Epidemiology of infections requiring hospitalisation during long term follow-up in kidney-transplant patients.

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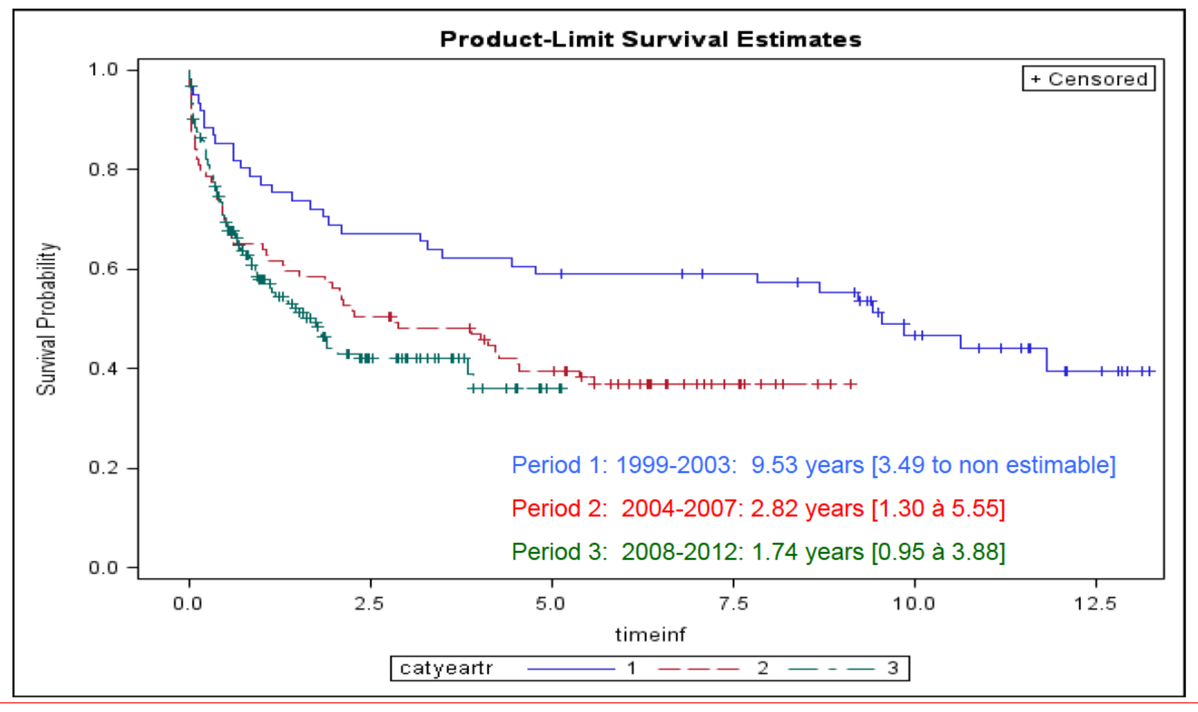
Background: Major progress has been made in protocols of immunosuppressive drug therapies to prevent acute kidney rejection but the occurrence of infections has been poorly monitored. Given that infectious complications are a major source of morbidity and mortality in transplant recipients, we sought to estimate the incidence of infections requiring hospitalisation (IRH) following renal transplantation over time, and risk factors of IRH.

Methods: We performed a retrospective cohort study of 314 consecutive renal transplant recipients from 1999 to 2012. We stratified the cohort in three periods according to the date of renal transplantation (P1:1999-2003: n=61; P2:2004-2007: n=89; P3:2008-2012: n=164). Data regarding the IRH, including bacterial, viral, parasites and fungal infections, were collected. We estimated the incidence rate of IRH (per 100 patients per year), the median time to the first IRH in the three time periods (P1 being the reference period) and the risk factors for the first and subsequent IRH during the study period using survival analysis (Kaplan-Meier curves and Cox proportional hazards models).

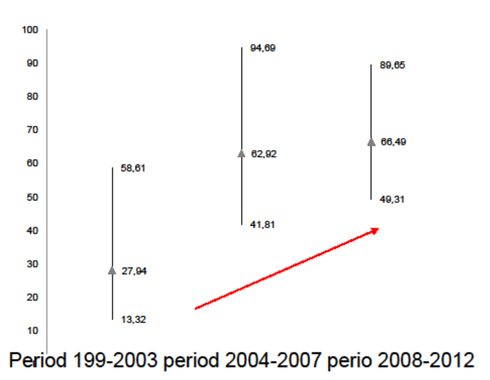
Results:

The median time to the occurrence of the first IRH was shorter for most recent transplant recipients: P1 : 9.53 years (IC-95% : 3.40 to non estimable) ; P2 : 2.83 years (1.30-4.55) ; P3 : 1,74 years (0.95-3.88) (p<0.05).



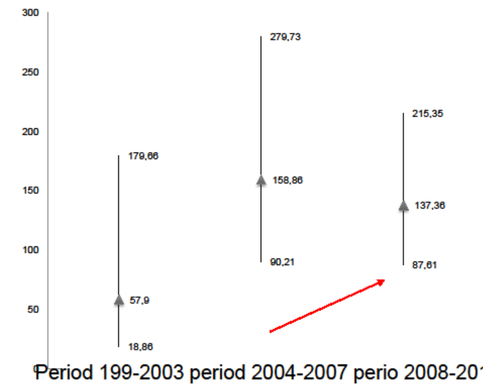
Incidence rate of IRH adjusted for sex and age (3.38; 9.1; 14.03), opportunist infection (0.90; 5.04; 8.48), late infection (8.3; 22.16; 36.05) and death rate increased over time (p<0.001 for all).

Number of events	Period 1999-2003 n=63	Period 2004-2007 n=143	Period 2008-2012 n=175	P value
Infectious events	9.49 (7.41-12.15)	27.05 (22.99-31.83)	44.20 (38.06-51.32)	p<0.0001 p<0.0001
Infectious events adjusted to age and sex	3.38 (2.03-5.64)	9.10 (5.51-15.0)	14.03 (8.27-23.81)	p<0.0001 p<0.0001
Opportunistic infection	0.90 (0.41-2.01)	5.04(3.45-7.34)	8.48 (6.03-11.93)	p<0.0001 p<0.0001
Opportunistic pathology	2.41 (1.48-3.93)	9.51 (7.23-12.52)	16.96 (13.32-21.59)	p<0.0001 p<0.0001
Acute rejection episode	1.69 (0.90-3.13)	5.62 (3.77-8.38)	6.83 (4.58-10.12)	p<0.0001 p<0.0001
Death	0.45 (0.14-1.40)	2.42 (1.40-4.18)	3.34 (1.94-5.75)	0.0014 p<0.0001



Period 199-2003 period 2004-2007 perio 2008-2012

Incidence of IRH during the first Month post transplantation



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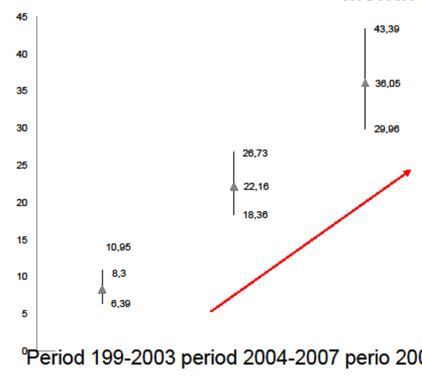
Incidence of IRH between the 2 nd ant the 6th Month post transplantation



Period 199-2003 period 2004-2007 perio 2008-2012

Incidence of IRH after the 6th Month post transplantation

In a multivariate Cox regression analysis, the potential risk factors for the first IRH were age, time under dialysis before transplant, induction by antithymocyte globulin induction, corticoid use, and a transplant after 2004.

variables	Hazard Ratio	95% IC	P value
Sexe	0.58	[0.42-0.80]	0.001
Recipient age	1.02	[1.01-1.04]	0.005
HIV	0.90	[0.34-2.49]	0.85
History of diabetes	1.19	[0.75-1.89]	0.45
Cardiovascular history	0.89	[0.62-1.26]	0.49
Dialysis time	1.07	[1.02-1.12]	0.003
PRA	0.63	[0.37-1.09]	0.12
Thymoglobulin	1.68	[1.02-2.78]	0.04
Tacrolimus	0.98	[0.64-1.50]	0.91
Mycophenolate mophetil	2.52	[0.77-8.29]	0.13
steroids	2.22	[1.38-3.57]	0.001
MDRD en post greffe immédiat	1	[0.99-1]	0.37
Episode of acute rejection	0.96	[0.63-1.47]	0.86
Period 2 versus 1	2.03	[1.15-3.59]	0.01
Period 3 versus 1	2.26	[1.20-4.28]	0.01

In a repeated events analysis taking all infections into account, Episode of previous IRH was an independent risk factor for a subsequent event as well as age, time on dialysis prior to transplant, induction by antithymocyte globulin induction, corticoids, and mycophenolate mophetil use.

Conclusion : The incidence rate of IRH increases over time. This higher incidence might be related to different patient profile and immunosuppressive protocols including antithymocyte globulin induction.

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