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Adherence to the Medical Regimen During the First Two Years After Lung Transplantation

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Abstract

Background—Despite the importance of adherence to the medical regimen for maximizing health after lung transplantation, no prospective studies report on rates or risk factors for nonadherence in this patient population. Whether adherence levels differ in lung versus other types of transplant recipients is unknown.

Methods—A total of 178 lung recipients and a comparison group of 126 heart recipients were enrolled. Adherence in nine areas was assessed in separate patient and family caregiver interviews 2, 7, 12, 18, and 24 months posttransplant. Potential risk factors for nonadherence were obtained at the initial assessment.

Results—Cumulative incidence rates of persistent nonadherence (i.e., nonadherence at ≥2 consecutive assessments) were significantly lower ($P < 0.05$) in lung recipients than heart recipients for taking immunosuppressants (13% non-adherent vs. 21%, respectively), diet (34% vs. 56%), and smoking (1% vs. 8%). Lung recipients had significantly higher persistent nonadherence to completing blood work (28% vs. 17%) and monitoring blood pressure (70% vs. 59%). They had a high rate of spirometry nonadherence (62%; not measured in heart recipients). The groups did not differ in nonadherence to attending clinic appointments (27%), exercise (44%), or alcohol limitations (7%). In both groups, poor caregiver support and having only public insurance (e.g., Medicaid) increased nonadherence risk in all areas.

Conclusions—Lung recipients were neither uniformly better nor worse than heart recipients in adhering to their regimen. Lung recipients have particular difficulty with some home monitoring

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activities. Strategies to maximize adherence in both groups should build on caregiver support and on strengthening financial resources for patient healthcare requirements.

Keywords

Adherence; Lung transplantation; Heart transplantation; Risk factors

The rate of lung transplantation has increased markedly in both the United States and worldwide within the last decade (1–3). This increase has coincided with improvements in posttransplant survival (1, 2). As for other types of organ recipients, lung recipients' adherence to the posttransplant medical regimen—the degree to which patients' behavior coincides with posttransplant medical recommendations (4, 5)—is important for maintaining health (6 –10). Indeed, adherence to the regimen is of heightened concern in lung transplantation relative to other types of transplantation because of the greater sensitivity of lung grafts to infection and both acute and chronic rejection (6, 9). Thus, careful adherence in areas such as taking immunosuppressants, attending clinic appointments, and home monitoring (e.g., spirometry) are widely agreed to be critical to minimize morbidity and mortality after lung transplantation (6, 9, 11).

It is striking, therefore, that only a handful of investigations have examined nonadherence rates in lung recipients. In a meta-analysis of the adherence literature in adult transplantation (12), we found that of the 147 studies published through 2005, merely 3% (n = 5) reported on lung recipients (10, 13–16). Aside from qualitative work (17), we have identified only one additional empirical study of adherence in lung recipients published since our meta-analysis (18). These few reports are all cross-sectional surveys, and most consider adherence to only a single component of the posttransplant regimen (e.g., substance use, or taking medications) (10, 13–16, 18). While our meta-analysis identified important differences in adherence rates across different types of transplant recipients (kidney vs. liver vs. heart), we could not include lung recipient reports in these comparisons due to the very small number of such studies. No study of adherence in lung recipients has itself included comparison groups of other transplant recipients.

In short, little is known about rates of nonadherence to the full range of components of the medical regimen after lung transplantation or whether these rates differ from those observed in other types of transplant recipients. Moreover, risk factors for nonadherence have yet to be determined prospectively in lung recipients (12, 19, 20). Absent risk factor identification, it is difficult to develop interventions to prevent or limit nonadherence.

The purpose of the present report is to determine both the rates and risk factors for nonadherence in lung recipients. We included a comparison group of heart transplant recipients. We judged that this would constitute the most appropriate comparison group since heart recipients are the only other major group of thoracic transplant patients, both groups generally receive care from the same or overlapping teams posttransplant, and they are required to adhere to similarly multifaceted medical regimens (19, 20).

Our study, therefore, prospectively evaluated a) whether lung recipients differed from heart recipients in the nature, rate, and pattern of nonadherence to each component of the medical regimen during the first 2 years posttransplant; and b) the extent to which persistent nonadherence to each component was predicted by a set of potential risk factors. We adopted the World Health Organization (WHO) conceptualization of risk factors (5), which posits that factors from multiple medical and psychosocial domains should predict nonadherence outcomes.

METHODS

Respondents

All adults (aged ≥18) receiving their first lung or heart transplant were contacted at 2 months posttransplant (n = 327). They were transplanted between November 1999 and August 2004 in the Cardiothoracic Transplantation (CT) Program, University of Pittsburgh Medical Center. (In the CT Program, a single nurse coordinator supervisor works with all CT physicians to monitor all of the clinical follow-up activities of individual nurse coordinators for both lung and heart recipients.) The sample refusal rate was 7.0% (n = 23). The 304 individuals enrolled (178 lung recipients; 126 heart recipients) did not differ from those who refused on type of transplant or demographic characteristics.

Across the study follow-up period, 30 of the 304 patients (9.9%, 19 lung recipients, 11 heart recipients) refused to continue their participation and 35 died (11.5%, 32 lung recipients, 3 heart recipients). Lung recipients were no more likely to drop out than heart recipients (χ^2(df = 1) = 0.31, P = 0.576), but they were more likely to be lost due to death (χ^2(continuity corrected; df = 1) = 16.12, P < .001). This difference is addressed in analyses below. There were no large or statistically significant differences between reason for loss to follow-up and any other variable.

Table 1 presents demographic and transplant-related characteristics for the sample. Patients were similar to the respective U.S. populations of lung and heart recipients transplanted during the same time period on distributions of gender, age, ethnicity, and indication for transplant (21). The significant between-group differences in Table 1 for several of these variables are also consistent with national data and led us to consider these variables as possible contributors to between-group differences in adherence. Although lung patients were hospitalized longer posttransplant than heart recipients, the groups were similar on functional status (Karnofsky Index) (22, 23) and proportions experiencing treated rejection episodes in the early posttransplant period.

Procedure

The protocol had Institutional Review Board approval. All respondents gave written informed consent. Data on patient adherence and psychosocial status were collected in individual 90- to 120-minute structured interviews conducted on three occasions during the first year posttransplant (2, 7, and 12 months) and two occasions thereafter (18 and 24 months). Interviews were conducted by trained interviewers with master's degrees in mental health or behavioral disciplines.

When possible, interviews were scheduled to coincide with routine outpatient CT Program evaluations. Otherwise, interviews were conducted in patients' homes or by telephone. There were no significant differences due to interview mode for any variable. Each recipient's primary family caregiver (the individual identified by the patient as providing the most daily care and assistance; the spouse for 66% of the sample) was also interviewed at each time point about the patient's adherence. Information on transplant-related characteristics (e.g., indication for transplant) was obtained from medical records.

Instruments

Nonadherence to the Posttransplant Medical Regimen—Meta-analyses (12, 24, 25) show that self-report (alone or combined with other assessment strategies, such as self-report+informant report) is more likely to yield evidence of nonadherence than any other approach (e.g., reliance on indirect methods such as medication monitoring or biologic measures). Other commentaries also recommend combined strategies (26). Thus, we

assessed patient adherence through a combination of patient and family caregiver report. We used the Health Habits Survey (patient and caregiver versions) that we developed and administered previously (27, 28). Its items derive from those originally administered to kidney recipients (29); the items were adapted to requirements specific to cardiothoracic recipients. The survey was designed using Feinstein's "clinimetrics" approach (30, 31) to maximize accurate reporting of adherence (i.e., attention to item wording and responses scales to encourage truthful answers; use of trained interviewers who took care to establish rapport with respondents). Regarding psychometric properties, interviewer interrater reliability exceeded an intraclass correlation of 0.97 on each item for the present sample. We have previously demonstrated that the items had predictive validity for health outcomes in heart recipients (28).

The survey assessed posttransplant nonadherence in nine areas: a) taking the primary immunosuppressant (cyclosporine or tacrolimus); b) clinic appointment attendance; c) completing blood work; d) home blood pressure monitoring; e) following a prescribed diet; f) following a prescribed exercise plan; g) abstaining from tobacco use; h) limiting alcohol consumption; and i) performing home spirometry (lung recipients only). Questions inquired about each area either since transplant (at the 2-month assessment) or since the previous assessment (at subsequent interviews). Although questions used an ordinal response format (e.g., respondents indicated how often patients missed taking medications: daily, several times a week, several times a month, etc.), responses on each item were dichotomized to indicate whether recipients adhered to the minimum level acceptable by the CT Program. These levels are specified in Table 2.

Recipients and caregivers showed high concordance in their reports of recipients' adherence in each area (85–97% at each assessment). To arrive at a single measure of nonadherence for each area, we judged that respondents were more likely to underreport nonadherence than to state that a recipient was nonadherent when he/she was in fact adherent. Thus, we took any report of nonadherence, whether from recipient or caregiver, as evidence of nonadherence in a given area.

Potential Risk Factors

These variables represented the five classes of factors in the WHO conceptualization of potential determinants of nonadherence (5).

Sociodemographic Characteristics—We obtained information on patients' gender, age, ethnicity, education, and income at the initial interview.

Healthcare System Access Factors—Distance of the patient's home address from the transplant center was determined. Insurance status at transplant was obtained from medical records and coded according to whether patients relied exclusively on public insurance (e.g., Medicaid).

Transplant-Related Health Characteristics—Patients' health status during the first 2 months of recovery was considered. Duration of posttransplant hospitalization and occurrence of treated acute graft rejection in the first 2 months were extracted from medical records. Physical functional status was assessed by the interviewers using the Karnofsky Index at 2 months posttransplant. Cognitive status was evaluated at the 2-month interview with the Mini-Mental State Exam (32). We also obtained pretransplant lifetime history of mood or anxiety disorders (major depression, generalized anxiety disorder, panic disorder) via the Structured Clinical Interview for DSM-IV (33) at the initial assessment.

Posttransplant Treatment-Related Factors—At the initial interview, patients answered a series of questions about effects of treatment. This included one item about whether or not they felt unhappy with any medications' effects on their physical appearance (29), and additional items about whether or not they felt that each component of their medical regimen (e.g., taking immunosuppressants, attending clinic appointments) interfered with daily life. These latter items were adapted from an instrument measuring opinions about medical treatment (34). Their primary maintenance immunosuppressant (cyclosporine or tacrolimus) was obtained from medical records.

Patient-Related Psychosocial Characteristics—Two types of characteristics, intrapersonal resources and interpersonal resources, were considered (19). Scales assessing each were administered at the initial interview. All have well-established psychometric properties. Internal consistency reliability coefficients reported below pertain to the present sample.

Seven measures of intrapersonal resources were administered. Feelings of emotional well-being were assessed with the depression, anxiety, and anger-hostility subscales of the Symptom Checklist 90 (35) (Cronbach's alpha = 0.88, 0.84, 0.84, respectively). To identify clinically significant distress on each subscale, individuals were categorized on each according to whether their scores were more than 1 SD above the gender-specific normative mean (i.e., higher than 84% of the normative sample) (35).

Optimism was measured with the Life Orientation Test (36), which assesses expectations about the future (alpha = 0.75). The Multidimensional Health Locus of Control Scale (37) measured the extent to which respondents believed that a) they could influence their health outcomes (internal locus of control, alpha = 0.65); b) their health outcomes were due to healthcare professionals (care provider locus of control, alpha = 0.74); and c) their health outcomes occurred by chance (chance locus of control, alpha = 0.71).

Two areas of interpersonal resources were assessed. The supportiveness (both emotionally and practically) of the recipient's relationship with their primary family caregiver was assessed with a measure adapted from Spanier (38) and Pearlin and Schooler (39) and used in other studies (40, 41) (alpha = 0.92). Friend support was assessed with a scale concerning the degree to which respondents believed they could rely on friends for emotional and practical support (42) (alpha = 0.89). These two measures had skewed distributions; scores were dichotomized to identify respondents with the poorest support (lower third of the distribution) relative to remaining respondents.

Statistical Analyses

Descriptive data were examined regarding proportions of patients who were nonadherent at each assessment. Survival analysis, using a life-table approach (43), was used to determine the cumulative incidence of persistent nonadherence (defined as nonadherence at ≥2 consecutive assessments). We used life-table rather than Kaplan-Meier methods because, by the design of this clinical epidemiologic study, individuals reported on nonadherence occurring during the period since last assessment. The survival analyses included all persons until the point of censoring.

The associations of potential risk factors with whether or not patients experienced persistent nonadherence during the 2-year study period were examined via bivariate analyses, followed by logistic regression analysis. We considered 24 potential risk factors. Given our total sample size, we maintained an appropriate respondent-to-variable ratio within the recommended range of 10:1 to 15:1 (44). Before multivariate analyses, risk factors were examined and found to adequately meet analytic assumptions (44).

RESULTS

Cross-Sectional Rates of Nonadherence

Table 2 shows the proportions of lung and heart recipients who were nonadherent in each area at each time point, based on data from all recipients available at the time point. Lung recipients showed significantly lower nonadherence rates than heart recipients in the areas of diet and tobacco use at most or all assessments. Lung recipients were significantly more nonadherent than heart recipients in monitoring blood pressure early posttransplant, but the groups did not differ by the final assessment.

Table 2 also shows that a) at each timepoint, nonadherence rates varied widely across the areas assessed, and b) the proportion of nonadherent patients increased from earlier to later assessments in all areas except diet (see tests for differences across assessments, last column of table). Despite uniform increases, the areas of nonadherence themselves were not highly intercorrelated among either lung or heart recipients. For example, at the 2-month assessment, the median intercorrelation among the nine nonadherence areas was 0.06 with an interquartile range of 0.02– 0.09 and (excluding the one outlier noted below) an absolute range of 0.00 – 0.15. Intercorrelations at other assessments were similarly small. The single exception was that nonadherence to spirometry was moderately correlated with nonadherence to blood pressure monitoring at each of the five assessments (median r = 0.36).

Longitudinal Pattern of Onset of Persistent Nonadherence

The data in Table 2 are cross-sectional “snapshots” of nonadherence at individual assessments. Persistent nonadherence across multiple assessments, and its timing of onset, may be of greater clinical significance than behavior at any single evaluation. Thus, for each area of the regimen, we identified individuals showing nonadherence at ≥2 consecutive assessments. Given our assessment schedule, this corresponds to nonadherence enduring for 6 months or more. Survival analyses comparing the timing of onset of persistent nonadherence (i.e., cumulative incidence rates) in lung versus heart recipients are shown in Figure 1. For example, Figure 1A shows that lung recipients had a significantly lower cumulative incidence of persistent nonadherence to the primary immunosuppressant by 2 years posttransplant (13%), compared to heart recipients (21%; Wilcoxon $\chi^2 = 4.46$, $P = 0.035$). Lung recipients were also significantly less likely to become persistently nonadherent in the areas of diet (Fig. 1F) and tobacco use (Fig. 1G). However, lung recipients showed significantly greater incidence rates of persistent nonadherence to completing blood work (Fig. 1C) and monitoring blood pressure (Fig. 1D). They had a high rate of persistent nonadherence to home spirometry (cumulative incidence, 62%; Fig. 1I).

To address the possibility that the differential death rates between lung and heart recipient were responsible for these findings, we repeated the survival analyses including only the recipients who remained alive throughout the study period (and among whom loss to follow-up was not associated with type of transplant). Results were identical to those described above (i.e., the shape of the incidence curves and the final rates were unchanged).

Risk Factors for Persistent Nonadherence

To limit the likelihood of type I error, we took several steps to control the number of tests examining risk factor–nonadherence associations. First, we grouped the nonadherence outcomes into four domains, corresponding to major components of the regimen: a) taking immunosuppressant medications; b) clinical monitoring (persistent nonadherence to either clinic appointments or completing blood work); c) home self-care (persistent nonadherence to either blood pressure monitoring, diet or exercise); and d) spirometry. (Spirometry was

considered separately from other home self-care activities because it was assessed only in lung recipients. We did not include a domain for substance use nonadherence because these behaviors were too rare.) Second, before the multivariate analyses, we examined bivariate associations of each risk factor with persistent nonadherence in each domain. Potential risk factors showing small associations (r = 0.15) with all four nonadherence domains were eliminated from further consideration (cf. Table 3, footnote b). Remaining risk factors were entered simultaneously into logistic regression analysis, with persistent nonadherence in a given domain (i.e., persistent nonadherence to any of the areas encompassed by the domain) as the outcome. Results are shown in Table 3. The table presents odds ratios (ORs), generated from the regression coefficients, and the 95% confidence interval for each OR. Each OR indicates the degree of increased risk of persistent nonadherence if a recipient possessed the risk factor.

Recipients relying on public health insurance were at heightened risk for nonadherence in all domains (ORs of 2.26 to 4.00). Poor caregiver support also predicted increased likelihood of persistent nonadherence in all domains (ORs of 1.81 to 2.59). Lower internal locus of control predicted increased risk of persistent nonadherence to home self-care in all recipients, and spirometry in lung recipients. Male gender was protective against home self-care nonadherence.

Finally, interaction terms between type of transplant and each factor were added to the regressions to determine whether any risk factor effects varied across lung versus heart recipients. Results indicated unique effects for two factors. First, feeling unhappy with medications' effects on one's physical appearance increased the risk for persistent immunosuppressant nonadherence in heart but not lung recipients (interaction effect, beta = 2.0, SE = 0.81, $P = 0.012$): heart recipients unhappy with such effects were more than 4 times more likely to be persistently nonadherent than remaining heart recipients (OR = 4.44, $P = 0.002$), while risk for persistent nonadherence was not related to this variable in lung recipients (OR = 0.70, $P = 0.498$). Second, poor support from friends predicted greater risk for persistent nonadherence to home self-care in lung but not heart recipients (interaction effect, beta = 1.9, SE = 0.74, $P = 0.008$): lung recipients with low friend support were almost three times more likely to be persistently nonadherent than lung recipients with higher support (OR = 2.94, $P = 0.010$). The risk of persistent nonadherence was not associated with friend support in heart recipients (OR = 0.58, $P = 0.213$).

DISCUSSION

Our study is the first to prospectively examine rates and risk factors for nonadherence to a full range of components of the medical regimen in lung transplant recipients. Moreover, we put our findings for lung recipients into a larger context by directly comparing them to heart recipients recruited from the same transplant program during the same time period. As such, the present report begins to address some of the key gaps in the literature on posttransplant adherence outcomes (12, 19, 20, 45).

The nonadherence rates in our lung recipient cohort show many similarities with those reported across the larger (nonlung) transplant literature (12). First, most recipients in our sample were adherent to each component of the medical regimen. The exceptions to this pattern were blood pressure monitoring and spirometry, as discussed further below. The second point of similarity is the marked variability in our sample's nonadherence rates across areas of the medical regimen, with nonadherence to tobacco and alcohol use being relatively rare while nonadherence to home monitoring activities, diet, and exercise was much more common (12). Third, our finding that nonadherence in most areas increased with time is consistent with the typical pattern reported in chronic disease and transplant

populations (4, 19, 27, 45– 48). Fourth, as observed in other transplant cohorts (27, 45, 49, 50), the areas of nonadherence in our sample were generally not highly interrelated. Thus, we found little evidence of an overall "profile" of typical nonadherence among respondents, with the exception that there was a moderate correlation between lung recipients' nonadherence to blood pressure monitoring and spirometry; a similar association was reported previously (16). This association, plus the high nonadherence rates in these two areas, suggests that a comprehensive plan to improve home monitoring activities could be beneficial for lung recipients.

In addition to general comparisons with the larger literature, our direct examination of differences between lung and heart recipients indicates that lung recipients were neither uniformly better nor worse than these other patients in adhering to their regimen. Given the importance of immunosuppressants for preventing graft rejection, it is noteworthy that lung recipients' cumulative incidence of persistent nonadherence in this area was significantly lower than that in heart recipients. Tobacco use, which has been linked to major morbidities and mortality after all types of organ transplant (51–53), was also significantly lower among the lung recipients. However, lung recipients were less adherent to blood work requirements and blood pressure monitoring. Moreover, we have already noted that, by 2 years posttransplant, a majority of lung recipients no longer performed spirometry several times weekly, as required. Indeed, among this nonadherent group, most performed spirometry less than monthly or not at all. This is of major concern given the importance of spirometry for providing early indications of possible infection and graft rejection (6, 9, 11).

Several small studies of interventions to promote home spirometry show that lung recipients will perform frequent spirometry according to protocol for extended time periods (54 –56). But our findings suggest that maintenance of this behavior outside of intervention research is more difficult. Some of our respondents spontaneously commented that they stopped spirometry because, beyond the first few months post-transplant, CT Program staff did not routinely review recipients' diaries of their spirometry readings. Similar comments were offered regarding blood pressure readings. Such remarks suggest that these recipients did not understand that these activities should be done entirely for recipients' own benefit. This point ties in with our risk factor findings: patients perceiving themselves to have little influence over their health were more than 1.5 times more likely to become persistently nonadherent to spirometry and other home self-care activities. The importance of this risk factor for lung recipient health outcomes has been noted elsewhere (57). In short, whether it is failure to fully understand that certain behaviors are important for health, or failure to believe that one can affect one's health, the implication may be that tailoring posttransplant education to "empower" (rather than only to instruct) patients is essential for maintaining adherence.

We examined a wide array of risk factors for persistent nonadherence. We found little to no impact for most demographic and transplant-related health history characteristics. This is not surprising; such variables have shown limited, contradictory effects on adherence in many transplant populations (12, 45). We also found no evidence that treatment-related characteristics were related to nonadherence, at least among lung recipients.

In contrast, variables reflecting healthcare system access and patient psychosocial characteristics were important risk factors for nonadherence in multiple areas. Of particular note, patients with only public health insurance were up to four times more likely to become persistently nonadherent to components of the regimen. Reliance on public insurance has repeatedly been found to increase the risk for poor health outcomes posttransplant (58 – 61), even controlling for income and other socioeconomic variables (59, 61). The mechanism for this effect may be due in part to reduced adherence, although the link between insurance

status and adherence has seldom been examined (58, 60). Our findings suggest the importance of identifying strategies to strengthen financial resources for patient healthcare requirements. This includes increasing the availability of low- and no-cost medication programs, increasing transplant teams' familiarity with such programs, and reducing patient perceptions of stigma associated with program participation (62). However, cost coverage options in areas beyond medications remain bleak. Third-party reimbursement for activities such as exercise, dietary counseling, and training in other home self-care activities is rare, particularly through publicly funded insurance (63).

Finally, we found that two types of patient psychosocial factors affected nonadherence risk. We commented earlier on the impact of patients' perceptions of control over their health. The second important type of psychosocial factor was patients' perceived social support. Recipients without a supportive relationship with their primary family caregiver were at increased risk of nonadherence in all outcome areas. In addition, at least for lung recipients, lack of support from friends increased their likelihood of nonadherence to home self-care activities. We and others have repeatedly observed patients' supports from family and friends to be critical predictors of a range of adult posttransplant emotional and behavioral outcomes (19, 20, 27, 45, 64, 65); the present study extends this finding to lung recipients.

There are limitations to our research. First, we studied recipients at a single site and this could affect our findings' generalizability. Second, there are other potential risk factors in each of the five WHO-based domains that we did not examine but which could influence posttransplant adherence. For example, other healthcare system access factors have been identified as important in other chronic disease populations (5), including the duration of face-to-face interactions with healthcare professionals and the extent of insurance reimbursements for specific components of the medical regimen. Other treatment-related variables—such as distress over a full range of side effects (18) and patient-related psychosocial characteristics such as beliefs about one's medical condition (66)—may affect posttransplant adherence. A sample size even larger than ours is required to examine the many additional potential predictors, as well as sensitively evaluate whether their effects vary by type of transplant. Third, concerning the measurement of nonadherence itself, we relied on patient and family caregiver reports and we did not collect information from clinician evaluations or indirect assessments (e.g., electronic medication monitoring). Our assessment strategy was based on meta-analytic findings, our own empirical comparisons of methods (27, 67), and other commentaries (26). Moreover, patient report, using techniques to maximize complete disclosure such as those we employed, has greater clinical relevance than many other research-based methods; it is less expensive and easier to integrate into routine clinical practice (12, 68).

For future work, our findings suggest that intervention development should be a priority for those areas where lung recipients' nonadherence rates are high and the consequences of nonadherence are significant. This should include, for example, home spirometry. Interventions to increase patients' feelings of competence and control at managing their health have proven useful in transplant and other chronic disease groups (69, 70). Involving family or even close friends in these efforts may enable patients to better draw on interpersonal relationships to promote adherence and optimal health outcomes. While risk factors such as type of health insurance may not themselves be easily modified through patient-focused interventions, assisting patients to seek alternative resources for cost coverage may reduce the likelihood of non-adherence for financial reasons (60, 71). Moreover, the impact of health insurance on our outcomes implies that not only patient-focused interventions but strategies to address healthcare system access factors are needed.

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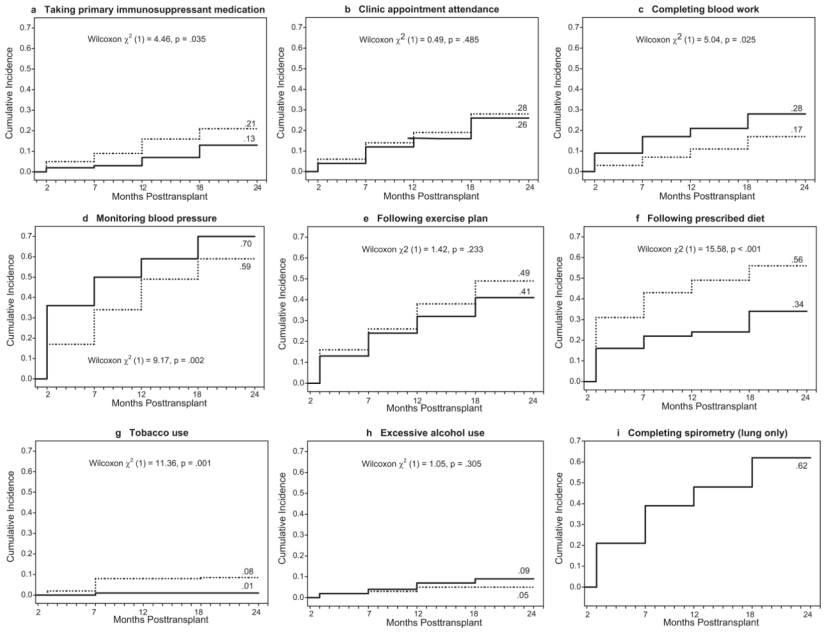

FIGURE 1.

Differences in time to persistent nonadherence in areas of the medical regimen between lung recipients and heart recipients during the first two years posttransplant. Solid line denotes lung recipients; dotted line denotes heart recipients.

TABLE 1

Patient demographic and transplant-related characteristics

Characteristic	Lung recipients (n = 178)	Heart recipients (n = 126)	Group comparison, χ^2 test
Sociodemographic			
Gender (% men)	52.2	68.3	7.81[b]
Age (% <50 years)	36.5	31.7	0.74
Race/ethnicity (%)			
European American	94.9	85.7	7.88[c]
African American	3.9	11.9	
Other	1.1	2.4	
Education (% <high school)	48.9	47.6	0.05
Marital status (% married)	70.8	75.4	0.79
Household income below U.S. poverty level (21) (% yes)	13.6[a]	25.4	6.72[c]
Insurance coverage at transplant (% public: Medicaid, other forms of public assistance)	16.9	22.2	1.38
Transplant related			
Indication for transplant (% lung recipients)			
COPD/emphysema	35.4		
Idiopathic pulmonary fibrosis	21.3		
Cystic fibrosis	16.3		
Other	27.0		
Indication for transplant (% heart recipient)			
Coronary artery disease		42.3	
Myopathy		41.3	
Other		16.6	
Length of hospitalization posttransplant (%>1 month)	30.9	18.3	6.18[c]
Functional impairment at 2 months posttransplant (% Karnofsky Index scores >3)[d]	29.0	28.8	0.00
Treated acute rejection by 2 months posttransplant (% yes)	39.3	39.7	0.00
Maintenance immunosuppressant posttransplant (%)			
Cyclosporine	12.9	27.0	9.58[b]
Tacrolimus	87.1	73.0	

[a] Two patients were missing data on household income level.

[b] $P<0.01$.

[c] $P<0.05$.

[d] Karnofsky score exceeding 3 indicates that significant functional impairment is present.

TABLE 2

Nonadherence to components of the medical regimen among 304 cardiothoracic transplant recipients at each of five posttransplant assessments

Nonadherence with regimen (% yes)	Months after transplantation[a] 2 months (n = 178 lung; n = 126 heart)	7 months (n = 170 lung; n = 122 heart)	12 months (n = 155 lung; n = 116 heart)	18 months (n = 144 lung; n = 113 heart)	24 months (n = 127 lung; n = 112 heart)	Test for differences across assessments[b]
Primary immunosuppressant medication (missed at least once a month)						33.44[d]
Lung recipients	9.6	8.3	14.3	14.5	19.7	
Heart recipients	11.1	14.0	19.8	21.4	30.6	
Clinic appointments (missed ≥1 visit)						35.97[d]
Lung recipients	11.8	22.0	22.2	33.3	27.8	
Heart recipients	14.3	24.0	28.7	23.9	37.3	
Blood work (missed ≥1 appointment)						19.24[e]
Lung recipients	15.3	24.3	24.8	25.4	28.3	
Heart recipients	11.9	14.9	22.6	18.6	26.6	
Blood pressure monitoring (less than several times a week)						122.20[d]
Lung recipients	42.1[a]	55.9[a]	59.2	67.4	68.5	
Heart recipients	28.6[a]	39.2[a]	57.9	59.3	65.8	
Exercise (less than several times a week)						27.49[d]
Lung recipients	31.5	29.4	38.3	35.8	41.3	
Heart recipients	34.9	32.8	41.7	46.9	49.1	
Diet (went off diet at least weekly)						4.72
Lung recipients	28.1[a]	33.3[a]	31.2[a]	30.4[a]	36.5	
Heart recipients	45.2[a]	46.7[a]	52.6[a]	44.2[a]	43.1	
Used tobacco (any use)[c]						9.56[f]
Lung recipients	0.0	0.6[a]	1.3[a]	0.7[a]	1.6[a]	
Heart recipients	3.2	8.3[a]	7.0[a]	8.0[a]	9.1[a]	
Excessive alcohol use (≥2 drink/day)[c]						11.10[f]
Lung recipients	3.9	4.1	9.1	10.9[a]	10.2	

Nonadherence with regimen (% yes)	Months after transplantation[a] 2 months (n = 178 lung; n = 126 heart)	7 months (n = 170 lung; n = 122 heart)	12 months (n = 155 lung; n = 116 heart)	18 months (n = 144 lung; n = 113 heart)	24 months (n = 127 lung; n = 112 heart)	Test for differences across assessments[b]
Heart recipients	3.2	5.8	6.1	3.5[a]	6.4	
Performed spirometry (less than several times a week)						89.06[d]
Lung recipients	24.2	47.1	54.6	64.5	65.9	

[a] χ^2 tests were used to compare pairs of proportions at each assessment. Proportions with identical superscripts differed significantly at $P<0.05$.

[b] Cochran's Q test for multiple proportions ($df = 4$). Q was based on the panel of 239 respondents with complete data from all assessments (127 lung recipients, 112 heart recipients); the proportions who were nonadherent at each assessment in the panel group were virtually identical to the proportions based on all available recipients at a given assessment time point. Q was also calculated separately for lung recipients and for heart recipients; the pattern of results was identical to that for the entire panel group of 239 respondents.

[c] Fisher exact test tests were used to determine P values due to the small proportions per cell.

[d] $P<0.001$.

[e] $P<0.01$.

[f] $P<0.05$.

TABLE 3

Logistic regression analyses examining potential risk factor associations with domains of nonadherence in cardiothoracic transplant recipients[a]

		Nonadherence outcome domains							
		Taking primary immunosuppressant		Clinical follow-up care		Home self-care		Completing spirometry (lung only)	
Potential risk factor	Percentage or mean ± SD for study sample	OR	CI	OR	CI	OR	CI	OR	CI
Sociodemographic characteristics[b]									
Gender, male	58.9	0.79	0.35, 1.73	1.06	0.60, 1.88	0.45[d]	0.22, 0.92	0.84	0.40, 1.77
Ethnicity, non-European American	8.9	0.91	0.28, 3.00	0.87	0.34, 2.25	2.18	0.70, 6.75	0.91	0.20, 4.26
Education, <high school	48.4	0.95	0.44, 2.07	0.64	0.37, 1.12	1.02	0.53, 1.99	1.00	0.48, 2.12
Household income, <U.S. poverty level	18.5	1.27	0.48, 3.39	0.64	0.31, 1.30	1.07	0.43, 2.66	1.43	0.47, 4.39
Health system access characteristics[b]									
Insurance, public	19.1	2.60[d]	1.06, 6.25	2.26[d]	1.11, 4.54	3.77[e]	1.27, 11.11	4.00[d]	1.18, 14.28
Health-related background characteristics[b]									
Length of hospitalization posttransplant, >1 month	25.7	0.61	0.23, 1.64	1.79	0.98, 3.22	1.19	0.56, 2.56	0.61	0.27, 1.33
Psychiatric history pretransplant, yes	46.4	0.83	0.39, 1.77	1.59	0.92, 2.74	1.23	0.62, 2.41	0.85	0.41, 1.75
Treatment-related characteristics[b]									
Unhappy with medication effects on physical appearance, yes	39.5	1.52	0.69, 3.33	1.20	0.69, 2.08	1.66	0.83, 3.33	0.98	0.48, 2.00
Area of treatment interferes with daily life, yes	__[c]	1.10	0.31, 3.86	1.59	0.77, 3.29	0.50	0.20, 1.25	3.40	0.89, 13.07
Patient psychosocial characteristics									
Intrapersonal									
High depression symptoms posttransplant, yes	44.9	0.62	0.23, 1.63	1.09	0.54, 2.18	0.63	0.27, 1.46	0.77	0.31, 1.95
High anxiety symptoms posttransplant, yes	47.8	1.03	0.41, 1.67	0.76	0.38, 1.52	0.70	0.30, 1.60	0.85	0.35, 2.07
High anger/hostility symptoms posttransplant, yes	21.9	1.42	0.53, 3.78	0.70	0.33, 1.46	1.62	0.67, 3.94	0.86	0.29, 2.56
Internal locus of control (1 = high, 6 = low)	2.78±0.79	1.09	0.68, 1.79	1.12	0.79, 1.56	1.71[d]	1.12, 2.63	1.75[d]	1.11, 2.78
Care provider locus of control (1 = low, 6 = high)	4.26±0.94	0.81	0.53, 1.23	0.92	0.68, 1.25	1.02	0.72, 1.45	1.04	0.71, 1.53
Interpersonal									
Social support from family caregiver, low	37.2	2.59[d]	1.20, 5.58	1.81[d]	1.03, 3.19	2.18[d]	1.04, 4.53	2.42[d]	1.09, 5.36
Social support from friends, low	34.3	1.86	0.84, 4.10	0.88	0.49, 1.57	1.63	0.79, 3.35	0.60	0.28, 1.27

Potential risk factor	Percentage or mean ± SD for study sample	Nonadherence outcome domains							
		Taking primary immunosuppressant		Clinical follow-up care		Home self-care		Completing spirometry (lung only)	
		OR	CI	OR	CI	OR	CI	OR	CI
Model improvement over null model, χ^2		29.9[d]		34.1[e]		38.2[e]		27.5[d]	
Nagelkerke R^2		0.18		0.15		0.19		0.20	

[a] All regressions examining potential risk factors controlled for transplant group (lung vs. heart recipients). The regressions for taking immunosuppressants, clinical monitoring, and home self-care outcomes were based on the 285 of 304 cases with complete data on all predictors. The regression for spirometry (lung recipients only) was based on the 168 of 178 cases with complete data. The following predictors had missing data: household income (n = 2 cases missing), psychiatric history pretransplant (n = 11), unhappy with medication effects (n = 8), depression, anxiety and hostility symptoms (n = 3 each), internal locus of control and care provider locus of control (n = 5 each), family caregiver support (n = 6), and friend support (n = 3).

[b] Additional sociodemographic (age), health system access (distance of residence from transplant center), health-related background (presence of cognitive impairment at 2 months posttransplant, Karnofsky index of functional impairment at 2 months posttransplant, occurrence of treated acute rejection episodes during the first 2 months posttransplant), and treatment-related characteristics (primary maintenance immunosuppressant) showed small bivariate associations with all nonadherence outcome variables (r = 0.15). Thus, they were not included in the multivariate models. Although household income also showed r = 0.15 with all outcomes, we retained it in the multivariate models in order to ensure that any impact of patient insurance status on the outcomes was not confounded by this variable. The correlation between insurance status and household income was 0.30.

[c] A separate item was used to inquire about each area of the regimen. For the primary immunosuppressant, 10.1% of the sample reported that it interfered with daily life; for clinical monitoring, 15.8% reported that either clinic appointments or blood work or both interfered with daily life; for home self-care, 13.2% reported that one or more components interfered (blood pressure monitoring, diet, exercise); for home spirometry, 6.1% reported that it interfered.

[d] $P<0.05$.

[e] $P<0.01$.

OR, odds ratio; CI, 95% confidence interval.