

Original article

Cytomegalovirus infection after kidney transplantation and long-term graft loss[☆]

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ARTICLE INFO

Article history:

Received 2 December 2015

Accepted 17 November 2016

Available online 27 September 2017

Keywords:

Cytomegalovirus infection

Graft loss

Mortality

Kidney transplant

ABSTRACT

Background: Despite the use of prevention strategies, cytomegalovirus (CMV) infection is the most common viral complication after renal transplant and its impact on long-term outcomes is still open to debate.

Objective: To evaluate the incidence of CMV infection and disease during the use of prevention strategies in our centre and to analyse the association between CMV infection and long-term patient and graft survival and other potentially clinical events related with CMV.
Methods: We reviewed the medical records of 377 recipients of kidney transplants performed between January 1998 and December 2008. Kaplan-Meier survival curve analysis was performed to analyse graft and patient survival by CMV infection/disease and Cox proportional hazards regression was used to identify factors associated with CMV infection/disease, graft loss and mortality.

Results: The incidence of CMV infection was 34.7% and CMV disease was 9.5%. Patient and graft survival was significantly lower in patients with CMV infection/disease. CMV infection/disease was associated with a higher risk of graft loss (HR 1.91, 95% CI 1.09–3.36, $p=0.023$), but not with a higher mortality (HR 1.29, 95% CI 0.7–2.38, $p=0.4$).

Conclusion: CMV replication after renal transplant is a risk factor for long-term graft loss but not mortality. Prevention strategies decrease post-transplant CMV infection and disease.

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[☆] Please cite this article as: López-Oliva MO, Flores J, Madero R, Escuin F, Santana MJ, Bellón T, et al. La infección por citomegalovirus postrasplante renal y pérdida del injerto a largo plazo. Nefrología. 2017;37:515–525.

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La infección por citomegalovirus postrasplante renal y pérdida del injerto a largo plazo

R E S U M E N

Palabras clave:

Infección por citomegalovirus
Pérdida injerto
Mortalidad
Trasplante renal

Antecedentes: A pesar del uso de estrategias de prevención y la mejora en los métodos diagnósticos, el citomegalovirus (CMV) continúa siendo la complicación viral más frecuente después del trasplante renal y su impacto en los resultados a largo plazo se sigue debatiendo. **Objetivo:** Conocer la incidencia de infección/enfermedad por CMV bajo estrategias de prevención y analizar su asociación con la supervivencia del paciente y del injerto y con otros eventos clínicos relacionados con el CMV.

Métodos: Revisión de las historias clínicas de 377 pacientes trasplantados de riñón entre enero de 1998 y diciembre del 2008. Se analizó la supervivencia por el método de Kaplan–Meier en función de la presencia o ausencia de infección/enfermedad CMV y se usó el modelo de Cox para identificar factores asociados con infección/enfermedad por CMV y para evaluar su impacto en la mortalidad y la pérdida del injerto.

Resultados: La incidencia de infección por CMV fue del 34,7% y de enfermedad del 9,5%. La supervivencia del paciente y del injerto fue significativamente inferior en los pacientes con infección/enfermedad CMV. La infección/enfermedad por CMV se asoció de forma significativa a mayor riesgo de pérdida del injerto (HR 1,91, IC del 95% 1,09-3,36, $p=0,023$) pero no con más riesgo de mortalidad (HR 1,29, IC del 95% 0,7-2,38, $p=0,4$).

Conclusión: La replicación viral después del trasplante es un factor de riesgo de pérdida del injerto pero no de mortalidad a largo plazo. Las estrategias de prevención disminuyen la incidencia de infección y enfermedad por CMV postrasplante.

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Introduction

Cytomegalovirus (CMV) infection is a common complication in patients receiving a kidney transplant. It usually appears during first year after transplantation and; if it appears, it has direct and indirect effects on the patient and the graft, both short and long term.¹ The direct effects are well known, they are associated with high rates of viral replication and they occur in the form of CMV infection/disease. However, indirect effects are more difficult to recognise and are caused by the interaction of low rates of viral replication with the immune system.²

In the period when viral prevention and monitoring strategies were not widely used, the incidence of CMV infection/disease was high (60% infection and 30% disease).³ Both donor and recipient CMV sero-pairing and the use of anti-lymphocyte antibodies were important risk factors for CMV disease.⁴ This served to identify the risk of infection of patients so they are classified as high, moderate or low risk of infection. This classification is still used to dictate the prevention strategy.⁵

Indirect effects have been associated with increased morbidity (opportunistic infections), graft loss and long-term mortality.⁶⁻¹³

The recent avenue of effective antiviral drugs in the control of CMV, such as ganciclovir and valganciclovir, improved diagnostic methods and the use of CMV prevention strategies (universal prophylaxis and early treatment) have represented an important milestone in improving transplant care and

outcomes, reducing the risk of CMV infection/disease,^{6,14} the risk of acute rejection and the risk of mortality and long-term graft loss.^{6,7,12,15-17}

This study aims not only to understand the cumulative incidence of CMV infection/disease in our setting, taking into account differences in prevention strategies over time, and to analyse whether there is a correlation between viral replication and patient and long-term graft survival, as well as other adverse events potentially related to CMV, such as cardiovascular disease, neoplasms and infections.

Patients and methods

Study design

An observational, retrospective and single-centre study was conducted, in which CMV infection/disease after renal transplantation was the main endpoint of interest. Two cohorts of patients were created based on the existence or not of CMV infection/disease after transplantation (CMV group and non-CMV group, respectively). The results were analysed globally and according to the prevention strategy used (universal prophylaxis or preemptive therapy).

Study population

Patients receiving a kidney graft in our centre between January 1998 and December 2008. Patients who lost the kidney graft, died or were lost to follow-up less than 3 months after

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