

Luciano De Carlis

Il Trapianto di Fegato da Vivente Adulto

STATI GENERALI



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LDLT in Italy – Background & Statistics

Italy [59.8 million inhabitants; 21.9 Deceased Donor (DD) pmp]

A-A LDLT from March, 2001 (1st performed by Milano-Niguarda)

392 LDLT performed in Italy up to December 2018

2001-2018: 15584 DDLT; 392 LDLT (2,5%); 798 DD-SPLIT (5,1%)

US (2013): 252 LDLT performed (252/6203 = 4% total LT volume)

43/166 (26%) LT centers active in LDLT; only 8 centers performing 10 or more cases

Italy: 4/22 (18%) LT centers still active in LDLT (>20 cases performed)

South Korea: more than 300 LDLT performed per year by a single center (Seoul)



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- 1) OPTN, Organ Procurement and Transplant Network
- 2) Testa G. HepatoBiliary Surgery and Nutrition, Vol5, No2 Apr 2016
- 3) CNT, Centro Nazionale Trapianti

LDLT: premises

- Ethical aspects and donor safety have been the principal concerns worldwide
- LDLT indications must be the same for deceased donor liver transplantation
- LDLT should be performed only if the risk of the donor is justified by an acceptable outcome of the recipient
- Both donor and recipient operations, still remain a technically demanding surgical procedure
- What extent must the recipient benefit to justify the use of a living donor for extended indications and marginal recipient benefits?

1) *OPTN, Organ Procurement and Transplant Network*
2) *Testa G. HepatoBiliary Surgery and Nutrition, Vol5, No2 Apr 2016*
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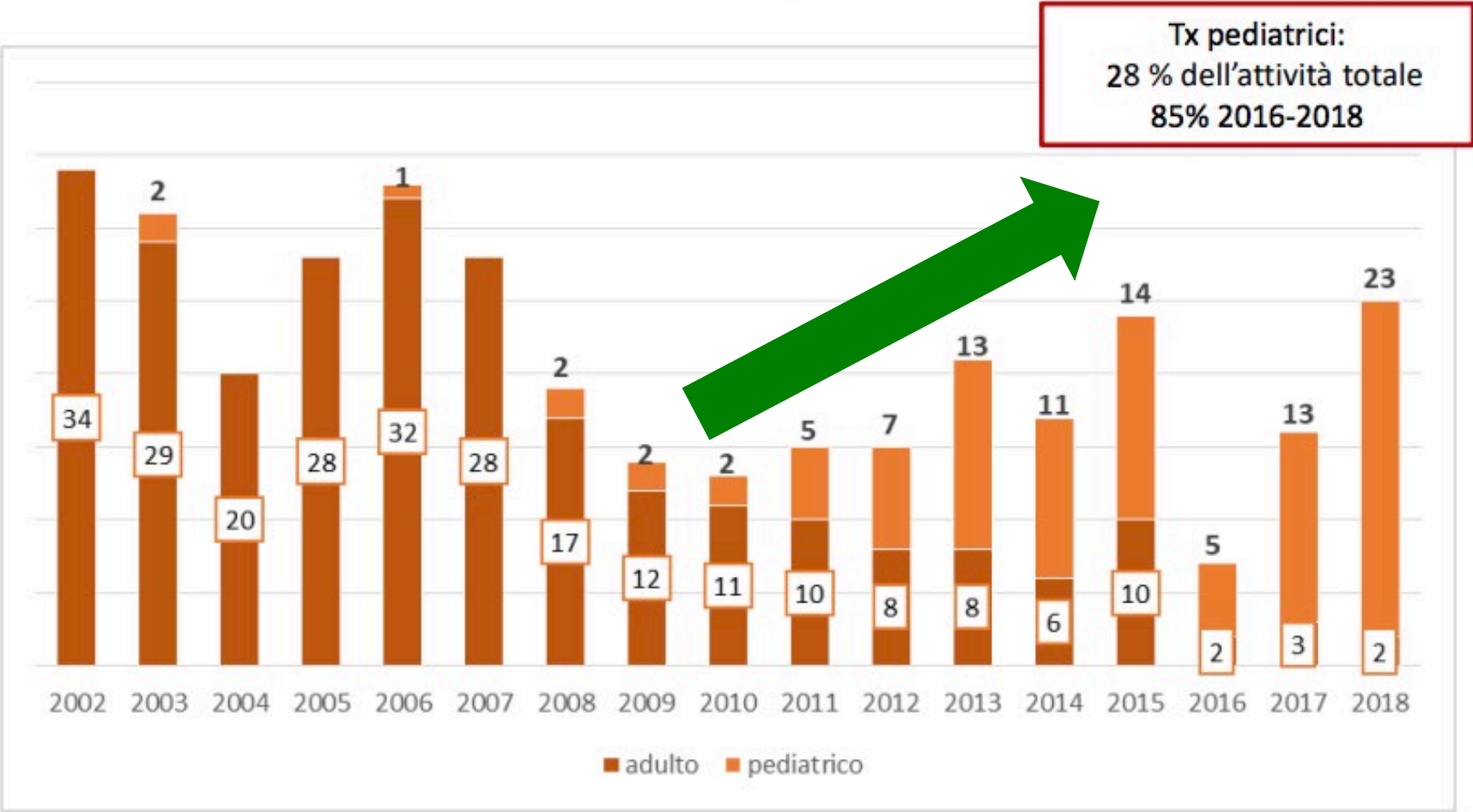


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LDLT: cases / year [2001-2018]



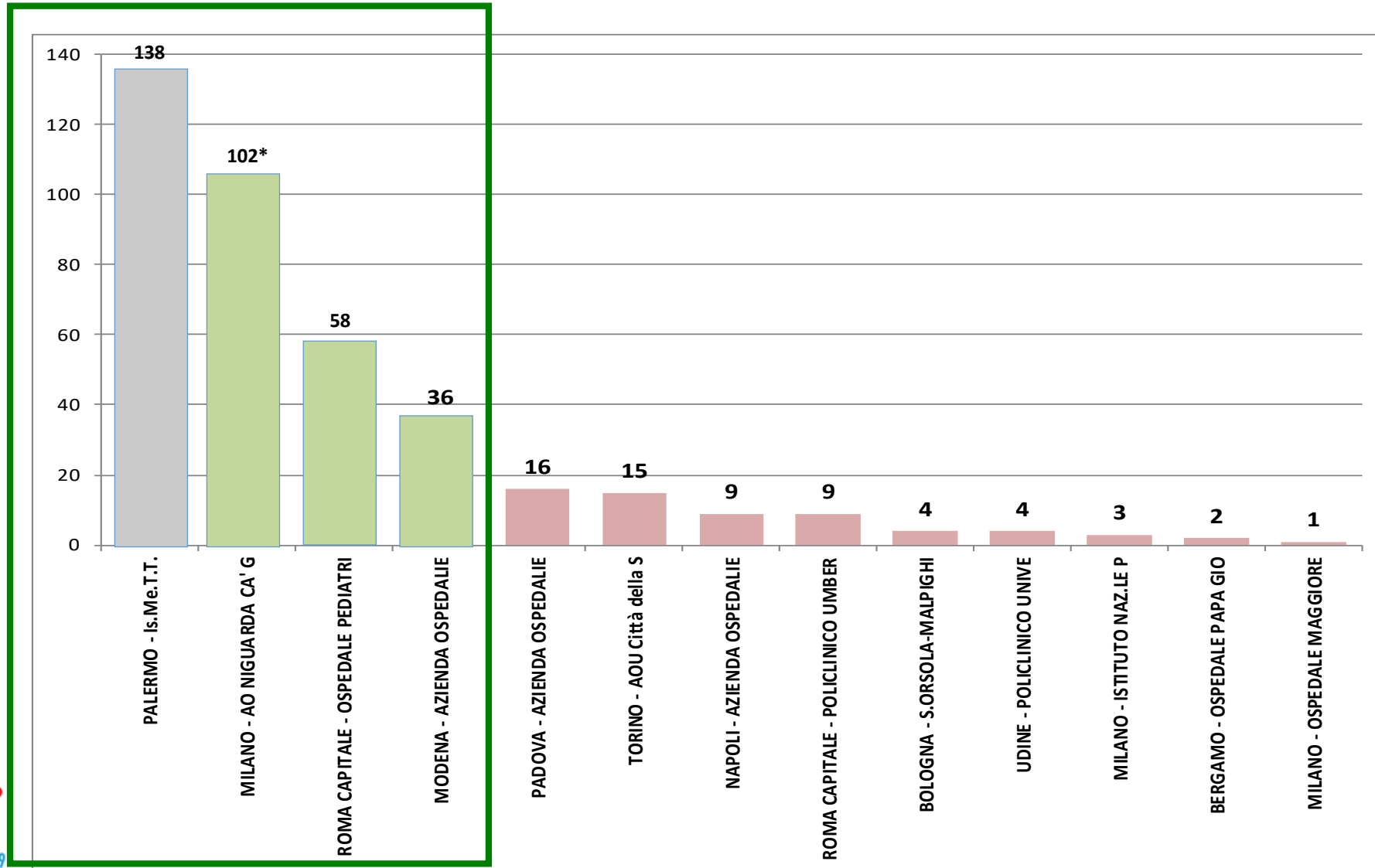
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Source: CNT, Centro Nazionale Trapianti

LDLT / Center Series [2001-2018]

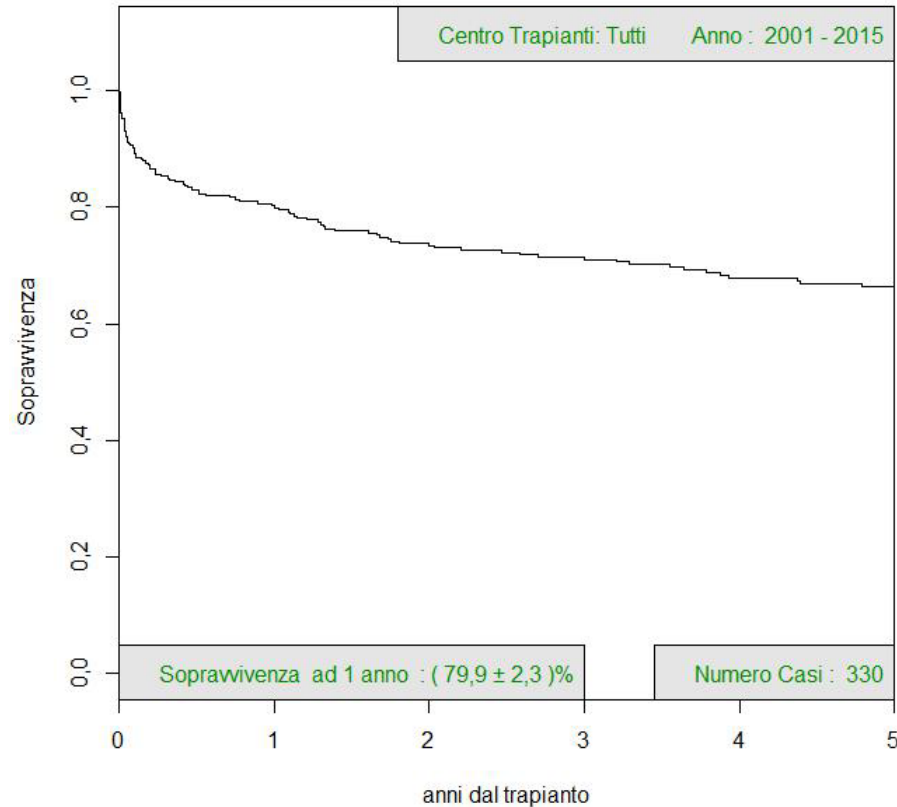


(*) 9 LDLT proctorship to other Institution worldwide

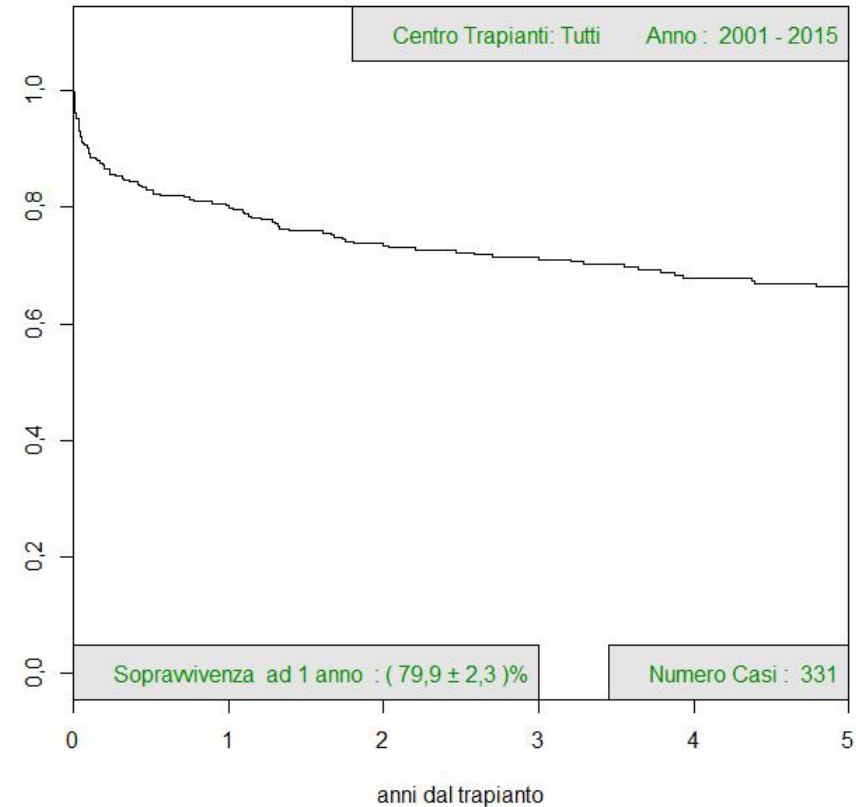
Source: CNT, Centro Nazionale Trapianti

LDLTs: Outcomes in Italy

Recipient Survival 1-year: 79.9%



Graft Survival 1-year: 79.9%



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LTx: Niguarda Experience (1986-10/2019)

Since 1986, > 2000 liver transplants performed in adult recipients

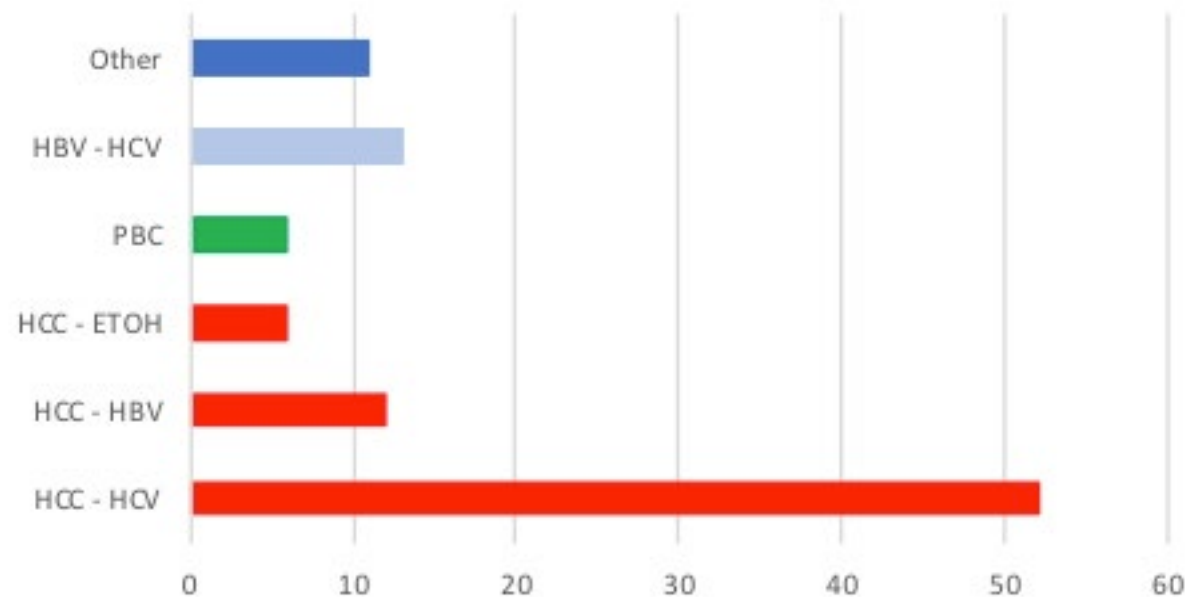
126 split-liver procedures (19 Adult/Adult; 107 Adult/Pediatric)

34 LT from DCD (since 2015) and 28 LT from donor in ECMO

102 cases performed (Right Lobe / 1 case with MHV)

(9 cases proctorship with University of Bucarest; Amman; Beirut)

Indications to LDLTx



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Pillars of Success

- Standardized surgical techniques (right lobe)
- Protocols for donor/recipient evaluation, and peri-operative management
- Adequate graft volume to avoid SFSS (GRWR > 0.8)
- Sufficient portal vein flow supporting liver regeneration
- Optimal hepatic vein outflow preventing graft congestion
- Surgical techniques for the RHV reconstruction

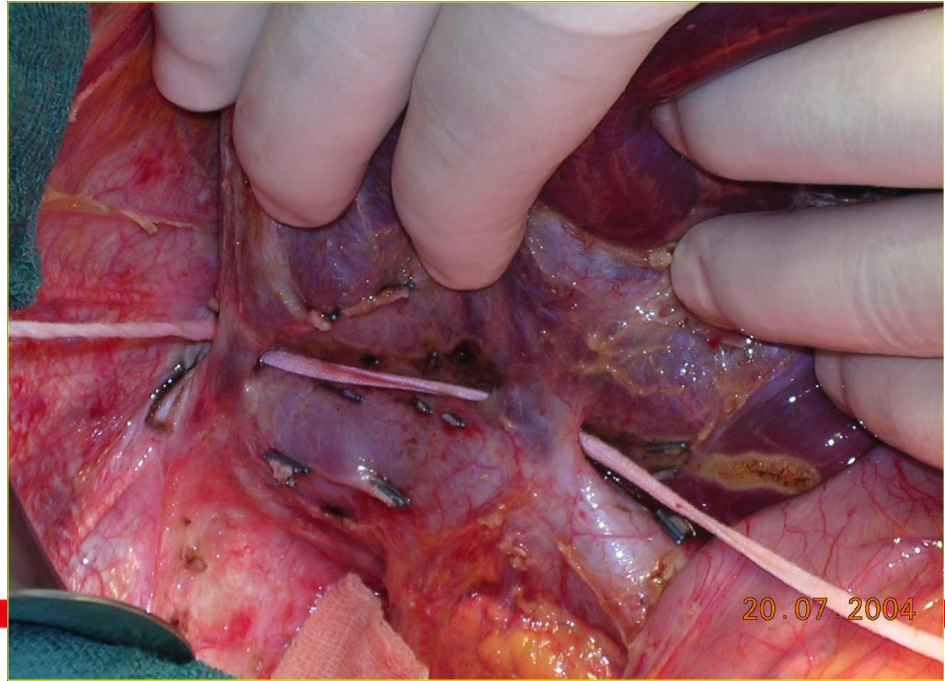
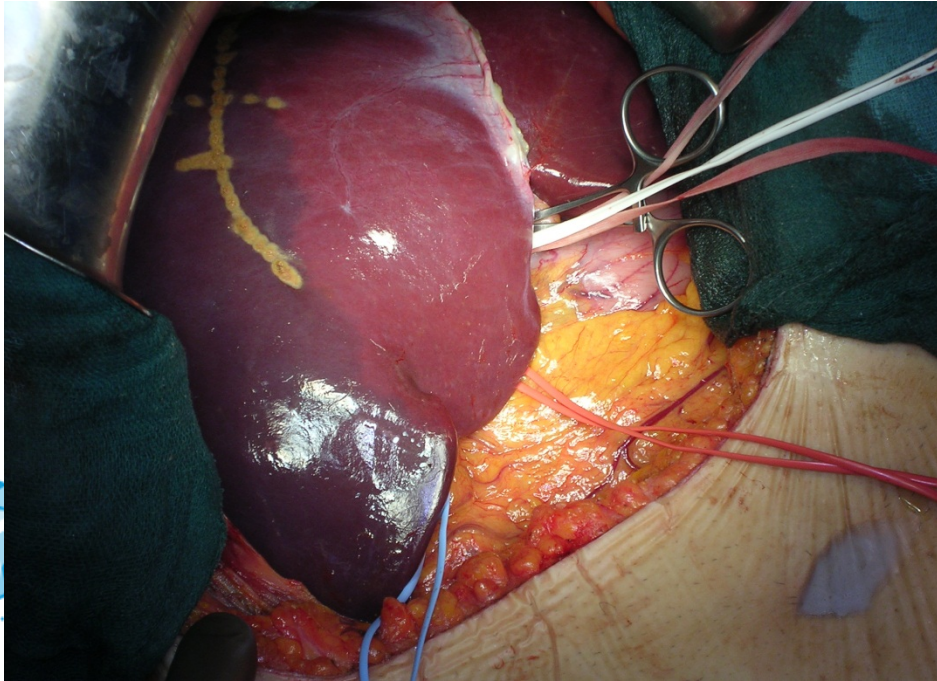
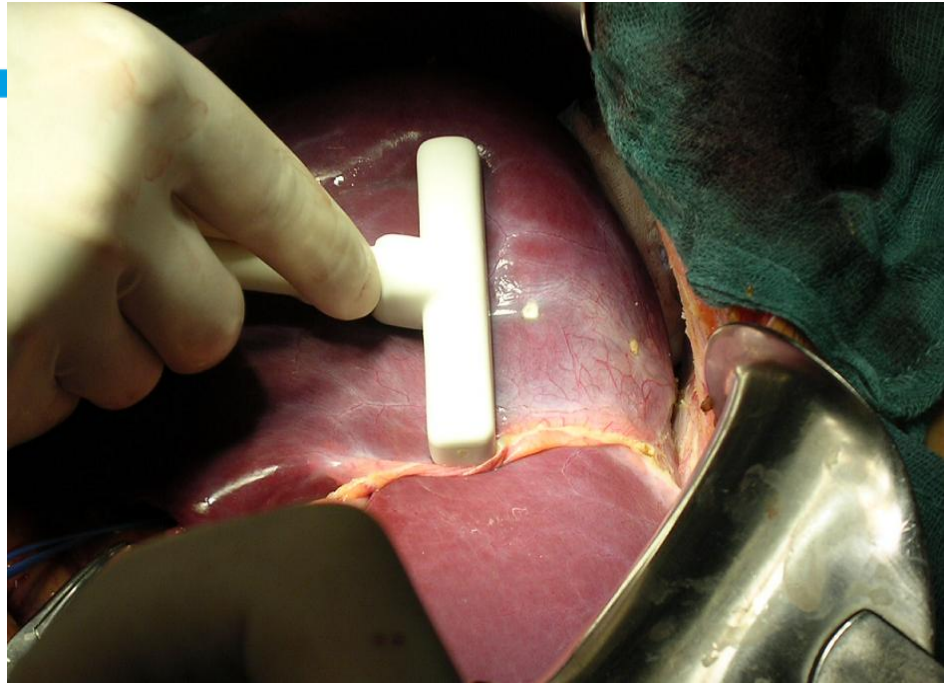
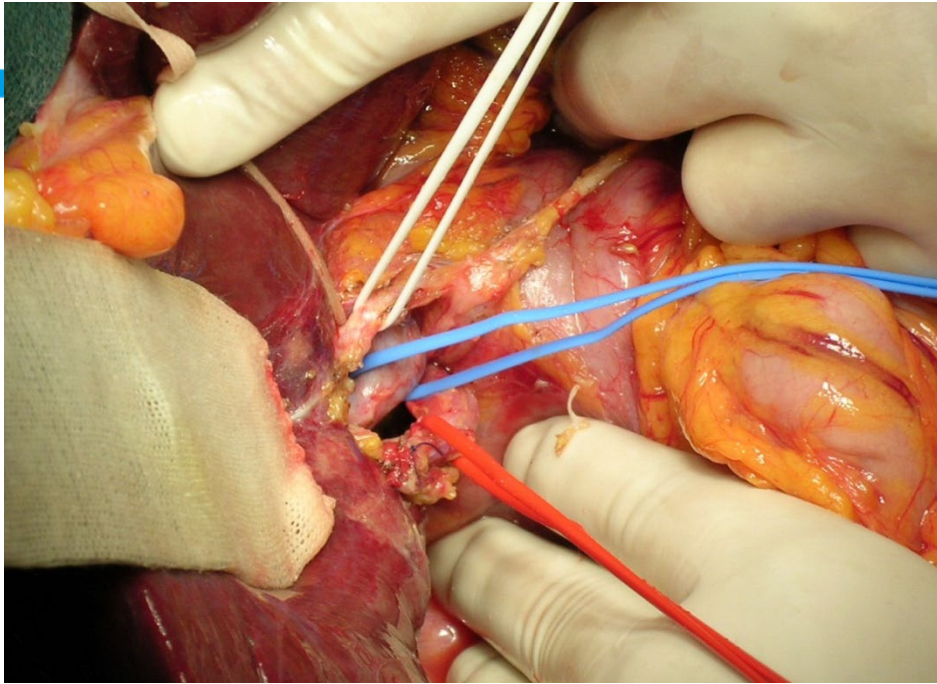


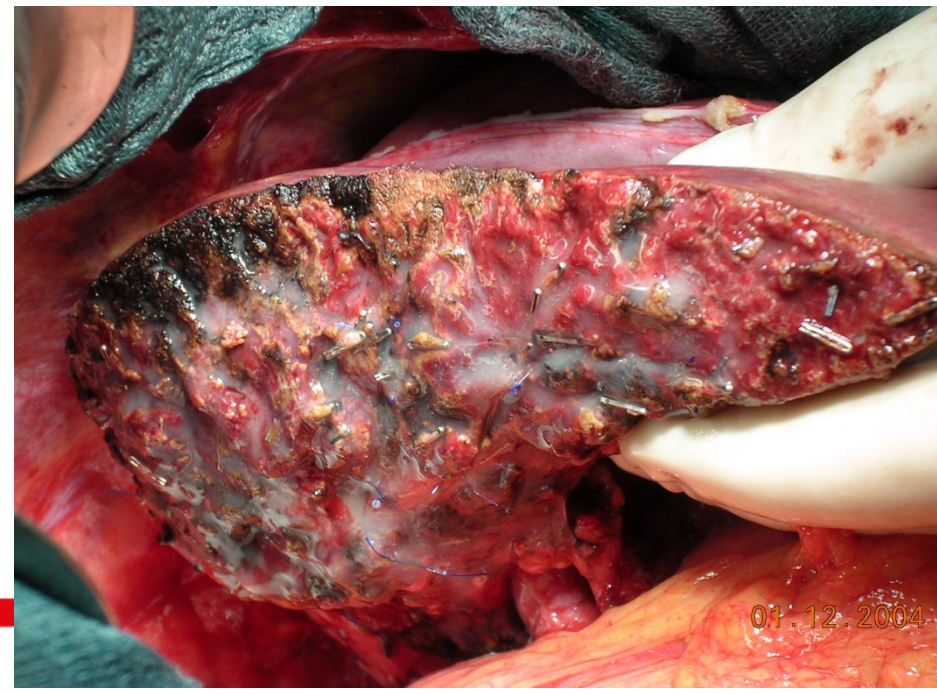
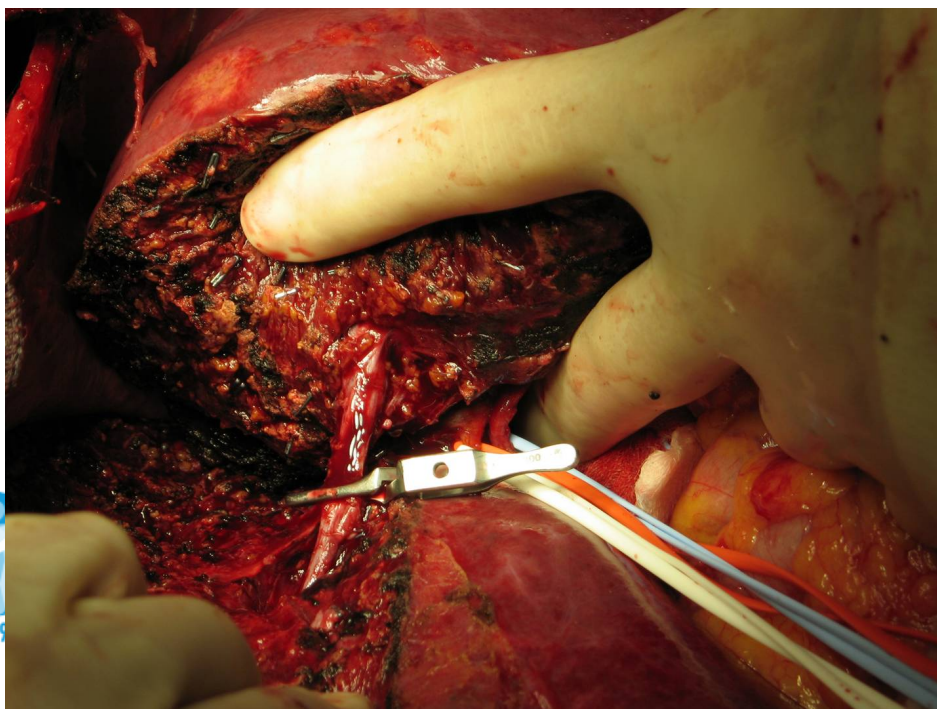
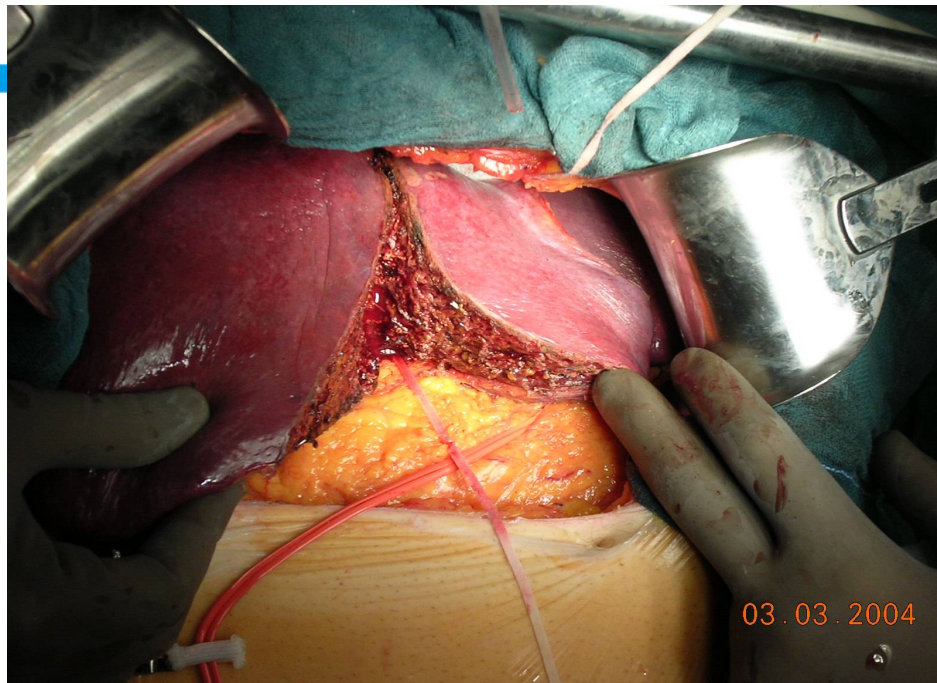
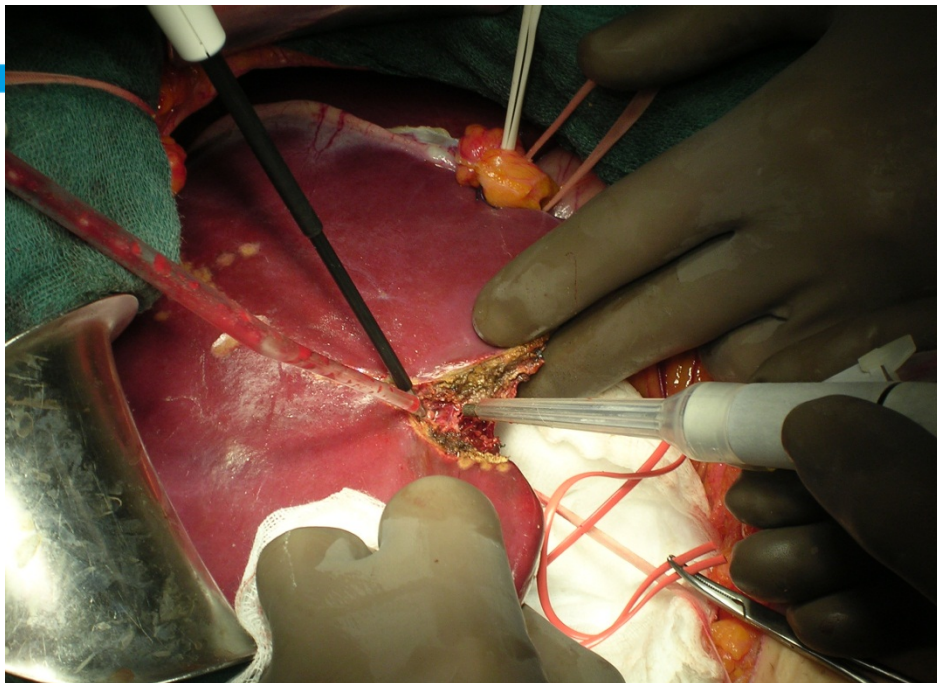
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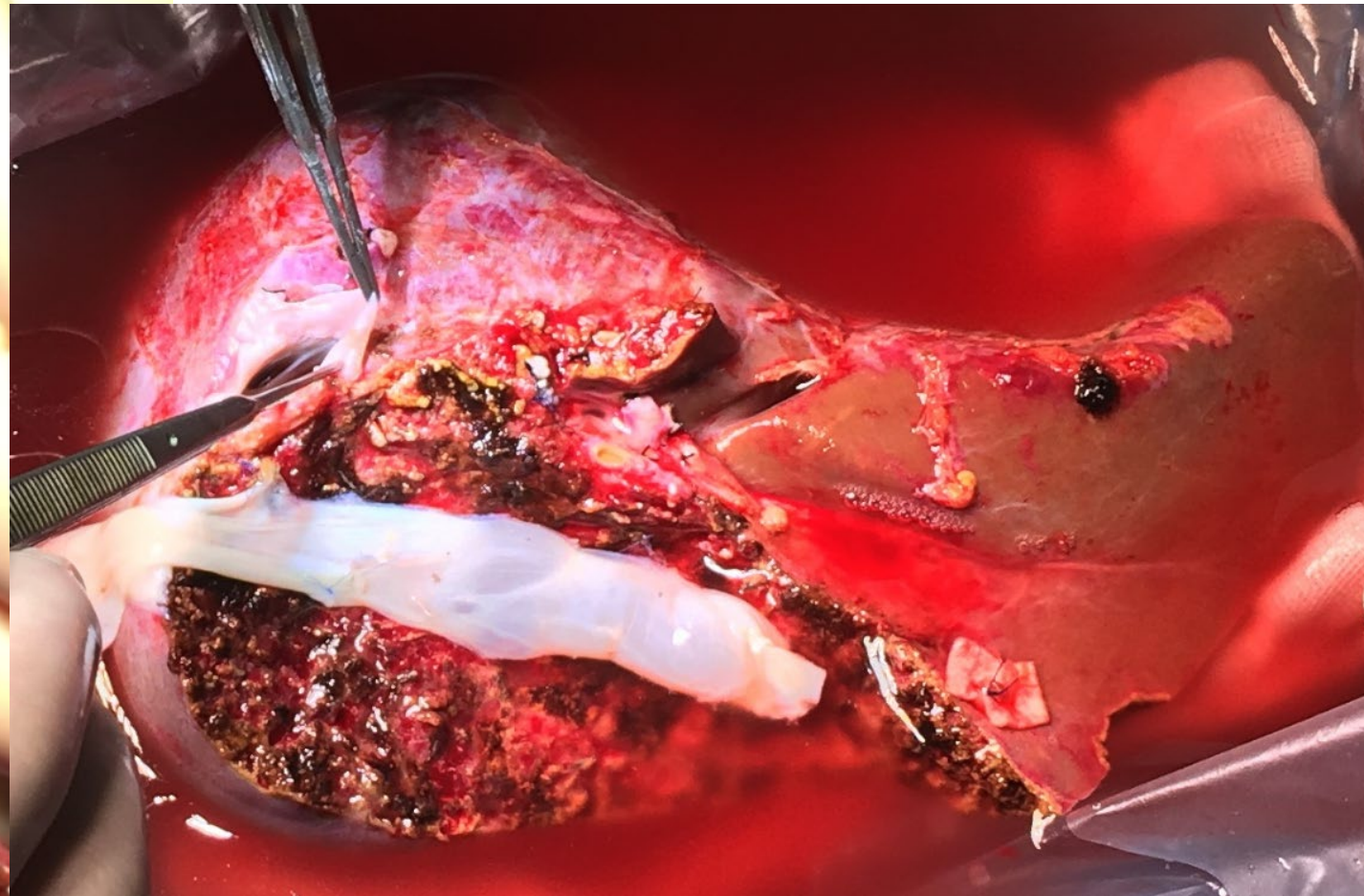
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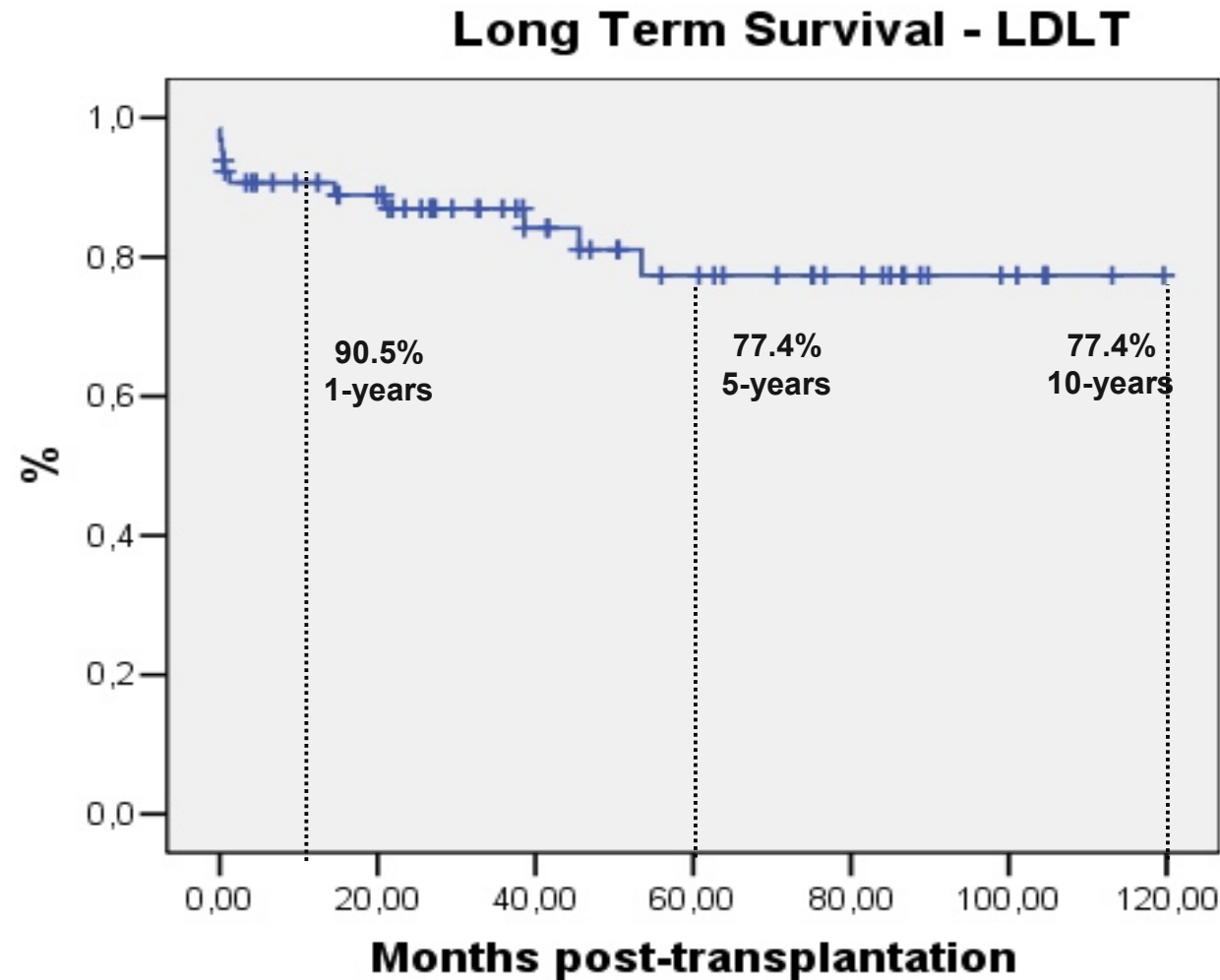
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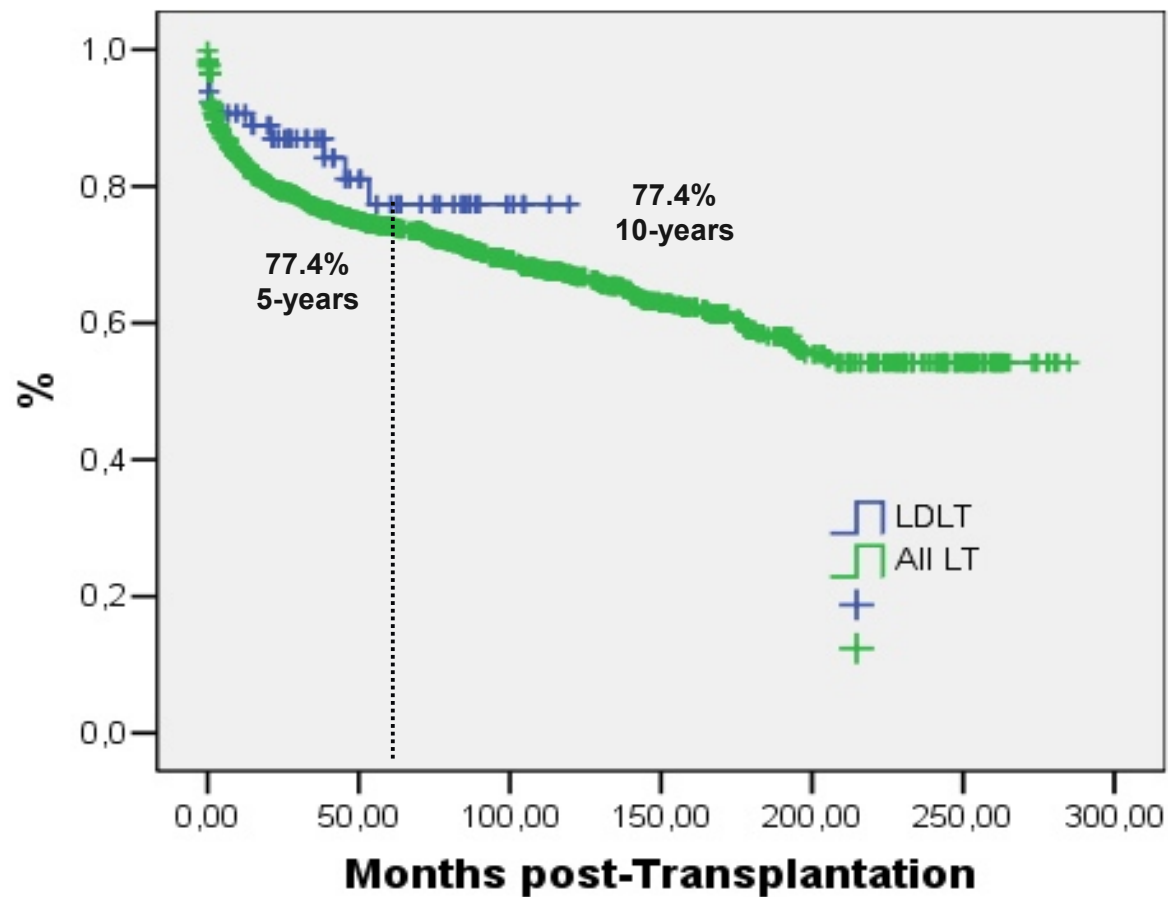


Patients overall survival LDLT cohort (2001-2018) 10-years Survival – NIGUARDA Experience



Patients overall survival LT vs LDLT cohort NIGUARDA Experience

Long Term Survival LDLT vs All LT



LDLT in Italy: Why isn't growing?

- Best allocation policy for HCC recipients
- Waiting list mortality is decreasing
- DDAs and “delisting of HCV patients”
- New options to expand the deceased donor pool
- Donor morbidity (and mortality)



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Donor morbidity and mortality (0.2%) still limit the use of LDLT

Morbidity and Mortality after Living Donor Liver Donation

Authors(year)	Country	Period	N. LD	Mortality	Morbidity (#)	Major complications (≥III Clavien grade)	Improvement with time
Suh KS (2015)	Korea	99-12	886	ZERO	26.4% - 5.8%	1.7% - 0.9%	Yes
Shin M (2012)	Korea	96-10	827	ZERO	10%	3% (25/827)	No
A2ALL (2012)	US	98-09	760	0.4% (3/760)	40%	20%-25%	No
Azoulay D (2011)	France	00-09	91	ZERO	47.3% (43/91)	37.3% (19/43) (°)	No
Iida (2010)	Japan	90-07	1262	0.08% (1/1262)	RG 40.9%-39.4% LG 17.5%-16%	17% (85/500) 2.6%(20/762)	No
Marsh JW (2009)	US	03-06	121	ZERO	20% (24/121)	10.7% (13/121)	Not evaluated

(#) N. of donors who had complications; (*) 4 grades Clavien classification; (°) proportion of ≥III Clavien grade complication



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Donor Safety in Living Donor Liver Donation: An Italian Multicenter Survey

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Liver Transplantation 23 184–193 2017 AASLD.
Received June 17, 2016; accepted August 31, 2016.

Study period: March 2001 - December 2014

[246/313 (78.6%) LDLT performed in Italy up to December 2014]

246 consecutive donor operations for LDLT were performed by 7 Centers in the Survey

- **Right Graft (RG): 220/246 (89.4%)**
- Left Graft (LG): 10/246 (4.1%)
- Left Lateral Segments (LLS): 16/246 (6.5%)

Outcomes were evaluated over two time periods (2001-2006 / 2007-2014)

[Clavien 5-tier grading system]

TABLE 2. Graft and Operative Characteristics Over Time

	All Donors (n = 246)	Period, 1-6 (n = 131)	Period, 7-14 (n = 99)	P Value
DRWR, %	1.0 (0.6-12.5)	1.0 (0.6-1.9)	1.0 (0.6-1.6)	0.06
Graft type				0.005
RL	220 (89.4)	121 (92.4)	99 (100.0)	
LL	10 (4.1)	10 (7.6)	0 (0.0)	
LLS	16 (6.5)	—	—	
Actual graft volume, g	780 (150-1482)	798.5 (220-1432)	790 (470-1482)	0.51
GRWR, %	1.2 (0.3-4.1)	1.2 (0.3-2.5)	1.2 (0.5-3.0)	0.35
GRWR < 0.8%	21 (8.5)	11 (8.4)	9 (9.1)	0.75
Remnant liver volume, %	39.9 (22.7-87.6)	39.0 (23.3-80.9)	38.7 (22.7-67.3)	0.45
Remnant liver volume < 30%	11 (4.5)	7 (5.3)	4 (4.0)	0.60
Blood loss, mL	300 (10-1680)	400 (50-1680)	300 (10-1115)	0.002
Blood loss > 300 mL	54 (22.0)	35 (26.7)	19 (19.2)	0.01
Intraoperative transfusion	38 (15.4)	27 (20.6)	10 (10.1)	0.07
Units of transfused blood				0.08
0	180 (73.2)	94 (71.8)	71 (71.7)	
1	16 (6.5)	9 (6.9)	6 (6.1)	
2	9 (3.7)	8 (6.1)	1 (1.0)	
3	9 (3.7)	8 (6.1)	1 (1.0)	
> 4	2 (0.8)	2 (1.5)	0 (0.0)	
Missing	30 (12.2)	10 (7.6)	20 (20.2)	
Intraoperative hypotension	12 (4.9)	12 (9.2)	0 (0.0)	0.002
Operative time, minutes	403 (270-754)	433 (295-754)	365 (270-705)	< 0.001
Operative time > 400 minutes	132 (53.7)	91 (69.5)	28 (28.3)	< 0.001
LOS, days	8 (3-45)	8 (6-34)	8 (3-45)	0.99
Hospital LOS > 13 days	22 (8.9)	14 (10.7)	8 (8.1)	0.53

NOTE: Data are given as n (%) and median (range). LLS excluded from the analyses over time.

TABLE 4. Type and Severity of All Complications Graded by the 5-Tier Clavien System

	Number of Donors	Clavien Grade				
		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Intraoperative complications	3 (1.2%)	—	—	—	—	—
Intraoperative hemorrhage	2	—	—	—	—	—
Common bile duct injury	1	—	—	—	—	—
Postoperative complications						
Ascites	5	4	1	—	—	—
Fever	9	8	1	—	—	—
Arterial hypertension	1	—	1	—	—	—
Skin rash	1	1	—	—	—	—
Nausea and pain	1	1	—	—	—	—
Hyperbilirubinemia	3	3	—	—	—	—
Pleural effusion	20 ●	14	2	4 (3a)	—	—
Urinary tract infection	3	—	3	—	—	—
Pneumonia	1	—	1	—	—	—
Clostridium difficile colitis	1	—	1	—	—	—
Wound infection/dehiscence	6	—	5	1 (3b)	—	—
Portal vein thrombosis	1	—	—	—	—	—
Pulmonary embolism	3	—	2	—	1	—
Bile leak/biloma	16 ●	1	5	4 (3a) + 6 (3b)	—	—
Biliary stricture	2	—	—	2 (3a)	—	—
Intraabdominal collection/abscesses	8	—	1	7 (3a)	—	—
Intraabdominal bleeding	1	—	—	1 (3b)	—	—
Incisional hernia	1	—	—	1 (3b)	—	—
Chylothorax	1	—	—	1 (3b)	—	—
Diaphragmatic hernia	1	—	—	1 (3b)	—	—
Pancreatitis	2	—	—	—	2 (4)*	—
Total	88 [†]	34	23	28	3	—

NOTE: 88 complications in all 246 LDs (3 complications not graded).

*2 donors had acute pancreatitis as a consequence of other complications.

[†]6 donors had more than 1 complication.

TABLE 7. Multivariate Risk Factors for Postoperative Donor Complications

Variable	<i>P</i> Value	OR	95% CI
<u>All postoperative donor complications</u>			
Portal vein abnormalities	0.02	2.95	1.22-7.15
Blood loss > 300 mL	0.04	2.43	1.06-5.58
Intraoperative hypotension (systolic < 100)	0.02	16.45	1.65-163.85
Operative time (>400 minutes)	0.04	2.21	0.93-4.17
<u>Major postoperative donor complications*</u>			
Intraoperative hypotension (systolic < 100)	<0.001	8.08	2.41-27.07

NOTE: LLS excluded from the analyses;

*Major complications are grade ≥ 3 .

LDLT in Italy: what's our perspectives?

LDLT continue to be a small, but important source to address the organ shortage in selected cases

Donor's outcome compare favourably with the overall outcomes reported

RL is the preferred choice (experience gained in HPB surgery, and a favourable GRWR)

We choose to preserve MHV in the donor to optimize liver function and remnant regeneration

Doubts on the role of laparoscopy in donor operation for adult recipients

A kind of “natural selection” of active centers were LD converges to make the best use of resources and knowledge

Transparency in reporting results after LDLT is mandatory and we should continue to strive for zero donor mortality

Continue vigilance in donor safety and optimal recipient selection are crucial to ensure LDLT growing

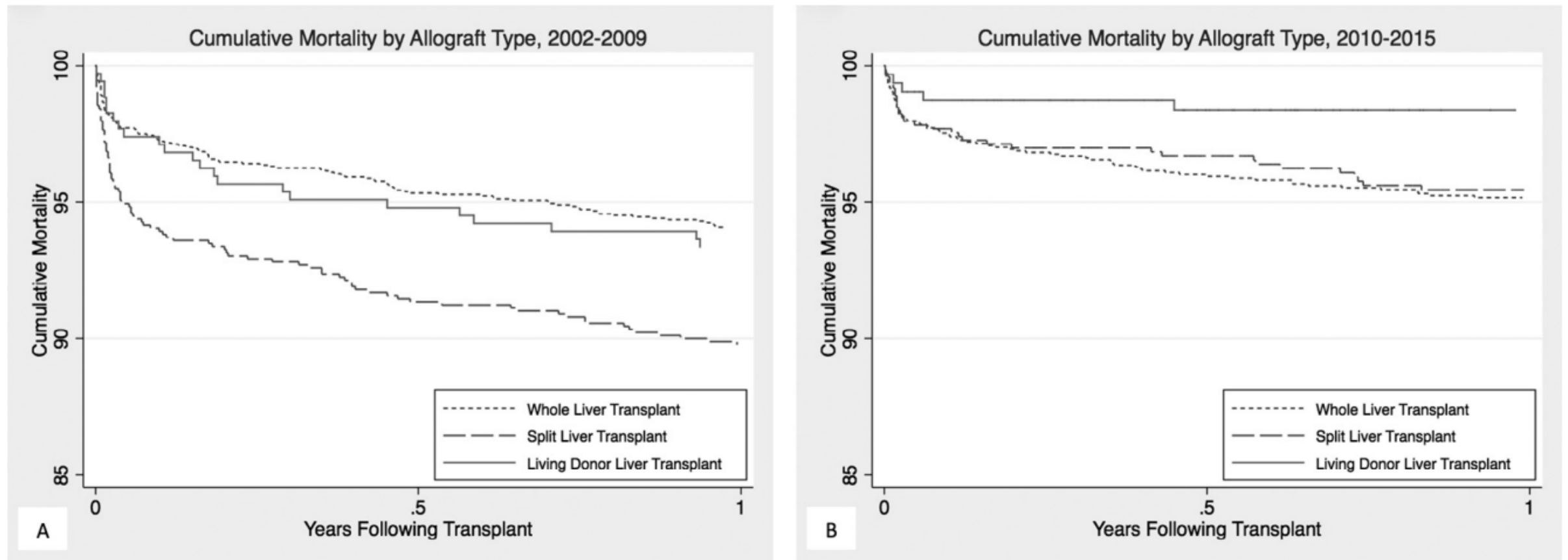


Figure 1. Kaplan-Meier curve of patient survival by allograft type in the first year after transplant from **A**, 2002 to 2009 and **B**, from 2010 to 2015.

LDLT in Italy: Future applications?

REVIEW

Auxiliary living donor liver transplantation combined Nadalin *et al.*

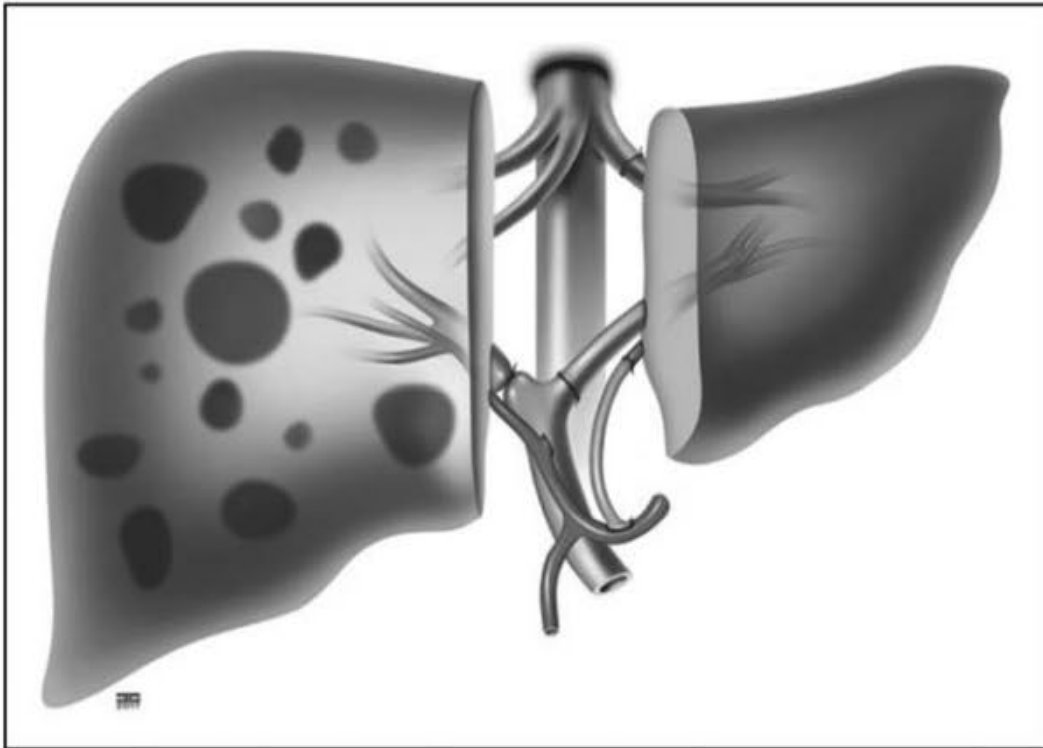


FIGURE 2. Implantation of left lateral graft according to the auxiliary partial orthotopic liver transplantation technique [39]

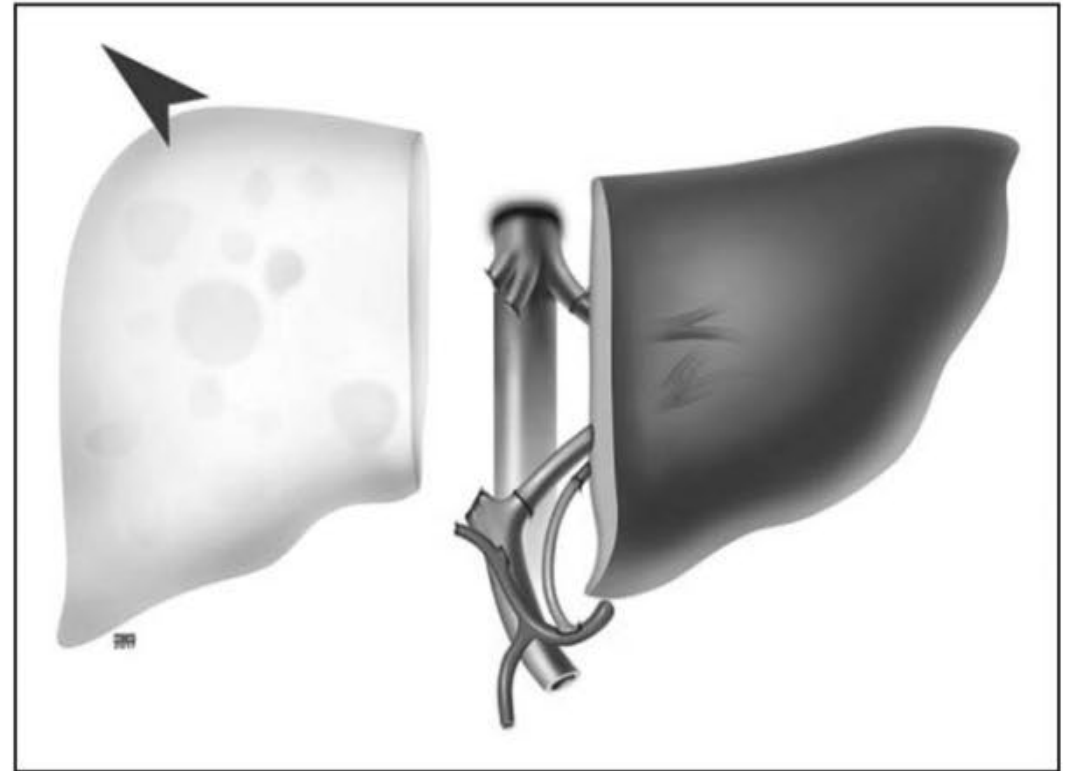


FIGURE 3. Removal of right hemiliver [39].