

## Research Article

# The Safety of Computed Tomography Angiography in Patients Suffering from Pre-Dialytic Renal Failure

Carmen Sebastià<sup>1\*</sup>, Miquel Blasco<sup>2</sup>, Lluís Peri<sup>3</sup>, Laura Buñesch<sup>1</sup>, Mireia Musquera<sup>3</sup>, and Carlos Nicolau<sup>1</sup>

<sup>1</sup>Department of Radiology, Hospital Clínic, Spain

<sup>2</sup>Department of Nephrology, Hospital Clínic, Spain

<sup>3</sup>Department of Urology, Hospital Clínic, Spain

**\*Corresponding author**

Carmen Sebastià, Department of Radiology, CDI, Hospital Clínic, Villarroel 170, Barcelona 08036, Spain, Email: msebasti@clinic.ub.es

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- End-stage renal disease
- Transplantation
- Preemptive

**Abstract**

**Background:** The aim of this study is to evaluate the prevalence of Contrast Induced Nephropathy (CIN) and the need for dialysis in pre-emptive living donor kidney recipients who undergo a Computed Tomography Angiography (CTA) after CIN prophylaxis to evaluate safety of iodinated contrast administration in these patients.

**Material and methods:** Thirty-eight patients with end-stage renal disease (ESRD), chronic kidney disease (CKD) stage 4 and 5, awaiting a pre-emptive living donor transplant underwent a CTA as part of the pre-transplant evaluation. All patients received a CIN prophylactic regimen using sodium bicarbonate 1/6M at 3 mL/kg/h starting 1 hour before the CTA and 1 mL/kg/h six hours following the procedure and three doses of N-Acetylcysteine (1200 mg/12h) starting 12 hours before CTA. The variables analyzed were plasma creatinine levels (15 days before and immediately before CTA and 48-72 hours after and 14 days after CTA) as well as the need for dialysis during the follow-up.

**Results:** Mean creatinine levels 14 days before and immediately before CTA, within 72 hours after and 14 days after CTA were 4.45 (R 1.76-7.30), 4.56 (R 2.00-7.0), 4.59 (R 2.09-6.98) and 4.73 (R 1.65-7.9) mg/dl respectively. Only four (10.5%) patients showed CIN, which was reversible in 3 cases. Further worsening of renal function was detected in only one patient (2.6%). None of the four patients required dialysis before transplantation.

**Conclusion:** In patients with CKD stages 4 and 5, the use of intravenous contrast media combined with CIN prophylaxis is safe not leading to an early initiation of dialysis.

**ABBREVIATIONS**

CTA: Computed Tomography Angiography; CIN: Contrast Induced Nephropathy; NAC: N-Acetyl Cysteine; ESRD: End-Stage Renal Disease; GFR: Glomerular Filtration Rate

**INTRODUCTION**

Pre-transplantation screening evaluation is compulsory to stratify the risks and leads of kidney transplantation. Computed tomography angiography (CTA) is used for pre-transplantation vascular mapping, in patients older than 40 years or with cardiovascular risk factors, mainly to assess atherosclerosis in the arterial iliac and splenic system. In patients with long time in

dialysis, contrast-enhanced CT may also be used to rule out the presence of renal cell carcinoma associated with acquired renal cystic disease [1-7]. Concurrent abdominal diseases and venous problems abnormalities can also be assessed by CTA [8].

CIN is defined as an increase in serum creatinine of 0.5mg/dl or more within 72 hours after contrast administration in absence of other causative factors [9]. In pre-dialysis patients awaiting for kidney transplantation, performing a CTA examination could be of concern as it may result in acute renal failure that could lead to an early initiation of dialysis. Although CIN incidence seems to be lower than previously described, it is well known that patients with a glomerular filtration rate (GFR) lower than 30 ml/min

are at a higher risk of increased creatinine levels, transient or permanent, or even of early initiation of dialysis [10,11].

The aim of this study is to evaluate the prevalence of CIN and the need for dialysis in pre-dialysis patients who underwent a CTA with intravenous iodinated contrast for pre-transplant evaluation with CIN prophylaxis to demonstrate the safety of administration of iodinate contrast in these patients. As far as we know, there is only one study that deals with this topic [12].

## MATERIAL AND METHODS

This is a prospective single-center study that was approved by the Ethics Committee of our hospital. Thirty-eight patients with chronic kidney disease (CKD) stage 4 and 5 who were candidates for pre-emptive living donor kidney transplantation for whom CTA was indicated were included between January 2011 and March 2013. All patients provided informed consent. All patients had a Modification of diet in renal disease estimated GFR lower than 30 ml/min. Exclusion criteria included patients [1] awaiting to kidney-pancreas transplantation [2] in whom prophylactic hydration is contraindicated (presence of uremic symptoms, symptoms suggestive of cardiac insufficiency class III-IV based on the New York Heart Association classification), and [3] with a history of allergy to iodinated contrast.

For CIN prophylaxis patients were instructed to take three doses of N-acetylcysteine (1200 mg every 12 hours starting 12 hours before the CT-scan). On the day of the procedure, the patients were infused with 3mL/kg/h of sodium bicarbonate 1/6M 1 hour before the CT examination and 1mL/kg/h six hours following the procedure. On average, 671 cc of saline were administered (2/3 after the examination). Patients were discharged six hours after the CT examination.

The CTA protocol involved scanning of the abdomen and pelvis using a Siemens Sensation 64 or Siemens Flash (Siemens, Erlangen, Germany) as part of the pre-transplantation evaluation. The study protocol involved an unenhanced phase CT (craniocaudal, from diaphragm to pubic symphysis, 30x1.2 mm) and two enhanced phases obtained after the injection of 100ml of a monomeric hypo-osmolar non-ionic contrast (iopromide Ultravist® 300mg/ml) + 40ml of saline at 4ml/s. Timing for arterial phase CTA (64x0.6 mm) was determined with CARE bolus, ROI at the abdominal aorta, a threshold of 120 UH; and six second delay. Nephrographic phase images were obtained 90 seconds following the administration of IV contrast material (30x1.2 mm). Axial reconstructions were obtained at the end of each phase. Multiplanar and volume rendering reconstructions of the aortoiliac system and branches were obtained in the post-processing workstation in all cases.

**Analysis:** All patients were closely followed before and after the CTA and until the time of transplantation. Blood samples were taken 14 days and immediately before CTA as within 48-72 hours and 14 days after the CTA. When no significant deterioration of the renal function was observed, patients continued the usual follow-up for renal insufficiency. In case of renal function decline, patients were appropriately managed.

**Variables analyzed:** The primary endpoint evaluated was the need for renal replacement treatment after CTA, before

renal transplant. Secondary endpoints were the appearance of CIN (increase of 0.5mg/dl in plasma creatinine within 72h after administration of contrast) and reversible or permanent increase of creatinine levels in CIN patients.

## Statistical analysis

Summary statistics were described as frequencies and proportions for categorical variables. Chi-square tests were used to determine the correlation between qualitative variables. Median values were compared using t-tests (95% confidence intervals). p-values <0.05 were considered statistically significant. Data documentation and analysis were performed using SPSS v.15 (IBM Corp., Somers, NY, USA).

## RESULTS

Thirty-eight patients were included in the study, with a mean follow-up of 5.23 months (range 0.23-36.83). The ratio male:female was 28:9, with a mean age of 52.7 years (range 32.1-77.25). Demographic data are shown in (Table 1). Of all these patients, 29 (78,4%) underwent kidney transplantation, with a mean time between the CTA imaging and the transplantation of 106 days (range 7-1105).

The average creatinine level 14 days before, immediately before, within 72 hours and 14 days after the CTA procedure were 4.45 (range 1.76-7.30), 4.56 (range 2.00-7.0), 4.59 (range 2.09-6.98) and 4.73 (range 1.65-7.9) mg/dl respectively. Four patients (10.5%) developed CIN, with a significant decrease in creatinine levels 15 days post-procedure in three of them, the fourth patient (2.63%) showed progressive worsening of creatinine levels (Table 2). Table 3 shows no significant differences in demographics between CIN and no-CIN patients.

None of the 29 patients that underwent kidney transplantation needed dialysis before surgery. Of the 9 patients who did not undergo kidney transplantation, 7 started dialysis 161 (range 33-346) days in average after the scan, one died due to a lymphoma and the other was submitted to a liver transplantation with improvement of the kidney function. None of these 9 patients developed CIN or early dialysis after CTA.

Despite the fact that there was a significant increase in

Variable	1
Age (y), mean ± SD	54.10 ± 11.64
Male, n (%)	28 (73.68%)
DM type II, n (%)	2 (5.26%)
Hypertension, n (%)	32 (84.21%)
ACE-inhibitor or ARB use, n (%)	19 (50%)
Diuretic use, n (%)	10 (26.31%)
Serum creatinine (mg/dL) mean ± SD	4.45 ± 1.26
eGFR (MDRD) mean ± SD	16.10 ± 7.07
Serum bicarbonate (mg/dL) mean ± SD	21.60 ± 3.39

CIN: Contrast-Induced Nephropathy; SD: Standard Deviation; ACE-inhibitor: Angiotensin-Converting Enzyme Inhibitor; ARB: Angiotensin Receptor Blocker

**Table 2:** Changes in creatinine levels in patients that developed CIN. Case 3 had a permanent worsening of the renal function. None of the patients needed dialysis before transplantation.

Creatinine (mg/dl)	15 days pre-CTA	day CTA pre-CTA	72h post-CTA	15 days post-CTA
Case 1	5.1	5.9	6.5	6
Case 2	4.4	4.9	5.5	5.2
Case 3	5.93	5.7	6.2	6.7
Case 4	3.47	3.9	5.04	4.2

**Table 3:** Comparison of baseline characteristics between patients who developed NIC and patient who did not.

Variable	CIN n = 4	Non-CIN n = 34
Age (y), mean ± SD	47 ± 10.39	54.96 ± 11.63
Male, n (%)	4 (100%)	24 (71%)
DM type II, n (%)	0 (0%)	2 (6%)
Hypertension, n (%)	4 (100%)	28 (82%)
ACE-inhibitor or ARB use, n (%)	2 (50%)	17 (50%)
Diuretic use, n (%)	1 (25%)	9 (26%)
Serum creatinine (mg/dL) mean ± SD	4.84 ± 0.87	4.40 ± 1.32
eGFR (MDRD) mean ± SD	14.5 ± 0.87	16.30 ± 7.54
Serum bicarbonate (mg/dL) mean ± SD	22 ± 3.68	21.55 ± 3.46

CIN: Contrast-Induced Nephropathy; SD: Standard Deviation; ACE-inhibitor: Angiotensin-Converting Enzyme inhibitor; ARB: Angiotensin Receptor Blocker

average creatinine between the levels obtained immediately before the CTA procedure and 14 days post-procedure in the patients of our series, the increases in creatinine levels obtained 14 days pre-procedure and immediately before CTA and between creatinine levels immediately before CTA and 14 days post procedure were similar (0,13 vs 0,30, respectively  $p > 0,29$ ) (Figure 1). The increase in creatinine observed in the only patient with CIN, whose renal function progressively worsened, could be due to the progression of the ESRD.

## DISCUSSION

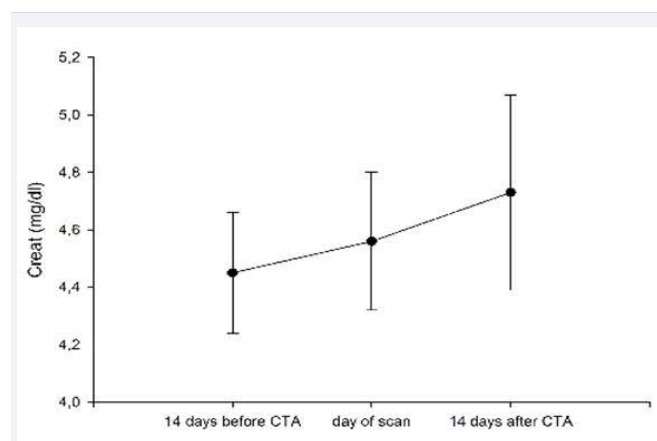
Enhanced CT is usually avoided in pre-dialysis patients with CKD stages 4 and 5, waiting for transplantation as it is considered to worsen the renal function, eventually leading to earlier dialysis initiation related to iodinated CIN [9]. The incidence of CIN following IV iodinated contrast administration has been recently reevaluated and its existence questioned even in end stage renal disease (ESRD) patients [11], but most of the literature states that chronic renal failure is an independent risk factor [10].

Several strategies have been used for the prophylactic prevention of CIN. Latest guidelines suggest that IV hydration with saline or bicarbonate is the most effective measure of prophylaxis [12]. The use of NAC is controversial, in fact, it has been excluded from the most recent guidelines [13].

The increasing number of living donor transplantations allows us to plan the surgery and to know the exact day of transplantation. In patients who receive transplants from living donors a CTA can be performed weeks before the transplantation date for vascular mapping and repercussions of a potential worsening of the renal function will not be relevant given the

proximity of transplant surgery. The evaluation of patients receiving transplants from living donors allows us to determine the actual incidence of NIC in CKD stage 4 and 5 patients after CIN prophylaxis.

We only found four patients (10.5%) with significant increase in creatinine levels consistent with CIN. This increase was reversible in three of the four patients. Newhouse et al. have reported that spontaneous oscillations of creatinine occur in the general population, with a similar incidence of CIN to that found



**Figure 1** Changes in creatinine levels 15 days before CTA, immediately before CTA and 15 days after CTA. No significant differences were found in creatinine increase from 15 days pre-CTA to immediately before CTA and from immediately before CTA and 15 days after CTA. The permanent worsening in the patient that presented CIN can be not related to contrast administration but to the progression of ESRD.

in patients with chronic kidney disease [14]. Newhouse and other authors also found that fluctuations in creatinine are greater in CKD stage 4 and 5. In our series the increase of creatinine between 14 days pre-CTA and the moment previous to the procedure was not statistically significant compared to the increase between two days post-CTA and 14 days post-procedure. This casts doubt on whether the increase in creatinine is not a result of the natural course of the disease if no contrast would have been administered. It is worth noting that the two patients that required dialysis before transplantation did not have CIN and that none of the four patients with CIN needed dialysis before surgery.

To our knowledge there is only one study that deals with prophylaxis of CIN in pre-dialysis living donor recipients undergoing CTA [12]. In this retrospective study, 43 patients in pre-dialysis were evaluated oral hydration was administered before and after CTA. Four out of the 42 patients (9%) showed an increase in creatinine levels greater than 0.5mg/mL (CIN definition), but none of them required dialysis. These results are similar to the results presented here. In this study by Smith et al. the theoretical clinical management of 22.9% of patients was modified because of the CTA findings. In 15.8% of patients the site of anastomosis was influenced by CTA findings and in 3.4% of patients CTA demonstrated renal cell carcinoma.

There are two other interesting publications about the effect of intraarterial contrast administration after coronary angiography (CA) in patients waiting for pre-emptive transplantation: One is a retrospective study in which 62 patients with CKD stage 4 and 5 underwent CA with a CIN prophylaxis regimen involving NAC and intravenous saline hydration. In this study all of the cases of CIN (22%) showed only a transient decline in renal function during the first week post-CA that was entirely reversible, suggesting that intraarterial iodinated contrast administration did not accelerate the decline in renal function in patients with ESRD [16]. In another series the need for dialysis in 23 patients waiting for pre-emptive kidney transplant who underwent CA with oral hydration prophylaxis was compared with a control group of 23 patients who did not undergo CA. No differences in the need for dialysis were found between the two groups [17].

The results of the present study are similar to those of Smith et al [12]: none of the patients evolved into dialytic renal failure, differently to Smith et al who utilizes no prophylaxis rather than hydration, we utilized a protocol comprising of N-acetyl cysteine and sodium bicarbonate in order to prevent worsening of renal function. The similar results seems to say that no matter which hydration protocol is utilized who present with pre-dialytic endstage renal failure tolerate performance of CT-Angiography without evolving into dialytic endstage renal failure. It seem confirmatory that hydration is the key.

One limitation of this study is patients waiting for kidney-pancreas transplantation have not been included, therefore the conclusions can no be extended to patients waiting for kidney-pancreas transplantation. Further works including these patients are needed to know CIN incidence after intravenous contrast injection in this specific group.

Another limitation of this paper is the small number of patients and the absence of a control group. However, comparison of our

results with those control groups (changes in creatinine levels in patients with CKD stage 4 and 5 after unenhanced CT) published in the literature has demonstrated similar results than ours [15].

## CONCLUSION

Our conclusion is that CTA is a safe procedure when performed with CIN prophylaxis in CKD stage 4 and 5 with low contrast induced nephropathy rate and not inducing to an early initiation of dialysis. In our series only four (10.5%) patients showed CIN, which was reversible in 3 cases. Further worsening of renal function was detected in only one patient (2.6%). CTA can be included safely in the clinical guidelines for the imaging examination of pre-emptive living donor kidney recipients.

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