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Reverse epidemiology and hemodialysis blood pressure

To the Editor: Analyzing reverse causality in dialysis, Kalantar-Zadeh et al [1] address the blood pressure (BP) control issue and refer to Tassin unit experience in this issue of *Kidney International*.

In the studies cited by the authors, BP figures used as risk predictor are baseline values, most patients are hypertensive, antihypertensives are used in 65%, follow-up time is <5 years, and extracellular volume (ECV) is not mentioned. Conversely, in our own studies [2, 3], integrated BP values are used, BP is strictly normal, antihypertensives are seldom used, follow-up time is >10 years, and ECV control is a key point. Among 1235 Tassin patients, the lowest initial predialysis BP decile (1st dialysis month mean arterial pressure <90 mm Hg) mortality is significantly high (2 years odds ratio = 1.96, $P < 0.02$). Therefore, in Tassin as elsewhere, initially low BP does predict early mortality.

BP predictive value at dialysis initiation is poor: 90% of patients then are hypertensive, whatever their former hypertension exposure duration, and whether or not they become normotensive in dialysis. The effect of hypertension on target organs takes many years and very often we don't know how long a patient starting dialysis has been hypertensive. A recent report [4] clearly confirms the crucial predictive importance of hypertension duration before dialysis.

Reverse epidemiology has misleading relevance on dialysis management. The high early mortality universally associated with low baseline BP figures does not contradict the need to achieve normal BP in dialysis patients to reduce long-term cardiovascular mortality. Besides, the eventual noxious/beneficial role of antihypertensive medications in dialysis patients needs to be investigated.

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REFERENCES

1. KALANTAR-ZADEH K, BLOCK GA, HUMPHREYS MH, *et al*: Reverse epidemiology of cardiovascular risk factors in maintenance dialysis patients. *Kidney Int* 63:793–808, 2003
2. CHARRA B, CALEMARD E, LAURENT G: Importance of treatment time and blood pressure control in achieving long-term survival on dialysis. *Am J Nephrol* 16:35–44, 1996
3. CHARRA B, CHAZOT C, JEAN G, *et al*: Long, slow dialysis. *Miner Electrolyte Metab* 25:391–396, 1999
4. FERNANDEZ LUCAS M, QUEREDA C, TERUEL JL, *et al*: Effect of hypertension before beginning dialysis on survival of hemodialysis patients. *Am J Kidney Dis* 41(4):814–821, 2003

Reply from the Authors

Charra et al [1] indicate that in Tassin, a low, rather than elevated, blood pressure (BP) is associated with an almost 2-fold increase in mortality among maintenance hemodialysis (MHD) patients, despite long hours of dialysis treatment. This is consistent with our stated theory of reverse epidemiology. The study quoted by the authors indicating a positive association between hypertension and mortality in 184 Spanish MHD patients had a relatively small sample size [2]. Moreover, patients in this study were, on average, 10 years younger than MHD patients in the United States [3]. On the contrary, the epidemiologic studies indicating a strong association between low BP and mortality in MHD patients, which we [1] referred to, or which have been published elsewhere [4], examined many thousands of MHD patients with a low likelihood of selection bias.

It is not well established that treatment of hypertension by altering hemodialysis techniques or lengthening dialysis hours improves survival by reducing BP. Such treatments almost certainly change many other physiologic and metabolic conditions concurrently. Nonetheless, it is quite possible that if MHD patients lived longer, traditional risk factors such as hypertension might have the time necessary to exert their long-term deleterious effects. However, in MHD patients, malnutrition-inflammation complex syndrome (MICS) may independently cause high early mortality and reverse traditional risk factors [1]. Thus, it is possible, although not proven, that alleviation of MICS saves lives. Given the high mortality in MHD patients and failure of traditional risk factors to explain this, randomized clinical trials that test whether treatment of MICS reduces mortality are strongly indicated.

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