Adverse Impact of Hypertension on Diabetic Recipients of Transplanted Kidneys

ELI A. FRIEDMAN, LUCIA M. CHOU, MONICA M. BEYER, KHALID M. H. BUTT, AND THOMAS MANIS

SUMMARY The effect of hypertension on patient and allograft survival in 60 diabetic recipients of transplanted kidneys was assessed by retrospective chart analysis. Hypertension was present in 81% of recipients. Of eight of these patients who became normotensive after transplantation, all had functioning allografts and one died. By contrast, persistent hypertension after transplantation was associated with a higher mortality rate (25 of 54, 48%) and loss of kidney graft function (19 of 54, 35%). At a mean of 21 months after transplantation, living hypertensive diabetic recipients had worse renal function (mean serum creatinine of 3.1 mg/dl) than did nonhypertensive recipients (mean serum creatinine of 1.6 mg/dl). It is concluded that hypertension is a significant risk factor for diabetic patients and kidneys after transplantation. (Hypertension 7 [Suppl II]: II-131-II-134, 1985)

KEY WORDS • allografts • survival

HYPERTENSION is more prevalent in patients with diabetes, insulin dependent (type I) or maturity onset (type II), than in nondiabetic persons of the same age, weight, and sex. As characterized by Kaplan and Punzi,1 diabetic patients pay a "particularly high price" for untreated hypertension due to accelerated kidney (glomerulosclerosis plus nephrosclerosis) or heart disease. Current medical regimens for diabetic management stress the importance of returning hypertensive blood pressures to normal as a means of reducing the frequency of stroke, heart attack, and blindness. Blood pressure reduction in hypertensive patients with type I diabetes will reduce the rate of loss of renal function by about one-half. 2 3 That hypertension threatens survival in patients with type I diabetes who receive a transplanted kidney (nearly all of whom are hypertensive) is a reasonable inference (although still a supposition) from studies in nonuremic diabetic persons. One explanation for the rapid (within 4 years) "reappearance" of glomerulosclerosis in transplanted kidneys may be the combined injurious effect on the kidney of diabetes plus hypertension. In this context, diabetes-induced glomerulopathy in a hypertensive recipient might progress to renal insufficiency in less than a decade; it requires 20 years, most of them normotensive, for this process to result in occlusive glomerulosclerosis in native kidneys.

To ascertain the effect of hypertension on the course of diabetic patients undergoing kidney transplantation, we reviewed the records of 684 recipients and compared patient and renal allograft survival.

Methods

The records of 684 kidney transplants performed at Downstate Medical Center between January 1977 and July 1983 were reviewed retrospectively. Patients diagnosed as having diabetes before transplantation were classified according to criteria proposed by the National Diabetes Data Group and the World Health Association4 as having type I disease if they were insulin-dependent, ketosis-prone, and had onset before age 35 years. Those who were not insulin-dependent and nonketotic, and had disease onset after the age of 35 years were said to have type II diabetes. Patients who first manifested hyperglycemia after kidney transplantation were analyzed separately3 and were not included in this study.

A total of 76 persons with previously diagnosed diabetes received a transplanted kidney, of whom 9 were excluded from this study because they underwent transplant nephrectomy within the first month after transplantation. The remaining 67 recipients consisting of 46 with type I (69%) and 21 with type II (31%) received 73 transplanted kidneys. Repeat transplantation was performed in five patients, four of whom received two kidneys, and one of whom received three kidneys.

Hypertension was defined as systolic blood pressure (BP) above 160 mm Hg and/or diastolic BP above 95
mm Hg. Patients receiving any antihypertensive medication for previously diagnosed hypertension were considered hypertensive. Mean BP was calculated as 
\[\text{diastolic BP} + \frac{1}{3} (\text{systolic BP} - \text{diastolic BP})\]. Blood pressure measurements as recorded in hospital records were collected for each subject on the day preceding, 7 days after, and 1 to 3 months after transplantation, and at the time of this study (May to July 1983). For recipients who died prior to May 1983, BP values recorded within 2 months of death were used for analysis. The date of transplantation was taken as the reference point for counting patient age, duration of diabetes, and duration of hypertension. For the five recipients of repeat kidney grafts, the most recent procedure was the event from which all timed observations in this study were made.

Statistical significance was calculated by Student's t test or chi-square analysis.

**Results**

A comparison of age, duration of diabetes, and duration of hypertension in living and dead patients is given in Figure 1. The proportion of functioning renal allografts in hypertensive and nonhypertensive patients is shown in Figure 2. Blood pressure measurements before and after kidney transplantation in 46 recipients with type I and 21 with type II diabetes are shown in Figure 3. Of the 67 patients studied, 60 (90%) were hypertensive before and 54 (81%) were hypertensive after transplantation, including 2 of 7 who had been normotensive before transplantation (Figure 4). Systolic, diastolic, and mean BP values, were compared for both types of disease on the day preceding transplantation and postoperatively on Day 7 and at 1 to 3 months and 11 to 24 months (Table 1). No difference in mean BP between groups was noted at any of these times. When the 60 hypertensive diabetic recipients were divided postoperatively into subsets of 52 (87%) who remained hypertensive and 8 (13%) who became normotensive, no significant group differences in age, duration of diabetes, or duration of hypertension prior to transplantation were discerned (see Figure 2). All of the normotensive recipients had functioning allografts at the time of study, while only 38 (63%) of the hypertensive recipients retained graft function (p < 0.04).

Diabetic recipients experienced a high mortality
HYPERTENSION IN DIABETIC KIDNEY TRANSPLANT RECIPIENTS/Friedman et al.

Only 39 (58%) of the group were alive at the time of this study (after a mean follow-up of 24.2 months). Death in 28 patients occurred after a mean of 11.0 months. The charted causes of death were sepsis, 7; myocardial infarction, 5; congestive heart failure, 4; gastrointestinal hemorrhage, 3; cerebrovascular accident, 2; and undetermined, 3. Surviving recipients had a significantly \( p < 0.01 \) lower mean BP (99.8 mm Hg) than did those who died (110.3 mm Hg). Further indicating the consequence of hypertension was its significantly \( p < 0.02 \) longer mean duration in recipients who died (8.5 years) than in survivors (3.5 years).

Poor or absent kidney graft function imparted a grim prognosis. Of the 20 (30%) recipients who required posttransplantation hemodialysis either short-term or long-term, only 12 were alive after 1 year; 11 were dead within 1 year. Nearly all survivors had normal graft function for at least 1 year after transplantation.

![Blood Pressure Pattern Before and After Transplantation](image)

**FIGURE 3.** Mean blood pressures before and at intervals after transplantation are shown. Mortality was higher in hypertensive recipients than in those who remained normotensive.

![Blood Pressure Pattern Before and After Transplantation](image)

**FIGURE 4.** Blood pressures before and after transplantation are shown for the entire study group. There were few normotensive diabetic recipients.

**TABLE 1.** Mean Blood Pressure (± sd) in Patients with Type I and Type II Diabetes Before and After Renal Transplantation

<table>
<thead>
<tr>
<th></th>
<th>Type I</th>
<th>Type II</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before transplantation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic/diastolic*</td>
<td>171.1 ± 28.4/98.7 ± 12.5</td>
<td>172.9 ± 32.5/95.2 ± 18.0</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>122.8 ± 16.0</td>
<td>121.1 ± 20.9</td>
<td>NS</td>
</tr>
<tr>
<td>1 wk after transplantation</td>
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<tr>
<td>Systolic/diastolic</td>
<td>167.8 ± 21.6/93.1 ± 10.1</td>
<td>163.7 ± 26.6/96.9 ± 11.7</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>118.0 ± 11.7</td>
<td>119.2 ± 15.1</td>
<td>NS</td>
</tr>
<tr>
<td>1-3 mo after transplantation</td>
<td></td>
<td></td>
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<tr>
<td>Systolic/diastolic</td>
<td>154.6 ± 24.7/91.1 ± 13.4</td>
<td>148.6 ± 29.3/84.0 ± 13.9</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>112.3 ± 15.3</td>
<td>105.5 ± 16.5</td>
<td>NS</td>
</tr>
<tr>
<td>Most recent†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic/diastolic</td>
<td>146.8 ± 23.7/86.8 ± 11.8</td>
<td>142.5 ± 21.0/87.2 ± 12.9</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>106.8 ± 14.5</td>
<td>105.6 ± 14.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

\*All values in mm Hg.
†Mean duration after transplantation was 19.6 months in patients with type I and 11.7 months in those with type II diabetes.
for as long as 14 months, 19 (95%) had been hypertensive throughout their course and 13 (65%) died. Successful establishment of allograft function (serum creatinine < 2 mg/dl) for from 1 to 107 months (mean 24.5 months at time of study) was attained in 47 recipients (70%). Of these 47, 33 who had been hypertensive before transplantation remained hypertensive after transplantation, 8 hypertensive recipients became normotensive, 2 normotensive recipients became hypertensive, and 4 normotensive recipients remained normotensive.

Discussion

The majority of patients in chronic renal failure are hypertensive; retention of salt and water that induces expansion of the intravascular volume is the most important mechanism underlying their raised BP. While contraction of intravascular volume by large doses of loop diuretics and/or ultrafiltration during hemodialysis will normalize BP in the majority of hypertensive nondiabetic uremic patients, 60 of 67 (90%) of the diabetics in this series were hypertensive at transplantation. Hypertension adversely affects the course of diabetic retinopathy and glomerulopathy. Sustained reduction of hypertensive BP slows the decline in renal function with time that is typical in patients with long-duration type 1 diabetes.6

In the current study, survival of diabetic kidney transplant recipients was inversely correlated with the presence of postoperative hypertension. One striking illustration of the negative impact was evident in the dissimilar proportion of functioning allografts in hypertensive and nonhypertensive diabetic recipients. All of 8 recipients (of 60 diabetic recipients in this series) who became normotensive after transplantation retained functioning kidneys, but only 63.5% of 52 recipients who were hypertensive after transplantation had functioning allografts when studied, a significant (p < 0.04) difference underscoring the negative effect on kidney graft survival of hypertension.

Interprogrammatic disparities in survival of diabetic kidney transplant recipients are marked.7,8 Gonzalez et al.,10 for example, reported 1-year patient and allograft survival of only 63 and 45%, while Sutherland et al.11 found no difference in patient or cadaveric graft survival 2 years after transplantation between patients with type I diabetes and nondiabetic recipients. Factors that account for inequality in series outcome, recently reviewed by Peter et al.,12 probably transcend basic competence of the surgical and supporting medical teams. Exclusion criteria, recipient age, severity of uremia at time of transplantation, preoperative manipulative (nephrectomy, splenectomy, and blood transfusions), and immunosuppressive regimens are variables known to influence allograft survival, and they must be equivalent in patient subsets in order to consider experimental groups to be at similar risk.

From the current study it seems apparent that hypertension must be included in the list of risk factors that threaten patient and graft survival in diabetic recipients of transplanted kidneys. Ethical constraints proscribe any prospective study of untreated versus treated hypertension in kidney transplantation. This series based on retrospective chart analysis, however, provides sufficient justification for aggressive treatment of hypertension in diabetic recipients of renal allografts. (These results were previously reported in preliminary form.13)

References

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