How Race and Ethnicity Affect the Relationship Between Quality of Life and Mortality in a Hemodialysis Population: "Quality of Life Is More Important Than Life Itself"

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The quotation in the title is attributed to Dr Alexis Carrel, a French surgeon and recipient of the 1912 Nobel Prize in Physiology or Medicine for pioneering vascular suturing techniques. Though his words were not

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in reference to the modern-day hemodialysis population, they are certainly fitting.

In 2016, approximately 125,000 new cases of end-stage renal disease (ESRD) joined an estimated 726,000 people already carrying this diagnosis.[1] The vast majority (87%) of incident dialysis patients initiated in-center maintenance hemodialysis, joining approximately 450,000 people already receiving dialysis in a hemodialysis facility.[1] It is well-established that mortality rates on hemodialysis are exceptionally high. Despite a decline in 5-year mortality rates for patients receiving hemodialysis during the past 2 decades, an estimated 55% of hemodialysis patients die within the first 5 years of initiating therapy.[1-3] Based on recent 5-year survival rate comparisons, adults initiating hemodialysis have lower life expectancy than most people who develop solid-organ cancers, including colorectal, breast, and prostate cancer.[2] This underscores the need to identify potentially modifiable risk factors and new treatments to improve hemodialysis outcomes.

Health-related quality of life (HRQoL) has emerged as one such factor. HRQoL is an important patient-reported outcome in its own right, with the burden imposed by maintenance dialysis well demonstrated by the fact that patients with ESRD report significantly lower HRQoL compared with the general population.[4] Additionally, low HRQoL is itself recognized as a risk factor for worse outcomes, including higher hospitalization and mortality rates among dialysis patients.[5,6] However, prior studies have been limited by the lack of robust longitudinal assessments of HRQoL and cohorts without adequate diverse racial/ethnic makeup.[5,7] This is critical because for reasons that remain not entirely delineated, Hispanics and African Americans have a survival advantage on maintenance hemodialysis compared with non-Hispanic whites.[8-13] Attempts to elucidate whether differences in HRQoL between Hispanics, African Americans, whites, and other races/ethnicities affect mortality risk are lacking.

In this issue of *Kidney Medicine*, Kalantar et al[14] address these gaps in the literature. The authors investigated the relationship between HRQoL and mortality in a subcohort of participants from the Malnutrition, Diet, and Racial Disparities in Chronic Kidney Disease (MADRAD) Study, an ongoing multicenter prospective cohort study at maintenance hemodialysis facilities in Southern California since 2011. The MADRAD Study was designed to recruit a racially/ethnically diverse cohort of maintenance hemodialysis patients with the goal of examining whether differences in diet and nutrition patterns affect outcomes across different racial/ethnic groups. The focus of the subcohort study reported by Kalantar et al was to determine whether social, psychological, and mental health factors contribute to the racial survival disparities observed in patients with ESRD.

MADRAD participants completed questionnaires related to HRQoL every 6 months, including the 36-Item Short Form Health Survey (SF-36), a questionnaire previously validated in hemodialysis populations.[15] The SF-36 has 2 main summary scores, the Physical (PCS) and Mental Component Summary (PCS and MCS) scores, along with 8 subscale scores (physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain, and general health). Lower SF-36 scores indicate worse HRQoL. The primary analysis examined the association of MCS and PCS scores with the outcome of mortality, while secondary analyses examined the association of the 8 subscale scores with mortality. The MCS, PCS, and subscale scores were treated in a time-varying fashion, in which scores were updated with repeat score measurements over time to account for changes over time.

Of the available 1,016 participants enrolled at the time of analysis, 263 (26%) were excluded due to missing SF-36 questionnaire components. The final study sample was composed of 753 hemodialysis patients recruited from 18 outpatient dialysis facilities in Southern California from October 2011 to August 2016. The 753 participants included for analysis had a racial/ethnic makeup of 49% Hispanic, 32% African American, 10% Asian/Pacific Islander, 9% non-Hispanic white, and 1% other. Included participants underwent a total of 2,461 repeated SF-36 measurements during about 5 years of follow-up.

The authors found that baseline MCS and PCS scores varied significantly by race/ethnicity. Although PCS and its subscale scores were similar in African Americans and Hispanics and lower in whites, MCS and its subscale scores tended to be higher in whites than African

Americans and Hispanics. The authors found that older individuals and those with lower serum albumin levels were more likely to have the lowest (worst) baseline PCS scores. Similarly, the presence of an arteriovenous fistula versus an arteriovenous graft was associated with higher baseline MCS scores.

The authors took into account broad sociodemographic and dialysis characteristics and found that participants with PCS or MCS scores in the lowest quartile (worse score group) had higher mortality risk compared with those with scores in the upper quartiles. When stratified by race/ethnicity, Hispanic and African American participants with PCS scores in the lowest quartile experienced higher mortality risk. This relationship was not observed between MCS scores and mortality when stratified by race/ethnicity. Secondary outcomes analysis revealed similar findings: being in the lowest quartile in 7 of the 8 subscale scores was associated with higher mortality risk (all subscale scores except emotional well-being) among Hispanic and African American participants. These associations remained true when analyzed in 10-point increments instead of in quartiles, with increasingly lower subscale scores associated with higher mortality risk.

As acknowledged by the authors, these results should be interpreted with certain limitations in mind. First, the preferred assessment tool for HRQoL in the ESRD population is a kidney-disease-specific HRQoL instrument, the Kidney Disease Quality of Life 36-Item Short-Form Survey (KDQOL-36)[16] because it is the annual HRQoL assessment required by the Centers for Medicare & Medicaid Services.[4] The authors intentionally used the SF-36 in the MADRAD population to allow for comparisons with other chronically ill populations given that it is a generic, rather than disease-specific, instrument.[17] Using this less preferred instrument may introduce bias into the results or make them less practical to clinicians.

Second, their results are applicable to patients receiving in-center hemodialysis. They should not necessarily be extended to adults receiving home dialysis modalities given the recognized differences in HRQoL based on treatment modality and venue.[18] Third, residual confounding remains due to the inability to account for several other factors that affect mortality in the ESRD population, including medications, cardiovascular comorbid conditions, and dialysis treatment variables such as treatment adherence.

Finally, although the authors should be lauded for inclusion of a diverse racial/ethnic population in this study, the relatively lower number of non-Hispanic whites and Asians may reduce the ability to make conclusions about these ethnic groups.

Despite these limitations, this study by Kalantar et al provides important and unique insight into the relationship between HRQoL and risk for mortality in a racially/ethnically diverse cohort of maintenance hemodialysis patients. First, their results confirm that HRQoL remains very low in maintenance hemodialysis patients and that certain components are especially low in certain racial/ethnic groups. Second, both the subscale findings and associations of potentially modifiable risk factors (eg, low albumin level) with worse MCS and PCS scores point to potential opportunities to improve HRQoL. Awareness of this information can allow clinicians to target strategies to improve HRQoL in a more patient-centered fashion. For example, clinicians may intervene to improve nutrition, improve vascular access, and address symptoms of depression or pain to effect improvement in HRQoL, though further studies are needed to confirm whether such strategies are effective. Additionally, their findings demonstrate that Hispanics and African Americans with lower HRQoL scores experience worse survival on hemodialysis, though the relationship between HRQoL and mortality did not reach significance in their white and Asian American counterparts. These findings suggest that racial/ethnic differences in HRQoL do not appear to explain the racial survival disparities observed in patients with ESRD.

The late comedian Robin Williams, in his role as a physician in the film *Patch Adams*, once said, "Our job is improving the quality of life, not just delaying death." As nephrologists, we should take these words to heart and perhaps pay closer attention to the annual KDQOL-36 results of our hemodialysis patients. The current study confirms the importance of HRQoL both as a patient-reported outcome and as a predictor of mortality and highlights the need for future studies to identify strategies to improve HRQoL in patients with ESRD.

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