Cumulative radiation dose from medical imaging in kidney transplant patients

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Abstract

Background. Although many patients undergoing kidney transplant are exposed to multiple examinations that increase cumulative effective doses (CEDs) of ionizing radiation, no data are available characterizing their total longitudinal radiation burden and relating radiation burden with risk factors for more exposure.

Methods. We did a retrospective cohort study of 92 patients (mean age 52 years; range: 20–75 years) who underwent kidney transplant at University Hospital, Novara, Italy, that evaluated all following medical imaging procedures involving ionizing radiation undergone beginning June 2007, and all subsequent procedures through August 2011, at the centre.

Results. The mean and median annual CED were 17.2 and 4.9 millisieverts (mSv) per patient-year. The mean and median total CED per patient over the study period were 46.1 and 17.3 mSv, respectively. Twenty-eight and 12% of patients had total CED >50 and 100 mSv, values which are associated with a good or strong evidence of an increased cancer mortality risk, respectively. Computed tomography scanning accounted for 73% of the total CED. The annual CED was significantly higher in incident patients and in patients with ischaemic heart disease and cancer.

Conclusion. In this institution, multiple testing of kidney transplant patients was common in many patients associated with high cumulative estimated doses of ionizing radiation.

Keywords: cancer risk; kidney transplant; medical imaging; radiation dose

Introduction

Renal transplantation is the treatment of choice for patients with end-stage renal disease, for it reduces the morbidity, improves the life expectancy, offers better quality of life and is more cost-effective than dialysis [1–3]. Although the advances in surgical techniques, organ preservation, immunosuppression therapy and prophylaxis or treatment of infections have improved the short-term graft and patients survival, there has been little or no improvement in late graft and patient survival [4, 5].

The main complications among kidney-transplanted patients (KTP) are cardiovascular disease, cancer and infections. They also represent the most important causes of death in patients with functioning graft [6], thus reducing the advantages of the graft in terms of life expectancy and quality of life.

KTP often require repeated exposure to ionizing radiation for both diagnostic and therapeutic purposes. To evaluate the early and late graft complications, which were often present with non-specific signs and symptoms, radiological procedures are necessary to allow specific treatment. For instance, morphological imaging may help to diagnose urologic complications, like obstructions or leakage of urine and vascular disorders, like arterial or vein stenosis or thrombosis [7]. In addition, non-surgical disorders such as acute rejection, drug toxicity, ischaemic damage and renal infarction require functional imaging procedures [8, 9]. Finally, diagnostic and interventional radiological procedures may be useful to diagnose and treat several pathological conditions in districts other than the graft.

The main deterrent that hampers the use of procedures with ionizing radiations is the increasing awareness about the long-term effects of the radiation exposure, namely the association between ionizing radiation and increase in cancer risk [10]; it has been estimated that ∼1.5–2.0% of all cancers in the USA may be attributable to the radiation from computed tomography (CT) studies [11] and that ∼29 000 future cancers could be related to CT scans performed in the USA in the 2007 [12].

KTP have a 2.5–5 times higher risk of cancer compared to the general population for both uraemia and drug-related immunosuppression [13, 14]. The role of ionizing radiation from medical imaging in the excess risk of cancer needs to be quantified since it represents a risk factor that might be reduced. Cumulative effective dose (CED) allows for comparisons/summation of radiation...
exposure generated from different origins and has been previously used to quantify the radiation exposure from medical imaging procedures [15].

Today, there is increasing concern that multiple imaging procedures leading to cumulative radiation exposure may increase the likelihood of developing cancer in the future, particularly when radiation exposure starts at an earlier age or when it is associated with other known carcinogens. Among these, specialized groups of patients are those undergoing kidney transplant.

The aims of this retrospective, descriptive observational study are to quantify the CED of ionizing radiation in KTP, to identify the subgroups that are at an increased risk and to consider the potential health consequences of this radiation exposure.

Materials and methods

Data sources and study population

We conducted a retrospective study of KTP attending a single university-based renal transplant centre, who were prevalent at 30 June 2007 and followed until 15 August 2011; incident KTP during this period were based renal transplant centre, who were prevalent at 30 June 2007 and waited for transplant of 4.3 (1.7–9.9) years, and the remainder 21 underwent transplant during the study period.

The distributions of total CED for all radiological procedures are shown in Figure 1.

At univariate analysis, the average radiation exposure was significantly associated with the older-aged patients who were exposed to higher total CED ( \( P = 0.002 \) ) and annual CED ( \( P = 0.004 \) ) than the younger patients (Figure 2). The ischaemic heart disease status was associated with a significantly higher (37.7 ± 50.4 versus 13.1 ± 24.6 mSv, \( P = 0.003 \) ) annual CED as well as the presence of cancer (35.0 ± 42.6 versus 14.2 ± 28.3 mSv, \( P = 0.04 \)).

Fig. 1. Frequency distribution of CEDs for all radiological procedures in KTP.
Average annual CED was not significantly different between males and females, in the case of a second kidney transplantation or for the remaining co-morbid conditions. The renal function was assessed according to the serum creatinine, measured at the beginning of follow-up for prevalent and after the post-surgical renal recovery for incident patients. Fifty-five (59.8%) of KTP had a serum creatinine >130 μmol/L, but their annual total CED was not higher than KTP with normal renal function (Table 1). The average annual CED was higher in incident than in prevalent patients (37.1 ± 46.3 versus 11.3 ± 22.5 mSv, P < 0.001). The two subgroups of incident and prevalent patients did not show any significant difference for the co-morbid conditions, for the serum creatinine or in the case of a second kidney transplantation (Table 2).

The regression equation that summarized the results obtained in a multiple regression model with annual CED as predicted variable and age, cancer, ischaemic heart disease and incident status as predictor variables may be written as:

Annual CED (mSv per patient year) = 5.8 + 19.8 × incident status + 20.4 × cancer status + 18.8 × ischaemic status

Detailed results are reported in Table 3. Age did not more result a significant predictor in this multivariable analysis. Thus, it cannot be considered as an independent risk factor. All the remaining variables inserted into the model were statistically significant predictors of annual CED, whose variance can be accounted for, in order of decreasing relevance, by incident status, presence of cancer and presence of ischaemic heart disease.

Among the subjects, 40 (43%) were in the low (<3 mSv/year), 32 (35%) in the moderate (3 to <20 mSv/year), 11 (12%) in the high (20 to <50 mSv/year) and 9 (10%) in the very high (≥50 mSv/year) radiation dose groups. Twenty-six patients (28%) had a total CED >50 mSv, and 11 patients (12%) had a total CED >100 mSv.

The total number of radiological procedures for all patients was 1472 and the annual median and mean CED are shown in Table 4. The median (IQR) total CED per

Fig. 2. Box plot showing median and IQR of annual CED of radiation in KTP and haemodialysis (HD) patients.

Table 1. Patient characteristics for the study population and comparison of average annual CED for age group, sex, second transplantation and co-morbid conditions

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Total N (%)</th>
<th>Yes</th>
<th>No</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (18–50 years)</td>
<td>39 (42.3)</td>
<td>13.6 ± 35.7</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>2 (51–65 years)</td>
<td>30 (32.6)</td>
<td>18.2 ± 27.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (&gt;65 years)</td>
<td>23 (25.0)</td>
<td>21.9 ± 27.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>62 (67.4)</td>
<td>14.4 ± 25.5</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Second kidney transplant</td>
<td>12 (13.0)</td>
<td>11.2 ± 12.4</td>
<td>0.63</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>16 (17.3)</td>
<td>16.5 ± 22.7</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Creatinine &gt;130 µmol/L</td>
<td>55 (59.8)</td>
<td>16.3 ± 29.3</td>
<td>0.70</td>
<td></td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>15 (16.3)</td>
<td>37.7 ± 50.4</td>
<td>0.003</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Patient characteristics for the incident versus prevalent status and comparison of average annual CED

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Incident (N= 21)</th>
<th>Prevalent (N= 71)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual CED (mSv per patient-year)</td>
<td>37.1 ± 46.3</td>
<td>11.3 ± 22.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.7 ± 14.1</td>
<td>51.4 ± 14.0</td>
<td>0.59</td>
</tr>
<tr>
<td>Male (%)</td>
<td>42.8</td>
<td>73.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Second kidney transplantation (%)</td>
<td>23.8</td>
<td>9.8</td>
<td>0.13</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>19.0</td>
<td>16.9</td>
<td>0.75</td>
</tr>
<tr>
<td>Creatinine &gt;130 µmol/L (%)</td>
<td>52.3</td>
<td>61.9</td>
<td>0.29</td>
</tr>
<tr>
<td>Ischaemic heart disease (%)</td>
<td>23.8</td>
<td>14.1</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Table 3. Results of multiple linear regression analysis with annual CED (mSv per patient-year) as the dependent variable

<table>
<thead>
<tr>
<th>β</th>
<th>Standard error of β</th>
<th>B</th>
<th>Standard error of B</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>5.8</td>
<td>3.5</td>
<td>1.64</td>
<td>0.105</td>
<td></td>
</tr>
<tr>
<td>Incident status</td>
<td>0.28</td>
<td>0.10</td>
<td>19.8</td>
<td>6.7</td>
<td>2.94</td>
</tr>
<tr>
<td>Cancer</td>
<td>0.24</td>
<td>0.09</td>
<td>20.4</td>
<td>8.1</td>
<td>2.53</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>0.23</td>
<td>0.10</td>
<td>18.8</td>
<td>7.7</td>
<td>2.46</td>
</tr>
</tbody>
</table>

KT, kidney transplant.
subject over the study period was 17.3 mSv (7.8–57.7). The mean total CED was 46.1 ± 80.6 mSv. The mean levels are much higher than the median annual and total CED which reflects the right skew in this distribution of patients with increasing CED.

The median (IQR) number of radiological procedures was 3.9 (2.8–5.7) per patient-year. All patients underwent at least one procedure involving exposure to ionizing radiation: 52% had at least one CT examination, 42 and 8.7% had at least one nuclear medicine and one interventional procedure, respectively. The proportion of total radiation exposure attributable to different types of investigations is also shown in Table 4. Accounting for only 10.3% of the total number of radiological procedures, CT examinations accounted for 73% of the total CED. Among the 152 CT procedures, 59 (38.8%), 39 (25.7%), 28 (18.4%) and 9 (5.9%) were performed to diagnose or to monitor a previously diagnosed cancer, cardiovascular disease, infection and urological disease, respectively.

Conventional diagnostic radiology, nuclear medicine and interventional procedures accounted for 84.2, 4.5 and 1.0% of the frequency in procedures and for 16.8, 7.1 and 3.4% of total CED, respectively. The proportion of total CED to different types of CT examinations is shown in Table 5. Although comprising only 44.7% of the CT procedures, abdominal/pelvic examinations resulted in 80.2% of the CT radiation exposure and 58.4% of the total CED. The main analyses were repeated in the subset of 79 non-cancer patients. Both the total CED and annual CED were significantly higher in the older than in the younger patients (P = 0.002 and P = 0.003). Also, in this subset, the ischaemic heart disease status was associated with a significantly higher annual CED and the average radiation exposure was higher in incident than in prevalent patients (Table 6).

### Table 4. Number of radiological procedures and annual and total CED by procedure type

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number of examinations N (%)</th>
<th>Number of scans (average N of scans per examination)</th>
<th>Annual CED (mSv per patient-year) median (IQR)</th>
<th>Annual CED (mSv per patient-year) mean ± SD</th>
<th>Total CED mSv (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall total</td>
<td>1472 (100)</td>
<td>68 (44.7)</td>
<td>4.2 (1.9–18.2)</td>
<td>16.3 ± 29.9</td>
<td>4256.8 (100)</td>
</tr>
<tr>
<td>Conventional diagnostic radiology</td>
<td>1239 (84.2)</td>
<td>52 (1.3)</td>
<td>2.0 (1.3–2.8)</td>
<td>2.4 ± 1.8</td>
<td>711.8 (16.8)</td>
</tr>
<tr>
<td>CT</td>
<td>152 (10.3)</td>
<td>70 (1.6)</td>
<td>0.5 (0.0–12.1)</td>
<td>12.1 ± 27.1</td>
<td>3097.0 (72.7)</td>
</tr>
<tr>
<td>Nuclear medicine</td>
<td>67 (4.5)</td>
<td>193 (2.8)</td>
<td>0.0 (0.0–0.8)</td>
<td>1.1 ± 1.7</td>
<td>302.5 (7.1)</td>
</tr>
<tr>
<td>Interventional</td>
<td>15 (1.0)</td>
<td>315 (2.1)</td>
<td>123 (4.0)</td>
<td>0.6 ± 2.5</td>
<td>145.4 (3.4)</td>
</tr>
<tr>
<td>Abdominal/pelvis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 5. Number of CT examinations, CT scans and related total CED

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number of examinations, N (%)</th>
<th>Number of scans (average N of scans per examination)</th>
<th>Total CED mSv (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall total</td>
<td>152 (100)</td>
<td>315 (2.1)</td>
<td>3097 (100)</td>
</tr>
<tr>
<td>Head/neck</td>
<td>41 (27.0)</td>
<td>52 (1.3)</td>
<td>123 (4.0)</td>
</tr>
<tr>
<td>Chest</td>
<td>43 (28.3)</td>
<td>70 (1.6)</td>
<td>490 (15.8)</td>
</tr>
<tr>
<td>Abdomen/pelvis</td>
<td>68 (44.7)</td>
<td>193 (2.8)</td>
<td>2484 (80.2)</td>
</tr>
</tbody>
</table>

### Table 6. Patient characteristics for the subset of 79 non-cancer patients and comparison of average annual CED for sex, prevalent versus incident status, second transplantation and co-morbid conditions

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Total N (%)</th>
<th>Yes</th>
<th>No</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CED (mSv per patient-year)</td>
<td>152 (64.5)</td>
<td>9.0 ± 14.9</td>
<td>23.9 ± 42.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Male</td>
<td>51 (64.5)</td>
<td>9.0 ± 14.9</td>
<td>23.9 ± 42.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Prevalent</td>
<td>61 (77.2)</td>
<td>6.7 ± 9.5</td>
<td>39.9 ± 49.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Second kidney transplantation</td>
<td>11 (13.9)</td>
<td>10.5 ± 12.7</td>
<td>14.8 ± 30.1</td>
<td>0.49</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>12 (15.2)</td>
<td>19.5 ± 25.3</td>
<td>13.3 ± 28.9</td>
<td>0.26</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>12 (15.2)</td>
<td>36.8 ± 52.6</td>
<td>10.2 ± 19.4</td>
<td>0.005</td>
</tr>
</tbody>
</table>

### Discussion

The association between the level of cancer risk from low-level radiation exposure over time assumes the validity of the linear no-threshold model [22] and is derived from analyses of mortality data based on Japanese atomic bomb survivors [23], which provides strong evidence of an increased cancer mortality risk at equivalent doses >100 mSv, good evidence of an increased risk for doses between 50 and 100 mSv and reasonable evidence for an increased risk for doses between 10 and 50 mSv [24].

This study demonstrated that the annual CED in 43% of patients falls in the ‘low-dose’ category and 35% of patients fall in the ‘moderate-dose’ category. Therefore, ~80% of the cases fall in the two lower dose categories that are of relatively low concern for radiation. On the other hand, this study demonstrated that, within only 4 years, ~28% of KTP received >50 mSv and 12% received >100 mSv, a level at which there is little controversy over the potential for increased cancer risks.

For external validity, it is important to know the generalizability of these findings. It must be acknowledged that the study cohort was selected since only patients from the neighbourhood of the centre were enrolled. However, the sampled patient population was similar to the generality of the 750 patients who underwent kidney transplant in our institution as for mean age (52.4 ± 14.0 versus 50.3 ± 16.7 years; P = 0.18), presence of diabetes (15.2 versus 20.0%; P = 0.11) and presence of ischaemic heart disease (16.3 versus 17.1%; P = 0.85).

This level of radiation exposure is relevant when considering the high incidence of cancer among patients suffering from renal chronic disease, excluding non-
melanoma skin cancer and those cancers known to frequently cause end-stage renal disease (myeloma and urinary tract tumours); Vajdic [13] found a standardized incidence ratio of cancer of 1.16, 1.35 and 3.27 among patients with chronic kidney disease before the replacement therapy, during haemodialysis and after kidney transplantation, respectively. Among KTP, cancer rates are similar to the ones observed in non-transplanted people who are 20–30 years older [25]. The causes of carcinogenesis in end-stage renal disease are not completely understood, but in KTP, we assist to a summation of several mechanisms. The first is the transplant-related immunosuppression, as demonstrated by the fact that the main percentage of tumours is viruses-related [14]. The second is the carcinogenesis due to lymphocytes dysregulation and DNA damage [26, 27]; the third is carcinogenesis related to underlying renal disease (e.g. the acquired polycystic kidney disease and renal carcinoma) [28]. The fourth is the carcinogenesis due to drugs given for the glomerulonephritides or vasculitides; cyclophosphamide and azathioprine could induce bladder, kidney, skin cancer or lymphomas [29, 30]. In this context, the ionizing radiations, which are recognized to induce DNA and RNA damage and to reduce the capacity of molecules’ repair, could enhance the carcinogenesis and represent the ‘fifth’ mechanism of cancer in KTP.

There is no question that minimizing the radiation to these patients must be a high priority in an effort to minimize the risk versus benefit ratio. However, the caution about radiation for this group of patients must not be overstated. The life expectancy post-transplantation varies greatly (between 5 to >20 years) and with recent advances it may be improved. At these levels, the effects of radiation are stochastic and the latent period can be longer than 20 years, with the exception of radiogenic leukaemia that has a much shorter latency (~5 years). Therefore, the stochastic radiogenic risk for the onset of carcinogenesis is comparable to the average survival post-transplantation.

This fact does not justify complacency about radiation but, given the alternatives, careful selection of radiological examinations and focussing on dose reduction techniques can greatly reduce the risk to benefit ratio. Moreover, in circumstances in which clinical management requires multiple imaging procedures, monitoring of the cumulative radiation dose and inclusion in the patients’ record have been suggested so that considerations of further exposure can be documented during the course of treatment [31]. One concern is the potential synergistic effect of immuno-suppressive drugs and radiation but we do not have adequate data to make any conclusion about this risk.

The comparison with the results of published studies regarding the radiation exposure in chronic or recurrent patients deserves further consideration. KTP receive on average a radiation dose higher than other chronically ill patients: Stein et al. [32] reported a mean total CED after 3 years of 12.3, 21.7, 18.7 and 14 mSv in patients with hydrocephalus, pulmonary thromboembolic disease, renal colic and cardiac disease, respectively. Kroeker et al. [33] reported a mean total CED of 14.3 mSv after 5 years in patients with Crohn’s disease. Chen et al. [34] reported a mean total CED over 3 years of 23.1 mSv in patients who underwent more than one cardiac imaging procedure. Einstein et al. [35] reported a mean total CED over 20 years of 96.5 mSv in patients undergoing myocardial perfusion imaging. Lawler et al. [36] documented a mean cumulative CED of 19.1 mSv due to cardiac imaging among patients with myocardial infarction in a 3 years period. However, the KTP radiation dose is lower than haemodialysis patients for whose a mean total CED over 3 years of 55.7 mSv was previously reported by our group [37]. These values must be compared to an estimate of mean total CED over 4.1 years of 46.1 mSv in renal KTP: the mean annual CED in KTP is significantly lower than in haemodialysis patients as illustrated in Figure 2, suggesting that kidney transplantation is a favourite renal replacement therapy also in the light of the radiological exposure. However, it must be considered that in the majority of KTP, the radiation doses experienced after kidney transplant added with the ones experienced during previous haemodialysis period: De Mauri et al. [37] reported an annual CED of 22 mSv/year in the whole group of haemodialysis patients that raises to 31 mSv/year in the subgroup of renal transplant eligible patients and lowers to 18 mSv/year in the subgroup with maintenance haemodialysis, against and average annual CED of 16 mSv/year post-transplantation.

To our knowledge, there is only one published study on the CEDs that KTP accrue over time [38]. Notwithstanding a similar period of median follow-up (4 years), the median estimated total CED was higher (17.3 versus 2.9 mSv) and, even more relevant, the median annual CED was almost 8-fold in our study (4.2 versus 0.52 mSv). This is mainly because of the severe underestimation in the study of Coyle et al. of the contribution of CT exposure. On average, in the study of Coyle et al., a CT study contributed an average 9.8 mSv to the CED compared with a corresponding figure of 20.3 mSv in our study. This is likely attributable to the non-consideration of the number of CT scans in a single CT study, which is a crucial factor in determining the total examination dose.

The results of this study should be interpreted in the context of several limitations. Firstly, it was conducted in a single centre, while the pattern of use of radiation-related procedures and the resulting patient exposure is highly variable depending on both available technologies and clinical practices. Moreover, we only registered total CED during the study period and as performed at our medical centre; this by definition underestimates the radiation exposure of the subjects. Secondly, the inclusion in the sample population of patients already affected by cancer could be criticized since these subjects may inflate the CED due to therapeutic imaging/monitoring. The main analyses were thus repeated in the subset of 79 non-cancer patients with similar conclusions. Thirdly, we did not use measures of radiation doses that are specific to the subject we studied but instead we relied on estimates of effective doses, which are neither precisely measured nor subject specific. This limitation was partly compensated in our study by careful recording of the number and location of scans in individual CT examinations, by the estimation of effective dose for CT examinations derived from the individual dose report and Monte Carlo-based dosimetry calculations and by the estimation of effective
dose from nuclear medicine procedures obtained from individual administered activities. Finally, although effective dose reflects cancer risk from radiation, it is a population-averaged metric that does not account for individual characteristics such as age and health status. Since there are no long-term outcome data in this study, the relationship between radiation exposure and the incidence of cancer in KTP cannot be directly assessed. The population of KTP patients is fundamentally very different in several respects from both the Life Span Study cohort and, more importantly, the general population. These differences favorably shift the balance of benefit versus risk of the ionizing radiation associated with KTP patients.

In conclusion, in our single-centre study and within a 4-year period, ~24% of the renal KTP received high cumulative estimated doses of radiation because of several co-morbidities requiring many diagnostic and therapeutic radiological procedures. The radiation doses experienced after kidney transplant added with those experienced during previous haemodialysis periods. Efforts are needed to reduce this cumulative dose and its potential attendant risks.

**Transparency declarations.** None declared.

**Conflict of interest statement.** None declared.

**References**


Steroid avoidance with intensified early EC-MPS

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Abstract

Background. Short-term intensified dosing using enteric-coated mycophenolate sodium (EC-MPS) reduces rejection after kidney transplantation without compromising safety and may facilitate steroid avoidance.

Methods. In a 6-month, multicentre open-label trial, 222 de novo kidney transplant recipients at low-immunological risk were randomized to steroid avoidance or maintenance steroids with interleukin (IL)-2 receptor antibody (IL-2RA) induction, EC-MPS (2160 mg/day to Week 6, 1440 mg/day thereafter) and cyclosporine.

Results. The primary end point; treatment failure at Month 6 [biopsy-proven acute rejection (BPAR), graft loss, death or loss to follow-up], occurred in 17.9% (20/112) of steroid-avoidance patients and 14.5% (16/110) of controls (difference 3.4%, 95% confidence interval −6.3 to 13.1, P = 0.47 for superiority testing). BPAR occurred in 11.6 and 7.3% of patients in the steroid-avoidance and control arms, respectively (P = 0.27). Creatinine clearance was similar at Month 6 (steroid-avoidance 56 ± 18 mL/min/1.73m², controls 60 ± 22 mL/min/1.73m², P = 0.34). Cytomegalovirus infection, as reported by investigators, occurred in 12.5% of steroid-avoidance patients and 22.7% of controls (P = 0.045).

Conclusions. A regimen of early intensified EC-MPS dosing with calcineurin inhibitor and IL-2RA induction permits oral steroid avoidance in adult kidney transplant patients at low-immunological risk without compromising efficacy at 6 months’ follow-up.

Keywords: EC-MPS; enteric-coated mycophenolate sodium; MMF; mycophenolic acid; myfortic

Introduction

Steroid-free immunosuppression is a long-standing goal for immunosuppression following kidney transplantation.