May 5, 2001

Circulating Endothelial Cells after Transplantation

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Fate of renal allografts that survive vascular rejection

Citation: **Salazar AB, McAlister VC, Gupta R, MacDonald AS.** [Circulating endothelial cells after transplantation.](#) Lancet. 2001 May 5;357(9266):1450. PMID: 11360956

Jordan Pober, in his Jan 6 commentary,¹ asks whether the vascular rejection after replacement of donor endothelium in transplanted kidneys, reported by Emma Lagaaij and colleagues,² presents the graft with an advantage in an alloreactive environment. Pober and Lagaaij and colleagues identify Sir Peter Medawar's priority with his hypothesis in 1965 that host acceptance of a graft might be induced by endothelial replacement.^[3] and ^[4] However, Lagaaij and colleagues point out the apparent anomaly that vascular rejection is associated with a very poor prognosis for graft survival.

We have seen loss of the graft through vascular rejection. This effect probably arises before there is an opportunity for endothelial repair, whether by replacement with recipient cells or not. To measure the outcome for grafts that survive early vascular rejection, we reassessed 411 biopsy samples taken from 260 patients in the first month after transplantation. Patients were separated into four classifications, according to Banff 1997 criteria: vascular rejection (36 patients); acute cellular rejection ([ACR] 30); no rejection (194); and 974 recipients from the same era who did not undergo biopsy. Other than graft histology, the groups did not differ for known adverse prognostic factors. The mean follow-up period was 6.03 years (SD 4.7).

Graft survival is presented in the [table](#). The graft attrition rate for the ACR group was significantly higher than for the no rejection group (6.5 vs 3.8% per year) and no biopsy groups (6.5 vs 2.8% per year).

Table. Graft loss and attrition by group

Group	Graft loss in first 6 months	Graft attrition (% per year) after 6 months (95%CI)	Number at risk
Vascular rejection	12 (33%)	2.3 (1.9–2.7)	36
ACR	8 (26%)	6.5 (3.9–9.1)*	30
Biopsy, no rejection	51 (26%)	3.8 (3.7–3.9)*	194
No biopsy	115 (12%)	2.8 (2.1–3.5) [†]	974

* p<0.0001.

[†] p>0.05 compared with vascular rejection group.

In the group that experienced vascular rejection in the 1st month after transplantation, 12 (33%) grafts were lost to the first episode. These grafts failed within 4.3 weeks (SD 3.3). Two grafts recovered marginal function and failed within the 1st year. However, after 6 months, the rate of graft loss for survivors of vascular rejection (2.3% per year) is significantly less than that seen in the ACR or no rejection groups. Only four (11%) grafts failed because of chronic rejection.

Although vascular rejection results in a high rate of early graft loss, few grafts fail because of chronic rejection. Grafts that recover from the first episode of vascular rejection seem to have a subsequent survival benefit. If as, Lagaaij and colleagues suggest, endothelial replacement has occurred in these grafts, these data are consistent Medawar's hypothesis.

References

- [1](#) JS Pober, Is host endothelium a silver lining for allografts?. *Lancet*, **357** (2000), pp. 2–3.
- [2](#) EL Lagaaij, GF Cramer-Knijnenburg, FJ van Kemenade, LA van Es, JA Bruijn and JHJM van Krieken, Endothelial cell chimerism after renal transplantation and vascular rejection. *Lancet*, **357** (2000), pp. 33–37.
- [3](#) PB Medawar, Transplantation of tissues and organs: introduction. *Br Med Bull*, **21** (1965), pp. 97–99.
- [4](#) RJ Tesi, EA Elkhammas, ML Henry, EA Davies, A Salazar and RM Ferguson, Acute rejection episodes: best predictor of long-term primary cadaveric renal transplant survival. *Transplant Proc*, **25** (1993), pp. 901–902.