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Social adaptability index predicts kidney transplant outcome: a single-center retrospective analysis

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Abstract

Background. Social adaptability index (SAI) is the composite index of socioeconomic status based upon employment status, education level, marital status, substance abuse and income. It has been used in the past to define populations at higher risk for inferior clinical outcomes. The objective of this retrospective study was to evaluate the association of the SAI with renal transplant outcome.

Methods. We used data from the clinical database at the Beth Israel Deaconess Medical Center Transplant Institute, supplemented with data from United Network for Organ Sharing for the years 2001–09. The association between SAI and graft loss and recipient mortality in renal transplant recipients was studied using Cox model in the entire study population as well as in the subgroups based on age, race, sex and diabetes status.

Results. We analyzed 533 end-stage renal disease patients (mean age at transplant 50.8 ± 11.8 years, 52.2% diabetics, 58.9% males, 71.1% White). Higher SAI on a continuous scale was associated with decreased risk of graft loss [hazard ratio (HR) 0.89, $P < 0.05$, per 1 point increment in the SAI] and decreased risk of recipient mortality (HR 0.84, $P < 0.01$, per 1 point increment in the SAI). Higher SAI was also significantly associated with decreased risk for graft loss/recipient mortality in some study subgroups (age 41–65 years, males, non-diabetics).

Conclusions. SAI has an association with graft and recipient survival in renal transplant recipients. It can be helpful in identifying patients at higher risk for inferior transplant outcome as a target population for potential intervention.

Keywords: allograft loss; renal graft outcome; social adaptability index; socioeconomic factors; transplant

Background

Historically, African-Americans [1], women [2] and residents of rural areas [3] are considered to be the groups that continue to experience health care disparities. However, since these populations at risk are defined based on the rigid criteria of race, gender or geographic location, they are more likely to represent a mix of genetic, socioeconomic and cultural factors. The effect of race, education and gender might be mediated by factors such as education, income, health insurance and employment. Studies have shown that low education level is associated with inferior health status [4]; income has substantial effects on mortality [5] and Medicaid beneficiaries are less likely to receive optimal treatment and more likely to experience inferior outcomes when compared with privately insured patients [6, 7]. Similarly, in the transplant population, socioeconomic variables such as employment status [8], education level [9], insurance status [9], marital status [10], substance abuse [11] and non-adherence [12] have been found to be associated with renal allograft loss. Furthermore, we recently demonstrated that education level noticeably reduces the association of race with inferior access to kidney transplantation [13].

Social adaptability index (SAI) is a composite index of various socioeconomic factors that could provide an overall measure of the 'social standing' of an individual and be helpful in accurately identifying individuals at the greatest health risk. SAI is comprised of five socioeconomic factors (employment status, education level, insurance status, marital status and substance abuse), each easily measured and quantified and each shown to be independently associated with allograft loss [8–11].

The role of SAI in clinical outcomes has been demonstrated in several patient groups, specifically in the general American population from the National Health and Nutrition Examination Survey data [14], patients with chronic kidney disease [15], including those on dialysis [16]. SAI

has also been shown to be significantly associated with access to renal transplantation [17]. SAI may be a more specific and sensitive indicator of socially disadvantaged groups prone to disparities rather than race, gender or geographic location. With that in mind, we aimed to test the association between the SAI and the renal transplant outcome. We hypothesize that the SAI has a significant and clinically relevant association with kidney allograft and recipient survival.

Materials and methods

Source of data

We used the data from OTTR (Organ Transplant Tracking Record) clinical database at the Beth Israel Deaconess Medical Center Transplant Institute, supplemented by the data from the United Network for Organ Sharing.

This study included all the patients who received a kidney transplant (including kidney/liver, kidney/pancreas and kidney/liver/pancreas) between 1 October 2001 and 30 September 2009. Patients who had multiple kidney transplants during the time period, the most recent kidney transplant date was used for calculating patient and graft survival. Patients under 18 years of age were excluded from the study.

As with other retrospective projects using data registry, one has to deal with the missing data. Specifically, some of components of SAI (education level, employment status, marital status, income level and substance abuse); human leukocyte antigen; recipient and donor body mass index (BMI) and panel reactive antibody counts had some missing entries. The most serious deficiency was the missing information for 55.7% ($n = 297$) of substance abuse data, 28.3% ($n = 151$) of panel-reactive antibodies, 13.9% ($n = 74$) of marital status data were missing. In the study population, 215 patients had complete information to calculate the SAI. Missing entries for categorical covariates (but not the primary variables of interest) were coded separately. Missing information for continuous variables ($n = 198$) was imputed using multiple imputations approach (standard procedure available in SAS: PROC MI and PROC MIANALYZE). Our initial approach was to exclude those records with missing information necessary for SAI calculation, but given limited sample size, we imputed the SAI components with the first value generated by multiple imputation procedure.

Outcomes

The primary outcome variables analyzed in this study were graft and recipient survival. Graft survival was defined as the time between the most recent kidney transplant procedure and the date of return to dialysis. Graft survival outcome was censored for recipient death. Recipient survival was defined as the time between the most recent kidney transplant procedure and the recipient death.

Primary variable of interest

The SAI was our primary variable of interest and has been described in detail in the past [14–17]. Briefly, the SAI is calculated based on five characteristics of socioeconomic status, each graded on a scale of 0–3 without additional weighting, as described below. Factors selected for SAI calculations were based on the previous studies of socioeconomic predictors of transplant outcome. Each of the five components of the SAI were studied separately in a series of retrospective analyses [8, 10, 11, 18]. In addition, we validated SAI in the general US population [14] and also in the cohorts of patients with chronic kidney disease [15] and those on dialysis [16]. Furthermore, the SAI demonstrated a strong association with access to kidney transplantation [17]. Despite hypothetical colinearity between SAI components, they actually demonstrated an independent association with the outcome and roughly equal effect size in their association with survival [14]. Based on that and also on the practicality of the index, the factors were weighted equally in the calculation of SAI.

Employment status: 0 = unemployed, not working due to medical conditions, not working by choice; 1 = retired; 2 = working part time; 3 = working full time.

Marital status: 0 = not married (including never been married and widowed); 1 = divorced or separated; 2 = married without children; 3 = married with children.

Education level: 0 = did not complete high school; 1 = high school graduate; 2 = college graduate; 3 = post-college education or doctorate degree.

Substance abuse: 0 = abusing drugs, alcohol and tobacco; 1 = abusing two of three substances; 2 = abusing one of three substances; 3 = none.

Income: In this particular study, we did not have specific information of patient income, therefore, the medical insurance status was used as a surrogate for income: 1 = Medicaid, 2 = Medicare, 3 = private insurance.

The SAI was calculated as a sum of grades for employment status, marital status, education level, substance abuse and level of income; therefore, the SAI scores in our dataset ranged from 0 to 15. In addition, we evaluated SAI as a categorical variable and divided SAI into two groups using the cut-point value of SAI = 9 (based on median SAI value in the study population).

Covariates

We used the following two covariates in multivariate analysis: recipient variables: age, gender, race, BMI, comorbid conditions (diabetes, hypertension, coronary artery disease, congestive heart failure), cause of end-stage renal disease (diabetes mellitus, hypertension, glomerulonephritis or other/unknown), total number of transplants, primary source of payment for medical services, number of human leukocyte antigen matches between donor and recipient, peak panel reactive antibody level (%) and induction and maintenance immunosuppression; donor variables: age, gender, race, BMI, donor type (living related, living unrelated or deceased).

Statistical analysis

Means and SDs were used to summarize continuous variables with normal distribution. Categorical variables were summarized as percentage of total. Cox model was used for time to outcome analysis. As measures of association between SAI and outcome variables, we estimated hazard ratios (HRs) and 95% confidence intervals. We tested proportionality assumption in the Cox models with graft survival and recipient survival as outcomes and the SAI in the continuous format. We used time-varying covariates for the SAI variable and demonstrated no significant deviations from the proportionality assumptions.

The data collected were analyzed using the SAS software version 9.2 (SAS Institute, Cary, NC).

Results

Baseline characteristics

The study population included 533 transplant recipients. Of 533 patients included in our study, 401 patients had only one kidney transplant, 52 patients had multiple kidney transplants, 21 had both kidney and liver transplant, 58 had both kidney and pancreas and 1 patient had kidney, pancreas and liver transplants. The study population had a mean age at transplant of 50.8 ± 11.8 years. For the purpose of subgroup analysis, patients were divided into three age groups using arbitrarily selected cut-points: 18.2% were 18–40 years, 69.4% were 41–65 years and 12.4% were >65 years. Of the study population, 58.9% were males, 71.1% white, 18.8% African-American and 5.6% were Hispanic; 52.2% of the study group had diabetes. The calculated mean SAI was 9.2 ± 2.5. Baseline characteristics of the study population are presented in Table 1.

Survival analysis in the entire study population

SAI was evaluated as a continuous variable in the entire study population using a proportional hazard model adjusted for potential confounding factors (Table 2). In our primary analysis, higher SAI was found to be associated with

Table 1. Baseline characteristics of the study population[a]

	Entire study population ($n = 533$)	SAI Group 1 (≤ 9) ($n = 269$)	SAI Group 2 (>9) ($n = 264$)	P-value
Age at transplant (years)	50.8 (11.8)	50.4 (12.6)	51.3 (10.8)	0.330
Age categories (years)				
18–40 years old	18.2	10.3	7.9	0.170
41–65 years old	69.4	33.2	36.2	0.070
>65 years old	12.4	6.9	5.4	0.330
Race/ethnicity				
Non-Hispanic white	71.1	33.2	37.9	<0.010
Non-Hispanic African-American	18.8	12.8	6	<0.001
Hispanic	5.6	3	2.6	0.750
Other	4.5	1.5	3.0	0.080
Sex				
Female	41.1	23.8	17.3	<0.010
Male	58.9	26.6	32.3	<0.010
BMI (kg/m^2)	27.2 (5.8)	27.3 (5.8)	27 (5.8)	0.550
Diabetes				
Yes	52.2	27.2	25.0	0.410
No	47.8	23.8	49.6	
Education level				
<12 years	5.6	4.9	0.7	<0.001
High school graduate	59.1	36.0	23.1	
Some college	27.4	8.6	18.8	
College graduate	7.9	0.9	7.0	
Marital status				
Not married	24.8	21.4	3.4	<0.001
Divorced or separated	12.9	7.5	5.4	0.180
Married without children	41.5	15.6	25.9	<0.001
Married with children	20.8	6.0	14.8	<0.001
Employment status				
Not working (but not retired by age)	46.3	37.5	8.8	<0.001
Retired	13.5	6.9	6.6	0.870
Working part time	6.4	2.4	3.9	0.140
Working full time	33.8	3.6	30.2	<0.001
Substance abuse				
Tobacco, alcohol and drugs	1.5	0.6	0.9	0.460
Two of three above	16.1	11.8	4.3	<0.001
One of three above	45.0	24.8	20.3	0.060
No substance abuse	37.3	13.3	24.0	<0.001
Insurance				
Medicaid	3.9	3.8	0.2	<0.001
Medicare	50.8	35.8	15.0	
Private insurance	45.2	10.9	34.3	
SAI	9.2 (2.5)	7.2 (1.4)	11.3 (1.5)	

[a]Continuous variables presented as mean (and SDs), categorical variables presented as percentage of total.

Table 2. The association between SAI and graft loss/recipient mortality in the entire study population by proportional hazards model[a]

	Graft loss		Recipient mortality	
	Adjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Total SAI score	0.89 (0.82–0.98)	<0.018	0.84 (0.74–0.95)	<0.005
Age at transplant (years)	1.01 (0.99–1.03)	0.413	1.04 (1.01–1.08)	<0.004
Sex: female	Reference			
Sex: male	1.51 (0.96–2.39)	0.075	1.84 (1.02–3.32)	<0.042
Race: non-Hispanic African-American	Reference			
Race: non-Hispanic white	0.94 (0.55–1.62)	0.834	1.91 (0.85–4.29)	0.115
Race: Hispanic	0.67 (0.19–2.33)	0.526	1.33 (0.27–6.49)	0.722
Race: Other	0.62 (0.14–279)	0.538	2.47 (0.49–2.47)	0.273
History of diabetes (compared to history of no diabetes)	1.08 (0.60–1.95)	0.790	0.93 (0.42–2.08)	0.863
BMI (kg/m^2)	0.99 (0.95–1.03)	0.547	0.97 (0.92–1.03)	0.323

[a]The Cox model was adjusted for human leukocyte antigen match level, diabetes, hypertension, coronary artery disease, congestive heart failure, cause of end-stage renal disease, peak panel reactive antibody gender, recipient (BMI, age, race) and donor (BMI, age, race) parameters.

decreased risk of graft loss (HR 0.89, P < 0.018 per 1 point increment in SAI) and decreased risk of recipient mortality (HR 0.84, P < 0.005 per 1 point increment in SAI) (Table 2). In a follow-up analysis trying to elicit the mechanism of the observed association, we included preemptive transplant as a covariate in the model. We found that the effect size of association decreased (HR 0.91, P < 0.058; HR 0.86, P < 0.01 per 1 point increment in SAI for graft loss and recipient mortality, respectively), indicating preemptive transplantation being one of the potential mechanisms of an association between the SAI and outcomes.

We also evaluated SAI as a categorical variable and divided SAI into two groups (SAI ≤9 and SAI >9). Using patients with SAI ≤9 as a reference, those with SAI >9 demonstrated a statistically significant association with decreased risk of recipient mortality (HR 0.54, P < 0.037). Using these two SAI groups, Kaplan–Meyer plots were constructed, suggesting an increase in graft survival (P < 0.001) and recipient survival (P < 0.001) associated with higher SAI (Figures 1 and 2).

Survival analysis in the subgroups

The association between the SAI and transplant outcome was also evaluated in several subgroups (Table 3). Higher SAI was shown to be associated with statistically significant reduction in patient mortality in age groups 41–65 years (HR 0.50, P < 0.049 per 1 point increment in SAI), however, this association has not been demonstrated in patients with age of 18–40 years (HR 1.55, P = 0.63) and in patients >65 years (HR 0.61, P = 0.51). Higher SAI was associated with a significant reduction in patient mortality in males (HR 0.49, P < 0.038 per 1 point increment in SAI) but failed to reach statistical significance in females (HR 0.89, P = 0.87). In addition, the SAI had significant association with decreased recipient mortality in patients with no history of diabetes (HR 0.34, P < 0.043 per 1 point increment in SAI) but not in the patients with positive history of diabetes (HR 0.74, P = 0.45). The association of SAI and patient mortality was not found to be significant in any of the racial subgroups. Additionally, there was no statistical significant association of SAI and graft loss in any of the subgroups.

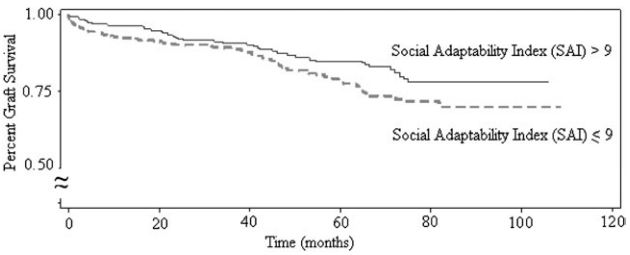

Fig. 1. Kaplan–Meier curves of the patients comparing graft survival between the group of patients with social adaptability index (SAI) ≤9 and those with SAI >9. Higher SAI was associated with superior graft survival (P-value <0.001). Note scale break introduced in Y-axis.

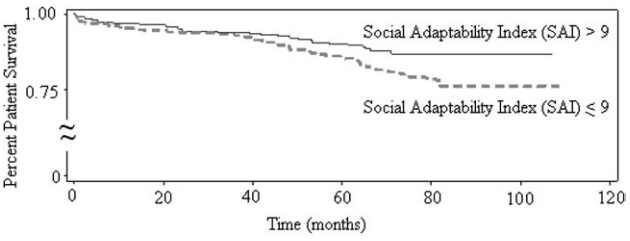

Fig. 2. Kaplan-Meier curves of the patients comparing survival between the group of patients with social adaptability index (SAI) ≤ 9 and those with SAI > 9. Higher SAI was associated with superior patient survival (P-value <0.001). Note scale break introduced in Y-axis.

Discussion

Improvements in organ preservation methods, advanced surgical techniques, availability of improved immunosuppressive agents and post-operative care have resulted in 1 year graft survival rates exceeding 90% in most transplant centers in the USA [19]. Recipient and graft survival rates are affected by a number of pre-transplantation and post-transplantation factors that have been studied in the past. Pre-transplantation factors may include donor characteristics, such as age, sex, donation post-cardiac death or post-brain death, pre-existing donor hypertension; and recipient factors such as age, BMI, number of human leukocyte antigen match and duration of pre-transplant dialysis [20–23]. Post-transplant causes include drug toxicity, viral infections, recurrent disease and as a result of the above chronic allograft nephropathy [24]. Besides these physiological factors, there are socioeconomic predictors that play a significant role in altering transplant outcomes. In the past, it has been shown that females [2], people living in rural areas [3] and African-Americans [1] have inferior transplant outcomes. Furthermore, previous studies in the transplant population have shown that various socioeconomic variables such as employment status [8], education level [9], insurance status [9], marital status [10], substance abuse [11] and non-adherence [12] have been found to be associated with renal allograft loss.

SAI being an integrative measure of the socioeconomic status reflects an individual's life patterns starting from obtaining education, securing a job, making reasonable income, having a support system and abstaining from any kind of substance abuse [14–17] (Figure 3). Theoretically, the SAI might be able to identify the group of patients at risk for disparities and inferior clinical outcomes better than individual indicators of race, gender or geographic location. In this study using a proportional hazards model, we demonstrated that higher SAI levels are associated with a significant reduction in risks for graft loss and recipient mortality. The trend is true for the entire study population and also for some of the subgroups. We hypothesize that factors leading to lower SAI and put recipients in a high-risk group for graft failure can be classified as extrinsic factors and those intrinsically associated with the individual (Figure 3) [15].

Based on this, the association observed between the SAI and clinical outcome may be explained by several potential mechanisms.

(1) Firstly, there are potential health care barriers that might be present in the patients with low SAI. It is quite

Table 3. The association between SAI and recipient survival in the entire population and study subgroups by proportional hazards model[a]

	Graft loss		Recipient mortality	
	Adjusted HR (95% CI) SAI Group 2 (SAI score >9) comparing to SAI Group 1 (SAI score ≤9)	P-value	Adjusted HR (95% CI) SAI Group 2 (SAI score >9) comparing to SAI Group 1 (SAI score ≤9)	P-value
SAI in the entire study population	0.65 (0.40–1.03)	0.069	0.54 (0.30–0.96)	<0.037
SAI in age subcategories (years)				
SAI in patients 18–40 years old	0.57 (0.10–3.33)	0.533	1.55 (0.26–9.12)	0.627
SAI in patients 41–65 years old	0.62 (0.35–1.08)	0.094	0.50 (0.25–0.99)	<0.049
SAI in patients >65 years old	0.92 (0.21–4.09)	0.909	0.61 (0.14–2.60)	0.509
SAI in subgroups divided by race				
SAI in non-Hispanic African-American	0.37 (0.11–1.20)	0.100	0.13 (0.01–3.14)	0.211
SAI in non-Hispanic white	0.76 (0.43–1.33)	0.333	0.63 (0.33–1.23)	0.181
SAI in subgroups divided by diabetes status				
SAI in subjects with no diabetes	0.53 (0.26–1.07)	0.078	0.34 (0.12–0.96)	<0.043
SAI in subjects with diabetes	0.75 (0.37–1.50)	0.418	0.74 (0.34–1.62)	0.450
SAI in subgroups divided by sex				
SAI in males	0.63 (0.37–1.08)	0.091	0.49 (0.25–0.96)	<0.038
SAI in females	0.77 (0.29–2.02)	0.598	0.89 (0.24–3.38)	0.869

[a]The data presented in the table was derived from five separate Cox models. Only HRs for SAI are indicated in the table. Each model was adjusted for human leukocyte antigen match level, diabetes, hypertension, coronary artery disease, congestive heart failure, cause of end-stage renal disease, peak panel reactive antibody gender, recipient (age, race, BMI) and donor (age, race, BMI) parameters.

possible that low SAI patients are unable to pay for their medications or may have poor access to health care facilities. In resolving objective barriers, problem-solving abilities of the individual become important. On the other hand, there is a hypothetical association between the SAI and problem-solving abilities. For example, it has been demonstrated that college graduates suggested more solutions for everyday problems as compared to the ones who had not completed college [25]. In addition, problem-solving abilities are predictive of medication adherence [26]. It has also been shown that early access to transplantation may be dependent on education, SAI, substance abuse and marital status [13, 17, 27, 28].

(2) Lower health literacy might be an issue. It is likely that patients with low SAI may have poor cognitive skills and due to poor health literacy, they are unable to keep up with their regular follow-up with their physicians and understand the complex immunosuppressive regimen. Additionally, previous studies have shown that the patients with low literacy level often feel shy admitting their inferior reading abilities and fail to seek the required help to understand and ask questions regarding their health [29]. Related to that might be a hypothetical association between lower SAI and inferior self-care behavior defined as 'the range of behavior undertaken by individuals to promote or restore their health' [30].

(3) It is also possible (although this has not been demonstrated) that patients with lower SAI might have lower degree of adherence to medical regimen.

(4) Subjects with lower SAI might also have a less developed social network. Specifically, a 'healthier' social network might provide better access to living donors and preemptive transplantation [31]. In a study by Coorey *et al.* [32], 25% of the patients said that living donors were suggested by people they know in their social network rather than by health care professionals. Interestingly, when preemptive transplant was included in our Cox model, the association between SAI and graft survival lost its statistical significance, indicating that preemptive transplantation might be one of the mechanisms of the observed phenomenon. In addition, the role of a social network in changes in behavior and an individual's health has been demonstrated in the past [33, 34].

(5) In addition to above-mentioned issues, it is conceivable that patients with low SAI may suffer from various psychological disorders (e.g. depression [35–37]) resulting in inferior clinical outcome. Furthermore, a study by Cukor *et al.* [38] demonstrated the association between depression and medication adherence in kidney transplant recipients.

Practical utility of the SAI deserves specific discussion. This composite index can help practitioners to identify high-risk patients who are likely to have inferior outcomes after renal transplantation. The SAI has been demonstrated in different populations to be a robust predictor of clinical outcome. The effect of the SAI has been previously demonstrated in different patient subgroups and it is 'dose dependent', meaning there is an incremental improvement in the outcome associated with higher SAI scores. We suggest that the SAI, as a composite score, can potentially be used in practice not only to identify patients with disadvantaged status but also quantify the degree of this status with objective measure. An advantage of SAI is that it allows researchers and practitioners to be more specific in identifying the population at risk for health care disparities and inferior clinical outcome. It is not clear what the mechanism of the association is; however, we hypothesize that it might be mediated by lower level of adherence, lower

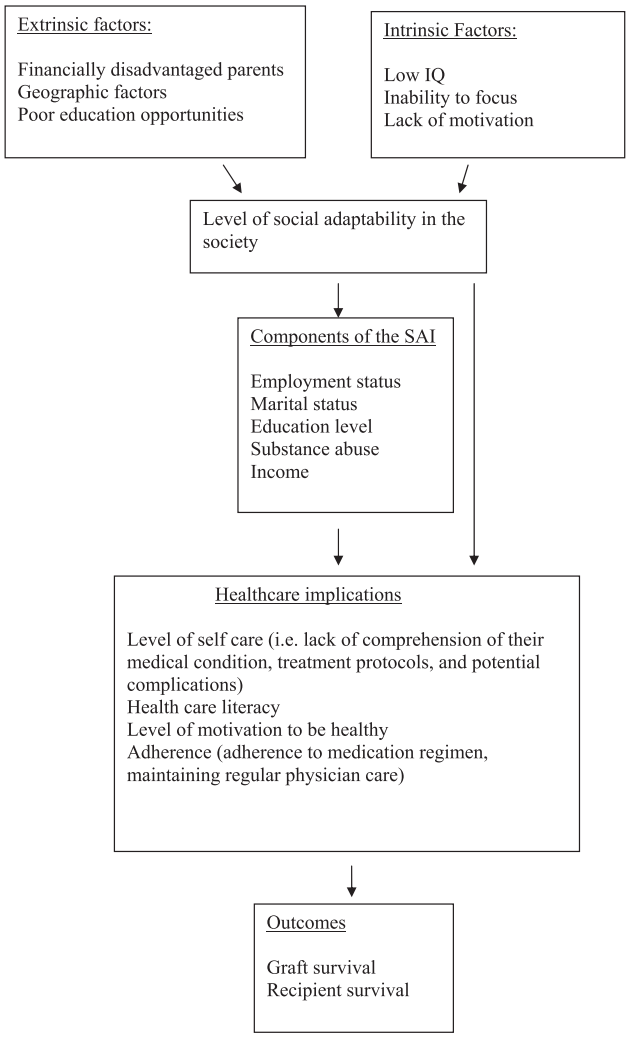

Fig. 3. In this model, social adaptability is a measure of individual factors either intrinsic or extrinsic to the individual. The level of social adaptability can be measured by five factors and combined in a social adaptability index (SAI). The level of social adaptability leads to health care implications, in particular, level of self-care, health care literacy and adherence to medical regimen. Those health care factors lead to specific outcomes, such as graft and recipient survival.

health literacy, possibly less developed social structure and greater degree of objective barriers to care. Therefore, further validation of SAI in transplant population, studying its association with adherence, health literacy and objective barriers will have practical implication for the future research and practice.

The important question becomes what would be an effective intervention to address these issues in patients with lower SAI score. Of course, this study did not address it.

Subsequently, interventions can be undertaken early in the course to improve graft and recipient survival. However, in this project, we did not address the role of any potential interventions. Any discussion on this subject would be purely hypothetical. It has been documented and validated in previous studies that patients with a higher education level have superior graft and recipient survival [9]. We have also demonstrated that education modifies the degree of racial disparities in kidney transplant outcome [13]. However, these studies are retrospective and only tangential to the idea of using education program as an intervention. There is a body of literature demonstrating the effect (or lack of thereof) of education approach [39]. We tend to believe that complex intervention addressing several potential mediators, such as poor adherence and health literacy, limited social structure as well as objective barriers has a potential of being effective.

There are a few limitations in our study of which the reader should be aware. Because our analysis is retrospective, it establishes association and not causality, which can only be addressed by a prospective study. Furthermore, there is a possibility of reverse causality [40] that may have confounded our results as patients with poor health status may drift toward poor SAI as they lose their jobs, families, income or begin substance abuse. However, in our analysis, the association between SAI and outcome was independent of comorbid conditions. Furthermore, previous reports of associations between socioeconomic factors and clinical outcome [11, 15–17, 18, 27, 28, 41] might be suggestive of potential cause–effect relationship. In this case, for practical purposes, SAI would still be a good indicator of the population at risk for inferior outcome. Another potential limitation of the analysis is being a single-center study. However, the patient population at the Beth Israel Deaconess Medical Center represents a heterogeneous mix of races, genders, urban and rural recipients, future work should focus on multicenter databases with less missing values to confirm the association of SAI across the different (US and non-US) patient population.

In conclusion, SAI has an association with graft and recipient survival in renal transplant recipients and might be used as a tool for the researchers and clinicians in accurately identifying patients at increased risk of inferior transplant outcomes. Once identified, strategies can be developed for these high-risk patients to improve graft and recipient survival.

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Conflict of interest statement. None declared.

Authors contribution: J.G., M.K., G.S.S., R.D., J.R.R., M.P., D.W.H., A.S.G.-R.—participated in the writing of the paper. J.G., M.K., H.T., G.S.S., R.D., J.R.R., M.P., D.W.H., A.S.G.-R.—participated in research design and H.T., B.C.B., A.S.G.-R.—participated in data analysis.

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