https://doi.org/10.23934/2223-9022-2020-9-4-539-544

Morphological Aspects of Acute Renal Injury in Cardiac Surgery

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SUMMARY The use of endoscopic transsphenoidal access is an effective and safe method for the surgical treatment of pituitary adenomas (PA). In endoscopic transsphenoidal surgeries, there is a need to control intracranial pressure (ICP) for reposition and expansion of the tumor capsule. Currently, the main method for reducing ICP in transsphenoidal surgery is installation of an external lumbar drainage, which is associated with a number of complications.

Aim of study To improve the results of surgical treatment of patients with arterial hypertension using hypertonic saline solution.

Material and methods A clinical and anatomical analysis of material from 27 deceased patients who were treated in the cardiac surgery department of the Institute was carried out. Valve replacement was performed in 11 patients, aortic replacement - 2, valves and aorta - 7, combined operations - 7. The patient' s records, autopsy protocols, results of histological examination of surgical and autopsy material were studied. Already on the next day after surgery, an increase in serum creatinine by more than 25% was noted under the conditions of CBR. Morphological examination of the kidneys revealed acute pathological processes - necrosis of nephrocytes of the convoluted tubules in 59.3% of cases and dystrophic changes in 40.7% of cases against the background of chronic pathology (nephrosclerosis, vascular atherosclerosis, glomerulosclerosis, pyelonephritis, secondary contracted kidney). After coronary angiography with a radiopaque contrast agent (RCA), signs of excretory nephrosis were noted, often with fixation of the RCA in the loop of Henle, with tubulorrhexis and the formation of cell casts.

Keywords: acute renal injury, cardiac surgery, morphology

For citation Zimina LN, Berdnikov GA, Rey SI, Kambarov SYu. Morphological Aspects of Acute Renal Injury in Cardiac Surgery. Russian Sklifosovsky Journal of Emergency Medical Care. 2019;9(4):539–544. https://doi.org/10.23934/2223-9022-2019-9-4-539-544 (in Russ.)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments, sponsorship The study had no sponsorship

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AH – arterial hypertension
AKI-C – acute renal injury in cardiac surgery
ARF – acute renal failure
ARI – acute renal injury
CABG/MCABG – coronary artery bypass grafting and mammary coronary artery bypass grafting
CI-ARI – contrast-induced acute renal injury
CKD – Chronic Kidney Disease
CPB – cardiopulmonary bypass

DIC syndrome – disseminated intravascular coagulation syndrome
DM – diabetes mellitus
GFR – glomerular filtration rate
PAS reaction – periodic acid-Schiff reaction
PCI – percutaneous coronary intervention
RCA – radiopaque contrast agent
RRT – renal replacement therapy
SC – serum creatinine
CHD – coronary heart disease

Acute renal injury (ARI) is a common complication in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB), with the incidence from 3.1% to 42% [1]. A recent meta-analysis showed that ARI occurs in 22.3% of cases in cardiac surgery patients with the need for a renal replacement therapy (RRT) of 2.3%, with hospital and long-term (up to 5 years) mortality rates of 10.7% and 30%, respectively. It should be noted that the 3rd stage ARI is associated with a hospital mortality rate of 36.7% [2].

The term ARI, which has replaced the concept of acute renal failure (ARF) since 2012, was proposed by the Kidney Disease Improving Global Outcomes (KDIGO) International Committee and has been used by nephrologists and critical care physicians around the world [3]. The ARI term reflects acute renal dysfunction, defined as the presence of at least one of the following criteria [3]: an absolute increase in serum creatinine (SC) concentration by 0.3 mg/dL (no lower than 26.4 µmol/L) within 48 hours; or a relative increase in SC by 1.5 times or more compared to the baseline (if known or assumed that this occurred within the previous 7 days); or the urine output less than 0.5 ml/kg per hour over 6 hours of observation.

The incidence of ARI in cardiac surgery (ARI-C) depends on many factors associated with the complexity and duration of surgery in CPB conditions, and in the perioperative period - with the negative effect of medicinal and diagnostic radiopaque contrast agents (RCA), hemodynamic state and glomerular filtration rate (GFR) [4, 5]. The premorbid factor plays an important role in the development of ARI-C. The presence of such chronic diseases as arterial hypertension (AH), diabetes mellitus (DM), chronic kidney disease (CKD), requiring RRT, greatly increases the risks of ARI and increases mortality by 1.5 times [4]. The impact of such a number of different damaging factors during cardiac surgery can cause damage to various structural elements of the kidney.

In the literature up to 2012, tubuloepithelial lesions were traditionally considered the morphological equivalent of ARF [6, 7]. Despite the fact that the term ARI is considered to have a broader concept than ARF [8], in the opinion of A.V. Smirnova et al. [4], it does not reflect damage to the renal parenchyma.

The aim of the research was to study the structural basis of ARI-C, which is a frequent complication in cardiac surgery, as well as an essential component of multiple organ failure as a cause of death.

MATERIAL AND METHODS

A clinical and anatomical analysis of material from 27 deceased patients with valvular heart disease, who had been hospitalized in the Cardiac Surgery Department of the Institute in 2017–2018, was preformed. There were 14 men (52%) aged 52 to 75 years, and 13 women (48%) aged from 46 to 79 years old. The inpatient medical records, autopsy protocols, the results of histological examination of the operation and autopsy material were studied. The histological examination was made using well-known methods, including the periodic acid-Schiff reaction (PAS reaction) with the amylase treatment of control sections. In some cases, MSB fibrin staining was used. To identify RCA with iodine in histological sections of the kidneys, we used our originally developed qualitative reaction based on the oxidation of ascorbic acid of the iodine with its discoloration. For this, the sections were treated with a freshly prepared alcoholic or aqueous solution of ascorbic acid, as a result of which RCA lost its black color, became discolored, or became blue or dark-blue with emerging crystal structures.

RESULTS AND DISCUSSION

All patients were admitted to the cardiology department. The hospital length of stay was 10.1 ± 9.5 days (from 1 to 39 days), the ICU length of stay was 6.8 ± 6.7 days. The surgery duration was 318.9 ± 109.4 minutes, the time of CPB made 152.7 ± 81.1 minutes, the myocardial ischemia was 88.0 (73.0 ± 138.0) minutes, the blood loss during surgery made 1900.0 mL (1000.0; 3000.0 ml). SC levels were 105.5 ± 26.4 µmol/L before surgery, 139.4 ± 29.23 µmol/L one day after surgery. GFR (Cockroft – Gault) was 76.19 ± 17.16 ml/min before surgery, 58.17 ± 17.4 ml / min on the 1st day after surgery.

The types of surgical treatment are shown in Fig. 1.

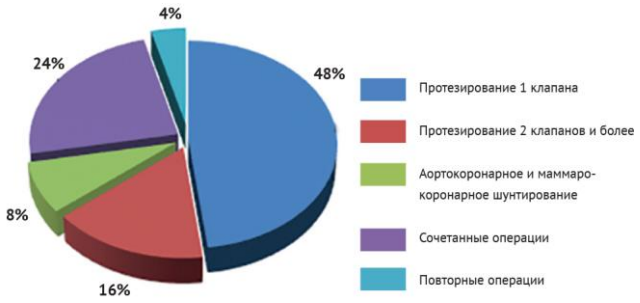

Fig. 1. Types of surgical treatment
1 valve prosthetics
Prosthetics of 2 or more valves
Coronary artery bypass grafting and mammary coronary artery bypass grafting
Combined operations
Repeated operations

Valve replacement was performed in 11 patients, aortic replacement in 2, valve and aortic replacement in 7, combined operations in 7 patients. Almost half of the patients underwent percutaneous coronary intervention (PCI) before surgery, followed by stenting (55.5%), coronary artery bypass grafting and mammary-coronary artery bypass grafting. (CABG / MCABG) in 8% of patients. The nature of the pathological impact on the heart valves was confirmed by morphological examination of the surgically obtained tissue material and is shown in Fig. 2.

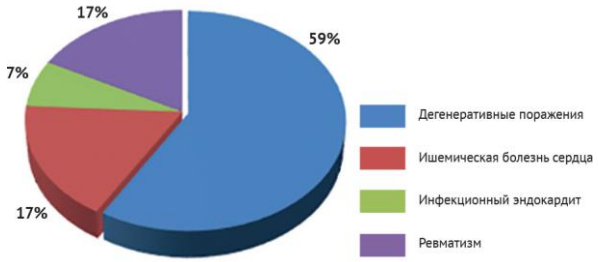

Fig. 2. The nature of valve damage
Degenerative lesions
Coronary heart disease
Infective endocarditis
Rheumatism

Morphological examination of biopsy material revealed predominant degenerative valve lesion (59%), rheumatic origin was noted in 17% and atherosclerotic origin was noted in other 17%, and infective endocarditis was identified in 7%.

In addition to the underlying disease - a heart defect, all patients had chronic diseases, which were registered in the clinical and anatomical diagnoses as the second underlying diseases, secondary or co-morbid ones (Table 1).

Table 1

Chronic diseases in operated patients

No.	The nature of the pathological process	Number of patients	
		n	%
1	Arterial hypertension	26	96.3
2	Atherosclerosis	26	96.3
3	Coronary heart disease	16	59.2
4	Type 2 diabetes mellitus	10	37.0
5	Primarily identified hyperglycemia	3	11.1
6	Chronic kidney diseases	11	40.7
7	Chronic lung diseases	16	59,2
8	Chronic diseases of the gastrointestinal tract	8	29,6
9	Obesity	3	11,1
10	Oncological diseases	4	14,8

According to clinical data, 92.6% of patients showed signs of ARI as early as on the next day after surgery, an increase in SC level in blood plasma by more than 25% and a decrease in GFR. On the next day after surgery, in most of the patients, the progression of ARF was observed, as a rule, which required the use of special treatments, including RRT.

Morphological examination of the kidneys revealed pathognomonic lesions both for acute lesions and for chronic pathological processes. When studying various structural elements of the kidneys, a mosaic pattern of changes was observed, as a rule. For example, against the background of widespread necronephrosis, it was almost always possible to find tubules with hydropic degeneration of nephrocytes as a result of the development of osmotic nephrosis during infusion therapy. Therefore, in the presence of both necrosis and dystrophic changes in nephrocytes, the pathological process was assessed by the significant predominance of certain changes. A histological examination of the kidneys in 26 non-survivals (96.3%) revealed lesions of the nephrocytes of the proximal tubules. The most severe damage in the form of nephrocyte necrosis was noted in 16 cases (59.3%), in 11 (40.7%) there were degenerative changes, of which in 4 cases (14.8%) these changes were insignificant. Dilation of tubules was noted in 15 cases (55.6%). In terms of scale, the nephrocyte necrosis was partial and total. In the partial variant, the apical sections were subjected to necrosis with subsequent sequestration (Fig. 3A). In the total variant, all nephrocytes were necrotic up to the basement membrane (Fig. 3C). In a 63-year-old patient with the kidney transplanted in 2012, ARI appeared on the 3rd day after surgery with progression and death on the 8th day. At the same time, no kidney transplant dysfunction was observed in this patient before surgery. Macroscopic examination of the transplanted kidney weighing 210 g revealed a pale and flabby cortex. Histological examination revealed widespread total necrosis of the tubular epithelium against the background of focal membranous glomerulitis and focal lymphocytic infiltrates in the stroma. The morphological pattern of the native kidneys corresponded to the secondarily wrinkled kidney with a total weight of 90 g. In 2 cases, in the patients suffering form the long-term DM who required RRT in the form of program hemodialysis, the hydropic dystrophy of nephrocytes was progressing into colliquation necrosis in a few preserved proximal tubules (Fig. 3C) ...

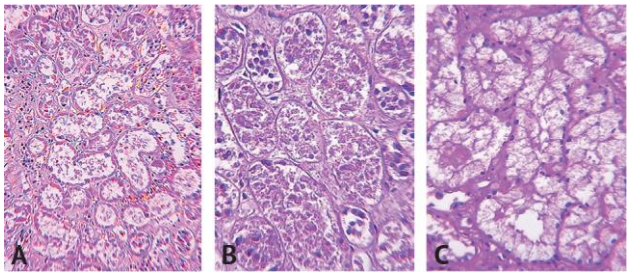

Fig. 3. Changes in the epithelium of the convoluted tubules: A — partial necrosis of the epithelium (x100 magnification); B — total necrosis of the epithelium (x200 magnification); C — hydropic dystrophy with progression to colliquation necrosis (x200 magnification). Hematoxylin and eosin staining

Almost all cases showed signs of circulatory disorders in the form of a sludge phenomenon, thrombosis of glomerular capillaries, and disseminated intravascular coagulation syndrome (DIC syndrome). Histological examination revealed a minor form of symmetric cortical necrosis with damage to all structural elements of the kidney and glomerular thrombosis (Fig. 4A). Acute impairments in the vascular bed were observed against the background of chronic pathological processes of various etiology (atherosclerosis, DM, AH, rheumatism, CKD, etc.). The most common were atherosclerotic vascular lesions and glomerulosclerosis of various types and scales. So, in glomerulosclerosis, the same deceased had its various forms of it: nodular, diffuse and mixed; in DM there were its pathognomonic signs the formation of lipo-hyaline cups and aneurysms of glomerular capillaries (Fig. 4 B, C).

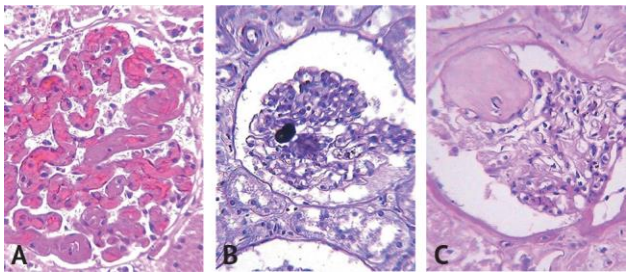

Fig. 4. Changes in the glomeruli: A — thrombosis of the glomerular capillaries in the syndrome of disseminated intravascular coagulation (x400 increase, staining with hematoxylin and eosin); B — nodes of glomerulosclerosis (x200 magnification, Schick test); C — aneurysmal peripheral capillary of the glomerulus (magnification x200, staining with hematoxylin and eosin)

After PCI, histological examination revealed RCA cylinders in the form of homogeneous and lumpy black masses of high density in the lumens of the loop tubules and distal nephrons.

After treatment of the sections with an ascorbic acid solution, the RCA cylinders discolored or became bluish-blue with the outlines of the developed crystal structures. In the area of RCA fixation in the lumens of the loop tubules, a complex of gross damage to both the epithelium and the basement membrane of the tubule itself was observed. In this case, the tubule itself was subjected to tubulorrhexis with the release of RCA fragments into the stroma (Fig. 5A). It is known that a ruptured tubule does not heal and creates conditions for urinary leakage, inflammation, and medullary fibrosis. In adjacent loop tubules with retention of RCA**,** the absence of epithelium and exposure of the basement membranes were noted (Fig. 5C). In these segments of the kidney, the lumens of the distal tubules were dilated and filled with desquamated epithelium, which formed cell casts with lumen obstruction (Fig. 5C).

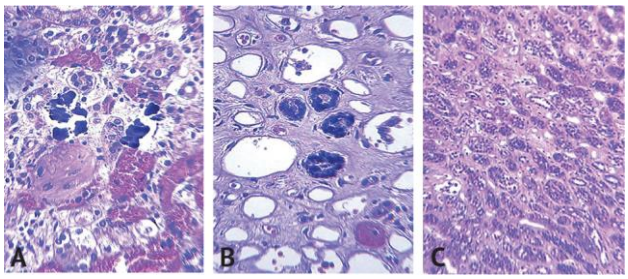

Fig. 5. Morphological changes in the kidney after percutaneous coronary intervention with a radiopaque contrast agent: A — rupture of the loop tubules with the release of the radiopaque agent into the stroma (x200 magnification); B — radiopaque agent — cylinders in the lumen of Henle's loop, absence and exposure of the tubular basement membrane (x200 magnification); C — cell cylinders in the lumen of the distal nephrons (x100 magnification). Hematoxylin and eosin staining

Thus, ARI-C in our studies had always a structural basis. Various elements of the nephron were subjected to acute injuries, as a rule, under the impact of several factors [4–6]. Thus, necrosis of the proximal tubule epithelium could result from ischemia during the surgery in combination with CPB, as well as from the direct toxic effect of iodine on the epithelium and a high osmotic pressure in the proximal tubules in diagnostic studies using RCA [4, 8]. Many unresolved questions remain, including the nature of kidney damage, in PCI with RCA. At the same time, the etiopathogenesis of contrast-induced nephropathy or contrast-induced ARI (CI-ARI) have been well developed. The main factors in the development of CI-ARI are: the toxicity of iodine itself, an increase in the osmolarity of the filtrate damaging the epithelium, the reperfusion and toxic effects of reactive oxygen species, high RCA viscosity, and a decrease in GFR with the expression of endogenous vasoconstrictor substances, a direct vasoconstrictor effect on vessels, and tubular obstruction [3, 4, 6, 9].

We should note that we have found no descriptions of renal morphology during PCI with RCA administration in available literature. There is an indication in the literature that RCA is not reabsorbed and is excreted by the

kidneys unchanged. Therefore, this process in the kidneys can be classified as excretory nephrosis, which morphological picture will reflect RCA transport through the nephron system.

Our studies have shown that RCA transport can be accompanied by gross kidney damage. This finding made it possible to formulate the main morphological criteria for CI-ARI: the presence of RCA fragments in the lumens of nephrons with RCA retention in the loop tubules with destruction, and in a number of cases, with irreversible damage - tubulorrhexis, trauma and desquamation of the epithelium of the loop tubules with the exposure of the basement membranes and the formation of cell casts in distal tubules by a tubular obstruction.

An essential role in ARI-CKP is played by the premorbid factor in the form of chronic diseases (DM, AH, CKD and others).

CONCLUSIONS

1. The structural basis of renal injury after cardiac surgery was tubuloepithelial damage in the form of dystrophic and necrotic abnormalities in nephrocytes, acute dyscirculatory disorders against the background of pre-existing chronic pathological processes in the kidneys with damage to the glomeruli, vessels and interstitium.

2.. Kidney injury caused by X-ray contrast agents are characterized by focal nature and typical damage, mainly to the loop and distal tubules, up to the irreversible injury of tubulorrhexis.

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Received on 05.05.2020

Review completed on 29.06.2020

Accepted on 30.06.2020