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Nonadherence to the medical regimen after lung transplantation: A systematic review

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ABSTRACT

This study reports on the first systematic review focused on lung transplant recipients (LTRs) and provides evidence regarding 1) prevalence of nonadherence to the post-transplant medical regimen; 2) risk factors for nonadherence; 3) impact of adherence-promoting interventions; and 4) transplant-related clinical outcomes of nonadherence in LTRs. Following the PRISMA guidelines, a literature search of 5 databases was conducted, yielding 30 relevant articles. Findings suggested that nonadherence rates varied greatly across regimen components and were not consistently associated with any single risk factor. Effect sizes in terms of correlation coefficients for adherence-promoting interventions ranged from .05 to .45. Mortality rates did not significantly differ by adherence levels. Major limitations across studies were weak methodologies for measuring nonadherence and small sample sizes. This review underscores the need for more rigorous and extensive studies of risk factors and clinical outcomes of nonadherence and for large-scaled theory-based trials to examine adherence-promoting interventions in LTRs.

Introduction

Lung transplantation is the optimal therapeutic option to improve quality of life for persons with end-stage lung disease.[1–7] While the first year survival rate among lung transplant recipients (LTRs) is similar to recipients of other solid organ transplants, the 3- and 5-year survival rates for LTRs are much lower.[8] One reason for this disparity is that LTRs are at a higher risk of developing transplant-related complications, such as graft rejection and infection.[9,10]

After transplantation, LTRs are expected to adhere to a lifelong medical regimen involving: 1) medication-taking, 2) self-monitoring of lung function and signs and symptoms of complications, and 3) healthy lifestyle requirements like abstaining from tobacco, limiting alcohol consumption, and following diet, nutrition, and exercise recommendations. Adhering to these elements of medical regimen has been widely recognized to have the potential to prevent complications and maximize health outcomes among LTRs.[11–16]

While there is a growing literature on adherence behaviors among LTRs, including investigations into key correlates and outcomes, translating this body of research to practice requires a systematic examination of the evidence. To date, one meta-analysis[13] and two reviews[11,17] have examined the prevalence and risk factors of nonadherence among adult heart transplant recipients, LTRs and heart-lung transplant recipients.[11,13,17] However, due to a limited number of published articles on LTRs, very few conclusions could be drawn regarding this patient population. In order to maximize their effectiveness in educating and supporting LTRs, nurses and other healthcare providers must be up to date on the scientific literature on adherence after lung transplantation. Therefore, our goal was to systematically review evidence

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regarding the 1) prevalence of nonadherence; 2) risk factors for nonadherence; 3) impact of interventions for promoting adherence; and 4) transplant-related clinical outcomes associated with nonadherence among LTRs. Our rationale for including articles on clinical outcomes of nonadherence was that although there is no doubt that the post-transplant medication regimen is effective for preventing complications,[18] less is known about the strength of the relationship between nonadherence and clinical outcomes such as mortality and morbidity.

Methods

Search strategies

An electronic literature search was conducted in PubMed MEDLINE, EBSCOhost CINAHL, Ovid PsycINFO, Ovid Global Health, and EMBASE. The keywords of "lung transplant" or "lung transplantation" were paired with combinations of the terms "(non) adherence", "(non)compliance", "medication", "monitoring", "diet", "exercise", "alcohol drinking", "smoking", "tobacco use", "substance use" and "spirometry". Truncation was used to ensure that both noun and verb forms of each word were captured. Databases were searched from the earliest available dates through April 1, 2015.

Inclusion and exclusion criteria

Articles included in this review met the following criteria: 1) reported LTRs' nonadherence to any element of the post-transplant medical regimen, 2) focused on adults (≥18 years old), 3) quantitative research study, and 4) English language. Articles were excluded if they met any of the following criteria: 1) did not report post-transplant nonadherence for adult LTRs, 2) case study, 3) clinical guideline, 4) conference abstract or proceeding, 5) commentary; 6) qualitative only study, and 7) review article.

Data extraction for review

This project was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[19] Each article was screened by at least two independent reviewers and if any discrepancies occurred, two reviewers discussed and reached agreement on whether to include the article or not. If no agreement was reached, further consultation was sought from the content experts on the team. The screening processes are reported in Fig. 1. Key information regarding the study was extracted from each article, including the first author, year, sample size, definitions and measures of nonadherence and findings. We assessed the quality of each article using the level of evidence by the Agency for Healthcare Research and Quality.[20] A summary of key characteristics for each study, organized by the aims of this review, are displayed in Tables 1–3.

Data analysis

To adjust for the different follow-up duration post-transplantation across studies, we calculated person-time incidence nonadherence rates. Specifically, we calculated the number of cases of nonadherence per 100 person-years for each component of the medical regimen examined in a given study. The effect sizes of intervention impact on promoting adherence were examined by extracting or calculating correlation coefficients (i.e., the association between intervention exposure and status on each outcome variable).

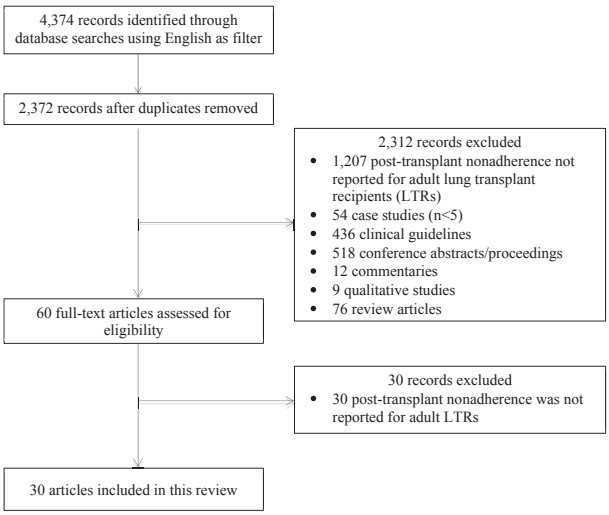

Fig. 1. Study flow chart.

Results

As shown in Fig. 1, 30 articles were included in this review: 22 (73.3%) focused on prevalence and/or risk factors of nonadherence (see Table 1), 6 (20.0%) examined the effects of interventions to promote adherence (see Table 2), and 2 (6.7%) explored clinical outcomes related to nonadherence (see Table 3). The study sample sizes ranged from 22 to 331 with a pooled total sample size of 3388. The study samples were predominantly comprised of individuals who were male, non-Hispanic white, and approximately 40–54 years of age with the diagnosis of chronic obstructive lung disease or cystic fibrosis as the indicator for transplant. These sample characteristics are consistent with the characteristics of the worldwide LTR population.[10]

Prevalence and risk factors of nonadherence to the medical regimen

Nonadherence to medication-taking

Medication nonadherence was examined in 13 articles,[6,14,21–31] with rates ranging from 2.3% to 72.2%. However, the period of observation time for nonadherence in each study varied, ranging from 2 weeks to 4 years. When taking different follow-up time into consideration, the medication nonadherence rates ranged from 4 to 100 cases for every 100 person-years of observation. Approaches to defining and measuring medication nonadherence varied within this set of articles. In some articles,[14,22,26] medication nonadherence was defined as any missing dose over a month or between study follow-ups, while in others[21,30] medication nonadherence was defined as following the medication instructions less than 80% of the days over 3 months. Across articles, self-report approaches (with or without collateral report) to measure medication nonadherence were the most common, with fewer articles incorporating measures like electronic medication event monitoring[21,22] or records of pharmacy dispensing.[30] One article used a combined approach of self-report and plasma concentration of immunosuppressant.[25] Notably, among the articles using self-report measures, a variety of scales were used with most scales having been validated in other chronic diseases or other solid transplant recipients, and their reliability and validity among LTRs was generally unreported.[6,22,23,25,26,29,31]

Among the 13 articles identified on medication nonadherence, 6 reported associated risk factors for nonadherence.[14,21,24,26–28] None of the factors were examined in a sufficient number of articles (i.e.,