

# Acute Renal Failure Following Intravenous Use of Radiographic Contrast Dyes in Patients with Diabetes Mellitus

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## SUMMARY

Acute renal failure following roentgenologic procedures employing intravenous administration of contrast media was observed in seven diabetic patients over an 18-month period. All had long-standing diabetes mellitus complicated by retinopathy and cardiovascular disease; six had mild impairment in renal function before x-ray studies. The renal failure occurred within 48 hours of the procedure and was of the oliguric type in six of the patients. Renal function returned toward the prestudy levels within four weeks.

None of the patients required dialysis. Combined analysis of our

data and those of 31 cases reported in the literature suggest that certain factors in diabetic patients make them prone to develop dye-induced acute renal failure: These include old age; long duration of diabetes; preexisting impaired renal function; the presence of diabetic complications such as retinopathy, neuropathy, and cardiovascular disease; and dehydration. All diabetic patients should be monitored closely after a radio-contrast study to detect the development of acute renal failure so that appropriate management can be instituted early in the course of the disease. *DIABETES* 26:643-49, July, 1977.

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Although currently used radiographic dyes for angiography, intravenous pyelography, oral cholecystography, and cholangiography are considered relatively safe, acute renal failure has been reported after their use in patients with multiple myeloma,<sup>1-9</sup> severe dehydration,<sup>7-10</sup> jaundice due to hepatocellular disease,<sup>9,11-15</sup> various vascular or renal lesions,<sup>9-16</sup> or diabetes mellitus.<sup>9,17-22</sup> If the diagnostic usefulness of a roentgenologic procedure using intravenous contrast media is to be weighed against the possibility of adverse side effects, clinical guidelines are necessary to identify those patients who may be at risk.

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We have encountered seven patients with diabetes mellitus who developed acute renal failure following intravenous administration of diatrizoates. The present report describes the course of the renal complication in these patients and provides a combined analysis of the clinical features of dye-induced acute renal failure in our diabetic patients and those reported in the literature.

## SUBJECTS AND RESULTS

Between July 1974 and December 1975 seven patients with diabetes mellitus were observed in whom acute renal failure developed after roentgenologic procedures entailing the intravenous use of contrast media. Table 1 shows the pertinent clinical and laboratory findings in these patients before administration of contrast media and the type of roentgenologic procedures performed. Of the seven patients who developed acute renal failure, four were

ACUTE RENAL FAILURE

TABLE 1

Clinical and laboratory data and radiologic procedures in our seven patients with diabetes mellitus and dye-induced acute renal failure

Patient	Age (yr.)	Sex	Duration (yr.)	Characterization of diabetes mellitus			Blood pressure (mm. Hg)	Dehydration	
				Treatment	Retinopathy	Complications			
1	69	F	9	D,I	+	+	MI CHF	114/100	0
2	64	F	26	D,I	+	+	MI CHF	180/110	0
3	66	F	25	D,I	+	+	CVA	180/90	possible
4	54	M	>20	D,I	+	+	CVA	180/100	0
5	22	M	17	D,I	+	0	0	130/90	0
6	60	F	10	D	+	+	MI CHF	190/100	0
7	42	M	20	D,I	+	+	CHF	190/100	0

D = diet; I = insulin; MI = myocardial infarction; CHF = congestive heart failure; CVA = cerebrovascular accident; + = present; 0 = none.

females and three males. Their ages ranged between 22 and 69 years. All had long-standing diabetes mellitus of at least nine years' duration. Six patients received insulin and one patient (case 6) was treated with diet only. All had clinical evidence of retinopathy, and six patients had neuropathy and cardiovascular disease manifested either by hypertension, myocardial infarction, heart failure, and/or cerebrovascular accident.

Before the injection of contrast media, serum creatinine values ranged from 1.2 to 3.5 [ $2.2 \pm 0.8$  (S.D.)] mg./100 ml. All patients had proteinuria ranging from 2.2 to 18.8 ( $6.0 \pm 5.8$ ) mg./24 hr. Three patients had positive urine cultures showing  $\geq 10^5$  Escherichia coli or cytotacter per milliliter of urine. None of the patients showed clinical evidence of dehydration before the x-ray procedure, although in case 3 the state of hydration was questionable since her fluid intake was restricted for 16 hours before the study. Two days before the x-ray procedure, one patient (case 2) was started on cephalothin, 1 gm. per day, for treatment of his urinary infection. The other six received no potentially nephrotoxic drugs.

The roentgenologic procedures performed were intravenous pyelography or inferior venacavography, each in two patients, and angiocardiology, inferior venacavography followed by renal visualization for renal biopsy, or biopsy visualization alone, each in one patient. During the procedure, all patients received meglumine and/or sodium salts of diatrizoic acid, with the total dose ranging from 36 to 90 gm. and the amount of iodine content of these doses ranging from 17 to 42 gm.

Figure 1 shows the changes in the concentration of serum creatinine and urinary output after the injection of the contrast media in all patients. Following the

radiographic study, an acute rise in serum creatinine and a marked increase in urinary volume occurred within 48 hours in each patient, and oliguria of less than 400 ml./24 hr. occurred in six. None of the

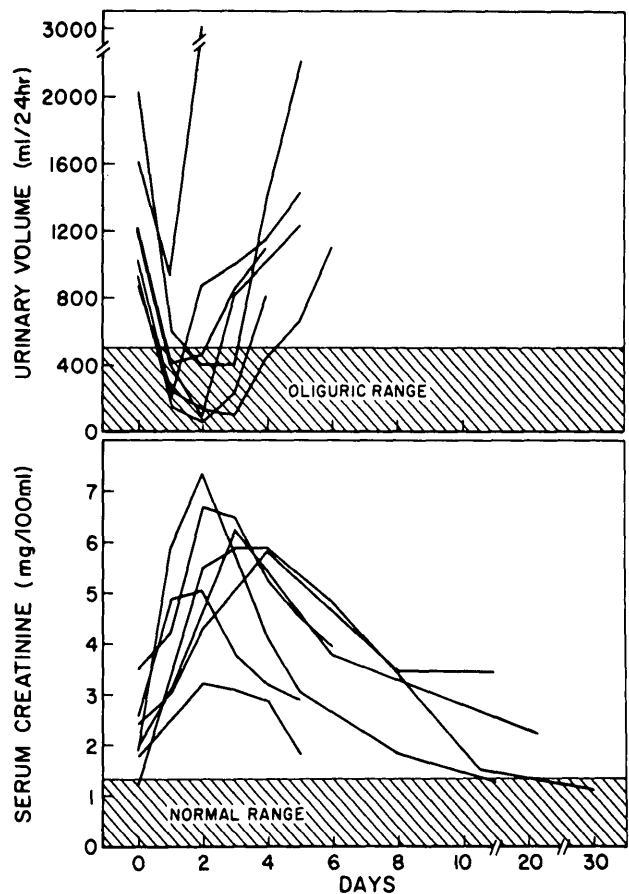


FIG. 1. Urinary volume and serum creatinine levels before and after intravenous administration of contrast media.

TABLE 1 (Continued)

Clinical and laboratory data and radiologic procedures in our seven patients with diabetes mellitus and dye-induced acute renal failure

Patient	Nephrotoxic drugs	Renal status prior to Contrast Study			X-ray procedure	Contrast media		
		Urinary protein (gm./24 hr.)	Urinary infection	Serum creatinine (mg./100 ml.)		Type	Total	Dose Iodine
1	0	2.9	+	1.2	ACG	MGD	90	42.3
2	cephalothin	3.2	+	2.4	IVP	MGD	60	28.2
3	0	2.2	0	2.0	IVP	NaD	60	28.2
4	0	4.2	0	3.5	IVC	MGD	90	42.3
5	0	4.5	0	1.9	IVC	MGD	60	28.2
					RV	NaD		
6	0	18.8	+	1.8	RV	NaD	36	16.9
7	0	6.5	0	2.9	IVC	MGD	60	28.2
					NaD			

ACG = angiocardigraphy; IVP = intravenous pyelography; IVC = inferior venacavography; RV = renal visualization for renal biopsy; NaD = sodium diatrizoate; MGD = meglumine diatrizoate; + = present; 0 = none.

patients showed signs of an allergic type of reaction such as fever, rash, hypotension, shock, or eosinophilia. Within two to four days from the time of administration of contrast media, serum creatinine levels reached their maximum, which ranged from 3.2 to 7.3 ( $5.8 \pm 1.3$ ) mg./100 ml. The clinical course of the renal failure was uncomplicated in each patient, and none of the patients required dialysis. Spontaneous diuresis in the six oliguric patients occurred three to five days after exposure to the contrast media. Following recovery from the acute renal failure, serum creatinine, levels returned toward initial values and ranged from 1.1 to 3.9 mg./100 ml.; the mean value after recovery was  $2.4 \pm 1.0$  mg./100 ml. and did not differ significantly from the mean prestudy level of  $2.2 \pm 0.8$  mg./100 ml.

#### DISCUSSION

Despite the wide use of intravenous contrast media for the diagnosis of various diseases, nephrotoxic complications are not common. Schwartz et al.<sup>23</sup> used larger than usual doses of contrast media to improve kidney visualization by intravenous pyelography in patients with renal failure. Furthermore, Schenker,<sup>29</sup> who introduced the drip-infusion technique, observed no serious adverse effects from this procedure in more than 200 patients. Since then, there have been numerous reports published of successful visualization of the urinary tract using high-dose urography in presence of renal insufficiency without further deterioration in renal function.<sup>23-26</sup>

Various authors, however, have drawn attention to the risks entailed. Manitz and Mathes<sup>27</sup> and Ansell<sup>28</sup> reported temporary anuria as a complication of intravenous pyelography in patients with preëxisting

renal failure. The danger of acute renal failure after pyelography in multiple myeloma is well known,<sup>4-6</sup> and the increased risk of this complication in the presence of dehydration was emphasized by Danford, Davidson, and Goldman.<sup>29</sup>

The seven patients described in this study had diabetes mellitus and developed acute renal failure following roentgenologic procedures that used intravenous administration of the contrast media, meglumine, and/or sodium diatrizoate. In these patients, the dye was given in conjunction with various tests, including inferior venacavogram, intravenous pyelography, angiocardigraphy, or visualization of the kidneys for renal biopsy.

Acute renal failure following the use of contrast media in diabetic patients has already been reported previously.<sup>9,17-22</sup> In the 31 cases reported in the literature, this complication occurred following intravenous pyelography in 22 (71 per cent) (table 2, figure 2). As in our patients, the contrast media used in 30 of these patients were salts of diatrizoic acid, and in one case meglumine iohalamate was utilized.<sup>19</sup> It is noteworthy to emphasize that there was no correlation between the occurrence of renal failure and the dose of contrast media or its iodide content. The mechanisms for the pathogenesis of the dye-induced acute renal failure are not elucidated: an effect of the contrast media on the renal microcirculation,<sup>30,31</sup> direct nephrotoxicity,<sup>9,32,33</sup> or the formation of immune complexes<sup>34</sup> have all been implicated.

Several predisposing or precipitating factors may also play a role in the genesis of this type of acute renal failure: these include dehydration,<sup>7,8,10</sup> vascular disease,<sup>18</sup> jaundice,<sup>9,11-13,15</sup> proteinuria,<sup>10,18,35</sup> marked uricosuria,<sup>14,36,37</sup> and arterial hypotension.<sup>28</sup> However, most of these factors did not appear to be of

TABLE 2

Clinical and laboratory data and radiologic procedures in 31 previously reported patients with diabetes mellitus and dye-induced acute renal failure

Patient	Age	Sex	Duration (yr.)	Characterization of diabetes mellitus			Complications			Blood pressure (mm. Hg)	Dehydration	Nephrotoxic drugs
				Treatment O	I	Retinopathy	Neuropathy	Vasculopathy				
1	52	M	NM	NM		+	NM*	NM*	normal	+	0	
2	57	F	10		+	NM*	+	+	200/85	+	cephalothin	
3	60	M	25		+	+	+	+	130/80	+	0	
4	42	M	22		+	+	+	+	increased	+	0	
5	51	F	20			+	+	+	200/100	+	0	
6	62	M	NM	NM		NM	NM	NM	NM	0	NM	
7	68	F	20	NM		+	NM*	+	200/80	+	0	
8	59	M	20	NM		+	NM*	+	180/100	0	kanamycin	
9	58	M	12	NM		0	NM*	+	NM	0	gentamycin cephalothin gentamycin	
10	60	M	6	NM		+	+	+	NM	0	gentamycin	
11	44	M	13	NM		+	+	+	200/120	+	0	
12	43	M	>10	NM		+	+	+	increased	0	0	
13	43	F	31		+	+	+	+	220/100	+	NM	
14	48	F	22		+	+	+	+	190/120	+	NM	
15	56	M	22		+	+	+	+	200/70	+	NM	
16	49	M	30		+	+	+	+	160/80	+	NM	
17	61	F	10	+		+	+	+	160/90	+	NM	
18	62	F	15		+	+	+	+	160/95	+	NM	
19	44	M	18		+	+	+	+	190/100	0	NM	
20	68	F	6	+		+	+	+	220/110	+	NM	
21	72	M	NM	NM		NM	NM	NM	NM	+	NM	
22	61	M	NM	NM		NM	NM	NM	NM	0	NM	
23	62	F	NM	NM		NM	NM	NM	NM	0	NM	
24	68	M	NM	NM		NM	NM	NM	NM	+	NM	
25	76	M	NM	NM		NM	NM	NM	NM	0	NM	
26	74	F	NM	NM		NM	NM	NM	NM	+	NM	
27	67	M	NM	NM		NM	NM	NM	NM	0	NM	
28	65	M	NM	NM		NM	NM	NM	NM	0	NM	
29	61	M	NM	NM		NM	NM	NM	NM	0	NM	
30	47	M	NM	NM		NM	NM	NM	NM	0	NM	
31	64	M	NM	NM		NM	NM	NM	NM	0	NM	

O = oral antidiabetic agents; I = insulin; NM = not mentioned; + = present; 0 = none.

\*Although the authors did not mention these complications, we assume they were not present since information on other diabetic complications was provided in these cases.

paramount importance in our patients. Jaundice, marked uricosuria, or decreased blood pressure during the x-ray procedure were not present in our patients and are not mentioned in those reported in the literature. Although dehydration was noticed in 58 per cent of the previously reported cases (table 2), it was possibly present in only one of our patients (table 1). Significant proteinuria was present in all of our patients and in eight of the 11 patients previously reported and in whom quantitation of urine protein was available.

Combined analysis of the 38 patients reported here and by others<sup>9,17-22</sup> reveals interesting information regarding the diabetic population that may be prone to develop acute renal failure following the intravenous use of contrast media. Age, duration of diabetes, severity of complications of diabetes, and presence of

renal insufficiency may all be important. The age of 60 per cent of the patients was greater than 55 years, while 97 per cent were older than 40 years. In addition, 88 per cent of the patients had had diabetes for more than 10 years.

The patients who developed renal failure had a high prevalence of complications associated with diabetes mellitus; thus, 85 per cent had arterial hypertension, 95 per cent had diabetic retinopathy, 92 per cent had vascular complications, and 81 per cent had neuropathy. Finally, 92 per cent had preëxisting renal insufficiency: serum creatinine levels ranging from 1.4 to 2.5 mg./100 ml. were noticed in 45 per cent of the patients and values ranging from 2.6 to 9.6 in 47 per cent. These data suggest that the patients with diabetes mellitus who are at risk of developing acute renal failure after the administration of contrast media

TABLE 2 (Continued)

Clinical and laboratory data and radiologic procedures in 31 previously reported patients with diabetes mellitus and dye-induced acute renal failure

Patient	Renal status prior to contrast study			Procedure	Contrast media			Source ref.
	Urinary protein* (gm./24 hr.)	Urinary infection*	Serum creatinine (mg./100 ml.)		Type	Dose Total iodine (gm.)		
1	1.3	NM	4.5	IVP	MGD	90	42.3	17
2	3+	+	1.9	IVP	MGD	90	42.3	18
3	3+	NM	2.3	IVP	MGD	30	14.1	"
4	4.6	NM	3.1	IVP	MGD	60	28.2	"
5	5.4	NM	9.6	IVP	MGD	90	42.3	"
6	NM	NM	1.2	A	MGI	24	12.3	19
7	0.28	+	2.4	IVP	MGD	90	42.3	20
8	5.5	+	2.9	IVP	MGD	135	63.5	"
9	0.01	+	2.2	IVP	MGD	270	127.0	"
				+RV				
10	0.37	+	2.1	IVP	MGD	90	42.3	"
11	8.6	0	5.0	IVP	MGD	90	42.3	"
12	10	NM	5.0	IVP + ACG	NaD + MGD	165	77.6	21
13	NM	NM	9.0	IVP	D	NM	0.93†	22
14	NM	NM	5.8	IVP	D	NM	0.42†	"
15	NM	NM	2.5	IVP	D	NM	0.58†	"
16	NM	NM	2.9	IVP	D	NM	0.27†	"
17	NM	NM	6.2	IVP	D	NM	0.31†	"
18	NM	NM	1.4	IVP	D	NM	0.30†	"
19	NM	NM	3.7	IVP	D	NM	0.64†	"
20	NM	NM	3.3	IVP	D	NM	>0.50†	"
21	NM	NM	2.8	IVP	MD	90	42.3	9
22	NM	NM	2.0	IVP	MD	90	42.3	"
23	NM	NM	2.8	IVP	MD	90	42.3	"
24	NM	NM	3.6	IVP	MD	90	42.3	"
25	NM	NM	1.8	A	MNaD	115.2	55.3	"
26	NM	NM	2.0	A	MNaD	228.4	110.0	"
27	NM	NM	2.6	A	MNaD	190	91.5	"
28	NM	NM	2.0	A	MNaD	152	73.2	"
29	NM	NM	2.3	A	MNaD	190	91.5	"
30	NM	NM	2.0	A	MGD	NK	NK	"
31	NM	NM	0.8	A	MNaD	214.9	103.5	"

\*NM = not mentioned; IVP = intravenous pyelography; RV = renal visualization for renal biopsy; A = angiography; MGD = meglumine diatrizoate; NaD = sodium diatrizoate; MGI = meglumine iothalamate; + = present; 0 = none; NK = not known.

†Expressed per kilogram body weight.

are usually those who are older than 40 years of age, have had the disease for at least ten years, have developed retinal, neural, and vascular complications of diabetes mellitus, and also have impaired renal function. Although diabetes mellitus is known to be more common in the female, renal impairment following contrast media has been observed more frequently in males (63 vs. 37 per cent) (figure 3).

This analysis also allowed us to arrive at some conclusions regarding the course of the dye-induced acute renal failure in patients with diabetes mellitus (figure 4). Oliguria occurred in 94 per cent of these patients, and it was usually of short duration (one to four days). The concentration of serum creatinine was already elevated within the first 48 hours after the x-ray procedure and reached its peak value within eight days. The renal failure was usually of a mild to moderate degree,

and only three of the 38 patients required dialytic therapy.

Following the acute episode, the majority of the patients showed recovery of renal function to prestudy levels (figure 4). However, persistent impairment in renal function was noted in five of the 38 patients (13 per cent). Two of these five patients had advanced renal failure, with initial serum creatinine levels of 6.2 and 9.2 mg./100 ml., respectively. Because of the further deterioration of renal function after the x-ray studies, they required chronic hemodialysis for their maintenance. In the other three patients, the last recorded serum creatinine levels were distinctly higher than the values observed before the administration of contrast media (figure 4).

From these observations it appears mandatory that diabetic patients be examined carefully for the pres-

ACUTE RENAL FAILURE

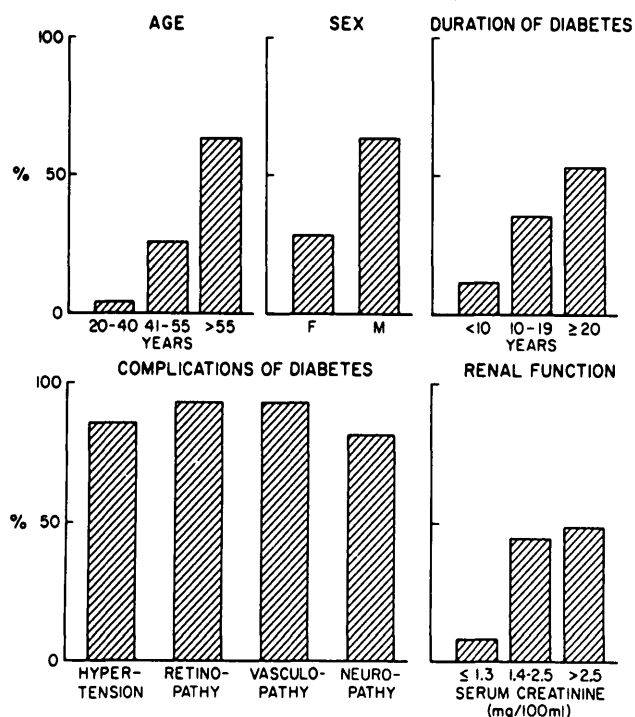


FIG. 2. Clinical features in patients with diabetes mellitus and dye-induced acute renal failure. Combined analysis of our own patients and those reported in the literature. Adapted from table 2.

ence of risk factors before they are subjected to roentgenologic procedures employing intravenous administration of contrast media. After the procedure, urine output and serum creatinine levels should be monitored closely for the first five days; this may allow for early detection of impaired renal function and for treatment should renal failure develop.

These data allow the conclusion that x-ray procedures using intravenous contrast media can still be considered safe procedures in patients with diabetes mellitus when they are young and well hydrated, have normal renal function, and show no evidence of retinal, neural, and vascular disease. However, the risks of performing these procedures should be weighed carefully against the possible diagnostic benefits, especially in middle-aged or elderly patients who have long-standing diabetes mellitus with impaired renal function and other complications of the underlying disease.

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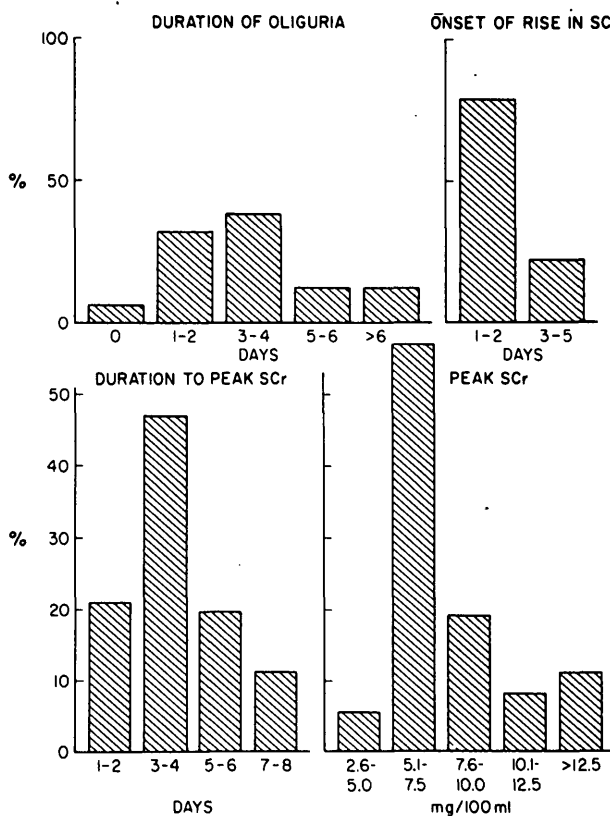
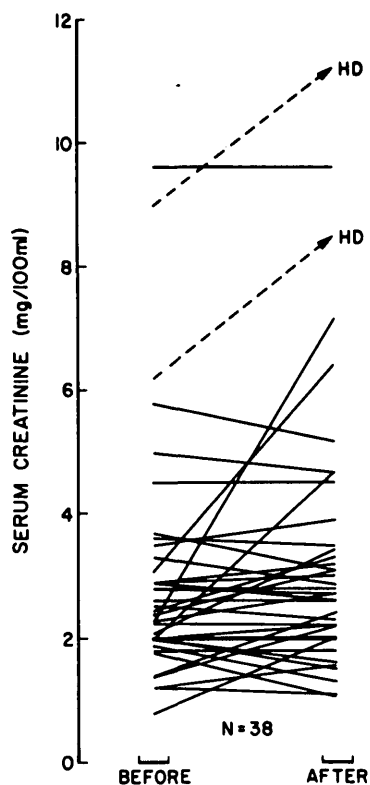


FIG. 3. Course of dye-induced acute renal failure in patients with diabetes mellitus. Combined analysis of our own patients and those reported in the literature.

FIGURE 4

Serum creatinine levels before and after dye-induced acute renal failure in patients with diabetes mellitus. Combined analysis of our own patients and those reported in the literature.



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