

# Gadolinium: Non-ionic contrast media (1:1) coronary angiography in patients with impaired renal function\*

Renal disfonksiyonu olan hastalarda gadolinium: Non-iyonik kontrast madde (1:1) karışımı ile koroner anjiyografi

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**Aim:** To evaluate efficacy and safety of gadolinium (magnetic resonance imaging contrast media): non-ionic low osmolar contrast media (1:1) in avoiding contrast nephropathy in patients with renal dysfunction referred for coronary angiography.

**Material and Methods:** Patients with a baseline creatinine of 1.5 mg/dl or more were included. In order to minimize contrast nephropathy risk all patients were thoroughly hydrated and treated by N-acetyl cystein. After coronary angiography and/or percutaneous coronary intervention renal function tests were re-measured on day 1,2 and 3. A rise of 0.5 mg/dl in creatinine value in the following 3 days or need for dialysis was considered as a contrast nephropathy event.

**Results:** Twenty six patients were enrolled in this study. Ten were women and 16 were men, mean age was 65.7 ± 11 Baseline creatinine value was 2.47 ± 0.74 mg/dl. Total amount of contrast media used on 1:1 fashion was 57.1 ± 27.2 ml. No procedure related cardiac complication or contrast nephropathy event occurred in this study. Although there was slight image quality loss what we had was adequate for performing the procedures.

**Conclusion:** Although "off label" using gadolinium contrast media in a 1:1 mixture with standard non-ionic low osmolar contrast media seems to be a viable option in decreasing the likelihood of contrast nephropathy.

Key words: **contrast nephropathy, coronary angiography, gadolinium.**

**Amaç:** Renal disfonksiyonu olan ve koroner anjiyografi planlanan hastalarda gadolinium (manyetik rezonans görüntüleme kontrast maddesi) : non-iyonik düşük ozmolar kontrast madde (1:1) karışımının kontrast nefropati gelişmesini önlemede etkinliğini değerlendirmek.

**Gereç ve Yöntem:** Bazal kreatinin değeri 1.5 mg/dl veya üzeri olan hastalar çalışmaya alındı. Kontrast nefropati riskini en aza indirebilmek amacıyla bütün hastalar yoğun bir şekilde hidrate edildi ve n-asetil sistein ile tedavi edildi. İşlemden sonra 1, 2 ve 3. günde böbrek fonksiyon testleri tekrar ölçüldü. Kreatinin düzeyinde 0.5 mg/dl ve üzeri artış veya diyaliz ihtiyacı kontrast nefropati olarak değerlendirildi.

**Bulgular:** Çalışmaya 26 hasta alındı. Hastaların 10'u kadın 16'sı erkek yaş ortalaması ise 65.7 ± 11 idi. Bazal ortalama kreatinin değeri 2.47 ± 0.74 mg/dl idi. Bire : bir derişiminde kullanılan ortalama opak madde miktarı 57.1 ± 27.2 ml idi. Çalışma grubunda işleme ilgili kardiyak komplikasyon veya kontrast nefropati izlenmedi. Hafif bir görüntü kalite kaybı yaşanmakla beraber karar vermek ve işlem yapabilmek için yeterli görüntü kalitesine ulaşılabildi.

**Sonuç:** Gadolinium X-ışını anjiyografisi için üretilip ruhsatlandırılmamış olmasına rağmen 1:1 derişiminde non iyonik düşük ozmolar kontrast ajanla kullanımı kontrast nefropati ihtimalini azaltabilmek için etkin bir alternatif olabilir.

Anahtar kelimeler: **kontrast nefropati, koroner anjiyografi, gadolinium.**

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**D**espite 40 years of experience radiocontrast induced nephropathy (RCIN) is a never resolved issue. Implications of RCIN may be disastrous with an in-hospital mortality rate of 20 % in non-emergency patients (1-3). The incidence of RCIN depends on a number of factors ; preexisting renal insufficiency (most significant), diabetes, congestive heart failure, volume depletion, dose of contrast agent (4,5). So far, the only consistently proven effective intervention to avoid RCIN among high risk patients is vigorous hydration and the use of low osmolar and non ionic agents instead of high osmolar contrast media at the lowest possible dose (6).

**Table 1.** Renal function data of the study group

Baseline urea (mg/dl)	75.4 ± 18.4
Baseline creatinine (mg/dl)	2.47 ± 0.74
Baseline creatinine clearance (ml/min)	30.6 ± 10.2
Creatinine – day 1 (mg/dl)	2.34 ± 0.7 *
Creatinine – day 2 (mg/dl)	2.3 ± 0.74 †
Creatinine – day 3 (mg/dl)	2.2 ± 0.74 ‡
Total contrast used (ml/patient)	57.1 ± 27.2

\*, †, ‡ P<0.001 for all days with respect to baseline value.

**Table 2.** Clinical characteristic of the study group

Number of patients	26
Age	66.5 ± 10.2
Women n, (%)	10 (38.4 %)
Diabetes Mellitus n, (%)	10 (38.4 %)
Hypertension n, (%)	22 (84.6 %)
Compensated heart failure n, (%)	2 (7.6 %)
Previous CABG * n, (%)	1 (3.8 %)
Previous myocardial infarction n, (%)	8 (30.7 %)
Stable angina pectoris n, (%)	7 (26.9 %)
Unstable angina pectoris n, (%)	13 (50%)

\*: coronary artery by-pass graft surgery

Gadolinium chelates are used for magnetic resonance imaging (MRI). They are proposed to have no adverse effects on renal function within recommended doses up to 0.3-0.4 mmol/kg. Given no or very little nephrotoxic effect as a contrast agent several articles related with gadolinium chelates (although “off label”) have been published in imaging different vascular territories during digital subtraction angiography (DSA) or coronary angiography in patients with moderate to severe renal dysfunction (9-12). In these reports gadolinium chelates have been used as the sole agent (9), in conjunction with carbon dioxide (10) or non-ionic low osmolar contrast media (11) with adequate image quality and almost no nephrotoxicity.

## Material and Methods

In order to evaluate the potential benefit of gadolinium as a contrast media during coronary angiography in patients with renal dysfunction we performed the present study. Twenty-six patients with a baseline serum creatinine of 1.5 mg/dl or more were included in this study. We used gadopentetate dimeglumine based contrast material (0.5

mmol/L; Magnevist, Schering, Berlin, Germany) and a low osmolar non ionic contrast agent (Iohexol, Omnipaque; Nycomed, Cork, Ireland) on a 1:1 basis.

To minimize renal injury all patients had intravenous saline hydration 1 ml/kg/hr 12 hours before and after the procedure. Patients were also motivated for liberal fluid intake one day before, on the day of the procedure and afterwards. N-asetyl cystein 1200 mg daily po before the day, on the day and the day after the procedure is part of routine practice for patients with a baseline creatinine value of 1.3 mg/dl or more in our institution. Renal function was assessed before the procedure and on a daily basis during the following 3 days using serum creatinine, urea, sodium, potassium, and creatinine clearance. Cockcroft-Gault formula (13) was used to estimate creatinine clearance. An increase of 0.5 mg/dl in 72 hours of follow-up period or need for dialysis during hospitalization period was considered to reflect an RCIN event for research purposes. Total amount of contrast used on average (1:1 fashion) was 57.1 ± 27.2 ml. Renal function data is presented in Table 1.

### Statistical analysis

Statistical analysis was performed using a SPSS 10.0 computer program. Continuous variables are presented as mean ± standard deviation. To compare pre and post coronary angiography values we used paired t-test.

## Results

There were 10 women and 16 men, mean age was 65.7 ± 11, 10 patients were diabetic (38 %), 2 patients had compensated heart failure (8 %), 22 patients had history of hypertension (85 %). Mean baseline serum creatinine was 2.47 ± 0.74 mg/dl. Two of the patients had staged coronary angiography (CAG) and percutaneous coronary intervention (PCI), 5 had an PCI extended to a CAG and 10 patients were recommended by-pass surgery. Clinical characteristics and cardiovascular background is given in Table 2.

Coronary angiography and where necessary PCI was successfully performed in all cases. Although we felt a slight loss of image quality what we had was satisfactory enough to reach diagnostic conclusions and perform subsequent therapeutic interventions.

None of the patients in this study had a RCIN event. Interestingly renal functions slightly but statistically significantly improved. Similar findings were reported by Rieger et al (10). The most likely explanation for this effect seems to be vigorous hydration.

## Discussion

Gadolinium, although produced for MRI studies, is definitely an attractive agent for “off label” DSA and coro-

nary angiography studies in patients with moderate to severe renal insufficiency. Now, there are several case reports, small series, larger retrospective analysis indicating no or minimal nephrotoxicity of gadolinium in patients with moderate to severe renal dysfunction. However, there are some limitations of using gadolinium other than being "off label". During coronary angiography, since maximum recommended dosage is 0.3-0.4 mmol/kg or 0.6-0.8 ml/kg, in many instances, there would be a need for an excess of the maximum recommended dosage. For example in an averaged sized adult of 70 kg 40-55 ml of gadolinium is in the recommended range and this amount may not be enough for many patients especially if the procedure would be extended with PCI. In this context it may be prudent to use gadolinium with a non-ionic contrast so as to be able to increase the total amount of contrast media without increasing the risk of gadolinium related toxicity and cost.

Another issue is image quality. Although there is some loss of image quality (especially when gadolinium is the sole agent), and our experience are in parallel that satisfactory enough results could be achieved especially with a mixture of gadolinium and non ionic contrast media (11). In a recent optical density DSA study, gadolinium-iodinated media mixture was documented to be visualized markedly better than gadolinium only through a phantom study (14).

Cost is another important issue. Generally gadolinium chelates are approximately fivefold expensive than non ionic low osmolar contrast media in many countries. In a

very similar group of patients (with respect to renal function and total contrast media used) Sarkis et al (11) demonstrated efficacy and safety of 2:1 gadolinium:non-ionic low osmolar contrast media coronary angiography. Our data confirms and further extends contrast nephropathy literature in terms of efficacy and safety of gadolinium/non ionic low osmolar contrast mixture in performing coronary angiography/PCI. One to one basis of gadolinium : non ionic low osmolar contrast media will be less costly.

To the best of our knowledge, there is no head to head comparison of non ionic low osmolar contrast media and gadolinium based (sole agent or in mixture) coronary angiography or other X-ray examination in terms of prevalence of contrast nephropathy. Since gadolinium for X-ray examinations is "off label" such a study may never be performed. Although methodological validity is questionable, a hydration contrast nephropathy study, with similar baseline renal function tests revealed a 11 % incidence of contrast nephropathy (15) .

In summary, we conclude that coronary angiography/ PCI with a 1:1 mixture of gadopentetate dimeglumine: non ionic low osmolar contrast media added to well hydration and n-acetyl cystein treatment is a safe, efficacious procedure for avoiding RCIN in patients with moderate to severe renal dysfunction. Given increasing number of efficacy and safety data authorities may possibly re-evaluate gadolinium chelates as a X-ray contrast media in renal failure patients.

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