Accelerated Renal Death After Unilateral Nephrectomy in a Rat Strain Suffering From Autosomal Dominant Polycystic Kidney Disease¹,²

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Recently, Zierer et al. (1) reported in this journal that, in polycystic kidney disease (PKD) patients, unilateral nephrectomy (UNX) had no adverse effect on the occurrence of renal death. In that study, the age at which UNX was performed was highly variable (22 to 54 yr). Therefore, the time elapsing until end-stage renal failure was reached might have been too short in some patients to have any effect on progression. Thus, reproducing these data under more standardized conditions in a rat model of PKD (2) could be helpful in defining the effect of UNX on the occurrence of renal death. The rats of this model of autosomal-dominant PKD exhibit typical histologic lesions and develop terminal renal failure, the course of which is ill defined (2–5).

ANIMALS AND METHODS

Han:SPRD rats exhibiting PKD were obtained from Dr. Deerberg (Central Institute for Laboratory Animal Breeding, Hanover, Germany). One hundred four randomly selected male rats inbred in our unit to the third generation were entered into this trial: Group 1 (N = 40), UNX was performed in heterozygous PKD rats at the age of 3, 5, 6, or 7 months (10 animals/age group); Group 2 (N = 40), age-matched heterozygous PKD rats (10 animals/age group) (inadvertently, 2 animals entered at the age of 3 months were euthanized when it was thought that they would belong to another experiment. Thus, data of only 38 animals were available for evaluation.); Group 3 (N = 12), age-matched homozygous unaffected animals, with UNX performed at 3, 5, 6, and 7 months (3 animals/age group); and Group 4 (N = 12): age-matched homozygous unaffected animals serving as controls for Group 3 (3 animals/age group). Thus, the age structure of all groups was exactly the same. Therefore, the data of the animals could be combined for survival analysis.

All animals had free access to tap water and standard rat chow containing 19% protein. Blood sampling from the retro-orbital plexus was performed monthly for the determination of serum urea. For the data evaluation we applied the Kaplan-Meier method.

RESULTS

The overall observation period was 13.4 months after nephrectomy. Thereafter, all surviving rats were euthanized, and the data about them were regarded as censored in the survival analysis.

A considerable number of rats in Groups 1 and 2 died as a result of uremia (defined as having a serum urea concentration above 200 mg/dL), with non-UNX animals surviving significantly longer than UNX rats (log rank test, P = 0.001) (Figure 1). During the observation period, no animal of Group 4 died because of uremia, but two of Group 3 did. Thus, UNX accelerated renal death in PKD rats.

DISCUSSION

Our data reveal that UNX in PKD rats results in an earlier occurrence of renal death than in non-UNX animals, whereas Zierer et al. (1) observed no difference in the time to ESRD or death in UNX-PKD patients as compared with non-UNX-PKD patients. Several factors could contribute to this differing observation. First of all, there was a considerable variability in the patients’ age when UNX was performed (range, 22 to 54 yr). Therefore, the time elapsing until end-stage renal failure supervened in the UNX group might be too short for the occurrence of any adverse effect on renal survival. In contrast, UNX was performed fairly early in the life of the rats, thus allow-
ing sufficient time to elapse for UNX to display its effect on "renal" death. Furthermore, a considerable gap between the survival curves of the two patient groups was reported for the early course of the survival curves. Unfortunately, statistical tests giving weight to these parts of the curves were not applied. A further explanation for not detecting a difference might be the small number of patients (28 of 47) coming to end-stage renal failure.

This article also provides a formal survival analysis in this PKD rat strain. When planning our study, the average survival time of these rats was unknown (3). As we know by now all chosen times for UNX have to be regarded as fairly early in the life of animals having a median survival time of 17 months. Thus, our study provides no answer as to the effect of late-performed UNX on renal survival.

Renal survival compares well, as does histology and renal function (3–5), with that of humans coming to end-stage renal failure at the age of about 50 yr. In comparison, PKD rats are dying from uremia at the age of about 17 months, whereas the overall survival time in Sprague-Dawley rats is about 30 to 36 months.

The fact that UNX leads to an earlier development of the disease and results in a constant rate of progression once the disease starts is demonstrated by the parallel course of the survival curves of the UNX and non-UNX rats. The same is suggested by the early course of the survival curves in the article by Zeier et al. (1). Thus, our data and the reviewing of the literature still suggest that UNX could have an adverse effect on renal survival in PKD.

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