Initiation of dialysis: is the problem solved by NECOSAD?

Sir,
We are pleased with the editorial comment by Lameire and colleagues [1] on our article regarding the effect of the timing of initiation of dialysis treatment on survival [2]. We would like to add some remarks to the debate on the timing of dialysis treatment. We studied the effect of the timing of dialysis initiation on survival in a large cohort in The Netherlands, but it is obvious that more studies are a necessity. These studies should address different populations, or should study different outcomes like quality of life, as is suggested by Lameire et al.

In a recently published study of our group, we presented the findings of the effect of timing of dialysis treatment on health-related quality of life [3]. In this study we found that a timely start was associated with a significantly better HRQOL during the first months after the initiation of dialysis. Yet, within 1 year after the start of dialysis treatment this benefit had disappeared. A potential advantage of a late start is the extra time without the strict rules of dialysis therapy. So the deliberation is between extra dialysis free time, accompanied by a worsening in HRQOL that can most likely be made up for within 12 months, vs less time free of the strict rules of dialysis therapy and an earlier improvement in HRQOL that is not certain to last. Only the patient, in consultation with the nephrologist, is able to weigh both sides.

Regarding the comment on the relatively low incidence of renal replacement therapy in The Netherlands, Lameire et al. cite USA figures, instead of the most recent ones reported by the renewed ERA–EDTA Registry [4]. It appears from these figures that both the incidence and prevalence of renal replacement therapy in The Netherlands are similar to those in Norway, Finland and Scotland. For Belgium, only data from the French-speaking area are available, showing the highest figures in Europe. It is speculative whether this may be related to a high incidence of analgesic nephropathy. Based on these data we think it rather unlikely that the NECOSAD results have been influenced by a selection bias towards taking only relatively healthy patients in dialysis treatment.

As mentioned in the Editorial Comment, one of the issues in determining the effect of timing on outcome is lead-time; i.e. the effect that the observed benefit of an early start is merely a reflection of studying patients at an earlier stage of their disease instead of a real gain in outcome. The best method of handling this problem is to include all patients at the same stage of their disease; for example, with the same residual renal function. Unfortunately, we included patients at the start of dialysis, instead of at the time of equal renal function. So to be able to adjust for lead-time, we had to estimate the lead-time from the literature. Based on this search, the lead-time could range between 4.1 and 8.3 months. Even taken the shortest lead-time into account (4.1 months), the gain in survival of 2.5 months after 3 years of follow-up was less than the lead-time. Next, to verify whether the lead-time as estimated from the literature might be applicable in Dutch patients, we determined the actual lead-time in a small sample of 60 patients. Thus, we collected additional data from these patients during the pre-dialysis phase, resulting in an average lead-time of 6 months. This result supported the use of the literature findings in our study. More importantly, however, in a recent publication by Traynor et al. [5], in which the effect of an early initiation on survival was studied, lead-time was determined for all patients. Adjusting for the actual lead-time, these authors also could not find any support for a policy of earlier initiation of dialysis treatment for patients with ESRD.

On the last page of this Editorial Comment, Lameire et al. handle some statistical problems. First, they address the sample size. The authors suggest that with a larger sample the results of the Cox regression analysis would become statistically significant. However, whether these findings were statistically significant or not (apart from sample size), is not the main issue in this particular case, as these findings were merely the first step in the total analyses, i.e. these were the results before adjusting for lead-time. The comparison of the effect of an early start vs a late start is only meaningful after including the effect of lead-time. Drawing attention to statistical significance of the crude effect without taking into account the effect of lead-time would be misleading. In our study, the effect of lead-time was larger than the effect of an early start, so the apparent gain in survival presumably did not represent an actual improvement in the course of the disease. Next, Lameire et al. seem to have made a miscalculation in their discussion on statistical problems. They claim that the time span between January 1997 and August 2000 is only 32 months, so we could not possibly draw a conclusion based on 3 years of follow-up. However, after recalculation, we can only conclude that there is a time span of 43 months between January 1997 and August 2000. Therefore, we were perfectly able to value the effect of a 3-year follow-up (a period of 36 months).

In conclusion, the decision on the timing of dialysis initiation remains an important subject. New results from the Netherlands and Scotland showed that the differences in survival and quality of life between patients who started early compared to patients who started late were small [2,3,5]. Consequently, the decision on when to initiate dialysis has to be the result of a comprehensive comparison. The potential risks and benefits of all options have to be weighted by the nephrologist, in consultation with the patient. Current published findings do not support a policy of earlier initiation of dialysis for patients with ESRD.

Conflict of interest statement. None declared.


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