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RESEARCH ARTICLE

THE CHALLENGE OF KIDNEY DAMAGE DURING INTERVENTIONAL CARDIOLOGY PROCEDURES

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Abstract

Introduction: Contrast nephropathy (CN) is a frequent cause of acute renal failure (ARF). The diagnosis is based on an elevation of serum creatinine of 0.5 mg/dl (= 44.2 μ mol/l) and/or \geq 25% of baseline creatinine. In 90% of patients developing AKI on PC, it classically occurs between 24 and 72 hours after the examination. Diuresis is generally preserved, proteinuria is minimal, and urine sediment shows only granular cylinders and few cells. The differential diagnosis is that of ARF caused by cholesterol emboli from invasive procedures in the suprarenal aorta. In the short term, AKI following coronary angiography is associated with procedural complications, a longer hospital stay (8.1 days versus 4.7 days; $p < 0.001$), and higher one-year mortality (12.1% versus 3.7%). Patients at risk of developing PC-related nephropathy, particularly those with chronic renal failure or concomitant hypovolemia, have the need for extrarenal purification in some cases, in addition to the risk of cardiovascular mortality. This makes contrast media nephropathy a serious event for which clinicians must be prepared.

Objective: the aim of this work was to determine the incidence of NIPC in patients undergoing primary angioplasty and/or coronary angiography procedures and generate hypotheses about risk factors. **Materials and methods** In collaboration with the cardiology department, we conducted a longitudinal descriptive study between January 2019 and January 2021. It included a cohort of 180 patients undergoing emergency or cold angiocoronary angiography for diagnostic or therapeutic purposes. Clinical and biological follow-up was 3 months for all patients. Patients with a blood test including creatinine levels before the examination and creatinine levels at 3 days, 15 days, 1 month, and 3 months after the procedure were included. Those who had undergone PCI for an examination other than coronary Results Characteristics of the overall population All patients had normal creatinine levels and were predominantly male (70.0%) with an average age of 60.8 years. Of these patients, 20.6% had diabetes, 18.2% hypertension and 6.4% heart failure (HF). The rate of IR was 20.8%. **Descriptive study; Comparison of patient characteristics with and without NCI:** The multivariate logistic regression study demonstrated that diabetes mellitus (Odds Ratio (OR)=2.26; 95% confidence interval (CI95%): 1.29-3.98, $p=0.005$), a left ventricular ejection fraction (LVEF) $< 45\%$ (OR=2.03; IC95% :1.22-3.39, $p=0.007$) and a quantity

of iodinated contrast medium (ICP) > 90ml (1.72; IC95%: .of iodinated contrast medium (ICP) > 90ml (1.72; IC95%: 0.99-2.99, p=0.05) were predictive of the occurrence of NCI. It should be noted that age was linked to creatinine clearance, and it was through a reduction in renal function that advanced age was responsible for a higher incidence of CIN. Furthermore, the search for correlations between these five independent factors 2 by 2 showed a significant relationship between diabetes and reduced renal function; in the co-presence of these two factors, their effects are reciprocally potentiated and are responsible for an increased risk. Preventive measures showed their efficacy only in the diabetic group, where prior hydration with saline significantly reduced the incidence of CIN: 16% versus 50% in diabetics who did not receive saline infusion

Conclusion: Despite current management, this pathology affects the cardiovascular prognosis of patients, even though normalization of renal function is usually achieved within a month of exploration. In addition to identifying factors predictive of NIPC with a view to implementing appropriate preventive measures in patients at risk, we stress the importance of ensuring a good hemodynamic state intra-procedurally²⁷.

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Introduction:

Millions of iodinated contrast media (CP) injections are performed worldwide every day. When administered to ambulatory patients with no morbidity, no specific preventive measures are usually taken, given the very low risk of contrast-induced nephropathy (CIN). Contrast-induced nephropathy is common in elderly patients with chronic renal failure or diabetes. In fact, CIN is the third leading cause of acute renal failure (ARF) in hospitals, after functional ARF and drug-induced causes. Prevention is therefore essential for these at-risk patients.

Contrast nephropathy (CN) is a frequent cause of acute renal failure (ARF). Diagnosis is based on an elevation of serum creatinine ≥ 0.5 mg/dl ($= 44.2 \mu\text{mol/l}$) and/or $\geq 25\%$ of baseline creatinine. In 90% of patients developing AKI on PC, it classically occurs between 24 and 72 hours after the examination. Diuresis is generally preserved, proteinuria is minimal, and urine sediment shows only granular cylinders and few cells. The differential diagnosis is that of ARF caused by cholesterol emboli from invasive procedures in the suprarenal aorta. In the short term, AKI following coronary angiography is associated with procedural complications, a longer hospital stay (8.1 days versus 4.7 days; $p < 0.001$), and higher one-year mortality (12.1% versus 3.7%). 2 Patients who have chronic renal failure or concomitant hypovolaemia are more likely to develop PC-related nephropathy.

The need for extrarenal purification in some cases, in addition to the risk of cardiovascular mortality, makes contrast media nephropathy a serious event for which clinicians must be prepared.

Objective:

The aim of this work was to determine the incidence of NIPC in patients undergoing primary angioplasty and/or coronary angiography procedures and generate hypotheses about risk factors.

Materials and Methods:

Study population

In collaboration with the cardiology department, we conducted a longitudinal descriptive study between January 2019 and January 2021.

It included a cohort of 180 patients undergoing emergency or cold angiocoronary angiography for diagnostic or therapeutic purposes. Clinical and biological follow-up was 3 months for all patients. Patients with a blood test including creatinine levels before the examination and creatinine levels at 3 days, 15 days, 1 month, and 3 months

after the procedure were included. Those who had undergone PCI for an examination other than coronary angiography were included.

Definition

NCI was defined by a rise in creatinine levels ≥ 5 mg/l (44 μ mol/l) or an increase of more than 25% from baseline within 72 hours of examination [1–3]. Renal function was estimated by calculating the glomerular filtration rate using the CKD EPI formula.

Iodinated contrast-induced nephropathy (ICIN) is defined as "acute renal failure (ARF)" occurring within 48 hours of exposure to iodinated contrast medium (ICP) and after excluding other nephrotoxic agents. The European Society of Urogenital Radiology (ESUR) [1] recommends that the KDIGO definition [2] be adopted as the definition of CINP, i.e., an increase in serum creatinine ≥ 26.5 μ mol/l (0.3 mg/dl), or ≥ 1.5 to 1.9 times the initial value, within 48 to 72 hours of intravascular injection of an ICP.

This nephropathy poses a number of terminological problems. According to some studies, it has not always been possible to exclude other potential causes of nephropathy from the protocols adopted and patient follow-up.

Preventive protocols were applied to patients with diabetes and/or moderate chronic renal failure or more for scheduled coronary angiography. No preventive measures were recommended for patients undergoing emergency coronary angiography. Prevention was started 24 hours before iodinated contrast injection by intravenous administration of one liter of 9% saline. Keeping the same protocol for the two days following the procedure. Patients had clinical and biological follow-up within 72 hours, 15 days, 1 month, and 3 months of coronary angiography.

Results:-

Characteristics of the overall population

All patients had normal creatinine levels and were predominantly male (70.0%) with an average age of 60.8 years. Of these patients, 20.6% had diabetes, 18.2% had hypertension, and 6.4% had heart failure (HF). The rate of IR was 20.8%.

Descriptive study:

Comparison of patient characteristics with and without NCI:

The multivariate logistic regression study demonstrated that diabetes mellitus (Odds Ratio (OR)=2.26; 95% confidence interval (CI95%): 1.29-3.98, $p=0.005$), a left ventricular ejection fraction (LVEF) $< 45\%$ (OR=2.03; IC95%:1.22-3.39, $p=0.007$), and a quantity of iodinated contrast medium (ICP) > 90 ml (1.72; IC95%: 0.99-2.99, $p=0.05$) were predictive of the occurrence of NCI.

It should be noted that age was linked to creatinine clearance, and it was through a reduction in renal function that advanced age was responsible for a higher incidence of CIN. Furthermore, the search for correlations between these five independent factors 2 by 2 showed a significant relationship between diabetes and reduced renal function; in the co-presence of these two factors, their effects are reciprocally potentiated and are responsible for an increased risk.

Preventive measures showed their efficacy only in the diabetic group, where prior hydration with saline significantly reduced the incidence of CIN (16% versus 50% in diabetics who did not receive a saline infusion).

Discussion:-

We identified several observational studies examining the risks of mortality, cardiovascular events, and renal failure associated with MI after coronary angiography. Myocardial infarction was associated with an 8-fold increase in the risk of death after coronary angiography in studies without adjustment. Among studies adjusted for baseline clinical features that simultaneously predispose to ICU and mortality, ICU remained an independent predictor of long-term mortality, but with a pooled RR reduced by around 2. Our results show that, although UHI is consistently associated with mortality after coronary angiography, the strength of this association varies from study to study, and the risk associated with UHI in adjusted studies represents only a fraction of the overall risk reported by unadjusted observational studies. These results suggest that the independent association between myocardial infarction and

mortality is more modest and attenuates further after accounting for publication bias, resulting in a remaining 79% independent increase in the adjusted risk of death associated with myocardial infarction in our meta-analysis.

There is a wide disparity in the incidence of NCI reported in the literature, ranging from 2 to 50(4–6). In the study by Budano et al. (7), the incidence of NCI after coronary angioplasty in an unselected population ranged from 6.9 to 15.9, depending on the definition adopted. Sweatshots are performed to determine which definition would best correlate with the subsequent prognosis. The definition we adopted (addition of creatinine levels of more than 5 mg/l or more than 25) is the one used by the majority of studies (9–11) and by the European Society of Urogenital Radiology. The disparity in NCI incidence is also due to the heterogeneity of the populations studied (21–4). In an unselected population, the incidence of AKI with PCI is around 2. In salty cases, the incidence is higher, ranging from 12. to 30.6. The incidence found in our population, which included over 40 diabetic subjects and where two-thirds of procedures were carried out as emergencies, was 17.2, which is close to the incidence reported in high-risk subjects (30).

Risk factors for NCI

- The most important patient-related risk factors are eGFR < 60 ml/min/1.73 m² and diabetes mellitus. 15
- The risk of CIN is significant if baseline creatinine is ≥ 1.3 mg/dl in men and ≥ 1.0 mg/dl in women, i.e., an eGFR < 60 ml/min/1.73 m². However, according to observational studies, this risk is:
 - Nil for an eGFR ≥ 45 ml/min/1.73 m²
 - between 0 and 2% for an eGFR between 30 and 44 ml/min/1.73 m².
 - Between 0 and 17% for eGFR < 30 ml/min/1.73 m², 11, 12.
- For other authors (13, 14), this risk is:
 - Negligible for eGFR ≥ 45 ml/min/1.73 m²
 - High for eGFR < 30 ml/min/1.73 m², even with intravenous administration of PCI
 - Intermediate when eGFR is between 30 and 44 ml/min/1.73 m², except for diabetic patients and/or when PCI is administered intra-arterially, situations that place these patients in the high-risk group for AKI Other patient-related risk factors need to be taken into consideration. These include
 - Age > 65, given the presence of one or more risk factors
 - some medications: NSAIDs, diuretics, renin-angiotensin-aldosterone system (RAAS) blockers, calcine urine inhibitors, aminoglycosides, amphotericin B, etc.
- Situations of renal hypoperfusion
 - The presence of multiple myeloma

Finally, some risk factors are procedure-related, such as hyperosmolar PCI, the volume of PCI injected, repeated injections of PCI 48 or 72 hours apart, and intra-arterial injection of PCI.

Thus, after coronary angiography coupled with endoluminal angioplasty, the risk of AKI appears higher after CT with PCI injection due to the severity of the clinical picture, associated comorbidities, and the route of PCI administration 15.

In our study, the incidence of AKI among diabetics was 27%, and the 80 mL/min threshold for creatinine clearance was distinctive for the risk of AKI occurrence, since 83.9% of subjects who presented with AKI had a clearance <80 mL/min. In our study, the risk of NCI was multiplied

In our series, NCI was three times more frequent in patients aged over 60, but age was not an independent factor in NCI; according to our results, the occurrence of NCI was not related to patient gender. Hydration inhibits the renin-angiotensin-aldosterone system and reduces the release of vasoconstrictors and oxygenated free radicals. It also dilutes ICP, reducing its viscosity and direct tubular toxicity. Therefore, it remains the most important preventive measure.

It is recommended for all patients at high risk of developing ARF after ICP injection, unless they are hypervolaemic or on dialysis 29.

Which route should be used for rehydration?

Agarwal et al. (15) and Hiremath et al. (17) concluded in their meta-analysis that the incidence of AKI after ICP injection is statistically similar whether rehydration is oral or intravenous. This incidence is also statistically

identical, whether renal function is normal or impaired. However, patients with an eGFR ≥ 60 ml/min/1.73 m² have a very low risk of developing AKI after ICP injection, and therefore oral rehydration on an outpatient basis seems appropriate²⁷. But for patients at high risk of AKI after PCI injection (with the exception of those with hypervolaemia and dialysis), the National Institute for Health and Care Excellence (NICE) 18 and KDIGO [2] recommend intravenous rehydration.

What volume should be infused for this prevention?

The Canadian Association of Radiologists (19) recommends infusing isotonic saline at a rate of 1 to 1.5 ml/kg/h, 1 to 12 h before, and up to 24 h after the procedure. In emergencies, hydration should be performed after PCI injection. This infusion should be administered cautiously to subjects suffering from heart failure and/or the elderly, given the risk of OAP. A new strategy based on forced diuresis with furosemide and intravenous hydration using the Renal Guard system appears to be effective in preventing AKI after PCI injection (20).

Statins

Statins have antioxidant, anti-inflammatory, and antithrombotic properties²¹. Several clinical trials and meta-analyses have demonstrated the benefit of statins in preventing AKI after ICP injection. In the meta-analysis by Zhou X et al. ²², administration of a statin (atorvastatin or rosuvastatin) prior to PCI injection for cardiac catheterization was associated with a significant reduction in the risk of worsening renal function in CKD patients. Similar results have been reported previously in the meta-analysis by Liu et al. (23 and Singh et al. (24, and more recently in that by Zhou Y. L. et al. (2021).

Most patients referred for coronary angiography are already on statins for secondary prevention or will be prescribed a statin given its preventive efficacy, as reported in the PRATO-ACS study (the protective effect of rosuvastatin and antiplatelet therapy on contrast-induced acute kidney injury and myocardial damage in patients with acute coronary syndrome trial) ²⁵. "The ESC/EACTS guidelines on myocardial revascularization therefore suggest statin prescription²⁵. However, there are insufficient arguments to recommend statin administration to patients at the point of first-line treatment, prior to PCI injection. In our series, saline hydration was only effective for diabetic patients. As mentioned above, prevention is based on limiting the amount of PCI used.

Is there a place for prophylactic hemodialysis or hemofiltration?

As demonstrated in the meta-analysis by Cruz et al ²⁶, prophylactic hemodialysis or hemofiltration are not indicated to prevent the occurrence of AKI after ICP injection. On the contrary, hemodialysis appears to increase the risk of worsening pre-existing ARF. Prophylactic extra-renal purification is therefore not recommended after ICP injection. In chronic hemodialysis patients, there is no benefit in dialyzing immediately after ICP injection, except in emergency situations²⁸.

Conclusion:-

Despite current management, this pathology affects the cardiovascular prognosis of patients, even though normalization of renal function is usually achieved within a month of exploration. In addition to identifying factors predictive of NIPC with a view to implementing appropriate preventive measures in patients at risk, we stress the importance of ensuring a good hemodynamic state intra-procedurally²⁷.

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