Survival of Diabetic and Non-Diabetic Patients on Hemodialysis is Similar : Reasons for another (French) Paradox.

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Diabetes is the most common cause for new patients requiring Renal Replacement Therapy (RRT) accounting for approximately 45% of new cases in the United States [1], 23 % in ERA-EDTA Registry [2], and 21.5% in France [3]. The most frequent modality of RRT utilised in the diabetic patients remains Hemodialysis, but this method is associated with many clinical problems, in particular vascular access, frequent intra-dialytic hypotension, cardiovascular conditions, and diabetic foot, and poor survival.

Diabetic patients undergoing Hemodialysis demonstrate all over the world worse survival rates than Non-Diabetic patients undergoing hemodialysis. Whilst caring for Diabetic patients for more than 40 years [4], we have not noted a similar pattern during the last decade.

The aim of this study was to analyze survival rates, clinical conditions, hospitalisation of Diabetic patients and Non-Diabetic patients during the last decade to offer possible explanations to this paradox. These findings may help to optimise management of Diabetic patients on RRT treated by Hemodialysis.

Patients & Methods

During the last decade, 408 patients were treated by hemodialysis in our unit. Patients were assigned to the diabetic patient cohort when Diabetic Nephropathy was the primary cause of End Stage Renal Disease (ESRD). Diabetes Mellitus as co-morbidity was recorded in the Non-Diabetic Group of patients.

Main characteristics of both groups were reported on Table 1:

Parameters	Diabetic Patients	Non-Diabetic Patients	p value
Numbers &(%)	101 (25%)	307 (75%)	
Sex: M/F %	63 / 37	65 / 35	NS
Age: years (SD)	60.2 (12.5)	53.5 (17.2)	0.0001
BMI: Kg/m² (SD)	24.6 (4.9)	22.2 (3.9)	0.001
Co-Morbidity: Charlson Index: mean (SD)	11.2 (2.7)	6.9 (3.3)	0.00001
0 à 5 N (%)	0	119 (39)	
6 à 10 N (%)	45 (45)	153 (50)	
11 à 18 N (%)	56 (55)	35 (11)	
Start Dialysis in the Unit: N(%)	70 (70)	165 (54)	
Vascular access at Start: N (%)			NS
AV Fistula	88 (87)	273 (89)	
Transient Catheter	11 (11)	27 (9)	
Graf	2 (2)	7 (2)	

Modalities of treatment were similar using Hemodial® software (PHP Développement, Roubaix, France) during the last decade : Dialysis was performed 3 times a week for a mean time of 3.5 - 4 hours, and using the same dialyzer membranes for both groups. Blood flow rate was maintained at 300 to 350 ml/min. Arterio-venous fistulas were the predominant access for both groups.

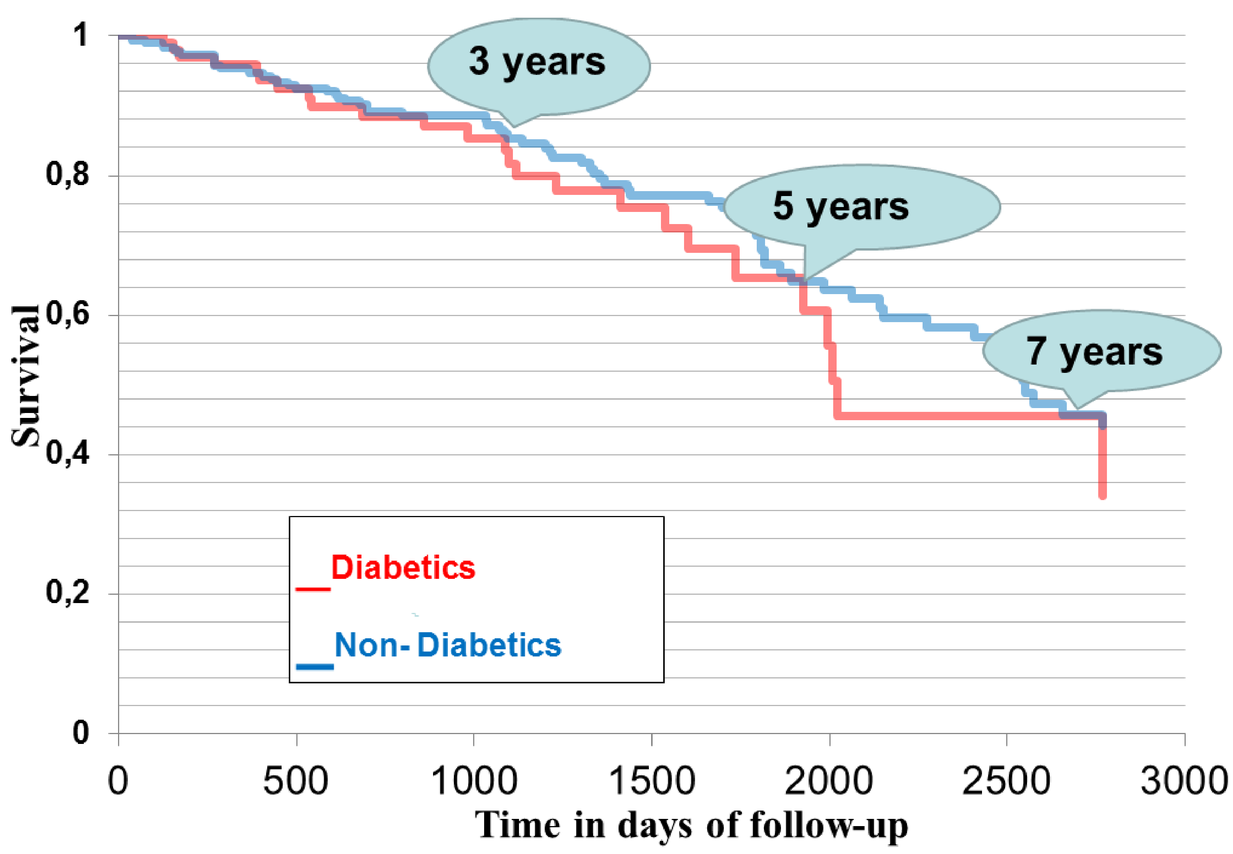
Kt/V was assessed every three months and recently at every dialysis on the dialysis machine.

Main biological parameters were controlled on the mean week dialysis session every other week, or for some of them every three months at the same period (albumin, CRP, iPTH, Ferritin, TSAT, LDL-cholesterol, and for diabetics HbA1c). If necessary, IV erythropoietin-stimulating agents (ESA) (mostly darbepoetin alfa [DA]) was administered every two weeks, with a target level for hemoglobin between 11.5 and 12 g/dL, and IV iron (mostly iron sucrose) once a week with a target level for TSAT around 40% and a ferritin level around 500µg/L.

Patient's follow up was assumed at least twice a week by the same physician, and a diabetic foot program was assessed with a visit at least every two weeks all over the decade.

Hospitalisation, reasons and duration, were recorded for all patients, excluding only one day-hospitalisation (for cataract surgery for example). Data were presented as mean ± standard deviation (SD). The Student t-test used for comparison between both groups, and survival were constructed using the Kaplan-Meier method.

RESULTS



The survival curves of both groups were presented on Figure 1.

Table 2: Summary of key biological data and hospitalisations of both groups during the decade of follow-up:

Parameters	Diabetic Patients	Non-Diabetic Patients	p value
Numbers	101	307	
Hemoglobin : g/dL mean (SD)	11.41 (0.89)	11.31 (0.92)	0.31
Pts receiving ESA , N	100	295	
Darbepoetin alfa	71.78 (44.75)	65.76 (43.35)	
Mean Dose per injection: µg(SD)	62.66	61.33	0.23
Median Dose: µg/per injection	0.51 (0.51)	0.53 (0.35)	0.52
Mean Dose: µg/Kg/week (SD)			
Albumin: g/L mean (SD)	38.1 (3.4)	38.7 (3.4)	0.12
CRP: mg/L mean (SD)	11.3 (11.7)	10.9 (16.4)	0.18
iPTH: pg/ml mean (SD)	396 (279)	394 (313)	0.9
Ferritin: µg/L mean (SD)	473 (280)	513 (305)	0.22
TSAT: % mean (SD)	34.7 (11.3	35.8 (10.0)	0.36
LDL-Cholesterol: mmol/L (SD)	2.13 (0.86)	2.13 (0.78)	0.9
Kt/V: mean (SD)	1.38 (0.12)	1.41 (0.14)	0.65
Hba1c: % (SD)	7.4 (1.2)		
Hospitalisation: % of Pts	52	43	0.05
All patients (days/pt/year)	5.52	3.14	0.05
Hospitalised pts (days/year)	10.5	7.3	0.24

Table 3:Key outcomes of the observed patients.

Outcomes	Diabetic Patients	Non-Diabetic Patients	p value
Number of patients	101	307	
Still on Dialysis: N (%)	45 (45)	89 (30)	0.05
Transplanted : N (%)	22 (21)	114 (37)	0.001
Kidney alone	20		
Kidney and Pancreas	2		
Transferred to other Unit: N(%)	8 (9)	30 (11)	NS
Death : N(%)	26 (25)	74 (24)	NS

Table 4: Primary causes of death.

Causes of Death	Diabetic Patients	Non-Diabetic Patients	p value
Total N of Deaths: N (%)	26 (25)	74 (24)	NS
Cardio-Vascular :N (%)	17 (66)	33 (44.5)	0.05
Myocardial Infarction	14	17	
Heart Failure	3	6	
Cerebro-vascular		10	
Infection: N (%)	3 (12)	4 (0.5)	0.03
Other causes: N (%)	6 (26)	37 (50)	
Cancer	2	6	
Hyperkaliemia	2	6	
Various	2	25	

DISCUSSION & CONCLUSIONS

The main findings of this study were the similar survival of Diabetic and Non-Diabetic Patients treated by Hemodialysis in our Unit over the last decade. The survival curves indicate survival rates of 95%, 85%, 65%, 45% for both groups at 1, 3, 5, and 7 years respectively. Hence, whilst cardiovascular and infection mortalities were more frequent in the diabetic group the overall survival did not differ between groups.

These results differ from data published over the last decade – especially for diabetic patients. For instance in 1995 the Lombardy Registry demonstrated survival rates of 82% at 1 year, and 48% at 3 years [5]; in 1997 a German prospective multi-centre study showed a extremely low 5 years survival of 10% [6]; in 2007 a group of Croatia showed a 35% survival at 2 years [7]; in 2011 for a group of Netherlands the survival was 25% at 5 years [8]; in 2012 the Da Vita group reported a 3 years survival of 30% [9]. In the French registry the 5 years survival rate was recently 40%[3].

Some studies have recently suggested that intensive glucose control, with HbA1c < 7% could have in incidence on patient's survival [10]. Our mean HbA1c was 7.4±1.2, however the survival rate of the group lower and higher was identical with 55% at 6 years.

Reasons for the equivalent mortality between groups may be explained by similar Hb level, similar ESA dosing, similar albumin levels, and/or similar CRP levels. However we believe that two major aspects should be underlined and may attribute possibly even more strongly, to observed outcomes:

1. Patient-doctor contact program with at least two visits per week with the same physician, recently pointed out in a study [11].
2. Diabetic foot program: this has been standard at our unit since inception, with an obligatory foot examination every two weeks by the nephrologist and a dedicated nurse; we believe that the early identification and treatment of diabetic foot complications is a team effort, where the nephrologist has a unique position to take action in this high risk population[12].

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