

Life after kidney allograft failure (KAF)

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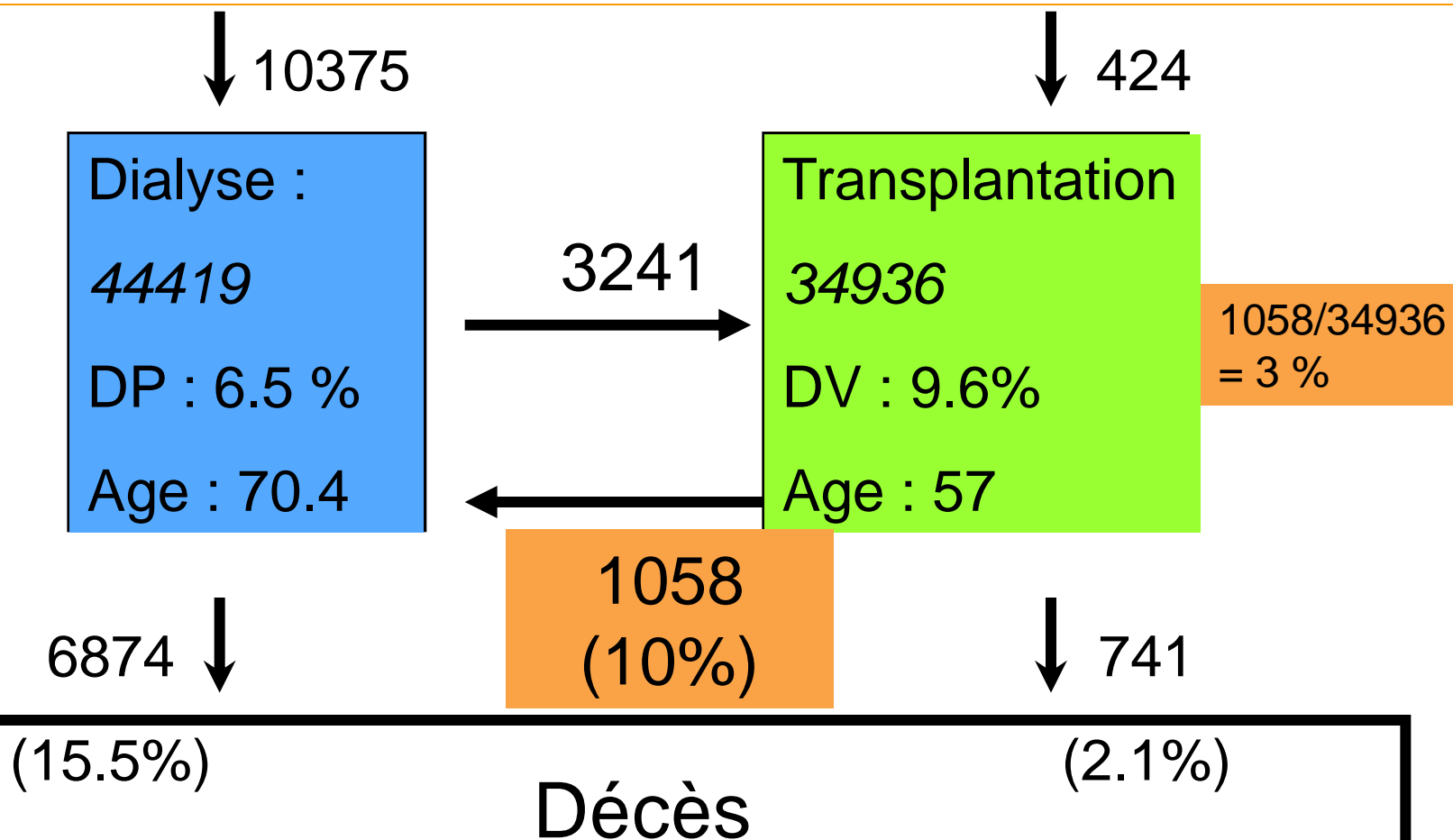
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IRC stade V en 2014 en France



Specific features (KAF vs Transplant-naïve patients)

- - ***Long Period of immunosuppression :***
Increased risk of infection and cancer
- - ***Presence of an « allogenic » graft :***
Inflammation, graft intolerance syndrome, acute rejection.
- - ***Regular FU by a transplant team :***
Preparation to dialysis.



Life after KAF : 3 important decisions :

- 1- Preparation and timing of dialysis initiation
- 2- What to do with immunosuppressive treatment?
- 3- What to do with the failed graft?



Life after KAF : 3 important decisions :

1- Preparation and timing of dialysis initiation:

- *Late referral ?(Gill et al. Kid Intern. 2002)*

- *Increased mortality? (Rao et al, AJKD, 2007)*

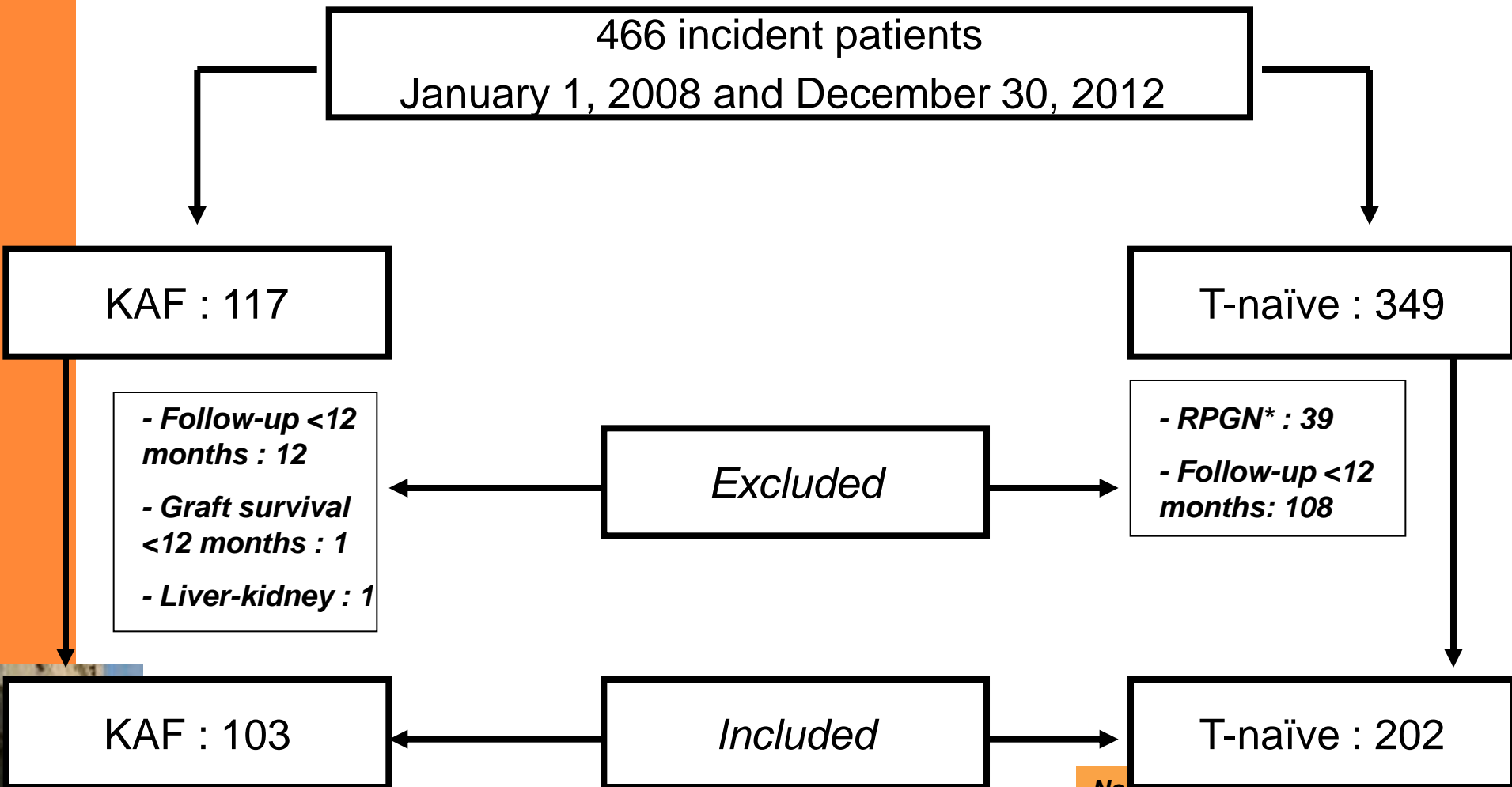
2- What to do with immunosuppressive treatment?

3- What to do with the failed graft?

Case control analysis

			Cases N=778		Controls N=778		P value**
			n*	Value	n*	Value	
	Albumin (g/L), mean ± SD			276	34.6 ± 5.8	248	
Hemoglobin (g/dL), mean ± SD			175	10.4 ± 1.8	146	10.8 ± 1.7	<0.001
Peritoneal Dialysis			0	26 (3.34)	0	148 (19.02)	<0.001

Return to dialysis after kidney allograft failure : evolution of clinical and biological parameters 12 months before and after dialysis initiation.



Necker 20/04/10

*RPGN : Rapidly progressive glomerulonephritis

	KAF patients (n=103)	T-naïve patients (n=202)	p-value
Age (years)	53.6 ± 14.2	63.9 ± 15.6	<0.001
Sex (% male)	69	63.4	ns
CV disease (%)	26.2	44.1	0.002
Diabetes Mellitus (%)	23.3	35.6	<0.01
Cognitive disorders (%)	1.9	6.4	0.09
Pulmonary disease (%)	1	14.8	0.002
Chronic liver disease (%)	12.7	9.9	ns
Neoplasms (%)	9.7	15.3	ns
HIV (%)	0	1	ns
Tobacco (%)	27.2	31.0	ns
Charlson comorbidity index			<0.001
0-3 (%)	43	19	
4-5 (%)	35	23	
≥6 (%)	22	58	

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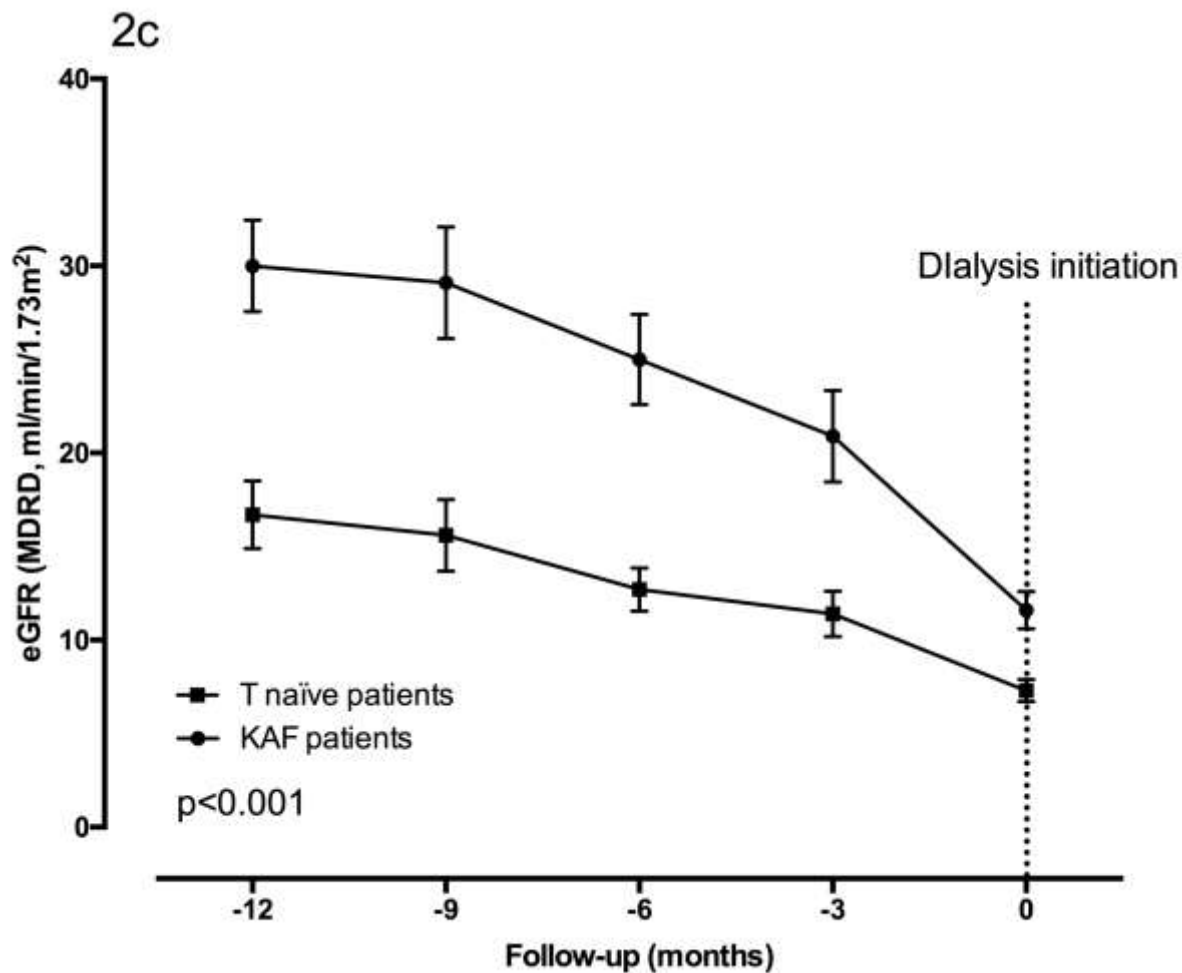
1- KAF and T-naïve cohorts are obviously two different populations, which significantly differ in terms of age, BMI, prevalence of diabetes mellitus, cognitive disorders and pulmonary disease.



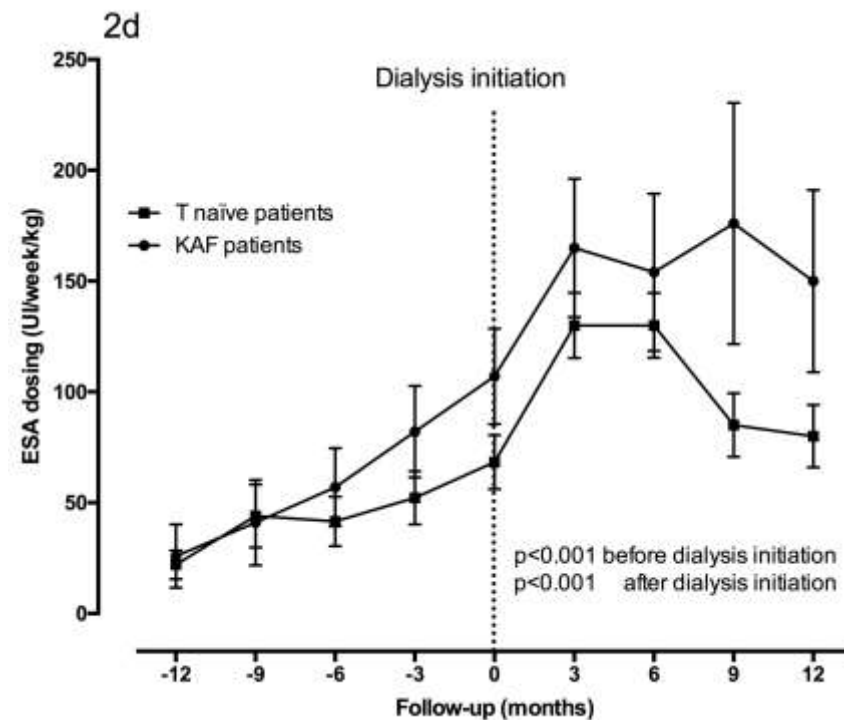
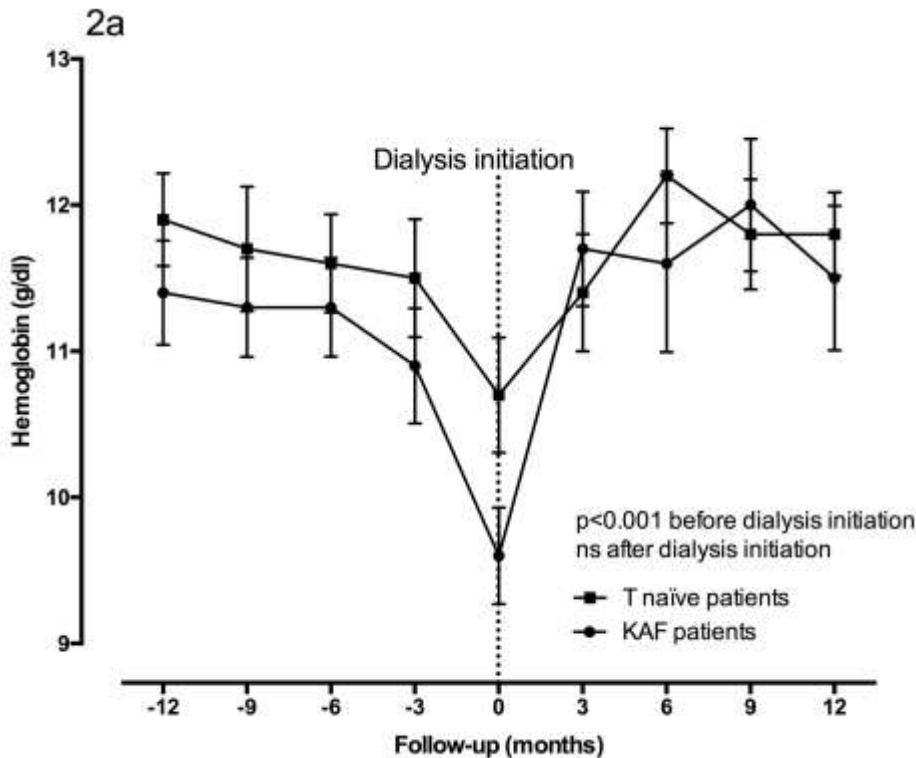
	KAF patients (n=100)	T-naïve patients (n=100)	p-value
Age (years)	53.3 ± 14.3	57 ± 14.7	0.03
Sex (% male)	68	59	ns
CV disease (%)	25	30	ns
Diabetes Mellitus (%)	23	23	ns
Cognitive disorders (%)	0	0	ns
Pulmonary disease (%)	0	0	ns
Chronic liver disease (%)	13	12	ns
Neoplasms (%)	11	20	ns
HIV (%)	0	2	ns
Tobacco (%)	28	33	ns
N° of visits on the last year	2.9 ± 1.5	3.5 ± 1.7	ns
On KT waiting list (%)	64	57	ns
HD (vs PD, %)	97	89	<0.05
AV fistula (presence, %)	68	56	0.052
1st dialysis on catheters (%)	31	44	ns
1st dialysis on emergency (%)	31	22	ns
BMI (kg/m2)	23 ± 4.2	23.7 ± 3.5	ns
SBP (mmHg)	152 ± 27	152 ± 24	ns
DBP (mmHg)	84 ± 14	83 ± 13	ns
ESA dosing (UI/Kg/week)	107 ± 99	68 ± 59	<0.001

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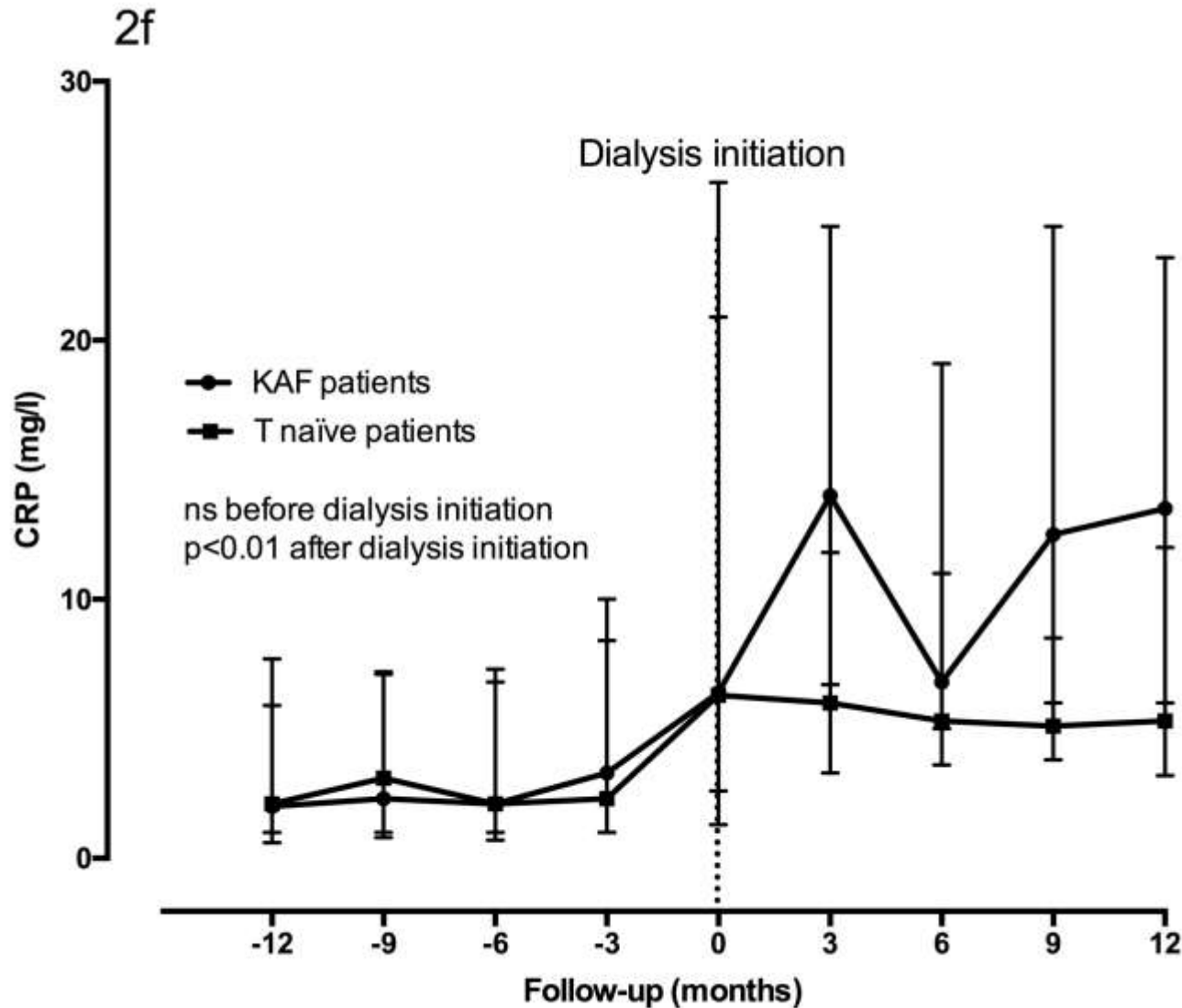
Quarterly values (mean \pm SD) of eGFR before dialysis initiation.



Quarterly values (mean \pm SD) of Hb and ESA before and after dialysis initiation.



Quarterly values (mean \pm SD) of CRP before and after dialysis initiation.



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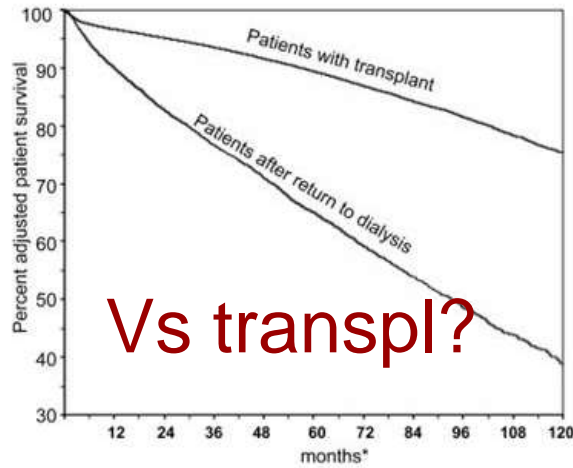
2- The majority of biological and endocrine abnormalities are already present 12 months before dialysis initiation and progress with the decline of renal function.

3- The rate of eGFR deterioration and need for ESA agents are significantly higher in the KAF group, suggesting that KAF is a particular type of CKD.

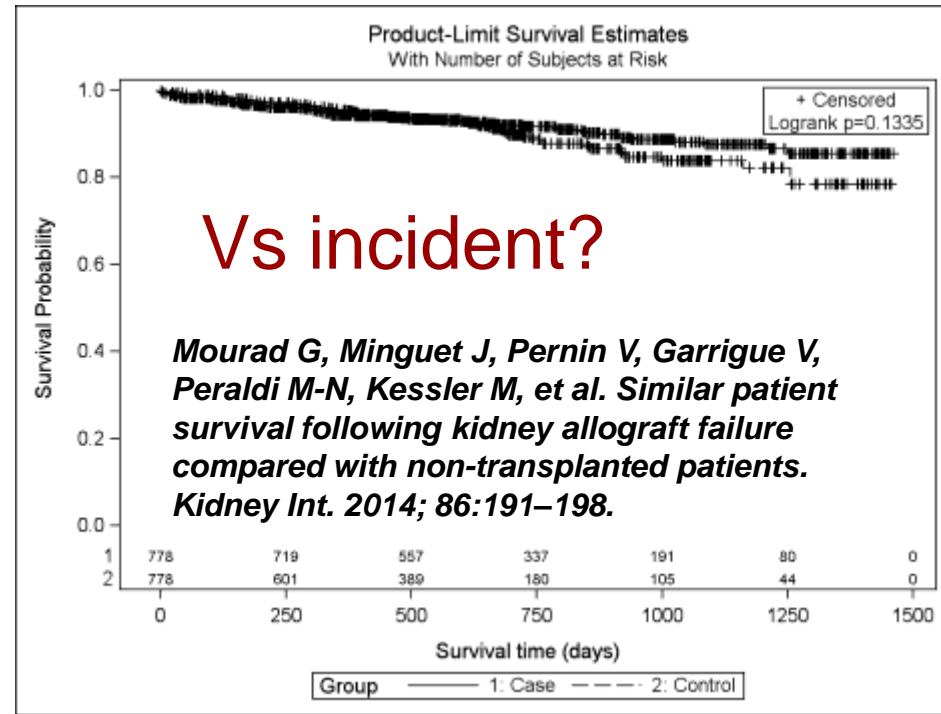
KAF patients receive similar nephrological care as T-naïve controls.

	KAF (103)	T naïve (202)	P value
N° of visits on the last year	2.9 ± 1.4	3.39 ± 1.7	ns
On KT waiting list (%)	81.6	60.4	<0.001
HD (vs PD, %)	96	92.6	ns
AV fistula (presence, %)	72	54	0.003
1st dialysis on catheters (%)	44.7	65.8	0.02
1st dialysis on emergency (%)	32	32.7	ns
BMI (kg/m ²)	23 ± 4.2	27 ± 7.9	<0.001
SBP (mmHg)	152 ± 26.4	154 ± 25.3	ns
DBP (mmHg)	83.7 ± 13.6	82.1 ± 12.7	ns
Hypertension (%)	97	96	ns
ESA dosing (UI/week)	6820 ± 6102	4672 ± 3913	<0.001
ESA dosing (UI/Kg/week)	106 ± 96	63 ± 54	<0.001
>1 IS drug (%)	93	NA	

Increased Mortality?

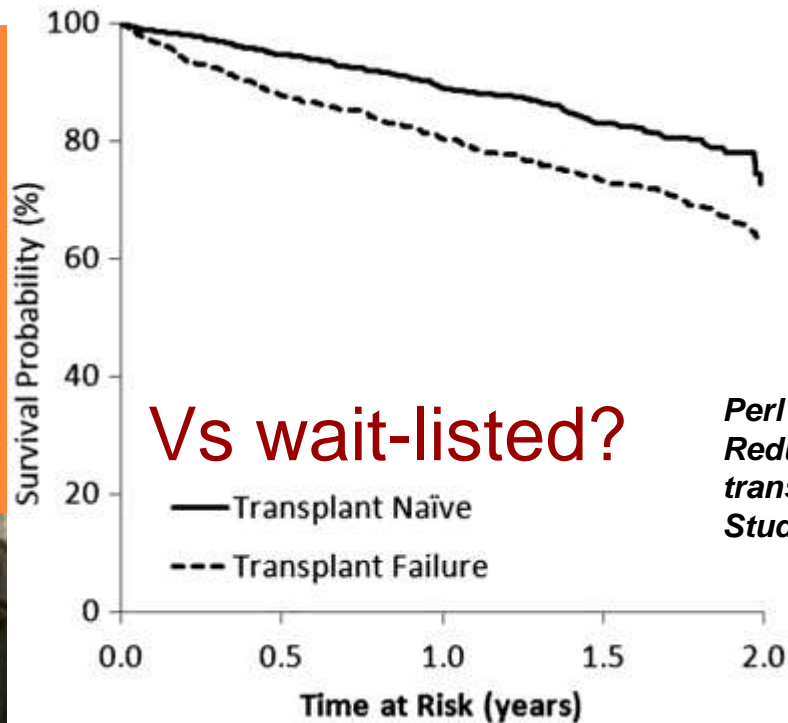


From Kaplan, Bruce & Meier-Kriesche, Herwig-Ulf
 Death After Graft Loss: An Important Late Study Endpoint in Kidney Transplantation.
 American Journal of Transplantation 2002, 2 (10), 970-974. Printed with Permission



Vs incident?

Mourad G, Minguet J, Pernin V, Garrigue V, Peraldi M-N, Kessler M, et al. Similar patient survival following kidney allograft failure compared with non-transplanted patients. Kidney Int. 2014; 86:191-198.



Perl J, Zhang J, Gillespie B, Wikström B, Fort J, Hasegawa T et al. Reduced survival and quality of life following return to dialysis after transplant failure: the Dialysis Outcomes and Practice Patterns Study. Nephrol Dial Transplant. 2012; 27: 4464-4472.

Life after KAF : 3 important decisions :

- 1- Preparation and timing of dialysis initiation
- 2- What to do with immunosuppressive treatment? Cessation or withdrawal?
- 3- What to do with the failed graft?



Continuation of immunosuppression :

Potential adverse effects:

- Infection and cancers

SmakGregor et al. Clin Transpl 2001.

Infections : 1.7 vs 0.51 pt/année (OR 3.4).

- CV complications

-Décès : OR 2.8

-CV : OR : 3.

- Metabolic complications (DM, HT)

- C.S. adverse effects

Withdrawal of immunosuppression



- *Early failure :*
- Stop Immunosuppression and immediate Graft nephrectomy.
- (DSA: 57 %; Del Bello et al. Transplantation 2012)

- *Late Failure:*
- Rapid withdrawal of IS.
- Graft nephrectomy in cases of AR or graft intolerance syndrome.
- (DSA 70%; Scornik et al, Hum Immun; 2011

Increased risk of sensitization after KAF :

- Weaning of immunosuppression +++
- Graft Nephrectomy
- **Blood Transfusions ++**, often needed in the setting of graft failure: surgery, blood loss during hemodialysis, myelosuppressive effect of IS



Scornik et al. HLA sensitization after transplant loss. Hum Immunol 2012; 72 : 398-401

Abs after T	N	G.N.		IS		TF	
		Yes	No	Off	On	Yes	No
Yes	38	31	7	38	0	26	12
No	31	8	23	20	11	12	19
% pos	55	79	23	66	0	68	39
<i>P value</i>		<i><0.001</i>		<i><0.001</i>		<i>0.016</i>	

Continuation vs Withdrawal of immunosuppression :

Prevention of graft intolerance syndrome, AR and the need for graft nephrectomy

- Graft intolerance syndrome, Acute rejection and need for transplant nephrectomy

Minimization of allosensitization

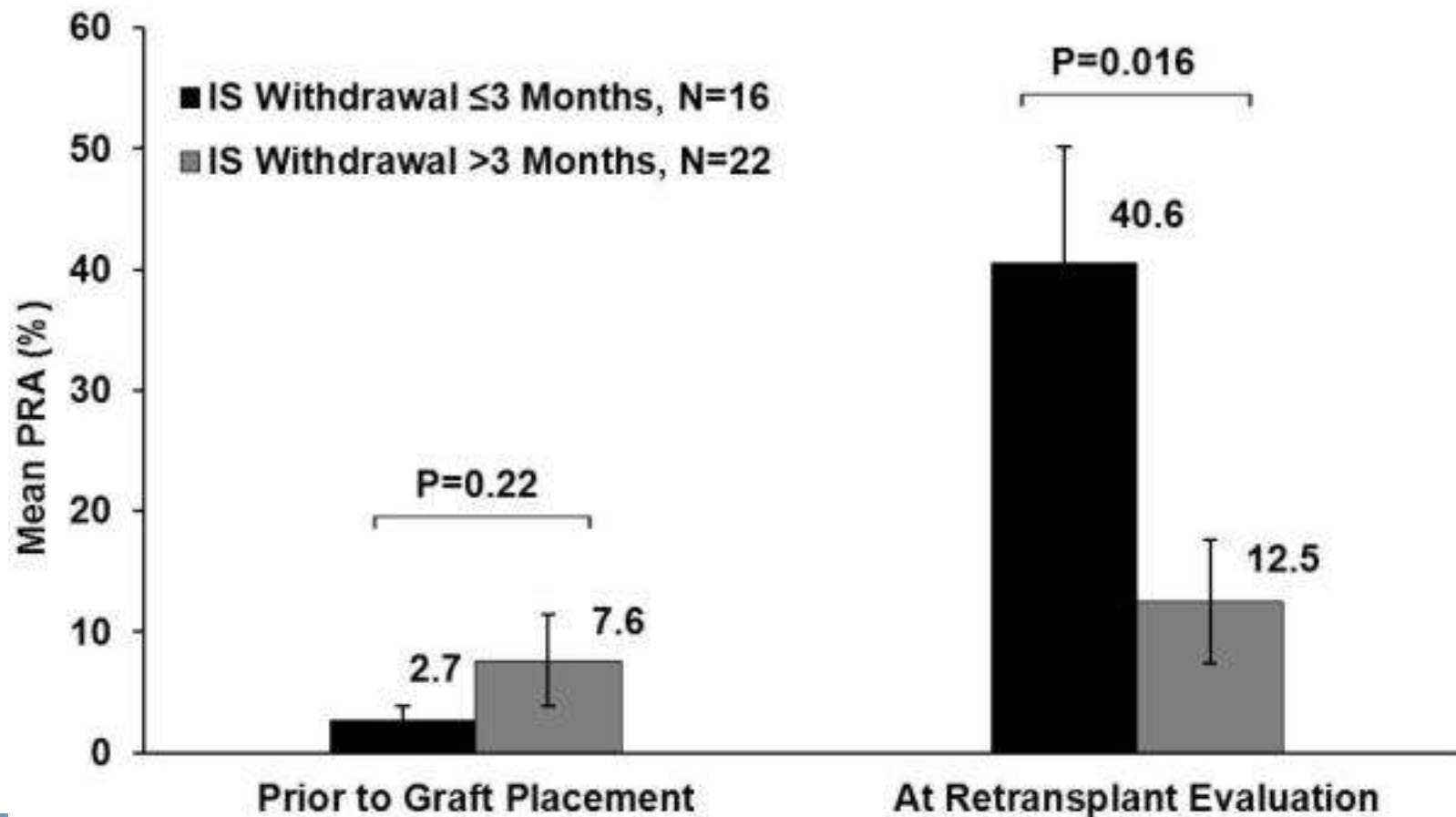
- Anti-donor Immunisation

Residual renal function

Prevention of adrenal insufficiency, reactivation of systemic disease

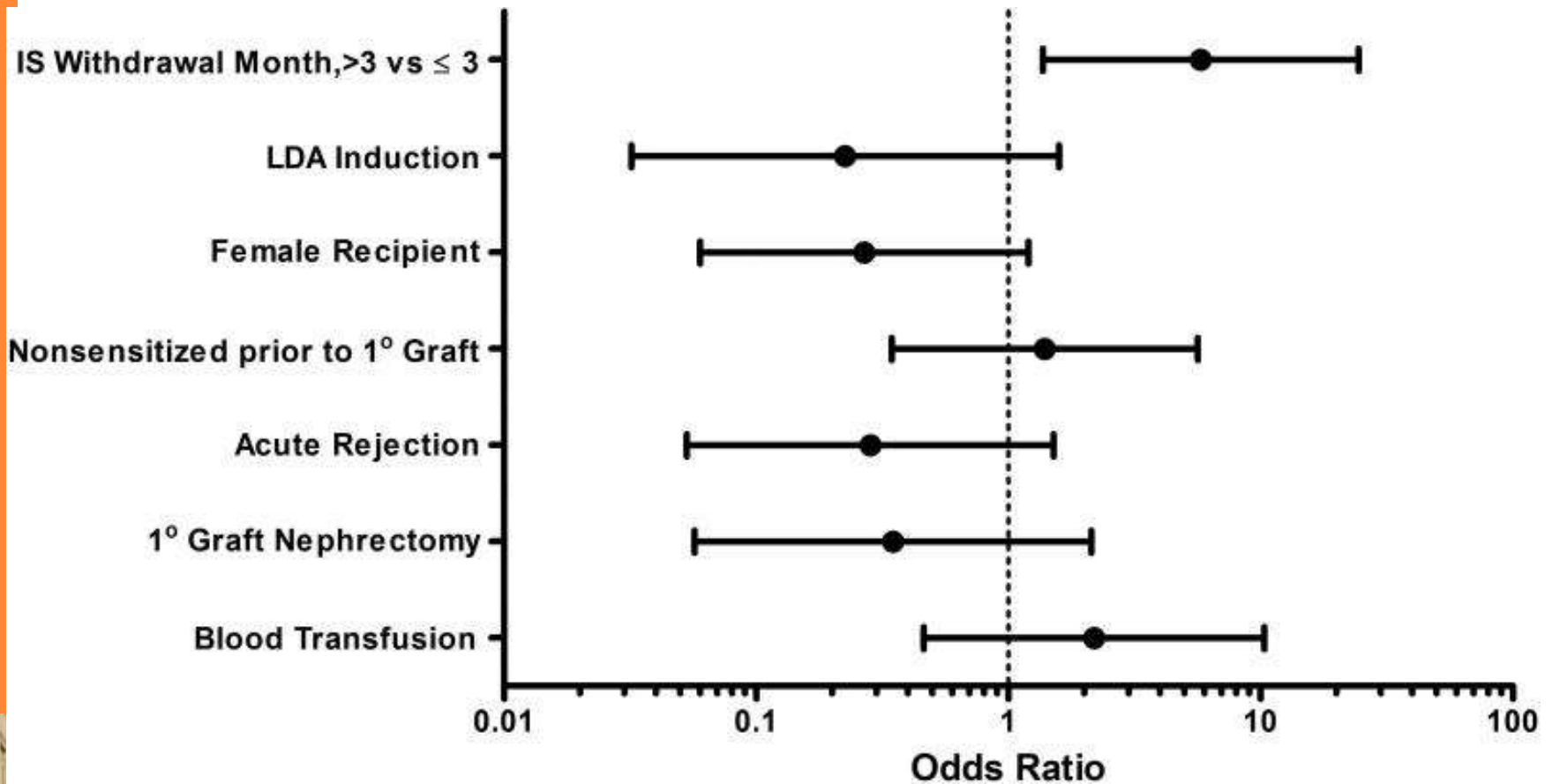
Transplantation. 2014;98:306-11. Prolonged immunosuppression preserves nonsensitization status after kidney transplant failure.

Casey MJ1, Wen X, Kayler LK, Aiyer R, Scornik JC, Meier-Kriesche HU



Transplantation. 2014;98:306-11. Prolonged immunosuppression preserves nonsensitization status after kidney transplant failure.

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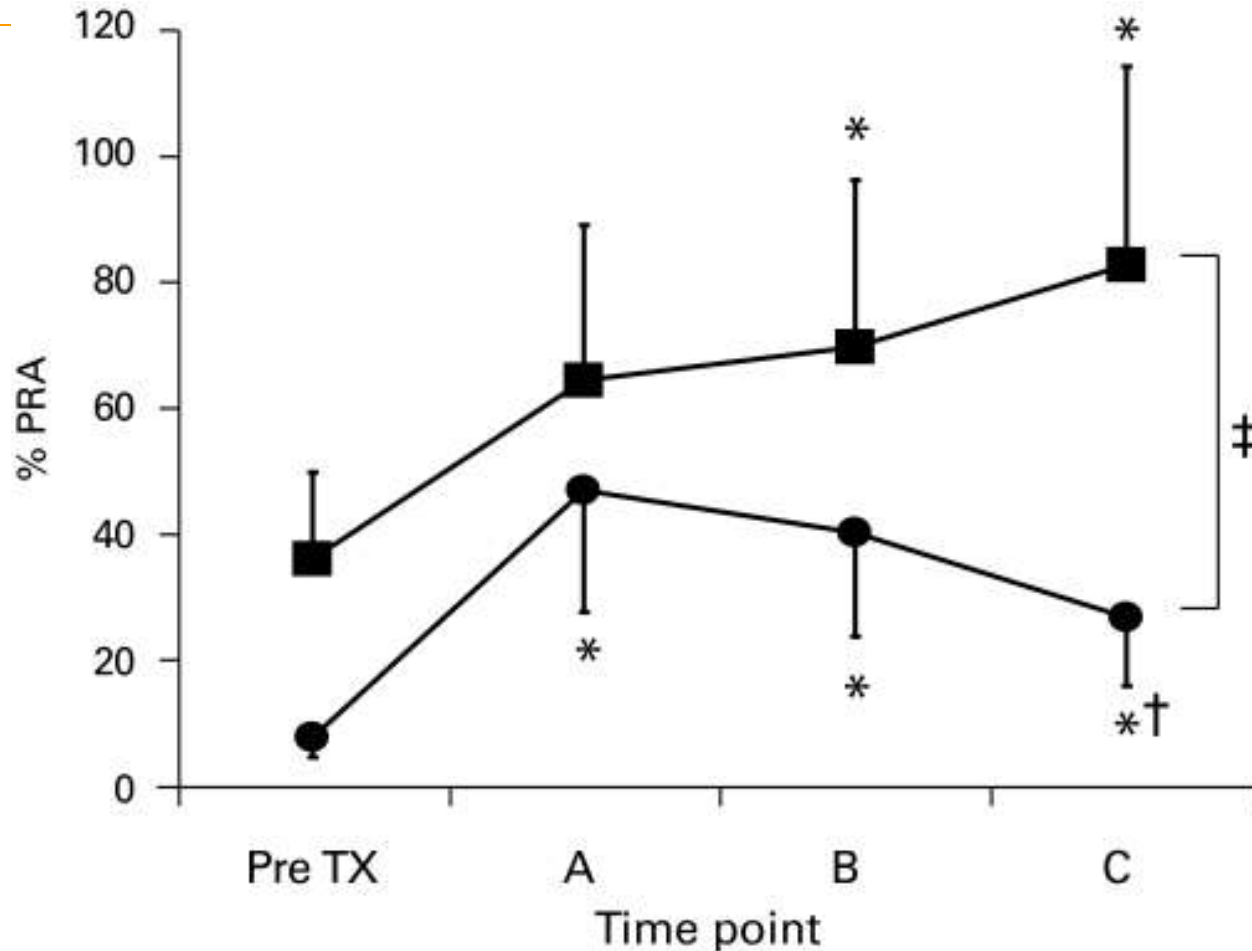


Life after KAF : 3 important decisions :

- 1- Preparation and timing of dialysis initiation
- 2- What to do with immunosuppressive treatment?
- 3- What to do with the failed graft? Allograft nephrectomy or not?



Regularly done in early failure. Probably beneficial



Can Urol Assoc J. 2011;5:142-7. Early but not late allograft nephrectomy reduces allosensitization after transplant failure. Sener A, Khakhar AK, Nguan CY, House AA, Jevnikar AM, Luke PP.

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Graft Nephrectomy after late graft failure.



George P. Bayliss et al. Immunosuppression after renal allograft failure: a survey of US practices. Clinical Transplantation 2013; 27 : 895-900.

Graft Nephrectomy after late graft failure : usually not done

- **Surgery related mortality and morbidity (16% : *graft site hematoma or infection; septicemia*).**
- **Allosensitization**
- **Loss of residual kidney function**

Graft Nephrectomy and sensitization: Elution of antibodies or an other mechanism?

	<i>Eluates</i>	<i>Serum</i>		<i>P</i>
		<i>1 yr after Tx</i>	8/19 (42.1%)	<0.05
DSA	12/17 (70.6%)	<i>At Txectomy</i>	6/19 (31.6%)	<0.05
		<i>After Txectomy</i>	14/19 (73.6%)	NS

Martin L, Guignier F, Mousson C et al, Detection of donor-specific anti-HLA antibodies with flow cytometry in eluates and sera from renal transplant recipients with chronic allograft nephropathy. Transplantation, 2003; 76: 395-400.

Allograft Nephrectomy after Transplant Failure: Should It Be Performed in All Patients Returning to Dialysis?

Heidi M. Schaefer and J. Harold Helderma

Department of Medicine, Division of Nephrology, Vanderbilt University School of Medicine, Nashville, Tennessee

J Am Soc Nephrol 21: 207–208, 2010.

doi: 10.1681/ASN.2009121262

- Failing graft is a focus of a chronic inflammatory state

May reduce mortality rates

Presence of a failed kidney transplant in patients who are on hemodialysis is associated with chronic inflammatory state and erythropoietin resistance.
Juan M. Lopez-Gomez, Isabel Perez-Flores, Rosa Jofré & al.
J. Am. Soc. Nephrol 15 : 2494-2501, 2004

Table 5. Comparison of hematologic and biochemical data between group A1 and group A2 at 6 mo of follow-up^a

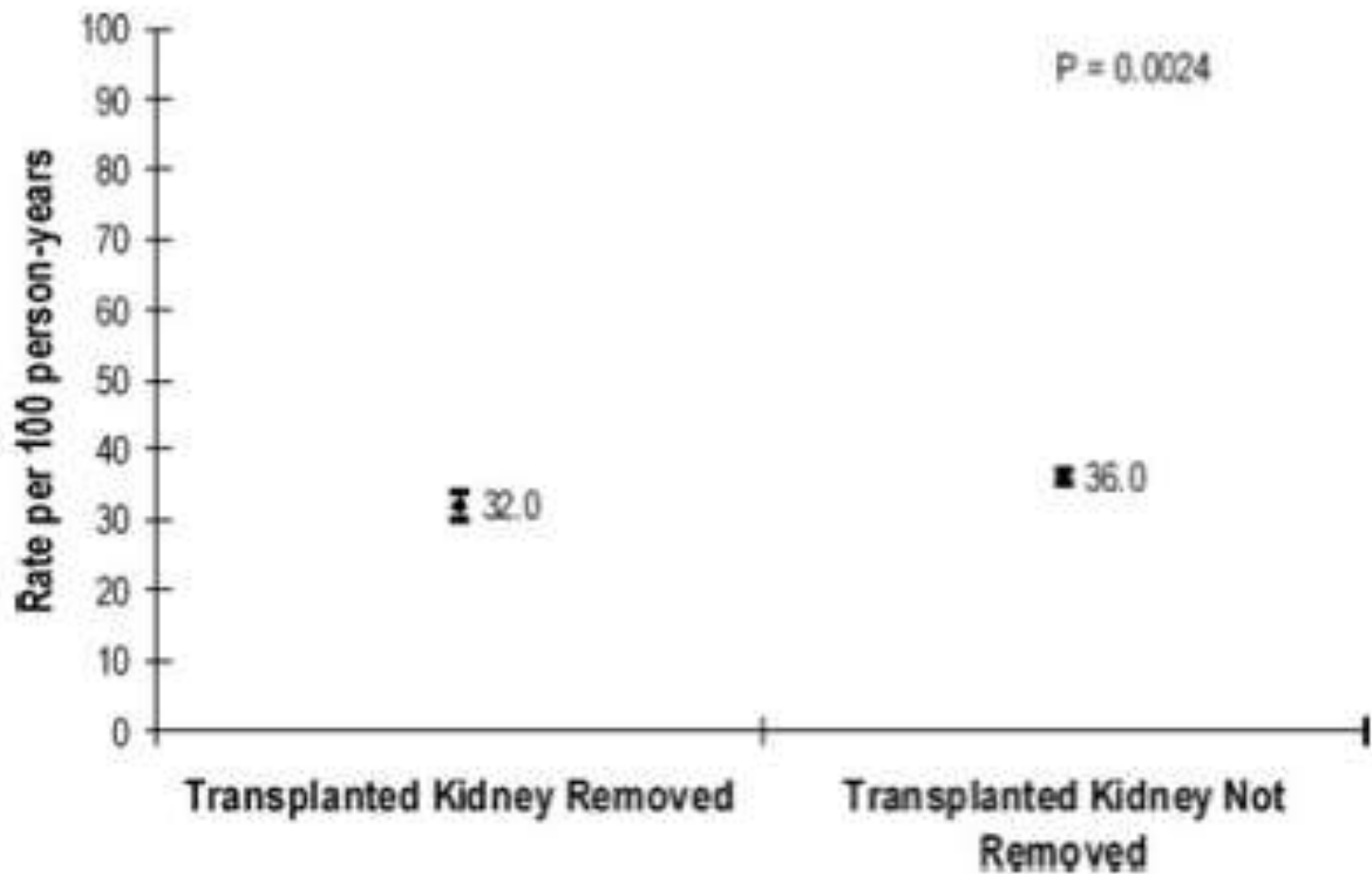
	Group A1 Transplant Nephrectomy Done	Group A2 Transplant Nephrectomy not Done
<i>N</i>	29	14
Hb (g/dl)	12.7 ± 1.1 ^c	10.9 ± 1.4 ^c
rHu-EPO dose (U/wk)	6925 ± 3173 ^c	12714 ± 8693 ^c
ERI (U/kg per wk per g/dl)	9.9 ± 5.5 ^c	20.2 ± 12.3 ^c
Ferritin (μg/L)	356.7 ± 268.6 ^{NS}	235 ± 119 ^{NS}
TSI (%)	37.9 ± 14.3 ^{NS}	38.7 ± 18.1 ^{NS}
Albumin (g/dl)	3.9 ± 0.6 ^b	3.3 ± 0.4 ^b
Prealbumin (mg/dl)	30.8 ± 8.6 ^c	27.6 ± 7.9 ^c
CRP (mg/dl)	0.9 ± 0.5 ^b	3.6 ± 6.0 ^b

^a Data are mean ± SD.

Significance between group A1 and group A2: ^b *P* < 0.001; ^c *P* < 0.005.

Transplant Nephrectomy Improves Survival following a Failed Renal Allograft

Juan Carlos Ayus,* Steven G. Achinger,[†] Shuko Lee,[‡] Mohamed H. Sayegh,[§] and Alan S. Go^{||¶}



IS and graft nephrectomy : a pragmatic decision!

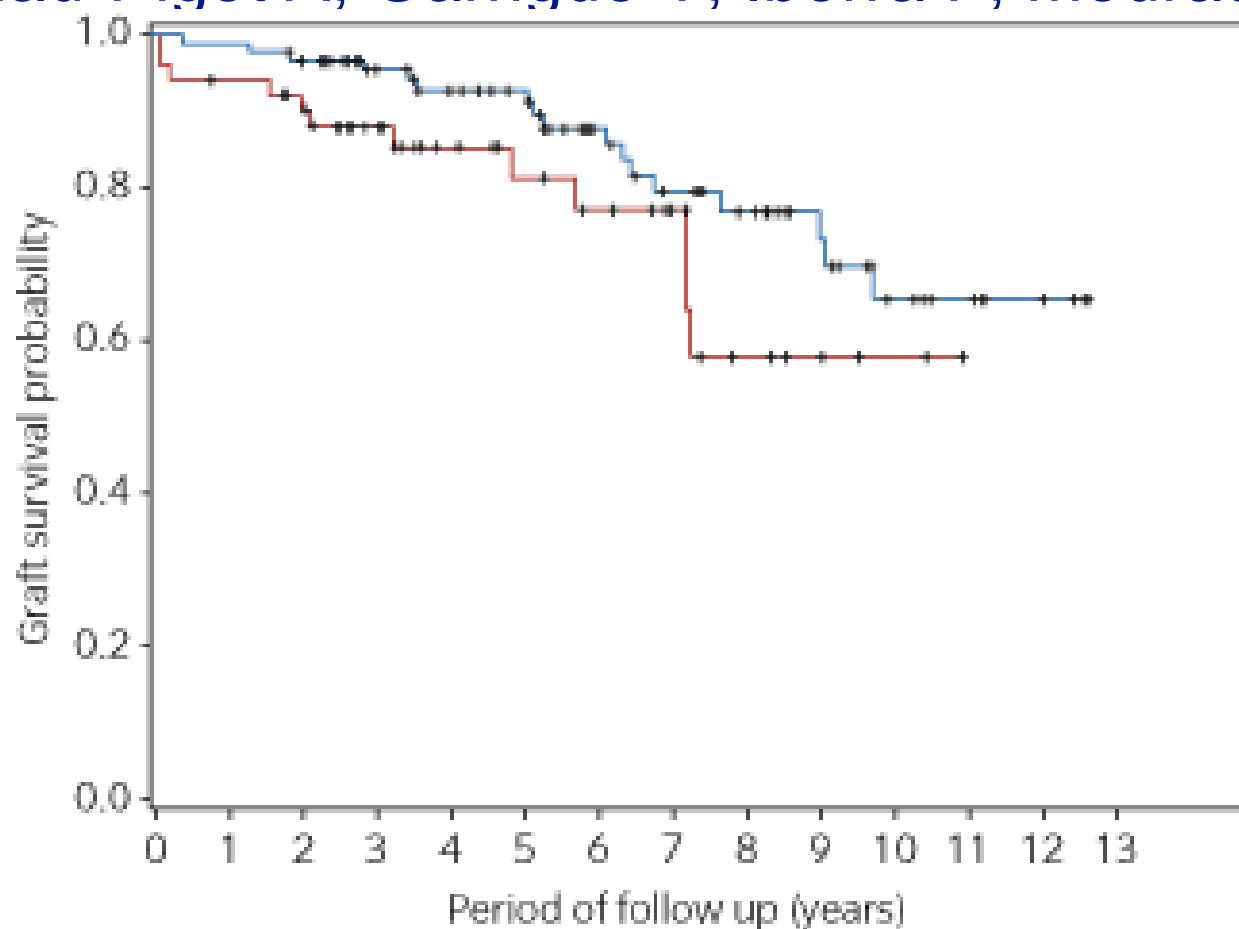


- ***No retransplant :***
- **Rapid IS withdrawal and Graft nephrectomy if needed.**

- ***Retransplant:***
- **Maintain IS until Retransplant (LD) or for > 3 months**

Int J Urol. 2014;21:797-802. Impact of graft nephrectomy on outcomes of second kidney transplantation.

Fadli SE1, Pernin V, Nogue E, Macioce V, Picot MC, Ramounau-Pigot A, Garrigue V, Iborra F, Mourad G.



No. patients at risk of failure

No graft nephrectomy	94	93	89	74	63	58	44	35	28	21	13	9	3	0
Graft nephrectomy	52	48	44	35	25	20	17	13	6	4	2	0	0	0



George P. Bayliss et al. Immunosuppression after renal allograft failure: a survey of US practices

