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STARTING DIALYSIS ON ONCE-WEEKLY SCHEDULE WITH SOFT, PRE-DILUTION HF OR HDF CAN PRESERVE RESIDUAL RENAL FUNCTION AND ALLOW LESS FREQUENT TREATMENT FOR YEARS, IN MANY ESRD PATIENTS

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INTRODUCTION. According to the current European guidelines, maintenance dialysis should be started before than GFR falls below 6 ml/min/ 1.73 m^2 (GFR_{min}). This could be interpreted to state that a GFR equal or greater than GFR_{min} provides a sufficient control of Uraemia. So that, one could argue that, as far as GFR is either greater or slightly lesser than GFR_{min}, a low dose and/or a less frequent dialysis could suffice to compensate for the difference between GFR_{min} and the actual GFR value. On this basis, at our unit it has been usual for years trying to start maintenance haemodialysis (HD) on once weekly schedule (1HD/w) for almost every patient with a significant residual renal function (RRF), soon increasing the frequency of treatment in the case of deterioration of either RRF and Urinary Output (UO) or clinical status. Quite unexpectedly, we have observed that such an approach seemed to preserve RRF in many patients. More recently, since we have observed that RRF could be preserved even better in patients undergoing once weekly soft Haemodiafiltration (HDF), we have devised to start all new patients on once-weekly pre-dilution HDF (1HDF/w). The aim of this study was to evaluate the impact of different initial dialysis schedules and/or modalities on RRF survival.

PATIENTS AND METHODS. We retrieved data of all ESRD patients started on HD or HDF at our Unit from January, 2000 to June, 2013, and followed-up for at least 6 months. For each patient, the following data set was obtained: date of birth, sex, primary renal disease (PRD), date of 1st dialysis, baseline (before the 1st dialysis) body weight, Body Mass Index (BMI), Body Surface Area (BSA), Mean Arterial Pressure (MAP), UO and GFR. Actually, some baseline UO and GFR values were only available within a few weeks after the dialysis inception. The data set also included the final UO and GFR values. The latter were obtained from the last (monthly) UKM study for which a measured UO of at least 500 mL/day was available. For the sake of simplicity, 500 mL/day was arbitrarily set as the critical level of UO used to define the RRF survival time as the time interval (i.e., follow up period, FUP) between the date of the 1st dialysis and that of the last measured UO equal or greater than 500 mL,/day. The rates of GFR loss and UO loss were computed as the difference between the initial and final GFR and UO values, respectively, divided by FUP. GFR was computed as the mean of urea clearance and creatinine clearance. The UO value refers to the last 24 hours before the studied dialysis session. BUN and Creatinine blood values were drawn at the start of the study session and used as a denominator of the clearance formula. The patients were divided into 3 groups (G), based on the initial schedule and or modality of treatment: standard HD, three sessions per week (3HD/w, G1); standard HD, once (or twice) weekly, (1HD/w, G2), and HDF (or HF), once weekly (1HDF/w, G3). Of note, due to the frequent variability of the operative parameters during the early sessions, we assumed as the effective initial treatment the one observed at the 2nd month. Within each group, all patients used the same dialyser membrane: a low flux Polysulfone, for G1 and G2, and Helixone membrane for G3 patients.

RESULTS. : We found a total of 150 patients fulfilling the inclusion criteria. The main characteristics of the patients are shown on table 1: most of them, such as age, body weight, and MAP were similar for the 3 groups. In contrast, the baseline GFR and UO values were significantly different among groups. The initial schedule and modality of treatment by year are shown on table 2: there is a progressive shift to 1HDF/wk. The Kaplan-Meyer plot of renal survival (UO=>500 mL/day) is given in figure 1: it shows a significant (Log Rank, $p<0.001$) difference among groups, with an impressive 2-year cumulative RRF survival of 89% for G3, vs 27% for G1, and 63% for G2 patients. The 3-year survival rate for G3 patients remained stable at 89%, but was 49% for G2, and 14% for G1 patients. As shown on table 3, the average rates of reduction in UO for the 3 groups were 210 (G1), 38 (G2) and 41 mL/month (G3). The corresponding rates of reduction in GFR values were, respectively: 0.76 (G1), 0.24 (G2), and 0.08 mL/month (G3).

DISCUSSION. Due to the observational nature of the study, the above results only suggest that starting HD on a less frequent schedule could allow a longer RRF survival time, further prolonged by using HDF or HF in the place of HD. Interestingly, similar data showing a beneficial effect of twice-weekly HD on RRF survival have recently been published for a large group of Chinese patients. Such an effect is usually explained by less hypotensive episodes on 2HD/w vs 3HD/w patients. However, it is also possible that less frequent dialysis could be more biocompatible. Moreover, the associated higher BUN levels could maintain a beneficial osmotic diuresis. A soft HDF or HF, using low volume flows, ultrapure dialysate and very compatible membranes, would both avoid too low BUN levels and increase biocompatibility. An important limitation of this study is that many patients of G1 were obliged to the 3 HD/w schedule due to an early RRF loss. However, the groups seems quite relatively well comparable, particularly G2 and G3. In any case, the estimated 2-year RRF survival of 63% and 89%, for G2 and G3 patients, respectively, is really uncommon for the common HD patients. The significant difference in GFR loss rate between G2 and G3 patients could point to an elective indication of pre-dilution (low efficiency) HDF (or HF), for starting the extracorporeal RRT.

In our experience, the patients that start on 1HD/w and particularly those on 1HDF/w are happy and fare well. Thanks to such a strategy, about 1/3 of our prevalent patients is currently on 1 or 2 HD or HDF per week, with sizable economical savings. While waiting for evidence-based new guide lines for dialysis start, we believe that everyone could safely test our approach by starting a few suitable patients on 1HDF or 1HF/w, being careful to increase the frequency on the basis of the observed GFR and UO (or interdialysis weight gain) values as well as clinical status, paying a particular attention to the control of biochemistries, ECF volume and blood pressure. We would stress that using the UKM-based incremental approach is not recommended because, due to the erroneous assumption of equivalency between renal and dialytic clearance, it overestimates the dialysis needs, so that 1 HD/w would be nearly impossible. Moreover, as hypothesised above, a high efficient treatment could increase the RRF loss rate.

Table 1 Patient characteristics by initial HD schedule/modality

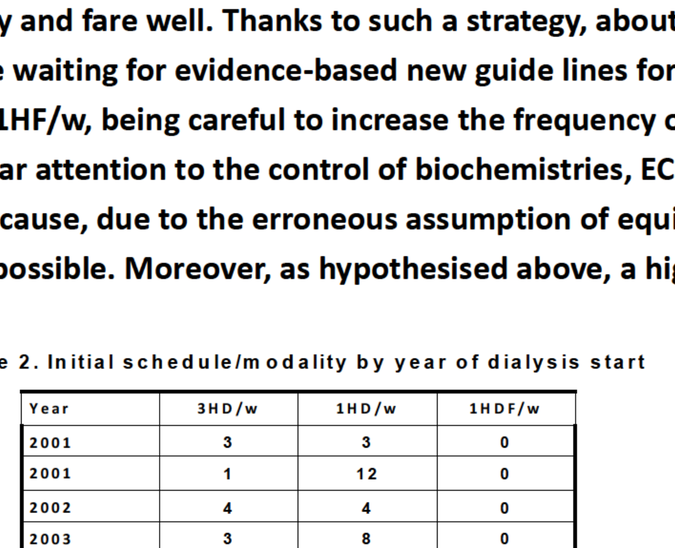
Group	tot	G1 (3HD/w)	G2 (1HD/w)	G3 (1HDF/w)
N	150	48	80	22
Male (%)	87 (58)	22 (46)	51 (64)	14 (64)
Age (years)	68±16	67±17	69±15	67±13
Body weight (kg)	65.0±14	68±17	63±12	68±16
Body mass index (kg/m^2)	26.4±6.1	28.1±8.4	25.3±4.3	26.7±5.1
Body surface area (m^2)	1.65±0.20	1.68±0.24	1.62±0.18	1.72±0.22
MAP (mmHg)	98.5±11.1	99.3±11.6	97.5±11.0	100±10.7
GFR (mL/min)	5.6±2.1	5.1±2.2	6.1±2.0	5.0±15
Urine output (L/day)	1.6±0.6	1.3±0.5	1.7±0.6	1.9±0.6
Causes of ESRD, N (%)				
Diabetes	28 (19)	11 (23)	14 (18)	3 (14)
Glomerular Diseases	22 (10)	7 (15)	12 (15)	3 (14)
Interstitial Diseases	26 (17)	7 (15)	14 (18)	5 (23)
Other	74 (49)	24 (50)	40 (50)	10 (46)

Table 2. Initial schedule/modality by year of dialysis start

Year	3HD/w	1HD/w	1HDF/w
2001	3	3	0
2001	1	12	0
2002	4	4	0
2003	3	8	0
2004	5	9	0
2005	2	7	0
2006	12	9	0
2007	8	11	0
2008	2	5	0
2009	4	6	2
2010	2	3	3
2011	1	3	4
2012	1	0	9
2013	0	0	4
Tot	48	80	22

Table 3. Average loss rate of U.O. and GFR, by group.

	UO loss rate (mL/month)	GFR loss rate (mL/min/month)
Group 1	210 ± 650	0.76 ± 1.26
Group 2	38 ± 44	0.24 ± 0.45
Group 3	41 ± 64	0.08 ± 0.24
P	0.04	0.001



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