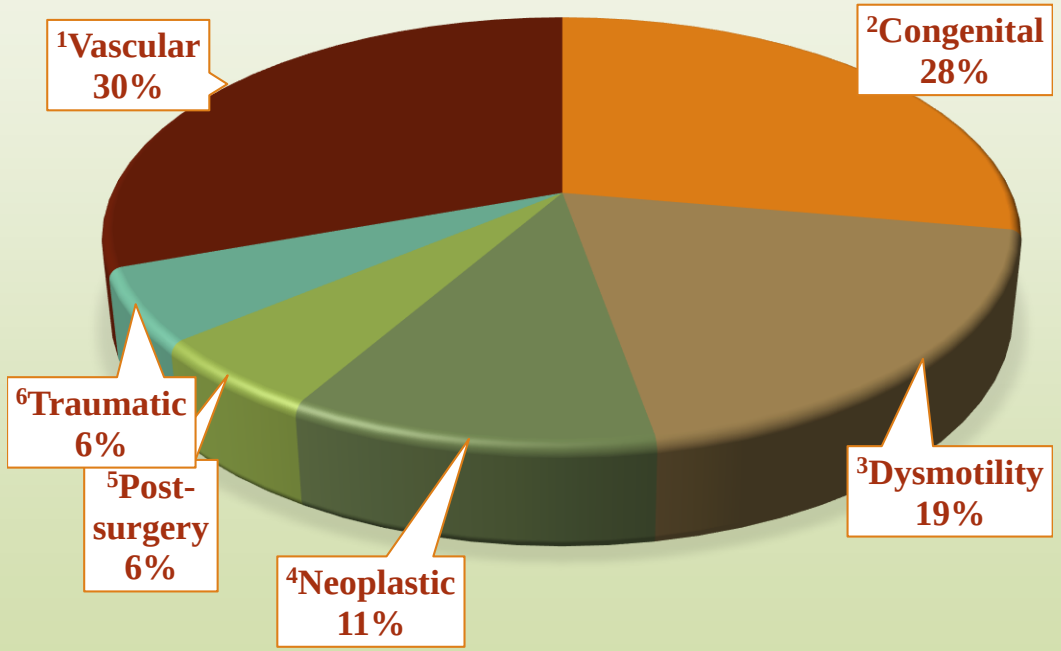
Other Baseline Variables	ISB Tx (n=13) Mean ± SE	Full MV Tx (n=36) Mean ± SE	P-value
A. Donor Age (years)	15.4 ± 3.7	18.3 ± 2.8	0.58
1. Adult (≥18 years)	23.1% (n=3/13)	52.8% (n=19/36)	0.06
B. Donor BMI (Kg/m^2)	20.6 ± 0.9	20.9 ± 0.7	0.43
C. Ischemia times			
1. Cold ischemia time (CIT) (hours)	6.7 ± 0.32	7.8 ± 0.27	0.04
2. Warm ischemia time (WIT) (minutes)	25.2 ± 1.5	29.4 ± 1.4	0.11
D. T/B Cell Cross-match			0.76
1. T-/B-	83.3% (n=10/12)	85.7% (n=30/35)	
2. T-/B+	0% (n=0/12)	2.9% (n=1/35)	
3. T+/B+	16.7% (n=2/12)	11.4% (n=4/35)	
E. Abdominal Wall Closure			0.68
1. Primary Abdominal Wall Closure	*53.8% (n=7/13)	47.2% (n=17/36)	
2. Vacuum Assisted Closure	46.2% (n=6/13)	52.8 (n=19/36)	
F. Stoma			0.005
1. Ileostomy	53.8 (n=7/13)	13.9% (n=5/36)	
2. Colostomy	38.5% (n=5/13)	36.1% (n=13/36)	
3. No Stoma	7.7% (n=1/13)	50.0% (n=18/36)	

RESULTS

Indications for ISB Tx



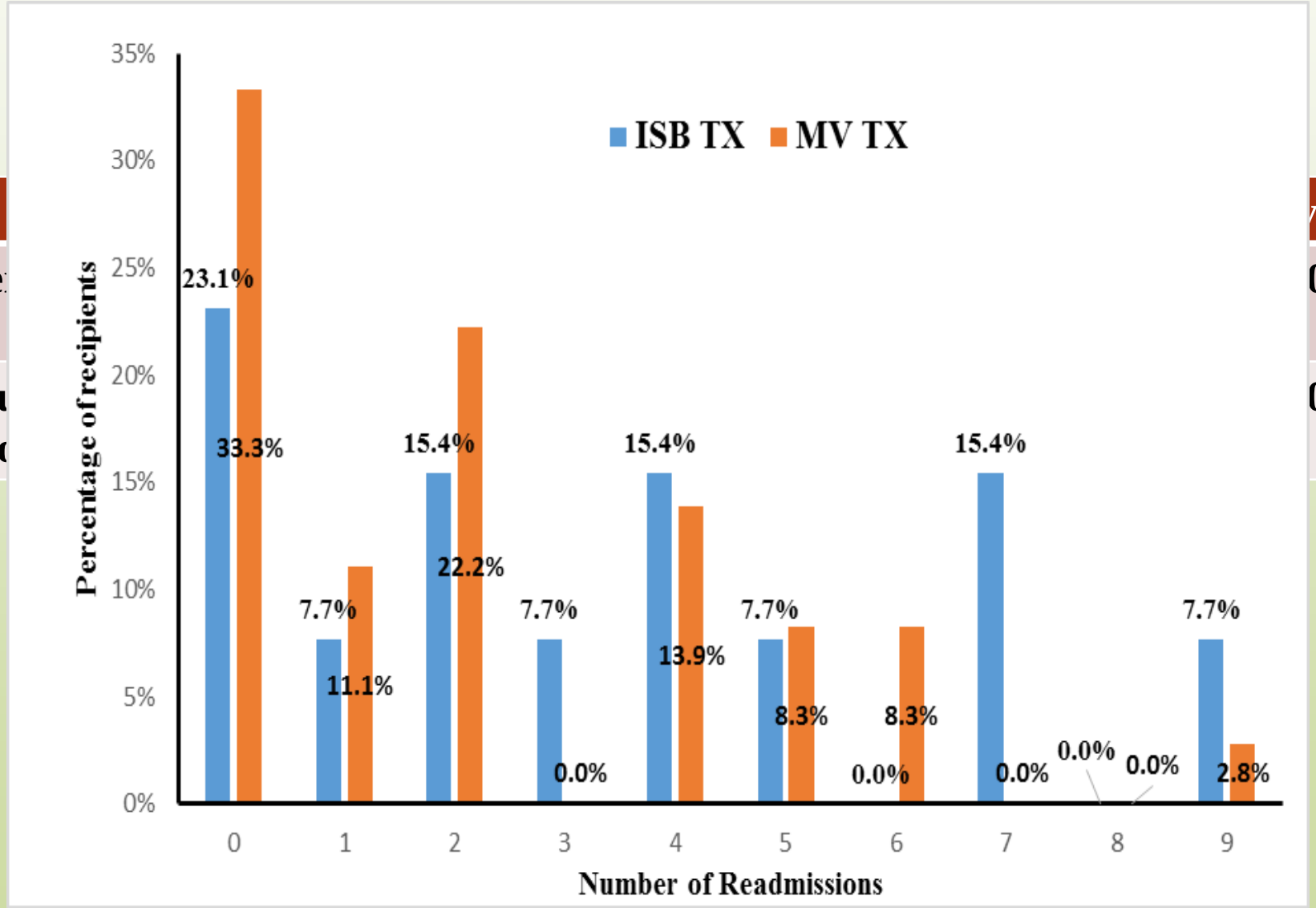
Indications for full MV Tx



RESULTS

Length of hospital stay and readmissions

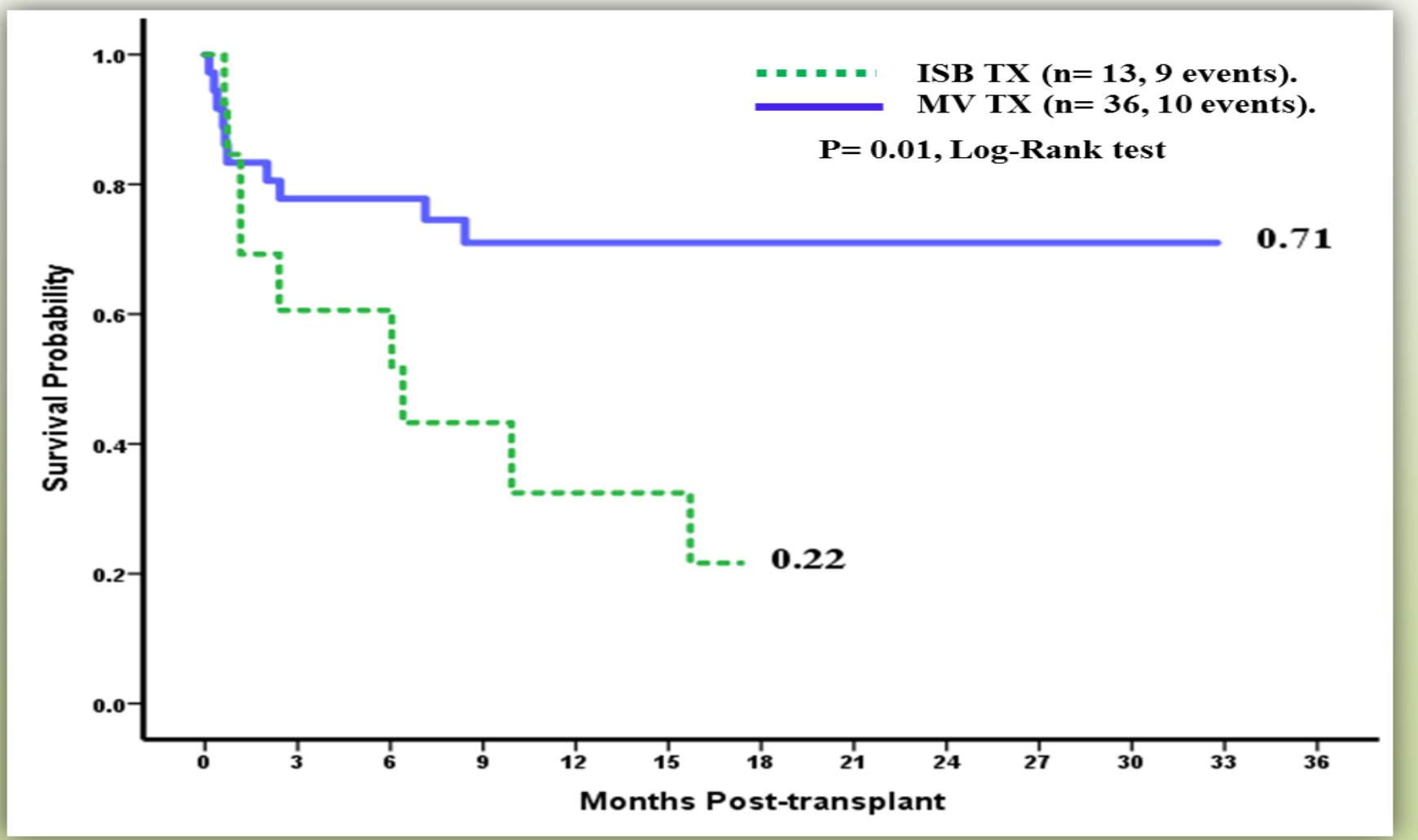
	value
Median le	0.5
Median nu readmissio	0.2



RESULTS

Rejection

Kaplan-Meier curve: any biopsy-proven acute rejection free survival by the type of transplant (ISB Tx vs. full MV Tx)



RESULTS

Rejection

- **Median time to develop a biopsy proven acute rejection (BPAR)**
  - ❖ **2.4 (0.6-15.7) months ISB Tx**
  - ❖ **0.7 (0.1-8.4) months Full MV Tx**

Sites of first rejection

Site of first rejection	ISB Tx (n=9)	Full MV Tx (n=10)
Small bowel	n=9	n=7
Colon	n=4	n=6
Colostomy		n=2
Stomach		n=2

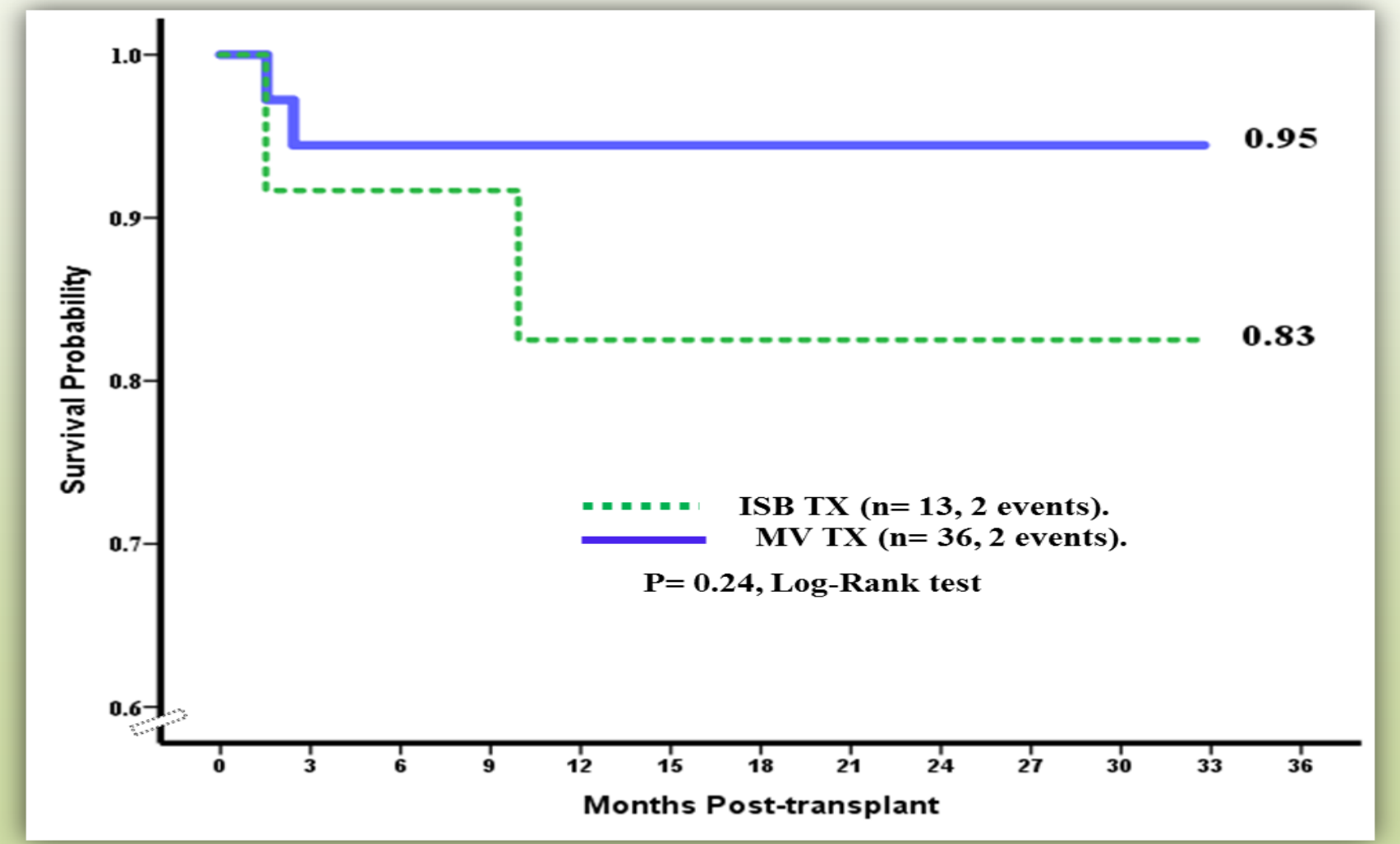
Grades of rejection

Grade of BPAR	ISB Tx (n=9)	Full MV Tx (n=10)
Grade I	n=7	n=4
Grade II		n=4
Grade III	n=2	n=2

RESULTS

Rejection

Kaplan-Meier curve: severe rejection free survival by the type of transplant (ISB Tx vs. full MV Tx)



RESULTS

Rejection

- **Median time to develop an episode of severe rejection**
  - ❖ **5.7 (1.5-9.9) months ISB Tx**
  - ❖ **2 (1.5-2.4) months Full MV Tx**

- **Sites of severe rejection**

ISB Tx **Both the small bowel and the colon in the 2 cases.**

Full MV Tx **The small bowel in one case and the colon in the other case.**

RESULTS

Rejection

Stepwise Cox regression results for the hazard rate of developing BPAR during the first 36 post-transplant months (n=49, 19 events)

Baseline Variable	Univariable P-value	Multivariable Model	
		P-value	Coeff ± SE
Transplant Type (ISB Tx)	0.01	0.01	1.085 ± 0.463
Systemic Drainage	0.004		
Citrulline Level at 1st month	0.05		

Cox regression model for the hazard rate of developing BPAR during the first 36 months post-transplant (49 cases, 19 events) that includes the 2 variables transplant type, and citrulline level at the 1st month (n=43, 17 events)

Baseline Variable	Multivariable Model	
	P-value	Coeff ± SE
Transplant Type (ISB transplant)	0. 09	0.960 ± 0.578
Citrulline Level at 1st month	0.46	0.022 ± 0.030

RESULTS

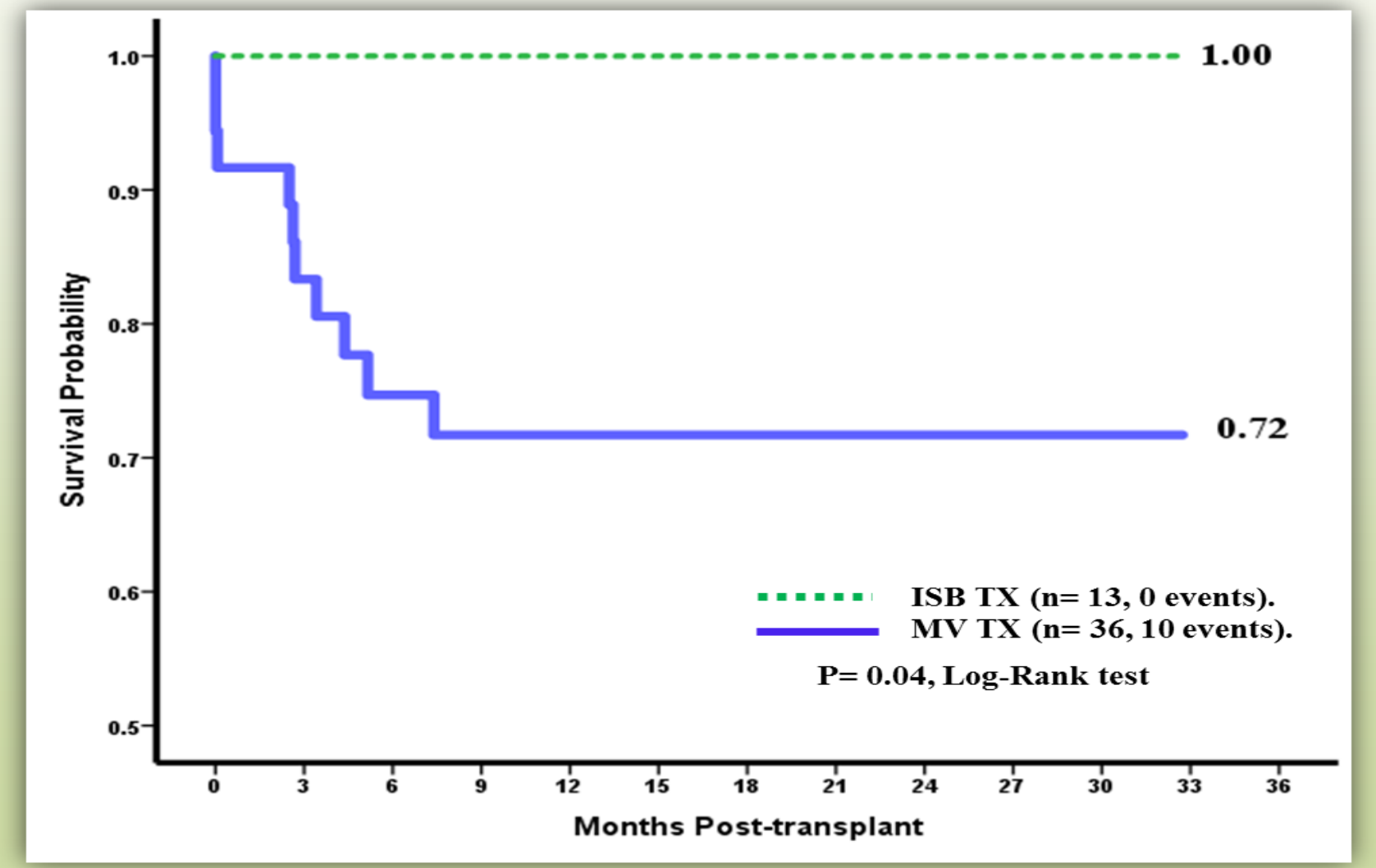
Graft failure

- **Causes of intestinal graft failure among ISB transplant recipients**
  - ❖ **Rejection (n=1).**
  - ❖ **Volvulus (n=1).**
- **Causes of intestinal graft failure among the full MV recipients**
  - ❖ **Rejection (n=2).**
  - ❖ **Enterocutaneous fistulas (n=1).**

RESULTS

Patient survival

Kaplan Meier curve: patient survival during the first 36 post-transplant months by the type of transplant (ISB Tx vs. full MV Tx)



RESULTS

Patient survival

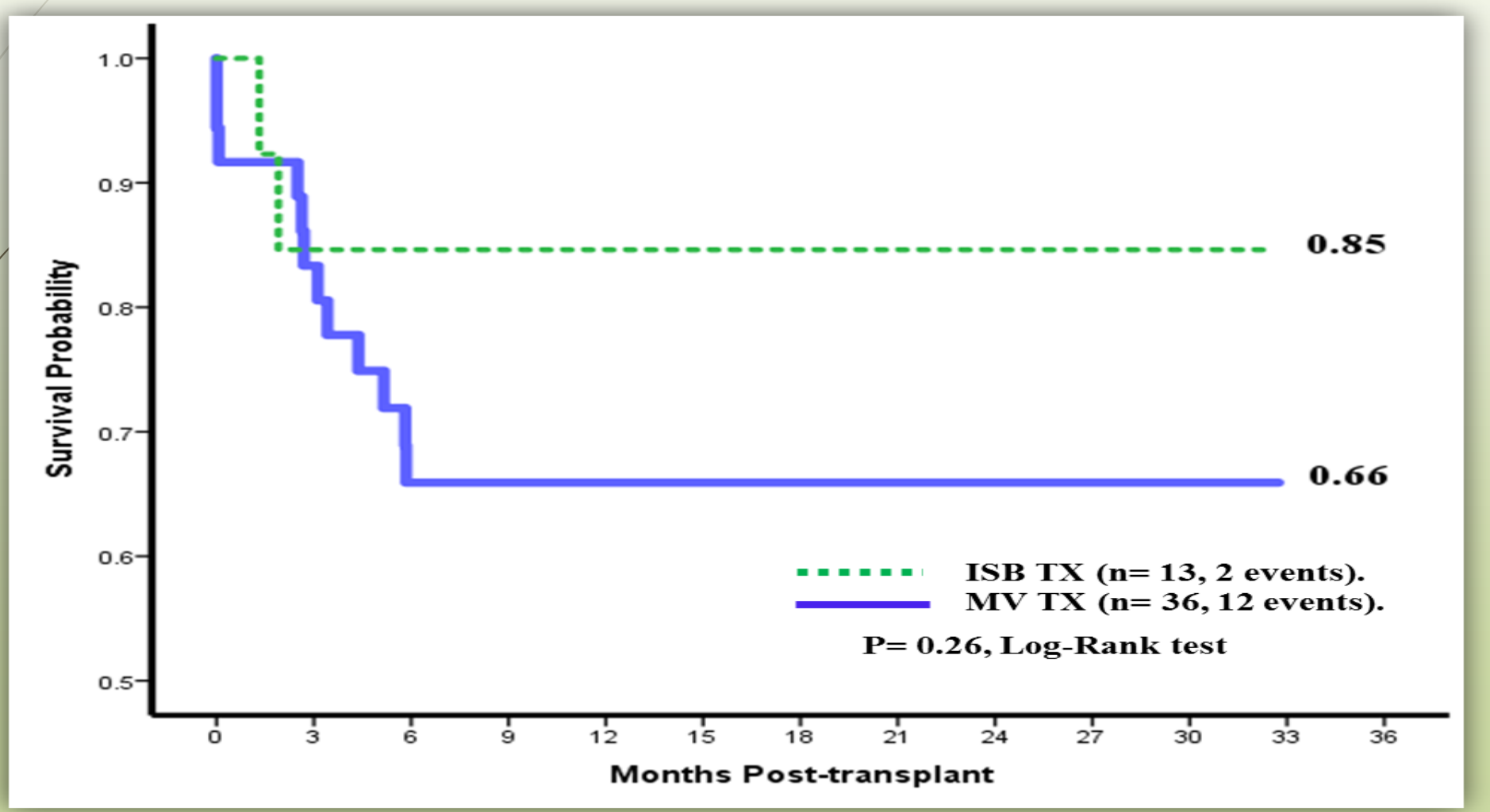
Full MV transplant recipients

- **Median time to patient death within the first 3 post-transplant months** — **1.3 (0-2.7) months**
- **Median time to patient death during the first 36 months** — **2.7 (0-7.4) months**
- **Causes of patient death**
  - ❑ GVHD (n=4).
  - ❑ Sepsis (n=2).
  - ❑ Intra-operative coagulopathy (n=1).
  - ❑ Intra-operative cardiac thrombosis (n=1).
  - ❑ Superior vena cava syndrome (n=1).
  - ❑ Rejection (n=1).

RESULTS

Graft survival

Kaplan Meier curve: freedom from graft failure or patient death from any cause (death-uncensored graft survival) during the first 36 post-transplant months by the type of transplant (ISB Tx vs. full MV Tx)



CONCLUSION

- **The results of our study support the worldwide agreement about the advantage of the visceral Tx either ISB Tx or full MV Tx in the management of patients with chronic IF.**

- **Early surgical intervention provides an efficient solution, compatible survival rate and satisfactory quality of life in the management of chronic IF in patients who cannot tolerate the life-long PN.**

Thank you