



Meeting del 45° parallelo

IBD and liver hemisphere

30 Maggio 2024

Salone del Grano

Piazza Giuseppe Garibaldi, 2
Rovigo

Lifestyle after Liver Transplantation

Maria Cristina Morelli

Laura Turco

IRCCS AOU Bologna Policlinico S.Orsola

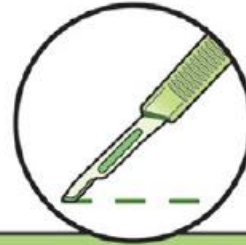
The Changing Landscape of Liver Transplantation

Recipient phenotypes has changed



Recipient phenotype

- Older
- Higher frailty status
- More obesity
- Higher frequency of comorbidities (CVD, CKD)



Transplant indication

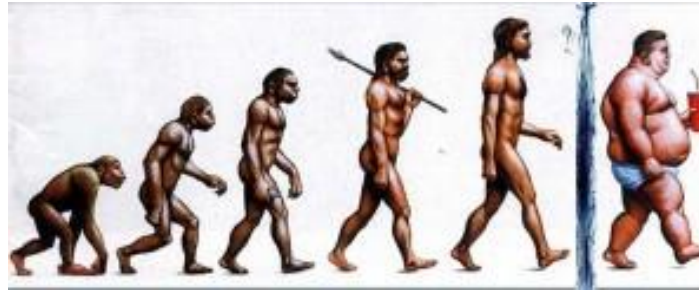
- Less HCV
- More NAFLD
- More alcohol
- Non-HCC oncologic indications



Disease severity

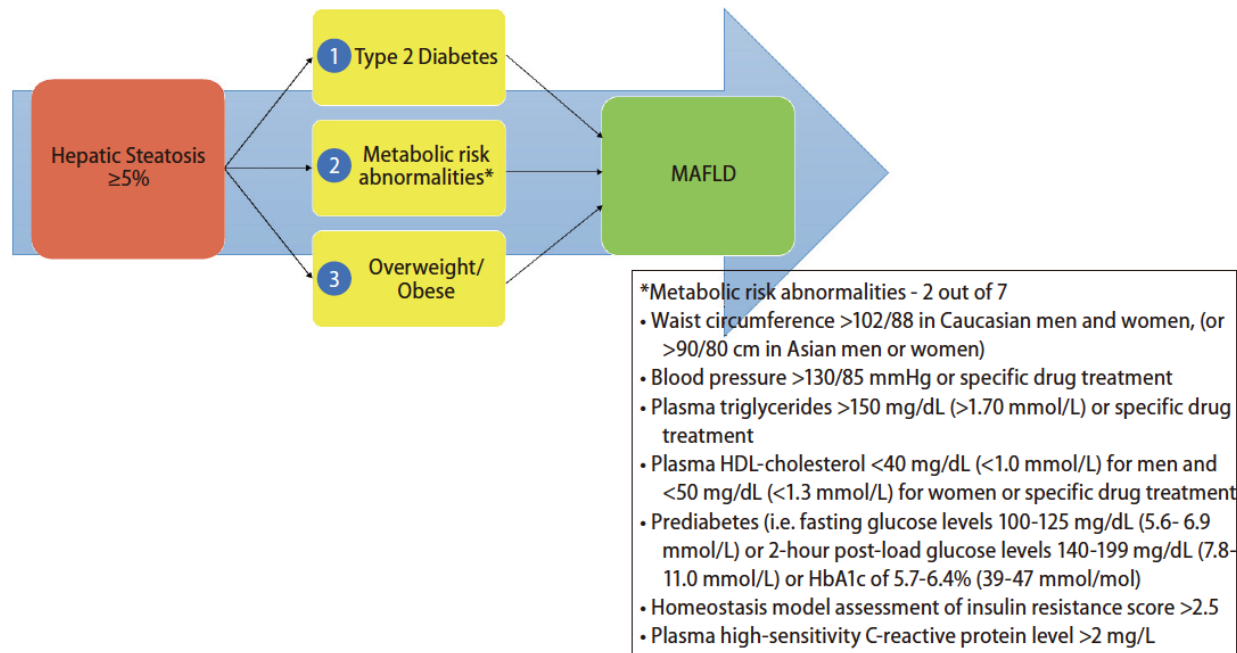
- Higher acuity
- Higher MELD score
- More ACLF and AH
- Expanded HCC

The Changing Landscape of Liver Transplantation

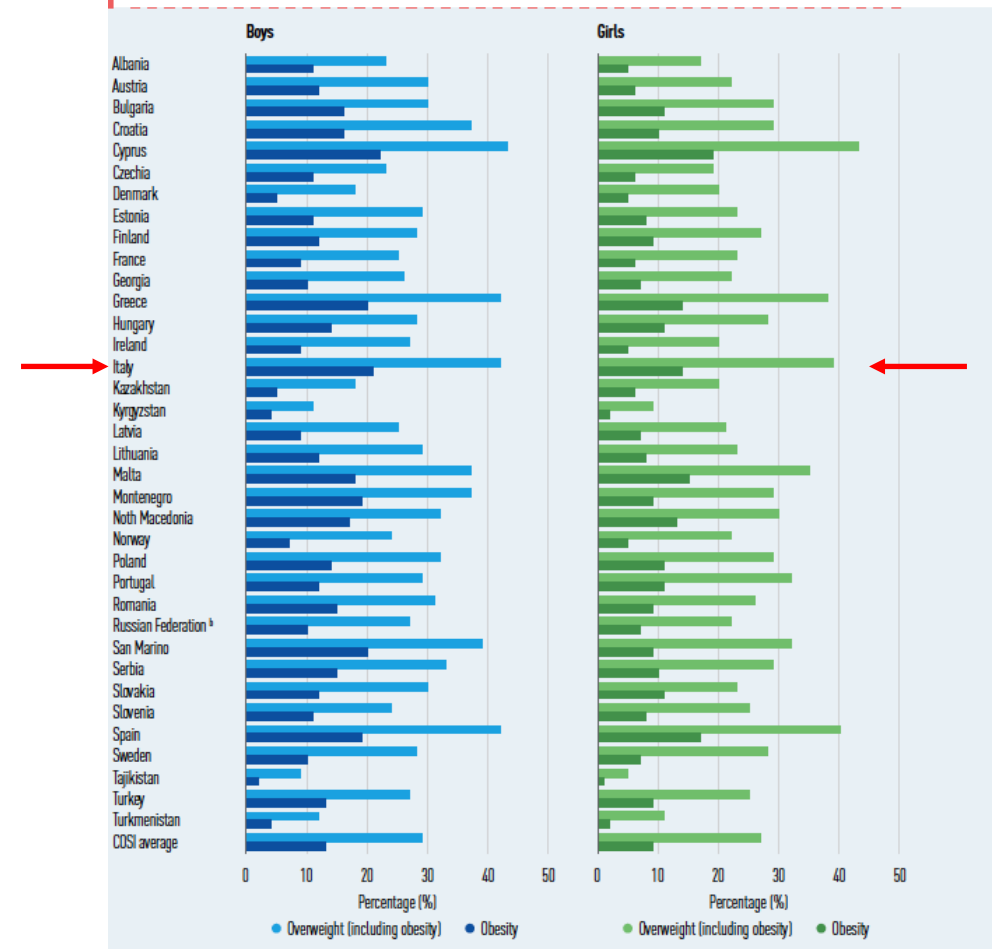


WHO EUROPEAN REGIONAL OBESITY REPORT 2022

- In parallel to that of metabolic syndrome, the prevalence of MAFLD is increasing Worldwide.
- High prevalence (36-44%) was found in obese children.
- Shift in indications for liver transplantation from viral to metabolic liver diseases



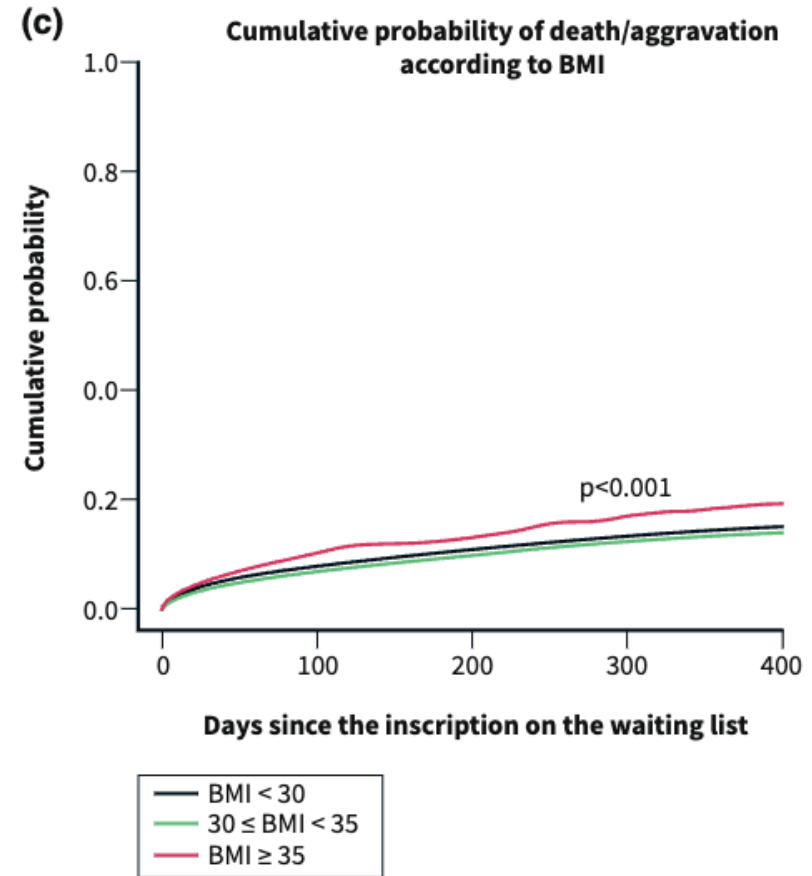
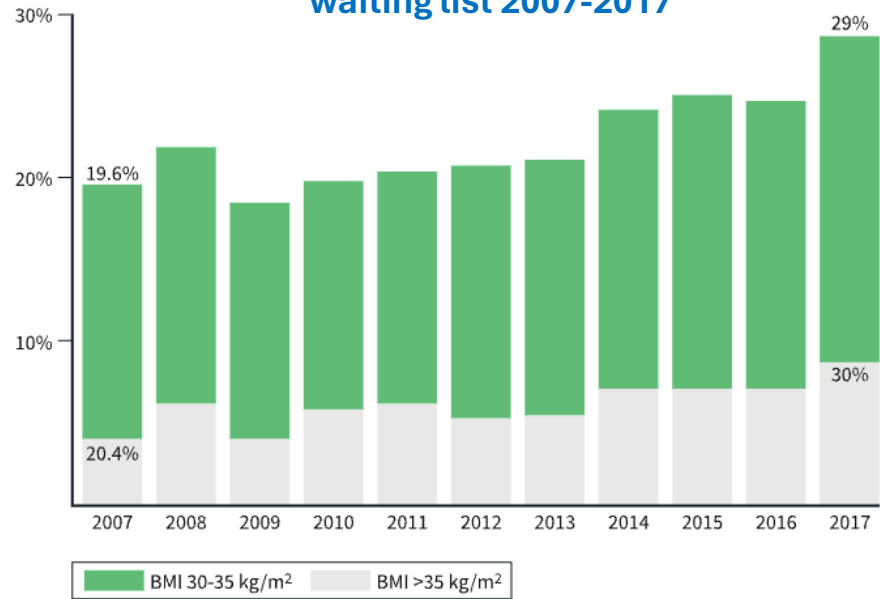
Prevalence of overweight and obesity among children aged 7–9 years in 36 countries of the WHO European Region, by sex (2015–2017) *



Morbid obesity increases death and dropout from the liver transplantation waiting list: A prospective cohort study

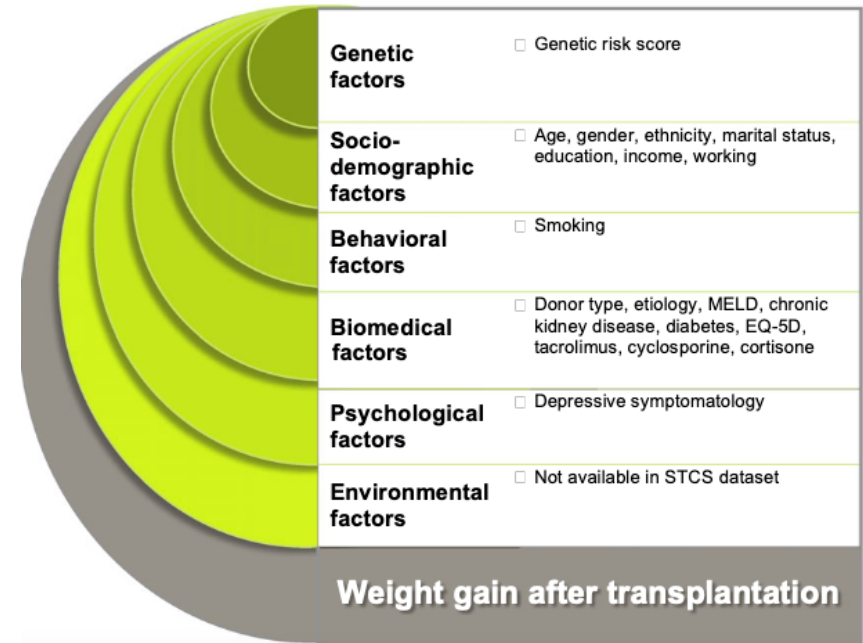
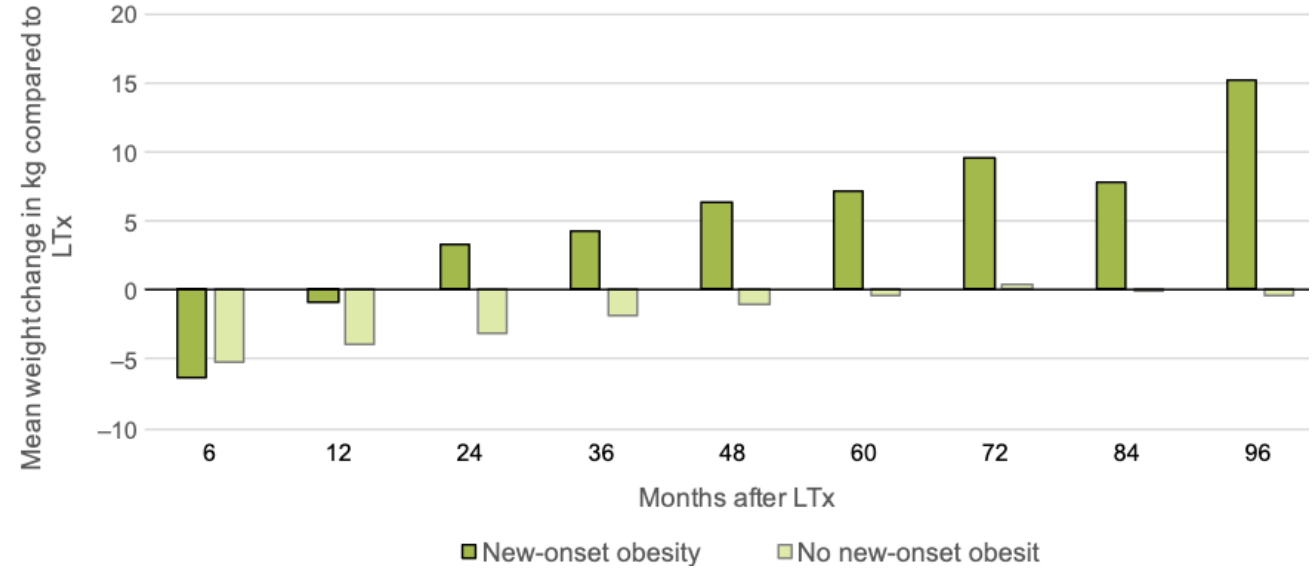
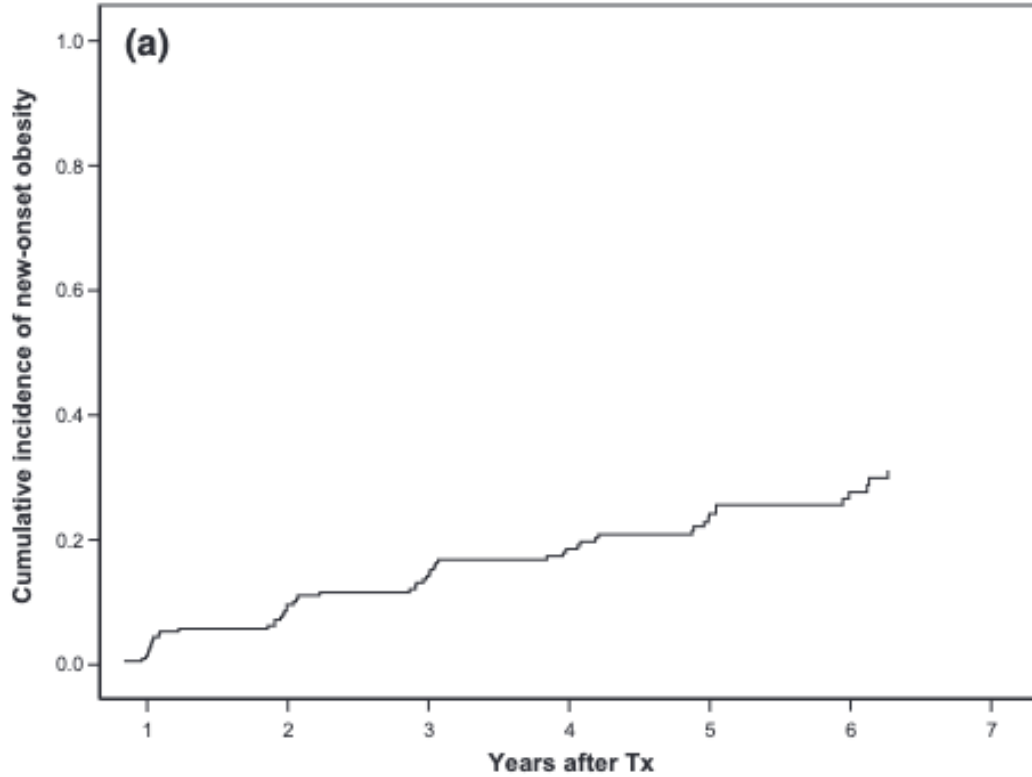
Claire Delacôte¹ | Mathilde Favre² | Medhi El Amrani³ | Massih Ningarhari^{1,2} |
Elise Lemaitre¹ | Line Carolle Ntandja-Wandji^{1,2} | Pierre Bauvin¹ |
Emmanuel Boleslawski³ | Guillaume Millet³ | Stephanie Truant³ |
Philippe Mathurin^{1,2} | Alexandre Louvet^{1,2} | Valérie Canva² | Gilles Lebuffe^{3,4} |
François René Pruvot³ | Sébastien Dharancy^{1,2} | Guillaume Lassailly^{1,2}  |
The French ABM study group

Prevalence of obesity in waiting list 2007-2017



Obesity after LT

Swiss transplant cohort study of 235 patients



Inevitability of disease recurrence after liver transplantation for NAFLD cirrhosis

JHEP Reports **2023**.

Authors

François Villeret, Sébastien Dharancy, Domitille Erard, Armand Abergel, Louise Barbier, Camille Besch,

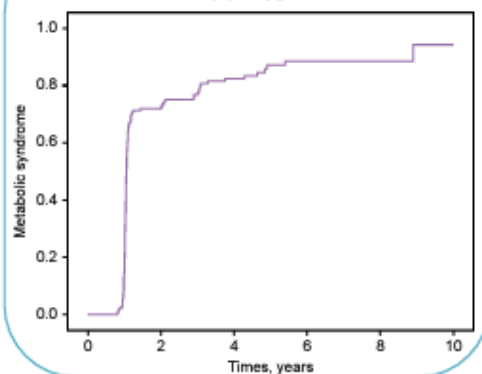
Disease recurrence at 5 years after liver transplantation for NAFLD cirrhosis

French retrospective cohort of 361 patients
150 patients with at least one graft biopsy performed ≥ 6 months after LT



Metabolic syndrome

86.2%



Inevitability of disease recurrence after liver transplantation for NAFLD cirrhosis

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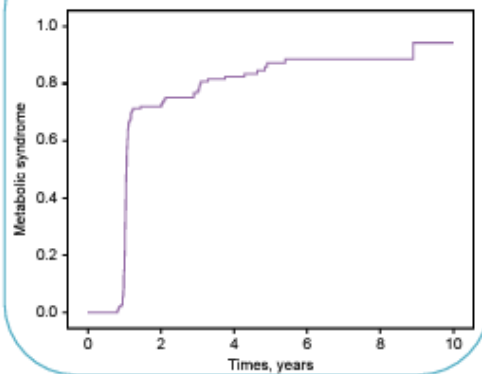
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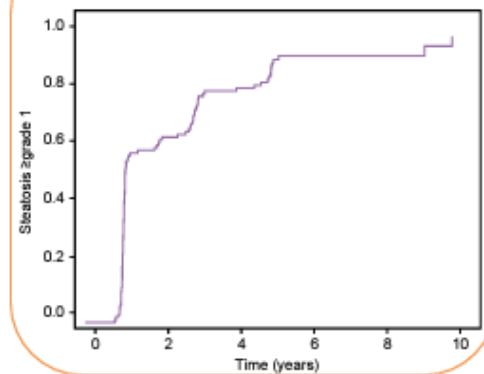
Metabolic syndrome

86.2%



Steatosis

85.0%



Inevitability of disease recurrence after liver transplantation for NAFLD cirrhosis

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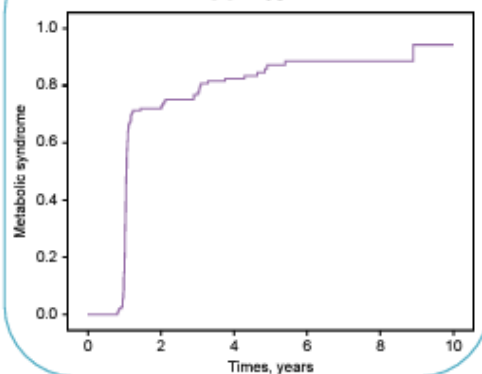
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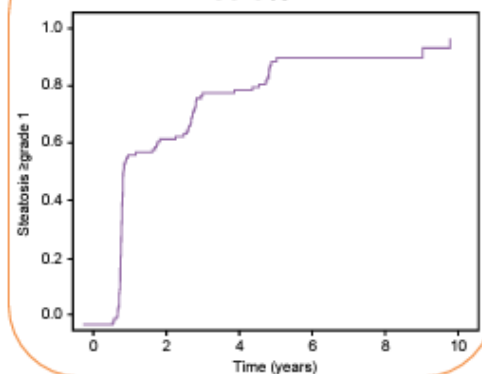
Metabolic syndrome

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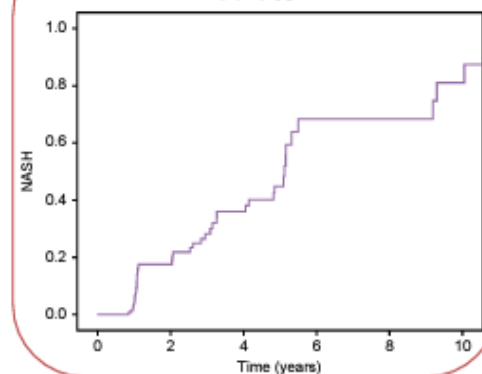
Steatosis

85.0%



NASH

60.3%



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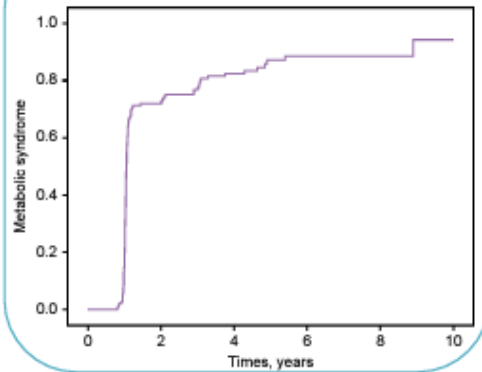
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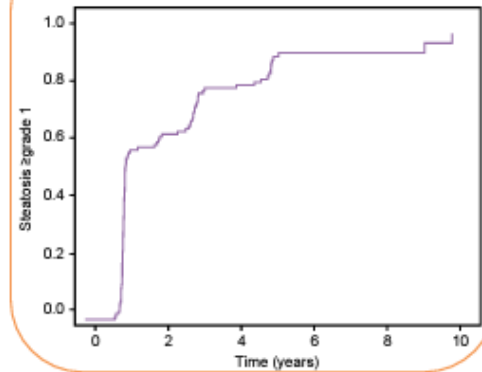
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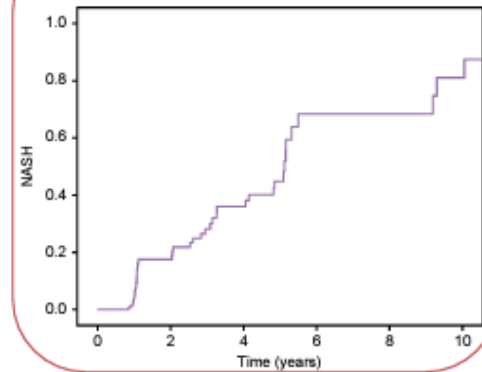
Steatosis

85.0%



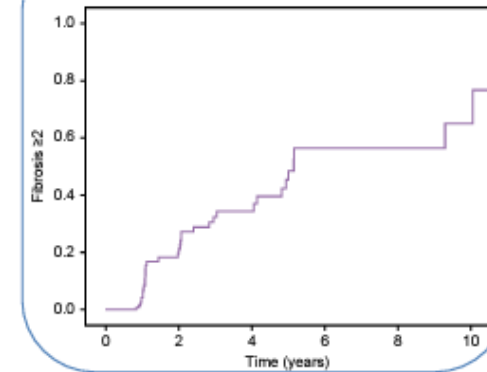
NASH

60.3%

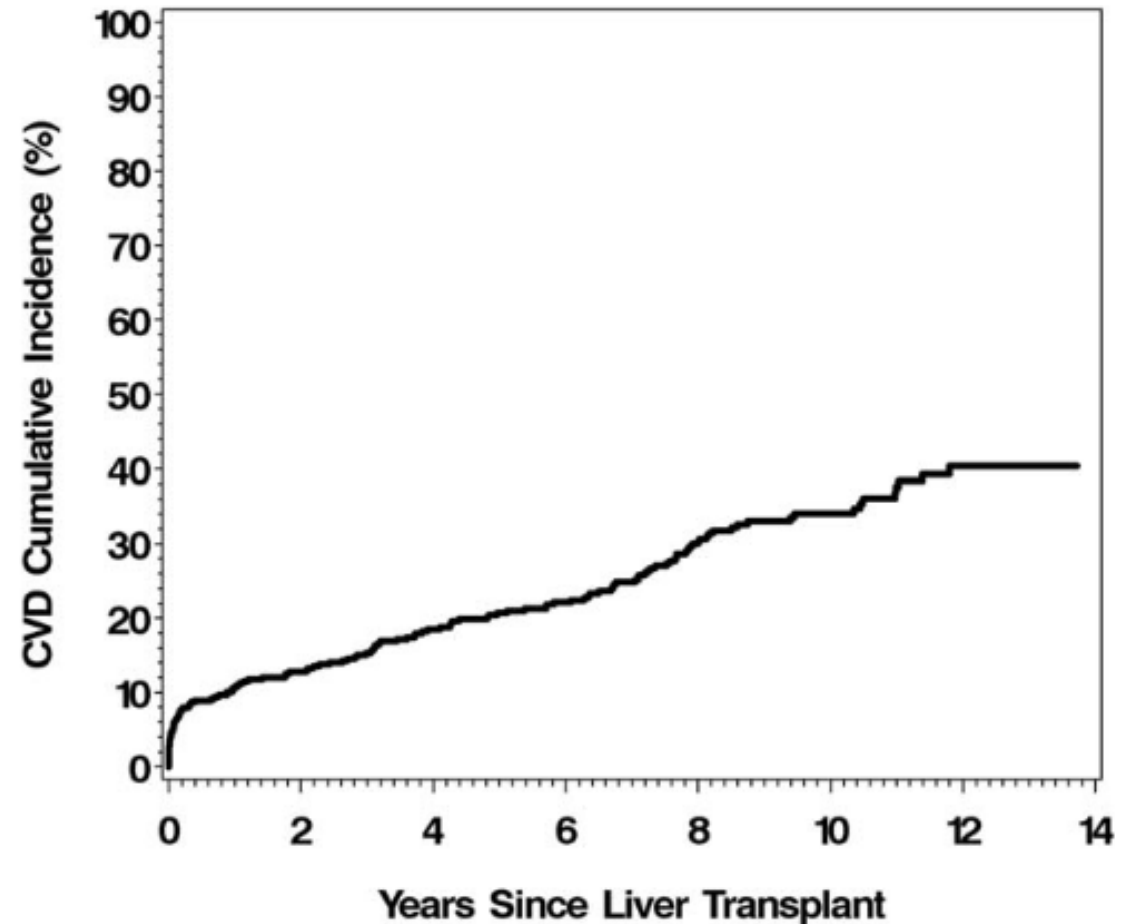
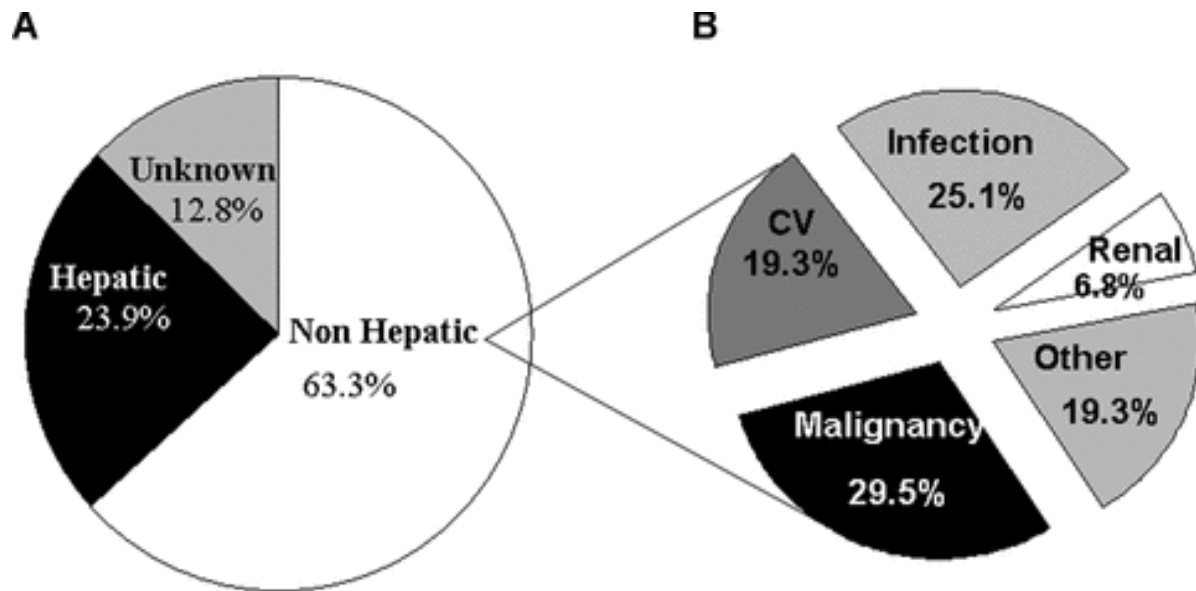


Significant fibrosis

48.0%

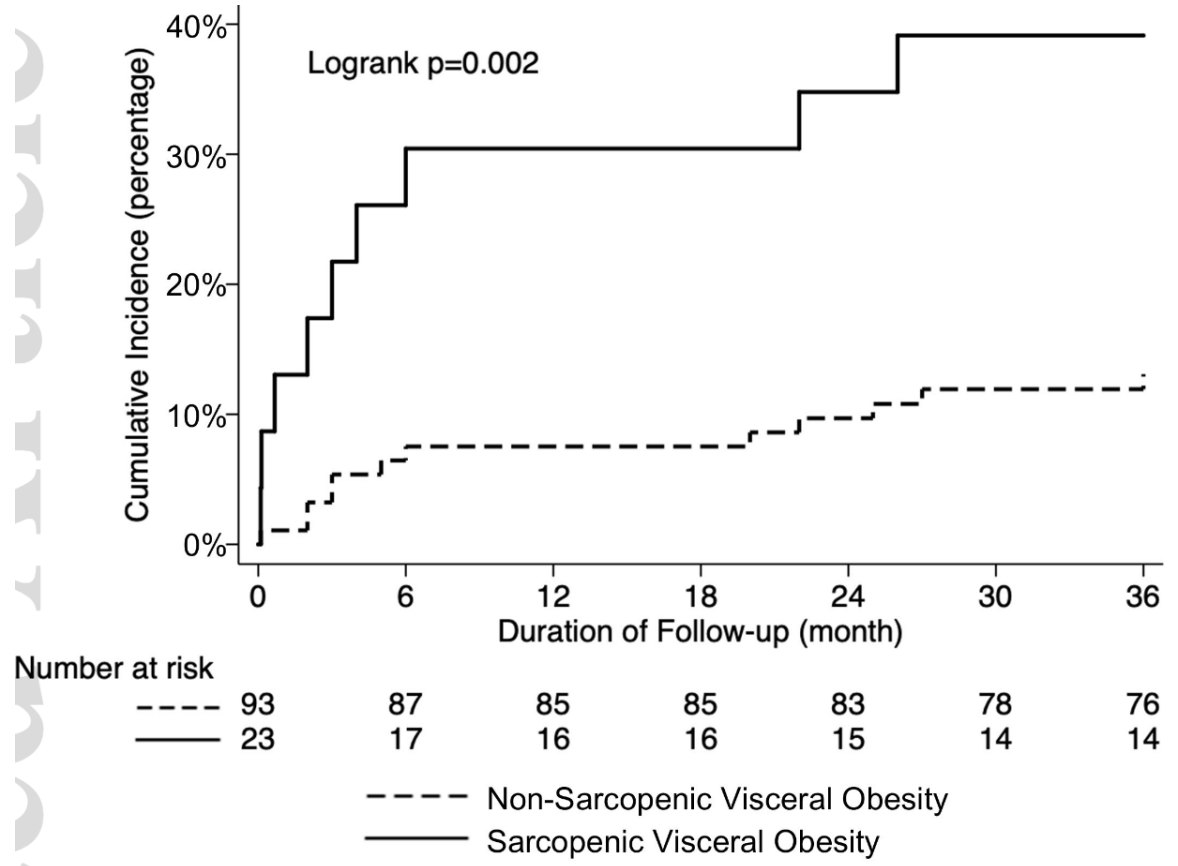
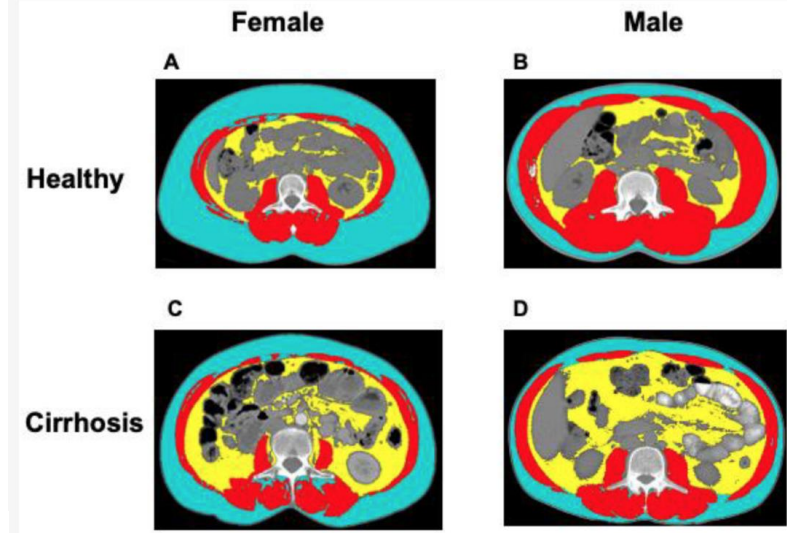


Cardiovascular Disease After Liver Transplantation

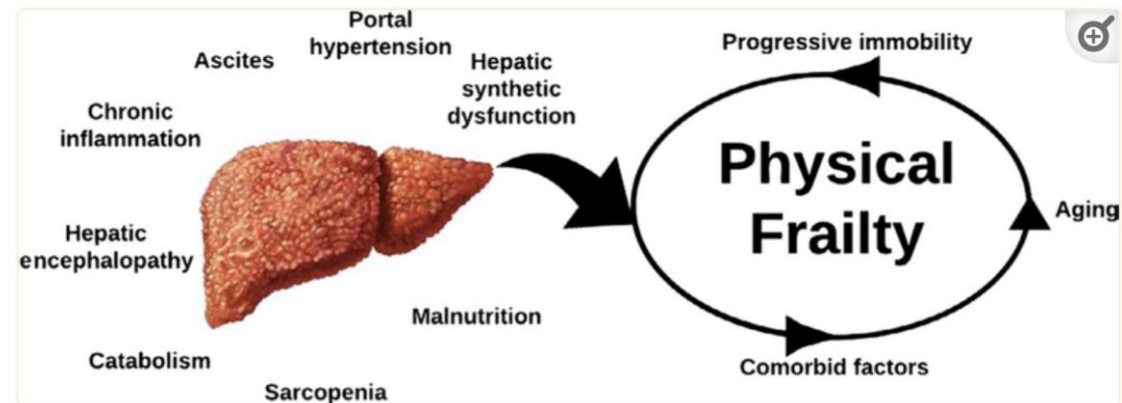


Sarcopenic visceral obesity is associated with increased mortality after LT

- N.116 cirrhotic patients urgently listed and transplanted (2005-2017)
- Sarcopenic visceral obesity
 - Visceral Obesity : VSR >1.54 men >1.37 women
 - Sarcopenia (men SMI <50 cm²/m², women <39 cm²/m²)

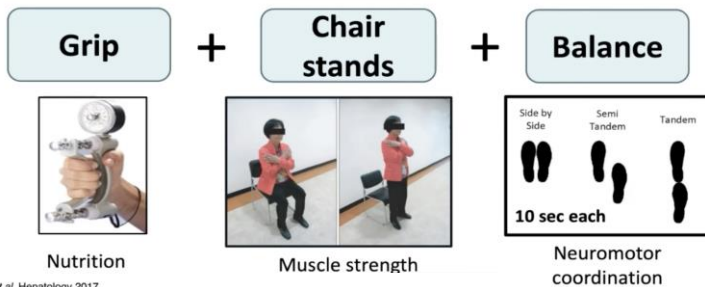


Frailty : decreased physiologic reserve to perform daily activities, fulfill social roles, and maintain health/well-being



Lai JC Am J of Transpl 2020

FrAILT
The Liver Frailty Index
liverfrailtyindex.ucsf.edu



Lai et al. Hepatology 2017.

Received: 4 August 2021 | Revised: 14 November 2021 | Accepted: 20 November 2021

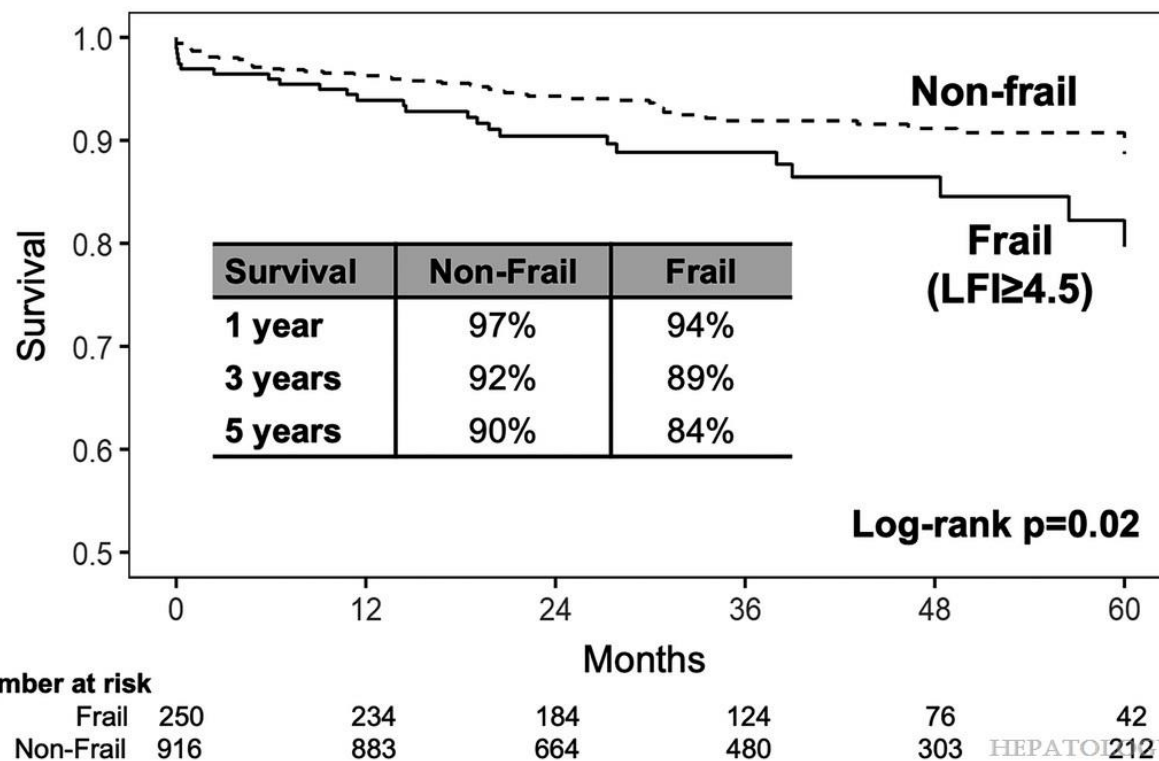
DOI: 10.1002/hep.32268



ORIGINAL ARTICLE

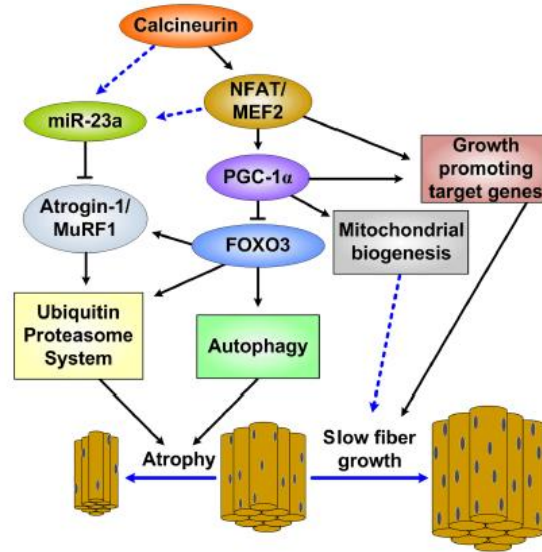
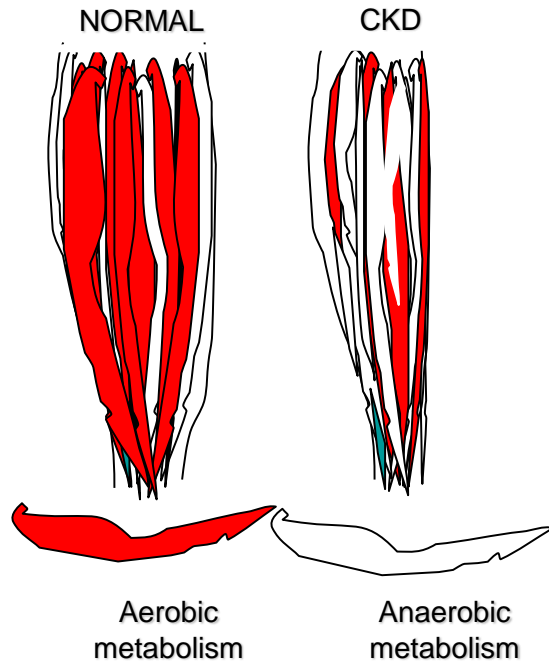
Frailty, mortality, and health care utilization after liver transplantation: From the Multicenter Functional Assessment in Liver Transplantation (FrAILT) Study

Jennifer C. Lai¹ | Amy M. Shui² | Andres Duarte-Rojo^{3,4} | Daniel R. Ganger⁵ |



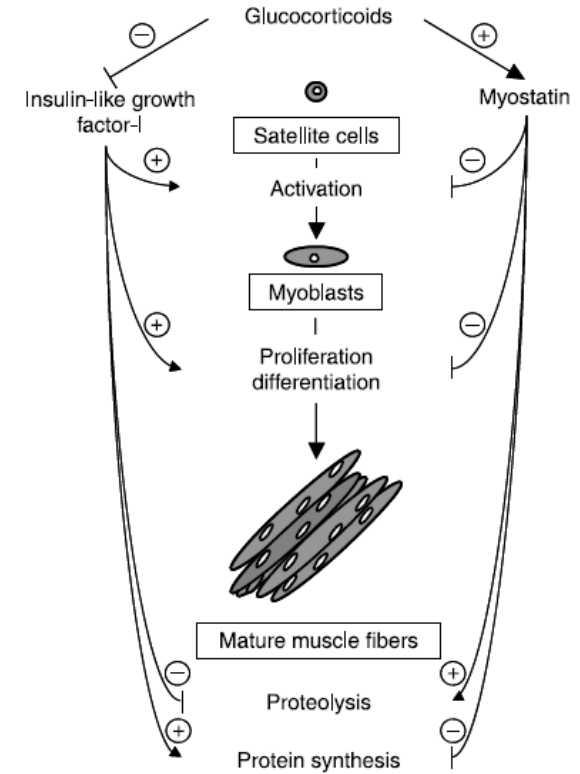
Drugs-induced myopathy in Liver Transplantation

Calcineurin Inhibitors



Hudson MB 2013

Glucocorticoids



Schakman O Int J Bioch Cell Biol 2013

Controlling Diabetes After Liver Transplantation: Room for Improvement

Diego Alvarez-Sotomayor, MD,¹ Carla Satorres, MD,¹ Beatriz Rodríguez-Medina, MD,²
Ignacio Herrero, MD, PhD,^{3,4} Manuel de la Mata, MD,⁵ Trinidad Serrano, MD,⁶ Manuel Rodríguez-Perálvarez, MD,⁵
Delia D'Avola, MD,^{3,4} Sara Lorente, MD,⁶ Angel Rubín, MD,¹ and Marina Berenguer, MD, PhD⁷

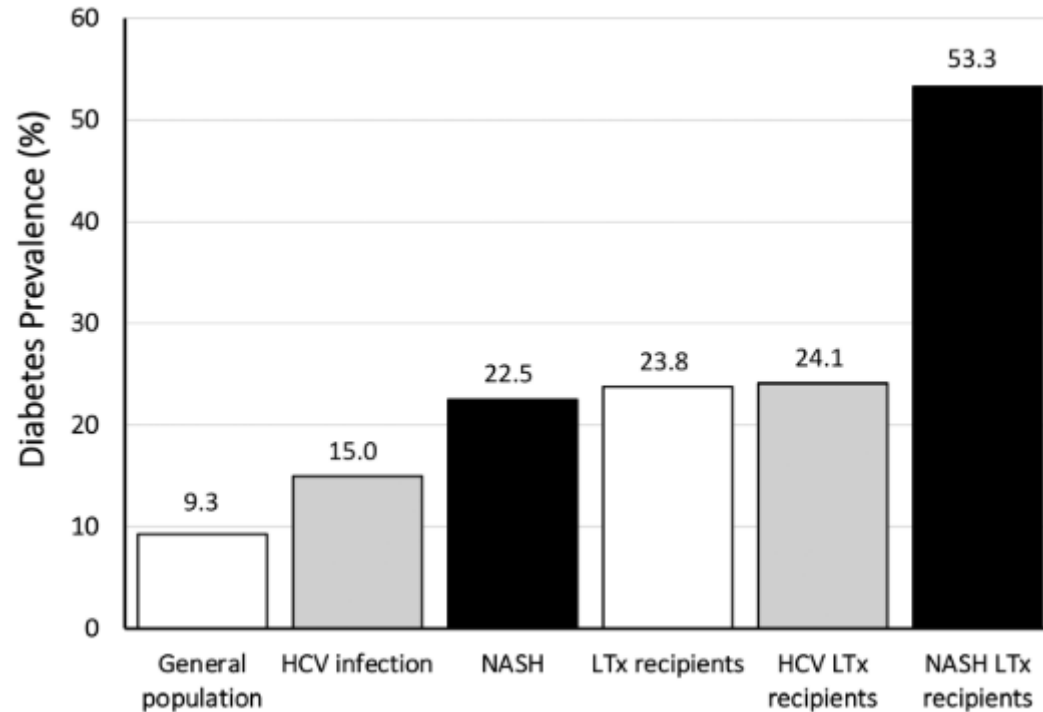
Transplantation ■ October 2016 ■ Volume 100 ■ Number 10

Glycemic control, management of diabetes mellitus and screening of associated conditions

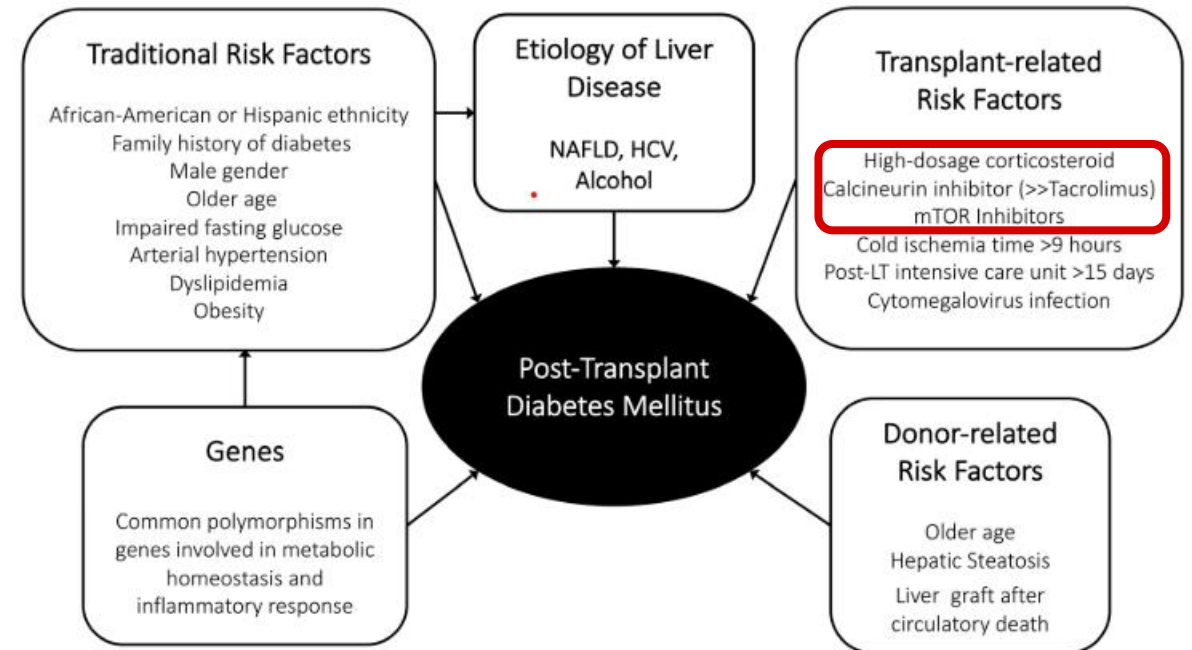
Diabetes (n = 157)	No. (%)
Adequate glycemic control (HbA1c < 7%)	94 (66.7) ^a
Physician responsible for management of DM	
Endocrinologist	28 (17.8)
Hepatologist	76 (48.4)
General practitioner	42 (26.8)
Self-control	11 (7.0)
Exercise	
None/Light	106 (67.5)
Moderate/Vigorous	51 (32.5)
Diet	
Free	56 (35.7)
Restricted	101 (64.3)
Retinopathy screening ^b	76 (48.4)
Nephropathy screening ^c	74 (47.1)
Neuropathy screening ^d	7 (4.5)
Diabetic foot screening ^e	9 (5.7)

Diabetes After Liver Transplantation

Pre-Transplant Diabetes Mellitus type 2



Post- Transplant Diabetes Mellitus (PTDM)



Management of Diabetes in Candidates for Liver Transplantation and in Transplant Recipients

- Offer counseling for diet and moderate physical activity
- Provide intensive programs of cognitive behavior therapy by dedicated
- Define HbA1c target considering patients' frailty
- **Limit the use of insulin to the sole basal insulin as long as possible**
- **Modulate immunosuppressive therapy, using mycophenolate mofetil or basiliximab to mitigate the diabetogenic effects of CNIs**
- In selected cases, consider bariatric surgery

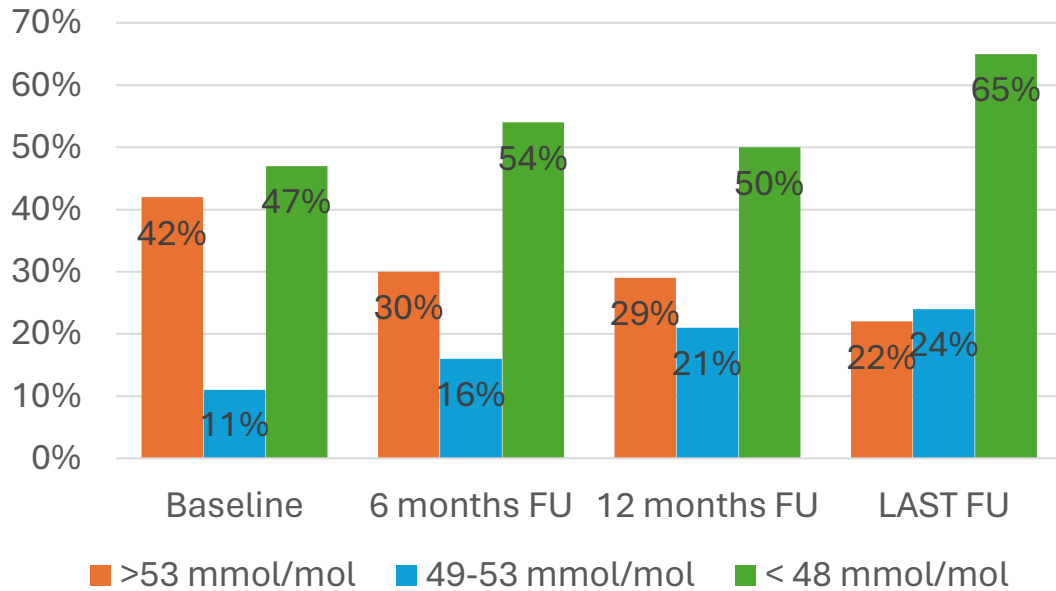
FIRST LINE	SECOND LINE	THIRD LINE	FOURTH LINE
<p>Test Metformin</p> <p>Move to 2nd line treatment in case of intolerance or contraindication</p>	<p>Use either GLP-1RAs or SGLT-2Is or pioglitazone, according to CV, HF, renal or liver risk</p> <p>Alone or in combination with metformin if not contraindicated</p>	<p>Combine 2nd line drugs with DPP-4Is (except GLP-1RAs) or with basal Insulin, according to registered indications</p> <p>Consider specific contraindications</p>	<p>Move to intensified insulin treatment</p> <p>Adjust glycemic targets to reduce the risk of hypoglycemia</p>

Short-term safety and efficacy of new hypoglycemic drugs in patients undergoing orthotopic liver transplantation: interim analysis from the DiaBoLT2021 study

	Baseline (patients n = 62)	6 months FU (patients n = 62)	12 months FU (patients n = 53)	LAST FU (21 ± 14 months) (patients n = 62)
Therapy	percent (%)	percent (%)	percent (%)	percent (%)
Insulin	73	52	50	47
- Basal	- 24	- 81	- 93	- 86
- Basal-bolus	- 76	- 19	- 7	- 14
Daily insulin unit (media ± st. dev.)	43,9 ± 31,25	28,9 ± 17,24	25,7 ± 13,94	27,2 ± 15,37
Metformin	35	81	80	82
Pioglitazone	0	2	2	2
Sulfonylureas	3	0	0	0
Acarbose	0	2	2	2
New antiadiabetic drugs	15	76	74	82
GLP-1RA	8	47	52	47
DPP-4I	5	16	15	23
SGLT-2I	5	26	28	39

Efficacy: glycemic control and changing in weight

Glycated Hb target



BMI 25-30 kg/m²

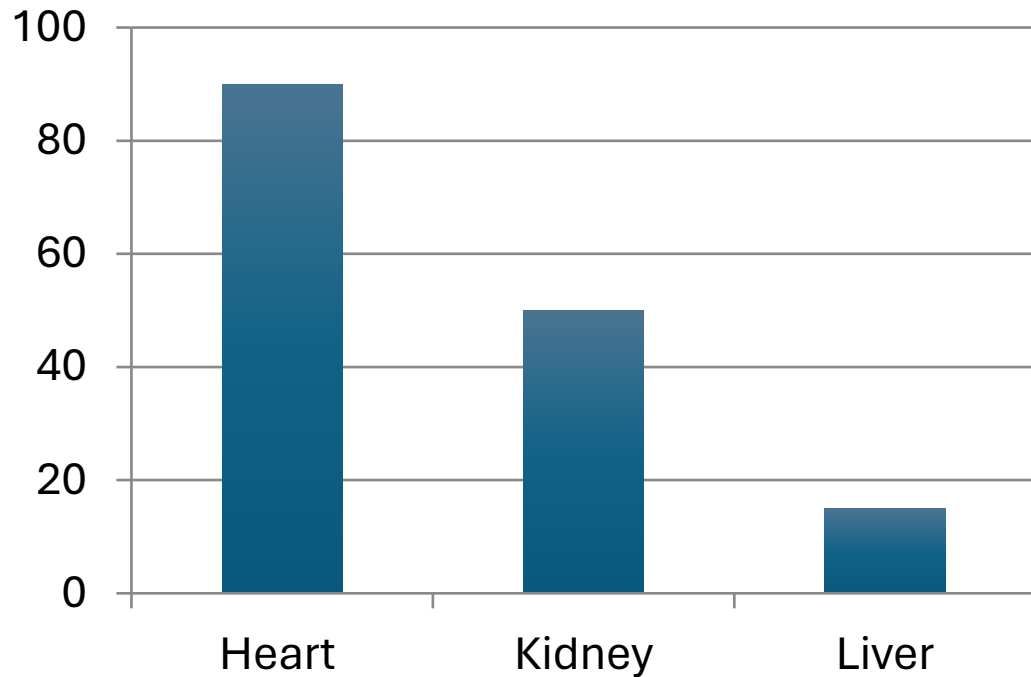
	Weight – mean (kg)	Δ weight – mean (kg)
6 months	77,4	-2,9
12 months	79,3	-4,3
Last FU	76,6	-3,8

BMI > 30 kg/m²

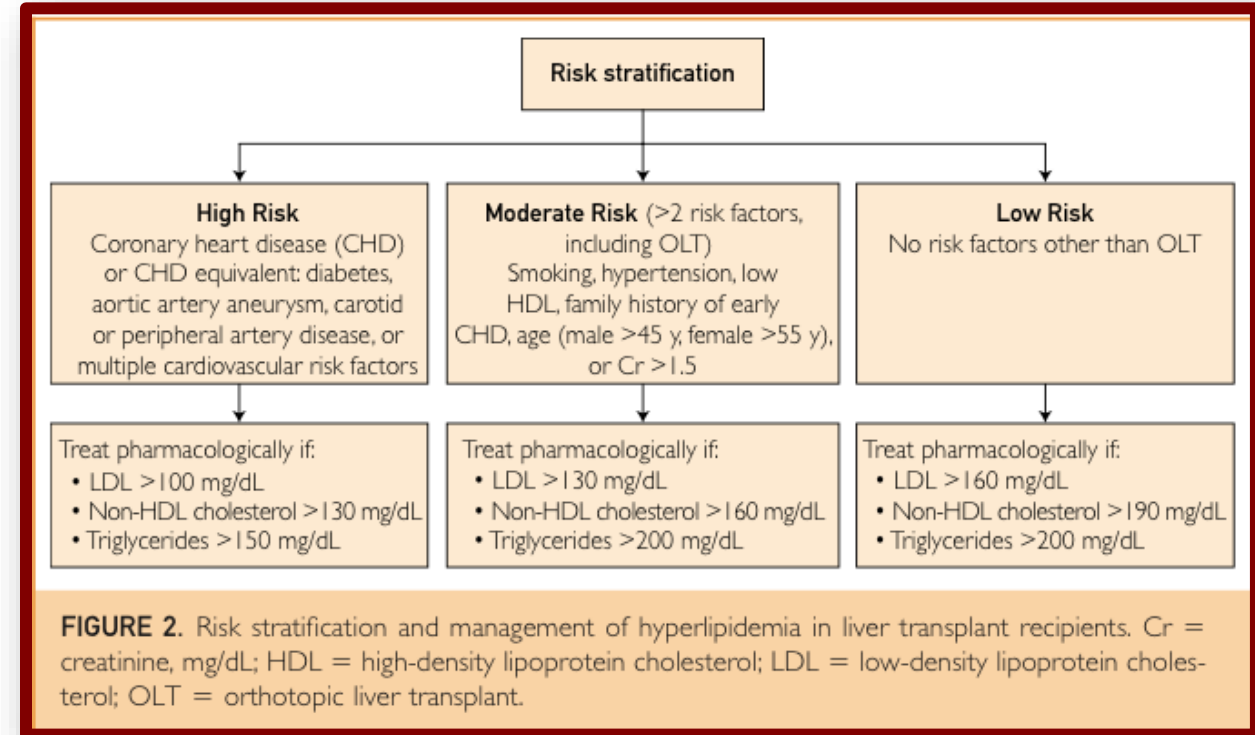
	Weight – mean (kg)	Δ weight – mean (kg)
6 months	91,8	-5,9
12 months	89,9	-8,9
Last FU	88,9	-8,9

Controlling Hyperlipemia After Liver Transplantation: Room for Improvement

Rate of transplant recipients receiving statins



Holdaas H, Potena L et al, Transplant Rev(2014)

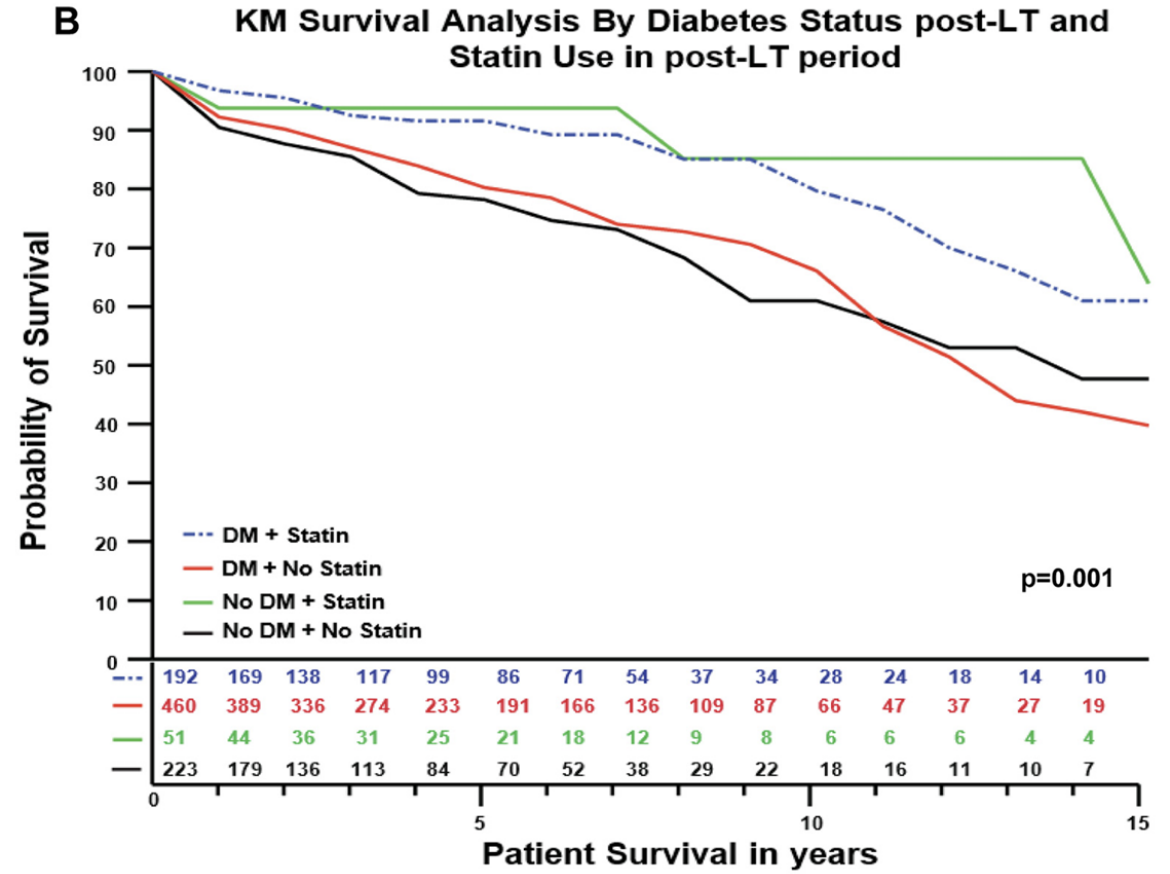
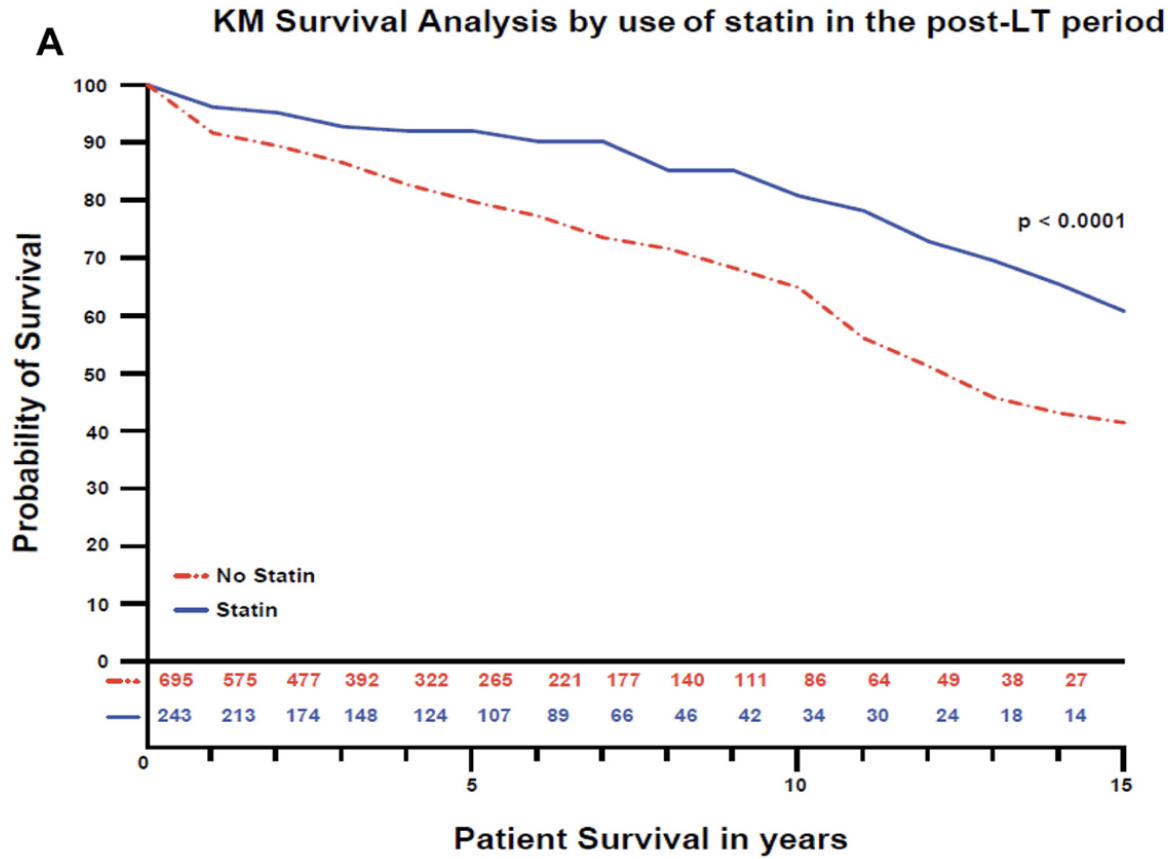


Factors Impacting Survival in Those Transplanted for NASH Cirrhosis: Data From the NailNASH Consortium



Mary E. Rinella,^{*,†,a} Sanjaya K. Satapathy,^{§,a} Danielle Brandman,^{||} Coleman Smith,^{||} Sal Elwir,[#] Jonathan Xia,[‡] Meg Gibson,[‡] Carlos Figueredo,^{**} Mounika Angirekula,^{‡‡} Jason M. Vanatta,^{§§} Raiya Sarwar,^{||||} Yu Jiang,^{§§} Dyanna Gregory,[‡] Tandy Agostini,^{||} JimIn Ko,^{||} Pradeep Podila,^{|||} Grace Gallo,[‡] Kymberly D. Watt,^{‡‡,b} and Mohammad S. Siddiqui^{##,b}

Clinical Gastroenterology and Hepatology 2023;21:445–455





Physical activity in liver transplant recipients: a large multicenter study

Stefano Gitto¹ · Lucia Golfieri² · Filippo Gabrielli³ · Margherita Falcini¹ · Francesco Sofi⁴ · Maria Rosa Tamè⁵ · Nicola De Maria⁶ · Luca Marzi⁷ · Andrea Mega⁷ · Giovanna Valente⁸ · Alberto Borghi⁹ · Paolo Forte¹⁰ · Matteo Cescon¹¹ · Fabrizio Di Benedetto¹² · Pietro Andreone³ · Marco Petranelli¹³ · Maria Cristina Morelli² · Paolo De Simone¹⁴ · Chloe Lau¹⁵ · Laura Stefani¹⁶ · Francesco Vizzutti¹ · Francesca Chiesi¹⁷ · Fabio Marra¹ · MEDITRA Research Group

511 subjects (71% males, mean age 63 years)

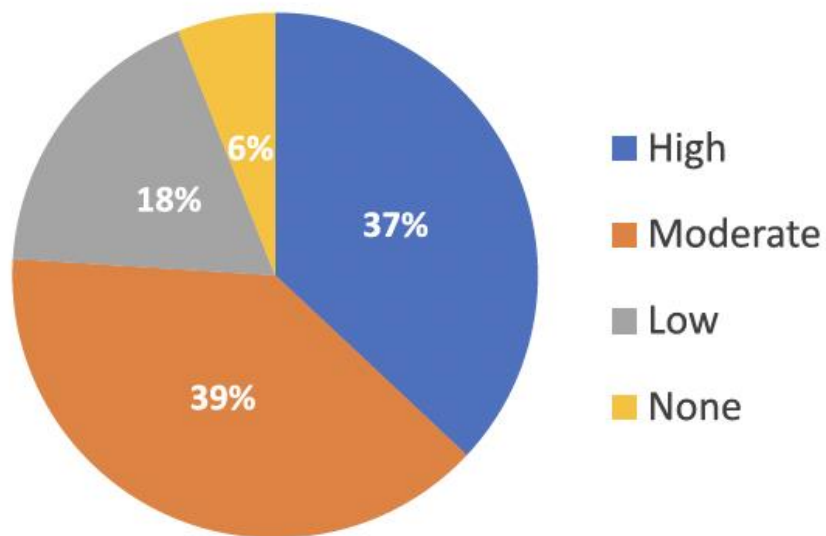


Fig. 1 Physical activity levels derived from the International Physical Activity Questionnaire

Factors associated with total inactivity.

Variable	β	SE β	Wald's χ^2	df	p	Odds ratio (e^β)	95% CI (e^β)
Time from LT	0.07	0.03	5.70	1	0.017	0.94	0.89–0.99
Sedentary activity	-0.94	0.37	6.28	1	0.012	0.99	0.19–0.81
Medi-Lite	0.20	0.10	3.89	1	0.049	1.22	1.01–1.48
PCS-12	0.21	0.02	32.69	1	<0.001	1.13	1.08–1.17

Overall model evaluation: Hosmer and Lemeshow: $\chi^2 = 6.53$, $df = 8$, $p = 0.59$. Nagelkerke $R^2 = 0.32$

LT, Liver Transplant; Medi-Lite, adherence to the Mediterranean diet score; PCS-12, Physical health score; Variable coding: 0 = inactive, 1 = active

Time from LT, sedentary lifestyle, low adherence to Mediterranean Diet and low level of QoL were independently associated with total inactivity

Trapianto... e adesso Sport



Physical Activity in Solid Organ Transplant Recipients: Organizational Aspects and Preliminary Results of the Italian Project

G.S. Roi^a, S. Stefoni^b, G. Mosconi^c, E. Brugin^d, P. Burra^e, A. Ermolao^f, M. Granito^g, P. Macini^h, S. Mastrosimoneⁱ, F. Nacchia^j, C. Pegoraro^k, P. Rigotti^l, G. Sella^m, S. Sgarziⁿ, M.R. Tamè^o, V. Totti^p, M. Trerotola^q, F. Tripi^r, and A. Nanni Costa^{s,*}

Kidney & Blood Pressure Research

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www.karger.com/kbr
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1423-0143/14/0393-0220\$39.50/0
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Original Paper

Physical Activity in Solid Organ Transplant Recipients: Preliminary Results of the Italian Project



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World J Transplant 2018 February 24; 8(1): 13-22

DOI: 10.5500/wjt.v8.i1.13

ISSN 2220-3230 (online)

ORIGINAL ARTICLE

Clinical Trials Study

Renal function and physical fitness after 12-mo supervised training in kidney transplant recipients

Giulio Sergio Roi, Giovanni Mosconi, Valentina Totti, Maria Laura Angelini, Erica Brugin, Patrizio Sarto, Laura Merlo, Sergio Sgarzi, Michele Stancari, Paola Todeschini, Gaetano La Manna, Andrea Ermolao, Ferdinando Tripi, Lucia Andreoli, Gianluigi Sella, Alberto Anedda, Laura Stefani, Giorgio Galanti, Rocco Di Michele, Franco Merni, Manuela Trerotola, Daniela Storani, Alessandro Nanni Costa



Physical Condition, Glycemia, Liver Function, and Quality of Life in Liver Transplant Recipients After a 12-Month Supervised Exercise Program

Valentina Totti^{a,b}, Mariaros Tamè^c, Patrizia Burra^d, Giovanni Mosconi^e, Giulio Sergio Roi^f, Gianluigi Sella^g, Andrea Ermolao^h, Alberto Ferrareseⁱ, Sergio Sgarzi^j, Gustavo Savino^k, Giuseppe Parodi^l, Giacomo Poggioli^l, Alessandro Ricchiuti^m, Rocco Di Michele^a, Manuela Trerotolaⁿ, and Alessandro Nanni Costa^{o,*}



Article

Longitudinal Analysis of Cardiovascular Risk Factors in Active and Sedentary Kidney Transplant Recipients

Valentina Totti^{1,*}, Bo Fernhall², Rocco Di Michele¹, Paola Todeschini³, Gaetano La Manna³, Maria Cappuccilli³, Maria Laura Angelini⁴, Marco De Fabritiis⁴, Franco Merni¹, Enrico Benedetti⁵, Giulio Sergio Roi⁶, Alessandro Nanni Costa⁷ and Giovanni Mosconi⁴

Sicurezza. Nessun drop-out legato ad attività fisica.
Nessun episodio di rigetto

Miglioramento capacità cardiopolmonare
Aumento massima potenza aerobica

Incremento forza arti inferiori (+4 - 25%); arti superiori (1 - 2%)

Stato Nutrizionale. Riduzione BMI e massa grassa

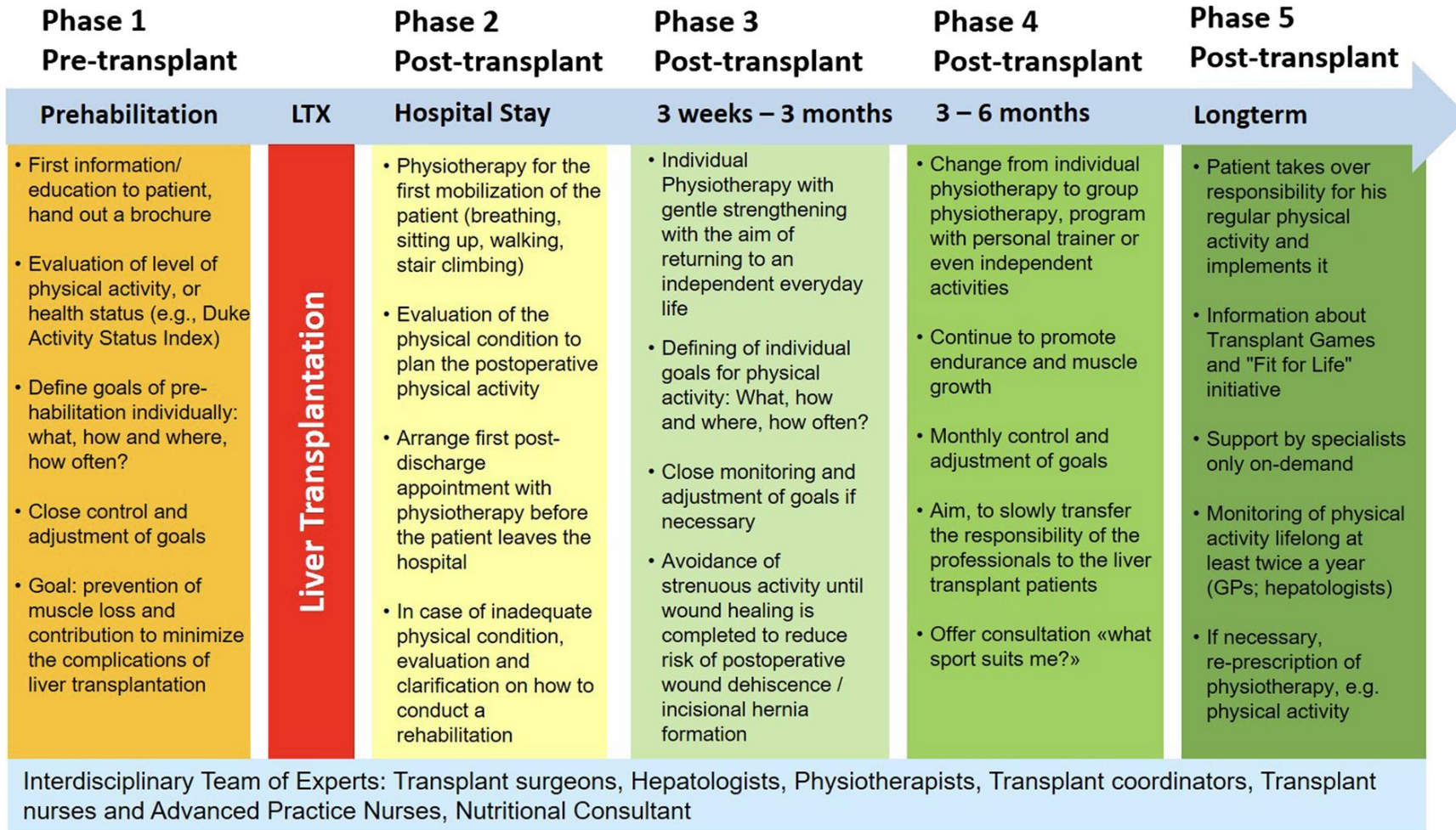
HRQoL. Miglioramento percezione qualità della vita (+3% / 16%)

Funzionalità Renale: stabilità indici funzionali



Physical Activity in Liver Transplantation: A Patient's and Physicians' Experience

Lara Beekman · Annalisa Berzigotti · Vanessa Banz



→ Implement supporting tools: brochures, Apps and wearables with pedometers, videos

→ Take into account patient barriers and use patient motivation – suiting patients individually

Conclusions:

- The recipient's lifestyle significantly affects the long-term outcome of a liver transplant.
- Managing immunosuppressive therapy should be accompanied by careful control of metabolic syndrome components.
- Lifestyle intervention should begin before the transplant and continue without interruption afterward.