

Prevalence and correlates of influenza vaccination among kidney transplant patients

Context—Immunosuppressive regimens increase kidney transplant patients' risk of contracting life-threatening influenza. However, little information exists about the prevalence and correlates of influenza vaccinations in this population.

Objective—To determine the prevalence and explore correlates of influenza vaccination in kidney transplant recipients.

Design, Sample, and Setting—This cross-sectional study used data from the Supporting Medication Adherence in Renal Transplantation study. The convenience sample consisted of 356 adult kidney transplant recipients (58.1% male; mean age, 52.9 [SD 13.53] years) recruited from 2 Swiss transplant outpatient clinics. Influenza vaccination status was assessed by self-report (yes/no).

Main Outcome Measure—Known correlates of vaccination in chronically ill patients (older age, cohabitation, higher education, higher socioeconomic status, financial stability, more comorbid diseases, nonsmoking status, and clinical site where care is received) were entered into a multiple logistic regression model.

Results—Of the 356 patients, only 83 (23.3%) reported having been vaccinated against influenza in the previous year. Positive vaccination status was significantly related to older age (odds ratio, 1.04; 95% confidence interval, 1.02-1.06).

Conclusion—Despite national and international guidelines recommending influenza vaccination in kidney transplant recipients, the prevalence of influenza vaccination in this sample was low. This study's results suggest that transplant centers need to implement policies to maximize influenza vaccination of their patients. (*Progress in Transplantation*. 2009;19:312-317)

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Receiving a kidney transplant entails lifelong intake of immunosuppressive medication that prevents rejection of the transplanted kidney, but also increases the risk of infections,¹⁻⁸ a major cause of morbidity and mortality after transplantation.⁹

One common but often life-threatening infectious disease in immunocompromised patients is influenza, an acute contagious viral infection characterized by inflammation of the respiratory tract, fever, chills, muscular pain, and prostration.^{10,11} A 10-year single-center longitudinal study of solid-organ transplant recipients showed that the incidence of influenza infection in kidney transplant recipients was 4.3 cases per 1000 person years.¹² Solid-organ transplant recipients have been reported to be more susceptible to influenza virus than healthy persons.¹² One common complication is secondary pneumonia infection, caused by any of a variety of bacteria, viruses, parasites, and fungi that attack the lung parenchyma.^{4,5,9} Left untreated in kidney transplant recipients, 40% to 50% of cases of pneumonia are fatal.⁵

Vaccination has been proven effective in reducing the risk of influenza and pneumonia infections in transplant patients.^{5,6,13-15} For immunocompromised patients, the World Health Organization and the Swiss Federal Office of Public Health, therefore, recommend yearly vaccination using a deactivated vaccine.¹⁶⁻¹⁹

Prevalence of Influenza Vaccination

Despite its proven effectiveness,^{5,6,13-15} vaccination of kidney recipients against influenza is not yet standard practice in transplant centers. According to Dinits-Pensy et al,² many nephrological practices are reluctant to administer vaccines, partly because of a lack of understanding regarding their risk/benefit ratio. In a US survey, Batiuk et al²⁰ found that only 59 of the 138 kidney transplant centers queried (43%) offered routine vaccination against influenza before transplantation. After transplantation, 74 (54%) routinely vaccinated or recommended vaccination to all patients. Twenty-two percent indicated that they did not recommend vaccination to any of their patients, and 24% reported recommending

vaccination only to specific subgroups of transplant patients.²⁰

Slightly different results were found among heart transplant centers. Of the 28 transplant centers investigated in a multicenter study by White-Williams et al,²¹ 25 recommended influenza vaccination. The remaining 3 centers did not recommend influenza vaccination because of a purported association with allograft rejection.

Among kidney transplant centers, however, policies vary widely. The United States Renal Data System reported an increase in the prevalence of influenza vaccination among kidney transplant patients from 43.1% in 1996 to 50% in 2004, far from the Healthy People 2010 goal of 90%.²²

Because successful vaccination requires a partial activation of the immune system, doubts have been raised about a possible increase in the risk of acute rejection episodes, and thus about the safety of influenza vaccination in transplant patients. This fear, however, has not been substantiated by scientific evidence.^{5,6,8,13-15} White-Williams et al²¹ concluded that the rate of rejections did not increase in the months before, during, or after the administration of the influenza vaccination.

Concerns also exist about decreased serological efficacy in transplant patients compared with healthy persons making vaccination ineffective. However, in spite of the kidney transplant recipients' lower immune response, various studies have shown that their antibody response to the influenza vaccine still significantly decreases the probability of contracting influenza.^{5,6,13,23,24}

Determinants of Influenza Vaccination

Because influenza vaccination reduces mortality risk in the immunocompromised population,^{10,11} it is vital to know what prevents kidney recipients from being vaccinated. Little is known about predictors of vaccination in transplant recipients, except that the policy of the transplant center is an important determinant.^{20,21} Studies in other populations have explored patient-related factors. Landi et al²⁵ studied predictors of influenza vaccination in a European population of frail community-dwelling elders. Living alone, cognitive impairment, and having economic problems were associated with a lower likelihood of being vaccinated, whereas advanced age and a higher number of comorbid diseases were associated with a higher probability of vaccination. In a similar sample, Burns et al²⁶ confirmed the relationship between vaccination and socioeconomic status but found no significant association with age or sex of the patient. They did, however, report a positive association with the ability to travel independently and not having to depend on public transportation to see their general practitioner, and

a negative relationship with smoking. No significant association was found between vaccination and either alcohol consumption or chronic disease status.

In a retrospective cross-sectional study²⁷ in adults older than 50 years, being white, having at least a high school education, having a comfortable household income, having visited a physician in the last year, and having comorbid diseases were all related to being vaccinated. This finding in relation to comorbid diseases is consistent with the findings of Landi et al.²⁵ Marital status was not related to getting the influenza vaccine.

Research Aims and Objectives

The aims of this study were to investigate the prevalence and correlates of influenza vaccination in a sample of kidney transplant recipients with functioning grafts more than 1 year after transplant in 2 kidney transplant outpatient clinics in Switzerland.

Methods

Research Design

This cross-sectional study used data of the Supporting Medication Adherence in Renal Transplantation study,²⁸ which aimed to determine the prevalence, risk factors, and consequences of nonadherence to immunosuppressive drug regimens in a sample of kidney transplant recipients.

Sample and Setting

The convenience sample consisted of 356 German- or French-speaking adult (≥ 18 years) kidney transplant recipients who were literate, were being followed up at 1 of the 2 Swiss outpatient transplant centers included in this study, and had undergone kidney transplant surgery at least 1 year before the study. Patients lacking the mental capacity to answer the questions and patients unable to read the study forms were excluded from the study.

Switzerland has an obligatory health insurance system. The standard health care package, which excludes no one, covers transplantation along with the majority of costs for follow-up care, including vaccination.

Data Collection

Once approval had been received from the institutional review board of each center, and after patients had given their informed consent, data were collected through structured face-to-face interviews and medical record reviews. The structured interviews were carried out by 4 qualified research staff members when patients visited their transplant centers for yearly check-ups.

Variables and Measurements

Influenza vaccination status was measured by self-report; participants were asked if they had received an

influenza vaccination during the previous year (yes/no). Data were collected on possible predictor variables: demographic characteristics, comorbid diseases, other health behaviors, and system factors. Data on patients' age, sex, and nationality were extracted from the patients' medical files. Other demographic factors, including living status (alone/cohabitation) and educational level (measured with a 4-point ordinal variable reflecting how long patients had attended school, that is, until 11/12, 14/15, or 18/19 years of age or longer) were assessed via structured interviews.

We extracted the Charlson Comorbidity Index from each participant's medical files. This index includes 19 categories of diseases, all weighted on the basis of their association with mortality.^{29,30} The health behavior factors assessed via structured interviews were current smoking status (yes/no) and the frequency of alcohol consumption (on a 6-point scale, ranging from never to daily). As system-related factors, we asked subjects which outpatient center they attended for follow-up, and, via structured interviews, assessed their perceptions of the adequacy of their financial resources (on a 4-point scale ranging from more than adequate to inadequate) to cover medication costs.

Data Analysis

Before the outcome data were modeled, a detailed descriptive analysis of all data was performed, involving the summarization of the data and the use of exploratory data analytical techniques. To identify correlates of vaccination status, we conducted a multiple logistic regression analysis in which we included each candidate correlate as a predictor variable, with vaccination status as a dichotomous outcome variable. We set the α level at 0.05. Descriptive statistical analyses were performed by using SPSS 14.0 (SPSS Inc, Chicago, Illinois), and inferential statistics were analyzed in SAS 9.1 (SAS Institute Inc, Cary, North Carolina).

Ethical Considerations

The Supporting Medication Adherence in Renal Transplantation study was approved by the ethics committees of the Basel University Hospital and the Cantonal Hospital of Aarau, as well as by the Federal Ethics Committee of Switzerland. All participants provided written informed consent.

Results

Sample Size and Demographic Characteristics

Of the 413 adult kidney transplant recipients visiting the outpatient clinics for their annual check-ups, 86% (N = 356; 207 males (58.1%); mean age 52.9 [SD, 13.5] years) agreed to participate in the study. Sample demographics and clinical characteristics are summarized in Table 1. The majority of participants were Swiss. The median time between transplantation and

Table 1 Demographic and clinical characteristics of the sample

| Variable | No. (%) of patients (N = 356) |
|-------------------------------|----------------------------------|
| Influenza vaccination | |
| Yes | 83 (23.3) |
| <65 years old | 58 (16.3) |
| ≥65 years old | 24 (6.7) |
| Unknown | 1 (0.3) |
| Sex | |
| Men | 207 (58.1) |
| Nationality | |
| Swiss | 291 (81.7) |
| Austria and Germany | 29 (8.1) |
| Italy | 15 (4.2) |
| Balkan | 9 (2.5) |
| Other | 12 (3.4) |
| Living alone | |
| Yes | 83 (23.3) |
| Paid work | |
| Yes | 187 (52.5) |
| Financial situation | |
| More than enough money | 9 (2.5) |
| Enough money | 277 (77.8) |
| Sometimes not enough money | 45 (12.6) |
| Not enough money | 24 (6.7) |
| Unknown | 1 (0.3) |
| Educational level | |
| Very low | 50 (14.0) |
| Low | 170 (47.8) |
| Medium | 36 (10.1) |
| High | 97 (27.2) |
| Unknown | 1 (0.3) |
| Smoke currently | |
| Yes | 76 (21.3) |
| Frequency of drinking alcohol | |
| Never | 134 (37.6) |
| Less than 1 time a month | 19 (5.3) |
| 1 to 2 times a month | 46 (12.9) |
| 1 to 2 times a week | 78 (21.9) |
| 3 to 4 times a week | 25 (7.0) |
| Daily | 47 (13.2) |
| Unknown | 7 (2.0) |
| Type of donor | |
| Living donor | 145 (40.7) |
| No. of transplantations | |
| First kidney transplant | 312 (87.6) |
| Not first kidney transplant | 44 (12.4) |
| Center | |
| 1 | 225 (63.2) |
| 2 | 131 (36.8) |

inclusion in the study was 6.54 years (interquartile ratio, 8.00). Almost two-thirds (63.2%) of the participants visited center 1 for follow-up; 36.8% went to center 2.

Prevalence and Correlates of Influenza Vaccination

Of the 356 participants, 83 (23.3%) reported having been vaccinated against influenza in the previous

Table 2 Multiple logistic regression analysis

| Variable | Odds ratio (95% CI) | <i>P</i> | More vaccination if |
|-------------------------------|---------------------|----------|------------------------------------|
| Age | 1.04 (1.02-1.06) | <.001 | Older |
| Sex | 0.84 (0.47-1.48) | .54 | Man |
| Nationality | | | |
| Swiss | Reference category | | |
| Austrian and German | 1.05 (0.40-2.78) | .92 | Austrian or German |
| Italian | 3.48 (1.00-12.24) | .05 | Italian |
| Balkan | 0.89 (0.10-7.80) | .92 | Swiss |
| Others | 0.27 (0.03-2.24) | .23 | Swiss |
| Living alone | 0.79 (0.40-1.54) | .48 | Not living alone |
| Financial situation | 1.07 (0.68-1.70) | .76 | Better financial situation |
| Educational level | 1.05 (0.80-1.37) | .70 | Higher educational level |
| Current smoking status | 0.89 (0.45-1.75) | .73 | Not smoking currently |
| Frequency of alcohol drinking | 1.14 (0.97-1.35) | .11 | More frequency of alcohol drinking |
| Center | 1.41 (0.91-2.18) | .12 | |
| Comorbid diseases | 1.06 (0.93-1.20) | .37 | More comorbid diseases |

year. Only 4 participants (1.1%) did not provide data on their vaccination status. Twenty-four of 79 participants (30.4%) who were 65 years of age or older received an influenza vaccination, whereas 59 (21.5%) of the 274 participants who were under 65 years of age reported being vaccinated against influenza. The results of the multiple logistic regression model testing correlates of influenza vaccination are summarized in Table 2. Being vaccinated was significantly related to older age ($P < .001$). Vaccination status also differed significantly between nationalities: patients who were Italian citizens had a higher prevalence of influenza vaccination than did patients who were Swiss ($P = .05$, odds ratio, 3.48).

Discussion

Ours is the first study that we know of to investigate the prevalence and correlates of influenza vaccination among kidney transplant patients. In our sample, the number of patients who had received influenza vaccinations was low. Older age was the only characteristic examined that was significantly related to influenza vaccination status. Patients who were Italian citizens were more likely to report receiving the influenza vaccination than were patients who were Swiss. However, the large 95% confidence interval of the 3.48 odds ratio (1.00-12.20) casts doubt on the reliability of this result.

Prevalence of Influenza Vaccination

Less than one-quarter of our sample group had received a vaccination against influenza in the year preceding the study. Compared with the 50% of vaccinated kidney transplant recipients in the United States,²² this is a very low prevalence. In our study, 30% of the participants who were 65 years or older reported having received an influenza vaccination in the previous

year. In the US renal population, the prevalence of influenza vaccination in the same age group was 56%.²² Further, despite national and international guidelines recommending annual influenza vaccination in kidney transplant patients,¹⁶⁻¹⁹ neither of the centers included in this study had implemented any policy concerning these guidelines. Another possible explanation (in addition to this striking gap between guidelines and clinical practice) for the low prevalence rate is that Swiss kidney transplant recipients are unaware of the danger of influenza and its possible complications, such as secondary pneumonia infection.⁵ As physicians play a key role in forming the vaccination attitudes of their patients,^{31,32} they and other health care providers can influence immunization rates by recommending vaccination, encouraging and answering questions, and addressing misconceptions.³¹ Naturally, this requires that each kidney transplant patient's physician have up-to-date knowledge of influenza vaccination studies, particularly of studies focused on transplant patients.

One alternative interpretation of such pronounced national differences in influenza vaccination rates is that physicians in the United States may be more motivated to vaccinate patients because of the extraordinarily high number of malpractice lawsuits there.³³ From this perspective, it would logically follow that the high incidence of legal complications would lead to a correspondingly high prevalence of preventive clinical practices. In fact, both are higher in the United States than in any other country.³⁴ Another possible explanation for the higher rate of influenza vaccination in the United States is the many clinical practice guidelines that include recommending influenza vaccine as well as immunization promotion programs in many hospitals and clinics.

A difference in influenza vaccination rates between the 2 countries also is apparent for the general population, although the disparity between similar samples of Americans and Swiss persons is somewhat smaller than that found in this study. In the 2000-2001 winter season, 51% of surveyed patients more than 65 years of age in Switzerland reported having received influenza vaccination,³⁵ compared with 64.3% of the same age group in the United States.³⁶ Such differences in prevalence, both in the kidney transplant population and in the general population, suggest that characteristics of the health care system might affect influenza vaccination status. Further research is needed to investigate whether, under what circumstances, and to what extent characteristics of the health care system, such as the extent to which influenza vaccination costs are covered or the quality control of transplant centers shape the prevalence of influenza vaccination.

Given the increased risk of influenza infection in immunocompromised patients, annual influenza vaccination of health care workers and household contacts of patients is strongly recommended.^{37,38} Therefore, annual vaccination of the most relevant potential carriers should be included in each center's policy.

Correlates of Influenza Vaccination

Of several potential correlates of influenza vaccination suggested by the literature, this study reliably identified only one correlate. Our finding that positive vaccination status is related to older age confirms the finding of Landi²⁵ but contradicts the result of Burns,²⁶ whose research showed no significant association between age and influenza vaccination.

A limitation of this study is that the policy of the transplant center—a known predictor of vaccination in transplant patients^{2,20}—could not be investigated in this study because this parameter did not vary in our study. A larger study including more centers would be better for investigating center characteristics in relation to the prevalence of vaccination.

A further limitation of this study is that it influenza vaccination was assessed by self-report. People might not remember any more if they received an influenza vaccination in the previous year. Furthermore, this study investigated mainly patient-related factors. Yet, human behavior is influenced not only by the characteristics of the individual, but also by environmental factors. A conceptual framework that serves to direct attention to both individual and environmental determinants of behavior is the ecological model.³⁹ This model examines behavior determinants on 5 levels of influence: intrapersonal factors (ie, characteristics of the individual), interpersonal processes and primary groups (eg, social networks and social support systems), institutional factors (eg, the management style of the institution), community factors

(eg, values and cultural norms in the community), and public policies (eg, local, state, and national laws and policies). It is recommended that subsequent research aimed at isolating and explaining determinants of influenza vaccination among kidney transplant patients be based on such an ecological model.

Conclusion

In spite of national and international guidelines recommending influenza vaccination of kidney transplant recipients, the prevalence of vaccination in this sample was low. This finding highlights the importance of transplant centers in formulating and implementing vaccination policies. Pronounced disparities in vaccination prevalence rates between Switzerland and the United States suggest that characteristics of the overall health care system influence national influenza vaccination status.

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