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CONTRAST-INDUCED NEPHROPATHY IN POST-COVID-19 PATIENTS

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Abstract. Introduction. Contrast-induced nephropathy is a serious cause of acute kidney injury and represents an urgent problem in clinical practice. Until recently, there are contradictions in the understanding of many aspects of contrast-induced nephropathy. However, the current situation with using CAs in patients with COVID-19, thus causing contrast-induced nephropathy, has become an urgent issue for clinical physicians and radiologists. **Aim** of this study is to review some up-to-date information on the use of newer and less nephrotoxic drugs among post-COVID-19 patients with a previous renal impairment. **Material and Methods.** Topical studies published on studying contrast-induced nephropathies in post-COVID-19 patients have been reviewed herein. **Results and Discussion.** In case of developing the acute renal failure syndrome caused by using CAs in past-COVID-19 patients, first it is necessary to exclude alternative (non-contrast-induced) causes of its occurrence, such as thromboembolism syndrome that may develop upon angiography, ischemic nephropathy, nephrotoxic effects. Upon administration of the X-ray ca, a short-term increase in creatinine levels is possible after 24 hours, but this does not mean the development of contrast-induced nephropathy. **Conclusions.** To prevent the development of contrast-induced nephropathies, patients must be adequately hydrated. Nephrotoxic drugs should be discontinued at least 24 hours before ca administration. Moreover, the choice of a suitable ca is important.
Keywords: contrast-induced nephropathy, contrast media, COVID-19.
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КОНТРАСТ-ИНДУЦИРОВАННЫЕ НЕФРОПАТИИ У ПАЦИЕНТОВ, ПЕРЕНЕСШИХ COVID-19

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Реферат. Введение. Контраст-индуцированная нефропатия является серьезной причиной острого поражения почек и представляет собой актуальную проблему в клинической практике. До настоящего времени остаются противоречия в понимании многих аспектов контраст-индуцированной нефропатии. Однако нынешняя ситуация при применении контрастных веществ у пациентов с COVID-19, вызывая контраст-индуцированную нефропатию, стала актуальным вопросом у клиницистов и радиологов. **Целью** текущего исследования является обзор актуальной информации об использовании более новых и менее нефротоксичных препаратов среди пациентов с предшествующим нарушением функции почек, перенесших коронавирусную инфекцию. **Материал и методы.** Проведен обзор актуальных опубликованных исследований, посвященных изучению контраст-индуцированных нефропатий у пациентов, перенесших COVID-19. **Результаты.** При развитии синдрома острой почечной недостаточности вследствие применения контраста у пациентов, перенесших COVID-19, прежде всего необходимо исключить альтернативные причины его возникновения – синдром тромбоэмболии, который может развиться после ангиографии, ишемическую нефропатию, нефротоксические эффекты, не связанные с введением контраста. Через 24 часа после введения рентгенконтрастного препарата возможно кратковременное повышение уровня креатинина, однако это еще не означает развития контраст-индуцированной нефропатии. **Выводы.** Чтобы предотвратить развитие контраст-индуцированной нефропатии у пациентов, перенесших COVID-19, они должны получать достаточное количество жидкости. Прием нефротоксичных препаратов следует прекра-

тить по крайней мере за 24 часа до введения контрастного вещества. Кроме того, важен выбор подходящего контрастного вещества.
Ключевые слова: контраст-индуцированная нефропатия, рентген-контрастные средства, COVID-19.
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Introduction. Contrast-induced nephropathy is an acute renal failure that occurs within 48–72 hours after intravenous administration of a ca. In the absence of other possible CAs, contrast-induced nephropathy manifests itself in an increase in blood creatinine by 44 mmol/l (by 0.5 mg/dl) or more, or an increase in creatinine levels by more than 25% compared to the initial level. Acute kidney injury is a sudden and sustained decrease in glomerular filtration, or urine volume, or both. In this context, the renal dysfunction existing for more than 1 month upon administration of the ca shall be considered as acute. Usually, the development of acute renal failure occurs within 1-7 days. The criterion for the sustainability of dysfunction is its being registered for 24 hours or more [1].

The aim of the current study is to review some up-to-date information on using newer and less nephrotoxic drugs among post-COVID-19 patients with previous renal impairment.

Material and methods. We used literature found in databases, such as PubMed, Scopus, Embase, Web of Science, and ProQuest by keywords: contrast-induced nephropathy, contrast media, COVID-19. The analysis included literature reviews, meta-analyses, systematic reviews, and clinical studies. The most informative and relevant publications were selected. The search was not limited by depth, since the absolute number of the works found was published within the last 2 years.

Results. Contrast-induced nephropathy is an acute renal failure that occurs within 48–72 hours after intravenous administration of a ca. In the absence of other possible CAs, contrast-induced nephropathies manifest themselves in an increase in blood creatinine by 44 mmol/l (by 0.5 mg/dl) or more, or an increase in creatinine levels by more than 25% compared to the initial level. Acute kidney injury is a sudden and sustained decrease in glomerular filtration, or urine volume, or both. In this case, renal dysfunction existing even for more than 1 month can be considered as acute. Usually, the development of acute renal failure occurs within 1-7 days. The criterion for the sustainability of dysfunction is its being registered for 24 hours or more [1].

Epidemiology. The prevalence of contrast-induced nephropathies in the population is 2–8%. The likelihood of this phenomenon may increase up to 50% among patients with underlying renal pathology or exposed to some risk factors. The likelihood of developing contrast-induced nephropathies depends on both the patient's somatic status and the examination technique and the type and volume of the ca administered. It was found that in patients with normal renal function, contrast-induced nephropathies developed rarely, in 0 to 5% of cases. When analyzing the results of a study of more than 16,000 patients (Computer tomography of the head and internal organs, cardiac and peripheral angiography), contrast-induced nephropathies was detected in 1% of patients (*n*= 174). In another large epidemiological study, contrast-induced nephropathies was diagnosed on average in 14.5% of patients, but its frequency varied significantly from 0 to 90% depending on the presence of risk factors, especially previous renal impairment, diabetes mellitus, class and volume of CSW (Cerebral salt wasting) [6]. So, if in patients with diabetes mellitus (DM) with a slight decrease in kidney function, the frequency of nephropathy was 9–40%, then with a significant violation, it increases to 50–90%. In-hospital mortality in acute renal failure among patients undergoing coronary angiography is 35.7%, and two-year survival these patients - 18.8%. An increased risk of death, however, was due to both pre-existing non-renal disease and association with conditions such as sepsis, bleeding, coma, or respiratory failure.

Pathogenesis. The mechanisms underlying the development of acute kidney injury associated with the use of radiocontrast agents are not fully understood, but most likely they include several pathogenetic links. There are five most important pathogenetic mechanisms that provoke the development of nephropathy [9]. 1. Direct toxic effect of the ca on the epithelium of tubular cells. Since the ca is freely filtered and not reabsorbed, it increases the osmolarity in the tubules, as contrast-induced nephropathies occurs in patients who have had COVID-19 in 18% of cases. 2. Contrast-induced change in renal microvascular hemodynamics. Studies investigating changes in blood flow in renal arteries exposed to a contrast medium have shown an initial increase in blood flow (increased activity of renal vasoconstrictors - vasopressin, angiotensin II, endothelin, adenosine) followed by a steady decline. The toxic effects of reactive oxygen species released during reperfusion also contribute to kidney damage. 4. Toxicity due to inflammation. As in other tissues, renal parenchymal lesions can be exacerbated by contrast-mediated activation of the compliment cascade and release of inflammatory cytokines. 5. Activation of the tubuloglomerular feedback mechanism: due to an increase in hydrostatic pressure in the renal tubules, a spasm of the vessels of the glomerular substance of the kidneys occurs, which leads to a decrease in renal filtration and an increase in vascular resistance [10]. It is assumed that contrast-induced nephropathies arises as a result of a synergistic combination of the direct toxic effect of radiocontrast agents on tubular epithelial cells,

Intrarenal mechanisms for the occurrence of contrast-induced nephropathies include: 1) an increase in pressure inside the tubules due to osmotic diuresis; 2) increased viscosity of urine; 3) direct toxic effect on tubular epithelial cells; 4) tubular obstruction; 5) increased activity of renal vasoconstrictors (vasopressin, Angiotensin II, dopamine-1, endothelin,

adenosine); 6) reduction of vasodilation mediated by local prostaglandins and nitric oxide; 7) increased oxygen consumption; 8) ischemia of the renal medulla. Radiocontrast agents studies have shown that the osmolarity of RCC (Red Blood Cell Counting) plays an important role in the development of nephropathy. Cas are freely filtered in the renal glomeruli and are not reabsorbed by the tubules, and therefore their concentration in the urine is 50-100 times higher than the concentration in the blood plasma. Experimental studies have shown that hyperosmolar radiocontrast agents cause changes in renal hemodynamics and have direct toxic effects on renal epithelial cells. Similarly, non-contrasting hyperosmolar solutions (eg, mannitol) can cause vasoconstriction, resulting in a decrease in renal blood flow and glomerular filtration rate (GFR), although to a lesser extent than with radiocontrast agents [6]. The main hemodynamic effect caused by radiocontrast agents is vasoconstriction with decreased renal blood flow and GFR (glomerular filtration rate). These shifts are accompanied by some other non-specific mechanisms - activation of the tubular-glomerular feedback mechanism due to osmotic diuresis, stimulation of the renin-angiotensin system (RAS), increased hydrostatic pressure in the tubules, causing compression of the intrarenal microcirculation. Prolonged vasoconstriction of afferent arterioles with a decrease in filtration pressure in the glomeruli is inevitably accompanied by subsequent ischemia of the medulla. It was found that radiocontrast agents, even iso-osmolar, despite moderate diuresis and natriuresis, also cause greater vacuolization of proximal tubular cells and promote erythrocyte aggregation compared to other classes of contrasts. From this, it was concluded that not only the osmolarity of the contrast medium, but also the increased viscosity of iso-osmolar agents and erythrocyte aggregation induced by PKC (protein kinase C) are critical determinants of the degree of cellular damage. At the same time, no correlation was found between the degree of vacuolization of tubular cells and a decrease in kidney function [7]. A certain role in the pathogenesis of acute renal failure is assigned to the ability of radiocontrast agents to have a direct cytotoxic effect, proven at the level of tubular epithelial cells (vacuolization of epithelial cells of the proximal tubules, cell necrosis and interstitial inflammation) and independent of hypoxia. Structural damage to the cell surface is mainly due to dysregulation and damage to the actin cytoskeleton, loss of cell polarity. In addition, active transport of the ca increases metabolic activity with increased energy expenditure by the tubular epithelium due to osmotic loading, causing oxygen depletion, which in turn leads to increased renal hemodynamic effects. Ischemic damage to the structure and function of the surface membrane of the epithelium of the proximal tubules is the main mechanism of acute cell and organ dysfunction. When the plasma membranes of tubular cells are damaged, their permeability to calcium increases, its intracellular concentration changes, which leads to an increase in constrictive stimuli on the vessels of the kidneys. But first of all, the nephrotoxicity of a ca is determined by its osmolarity. According to chemical and pharmacological properties, radiopaque preparations can be divided into high-osmolar, low-osmolar and iso-osmolar; ionic and non-ionic, as well as monomers and dimers. which leads to increased constrictive stimuli on the vessels of the kidneys. But first of all, the nephrotoxicity of a ca is determined by its osmolarity. According to chemical and pharmacological properties, radiopaque preparations can be divided into high-osmolar, low-osmolar and iso-osmolar; ionic and non-ionic, as well as monomers and dimers, which leads to increased constrictive stimuli on the vessels of the kidneys. But first of all, the nephrotoxicity of a ca is determined by its osmolarity. According to chemical and pharmacological properties, radiopaque preparations can be divided into high-osmolar, low-osmolar and iso-osmolar; ionic and non-ionic, as well as monomers and dimers.

A meta-analysis of several randomized trials showed that the use of high-osmolar CAs increases the risk of complications more than the use of hypo- or iso-osmolar agents, especially among patients with severe comorbidities. Currently, the iso-osmolar non-ionic dimer iodixanol (vasipak) is considered the safest ca. The use of gadolinium-containing CAs used in MRI, in X-ray studies as an alternative is not advisable since they have a greater nephrotoxic effect than equivalent doses of iodine-containing CAs.

Toxicology of radiopaque agents in post-COVID-19 patients. The toxicity of radiocontrast agents is determined by the structure of their molecule and its ability to dissociate into ions in an aqueous solution [2]. Until recently, only ionic or dissociating radiopaque agents (sodium amidotrizoate(urographin, verografin, etc.), which consist of salts that dissociate into cations and anions. They have a high osmolarity (5 times that of plasma) and are therefore also called high osmolar CAs and can cause local ion imbalance. When using them, side effects often develop, up to the most severe. Safer are non-ionic or non-dissociating, low-osmolar radiopaque agents (iohexol (omnipak), iopromide (ultravist), iodixanol (visipak)). They do not dissociate into ions, are characterized by a higher ratio of the number of iodine atoms to the number of drug particles per unit volume of the solution (that is, good contrast is provided by a lower osmotic pressure), iodine atoms are protected by hydroxyl groups, which reduces chemotoxicity. At the same time, the cost of low-osmolar radiopaque agents is several times higher than that of high-osmolar ones. In addition, radiopaque agents are divided according to their structure into monomeric and dimeric depending on the number of benzene rings with embedded iodine atoms [3]. When using dimeric preparations containing six instead of three iodine atoms in one molecule, a smaller dose of the drug is required, thereby reducontrast-induced nephropathy g osmotoxicity. According to the mechanism of development, side effects are divided into:anaphylactoid, or unpredictable(anaphylactic shock, angioedema, urticaria, bronchospasm, hypotension);direct toxic(nephrotoxicity, neurotoxicity, cardiotoxicity, etc.);local(phlebitis, soft tissue necrosis at the injection site).

Clinical characteristics of contrast-induced nephropathy, in post-COVID-19 patients. With the

development of the contrast-induced acute renal failure syndrome, first it is necessary to exclude alternative causes of its occurrence - atheroembolism syndrome, which can develop after angiography, ischemic nephropathy, nephrotoxic effects not associated with the administration of contrast, etc. After the introduction of radiocontrast agents, a short-term increase in creatinine levels is possible after 24 h, however, this does not yet mean the development of contrast-induced nephropathy. With the development of the latter, the serum creatinine level increases by 0.5 mg / dl or more. In most cases, contrast-induced nephropathy manifests as a non-oliguric and asymptomatic transient acute decrease in kidney function. The maximum peak of serum creatinine concentration is noted on the 3-5th day, and it usually lowers to the initial level within 10-14 days but can last up to 3 weeks. In some cases, oliguric acute renal failure occurs, and hemodialysis may be required. The peak serum creatinine concentration in oliguric acute kidney injury usually persists for 5–10 days and returns to the baseline after 14–21 days. Mortality in this group of patients is significantly higher than in non-oliguric acute renal failure. It must be emphasized that the degree of increase in serum creatinine has prognostic value for both short-term and long-term prediction of adverse outcomes *(diagram 1)*.

Changes in urinalysis in contrast-induced nephropathy are nonspecific. In some observations, these are: Turbidity of urine, its dirty brown color, minimal proteinuria in the absence of hematuria, granular casts, epithelial cells of the renal tubules, amorphous sediment, and urate and oxalate crystals. In most patients, the excreted sodium fraction is less than 1%.

Representatives of three nephrological associations (American Society of Nephrology, International Society of Nephrology and National Kidney Foundation) and the European Society of Intensive Care Medicine discussed contrast-induced nephropathy at a meeting in Vicenza (Italy) and proposed the concept of *acute kidney injury* (AKI) [11]. The first results of the work of this group were published in 2007 and touched upon the issues of clarifying diagnostic criteria and stratifying the severity of acute kidney injury. Risk factors for contrast-induced nephropathy may be related to RCD and/or directly to the patient [4,5]. With radiocontrast agents: Their osmolarity, large volume, route of administration, re-application after 72 hours, and complications from the previous application. Directly with the patient: 1) Previous renal failure; 2) diabetes mellitus with renal insufficiency; 3) decrease in effective intravascular volume (heart failure (NYHA – New York Heart Association, class III and IV), myocardial infarction, liver cirrhosis, nephrotic syndrome, diuretics (especially furosemide), abdominal fluid loss, dehydration); 4) prolonged hypotension (concomitant use of a diuretic and Angiotensin-Converting Enzyme inhibitors); 5) metabolic disorders (diabetes mellitus, hyperuricemia, hypercalcemia, hypercholesterolemia); 6) multiple myeloma; 7) nephrotoxic drugs (non-steroidal anti-inflammatory drugs, aminoglycosides, amphoteric contrast-induced nephropathy B, cyclosporine A, platinum-based drugs, sulfonamides); 8) older age; 9) arterial hypertension; 10) anemia; 11) proteinuria; 12) sepsis; and 13) atopic allergy. The standard critical level of normal kidney function has long been considered a serum creatinine concentration of 1.5 mg/dL (132.8 μmol/L) or an estimated GFR (glomerular filtration rate) of 60 mL/min [8]. The European Society for Urogenital Radiology (ESUR, ESUR) recommends slightly different indicators: serum creatinine - more than 120 μmol / l, GFR (glomerular filtration rate)- less than 50 ml / min / 1.73 m² of body surface area. The acute kidney injury Consensus Working Panel agreed that the risk of acute kidney injury becomes clinically significant at serum creatinine ≥ 115 μmol/L in men and ≥ 88.4 μmol/L in women [9], serum creatinine - more than 120 μmol/l, GFR (glomerular filtration rate) - less than 50 ml/min/1.73 m² of body surface area. The acute kidney injury Consensus Working Panel agreed that the risk of acute kidney injury becomes clinically significant

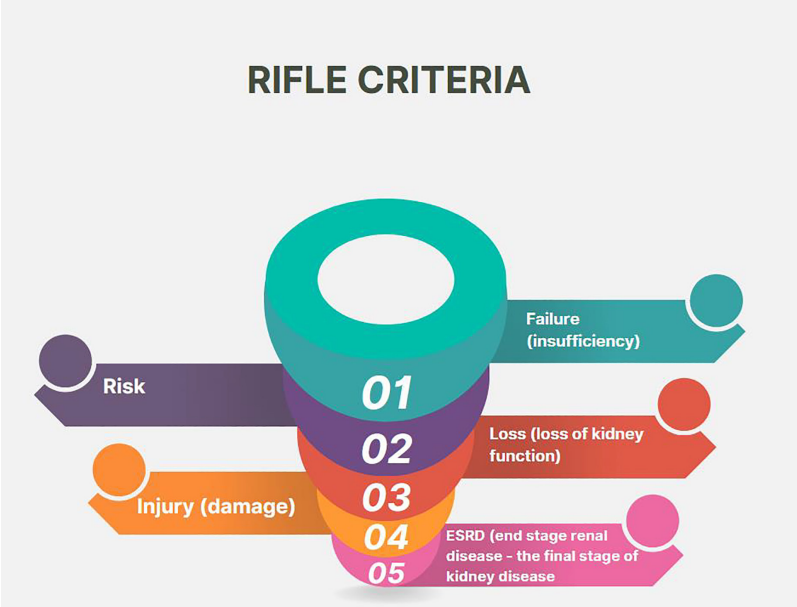

Diagram 1. **RIFLE CRITERIA.** The system of such criteria, proposed by ADQI experts, was abbreviated as RIFLE (English acronym for “Risk, Injury, and Failure; and Loss; and End-stage kidney disease”).
Диаграмма 1. **КРИТЕРИИ RIFLE.** Система таких критериев, предложенная специалистами ADQI, получила название RIFLE (аббревиатура от англ. «risk» (риск), «injury» (повреждение), «failure» (недостаточность), «loss» (утрата), «end-stage» (терминальная стадия) заболевания почек).

at serum creatinine ≥ 115 μmol/L in men and ≥ 88.4 μmol/L in women [9], serum creatinine - more than 120 μmol/l, GFR (glomerular filtration rate) - less than 50 ml/min/1.73 m² of body surface area. The acute kidney injury Consensus Working Panel agreed that the risk of acute kidney injury becomes clinically significant at serum creatinine ≥ 115 μmol/L in men and ≥ 88.4 μmol/L in women [9].

Risk factors associated with radiopaque drugs. Among the risk factors associated with radiopaque preparations, the following can be distinguished: 1) the type of ca (its osmolarity) and 2) the technology of application - volume (dose), route of administration, repeated use of the drug for a short period of time, the presence of complications in the previous application. The CA is not reabsorbed in the renal tubules. The half-life of its intravascular use in patients with normal renal function is about 2 hours and 75% is excreted within 4 hours, and 98% of the prescribed dose is excreted within 24 hours. After approximately 150 minutes, the concentration of radiocontrast agents rapidly decreases in patients with normal renal function, but in patients with severe renal impairment, this phase is prolonged. Radiocontrast agents are classified into ionic and non-ionic, monomers and dimers. First-generation or high-osmolar ionic contrast media (osmolarity > 2000 mosm/kg H2O), such as diatrizoate, have the highest percentage of various adverse reactions (10–12% in patients with an uncomplicated anamnesis and up to 50% in patients at risk). Second generation CAs or nonionic, low osmolar, high viscosity (osmolarity 600–1000 mosm/kg H2O), such as iohexol and iopromide, have fewer adverse reactions, less acute toxicity, and are widely used in clinical practice. Various adverse reactions were noted in 1-3% of patients with an uncomplicated anamnesis and in 16% of patients at risk.

In a large randomized trial including 1196 patients, there was no difference in nephrotoxicity between high and low osmolar radiocontrast agents in patients with intact kidney function (with and without diabetes mellitus). However, in patients with one or two risk factors, the use of low-osmolar monomeric Radiocontrast agents reduced the risk of contrast-induced nephropathy by 3.3 times. A meta-analysis of 31 randomized controlled trials including 5146 patients confirmed that low-osmolar Radiocontrast agents are less nephrotoxic than high-osmolar ones, especially in patients with pre-existing renal impairment, especially diabetic nephropathy.

Third-generation CAs or non-ionic iso-osmolar (osmolarity 290 mosm/kg – iso-osmolar blood at all concentrations) are the most modern class of radiocontrast agents (iodixanol – vizipak). Visipak causes less osmotic diuresis, natriuresis and, accordingly, a smaller decrease in effective intravascular volume. When it is used, the level of blood pressure does not decrease, cardiac arrhythmias do not occur, and allergic reactions are rare [10]. The risk of nephrotoxicity associated with the administration of iodixanol has been studied in patients with varying degrees of risk of nephropathy. When comparing iodixanol with low-osmolar radiocontrast agents in individuals with normal renal function, there was no difference in the incidence of nephropathy. The nephric multicentre study found that that in patients at risk (with renal failure in combination with diabetes and without diabetes) with the introduction of iodixanol, the likelihood of developing nephropathy was 11 times lower, and the incidence of serious cardiovascular complications was 45% less without additional preventive measures compared with low osmolar radiocontrast agents. This study demonstrated that iodixanol has a more favorable safety profile in at-risk patients.

Risk Factors Associated with Post-COVID-19 Patients. Factors that increase the risk of kidney damage to radiocontrast agents include: previous renal dysfunction, diabetic nephropathy with renal failure, a decrease in effective intravascular volume, competitive use of nephrotoxic drugs, advanced age, and some others [8].

Other risk factors for the development of contrast-induced nephropathies. Despite a significant body of research, controversy and disagreement remain regarding risk factors for contrast-induced nephropathy, the use of CAs, and the nephrotoxic effects of radiopaque agents on the kidneys. In an attempt to document the current understanding of contrast-induced nephropathy and develop strategies to prevent this condition, the ECSD (end stage renal disease) established the Committee on the Safe Use of Cas to focus on the effects of CAs on kidney function [4]. Based on the results of a questionnaire sent to ESUR (European Society for Urogenital Radiology) members and experts in the field, predisposing and procedure-related risk factors were identified and simple guidelines for the use of CAs were published and can be found on the Internet at the ESUR website (www.esur.org).

Dose of CAs. Large volumes of CAs are associated with an increase in the prevalence of contrast-induced nephropathy. Experts in the field believe that smaller volumes of CAs needed for imaging should be used, since the risk of contrast-induced nephropathy increases with increasing doses of CAs, in particular, as was shown in the RECOVER study, with a volume of CAs ≥ 140 ml, the risk of developing contrast-induced nephropathy increases [five]. Contrast volume has been confirmed to be an independent risk factor for contrast-induced nephropathy. To date, there is no consensus on the optimal minimum dose of contrast volume [4]. With intra-arterial administration of ca, calculations of possible limits were proposed based on the fact that the dose of ca in grams of iodine should be equal in digital terms to GFR (glomerular filtration rate (ml / min)). For example, in a patient with a GFR (glomerular filtration rate) of 60 ml/min, the estimated dose of contrast volume at an iodine concentration of 320 is 187.5 ml.

Osmolarity of CAs. In patients with existing renal dysfunction, the risk of developing contrast-induced nephropathy was higher when high osmolar CAs were used compared to low osmolar CAs. To prevent the development of contrast-induced nephropathy, the ECSD (end stage renal disease) recommends the use of low- or iso-osmolar CAs. Several studies have shown that in high-risk patients, iso-osmolar CAs are

less nephrotoxic than low-osmolar CAs, but along with this, there are some studies where there was no significant difference between the iso-osmolar drug and comparator drugs [10,11]. Further work is needed to confirm this position.

CA type. Data from several studies indicate that the incidence of contrast-induced nephropathy with the useof low-osmolar CAs is lower than with the use of high-osmolar CAs in patients at risk for contrast-induced nephropathy. For example, in one large randomized trial, patients with kidney disease developed acute renal failure 3.3 times more often when they were injected with high-osmolar CAs (diatrizoate) rather than low-osmolar CAs (iohexol) [12,13]. We also compared the nephrotoxic effects of CAs with an osmolality equal to blood osmolality (iodixanol) with the effects of a low-osmolar ca (iohexol) in patients with diabetes mellitus and impaired renal function who underwent coronary or aorto-femoral angiography (p= 0.002) [9]. Moreover, the incidence of the most severe cases of contrast-induced nephropathies (increased SCr > 1 mg/dL, or > 88 μmol/L) was 0% in patients treated with iso-osmolar ca compared with 15% in patients treated with low osmolar ca. After this study, many studies have been conducted to research in the role of osmolarity in the development of contrast-induced nephropathy. One of them is the RECOVER study [5]. This study was designed to compare the nephrotoxicity of the iso-osmolar non-ionic dimer of iodixanol and the ionic dimer of ioxaglate. Patients received iodicanol or yoxaglat for coronary angiography. The primary point was to determine the frequency of contrast-induced nephropathy (an increase in [SCr] ≥ 25% or ≥ 0.5 mg / dL (44.2 mmol/L). The frequency of contrast-induced nephropathy in various groups of patients was also determined: with severe renal impairment (GFR < 30 ml / min), with diabetes, in patients who received large doses of ca (≥ 140 ml). According to the results of the study, the frequency of contrast-induced nephropathy was statistically significantly lower in the iodixanol group (7.9%) than in the ioxaglat group (17.0%; p= 0.021). In addition, the incidence of contrast-induced nephropathy was statistically significantly lower in patients with impaired renal function (p=0.023) with concomitant diabetes (p=0.041). In the study «Comparison of the safety and efficacy of iodixanol and iopromide in patients with chronic renal failure: a randomized controlled trial» postCovid-19 patients [7], the tasks were set to evaluate several endpoints when comparing iso-osmolar iodixanol and low osmolar iopromide *(table 1)*.

Based on the results of the study, the following conclusions were made.

The frequency of contrast-induced nephropathy was significantly lower in the iodixanol group compared to the iopromide group (5.7 vs. 16.7%; p= 0.011).

Prevention of contrast-induced nephropathie sincludes: 1) conducting a radiopaque procedure only for strict indications; 2) identification and stratification of risk factors for RCI (Revised Cardiac Index); 3) an adequate choice of volume and type of contrast substance (it is better to use iso- or low-osmolar contrasts); 4) if possible, refusal of repeated and multiple X-ray contrast studies; 5) cancellation of nephrotoxic drugs before X-ray contrast examination; 6) if possible,

Table 1

Comparison of the safety and efficacy of iodixanol and iopromide in patients with chronic renal failure: A randomized controlled trial in post-Covid-19 patients

Таблица 1

Сравнение безопасности и эффективности йодиксанола и йопромида у пациентов с хронической почечной недостаточностью: рандомизированное контролируемое исследование у пациентов, перенесших Covid-19

Primary:	Secondary:
	Average peak of contrast agents:
Determine CIN frequency (SC ⩾ 0.5 mg/dl or ⩾ 25% above baseline up to 3 days).	determination of independent risk factors for CIN;
	frequency of serious cardiovascular adverse events (MACE) at the hospital stage and up to the 30th day after discharge;
	the quality of the obtained diagnostic information.
	Responsibility for all business tasks

the use of alternative imaging methods or alternative contrasts; 7) adequate hydration. Since the risk factors for the occurrence of contrast-induced nephropathy are very diverse, and the consequences are serious or even life-threatening, doctors need to take measures to prevent it. Although the optimal strategy to prevent contrast-induced nephropathy has not yet been fully defined, it is important to first identify high-risk patients. The most common ways to identify high-risk patients are a survey, a study of the medical history, measurement of serum creatinine before the administration of a ca.

Conclusion. To prevent the development of contrast-induced nephropathy, patients must be adequately hydrated. Nephrotoxic drugs should be discontinued at least 24 hours before ca administration. Since the nephrotoxic effect of the CA is dose-dependent, it is recommended to use the lowest possible dose. Moreover, the choice of a suitable ca is important. It has been shown that the frequency of contrast-induced nephropathy in patients with renal insufficiency and diabetes mellitus is lower when using iso-osmolar CAs than when using low-osmolar ones (Iohexol). Some studies have shown that the administration of drugs from different pharmacological groups, i. e., calcium channel blockers, dopamine, and N-acetylcysteine, reduces the incidence of contrast-induced nephropathy.

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