

“G.E. Palade” University of Medicine, Pharmacy, Science and Technology of Targu Mures

Doctoral School

CONTRAST INDUCED NEPHROPATHY – Abstract

PhD Student: Cristina Somkereki

Scientific Coordinator: Prof. Dan Dobreanu, MD, PhD

Technological progress has recently led to more diverse and precise interventional techniques. Beyond the new techniques, the use of more advanced materials also provides additional benefits. The development of hybrid materials, combining excellent mechanical properties and increased biocompatibility, opens new horizons in treating congenital heart diseases and other complex heart conditions.

Percutaneous coronary interventions have evolved from the first balloon angioplasties to the stent angioplasties that are in use today, and bare metal stents have been replaced by drug eluting stents, which have also evolved over time.

In addition to that, angio-computed tomography and cardiac magnetic resonance imaging are increasingly being used in research and clinical practice, and are greatly contributing to further development, in both medical knowledge, and patient care.

However, although these interventional and imaging procedures have immensely improved medical practice and patient outcomes, they come at the cost of some complications, the most frequent of which is contrast induced nephropathy.

Considering this, the purpose of the current PhD thesis was to assess the incidence and progression of clinical and subclinical kidney injury in patients who are exposed to intraarterially-injected contrast. Also, we aimed to identify if the levels of neutrophil-gelatinase associated lipocalin (NGAL) and cystatin C, a low molecular weight protein, can be used to predict contrast induced nephropathy with more accuracy and sensitivity by comparison with commonly used parameters, such as serum creatinine. Another important goal was to test the ability of this biomarkers to identify not only clinical kidney damage, but also subclinical impairment. In the current research, we defined subclinical contrast induced nephropathy as an increase of at least 25% in NGAL and cystatin C levels by comparison with baseline values.

To reach these goals, we enrolled in our study 71 patients with vascular pathology (coronary or peripheral) who underwent interventional revascularization procedures. Beyond conventional parameters for kidney function assessment, such as creatinine and glomerular filtration rate, we determined the levels of cystatin C and NGAL to identify acute kidney injury.

In the first part of the current research, we approached the correlation between cystatin C and NGAL, and the presence of functional and structural renal injury, as well as other clinical and biological parameters. Although we could not identify new predictors of kidney injury, we identified several significant correlations between subclinical kidney injury and some biological parameters such as HDL cholesterol, or serum potassium, albumin or uric acid.

Although cystatin C and NGAL are sensitive markers for identifying subclinical acute renal injury, it is essential to bear in mind that these parameters are not entirely specific for kidney dysfunction, and their levels may be influenced by numerous other factors. Determining the levels of other biomarkers of renal dysfunction such as urine cystatin C and NGAL, retinol binding proteins and beta 2 microglobulin would have been useful, but was not, unfortunately, possible.

In the second sub-study, the main finding was that contrast induced nephropathy is a rare occurrence, which is mostly associated to previous kidney impairment (as assessed by serum creatinine), and the volume

of contrast that is being used during the procedure. While clinical contrast nephropathy was no longer present in any of the patients at one month after the procedure, subclinical impairment (defined as a $\geq 25\%$ increase in cystatin C and NGAL levels by comparison to baseline values) was identified in a large number of patients. In fact, half of the patients who developed subclinical kidney injury 48 hours after the procedure still had significant changes in cystatin C and NGAL levels at 1 month. The only predictor for this occurrence was the renal function at hospital admission.

In the third sub-study, we assessed the role of periprocedural intravenous hydration in preventing contrast induced nephropathy. Although periprocedural hydration is considered one of the most important preventive measures, we found no correlation between the lack of hydration and the development of contrast-induced nephropathy, and this is consistent with the results reported in other studies.

In the fourth sub-study we assessed the differences between MDRD, CKD-EPI creatinine and CKD-EPI cystatin filtration rate, and their relationship with NGAL and cystatin C. NGAL and cystatin C were not able to refine the diagnosis of contrast induced nephropathy, and CKD-EPI creatinine was non-inferior to CKD-EPI cystatin and MDRD in identifying patients with contrast induced nephropathy.

The main limitation of the current research project is represented by the relatively low number of enrolled patients. Consequently, the evidence we gathered is not enough to endorse the use of NGAL and cystatin C for identifying patients at risk of developing contrast induced nephropathy.

To that purpose, further research on a larger number of patients is needed. Until then, current data suggests that contrast induced nephropathy is still a significant complication of interventional procedures, and finding a valid and more sensitive predictor for the occurrence of this condition, as well as a solid prevention strategy, is crucial for improving patient outcomes.

Although contrast induced nephropathy rarely occurs, it is a severe condition, associated with a significant increase in morbidity and mortality, as well as prolonged hospitalization and elevated costs. As seen in previous works, most prevention methods have limited efficacy, and controversy regarding the best way to approach this condition.