

## **Prevalence of contrast induced nephropaty (CIN) in preemptive living renal donor recipients after enhanced CT with CIN prophylaxis**

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## Purpose

Non-dialysis patients with a glomerular filtration rate less than 20 mL/min are the best candidates for kidney transplantation (preemptive transplantation) because graft survival and patient survival are better than in dialysis patients. Therefore, it is necessary to carefully evaluate potential recipients of kidney transplant carefully to determine the feasibility of kidney transplantation and to detect and treat concurrent conditions that may affect graft survival (1).

The best technique to assess the vascular anatomy and concurrent illnesses of a potential candidate is the angio-CT scan. Angio-CT scan is an accurate technique for demonstration of both stenotic and aneurysmal disease, allowing definition of the site, grade, and extent of abnormalities in vascular caliber with substantial interobserver agreement (2). Nonetheless, there is always some fear associated with the use of contrast media in candidates for preemptive kidney transplantation because of the risk of contrast-induced nephropathy (CIN), which might induce acute renal insufficiency and eventually lead to an earlier start of dialysis.

CIN is defined as an acute reduction in renal function secondary to the administration of iodinated contrast material, which results in an increase  $> 0.5$  mg/dl of serum creatinine levels (3).

Several strategies have been studied for the prophylactic prevention of CIN (3). In a large prospective trial, hydration with one-half isotonic (0.45%) saline started in the morning of the contrast procedure and immediately before the procedure proved to reduce the incidence of CIN (4). Tepel et al. were the first to report the protective effect of n-acetylcysteine (NAC) in reducing CIN, and Marenzi et al. demonstrated a dose-dependent effect of NAC (5). Based on this, further studies have demonstrated the effectiveness of NAC in the prevention of CIN (6, 7). Better clinical outcomes have also been reported when combining NAC and NaHCO<sub>3</sub> compared with NAC alone (4).

However, a recent randomized trial showed that NAC failed to reduce the incidence of CIN (8), and another study has not provided conclusive evidence about the effective of NAC in preventing CIN (9). To date, no studies have demonstrated a decrease in mortality using NAC.

Despite this evidence, no studies have been conducted to evaluate the preventive effects of hydration, NAC and NaHCO<sub>3</sub> in candidates for preemptive kidney transplantation. Recipients of living-donor kidney are the best population to investigate CIN, because

transplantation is performed in a short time lapse, avoiding problems of worsening of renal function due to CIN.

The aim of this study is to describe the prevalence of CIN and the need for dialysis in recipients of preemptive living-donor kidney transplants after enhanced computed tomography (CT) with CIN prophylaxis.

## Methods and Materials

During 2010, 20 non-diabetic patients with renal insufficiency (IV-V) (15 men and 5 women; 32-77 years, mean 53) underwent an angio-CT scan one month before the living-donor renal transplantation. All the patients were informed about all aspects of this clinical trial and they signed an informed consent form.

In our series, the leading causes of chronic renal failure were polycystic kidney disease (3 patients), IgA-associated glomerulonephritis (3 patients), ischemic nephropathy (2 patients) and hypertension (2 patients). Table 1 shows the causes of renal failure in each patient.

cause	number of patients
Polycystic disease	3
IgA-associate glomerulonephritis	3
High blood pressure	2
Ischemic neuropathy	2
Sarcoidosis	1
Vesico-ureteral reflux	1
Radiotherapy-induced nephropathy	1
Secondary amyloidosis	1
Alport syndrome	1
Bilateral renal hypoplasia	1
Unknown cause	4

**Fig. 1:** Table 1. Causes of chronic renal failure.

**References:** Radiologia, Hospital Clinic - Barcelona/ES

In all cases, CIN prophylactic measures involved saline hydration and administration of n-acetylcysteine and sodium bicarbonate following the regimen described next.

The day before the angioCT scan, patients received 1200 mg of NAC every 12 hrs and a nonsteroidal anti-inflammatory drug. On the day of the procedure, patients were

administered 1200 mg of NAC every 12 hrs and sodium bicarbonate 3mg/kg, an hour before the study. In addition, patients received intravenous hydration with isotonic saline solution (0.45%). On average, patients were administered 671 cc (two thirds after the test) (Fig. 1).



**Fig. 2:** Figure 1. Diagram showing the management schedule of patients

**References:** Radiologia, Hospital Clinic - Barcelona/ES

The radiological contrast agent was Iopromide (300 mg/ml), a hyposmolar non-ionic monomer. 100 ml of Iopromide and 40 ml of saline solution were injected at 40 ml/s.

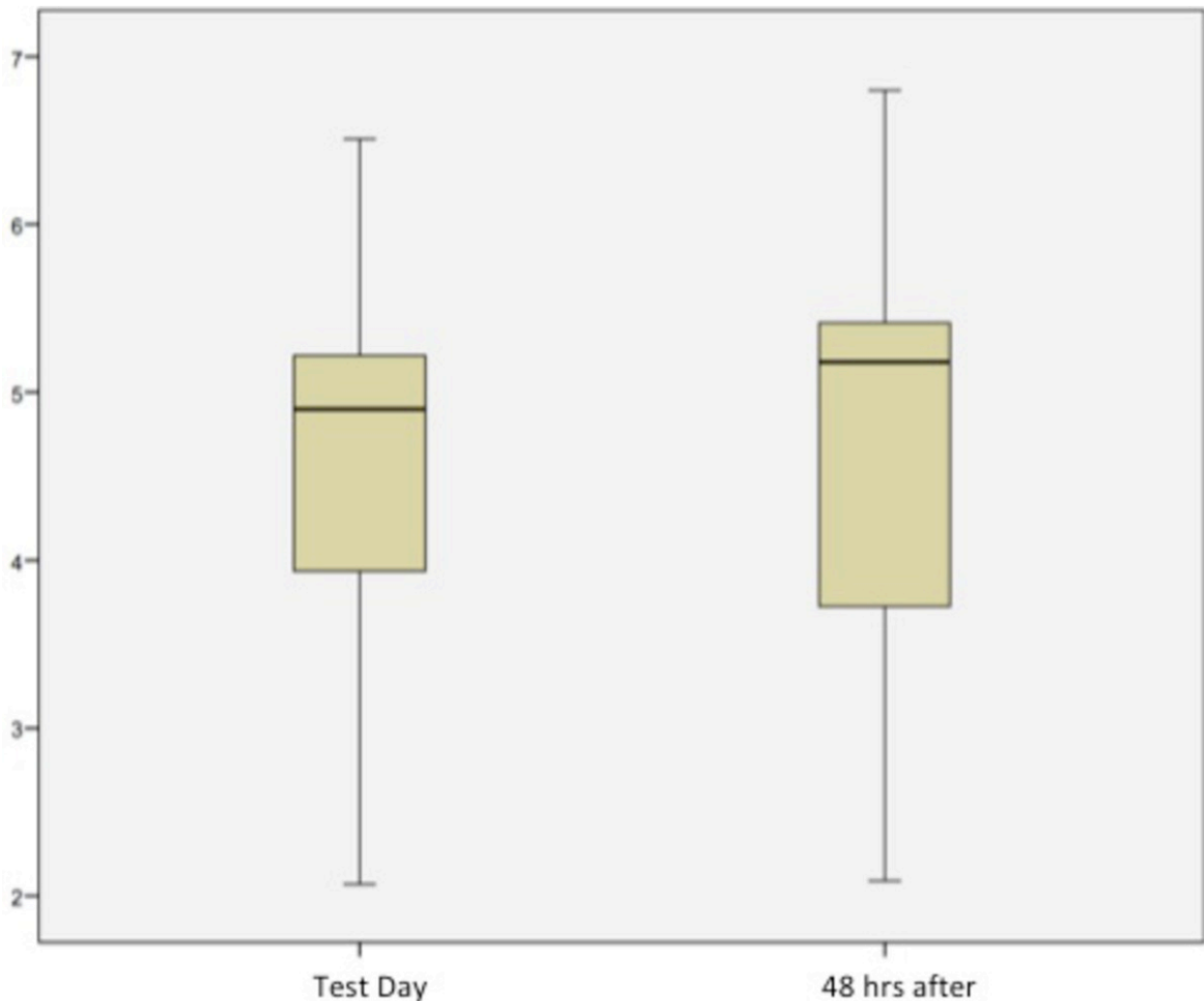
The creatinine levels were measured 15 days before and immediately before the angio-CT and 2 days after and 15 days after the angio-CT study. We also evaluated the dialysis requirements of the patients before the renal transplant.

## Results

The male:female ratio was 3.2:1, with a mean age of 53 years (R: 32-77).

Patients were followed up until transplantation. The mean follow-up was 80 days (R: 8-369).

The average creatinine level 15 days before, immediately before, 2 days after and 15 days after the angioCT scan were 4.43 (R:1.76-6,31), 4.6 (R: 2.07-6.64), 4.6 (R: 2.36-6.8) and 4.9 (R: 2.1-7.5), respectively. There were not significant differences between the levels of creatinine immediately before the CT and 2 days after the CT (0.300) (graph 1).



**Fig. 3:** Graph 1. Differences between creatinine levels immediately before the test and 48 hrs after the angio-CT scan. Statistical analysis for related samples (Wilcoxon) showed no significant differences.

**References:** Radiologia, Hospital Clinic - Barcelona/ES

Only two (9.5%) patients presented with an increase in creatinine levels > 0.5mg/dl 2 days after the angio-CT. However, no worsening in renal function was observed in these patients. In both cases, a significant decrease in creatinine levels occurred after 15 days. Table 2 shows variations in the creatinine levels in these patients.

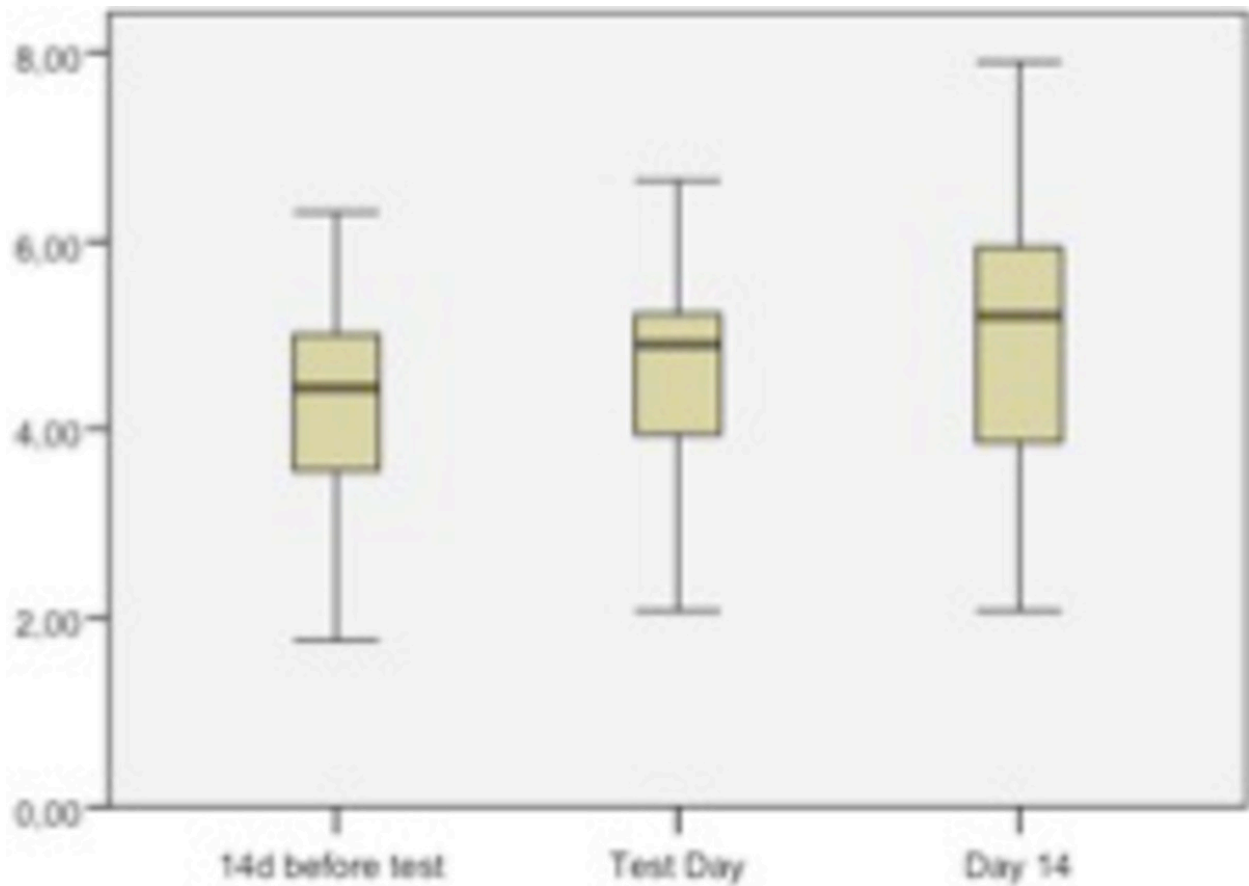
creatinine immediately before	creatinine 2 days after	creatinine 14 days after
5.1	6.65	6.05
4.9	5.5	5.2

**Fig. 4:** Table 2 shows the changes in creatinine levels in the two patients who fulfilled the diagnostic criteria for CIN

**References:** Radiologia, Hospital Clinic - Barcelona/ES

Although there was a significant increase in average creatinine levels between the measurement done immediately before and 14 days after the angio-CT (0.007), this difference was not significant if we compare it with the increase observed between creatinine levels measured 15 days before and immediately before the angio-CT (0.6). The increase observed after 15 days could be therefore attributed to the progression of disease itself. There is, however, some degree of bias due to the small sample size. Graph 2 shows the results of the statistical analysis.





**Fig. 5:** Graph 2. Differences between creatinine levels 14 days before, immediately before and 14 days after the angio-CT. Statistical analysis for related samples (Wilcoxon) showed no significant differences.

**References:** Radiologia, Hospital Clinic - Barcelona/ES

Only one patient started dialysis (37 days after the angio-CT) due to the impossibility of performing the living-donor transplantation. The patient did not develop CIN, showing an increase of 0.3 mg/dl (from 4.9 to 5.2 mg/dl) in his creatinine levels in the first 48 hrs.

Nineteen patients were transplanted during follow-up. The mean time between angio-CT and kidney transplantation was 49 days.

## Conclusion

Only two patients had a significant increase in creatinine levels compatible with CIN, but showing no persistent worsening in renal function. This increase may be related to the use of iodinated contrast, but a number of studies have reported an increase in creatinine level in patients who do not receive contrast material similar to that reported in series of patient receiving contrast material (10).

The patient who required dialysis 37 days after the angio-CT scan had no significant increase in creatinine levels compatible with NIC and the requirement for dialysis was due to the natural course of his renal disease and the impossibility of performing the living-donor transplantation.

The increase in creatinine levels observed between the day of the procedure and the levels at 15 days could be attributed to the progression of the disease itself, because they are not significantly different when compared with creatinine levels measured 15 days before the angio-CT. However, a larger sample size is needed to confirm these results.

The use of contrast media combined with prophylaxis with sodium bicarbonate and n-acetylcysteine in patients with end-stage renal disease will not induce an early start of dialysis. CIN appeared only in 9.5% of patients, with only a transient raise of creatinine and without permanent worsening of renal function.

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