Posture-Induced Disturbance of Pertechnetate Flow and I-123 Iodohippurate Transport in Some Renal Graft Recipients with Hypertension

John H. Clorius, Kurt Dreikorn, Joachim Zelt, Peter Schmidlin, Ekaterini Raptou, and Peter Georgi

German Cancer Research Center, the University of Heidelberg, and the Stiftung Rehabilitation, Heidelberg, Germany

Iodohippurate renography and rapid serial scintigrams with pertechnetate were done in 27 allograft recipients in supine and standing positions. Posture-dependent iodohippurate transport and/or disturbance of pertechnetate flow pattern was found in nine of those examined. Patients demonstrating these abnormalities were found to be hypertensive. We suggest a causal relationship between posttransplant hypertension and the described posture-induced alterations of tracer transit.

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Posttransplant hypertension is a recognized major complication of transplantation. It may be due to acute or chronic rejection (*1,2*), to disease of the recipient's own kidneys, to stenosis of the transplant's vessels, to transplant glomerulonephritis, to essential hypertension (*3,4*), or to steroid therapy (*5,6*). Renal-artery stenosis is being recognized increasingly as a major complication of transplantation (*7–9*). Stenosis may go undetected due to the several factors involved in posttransplant hypertension. It was recently demonstrated that renal mobility can result in posture-dependent change of renal-artery stenosis, and that these posture-dependent vascular lesions could be detected with gamma camera imaging (*10*). We felt that stenosis in an allograft artery might be identified if stenosis were increased by change in a patient's posture. The goal of the present study was to determine whether posture-dependent change of iodohippurate transport, or of the pertechnetate flow pattern, could be demonstrated in renal allografts, and to search for correlation of such findings with the patient's blood-pressure status.

METHODS

Twenty-seven graft recipients were included in the study. Initially, 18 patients were selected if hospitalized for reasons other than for treatment of acute rejection. Toward the end of the study, we required a transplant angiogram for inclusion in the study. Patients were examined only during hospitalization. Selection was not influenced by the patient's blood-pressure history. Twenty patients were male and seven were female. Graft implantation preceded each study by at least 4 wk. All 27 implants were cadaver kidneys. Standard vascular anastomoses were made. The renal artery was anastomosed end-to-end with the internal iliac artery. Accessory renal arteries were seen in three grafts, and the secondary artery was anastomosed end-to-side with the external iliac artery. Patients were excluded from the study when biochemical examination suggested a sudden change in graft function, whether improvement or deterioration. Each patient was examined in supine and standing positions, the former preceding the latter by 1 day. We did not prepare these patients for the function studies. All were well hydrated with 3.5–5 l of fluid intake per day. Electrolytes were determined daily. To detect residual urine, patients were asked to void following renography. The pertechnetate study was then done at once.

Emission renography was carried out after i.v. injection of 200 μCi of ortho-iodohippurate, either I-131 or I-123. A 15-in. gamma camera was used, with 25% window over the main energy peak. The camera was equipped with a general-purpose, medium-energy, par-

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For reprints contact: John H. Clorius, MD, Institute of Nuclear Medicine, German Cancer Research Ctr., P.O. Box 10 9149, D-6900 Heidelberg 1, Germany.

allel collimator. Data were stored on magnetic tape and analyzed by minicomputer. Regions of interest (ROI) were placed over the graft and its time-activity curves were generated. One-minute scintiphotos were made starting at 0,1–4,7,9,14 and 19 min. Graft assessment was based on bladder appearance time and on intrarenal iodohippurate transport, as indicated by the change in tissue activity. This was visually determined by comparing the tissue activity at 14 min with that at 3 min or at bladder appearance time. The results of renography in supine and standing positions were then compared. While posture-induced graft movement was assumed to exist, we did not attempt to document the extent of such motion.

Immediately following rapid antecubital-vein injection of 7 mCi pertechnetate (Tc-99m) in 1–2 cc volume, the arm of the patient was raised. Rapid serial scintigraphy was then carried out in either supine or standing position. Camera, collimator, and data collection were the same as for renography. A scintiphoto was made every 5 sec for 40 sec, and data were collected on tape for 60 sec. To evaluate pertechnetate flow, ROIs were placed over the graft and over the A. iliaca of the other side. The background ROI was kept small (generally one fourth of that of the kidney ROI) and was prorated to correspond to the area used for the graft. The time-activity curve for the background area was subtracted from that for the transplant. We found that poor injection technique will retard the rise of the background curve, and we used this to check the injection. In evaluating the pertechnetate flow pattern of a graft, we considered both the time-activity curve and the series of scintiphotos.

Posture-dependent changes in renography and pertechnetate flow patterns were registered. Serum creatinine, serum urea, and blood pressure were noted on the days of the examination. Patients were included in the study only if the biochemical values were stable at the time of the study. Angiograms were not done specially for this study, but when they were part of the patient's record, we compared the findings with those of scintigraphy.

RESULTS

As long as graft function is stable and the patient is supine, we find that the renographic and perfusion results are reproducible from one examination to the next (Fig. 1). A change in position, however, can alter the patterns of iodohippurate transport and Tc-99m transit (Fig. 2), although this does not necessarily happen (Fig. 3). Six patients (Nos. 1, 2, 3, 5, 6, and 7) clearly showed delay in bladder appearance time for iodohippurate when they were changed from supine to standing positions (Table 1); in a seventh the effect was present but slight. In all seven the elevation of the third renogram segment showed posture-dependent disturbance of intrarenal iodohippurate transport. In all but two patients the Tc-99m perfusion scintigrams indicated impaired tracer transit (Table 1). One patient (No. 1) had angiograms at 5 and 10 mo after transplantation. The first angiogram revealed stenosis of the renal artery, and the 10-mo study found stenosis to be unchanged. At the same time, camera renography and perfusion scintigraphy demonstrated massive, posture-dependent change of iodohippurate transport and pertechnetate flow pattern (Fig. 4). Two other patients with renal-artery stenosis (Nos. 2 and 3) showed similar, posture-dependent alteration of intrarenal iodohippurate transport. Unsatisfactory injection prevented the Tc-99m flow study in Patient 2; in Patients 3 and 5 the flow curve was not deformed. One patient (No. 4) with vascular stenosis failed to demonstrate a posture-induced alteration of iodohippurate

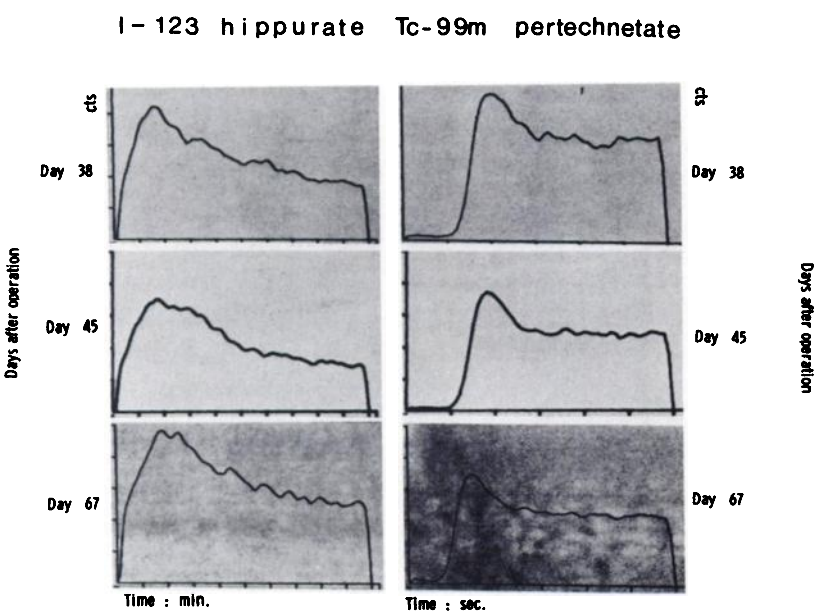

FIG. 1. Repeat renograms and pertechnetate flow curves obtained in normotensive transplant patient (No. 25), examined in supine position. Renal function was stable. Sequence demonstrates reproduceability of time-activity curves while renal function is unaltered.

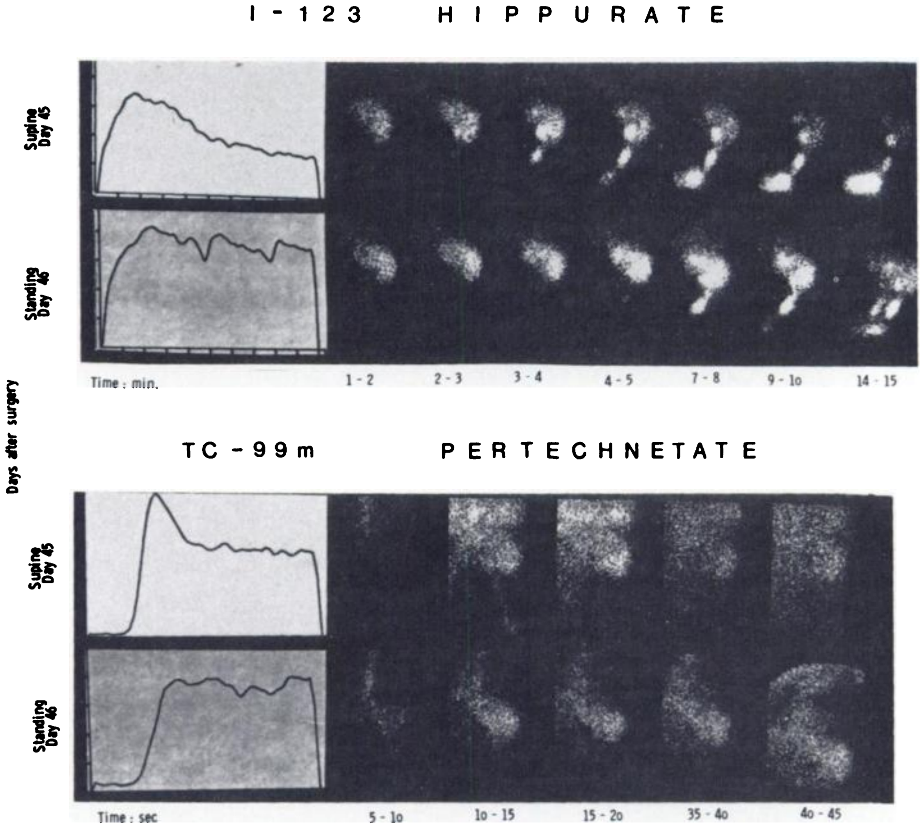

FIG. 2. Iodohippurate renography and pertechnetate perfusion scintigraphy in hypertensive patient (No. 6), examined in supine and standing positions on Days 45 and 46 after graft implantation. Biochemical data were stable at time of examinations. Change from supine to standing position disturbed intrarenal transport, delayed bladder appearance time, and markedly altered pertechnetate flow pattern.

transport, but had massive deformation of the pertechnetate flow curve. Angiography failed to demonstrate stenosis in one patient (No. 5) who showed a posture-dependent change in the iodohippurate images. The pertechnetate flow study was not posture-sensitive. Due to the angiographic finding, the patient was considered to have chronic rejection. Three further patients (Nos. 6–8) were found to have posture-induced change of iodohippurate transport and deformation of the pertechnetate flow curve. We had no angiograms for these patients. We find it noteworthy that all nine patients demonstrating posture-dependent change of iodohippurate renography, or of pertechnetate flow pattern, or both, were hypertensive at time of scintigraphy.

Fourteen of the 27 patients had renograms and perfusion scintigrams that failed to show any signs of de-

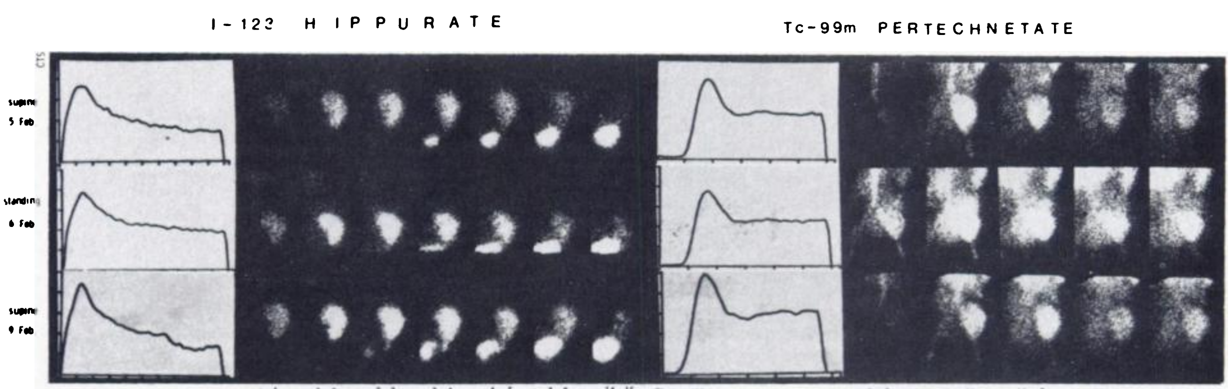

FIG. 3. Patient 25 again: Iodohippurate renography and pertechnetate perfusion scintigraphy in supine and standing positions. Sequence shows that change in posture will not necessarily influence renography. Intrarenal iodohippurate transport, as judged by tissue activities at 3 and 14 min, is stable; so is bladder appearance time. Change in posture did not influence pertechnetate time-activity curve in this normotensive patient.

TABLE 1. COMPARISON OF HIPPURATE SCINTIGRAPHY, PERTECHNETATE RAPID SERIAL SCINTIGRAPHY, BIOCHEMICAL DATA, MONTH OF GRAFT FUNCTION, BLOOD PRESSURE STATUS AND ANGIOGRAPHIC RESULTS OF 27 TRANSPLANT RECIPIENTS EXAMINED IN SUPINE AND STANDING POSITION

		Scintigraphy Hippurate			Pertechnetate	Biochemical data		
Patient	No. of mo since implantation	Supine position bladder appearance (min)	Standing position bladder appearance (min)	Intrarenal transport supine to upright	Flow pattern comparison supine to upright	Serum creatinin mg %	BP status	Angio-graphic results
1	11	3	9	deteriorated	deteriorated	1.6	+	vascular stenosis
2	14	7	14	deteriorated	—	1.9	+	vascular stenosis
3	3	3	19(7 pelvis)	deteriorated	stable	1.4	+	stenotic bruit
4	21	3	3	stable	deteriorated	1.3	++	vascular stenosis
5	17	4	7	deteriorated	stable	2.3	+	chronic rejection
6	2	2	4	deteriorated	deteriorated	1.4	+	—
7	19	4	9	deteriorated	deteriorated	2.5	++	—
8	7	3	4	deteriorated	deteriorated	1.8	+	—
9	21	4	4	stable	deteriorated	3.5	+	—
10	13	9	7	stable	stable	1.5	++	—
11	31	4	4	stable	stable	2.2	+	chronic rejection
12	23	7(4 pelvis)	4	stable	stable	2.7	+	chronic rejection
13	24	3	3	stable	stable	1.8	++	chronic rejection
14	41	4	7(4 pelvis)	stable	stable	6.9	+	chronic rejection
15	24	3	3	stable	stable	0.5	++	no vascular stenosis
16	24	4	4	stable	stable	2.5	+	chronic rejection
17	1	3	2	stable	stable	1.4	+	no vascular stenosis
18	1	7	7	stable	stable	2.3	+	chronic rejection
19	31	7	7	stable	stable	3.5	+	chronic rejection
20	1	2	3	stable	stable	1.2	−	—
21	10	2	3	stable	stable	1.5	−	—
22	1	2	2	stable	stable	1.5	−	—
23	3	—	—	—	stable	1.0	−	—
24	21	3	2	stable	stable	1.4	−	—
25	5	2	2	stable	stable	1.2	−	—
26	5	4	4	stable	stable	1.5	−	no vascular stenosis
27	4	3	4	stable	stable	1.3	−	—

— Normotensive; + under antihypertensive therapy; ++ hypertensive BP values plus hypertensive therapy.

terioration during standing. Three graft recipients (Nos. 20, 21, 27) showed discrete delay in bladder appearance time, but other signs of posture-dependent change of tracer transit were lacking. Renography was not done in Patient 23, and posture-induced changes failed to appear in the pertechnetate transit study. Eighteen patients were therefore considered to have scintigrams uninfluenced by posture. Ten of these patients were hypertensive at the time of scintigraphy, and nine (Nos. 11–19) had angiograms; none showed renal-artery ste-

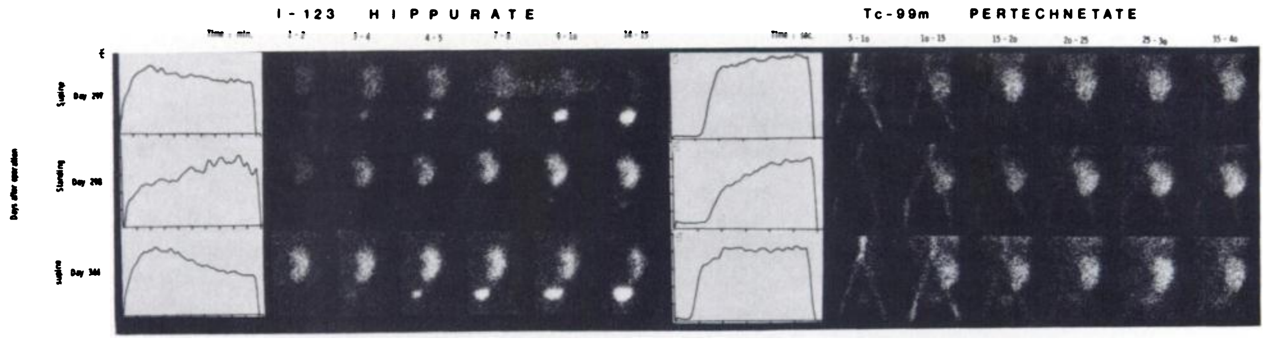

FIG. 4. Patient 1: Iodohippurate renography and perfusion scintigraphy in supine and standing positions. Standing produces sudden and massive deterioration of iodohippurate handling and pertechnetate flow. Note good repetition of supine flow curve on Days 297 and 344. Renal-artery stenosis was verified by angiogram.

nosis, but seven showed chronic rejection. The other eight recipients (Nos. 20–27) were normotensive at the time of scintigraphy, and showed no posture-induced changes. In Patient 26 an angiogram failed to show arterial stenosis. Because of the small population, our statistical analysis used the Fisher test, rather than chi squared, to examine the association between angiographic and scintigraphic findings. (The stenotic bruit in No. 3 was taken to verify stenosis.) The Fisher test indicates presence of a significant relationship between posture-dependent function abnormality and the existence of renal-artery stenosis. The demonstration of posture-dependent abnormality of iodohippurate transport or pertechnetate perfusion therefore makes the presence of a renal-artery stenosis probable, whereas vascular stenosis is unlikely in patients with function studies uninfluenced by posture. The probability (p) that the observed association was accidental is presented in Table 2.

DISCUSSION

Posture-dependent change of perfusion or iodohippurate transport has not been described as occurring in renal grafts. Neither renography nor pertechnetate rapid serial scintigraphy permits a direct evaluation of blood flow, but both examinations can be influenced by it. The methods used appear to us to be appropriate since the examinations were carried out on consecutive days, with clinical and biochemical data giving no evidence for the presence of acute rejection. Altered renographic or perfusion findings must therefore be due to the change in posture. We feel that posture-induced changes in iodohippurate transport and in pertechnetate flow pattern can only result from altered hemodynamics, and must therefore indicate change in renal blood flow. Note that repeat examinations in one position result in very similar time-activity curves whenever graft function is stable. Only the change in posture will provoke the described changes in renography and pertechnetate scintigraphy.

The data presented indicate that our examination sequence may identify transplant stenosis. We believe that change in posture can increase stenosis through movement of the transplant. We fully realize that massive adhesions exist, preventing movement of the graft in relation to its immediate surroundings, but we feel that movement can still occur, rather as a slide of the graft together with its surroundings. This could aggravate an existing stenosis and result in reduced perfusion, particularly since the transplant has an altered terminal vasculature (*11–13*). Busch described an active arteritis of the terminal vascular bed in transplanted kidneys (*14,15*). He demonstrated presence of obliterative arterial lesions. These result in elevated terminal resistance so that renal-artery stenosis, or increase in stenosis, may immediately influence function. The functional importance of a vascular stenosis in the presence of an altered microvasculature may be increased further when the patient stands up. Poor orthostatic regulation will decrease prestenotic pressure. This would reduce the intrarenal perfusion pressure and would be expected to increase renin secretion. Blaufox reports that denervated transplants are fully capable of renin secretion (*16*). Pollini pointed out that tilting will stimulate renin secretion, even in the absence of sympathetic stimulation (*17*).

TABLE 2. ANALYSIS OF RESULTS USING THE FISHER TEST*

Test	p (%)
Posture dependent alteration of hippurate transport vs. renal artery stenosis	3.3
Posture dependent alteration of pertechnetate perfusion scintigraphy vs. renal artery stenosis	3.3
Posture dependent alteration of either Hippurate transport or pertechnetate perfusion scintigraphy vs. renal artery stenosis	0.4

* Probability was calculated so that the observed association of vascular stenosis and posture dependent function was accidental.

We do not believe that renin determinations will help support our study or that they can serve as complementary screening tests. Numerous reports suggest that normotensive and hypertensive transplant recipients have similar renin values when salt intake is unrestricted (*18,19*). Pollini found normotensive as well as hypertensive graft recipients to have elevated, but similar, renin values (*17*). Furthermore, renal-artery stenosis was associated with low plasma renin values when patients with stenosis were compared with hypertensive graft recipients without stenosis. Rao reported similar results. He reminds us that the finding of normal or low renin levels in an ischemic graft with stenosis is not surprising, since the transplant represents, in many respects, the clinical counterpart of a Goldblatt single-kidney model (*4*). Sampson demonstrated elevated rates of aldosterone secretion in hypertensive transplant patients, with renin values in the normal range (*5*). He demonstrated, as did Holland (*6*), that mineralocorticoid administration can result in hypertension in the presence of low renin values. While low renin values fail to rule out stenosis, elevated renin is also difficult to interpret. High renin values may be found in ATN, acute and chronic rejection, vascular stenosis, and in many normotensive graft recipients (*4,17*). Elevated renin values may emanate from the patient's own diseased kidneys as well.

Our data indicate that graft quality will influence the ease with which posture-dependent alterations of iodohippurate transport and pertechnetate flow can be identified. Patients with elevated serum creatinine and serum urea demonstrate reduced iodohippurate uptake and often have abnormal perfusion patterns. Arrival at the bladder and intrarenal iodohippurate transport, as judged by tissue activity, become difficult to judge, and slight changes in pertechnetate flow may be missed. Thus problems of interpretation may arise.

We were astonished by the recorded results: the frequency of the postural changes exceeded our expectations. While disagreement exists as to the frequency with which renal-artery stenosis occurs in transplant recipients, it is commonly considered a rare complication (*20,21*).

We had suspected that the observed postural changes would be related to stenosis, and this was supported by the angiograms. We believe that the described scintigraphic pattern indicates a functional vascular abnormality that may be triggered by vascular stenosis. Our records show that many transplant recipients have posture-dependent swings in graft perfusion and that this may be common in patients having vascular stenosis.

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This paper is dedicated to Kurt E. Scheer, M. D., on the occasion of his 60th birthday.

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