PROGNOSTIC VALUE OF RADIOISOTOPE RENOGRAMS IN KIDNEY TRANSPLANTATION

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Radioisotope renography is used to monitor the function of kidney transplants in man and experimental animals (*1–8*). This study is a valuable aid for diagnosing the rejection reaction, especially if serial renograms are made (*3,4,6,8*). Nevertheless, little emphasis has been given to evaluating the prognostic significance of serial renograms in the rejection reaction.

This report presents an evaluation of the prognostic application of serial radioisotope renograms in 39 patients who received either a live human donor or cadaver renal transplant at the University of Minnesota Hospitals from June 1964 to January 1966.

METHODS

Radioisotope renography. A dual ratemeter system with 2-in. NaI(Tl) crystals was used (*7*). The crystals were collimated so that the distance from the crystal face to the skin surface was 8 in. This minimized differences due to kidney depth below the skin. Renograms were made with the patient in the dorsal decubitus position. One probe was placed over the easily palpable transplanted kidney in the anterior iliac fossa. The second probe, which served as a blood-activity monitor, was placed over the precordium. The system was calibrated before intravenous injection by directing the heavily collimated probes at the bolus-filled syringe placed 100 cm away. A dose of 20 μCi of ^{181}I-orthoiodohippurate was injected as a bolus.

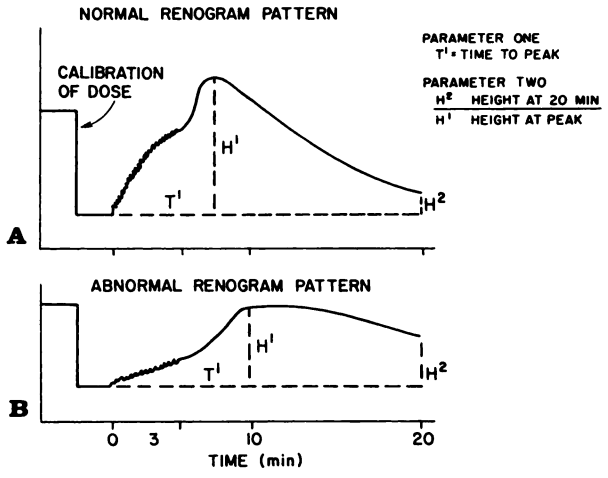

FIG. 1. Typical curves identifying renogram parameters: A is normal renogram pattern and B is abnormal renogram pattern.

The curve was recorded using a time constant of 3 sec and full-scale deflection of 10,000 cpm. Activity was displayed on a strip-chart recorder with overlapping pens. The recorder ran at 3 in./min during the first minute and 12 in./hr during the rest of the examination. Thirty-minute records were made. The normal renogram pattern using this method is shown in Fig. 1A.

Following transplantation, renograms were obtained while the recipient was in the postoperative recovery room and again within the first 24 hr after surgery. Renograms were then made on a daily basis for approximately 1 week and afterwards at various times dictated by the clinical course or renographic changes.

Renogram parameters. Based on the qualitative evaluation of the normal pattern (Fig. 1A) and definite abnormal patterns (Fig. 1B), arbitrary numbers were assigned to two parameters: (1) the "time to peak" in minutes and (2) the height at 20 min divided by the height at peak. These two parameters describe the renogram pattern numerically. Attempts by others at more sophisticated quantita-

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tion have been unsuccessful (*4*). The numerical values of the arbitrary parameters along with their suspected meanings are given in Table 1.

Rejection reaction. A clinical diagnosis of rejection was made based on enlargement of the transplanted kidney, fever, hypertension and various chemical determinations (primarily BUN, creatinine and creatinine clearance). Prednisone was held in reserve until a clinical diagnosis of rejection reaction was made. Thus the treatment policy permitted precise clinical definition of the rejection reaction.

Immunosuppression. Immuran (azothioprine) was used as the basic immunosuppressive drug with corticosteroid used only with significant transplant deterioration. The dose and schedule used in these patients have been reported (*9*).

RESULTS

Thirty-nine patients received either a living donor or cadaver kidney between June 1964 and January 1966 at the University of Minnesota Hospitals. Three of the 39 patients were not studied with serial renograms. Grossly abnormal renograms were obtained in 17 patients whose transplants never functioned. The remaining 19 patients had a clinical diagnosis of transplant rejection on 30 separate occasions (Table 2).

TABLE 1. RENOGRAM PARAMETER VALUES*

Categories	Time to peak (T′) (min)	Height at 20 min† / Height at peak
Abnormal	10+	0.75+
Borderline	8–10	0.6–0.75
Normal	0–8	0–0.6

* Arbitrary figures based on qualitative evaluation of serial renograms in present series of patients.
† H_3/H_1.

TABLE 2. CORRELATION OF RENOGRAMS WITH CLINICAL DIAGNOSES OF TRANSPLANT REJECTIONS

Renogram interpretation	Clinical impression	
	Rejection	Normal
Normal	4	—
Abnormal		
Before	10	16*
After	3†	
Simultaneously	13	
Total	30	16

* All cases had abnormal parameters. On occasions normal renograms were found before and after abnormal tracing.
† 2 with renograms every 24 hr. 1 with renograms after diagnosis.

On four occasions the renograms were normal at the time of clinical impression of rejection. These patterns remained normal throughout the period that active rejection was considered present. Moderate to rapid recovery was recorded in all four following additional therapy.

Sixteen were read as abnormal in patients who did not have the clinical findings of rejection. Normal renograms were obtained shortly before and immediately after the abnormal patterns in all these cases.

On 26 occasions renograms were obtained that correlated with the clinical impression. Ten predicted the rejection before the diagnosis was made clinically. In some cases abnormal renograms were obtained 2 days before any sign of deterioration was recorded clinically. Progressive deterioration in the patterns uniformly took place before steroid treatment was begun.

The clinical diagnoses of rejection preceded the appearance of abnormal renogram patterns in three patients. This was true in two of these patients despite serial renograms on a 24-hr basis. In one case the renogram was not obtained until after rejection was suspected on a clinical basis.

In 13 cases the renogram became abnormal on the day of frank clinical deterioration. These uniformly coincided with rapid renal deterioration and easy clinical diagnosis.

As the clinical state improved, reversal of the deteriorating renogram patterns takes place. The time parameter returns to normal values before the height-ratio parameter. Conversely, height-ratio parameter changes generally heralded the onset of rejection.

In one case the kidney transplanted into the left iliac fossa functioned while that in the right fossa never functioned adequately. Eventually the kidney on the left underwent complete rejection. The renogram patterns were consistent with the renal functional status in each of the transplanted kidneys.

Sixteen cases were tabulated in which the transplant survived 2 or more months associated with consistently normal renograms.

Five cases with normal renograms during the first week had early apparent rejections. Only one case without a normal renogram during the first week had a functioning transplant. Twenty with abnormal renograms in the initial week failed to function.

DISCUSSION

Whether abnormal patterns appear before, simultaneous with or after other clinical and chemical changes of renal transplant rejection has not been

ascertained. This task is complicated by numerous factors including (1) the nonphysiologic location of the transplant (thus, routinely normal renogram patterns do not necessarily represent the norm for the transplanted kidney), (2) causes other than rejection for alterations in renogram pattern and (3) difficulty in establishing a definite time for the clinical diagnosis of rejection. We attempted to control these various factors. First, we established norms for the renogram parameters based on retrospective observations. Excellent correlation between the renogram parameters and the condition of the graft was obtained in this series. Frequent renograms in some cases showed rejection patterns 2 days before the clinical diagnosis was established. Second, surprisingly, we encountered very few additional causes for abnormal renogram patterns. Finally, the treatment policy of withholding corticosteroids until a definite diagnosis of rejection established a point in time to determine the prognostic significance of the renogram.

On sixteen occasions single renograms suggested rejections. Repeat studies on the following day showed all of these to be isolated abnormal tracings, corroborating previous investigators' conclusions that serial tracings are necessary for full evaluation (*3, 4,6,8*).

This and previous studies also suggest that the renogram is helpful in determining the efficacy of therapy for rejection. A difference in the recovery time of the parameters studied was noted; the time parameter returned to normal before the height-ratio measurement. No attempt was made to determine the physiological significance of this finding. Possibly there is an initial increase in renal blood flow followed by a more gradual return of tubular function.

SUMMARY

Serial renograms after renal transplantation in 36 patients were analyzed using two parameters; (1) time in minutes to peak and (2) height at 20 min over height at peak. Excellent correlation between abnormal serial renogram patterns and the clinical diagnosis of rejection reaction was established. In some cases the renogram changes distinctly preceded the clinical diagnosis.

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