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PROGNOSTIC VALUE OF URINARY TISSUE INHIBITOR OF METALLOPROTEINASE-2 (TIMP-2) AND INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN 7 (IGFBP-7) FOR CONTRAST-INDUCED ACUTE KIDNEY INJURY: A LITERATURE REVIEW

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ABSTRACT

Relevance: *Contrast-induced acute kidney injury (CI-AKI) is a serious complication of medical procedures using contrast agents. Despite the decrease in the incidence of acute kidney injury (AKI), CI-AKI remains one of the leading causes of renal function deterioration, especially in emergencies. Serum creatinine (SCr) is not a reliable biomarker for early diagnosis since its level increases only when more than 50% of renal mass is lost. Modern iodinated contrast agents (ICA) reduce the risk of AKI but remain dangerous for patients with chronic kidney disease (CKD) and diabetes.*

The study aimed to *summarize published studies of TIMP-2 and IGFBP-7 early biomarkers to improve the diagnosis and prognosis of contrast-induced acute kidney injury.*

Methods: *The sources were searched in Pubmed, Web of Science, and Cochrane databases. The review included 21 sources published from 2014 to 2025.*

Results: *Iodized contrasts are widely used in clinical procedures. They increase the risk of CI-AKI, with intensive therapy remaining the only supportive measure. [TIMP-2]·[IGFBP7] biomarkers predict the development of severe AKI (KDIGO stage 2/3), mortality, and AKI severity with high sensitivity and accuracy. Elevated levels of these biomarkers are associated with the risk of death or dialysis within 9 months, making them useful for close patient monitoring.*

Conclusion: *Recent studies have highlighted the importance of early diagnosis of CI-AKI using IGFBP-7 and TIMP-2 biomarkers, which is important for early intervention and improved treatment outcomes. Further studies will help improve the understanding and management of this complication, considering risk factors such as creatinine levels, diabetes, and heart failure. The need for safe and effective methods for diagnosing and preventing CI-AKI is relevant both in Kazakhstan and abroad. Careful monitoring of high-risk patients and tailoring AKI management to individual patient needs can improve clinical practice and reduce the incidence of end-stage kidney failure.*

Keywords: *urinary tissue metalloproteinase-2 inhibitor (TIMP-2), insulin-like growth factor 7 binding protein (IGFBP7), contrast-induced acute kidney injury (CI-AKI), biomarkers.*

Introduction: Serum creatinine (SCr) is unreliable for detecting changes in renal function since its increase becomes noticeable only when more than 50% of the renal mass is lost. It delays the diagnostics of acute renal failure (ARF) and complicates corrective interventions. Therefore, early biomarkers of contrast-induced acute kidney injury (CI-AKI) are important for prognosis improvement. CI-AKI is defined as an absolute (0.5 mg/dL, 44 μmol/L) or relative (25%) increase in SCr in 48-72 hours after exposure to contrast medium [1].

Typically, the contrast medium causes rapid non-physiological vasodilation followed by prolonged vasoconstriction, rapidly decreasing renal blood flow. Further, this process results in a vicious cycle of medullary ischemia, which, in turn, causes the generation of reactive oxygen species and, therefore, damage to the endothelium and tubules of the vessels. The direct effects of kidney damage from contrast exposure are due to the toxicity of the tubular epithelium, confirmed by the violation of cell integrity, which leads to loss of function, apoptosis, and, ultimately, necrosis. The contrast dye also increases blood viscosity, reduces microcirculation, and lowers urine flow rate. It increases the time CM stays in the body and can cause microvascular thrombosis. All this results in a sharp decrease in the glomerular filtration rate (GFR) and kidney function. In 2012, 33,249 hospitalizations for acute myocardial infarction were reported in 31,532 patients in the United States and showed that the incidence of ARF decreased from 26.6% in 2000 to 19.7% in 2008 (a decrease of 26%). Although the incidence of CI-AKI may have historically declined over the past decade, the risk is still significant in patients with the greatest need for urgent percutaneous coronary intervention, including patients with ST-elevation myocardial infarction and patients with cardiogenic shock [2].

In hospitals, CI-AKI is one of the most common iatrogenic causes of ARF. As a result of the development of

diagnostic and interventional imaging methods, contrast-induced renal injury was the third leading cause of iatrogenia in hospitalized patients undergoing diagnostic and interventional procedures in Greece, Germany, and the United States in the 2010s [1]. Mild forms of acute kidney injury (AKI) are associated with high mortality and morbidity. The toxicity of iodinated contrast media (ICM) is an important cause of ARF in the intensive care unit (ICU). Modern ICMs with low osmolarity are less likely to cause ARF than older drugs. Over the past 40 years, the osmolality of available contrast agents has gradually declined to physiological levels. Only high-osmolar products (e.g., diatrizoate) with 5 to 8 times higher osmolality than plasma were used in the 1950s. Red blood cell deformity, systemic vasodilation, intrarenal vasoconstriction, and direct toxicity of the renal tubules are more common with contrast agents with osmolality greater than that of blood. This is confirmed in a meta-analysis of studies up to 1992 [3]. ICMs are water-soluble benzene rings in the form of monomers or dimers. Modern ICMs for intravascular injections are iso-osmolar iodixanol and low-osmolar non-ionic monomers. Highly osmolar ICMs are no longer used. The viscosity of iodixanol (11.8 cPs) is significantly higher than that of yohexol (6.3 cPs), the lowest in the category with a low osmolar content. Urine viscosity may be significantly higher with iodixanol in an experimental rat model. Temporary dilation may be followed by a period of sustained vasoconstriction that lasts several hours in the renal arcade of blood vessels subdivided into afferent glomerular arteriole serving the glomerulus, efferent arteriole dividing and forming a peritubular network. As a result, contrast stasis is observed in the kidneys after the completion of the procedure. The uptake of ICM by cells leads to cell swelling and apoptosis [4].

According to the neutrophil gelatinase-associated lipocalin (NGAL) assay results, a subclinical CI-AKI microembolism not found clinically may explain part of CI-AKI since the kidneys receive 25% of cardiac output. Direct complications include volume overload, hyperkalemia, end-stage chronic renal failure, and death. Patients with CI-AKI have a higher risk of myocardial infarction, bleeding, and mortality [4].

To date, there are no effective pharmaceuticals for the prevention or treatment of CI-AKI. Diagnostic procedures using ICM are often denied for patients with chronic kidney disease (CKD). Early detection of ARF is difficult, as it is diagnosed only with an increase in SCr or a decrease in diuresis [3].

ICMs are widely used for diagnostics and surgical treatment but cause iatrogenic renal dysfunction. With a decrease in renal parenchyma mass and fewer nephrons in patients with CKD and diabetes, the decrease in renal blood flow can be quite persistent. It impairs oxygenation of the external medulla and leads to ischemia of the proximal and distal tubules. Besides, water-soluble contrast is readily absorbed by the apical surface of the proximal tubular cells and from the basal-lateral surface into the tubulointerstitial space. Tubular cells undergo swelling and apoptosis.

Attempts to make iodine-based radiographic contrast medium less toxic are promising, especially with cyclodextrin, which retains contrast in the urinary space and reduces the likelihood of its penetration into kidney tissue and kidney damage. Today, significant funds in invasive cardiology have been invested in fluoroscopy and cineangiography for many years [4].

In severe cases, CI-AKI causes progressive oliguria requiring dialysis associated with high mortality. This is about 10% of all cases of iatrogenic kidney disease. Although the incidence is low (1-6%), this rate is high in at-risk groups. Therefore, early identification of high-risk patients is important to improve treatment outcomes [5]. In Kazakhstan, NGAL testing is still conducted only by commercial laboratories according to the AKI diagnostic protocol. The U.S. Food and Drug Administration (FDA) has authorized the marketing of the NephroCheck test. NephroCheck® is a commercial product combining two urinary biomarkers, TIMP-2 and IGFBP-7, to assess the risk of ARF.

Tissue inhibitor of matrix metalloprotease (TIMP-2) is a regulatory protein of 194 amino acids (21 kDa) with two domains: N-terminal and C-terminal. It reduces MMP activity and activates pro-MMP-2. The N-terminal domain (the first 125 amino acids) inhibits active MMPs by binding to their active site. This domain can change its conformation, affecting the binding affinity and specificity of the MMP. The C-terminal domain participates in pro-MMP-2 modulation. TIMP-2 forms a non-covalent bond with MMP-2 (gelatinase A) and is activated on the cell surface by interaction with MT1-MMP, which is required for collagenolysis and tissue remodeling. TIMP-2 is expressed in the glomeruli and tubular cells of the kidneys, regulating ECM components and maintaining the integrity of the kidneys. Its expression is regulated by cytokines and such growth factors as TGF-β and has been linked to fibrosis and kidney disease. TGF-β activates TIMP-2 expression via the Smad and MAPK pathways, increasing transcriptional activity and regulating ECM turnover. Other cytokines and growth factors, such as FGF and EGF, also affect the production of TIMP-2 but have been studied less [6].

Insulin-like growth factor 7 binding protein (IGFBP7) is a novel biomarker for predicting AKI that has gained attention as a biomarker in urine. IGFBP7 is highly expressed in the blood and urine of patients and mice with AKI through a c-Jun-dependent mechanism, correlating with renal dysfunction and programmed cell death. IGFBP7 originates from the epithelial cells of the renal tubules and acts as a biomarker and key mediator of AKI, inhibiting RNF4/PARP1-mediated tubular damage and inflammation [7].

TIMP-2 and IGFBP7 can be detected and measured using a variety of methods, including enzyme-linked immunoassay (ELISA), zymography, reverse transcription-polymerase chain reaction (RT-PCR), and surface plasmon resonance (SPR).

The study aimed to summarize published studies of TIMP-2 and IGFBP-7 early biomarkers to improve the diagnosis and prognosis of contrast-induced acute kidney injury.

Materials and methods: The analysis of articles indexed in the Pubmed, Web of Science, and Cochrane databases over the past 10 years has been conducted (Figure 1). We found 10 results in Pubmed and 3 in Web of Science for "contrast-induced nephropathy timp 2 igfbp 7" or "contrast-induced acute kidney injury timp 2 igfbp 7". 21 articles were selected after filtering. Most of the studies were conducted in America, China, and Europe.

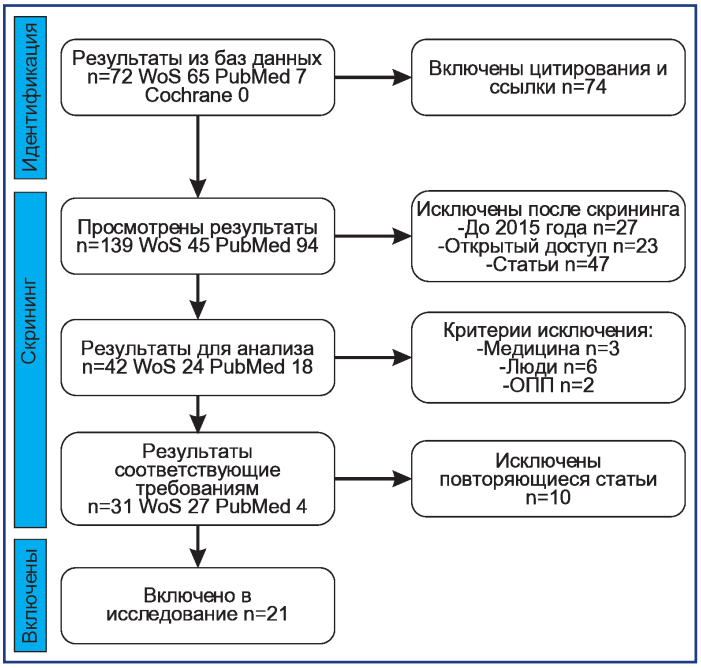

Figure 1 – Algorithm for selection of sources for analysis

Results: In the study by Q. Sun et al., the average dose of contrast medium was 3 ml/kg in 107 of the 137 children who received iodixanol injections. The mean volume was 2 ml/kg in the remaining 30 patients with heart disease who received yopamidol. The incidence of CI-AKI was 14.59% based on the SCr result [1]. In the CI-AKI group, urinary levels of NGAL, IGFBP-7, TIMP-2, and [IGFBP-7][TIMP-2] increased significantly at 2 and 6 hours and increased more rapidly than SCr, remaining high at 12 hours, in contrast to the group without CI-AKI. ROC analysis of CI-AKI diagnostics showed that [IGFBP-7][TIMP-2] was more effective for early diagnostics than IGFBP-7 or TIMP-2 alone. The authors note that the study is small and requires confirmation in multicenter studies. The lack of sensitive biomarkers for children with CI-AKI reduces the ability to intervene on time. Urinary NGAL, IGFBP-7, and TIMP-2 have shown sensitivity in CI-AKI diagnostics (Table 1) [1].

A. Breglia et al. noted that the incidence of CI-AKI was 3-fold higher in patients exposed to iopamidol than in those treated with iodixanol. There were no differences in age, sex, BMI, comorbidities, or use of nephrotoxic drugs [2]. The yopamidol group was exposed 4.5 times more than the iodixanol group, confirming a higher risk of CI-AKI [2].

Increases in IGFBP-7 and TIMP-2 after bypass surgery predicted a higher incidence of ARF in a study by A. Saad et al. Urine readings of these biomarkers predicted the development of ARF, protecting the kidney from tubular damage. Renal hypoxia developed in 50% in 24 hours; R2* levels rose but returned to baseline in 3 months. Patients with higher levels of TIMP-2 and IGFBP-7 responded better to revascularization. No sustained changes in serum creatinine or NGAL, KIM-1, TNF-α, IGFBP-7, or TIMP-2 levels were observed with ARAS [8].

Figure 2 shows an example of parametric maps after contrast imaging and renal stenting for a subject with ARAS at baseline and in 24 hours and 3 months. Maps obtained using the color scale for R2* demonstrate the development of transient widespread tissue hypoxia 24 hours after contrast imaging and renal stenting. This study was not randomized; people with diabetes were excluded, and most patients were men. Revascularization and contrast injection were performed as part of the same procedure. It did not allow the effect of each factor on hypoxia to be determined. The control group included patients with EH of similar age rather than "normal" people. Individuals with ARAS had lower GFR, and 30% had bilateral stenosis with extensive kidney damage. Levels of IGFBP-7 and

TIMP-2 in the renal veins, as well as NGAL, were elevated and inversely correlated with hypoxic changes in 24 hours in patients with chronic renal ischemia due to ARAS. Early hypoxic changes were transient and resolved in 3 months, highlighting the ability of the kidney to adapt to hypoxia even in elderly patients with low GFR. Among patients undergoing angioplasty, ARF was observed in 5.6% and subclinical ARF (increased lipocalin, without Cr increase) in 17.9%. Lipocalin levels remained elevated in one month in half of those with subclinical ARF [8].

Table 1 – Efficacy of uNGAL, ulGFBP-7, uTIMP-2 and [ulGBP7]*[uTIMP-2] biomarkers for the diagnostics of CI-AKI [1]

Area under the curve	Biomarkers			
	uNGAL	ulGFBP-7	uTIMP-2	[ulGBP7]* [uTIMP-2]
	0.718	0.779	0.779	0.811
CI 95%	0.575-0.860	0.658-0.901	0.650-0.908	0.681-0.941
Limit value	36.274	153.061	2.951	0.417
Sensitivity, %	0.70	0.80	0.75	0.80
Specificity, %	0.684	0.667	0.821	0.812

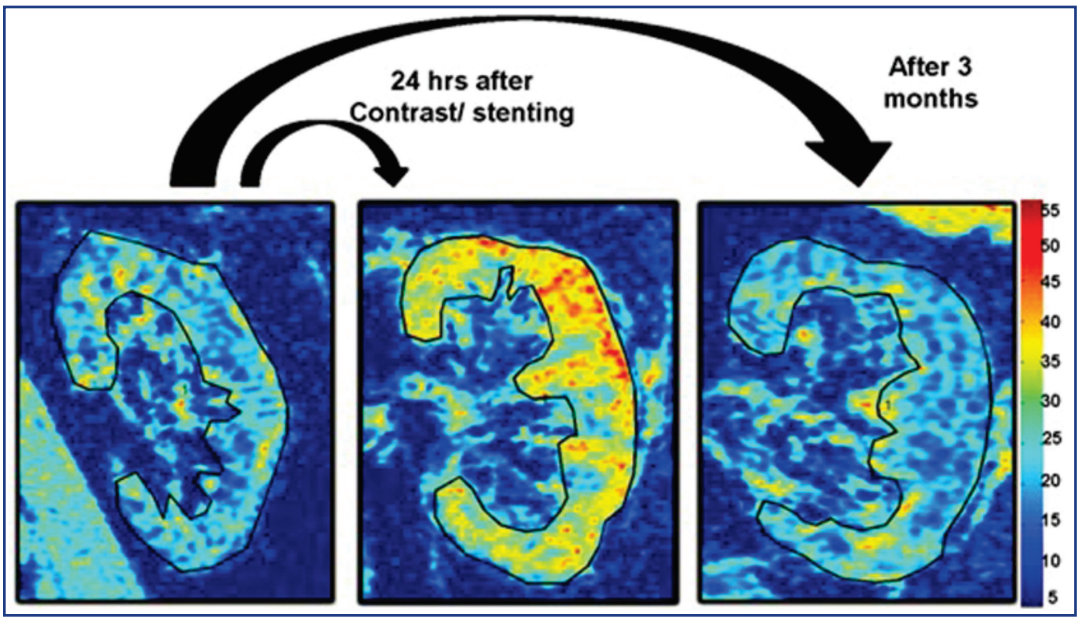

Figure 2 – Example of parametric maps [8]

A very interesting observation is made by S. Martin-Cleary et al.: after the marathon, serum creatinine increased by 40%, urinary TIMP-2 by 555%, and IGFBP-7 by 1094%. The values returned to baseline levels in 24 hours [9]. The PRESERVE randomized clinical trial "Prevention of Serious Adverse Events After Angiography" enrolled 922 participants who underwent coronary or non-coronary angiography at 53 health centers in the U.S., Australia, Malaysia, and New Zealand, making it the largest study to examine this marker in CKD patients undergoing angiography. 7.9% of the 922 participants in the study conducted by R. Murugan et al. developed CI-AKI, and 6.5% had adverse renal events by Day 90. The use of contrast medium was higher in patients who developed CI-AKI. There was no difference in the risk of death (2.7% versus 3.1%). 18% developed adverse events (persistent kidney dysfunction – 11% versus 2%). Patients with low GFR and high albumin-to-creatinine ratios had a high risk of adverse events. Thus, Stage 1 CI-AKI developed in 22% of them (vs. 7%). 46.7% of the 28 patients with adverse events died, 20% were on dialysis, and 43.3% had persistent renal dysfunction by Day 90. A high concentration of the [TIMP-2]•[IGFBP7] index was associated with a low risk of CI-AKI (aOR=0.59; P=0.002), but the predictive value of this index was low (AUROC=0.59). The [TIMP-2]•[IGFBP7] index was more sensitive and superior to other biomarkers for the early detection of ARF. Urinary levels of [TIMP-2]•[IGFBP7] did not increase after angiography in patients with mild ARF, indicating that cell cycle arrest is not the main factor in ARF [10]. This is confirmed in the study conducted by Rouve et al. [3]. It showed slight changes in [TIMP-2]•[IGFBP7] after exposure to the contrast medium.

According to R. Murugan et al. [10], the level of [TIMP-2]•[IGFBP7] may help in early risk stratification and rule out concerns about CI-AKI. A unique finding was a higher pre-angiographic urinary value [TIMP-2]•[IGFBP7] in patients without CI-AKI. This finding may be the result of chance alone or suggest that a higher pre-angiographic concentration of [TIMP-2]•[IGFBP7] in urine may

serve as a protection against the risk of CI-AKI, although the predictive accuracy of this index was low. The mechanisms associated with increased pre-angiographic urinary concentrations of [TIMP-2]•[IGFBP7] and a reduced risk of CI-AKI are unclear, and our findings require further confirmation in future studies. Limitations of this study included one-time urine and plasma collections, limited time intervals for biomarker assessment, and predominant male participation.

The Discovery Study showed that the urinary biomarkers - TIMP-2 and IGFBP7 are better predictive of the risk of ARF in critically sick patients than other biomarkers [11]. The combination of [TIMP-2]•[IGFBP7] and a furosemide (FST) stress test has also been shown to improve the prediction of ARF progression [12].

Biomarkers such as TIMP2•IGFBP7 appear to be a reasonable and effective method for early AKI prediction based on the analysis of existing studies. K.J. Gunnerson et al. showed high accuracy in predicting ARF based on a single measurement of urinary TIMP2•IGFBP7 after admission to the ICU [13]. M. Meersch et al. confirmed this biomarker's high sensitivity and specificity for ARF after cardiac surgery [14]. A study by K. Lakhal et al. also found that contrast-induced nephropathy was associated with higher mortality and the need for renal replacement therapy among patients who received contrast media [7].

The study conducted by E. Rouve et al. showed a significant increase in [TIMP-2]•[IGFBP-7] levels in 30% of patients after contrast media infusion, with 66% of them experiencing a worsening of KDIGO classification within 72 hours. However, the threshold of change in [TIMP-2]•[IGFBP-7] was not associated with CI-AKI, which may indicate the relative harmlessness of contrast agents [3].

Moreover, the incidence of ARF was similar in patients with STEMI who underwent angiography to that of the control group. This fact confirms the low incidence of ARF with contrast agents [10].

Other studies also support these findings. For example, [TIMP-2]x[IGFBP7] levels in a study with 42 participants were not significantly elevated in 4 hours after surgery and until the first day after surgery, highlighting the importance of measurement time for interpreting results [12].

Drug-induced nephrotoxicity is associated with 20% of ARF cases acquired in the hospital and 25% of ARF cases occurring in the ICU. Early detection of nephrotoxicity is critical, but TIMP-2 and IGFBP7 have not yet been used for these purposes outside of the ICU [12]. The toxic effect of ICM is minimal in ICU patients with multiple renal aggression. Disease severity and nephrotoxic load are risk factors for ARF independent of contrast agent infusion [15]. In a large study involving 6877 ICU patients (4351 with contrast, 2526 without contrast), after adjustments, ARF predisposition, dialysis, and mortality were not significantly higher in the contrast group in GFR >45. An increased risk of dialysis was observed with GFR ≤45 [11]. In another study, contrast administration was not associated with increased incidence of ARF, chronic kidney disease, dialysis, or transplantation at 6 months [16].

In the study by R.J. McDonald et al. [17], the ARF incidence was 5.0% (1059 of 21,346). The ARF incidence did not differ between the contrast (4.8%) and non-contrast (5.1%) groups; OR=0,94; P=0,38). In the "risk group" subgroups, the ARF incidence was higher in patients with a history of ARF, CKD, and CHF, but the differences were not significant for ARF (OR 1.10; P=0.36) or CHF (OR 1.18; P=0,18). After adjustment, the rate of emergency dialysis (OR 0.96; P=0.89) and short-term mortality (HR 0.97; P=0.45) was not different in patients who underwent computed tomography with and without contrast agents. Patients with AKI had a higher risk of dialysis (OR 15.75; P<0.0001) and mortality (OR 4.51; P<0.0001), regardless of the administration of the contrast agent. Besides, patients with high creatinine levels, diabetes, CHF, or renal dysfunction had higher rates of ARF, dialysis, and mortality regardless of contrast agent.

It can be noted that the results obtained by J.S. McDonald et al. [11, 18] are closely intertwined with the findings presented in S. Ehrmann et al. [15]. In particular, McDonald et al. showed that a reduced GFR was associated with an increased risk of ARF after computed tomography, and this risk was independent of the use of contrast, even with a GFR of less than 30 ml/min/1.73 m^2. This finding is reflected in a study by Ehrmann et al., where the AKI incidence was also similar between the contrast and control groups, with no significant difference (0%) observed. Moreover, both authors had comparable in-hospital mortality in the groups, highlighting no significant difference in outcomes when contrasting was used. The main risk factors, such as the assessment of sequential organ failure and the number of nephrotoxic agents used, were also similar in both studies. This calls into question the need to avoid contrast agents in patients with low GFR.

Discussion: Thus, the results of numerous studies confirm the feasibility of using biomarkers for the early diagnostics and prediction of CI-AKI and ARF. However, further multicenter studies must confirm these findings and address existing limitations. Early detection of nephrotoxicity remains critical, but TIMP-2 and IGFBP7 have not yet been used outside the ICU [12]. Clinical data show that intra-arterial injection of contrast agents is often associated with increased renal toxicity, but this belief is controversial and requires additional research [19]. It is also important to note the importance of hydration for the protection of the kidneys when using contrast agents [18].

ICMs are widely used in clinical procedures, increasing the risk of CI-AKI. Intensive care is the only supportive

agent in AKI, so new diagnostic approaches are required [5]. Daily measurements are not recommended, except in cases of a change in the clinical situation. Assessment of CI-AKI biomarkers, together with clinical information, should tailor the management of ARF to patients' individual needs. It will improve clinical practice and reduce the incidence of end-stage renal disease [17].

[TIMP-2] · [IGFBP7] predicts the development of severe ARF (KDIGO stage 2/3) with an area under the curve of 0.80-0.82. IGFBP7 predicts mortality, kidney recovery, and severity of ARF [20]. Increased [TIMP-2]·[IGFBP7] is associated with a composite endpoint of death or dialysis within 9 months. These markers can predict kidney damage, prompting closer monitoring of patients [21]. TIMP-2 increases earlier and longer than IGFBP7, as it is involved in cell cycle arrest, inflammation, and tubular regeneration after injury.

Conclusion Recent studies [1, 3, 8, 10, 11, 14] have shown the importance of early CI-AKI diagnostics using novel biomarkers such as IGFBP-7 and TIMP-2. Urine tests for these biomarkers allow CI-AKI detection much earlier than traditional methods based on serum creatinine levels. This finding has important implications for early intervention and improved patient outcomes.

Studies by Q. Sun et al. [1] and A. Saad et al. [8] demonstrate that using these biomarkers effectively diagnoses CI-AKI in children and post-bypass patients. At the same time, studies conducted by A. Breglia et al. show that the CI-AKI incidence is significantly higher in patients treated with iopamidol compared to iodixanol. This fact highlights the need to choose less toxic contrast agents [2].

The PRESERVE clinical trial confirms that the combination of TIMP-2 and IGFBP-7 is the most sensitive biomarker for early diagnostics and prediction of the CI-AKI risk [10]. Despite this fact, there are still unresolved questions, such as the mechanisms associated with the increase in the level of these biomarkers and their predictive accuracy, which requires further research.

Besides, a study by R.J. McDonald et al. [17] and J.S. McDonald et al. [11, 18] showed that the incidence of ARF does not differ between the contrast medium and non-contrast groups, indicating the need to consider other risk factors such as creatinine, diabetes, and heart failure. Patients with high creatinine levels, diabetes, chronic heart failure, or renal dysfunction have higher rates of ARF, dialysis, and mortality regardless of contrast medium use.

In general, the need for safer and more effective CI-AKI diagnostics and prevention remains relevant in Kazakhstan and abroad. Further multicenter studies will help improve the understanding and management of this serious complication.

Studies also highlight the importance of revascularization procedures and contrast media selection to minimize the CI-AKI risk in patients with chronic renal failure and other comorbidities. Closer follow-up of high-risk patients and tailoring the ARF management to patients' individual needs can significantly improve clinical practice and reduce the incidence of end-stage renal disease.

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АҢДАТПА

МЕТАЛОПРОТЕИНАЗА-2 ЗӘР ШЫҒАРУ ТІНІНІҢ ИНГИБИТОРЫНЫҢ (TIMP-2) ЖӘНЕ ИНСУЛИНГЕ ҰҚСАС ӨСУ ФАКТОРЫН БАЙЛАНЫСТЫРАТЫН АҚУЫЗ 7 (IGFBP-7) КОНТРАСТПЕН ТУЫНДАҒАН ЖЕДЕЛ БҮЙРЕК ЖАРАҚАТЫНДАҒЫ БОЛЖАМДЫҚ МӘНІ: ӘДЕБИЕТКЕ ШОЛУ

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Өзектілігі: *Бүйректің контрастты әсерінен жедел зақымдануы (БК-ӘЖЗ)контраст агенттерін қолданатын медициналық процедуралардың ауыр асқынуы болып табылады. Бүйректің жедел зақымдануы (БЖЗ) жиілігінің төмендеуіне қарамастан, (БК-ӘЖЗ) әсіресе төтенше жағдайларда бүйрек функциясының нашарлауының жетекші себептерінің бірі болып қала береді. Қан сарысуындағы креатинин (SCr) ерте диагностика үшін сенімді биомаркер болып табылмайды, өйткені оның деңгейі бүйрек массасының 50%-дан астамын жоғалтқанда ғана жоғарылайды. Заманауи йодталған контрастты заттар БЖЗ қаупін төмендетеді, бірақ созылмалы бүйрек ауруы және қант диабеті бар науқастар үшін қауіпті болып қала береді.*

Зерттеудің мақсаты *– TIMP-2 және IGFBP-7 ерте биомаркерлері туралы жарияланған зерттеулерді қорытындылау болды, бұл контрастпен туындаған жедел бүйрек жарақатының диагностикасы мен болжамын жақсарту.*

Әдістері: *Дереккөздерді іздеу Pubmed, Web of Science, Cochrane дерекқорларында жүргізілді. Шолу 2014 жылдан 2025 жылға дейін жарияланған 21 дереккөзді қамтиды.*

Нәтижелері: *ЙКЗ клиникалық процедураларда кеңінен қолданылады және БК-ӘЖЗ қаупін арттырады, қарқынды терапия жалғыз қолдау шарасы болып қала береді. [TIMP-2]·[IGFBP7] биомаркерлері жоғары сезімталдық пен дәлдікпен ауыр ЖБЖ (KDIGO 2/3 сатысы), өлім және ЖБЖ ауырлығының дамуын болжайды. Бұл биомаркерлердің жоғары деңгейлері 9 ай ішінде өлім немесе диализ қаупімен байланысты, бұл оларды пациенттерді мұқият бақылау үшін пайдалы етеді.*

Қорытынды: *Жақында жүргізілген зерттеулер IGFBP-7 және TIMP-2 биомаркерлерін пайдалана отырып, CI-AKI ерте диагностикасының маңыздылығын атап көрсетті, бұл ерте араласу және емдеу нәтижелерін жақсарту үшін маңызды. Кейінгі зерттеулер креатинин деңгейі, қант диабеті және жүрек жеткіліксіздігі сияқты қауіп факторларын ескере отырып, осы асқынуды түсіну мен басқаруды жақсартуға көмектеседі. CI-AKI диагностикасы мен алдын алудың қауіпсіз және тиімді әдістерінің қажеттілігі Қазақстанда да, шетелде де өзекті болып табылады. Тәуекелділігі жоғары емделушілерді мұқият бақылау және ЖРЖ басқаруын пациенттің жеке қажеттіліктеріне бейімдеу клиникалық тәжірибені жақсартуға және соңғы сатыдағы бүйрек ауруларының жиілігін төмендетуге мүмкіндік береді.*

Түйінді сөздер: *Металопротеиназа-2 зәр шығару тінінің ингибиторының (TIMP-2), инсулинге ұқсас өсу факторын байланыстыратын ақуыз 7 (IGFBP7), контраст-бүйректің жедел зақымдануы (ki-OPP); биомаркерлер.*

АННОТАЦИЯ

ПРОГНОСТИЧЕСКАЯ ЦЕННОСТЬ ТКАНЕВОГО ИНГИБИТОРА МЕТАЛЛОПРОТЕИНАЗЫ-2 (TIMP-2) МОЧИ И БЕЛКА, СВЯЗЫВАЮЩЕГО ИНСУЛИНОПОДОБНЫЙ ФАКТОР РОСТА 7 (IGFBP-7), В ОТНОШЕНИИ КОНТРАСТ-ИНДУЦИРОВАННОГО ОСТРОГО ПОВРЕЖДЕНИЯ ПОЧЕК: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: *Контраст-индуцированное острое повреждение почек (КИ-ОПП) – это серьезное осложнение медицинских процедур с использованием контрастных веществ. Несмотря на снижение случаев острой почечной*

недостаточности (ОПН), КИ-ОПП остается одной из ведущих причин ухудшения функции почек, особенно в неотложных ситуациях. Сывороточный креатинин (SCr) не является надежным биомаркером для ранней диагностики, так как его уровень повышается только при утрате более 50% почечной массы. Современные йодированные контрастные вещества (ЙКВ) снижают риск ОПН, но остаются опасными для пациентов с хронической болезнью почек и диабетом.

***Цель исследования** – обобщение опубликованных данных исследований ранних биомаркеров TIMP-2 и IGFBP-7 для улучшения диагностики и прогнозирования контраст-индуцированного острого повреждения почек.*

***Методы:** Проведен поиск источников в базах данных Pubmed, Web of Science, Cochrane. В обзор включен 21 источник, опубликованный с 2014 по 2025 гг.*

***Результаты:** ЙКВ широко используются в клинических процедурах и увеличивают риск КИ-ОПП, при этом интенсивная терапия остается единственным поддерживающим средством. Биомаркеры [TIMP-2]·[IGFBP7] предсказывают развитие тяжелой ОПН (стадия 2/3 по KDIGO), смертность и тяжесть ОПН с высокой чувствительностью и точностью. Повышенный уровень этих биомаркеров связан с риском смерти или диализа в течение 9 месяцев, что делает их полезными для тщательного наблюдения за пациентами.*

***Заключение:** Последние исследования подчеркнули значимость ранней диагностики КИ-ОПП с использованием биомаркеров IGFBP-7 и TIMP-2, что важно для раннего вмешательства и улучшения исходов лечения. Дальнейшие исследования помогут улучшить понимание и управление этим осложнением, учитывая факторы риска, такие как уровень креатинина, диабет и сердечная недостаточность. Необходимость в безопасных и эффективных методах диагностики и профилактики КИ-ОПП актуальна как в Казахстане, так и за рубежом. Тщательное наблюдение за пациентами с высоким риском и адаптация ведения ОПН к индивидуальным нуждам пациентов могут улучшить клиническую практику и снизить частоту терминальной стадии почечной недостаточности.*

***Ключевые слова:** ингибитор металлопротеиназы-2 (TIMP-2) мочи, белок, связывающий инсулиноподобный фактор роста 7 (IGFBP7), контраст-индуцированное острое повреждение почек (КИ-ОПП); биомаркеры.*

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