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Causes of re-hospitalization in different post kidney transplantation periods

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	<p>Summary</p>
<p>Background:</p>	<p>Post kidney transplantation Re-admissions are focused because they are costly and cause morbidity, or may end with unsatisfactory endpoints namely graft loss or death. We compared the pattern, outcome and cost of re-admissions in different post-kidney transplantation periods.</p>
<p>Material/Methods:</p>	<p>In a retrospective study, 562 consecutive re-admissions of kidney recipients categorized to early (during first 6 months; n=278); intermediate (6–24 months; n=115); and late (24 months and afterwards, n=169) hospitalizations. Primary outcome measures included hospitalization pattern (cause and length of hospital stay), and secondary outcome measure were assessed (mortality and graft loss during hospitalization) and costs.</p>
<p>Results:</p>	<p>The causes of rehospitalization were surgical complication (84 percent), infection (51 percent), graft rejection (45 percent), and malignancy (0.6 percent), in early phase, graft rejection (44 percent), infection (42 percent), surgical complication (13 percent), and malignancy (5 percent), in intermediate phase, and graft rejection (45 percent), infection (39 percent), surgical complication (3 percent), and malignancy (0.06 percent), in late phase. So, infections and surgical complications showed a decreasing trend from early to late post transplant phase, while malignancies showed a peak in intermediate phase. The length of hospital stay (12±11, 10±10, 9±7, p=0.001) and hospitalization charges (708±36, 468±333, 413±262 united states Dollars, p=0.035) were significantly higher in the early post transplant phase. Mortality (p=0.755) and graft loss during hospitalization (p=0.246) remained the same in all time intervals.</p>
<p>Conclusions:</p>	<p>Early post-kidney transplantation phase, with a higher risk of infections and surgical complications, health care system experience longer and more costly hospitalizations.</p>
<p>Key words:</p>	<p>hospitalization • renal transplantation • infections • surgical complications</p>
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BACKGROUND

In order to decrease the costs, morbidity and mortality as the major concerns of any health system, transplantation systems try to better understand the post transplantation re-hospitalization [1], because they are costly, fatal [2], and may cause graft loss [3]. Newly, study of re-hospitalizations has been named as a tool for transplantation monitoring [4].

As a result, there is a wide interest toward epidemiologic studies assessing different causes of post renal transplantation rehospitalization [5-7]. From the large body of these studies, most have focused on a single cause [8,9], length of stay [10], or recipient characteristics [11-13].

There are few evidence regarding that post transplantation hospitalization causes more likely to occur at different time periods [14]. For example, for the case of lymphoma among transplanted patients, one study reported the highest rate in the first 12 months [15]. As well, one study demonstrated that length of post transplantation hospitalization stay is affected by the time interval between transplantation and admission [16]. However, most studies in the field of post renal transplantation rehospitalizations have neglected the time interval between transplantation and hospitalization.

It has been suggested that comparison of post-transplant complications over time may help guide the timing and intensity of posttransplant monitoring [15]. Due to this different pattern of hospitalization, investigating what factors play the main role in hospitalization in different time interval post renal transplantation was aim of our study.

MATERIAL AND METHODS

This is a retrospective study of 562 consecutive readmissions of renal transplanted patients at Baqiyatallah Hospital from January 1994 to April 2006. We conducted a retrospective study of 562 consecutive re-hospitalizations of kidney recipients in Baqiyatallah Hospital, Tehran, Iran, from 2000 to 2006.

Re-hospitalization was defined as a hospital admission that occurred for any reason after discharge from the initial transplantation hospitalization. In the 3 periods, rehospitalization were defined same. Admissions were decided by all transplantation team including 3 nephrologists and 1 urologist. According to time interval after transplantation,

re-hospitalizations were divided into early (within the first six month; n=278), intermediate (between six and 24 months; n=115), and late (beyond 24 months, n=169). The 6 and 24 months were selected because of the importance of these time intervals according to the previous studies especially by means of infection and graft rejection [17].

Charts of readmission were reviewed in terms of patients' age at rehospitalizations, gender, cause of end stage renal disease (ESRD), causes of admission, length of hospital stay and hospitalization charges. For mortality and graft loss, we determined mortality and function of kidney at the time of discharge. Primary diagnoses recorded in patients' hospital discharge records included broad categories. We categorized them to infection, graft rejection, surgical complication, and malignancies. Miscellaneous etiologies included post transplant diabetes melitus (PTDM), benign prostatic hyperplasia (BPH), post-transplant hypertension, anemia, intestinal necrosis, transient thrombotic purpura, and cholestasis. Such categorization has been previously used for post renal transplantation rehospitalization. As the admissions are possible for more than one cause, this makes that the sum of the frequencies of hospitalization causes to be more than 100%, in each time period [11,18].

The hospitalization cost was defined as the total costs patients were charged by the hospital for rehospitalization including the costs of hospital stay, medications, surgical procedures, laboratory and imaging tests, as well as miscellaneous costs. The costs included direct medical costs but not the indirect costs, such as those related to productivity loss due to days off work owing to the disease. Since the costs of hospitalizations were recorded in different years, it was necessary to adjust them for the inflation rates so that comparing costs across different years would make sense. Considering year 2006 as our adjustment reference, the costs recorded across years 1994 to 2005 were inflated to those of year 2006 assuming an annual inflation rate of ten percent [18]. To make the final costs internationally comparable, the costs in Iranian Rial were converted to \$ US (10,000 Rials = one US \$).

Statistical analysis

All analyses were performed using SPSS 11.5 (SPSS for Windows, SPSS Inc., Chicago, U.S.A.). Our analysis was performed with chi square testing for categorical variables and one way ANOVA for continuous variables. $P < 0.05$ considered as significant.

Table 1. Comparison of age at transplant and admission, ESRD cause, graft and patient status at discharge.

		Frequency (%)									Mean \pm Std. Deviation	
		Gender		ESRD cause			Graft loss		Mortality		Age in tx	Age at admission
		Female	Male	DM	HTN	other	Loss	Active	Live	Death		
Tx_admission_cat	Early	92 (33%)	189 (67%)	46 (22%)	45 (21%)	123 (57%)	14 (6%)	206 (94%)	213 (94%)	14 (6%)	41 \pm 14	41 \pm 15
	Intermediate	34 (29%)	83 (71%)	11 (14%)	21 (28%)	44 (58%)	8 (11%)	64 (89%)	74 (96%)	3 (4%)	39 \pm 15	40 \pm 14
	Late	61 (34%)	119 (66%)	11 (15%)	10 (14%)	52 (71%)	11 (11%)	88 (89%)	99 (94%)	6 (6%)	39 \pm 14	40 \pm 13
Sig.		0.673		0.117			0.246		0.755		0.201	0.588

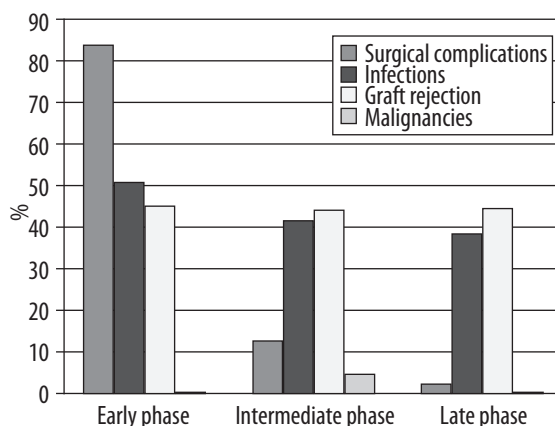
RESULTS

Among 562 rehospitalizations with a mean age at rehospitalizations of 40 \pm 14 (range: 16–73 years), 378 (67%) were due to male patients. The patients received grafts from living related donors (58; 10%), living unrelated (455; 81%) and cadaveric (49, 9%). Cause of ESRD were hypertension (20%), diabetic nephropathy (19%), urologic disorders (7%), autosomal-dominant polycystic kidney disease (6%), glomerulonephritis (5%), others (0.5%), and unknown (42%).

The readmissions in different post transplantation periods were not significantly different by means of age at transplantation (0.201), age at admission (0.588), gender (0.673), and cause of ESRD ($p=0.117$) (Table 1).

The causes of re-hospitalization in early phase were surgical complication (84%), infection (51%), graft rejection (45%), and malignancy (1%). These causes were graft rejection (44%), infection (42%), surgical complication (13%), and malignancy (5%) in intermediate phase. The causes of readmissions in late phase were graft rejection (45%), infection (39%), surgical complication (3%), and malignancy (0.06%). Infections (51%, 42% and 39% $p=0.016$) and surgical complications (84%, 13% and 3%, $p=0.03$) were significantly more common in early phase, but malignancies were more common (0.4%, 5% and 0.06%, $p=0.05$) in intermediate phase in comparison with the other two time intervals (Figure 1).

Length of hospital stay was longer in early phase in comparison to other time periods (12 \pm 11, 10 \pm 10, 9 \pm 7 group I, II, III, respectively, $p=0.001$). Hospitalization charges (709 \pm 366, 469 \pm 333,

**Figure 1.** Relative frequency of post renal transplantation admission causes for early, intermediate and late phase.

414 \pm 263 US \$, $p=0.035$) were significantly higher in the early post transplant phase.

Mortality ($p=0.755$) and graft loss during hospitalization ($p=0.246$) remained the same in all time intervals (Table 1).

DISCUSSION

This study showed a time dependent pattern of post kidney transplantation re-hospitalization, by means of cause, as seen a decreasing trend of infections and surgical complications from early to late phase, and by means of the same pattern in hospitalization length of stay and costs.

In our study, a decreasing trend of surgical complication was seen, but a proportion of these hospitalizations presented late, even after two years post transplantation. According to the literature, although most surgical complications present

early, but some surgical complications, for example obstruction or renal artery thrombosis, may present late, even after several years [19].

A great attention to decrease the surgical complications is necessary. Comparing different causes of post renal transplantation re-hospitalizations, admission due to surgical complications have been reported as predictor of renal recipient death and graft loss [3], and more than one of seven re-hospitalization of renal recipients for surgical complications are fatal [2]. Several surgical complications such as renal vein thromboses, renal artery thromboses, usually results in graft loss, and some others like arterial complications can be so fatal or devastating, by means of limb threatening [19,20].

Patients with old age at rehospitalizations, obesity, hypotension, multiple renal arteries, atherosclerotic disease, peripheral vascular disease, deep infections, insulin-dependent diabetes, hypercoagulable state, receiving antiplatelet agent or anticoagulation, history of deep venous thrombosis should be monitored because are at higher risk of surgical complications. Patients who receive newer, and more powerful immunosuppressive medications [21,22] or those who undergo kidney graft biopsy should be monitored as well. Technical problems, such as intimal dissection or kinking or torsion of the vessels, improper suturing technique, and donor artery trauma, angulation or kinking of the vein, compression by hematomas or lymphoceles, anastomotic stenosis, extension of an underlying deep venous thrombosis seem preventable with a better experience. Special interventions may also be beneficial, for example, prophylaxis with low-dose heparin for patients with hypercoagulable state. To minimize the detrimental impact on the graft and on the recipient, early diagnosis and appropriate intervention are crucial. It is crucial that all persons involved in the post-operative care of kidney transplant recipients be aware of the potential surgical complications that may occur, thus allowing for rapid diagnosis and treatment [19].

Similar to our results regarding the decreasing trend for infection, some have shown that infections are most common during the first six months post-transplant [23–26]. A study demonstrated that 50% of infectious episode occurred in first month [27], and two studies showed that one of the most common causes of death in early stage after renal transplantation is infection

[27,28]. The importance of infections in the first 6 month post transplant has been emphasized, repeatedly [29,30]. These may be due to the highest early doses of immunosuppressant. The key factors in preventing and minimizing the impact of posttransplantation infection in these patients are early diagnosis, low-dose immunosuppression, the experience of the transplantation team, and careful attention to the risks posed by endemic problems [31,32].

Regarding the peak in the rate of malignancy between six month and two year, literature shows a controversy. One study demonstrated that malignancy was one of the delayed causes of admission in kidney transplanted patients and in his study, late death (those after the first year) was caused predominantly by malignancy [17].

In our study, a great part of patients admitted to the hospital for more than one cause, mostly for surgical complications and infections. According to the literature, post transplantation admissions due to more than one cause is well known [19]. These include wound infections, aneurysms, lymphoceles, or urinary leaks [19,30,31].

Similar to our study, higher length of stay during first 6 month has been reported [16]. which may be due to higher rate of infections or surgical complications, because both have been reported to be accompanied with prolonged post renal transplantation hospitalizations [10,19].

It should be mentioined that readmissions especially late ones are underestimated as many patients can not admit in that hospital or they may prefer another hospitals. Hospital stay, the expenses and causes of admission were presented elsewhere [10,11,13]. As well, we did not focus on differences by means of age, gender, cause of renal failure, ptdm. As we aimed to compare the causes of admissions in different post transplantation periods, we did not describe any specific category of readmissions in detail in any time interval. By other means, in this study, all infections (respectless of site of infection or the organism) were viewed as infections and all readmissions needing surgical interventions were viewed globally as surgical causes. So, we did not need to analysis the detailed type of each category

CONCLUSIONS

To conclude, in early post-kidney transplantation phase, kidney transplant recipients are at

a higher risk of re-hospitalization secondary to infections and surgical complications. This will provide a better understanding of the time dependent pattern of post transplantation rehospitalizations which will be used for a better design of time-specific preventive programs.

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