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Incidence of osteonecrosis after renal transplantation

The incidence of osteonecrosis was 24% in 248 patients who had received 262 kidney transplants 1971–1982. However, based only on patients at risk, i.e. alive with functioning transplants, the incidence at 1, 3 and 6 years was found to be 13, 27 and 36%; after six years no new cases were found. The relative increase in body-weight at 180 days was predictive as regards risk for osteonecrosis, while the cumulative dose of steroids was not. This suggests that individual sensitivity to steroids rather than the absolute cumulative dose is involved in the development of osteonecrosis.

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The etiology of femoral head necrosis associated with renal transplantation is still controversial, corticosteroids and pre-existing osteodystrophy being the most likely causes, although post-transplant tertiary hyperparathyroidism may also play a role. We evaluated the incidence of osteonecrosis (ON) in the first 248 renal transplant patients at the University Hospital Rotterdam-Dijkzigt. The relationships between ON and other factors, like cumulative corticosteroid dose, increase in body weight and some biochemical parameters, were also studied.

Patients and methods

We reviewed the records of 248 patients, who received a total of 262 kidney transplants between 1971 and 1982.

Immunosuppressive treatment consisted of azathioprine (2–3 mg/kg body weight) and prednisone (30 mg) from the day of transplantation Rejection episodes, diagnosed in 90 per cent of the patients, were treated both by increasing the oral steroid dose and by i.v. administration of methyl-prednisolone.

For further analysis, 189 patients (127 male and 62 female) at risk for more than 1 year (alive with functioning transplant) were studied. The follow-up period ranged from 1–10 years.

Radiographic examinations of the hip and knee joints were routinely performed in the absence of complaints and more frequently when indicated. The diagnosis of ON was based on the radiographic appearance of bone changes. The actuarial incidence of ON was determined by a modification of the life table method, as described by Merrell & Shulman (1955).

For statistical analysis, the chi-square (χ^2) test and Student's t-test were used.

Results

ON was diagnosed in 61 out of 248 patients. However, 59 patients were at risk for less than 1 year and only two of them developed ON. In the remaining 189 patients ON was diagnosed in 59.

The actuarial risk of developing ON at 1, 3 and 6 years were 13, 27 and 39 per cent. After 6 years no new cases were diagnosed (Figure 1). There were no differences for sex, recip-

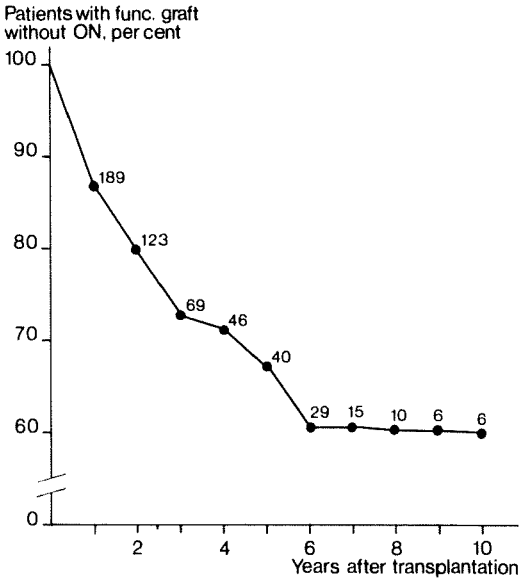

Figure 1. The actuarial incidence of ON.

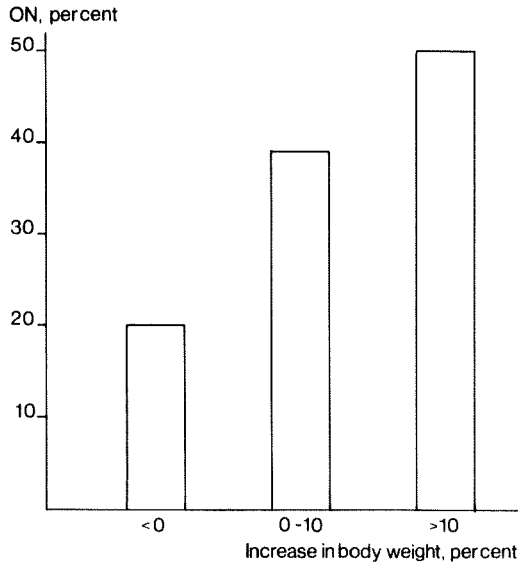

Figure 2. Relative increase in body weight 180 days after transplantation and the incidence of ON.

ient's age, time on hemodialysis before transplantation and number of second transplants between patients with and without ON. Hips, knees and shoulders were the predominantly affected joints (Table 1). In 16 patients only one joint was affected, in the others two or more joints were affected. Twenty-nine of 59 patients with ON had complaints before radiographic diagnosis with a median period of 3 (1–13) months. Four patients had ON without symptoms, and two of them developed symptoms later on.

The mean serum calcium and alkaline phospatase levels, 3 and 6 months after transplantation, were not higher in transplant patients with ON than in those without. The mean serum phosphate levels at these intervals were not lower in the group with ON than in those without. In patients with ON 12 had hypercalcemia 3 and 6 months after transplantation, 3 had hypophosphatemia at 3 months and none at 6 months post-transplantation. The prevalence of these biochemical abnormalities was not different in transplant patients with ON than in patients without ON. The number of parathyroidectomies because of hyperparathyroidism was the same in both groups. The cumulative dose of steroids after transplantation was not different in patients with and without ON. The relative increase in body weight at 6 months after transplantation showed a strong positive correlation with the incidence of ON (Figure 2). There was no correlation with body weight at time of transplantation and the incidence of ON.

Table 1. Location of osteonecrosis in 59 patients

L Hip	39
R Hip	28
L Knee	18
R knee	14
Ankle	2
L Shoulder	17
R shoulder	16
L Elbow	1
R Elbow	3

Discussion

The reported incidence of ON after renal transplantation is 4–37 per cent (Cruess et al. 1968, Harrington et al. 1971, Nelson et al. 1971, Griffiths et al. 1974, Ibels et al. 1978, Elmstedt 1982, de Graaf et al. 1982). Definition of ON, observer error and the method of analysis may account for part of the difference.

Of our 248 renal transplant patients 24 per cent developed ON. However, many patients lose their graft or die before they have the op-

portunity to develop ON. Calculating the actuarial risk for ON is thus in our opinion a more appropriate method, and we therefore used a modification of the life table as described by Merrell & Shulman (1955) to determine the freedom-index of ON. With this method the incidence of ON is based only on patients at risk (alive with a functioning renal allograft). It then appeared that the risk for ON was almost twice the overall estimate, that only 50 per cent of the total number of ON cases developed in the first 2 years and that no new cases of ON developed later than 6 years after transplantation.

Most authors agree that corticosteroids play a role in transplantation ON (Woods et al. 1972, Briggs et al. 1972, Pierides et al. 1975, Ibels et al. 1978, Nixon 1983). The exact mechanism is unknown, and even a correlation of the total dose of corticosteroids with the occurrence of ON is still controversial. However, Harrington et al. (1977) and Nelson et al. (1971) reported a significant reduction in the incidence of ON when the mean corticosteroid dose was reduced.

De Graaf et al. (1982) found that the total amount of prednisone administered during the first months after transplantation correlated positively with the incidence of ON. On the other hand, in this and other reports (Cruess et al. 1968, Bewick et al. 1976, Ibels et al. 1978), no differences were found in the total initial dose of prednisone between patients with and without ON. However, the individual susceptibility to corticosteroids may vary considerably (Ibels et al. 1978, Adinoff & Hollister 1983), and may therefore obscure dose effect correlations. The increase in body weight may be an indicator of the physical effects of corticosteroids. Indeed, we found a correlation of ON and the increase in body weight 6 months after transplantation.

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