

Indication et contre-indication à la greffe rénale: y a-t-il un âge ou un poids au-delà duquel la greffe de rein est contre-indiquée?

Dr Catherine Bonvoisin
Service de Néphrologie
CHU LIEGE

Mortalité annuelle comparée: population générale/Dialyse/Transplantation

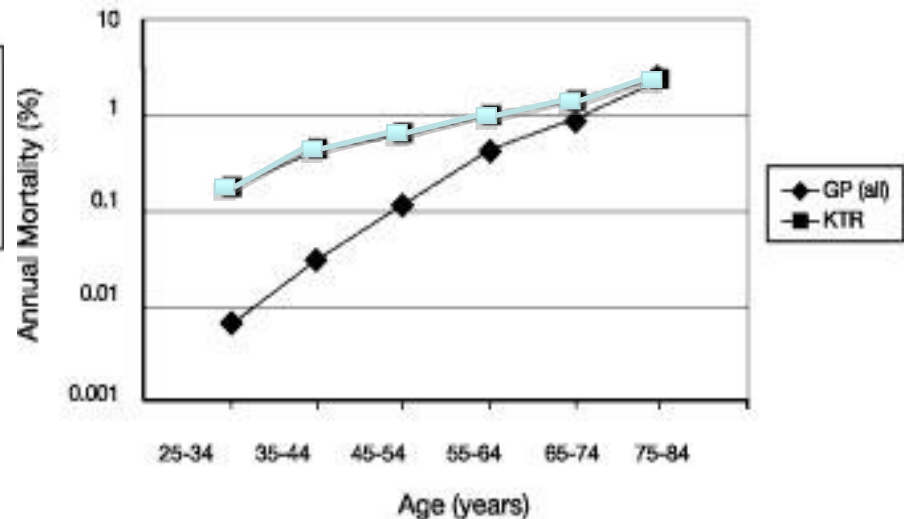
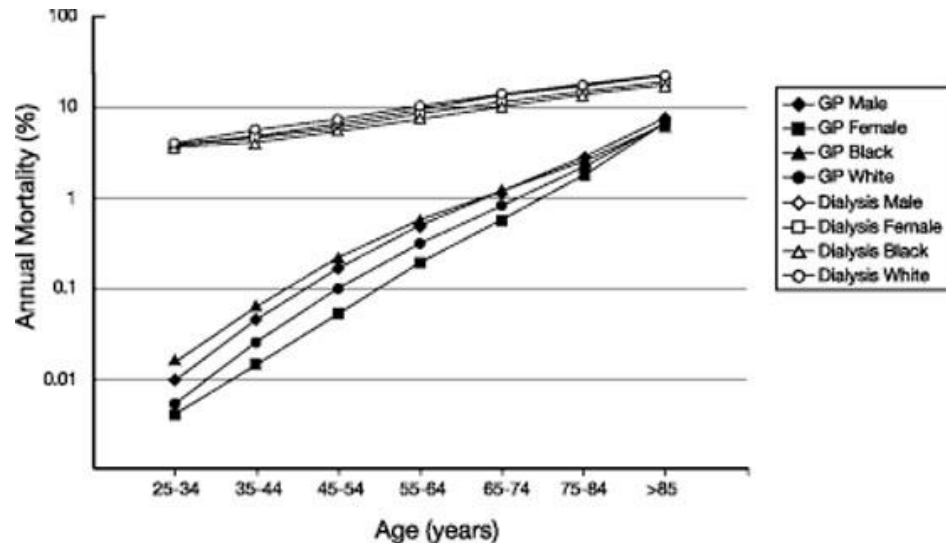


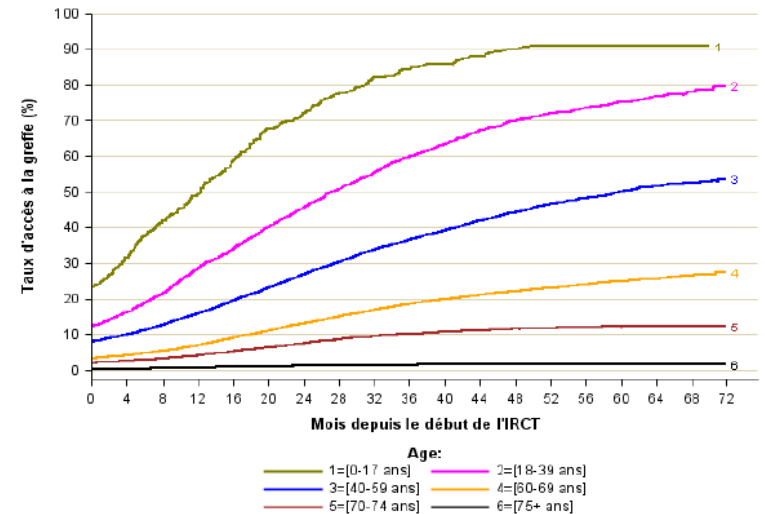
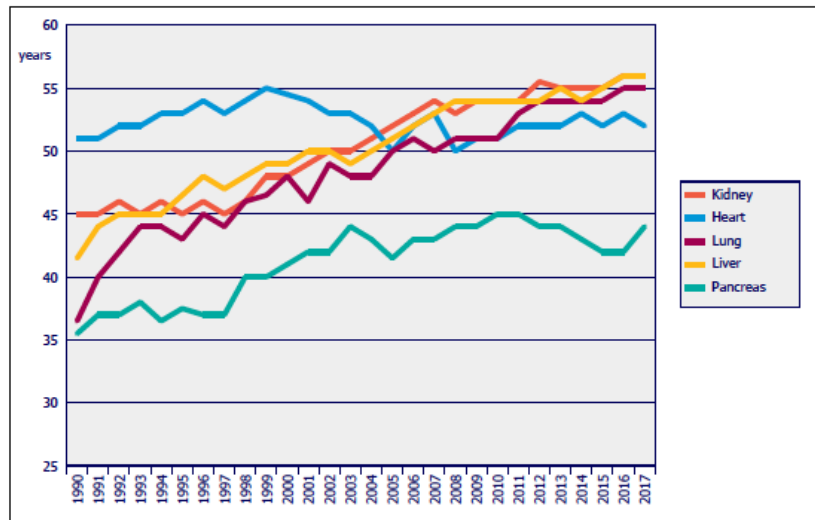
TABLE 3. OUTCOME AMONG RECIPIENTS OF FIRST CADAVERIC TRANSPLANTS, ACCORDING TO CHARACTERISTICS AT THE TIME OF INITIAL PLACEMENT ON THE WAITING LIST, 1991-1997.*

GROUP	RELATIVE RISK 18 Mo AFTER TRANSPLANTATION (95% CI)†	P VALUE	TIME AT WHICH RISK OF DEATH EQUALS THAT IN REFERENCE GROUP	TIME AT WHICH LIKELIHOOD OF SURVIVAL EQUALS THAT IN REFERENCE GROUP	PROJECTED YEARS OF LIFE (IN REFERENCE GROUP) WITHOUT TRANSPLANTATION‡	PROJECTED YEARS OF LIFE WITH TRANSPLANTATION‡
			days after transplantation			
All recipients of first cadaveric transplants	0.32 (0.30-0.35)	<0.001	106	244	10	20
Age						
0-19 yr	0.33 (0.12-0.87)	0.03	3	5	26	39
20-39 yr	0.24 (0.20-0.29)	<0.001	11	57	14	31
40-59 yr	0.33 (0.29-0.37)	<0.001	95	251	11	22
60-74 yr	0.39 (0.33-0.47)	<0.001	148	369	6	10

Foley et al, Am J Kidney Dis 1998; 32: S112-S119

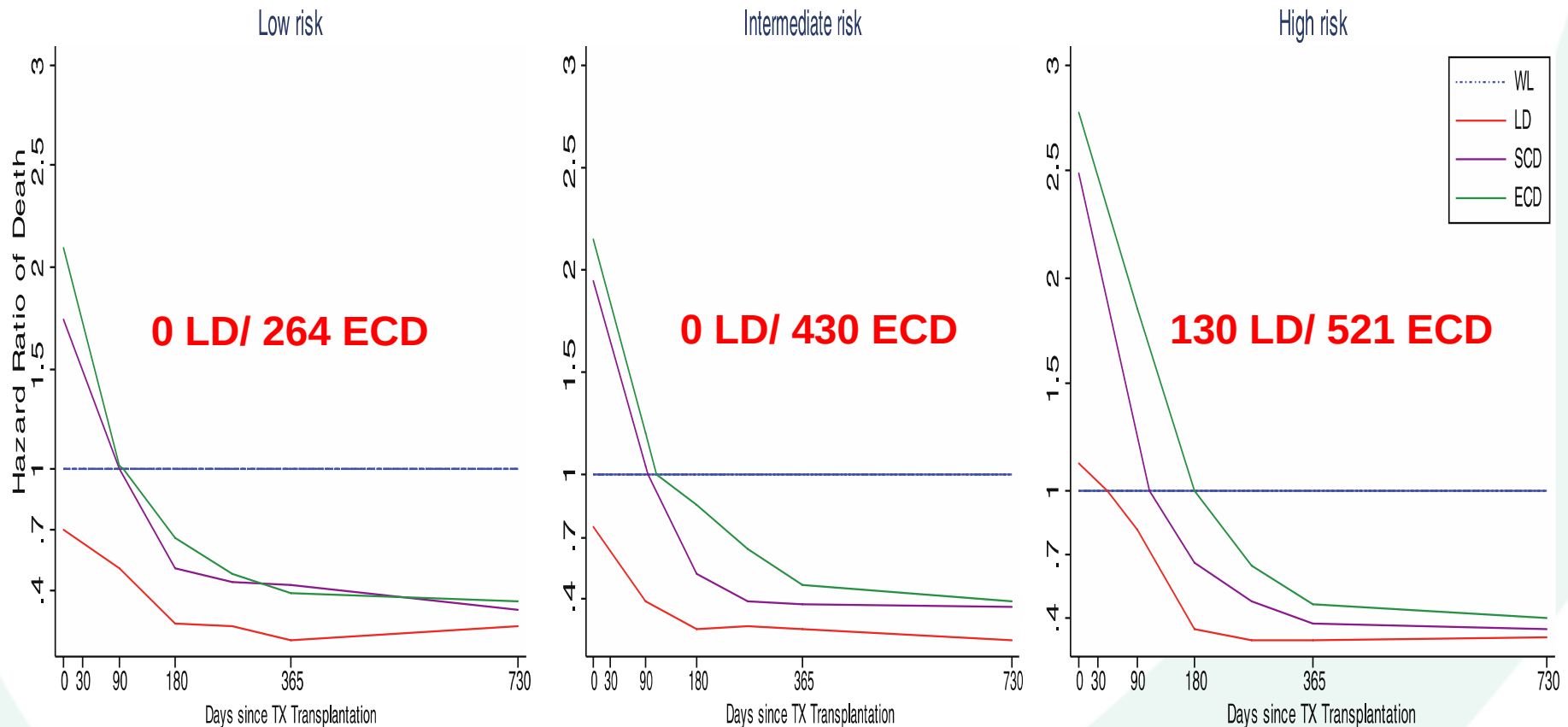
Wolfe RA et al, N Engl J Med 1999; 341: 1725-1730

Figure 1.6 Median age of transplant recipients (deceased donor transplants)



Age limite pour bénéficier d'une greffe rénale?

Risque relatif de décès chez receveur âgé de plus de 65 ans



Le vieillissement est hétérogène

MINIREVIEWS

Older candidates for kidney transplantation: Who to refer and what to expect?

Beatrice P Concepcion, Rachel C Forbes, Heidi M Schaefer



Succès: 20%



Pathologique: 50%



Fragilité: 30%

Criteria for and Appropriateness of Renal Transplantation in Elderly Patients With End-Stage Renal Disease: A Literature Review and Position Statement on Behalf of the European Renal Association-European Dialysis and Transplant Association Descartes Working Group and European Renal Best Practice

Liviu Segall, MD,¹ Ionuț Nistor, MD, PhD,^{2,3} Julio Pascual, MD, PhD,^{4,5,6} Istvan Mucsi, MD, PhD,⁷ Lluís Guirado, MD, PhD,⁸ Robert Higgins, MD, PhD,⁹ Steven Van Laecke, MD, PhD,¹⁰ Rainer Oberbauer, MD, PhD,^{6,11} Wim Van Biesen, MD, PhD,^{3,10} Daniel Abramowicz, MD, PhD,^{6,12} Cristina Gavrilovici, MD, PhD,¹³ Ken Farrington, MD, PhD,¹⁴ and Adrian Covic, MD, PhD²

CONCLUSIONS AND RECOMMENDATIONS

10. Several comorbidity scores can predict post-RT mortality and might be used to guide decision-making on eligibility. However, such scores should be validated in additional studies.
11. The assessment of frailty might also play a role in the selection of elderly patients for RT. Various scales have been proposed in this regard. However, there is still very limited information about the impact of frailty on mortality in elderly RT recipients, and there are no guidelines indicating at which level of frailty (if any) a patient should be excluded from a waiting list.
12. Psychosocial issues, including cognitive deterioration, depression, social isolation, and financial problems, are common in elderly patients and may have a significant impact on compliance to prescriptions and, ultimately, on patient and graft outcomes. Therefore, these issues should be assessed prior to RT waitlisting, as well as thereafter. Specific questionnaires can be used to identify patients who are more likely to be nonadherent.

Spécificité des receveurs âgés

- Multiplicité des comorbidités:
 - Augmentation du nombre de comorbidités avec âge
 - Augmentation de la mortalité après greffe avec le nombre de comorbidités

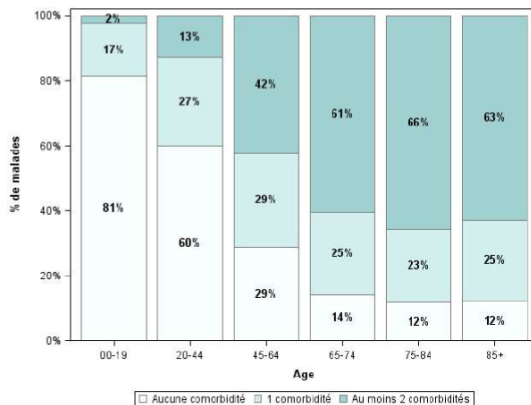


TABLE 1. Recipient 90- and 365-day mortality rates

	Age 18–59 years			Age ≥60 years		
	N (%)	90-day mortality	365-day mortality	N (%)	90-day mortality	365-day mortality
Overall	30,262	2.0%	4.4%	8,895	4.6%	10.5%
No comorbidity	21,506 (71.1%)	1.6%	3.5%	4,608 (51.8%)	3.9%	9.2%
With comorbidity						
Angina/coronary artery disease	2,483 (8.2%)	3.8%	8.1%	1,699 (19.1%)	6.0%	13.4%
Peripheral vascular disease	926 (3.1%)	3.7%	7.6%	480 (5.3%)	7.3%	14.2%
Cerebrovascular disease	616 (2.0%)	2.4%	7.8%	288 (3.2%)	4.5%	12.5%
History of malignancy	557 (1.8%)	2.9%	6.6%	483 (5.4%)	5.0%	10.6%
Chronic obstructive pulmonary disease	235 (0.7%)	3.0%	6.0%	117 (1.3%)	13.9%	21.4%
Diabetes	6,583 (21.8%)	3.0%	7.1%	2,875 (32.3%)	4.9%	11.4%

$P < 0.001$ for all age 18–59 vs. age ≥60 at both 90 days and 365 days.

Figure 4-1. Nombre de comorbidités selon l'âge chez les patients présents en dialyse au 31/12/2016
Number of comorbidities for patients on dialysis on December 31, 2016, by age

« Concept de Frailty ou Fragilité »

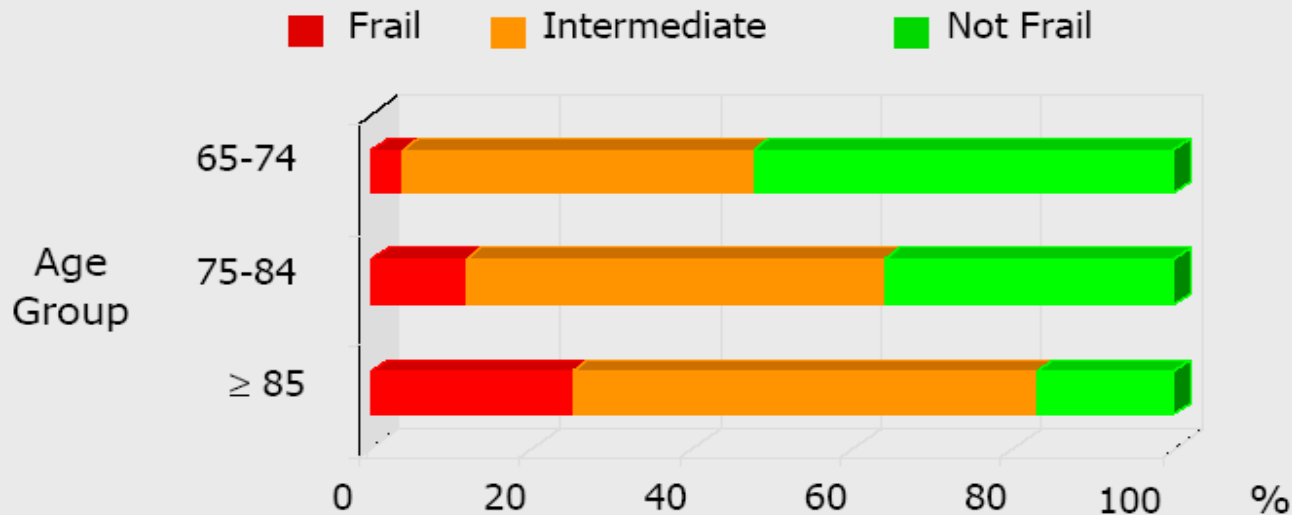
Etat instable, de forte vulnérabilité aux événements nécessitant une adaptabilité (mécanismes de compensation) aux stress physiques, psychiques, sociaux, environnementaux

Résultant d'une réduction des réserves adaptatives de multiples systèmes biologiques et physiologiques sous l'action conjuguée de l'âge, des maladies, du contexte de vie

Entraînant un risque élevé de dépendance, d'hospitalisations, d'entrée en institution, de mortalité

SCORE de FRIED

- F
- F
- /
- \
- F
- C



e)
ine)
l'une

Score :

3 ou plus : fragile

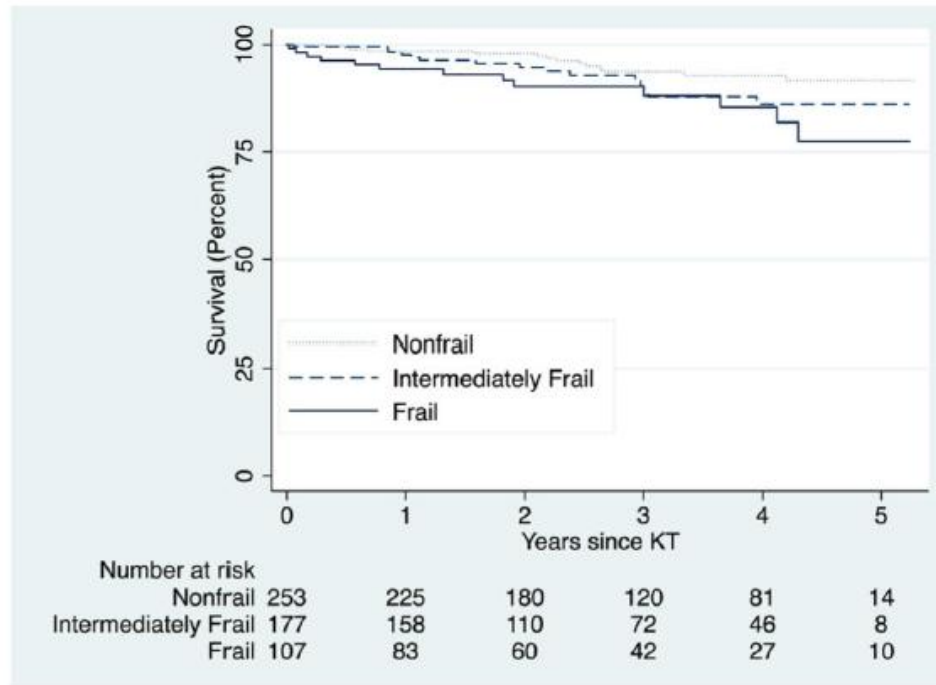
1 ou 2 : pré-fragile

0 : robuste

Frailty, Dialysis Initiation and Mortality in End-Stage Renal Disease

- 73% de sujets fragiles (63% pour les < 40 ans!)
Population générale (2200 Pts > 65 ans)
8% Fragile (41% pré-fragile) en 2011
- Fragilité = facteur indépendant de mortalité
suivi médian 2,9 ans
décès: 33% **HR: 1,57 [IC 95%: 1,25-1,97]**
- Hospitalisation
suivi médian 1,2 ans
taux hospitalisation: 73% **HR: 1,26 [IC 95% 1,09-1,45]**

Frailty and Mortality in Kidney Transplant Recipients



Hospitalisations x 2
 Perte d'autonomie x 3
 Fractures de hanche x 1,57

Syndromes gériatriques :
 Chutes/syndrome post-chute
 Syndrome confusionnel
 Syndrome d'immobilisation
 Syndrome de glissement

Figure 2. Survival, by frailty status at the time of transplantation (n = 537)

Log-rank test p-value = 0.0396. Nonfrail was defined as a score of 0 or 1, intermediately frail was defined as a score of 2 and frail was defined as a score of 3 or higher.

Obèses parmi les 15 ans ou plus

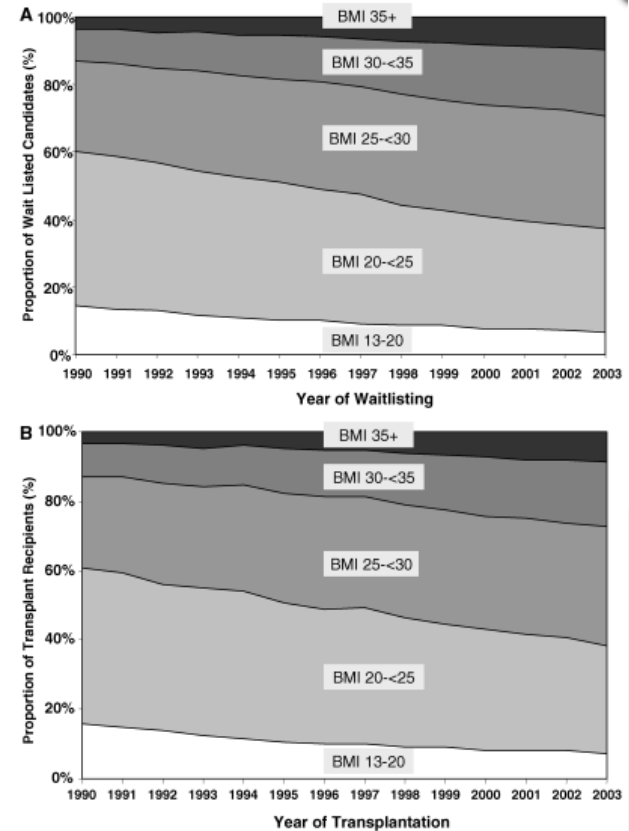
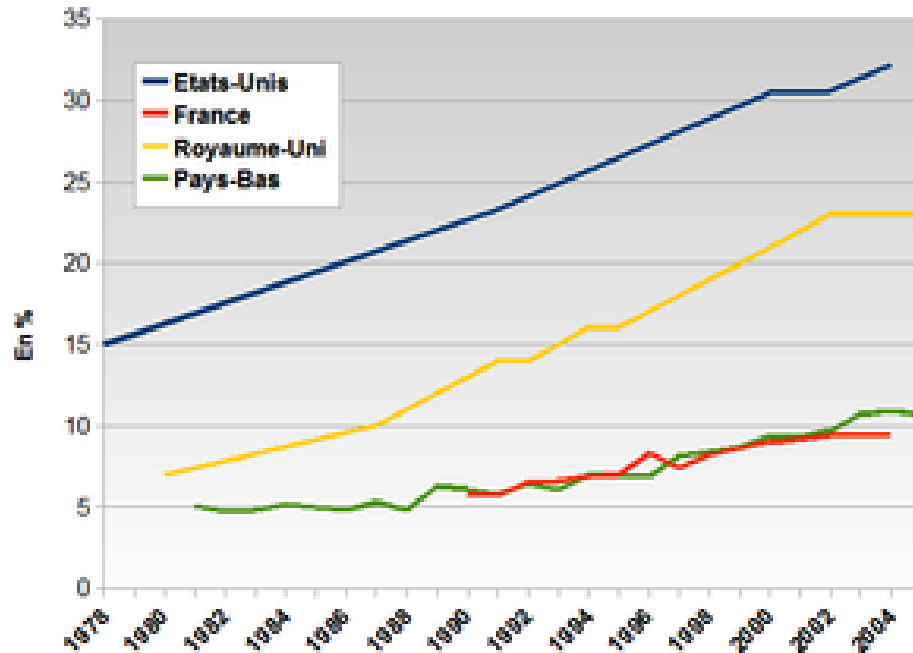


Figure 1. (A) Transplant candidate body mass indices by year of listing. (B) Transplant recipient body mass indices by year of transplant.

L'obésité, pourquoi un frein à la greffe rénale?

Pour rappel,

- Classification de l'obésité selon le BMI par l'organisation mondiale de la santé en 1997:

- $< 18,5 \text{ Kg/m}^2$ = Sous poids
- $18,5 - 24,9 \text{ Kg/m}^2$ = Normal
- $25 - 29,9 \text{ Kg/m}^2$ = Excès pondéral
- **$30 - 34,9 \text{ Kg/m}^2$ = Obésité**
- **$35 - 39,9 \text{ Kg/m}^2$ = Obésité sévère ou morbide**
- **$> 40 \text{ Kg/m}^2$ = Obésité très sévère**

Survie du patient obèse en EER versus en greffe

**Pourquoi existe-t-il un frein à
greffer un patient obèse?**

Months Post Transplant or Post 90 Days on Dialysis

Fig. 1. Actuarial patient survival with transplant (this series) compared to patient survivals on dialysis with BMI > 30.

Survie du receveur obèse à 1, 2 et 3 ans

- Si greffe avant 2003: RR x 1,5 à 2
- Depuis 2003: RR = 0,99 à 1,24

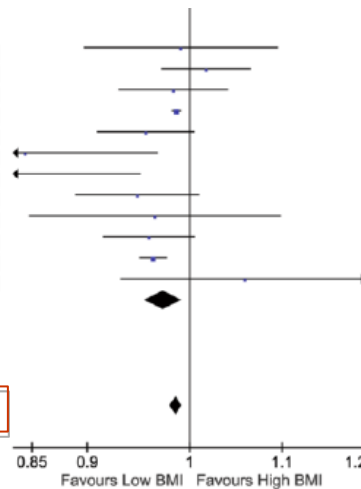
1.15.3 Patient Survival Year 3

Bardonnaud	20	21	172	179	0.4%	0.99 [0.90, 1.10]
Begov	339	358	175	188	1.6%	1.02 [0.97, 1.07]
Bennett	177	198	399	439	1.1%	0.98 [0.93, 1.04]
Cannon	20364	22315	48718	52668	13.1%	0.99 [0.98, 0.99]
Cockbain	177	197	687	731	1.4%	0.96 [0.91, 1.01]
Gill	65	85	77	85	0.2%	0.84 [0.74, 0.97]
Haime	28	47	188	235	0.1%	0.74 [0.58, 0.95]
Karabicak	140	160	445	482	0.9%	0.95 [0.89, 1.01]
Marks	21	23	212	224	0.2%	0.96 [0.85, 1.10]
Meier-Kriesche	149	160	233	240	1.5%	0.96 [0.91, 1.01]
Pieloch	4783	6055	19743	24077	8.1%	0.96 [0.95, 0.98]
Powers	19	20	61	68	0.2%	1.06 [0.93, 1.20]
Subtotal (95% CI)	29639	29639	79616	79616	28.6%	0.97 [0.95, 0.99]

Total events 26282 71110
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 28.49$, $df = 11$ ($P = 0.003$); $I^2 = 61\%$
Test for overall effect: $Z = 2.86$ ($P = 0.004$)

Total (95% CI) 66505 188383 100.0%
Total events 60797 173076
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 71.05$, $df = 36$ ($P = 0.0004$); $I^2 = 49\%$
Test for overall effect: $Z = 4.47$ ($P < 0.00001$)
Test for subgroup differences: $\chi^2 = 4.87$, $df = 2$ ($P = 0.09$), $I^2 = 58.9\%$

0.99 [0.98, 0.99]



2013
2007
2011
Grosso 2012
Hoogveen 2011

Weight

34.4%
30.6%
3.5%
7.1%
24.5%

Hazard Ratio [95% CI]

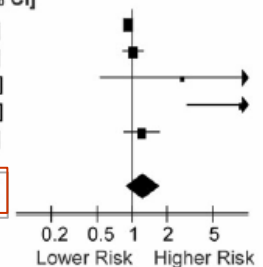
0.92 [0.86, 0.99]
1.02 [0.83, 1.25]
2.69 [0.53, 13.65]
8.74 [2.99, 25.55]
1.21 [0.85, 1.72]

Total (95% CI) 100.0%

Heterogeneity: $I^2 = 81\%$

Test for overall effect: $Z = 1.31$ ($P = 0.19$)

1.24 [0.90, 1.70]



Lafranca JA et al, *BMC Medecine* 2015;13:111

Hill CJ et al, *Nephrol Dial Transplant* 2015;30:1403-1411

Gore JL et al, *Am J Transplant* 2006;6:357-363

Survie du patient obèse greffé versus en EER en fonction du type de donneur

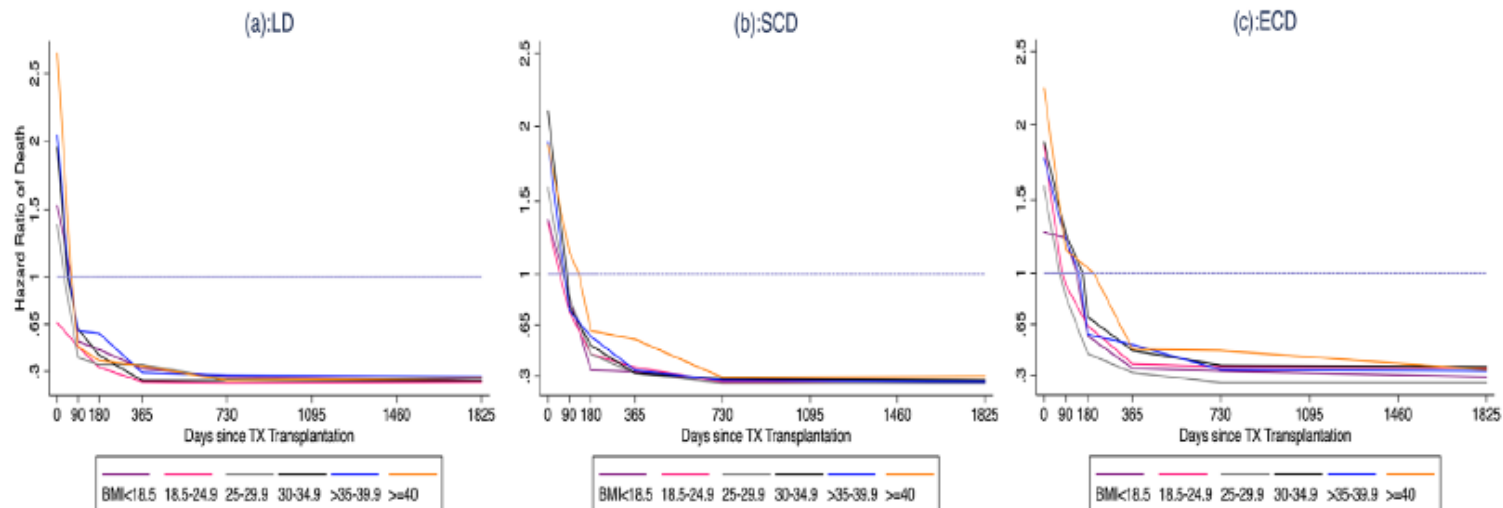


Figure 1: The figure shows the survival curves for deceased donor (SCD); b who had been on dialysis with a relative risk of 1 was higher than that among patients who remained on dialysis in each BMI group for all donor sources.

Table 5: Time (days) to equal risk of death and equal survival* in transplant recipients compared to wait-listed patients with the same body mass index

	<18.5 (n = 13 714)	18.5–24.9 (n = 67 260)	25–29.9 (n = 64 655)	30–34.9 (n = 37 453)	35–39.9 (n = 16 070)	≥40 (n = 9 346)
Death rate on waiting list per 100 patient years	5	5	6	6	6	6
Days to equal risk of death						
SCD	68	50	70	80	85	145
ECD	135	95	90	160	150	200
LD	55	Immediate	33	57	60	65
Days to equal survival						
SCD	118	100	137	210	179	245
ECD	216	226	210	331	257	387
LD	116	Immediate	75	121	135	157

*Calculated from separate multivariate nonproportional hazards regression models.

a), standard criteria for the same BMI group denoted in blue after transplantation. The point of intersection between the curves is at a relative risk = 1.0 among patients versus wait-listed patients at transplantation from

Survie greffon rénal chez le receveur obèse à 1, 2 et 3 ans

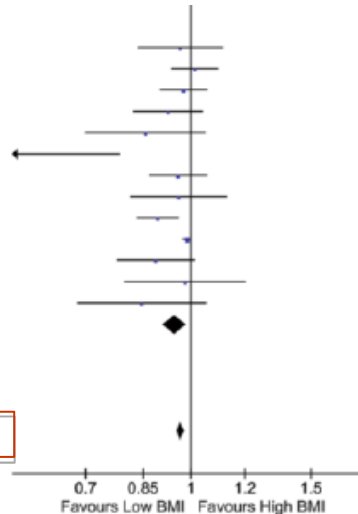
1.16.3 Graft Survival Year 3

Bardonnaud	19	21	168	179	0.6%	0.96 [0.83, 1.11]
Begov	301	358	156	188	1.9%	1.01 [0.94, 1.10]
Bennett	160	198	364	439	1.8%	0.97 [0.90, 1.06]
Chow	33	37	109	113	0.9%	0.92 [0.82, 1.04]
Gill	54	85	63	85	0.3%	0.86 [0.70, 1.05]
Halme	16	47	153	235	0.1%	0.52 [0.35, 0.79]
Karabicak	122	160	384	482	1.3%	0.96 [0.87, 1.06]
Marks	20	23	203	224	0.5%	0.96 [0.81, 1.13]
Meier-Kriesche	140	165	228	240	2.3%	0.89 [0.83, 0.96]
Pieloch	4662	6055	18780	24077	10.8%	0.99 [0.97, 1.00]
Pirsch	47	59	471	525	0.7%	0.89 [0.78, 1.01]
Powers	17	20	59	68	0.3%	0.98 [0.80, 1.20]
Yamamoto	22	28	26	28	0.3%	0.85 [0.68, 1.05]
Subtotal (95% CI)	7256		26883	21.8%		0.95 [0.91, 0.98]

Total events 5613 21164
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 24.01$, $df = 12$ ($P = 0.02$); $I^2 = 50\%$
Test for overall effect: $Z = 2.77$ ($P = 0.006$)

Total (95% CI) 22549 85859 100.0%
Total events 18582 72987
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 68.45$, $df = 47$ ($P = 0.02$); $I^2 = 31\%$
Test for overall effect: $Z = 5.87$ ($P < 0.00001$)
Test for subgroup differences: $\chi^2 = 2.79$, $df = 2$ ($P = 0.25$), $I^2 = 28.3\%$

0.97 [0.95, 0.98]



B

Study	Weight	Hazard Ratio [95% CI]
Cannon 2013	90.4%	1.05 [1.00, 1.11]
Chang 2007	6.1%	1.16 [0.95, 1.42]
Ditunno 2011	0.2%	1.42 [0.45, 4.48]
Grosso 2012	0.1%	0.98 [0.13, 7.39]
Hoogveen 2011	3.3%	1.27 [0.97, 1.66]

Total (95% CI) 100.0%
Heterogeneity: $I^2 = 0\%$
Test for overall effect: $Z = 2.46$ ($P = 0.01$)

1.06 [1.01, 1.12]

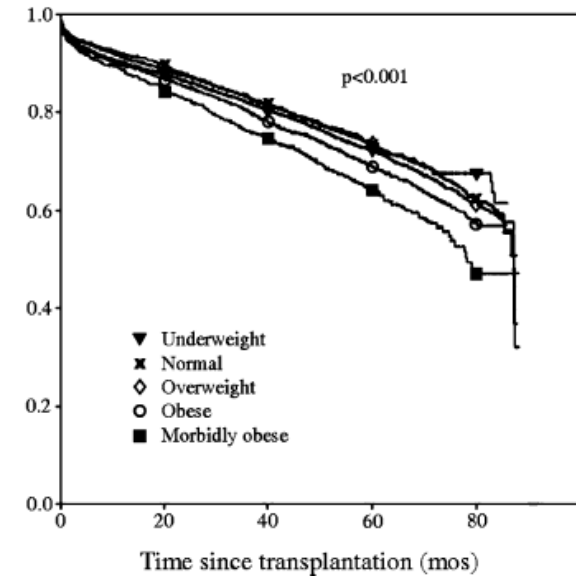
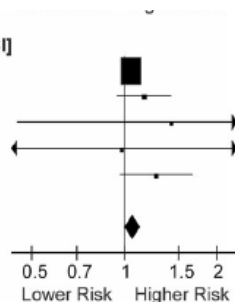


Figure 1: Graft survival following renal transplantation stratified by recipient BMI at the time of transplantation.

Lafranca JA et al, *BMC Medecine* 2015;13:111

Hill CJ et al, *Nephrol Dial Transplant* 2015;30:1403-1411

Gore JL et al, *Am J Transplant* 2006;6:357-363

Incidence de la DGF chez le receveur obèse

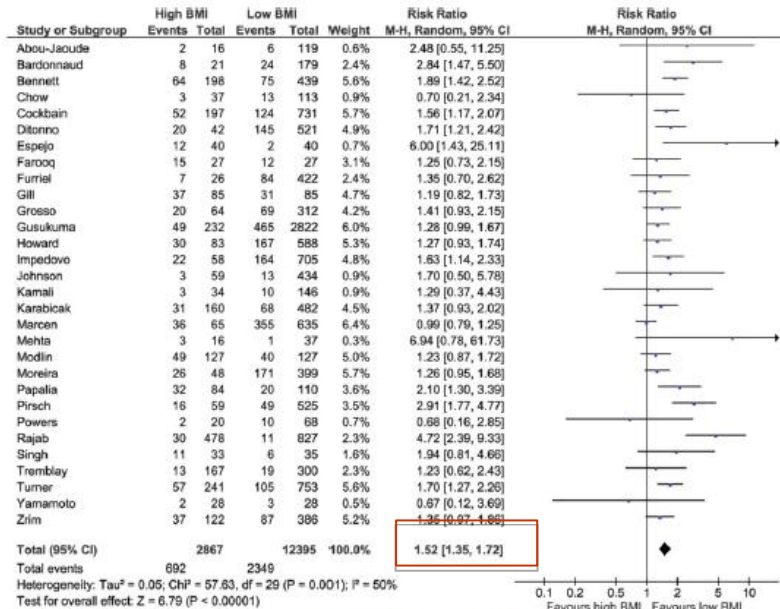
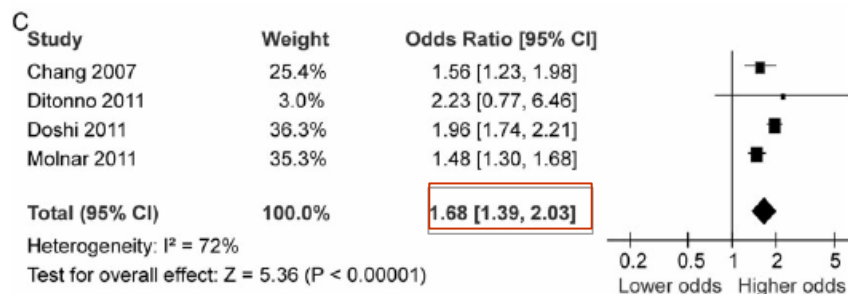


Figure 6 Forest plot of comparison: high versus low BMI recipients; outcome: delayed graft function.



⑩ ➡ DGF: RR x 1.5 à 1.7

- Augmentation du temps opératoire
- Augmentation de l'ischémie « tiède »

- x 1.3 à 1.9 si BMI 30-35
- x 1.7 à 4.5 si BMI > 35

Lafranca JA et al, *BMC Medecine* 2015;13:111

Hill CJ et al, *Nephrol Dial Transplant* 2015;30:1403-1411

Gore JL et al, *Am J Transplant* 2006;6:357-363

Incidence du rejet aigu chez le receveur obèse

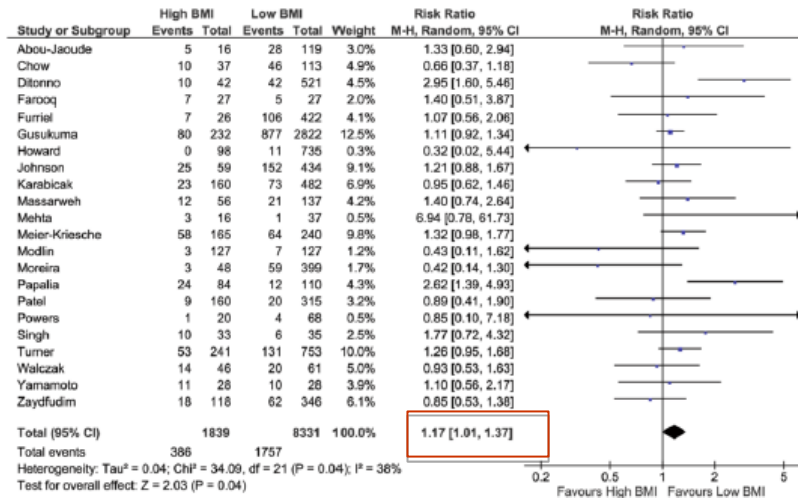
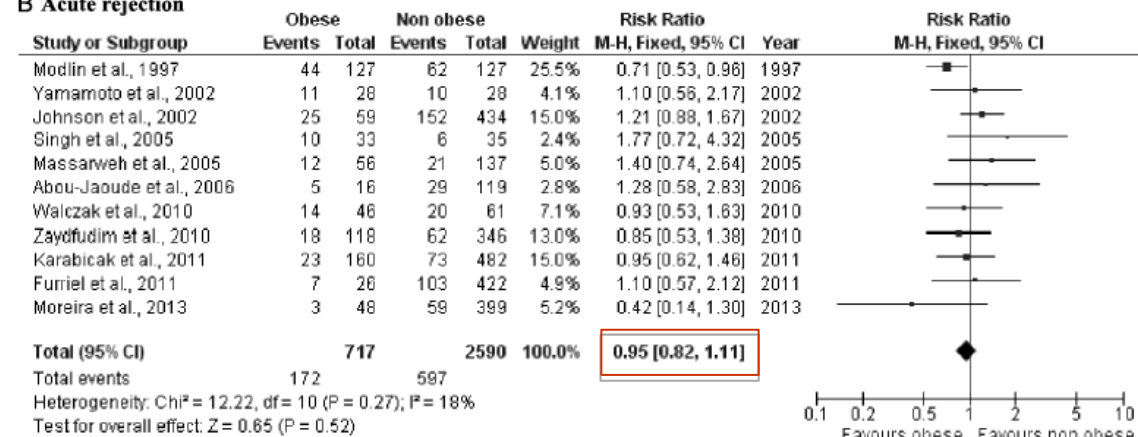


Figure 7 Forest plot of comparison: high versus low BMI recipients; outcome: acute rejection.

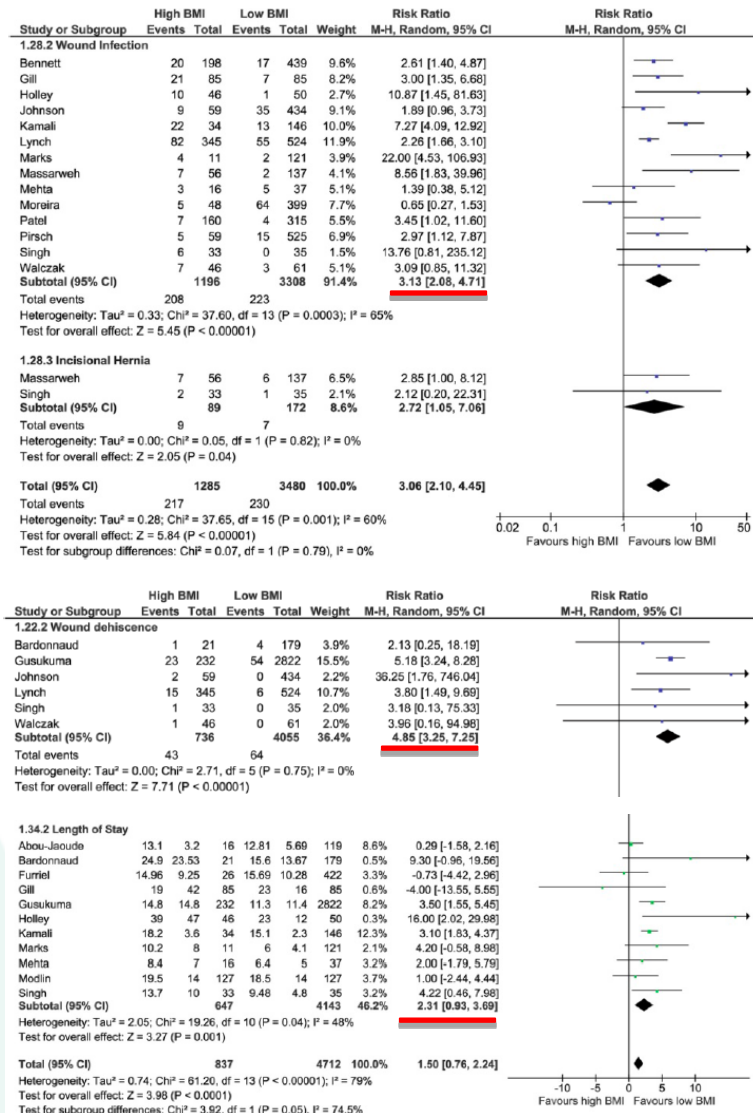
B Acute rejection



Lafranca JA et al, *BMC Medecine* 2015;13:111

Nicoletto BB et al, *Transplantation* 2014;98(2):167-176

Risques chirurgicaux chez le receveur obèse



- Retard de cicatrisation
- Infection pariétale (RR x 3 à 4)
- Eventration (RR x 4.8)
- Augmentation de la durée d'hospitalisation (+ 2.5 j)
- Lymphocèle?
- Hématome?
- Thrombose?

Autres risques médicaux

- Diabète de novo
 - Augmentation de la circonférence abdominale associée à un sur risque de NODAT (x 2 chez l'homme, x 5 chez la femme)
- Prise de poids
- Aggravation du syndrome métabolique
 - Hypertriglycémie
- FA en post-opératoire
- Protéinurie
 - Mécanisme d'hyper filtration
 - Risque de Protéinurie $> 0,5$ g/j est x 2 pour un BMI > 25 kg/m²
 - Risque majoré en cas de mismatch de taille

Challenge

