Literature Review-Clinical: Disparities in Access to Renal Transplantation for African Americans

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Background. Minority populations, especially African Americans (AAs), are disproportionately affected by deficiencies in our health care system. Because all Americans with end stage renal disease (ESRD) are eligible for government-funded care, one might expect ethnic discrepancies among patients with chronic kidney failure to be minimal. However, AAs have long been noted to be at a significant disadvantage when compared with other ethnic groups. **Methods**. To assess the impact of evolving trends in the management of ESRD on AAs, the authors reviewed published reports that examined the relationship between ethnicity, incidence of chronic renal failure, and access to optimal therapy. **Results**. The incidence of ESRD in AAs is 4 times greater than in Caucasians. African Americans remain substantially less likely than whites to be referred for, or undergo, renal transplantation, the preferred treatment for chronic renal failure. Comprehensive explanation of these ongoing observations remains elusive. **Conclusions**. Despite remarkable advances in ESRD management during the last decade, AAs in the United States remain significantly disadvantaged. Further evaluation of underlying causes and the development of specific remedies are warranted.

sIntroduction

Questions of equitability concerning African Americans (AAs) and health care, and more specifically renal transplantation, continue to permeate public discourse.[1] Of the myriad topics that have gained attention, the impact of ethnicity on the delivery of care for end stage renal disease (ESRD) remains especially controversial. One of the most troubling aspects of this problem is the exaggerated incidence of kidney failure among AAs. This has resulted in the demographic anomaly of AA overrepresentation in the ESRD population. Although the passage of the Social Security Amendments of 1972 entitled virtually all Americans with ESRD to Medicare-funded dialysis or transplantation, equal access is not apparent for all AAs with ESRD. This brief review will outline several factors that contribute to this discrepancy and will provide possible solutions.

Endstage Renal Disease in African Americans

First noted in the 1970s, AAs have a significantly greater risk of developing ESRD than Caucasians.[2,3] AA patients compose almost a third of those with ESRD, despite being less than 13% of the general population.[4] The incidence of ESRD in AAs in 1997 (873 per million) was more than 4 times that in the Caucasian population (218 per million), with 5 times greater prevalence (3579 per million vs. 803 per million). Although hypertension is the most commonly identified cause of kidney failure among AAs, those afflicted with other renal diagnoses are still at greater risk than Caucasians of ultimately requiring dialysis or transplantation.[5]

The prevalence of hypertension among AAs in the United States remains the highest in the world, with evidence that supports a role for environmental and genetic causes, that is, excess salt intake, superimposed on a genetic predisposition to salt retention, may lead to low-rennin hypertension.[6,7] Other research indicates a predisposition among AAs to deleterious effects of hypertension on renal function, even if blood pressures are well controlled.[3]

Recent studies documenting racial differences in the expression of transforming growth factor β, angiotensin receptor genotypes, and endothelial-dependent vasodilatation may provide a scientific basis to explain such observations.[8-11] Compounding these physiologic variables are socioeconomic and educational disadvantages often encountered by AAs, many of whom never received care for their hypertension prior to developing irreversible kidney failure.[1] Currently under way is an NIH sponsored project, the African American Study of Kidney Disease and Hypertension (AASK). The stated goal for AASK is to define the relationship between hypertension and renal disease in AAs and devise optimal strategies for intervention.[12] However, despite continued advances in understanding and treating some of these variables, ESRD in America is likely to remain disproportionately black.

ESRD Therapy in AAs

In the 1970s, dialysis was considered the optimal treatment for the patient with chronic renal failure.[13] Within a decade, improving outcomes in renal transplantation began to challenge this assumption.[2] Currently, more than 90% of transplant recipients maintain graft function for at least a year, and half-life for cadaver kidneys now exceeds 10 years.[4] In addition, renal transplantation reduces mortality, improves quality of life,

and is less costly than dialysis.[14,15] Recognizing these advantages, the federal government supports organ procurement, reimburses most costs associated with renal transplantation, and mandates that all ESRD patients undergo transplant evaluation.[16]

United States Renal Data System numbers indicate that the advantages of transplantation over dialysis, including significant prolongation of life expectancy, benefit AAs as much as other ESRD patients.[15,17] As early as 1988, Eggers noted that access of AA ESRD patients to transplantation was limited in relation to Caucasians.[2] The facts underlying this critical observation remain largely unchanged: an AA with ESRD is less than half as likely as a comparable Caucasian patient to receive a kidney transplant.[4] AA patients compose 37% of the U.S. dialysis population but receive only a quarter of cadaver kidneys and 14% of kidneys originating in live donors.[4,18] In addition, median waiting time for a cadaver kidney is twice as long (1185 vs. 605 days) for an AA candidate.[18] Although other minority patients (Asian/Pacific Islanders, Hispanics, and Native Americans) share lengthier waiting times with their AA counterparts, they are ultimately transplanted with a kidney at a rate proportionate to overall representation in the ESRD population. These differences are not evident in transplantation of other solid organs.

Racial disparity appears very early in the transplant process. Soucie found AA ESRD patients less likely to be identified as transplant candidates than Caucasians.[19] Other investigators in the early 1990s found AAs a third less likely than Caucasians to appear on a transplant waiting list within the first year of Medicare eligibility, a discrepancy not evident for other minority groups.[20] Given that Medicare mandates transplant evaluation for all dialysis patients, one might expect such differences to be waning. However, AAs accounted for only 28% of new listings in 1997, and current data indicate that a disparity in the number of referrals persists.[16,18] In a 1998 study, Kasiske found Caucasians more than twice as likely as AAs to be wait-listed before dialysis.[21] Another study found AA ESRD patients, once fully informed of their options, to prefer transplantation over dialysis as often as Caucasians but significantly less likely to proceed rapidly to transplantation.[22]

Ayanian found referred AAs less likely to actually appear on waiting lists or undergo transplantation (84% of Caucasians vs. 70% of AA), a discrepancy attributed to place of residence, educational levels, functionality on dialysis, and associated medical co-morbidity.[22] Epstein reiterated this observation when he reviewed 1518 patient records among those who started dialysis in 1996–1997 from 5 states and the District of Columbia.[23] Selected patients (ages 18 to 54 years) were stratified according to sex and ethnicity. AAs were less likely than Caucasians to be rated appropriate candidates for transplantation (9.0% vs. 20.9%) and were more likely to have incomplete evaluations (46.5% vs. 38.8%, $P < 0.001$). Of those deemed appropriate, AAs were less likely to be referred for evaluation (90.1% vs. 98% $P = 0.008$), to be placed on the waiting list (71% vs. 86.7%, $P = 0.007$), or to undergo transplantation (16.9% vs. 52%, $P < 0.001$). Moreover, among those patients deemed inappropriate for transplantation, Caucasians were more likely than AAs to be referred for evaluation, to be placed on the waiting list, and to undergo transplantation ($P < 0.001$). Epstein surmised that despite the limitations of the study, there exists a relative underuse of renal transplantation by AAs and an overuse by Caucasians.

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Living donor transplantation remains the optimal option for renal replacement therapy. However, once candidacy is established, AAs are significantly less likely to identify a potential live donor.[24] Thereafter, potential AA donors are more likely to be excluded because of previously undiagnosed co-morbidity, such as glucose intolerance or hypertension.[24] At the University of Alabama at Birmingham (UAB), only 13% of acceptable AA transplant candidates (versus 33% of Caucasians) ultimately received a kidney from a living donor, findings almost identical to those reported nationally.[18,25]

With fewer living donors available, AA transplant candidates are relatively more dependent upon cadaver kidneys, already noted to be of limited access.[18,26] Once again, socioeconomic disadvantage is important when a kidney becomes available. AA candidates may be more difficult to contact and less able to travel to the transplant center in a timely fashion.[27] Most agree, however, that immunologic variables are of greater importance.

First, given the medical necessity for compatibility of blood types and United Network for Organ Sharing (UNOS) allocation policy mandating ABO identity, AA candidates are disadvantaged by a predilection for ABO types associated with longer waits.[18] On the other hand, within blood groups, AAs waited from 23% (Type O) to 60% (Type B) longer than Caucasians, implying that ABO differences alone do not explain the racial discrepancy.[20] Second, AA transplant candidates are more likely to demonstrate significant anti–major histocompatibility complex (MHC) reactivity (presensitization) than comparable Caucasians, more often resulting in a positive

crossmatch that precludes transplantation from a given donor.[20,28] ESRD patients presensitized to 20% or more potential donors wait substantially longer for transplantation; an AA patient receiving a cadaveric transplant is 40% more likely than a Caucasian patient to have met this criterion.[18] Some attribute the difference in waiting times between AAs and Caucasians almost entirely to presensitization.[20]

There is, however, another immunologic variable at play: the relative weight of MHC matching in UNOS allocation algorithms. Wait-listed transplant candidates accumulate points. When a kidney becomes available, the candidate with the most points is designated to receive the organ. Based on the assumption that similarity in MHC antigen expression (i.e., matching) between donor and recipient optimizes outcomes, matching is the predominant variable determining allocation of cadaveric kidneys.[28] Racial implications arise due to the interaction among several immutable demographic and immunologic circumstances:

1. AAs are 12.6% of the population but account for 29% of new cases of ESRD and 37% of those undergoing dialysis.[4]
2. AAs with ESRD are less likely to receive kidneys from living donors.[24]
3. The donor pool is overwhelmingly Caucasian, with AAs donating at a rate commensurate with their representation in the general population.[29]
4. Some antigen species segregate almost exclusively according to race, with AAs having a greater HLA polymorphism.[30]
5. Allocation based on HLA matching diminishes interracial renal transplantation.[31]

However unintentional, the net result is preference for Caucasian transplant candidates. Data from the National Marrow Donor Program found AAs only 28% as likely as Caucasians to find a completely MHC-matched donor among 500,000 potentials.[30] The clinical implications are rather predictable. At UAB, despite a waiting list composed of more than 60% AAs, only 1 of 33 fully matched cadaver kidneys went to an AA recipient.

Takemoto reviewed the UNOS database from 1987 to September 1999 to determine the effect of sharing HLA-matched kidneys.[32] Although graft outcome was superior for well-matched grafts, AA patients received only 8% of 7614 matched kidneys. Conversely, 30% of mismatched kidneys go to AA recipients, approximating the frequency with which AA appear on the waiting list.[33]

Even proponents of the current allocation scheme concede that racial disparity exists,[34] but disagreement is centered on what benefits may be derived in exchange for modification of the system. Nevertheless, this question must be addressed because rapid advances in clinical transplantation have reduced the impact of matching on allograft survival.[35]

In the 1980s, when the core of the current point system originated, there was demonstrable incremental benefit of improved HLA compatibility between donor and recipient. The differential in 6-month graft survival between worst- and best-matched patients was 11% (76% vs. 87%), with a stepwise gradient for intermediate matches and a 64% longer half-life.[36] However, more recent data (1991–1997) show only marginal incremental improvement by reducing mismatches unless there is phenotypic identity (no mismatches). At 1 year, 82% of completely mismatched kidneys remain functional, versus 87% of kidneys with only 1 mismatch; corresponding half-lives improved only 30%. Since 1995, there has been remarkable improvement in short- and long-term graft survival across the entire match spectrum.[37]

Now, at least 2 groups of investigators estimate that the overall national impact of optimal HLA matching would be to improve graft survival by 1%-2%.[25,38] For AA recipients, benefits of HLA matching are even more elusive. Early reports documented no statistical benefit of matching among AAs, a finding attributed to the difficulty obtaining enough good matches in this population for meaningful analysis.[34] Current data indicate a benefit for AAs of 5%-6% (in graft survival at 3 years) in the few patients able to receive completely matched grafts, and improvement in allograft half-life from 5.4 to 8.4 years (the latter still less than the 9.7 years expected for Caucasian recipients of mismatched kidneys).[33] Overall, the primary benefit of the current allocation algorithm is conferred on the predominantly Caucasian recipients of completely matched grafts, with marginal impact on outcomes across other match grades, especially among AA recipients.

Possible Solutions

We are now faced with the daunting question of whether ethnic disparity in access to renal transplantation can be attenuated. A recent preliminary study by the Office of Civil Rights Region V found that culturally appropriate education materials were lacking for asymptomatic AAs at risk to develop ESRD.[39] Therefore, AA dialysis patients rarely received early diagnosis, treatment to prevent or delay ESRD, or early referral. In addition, there must be better education of primary care providers and nephrologists regarding the benefits of early referral. Without concerted efforts to remedy this problem, equal access will remain a specious promise.

The difficulties associated with ABO types and presensitization are likely to prove more daunting. Although eliminating the donor shortage would significantly alleviate ethnic disparities in the allocation process, there is no indication of an impending deluge of donated organs. Theoretically, more AA donors might provide more well-matched kidneys for AA transplant candidates.[40] However, given the prevalence of ESRD and MHC polymorphisms among AAs, this approach is unlikely to resolve the access issue.[26] Indeed, thanks to ongoing efforts to promote minority donation, the percentage of AA donors now corresponds to AA representation in the general population.[18]

Table 1 | **Current Point System (UNOS Policy 3.5—Organ Allocation) for Allocating Cadaver Kidneys in the Unites States[29]**

Criterion	Points Awarded
Zero antigen mismatch	Mandatory share
MHC mismatches	
0 BDR	7
1 BDR	5
2 BDR	2
Presensitization	
PRA ≥ 80%	4
Waiting time	
Longest wait (then fractional)	1
Each year on list	1
Age	
< 11 years	4
11-18 years	3

Inasmuch as the current UNOS algorithm perpetuates racial disparity, major changes may be necessary. Mandatory sharing of phenotypically identical (completely matched) kidneys should be retained: it improves transplant outcomes and, despite identifiable adverse impact on access for AAs, removes relatively few organs from the overall pool.[26,41] Beyond phenotypic identity, allocation of points for partial matching is less defensible.

A 1995 analysis confirmed that *matching points* were accumulated disproportionately by Caucasians and awarded for match quality that produced outcomes no better (2 mismatches) or worse (3 mismatches) than the national average.[28] In response, the algorithm was modified to its current form (Table 1); the impact of these modifications on minority access should be reassessed. A recent regional study involving the New England Organ Bank documented that elimination of points for partial matching indeed improved access for minorities without compromising outcomes.[42]

Other modifications are possible. Currently, UNOS allows local variances based on the concept of *acceptable mismatches* that, at least theoretically, preserve the benefits of matching while offering a more equitable allocation.[34] Although some remain unenthusiastic about the potential benefit of such an approach, evaluation of its merits is pending.[33] Alternatively, in light of increasing recognition of the influence of nonimmunologic factors (particularly early graft function and donor age) on long-term survival, it may be time to formulate a completely new paradigm for organ allocation.[43]

Conclusion

Formidable hurdles remain to equal access to renal transplantation for AAs. Although there remains a dearth of transplantable organs, the mechanism to transplant all appropriate candidates exists. To rectify this problem, several issues must be addressed:

1. Education of AAs to disease processes and prevention.
2. Improved access to basic health care for AAs.
3. Explain why the prevalence of ESRD is so high in the AA population.
4. Timely referral of appropriate ESRD patients to transplant centers.
5. Facilitate completion of pretransplantation evaluation.
6. Revisit national HLA matching criteria that result in longer waiting times for AAs.

With the advent of new immunosuppressive medications, acute rejection rates have fallen for all ethnicities. AAs have enjoyed improved early renal allograft survival, but long-term allograft survival remains sharply disparate between AAs and Caucasians. Renal transplantation is the modality of choice for ESRD. As such, ethnicity must not remain an obstacle to renal transplantation. Failure to address hindrances to equal access betrays the pioneering spirit of our predecessors and renders us impotent to care for those in the most need.

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Carlton J. Young, M.D.
Department of Surgery
University of Alabama at Birmingham
701 S. 19th
LHRB 728
Birmingham, Alabama, USA 35294
Tel.: 205.934.1393
Fax: 205.975.8452
email: carlton.young@ccc.uab.edu