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EVALUATION OF THE DYNAMICS OF ANTIPLATELET THERAPY IMPACT ON HEART REMODELING IN PATIENTS UNDERGOING REGULAR HEMODIALYSIS

***[1]Madaminov G. G., [2]Sabirov M. A. and [2]Munavvarov B. A.**

[1]Republican Specialized Scientific-Practical Medical Center of Nephrology and Kidney Transplantation, Andijan Branch, Andijan, Republic of Uzbekistan.
[2]Tashkent State Dental Institute.
[3]Tashkent Republic of Uzbekistan.

***Corresponding Author: Madaminov G. G.**
Republican Specialized Scientific-Practical Medical Center of Nephrology and Kidney Transplantation, Andijan Branch, Andijan, Republic of Uzbekistan.

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SUMMARY

Purpose: the article examines the six-month dynamics of indicators of cardiorenal syndrome and cardiac remodeling disorders in 101 patients with end-stage chronic kidney disease receiving regular hemodialysis, as well as the importance of antiplatelet therapy for the prevention of cardiovascular diseases and other thromboembolic complications caused by these disorders. These findings are reflected in the results of our research.

KEYWORDS: Chronic kidney disease, antiplatelets, planned hemodialysis, echocardiography, systolic, diastolic, altrombosepin.

RELEVANCE

Early signs of heart failure in patients with chronic kidney disease (CKD) are initially not diagnosed or poorly evaluated. According to echocardiography (EchoCG) results, more than 50% of CKD patients have left ventricular hypertrophy and heart failure without clinical manifestations.[7,9] In addition, left ventricular hypertrophy is detected in more than 75% of patients with end-stage renal disease. Undoubtedly, renal failure, which includes multifactorial inflammation, neurohumoral, homeostatic, hematological, rheological, metabolic, and hemodynamic disturbances, affects the cardiovascular system (CVS). According to studies, heart failure is found in more than 40% of patients with chronic heart failure (CHF).[7,11] Moreover, as heart failure worsens, kidney function declines. At this time, disruption of the water-electrolyte balance creates a basis for the pathological process to become more pronounced.[7,10]

In recent years, the term "cardiorenal syndrome".[15] has been used for patients with combined heart and kidney failure. In most cases, chronic cardiorenal syndrome is caused by heart failure that develops against the background of various forms of ischemic heart disease (IHD).[8] Along with several factors, the renin-angiotensin-aldosterone system (RAAS) and its last component, aldosterone, play a leading role in its development.[2,4,14] According to some specialists, the action of aldosterone is associated with an increase in cardiac rhythm disorders, an increase in liver inflammation, fibrotic processes in the heart and kidneys.[2,17,20] The term "fibrosis" refers to an increase in the collagen fraction 2-3 times higher than normal or a predominance of its breakdown over its synthesis.[13,18]

That is why we deemed it necessary to assess the indicators of heart remodeling in patients undergoing programmed hemodialysis, and to conduct scientific research on studying the state of blood rheology using antiplatelet drugs, as well as the impact on heart remodeling during correction of hemostasis system disorders.

Purpose of the study. To study the indicators of heart remodeling in patients undergoing scheduled hemodialysis and evaluate the effects of antiplatelet therapy.

MATERIALS AND METHODS

101 patients with stage 5 chronic kidney disease (CKD), developed as a result of non-diabetic etiology nephropathy of various genesis, who were under observation at the Regional Scientific and Practical Center of Nephrology and Hemodialysis and received scheduled hemodialysis treatment at this institution, were examined. The CKD stage was diagnosed based on the recommendations of the National Kidney Foundation of the USA (NKF K/DOQI, 2002).

From an etiological point of view, the majority of patients (77) had chronic glomerulonephritis, and 23

patients had chronic pyelonephritis. The nosology of chronic pyelonephritis includes secondary pyelonephritis caused by kidney stone disease and polycystic kidney disease. In addition, the study did not include CKD that occurs against the background of peptic ulcer disease, secondary nephropathies against the background of diabetes mellitus and other endocrine diseases, kidney tumors, and hematological diseases associated with blood clotting. The age of the patients ranged from 19 to 60 years, with an average age of 39.3±1.63 years. The duration of their planned hemodialysis did not exceed 5 years, on average it was 3.8±1.7 years. The patients were randomly divided into two groups: the first group (n=50) and the second group (n=51). Only the patients in the second group were prescribed Althrombosepin 200 mg/day (2 capsules of 100 mg each).

"Altrombosepin" is a powder with anticoagulant and antiplatelet properties obtained from local raw material (Allium cepa L.) using a special technology. The drug "Altrombosepin" 100 mg is produced in the form of capsules by the joint venture of OJSC "Remedy Group" in Uzbekistan. It underwent clinical trials in 2016 and was registered for use in medicine as an antiplatelet agent for the prevention and treatment of ischemic vascular disease by the Main Department of Quality Control of Medicines and Medical Devices of the Ministry of Health of the Republic of Uzbekistan (certificates of July 22, 2016: "Altrombosepin" No. DV/M 00913/07/16; Capsules "Altrombosepin" No. DV/M 00914/07/16).

For chronic kidney diseases, the daily dose of the drug Altrombosepin with titration control was established at a level of 200 mg/day, taking into account the clear severity of the hypercoagulation process.

All patients underwent echocardiography at the beginning of the study and after 6 months. The examinations were carried out at the functional diagnostic departments of the Andijan Regional Medical Center and the Clinic of the Andijan State Medical Institute. Echocardiography was performed using the traditional Simpson's method with a 3.5 MHz transducer on the SONOSCAPE S20 ultrasound machine. The following parameters were measured: left ventricular end-diastolic volume (LVEDV, ml), left ventricular end-systolic volume (LVESV, ml), left ventricular end-diastolic dimension (LVEDD, mm), left ventricular end-systolic dimension (LVESD, mm), interventricular septal thickness (IVST, mm), left ventricular mass (LVM, grams), left ventricular mass index (LVMI, g/m2), stroke volume (SV, ml), and left ventricular ejection fraction (LVEF, %). Stroke volume was calculated as LVEDV minus LVESV, and LVEF was calculated as (SV/LVEDV) x 100%. LVMI (g/m2) was calculated by dividing LVM by body surface area, using the formula by R. Devereux: LVM - 0.8 x [[1.04 x [(LVEDD + IVST + LVESD)3 - LVESD3] + 0.6]]. The obtained results were subjected to statistical analysis.

RESULTS AND THEIR DISCUSSIONS

During the six-month study, the following results were observed in the comparison groups: at the beginning of treatment in patients in the first group, the left ventricular end-diastolic volume (LVEDV) was 151.7±3.4 ml, and after 6 months of treatment, it increased to 160.1±2.64 ml. A significant increase in results compared to the control group was noted (R<0.001), and a less significant increase compared to the beginning of the study was observed (R<0.05). In the second group, at the beginning of treatment, LVEDV was 151.5±2.94 ml, and after 6 months, it increased to 154.1±3.01 ml. The results showed a significant (R<0.001) increase compared to the control group and an insignificant change compared to the beginning of the study.

In patients of the 1st group, the left ventricle end-systolic volume (LVESV) at the beginning of treatment was 69.8±1.69 ml, and after 6 months of treatment it increased to 79.4±1.27 ml. The results significantly increased (R<0.001) compared to the control group and significantly increased (R<0.001) compared to the initial level. In the 2nd group, the LVESV at the beginning of treatment was 69.1±1.65 ml, and after 6 months it increased to 73.6±1.59 ml. The results significantly increased (R<0.001) compared to the control group and changed less significantly (R<0.05) compared to the beginning of the study (Table 1).

Table 1: Dynamic of EchoCG on the background of antiplatelet therapy in patients receiving planned hemodialysis sessions.

Indicators	Control group (n-20)	1-group (n-50)		2-group + Altrombosepin (n-51)	
		At the start of treatment	in 6 months	At the start of treatment	in 6 months
EDVLV (End-diastolic volume of the left ventricle)	122.3±3.1	151.7±3.4***	160.1±2.64***^	151.5±2.94***	154.1±3.01***
ESVLV (End-systolic volume of the left ventricle)	47.7±1.1	69.8±1.69***	79.4±1.27***^^^	69.1±1.65***	73.6±1.59***^
EDSLV (End-diastolic size of the left ventricle)	31.5±0.7	41.7±0.51***	43.6±0.48***^^	41.9±0.51***	42.7±0.53***^

ESSLV (End-systolic size of the left ventricle)	45.7±1.2	57.8±0.65***	61.0±0.60***^^^	58.1±0.64***	58.8±0.69***
TPWLV (Thickness of the posterior wall of the left ventricle)	9.5±0.9	12.4±0.30**	13.5±0.23***^^	11.9±0.33**	12.5±0.26**^
LVMM (Left ventricular myocardial mass)	178.6±3.13	269.3±3.31***	286.2±3.30***^^^	267.6±3.27***	271.8±4.06***
LVMI (Left ventricular mass index)	109.1±1.2	159.2±1.73***	168.7±2.03***^^^	158.9±1.67***	161.8±1.97***^
SV (Stroke volume)	74.6±1.8	81.9±1.84***	80.7±1.68**	82.4±1.79***	80.8±1.82**
LVEF (Left ventricular ejection fraction)	60.4±1.37	53.9±0.84***	49.8±0.85***^^^	54.1±0.84***	52.2±0.76***

Note: * - differences are significant compared to the control group (*- p<0.05, **- p<0.01, ***- p<0.001); ^ - differences are significant compared to the values before treatment (^ - p<0.05, ^^ - p<0.01, ^^^ - p<0.001).

Left ventricular end-systolic dimension (LVESD), which is one of the parameters determining the volumetric dimensions of the heart in echocardiography, was 41.7±0.51 mm in the 1st group at the beginning of treatment and increased to 43.6±0.48 mm after 6 months of treatment. The results showed a significant (R<0.001) increase compared to the control group and a significant (R<0.01) increase compared to the baseline level. In patients of the 2nd group, LVESD was 41.9±0.51 mm at the beginning of treatment and increased to 42.7±0.53 mm after 6 months of treatment. A significant increase (R<0.001) in results compared to the control group was observed, as well as a less significant change (R<0.05) compared to the beginning of the study. At the beginning of the study, left ventricular end-diastolic dimension (LVEDD) was 57.8±0.65 mm in the 1st group and increased to 61.0±0.60 mm after 6 months of treatment. The results showed a significant (R<0.001) increase compared to the control group and a significant (R<0.001) increase compared to the baseline level. In the 2nd group, LVEDD was 58.1±0.64 mm at the beginning of treatment and increased to 58.8±0.69 mm after 6 months of treatment. It was noted that the results significantly increased (R<0.001) compared to the control group and were not significant compared to the beginning of the study. Note: * - significant differences compared to the control group (*- R<0.05, **- R<0.01, ***- R<0.001); ^ - significant differences compared to values before treatment (^ - R<0.05, ^^ - R<0.01, ^^^ - R<0.001).

In patients of the 1st group, the thickness of the interventricular septum (IVS) at the beginning of treatment was 12.4±0.30 mm, and after 6 months, thickening to 13.5±0.23 mm was observed. The results showed a significant (R<0.001) increase compared to the control group and a significant (R<0.01) thickening compared to the initial level. In patients of the 2nd group, the IVS thickness at the beginning of treatment was 11.9±0.33 mm, and after 6 months, this indicator was thickened to 12.5±0.26 mm. The values were evaluated as significantly (R<0.01) increased compared to the control group and less significantly (R<0.05) changed compared to the beginning of the study.

In the beginning of treatment, the left ventricular myocardial mass index (LVMI) in patients of the 1st group measured by EchoCG was 269.3±3.31 g, and after 6 months, it increased to 286.2±3.30 g. The results showed a significant increase (R<0.001) compared to the control group and a significant increase (R<0.001) compared to the initial level. In patients of the 2nd group, LVMI at the beginning of treatment was 267.6±3.27 g, and after 6 months, it increased to 271.8±4.06 g. Compared to the control group, LVMI significantly increased (R<0.001), and it was noted that this indicator did not change significantly compared to the start of the study.

In the 1st group of patients, the LVM index at the beginning of treatment was 159.2±1.73 g/m2, and after 6 months of treatment, it increased to 168.7±2.03 g/m2. The results showed a significant (R<0.001) increase compared to the control group and a significant (R<0.001) increase compared to the baseline level. In the 2nd group of patients, the LVM index at the beginning of treatment was 158.9±1.67 g/m2, and after 6 months, it increased to 161.8±1.97 g/m2. The LVM index values significantly (R<0.001) increased compared to the control group, and we observed a less significant (R<0.05) change in this indicator compared to the baseline level.

The stroke volume (SV), which is directly related to cardiac activity, on echocardiography in patients of the 1st group at the beginning of treatment was 81.9 ± 1.84 ml, and after 6 months of treatment, it decreased to 80.7 ± 1.68 ml. The results showed a significant (R<0.001)

increase compared to the control group and an insignificant change compared to the beginning of treatment. In patients of the 2nd group, SV at the beginning of treatment was 82.4 ± 1.79 ml, and after 6 months of treatment, it was observed that it decreased to 80.8 ± 1.82 ml. It was noted that left ventricular ejection fraction (LVEF) did not significantly change compared to the control group or compared to the beginning of the study.

In patients of the 1st group, the LVEF at the beginning of treatment was 53.9±0.84%, and after 6 months of treatment, a significant decrease to 49.8±0.85% was observed. The results showed a significant (R<0.001) decrease compared to the control group and a significant (R<0.001) improvement in heart function compared to the beginning of treatment. In patients of the 2nd group, the LVEF at the beginning of treatment was 54.1±0.84%, and after 6 months it decreased to 52.2±0.76%. We observed that LVEF showed significant (R<0.001) changes compared to the control group and insignificant decrease compared to the beginning of the study.

Now let's compare the values of the echocardiographic parameters in both groups. Looking at the diagram, it was noted that the parameters of LVEDV and LVESV significantly (R<0.001) increased in both groups of patients at the beginning of treatment and after 6 months compared to the control group. However, compared to the beginning of treatment, after 6 months in the first group, the values were less significant and significant (R<0.001), indicating that negative remodeling of the heart continued, while in patients in the second group receiving alteplase, there was an insignificant shift of these negative changes compared to the beginning of the study. We interpret these processes as the antiplatelet effect of alteplase (Figure 1).

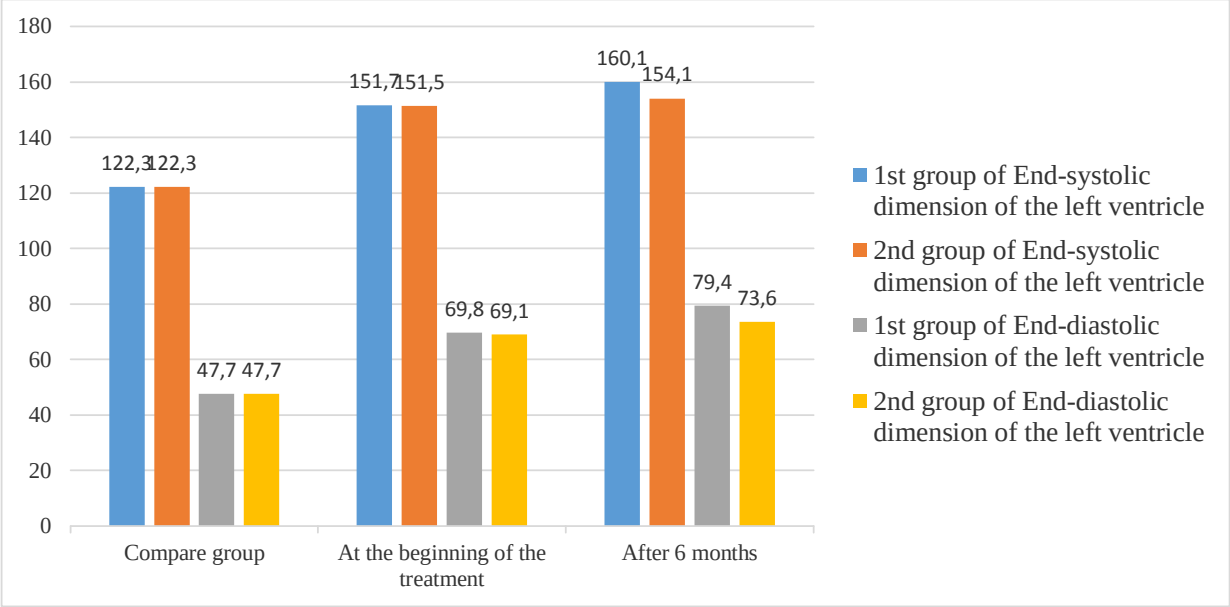

Fig. 1: Comparative dynamics of indicators of end-diastolic volume of the left ventricle and end-systolic volume of the left ventricle against the background of antiplatelet therapy.

On the echocardiogram, the parameters of left ventricular end-diastolic and end-systolic volumes, which determine the volumetric dimensions of the heart, showed a peculiar pattern on the diagram. According to it, there was a significant increase in the indicators (R<0.001) in both groups of patients compared to the control group at the beginning of treatment and after 6 months. However, after 6 months, compared to the beginning of treatment, the values in the 1st group significantly increased (R<0.001) and indicated the continuation of heart remodeling, while in patients of the 2nd group who received alteplase, the value of end-systolic volume was less significant (R<0.05) than at the beginning of the study, and the end-diastolic volume showed an incredible increase in value. Therefore, due to the action of antiplatelet agents on improving blood circulation in the myocardium, we can prevent further deterioration of heart remodeling (Figure 2).

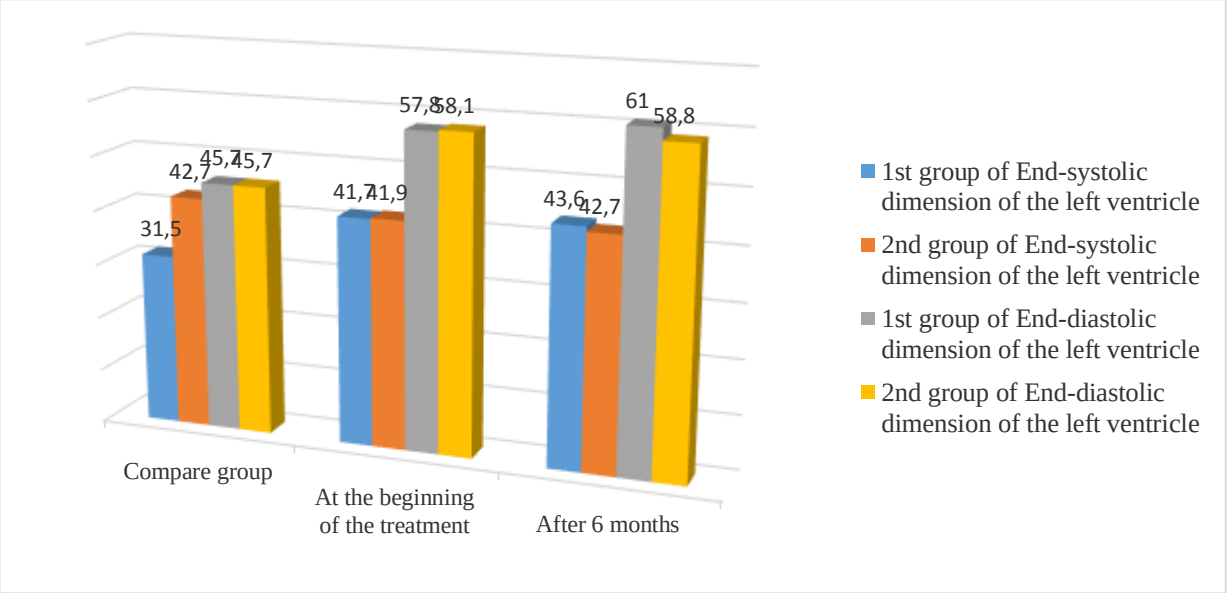

Fig. 2: Comparative dynamics of LVEDD and LVESD indices against antiplatelet therapy.

In the echocardiogram, the left ventricular mass (LVM) and indexed left ventricular mass (ILVM), which are parameters determining the weight dimensions of the heart, showed the following picture on the diagram. In both groups, these indicators significantly increased (R<0.001) compared to the control group at the beginning of the treatment and after 6 months, and in the first group, which did not receive antiplatelet therapy, these values significantly increased (R<0.001) compared to the start of the study. However, in patients of the second group, who regularly received alteplase, there was a relatively unreliable change in the LVM indicator. There was a less reliable change in the ILVM value (R<0.05) compared to the start of the study. Thus, it was shown that antiplatelet therapy also slows down the increase in myocardial mass and index values. (Fig. 3)

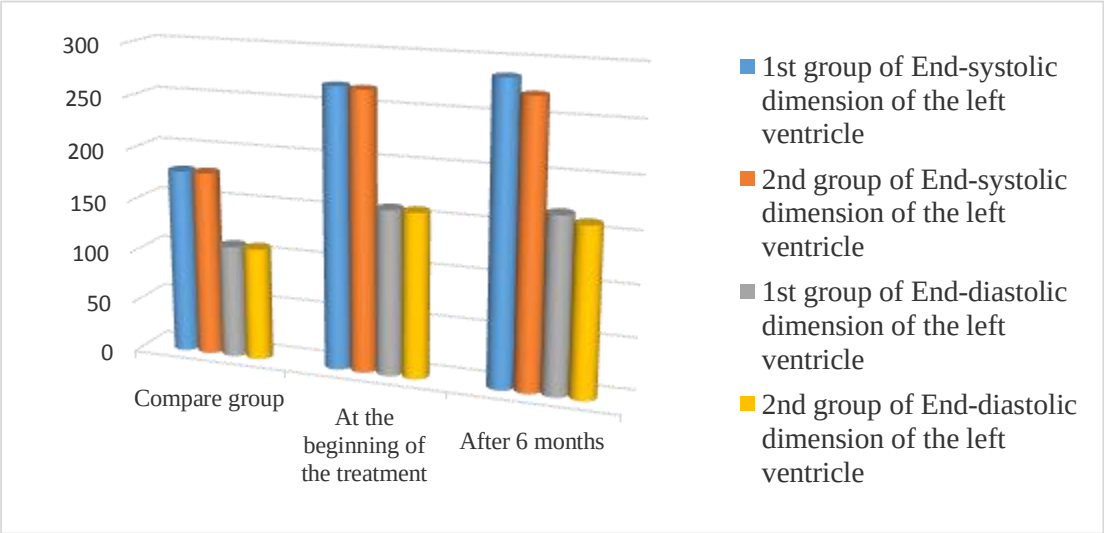

Fig. 3: Comparative dynamics of IVS and LVM indexes during antiplatelet therapy.

The table of indicators for assessing cardiac activity in the EchoCG showed the following picture. According to the results, the CO significantly increased (R <0.001) in both groups compared to the control group, and it was noted that the CO did not significantly change in both groups compared to the beginning of treatment and the beginning of the study.

A significant (R <0.001) decrease in LVESV compared to the control group was observed in both groups, while a significant (R <0.001) decrease in cardiac function was observed in the first group compared to the beginning of treatment. A decrease in LVESV with unreliable values was noted in patients in the second group who received antiplatelet therapy with abciximab.

Thus, inhibition of platelet aggregation occurs from the first days of using althrombosepin in patients undergoing regular hemodialysis. This improves the rheology of blood and the coordination of hemostasis system disorders, as well as prevents thromboembolic complications. This slows down the progression of chronic cardiorenal syndrome and relatively reduces the risk of death from end-stage renal disease (ESRD). Additionally, the progressive deterioration of the functional state of the heart activates the sympathetic-adrenal system and, as a result, leads to an increase in the renin-angiotensin-aldosterone system.[1,6,21] As a result, sodium, and water retention increase, leading to glomerular hypertension and damage. This reduces the effectiveness of detoxification treatment and increases the preload of the left heart chambers due to the increase in central venous pressure.[3,5] Currently, the accumulation of angiotensin II in association with the stimulation of angiotensin receptors leads to vasoconstriction and arteriolar hypertrophy, that is, to an increase in the cardiac afterload of the left ventricle.[16,19,22]

Therefore, by administering antiplatelet therapy to scheduled hemodialysis patients, it is possible to at least partially interrupt this pathological chain, minimize the consequences of cardiorenal syndrome, and relatively reduce the risk of death caused by it.

CONCLUSIONS

1. During hemodialysis procedures, sharp hemodynamic changes and heart remodeling occur in the body due to cardiorenal syndrome.
2. Antithrombotic therapy is necessary for patients undergoing regular hemodialysis to coordinate cardiorenal syndrome, slow cardiac remodeling, and prevent cardiovascular complications.
3. Regular use of antithrombotic agents in patients undergoing regular hemodialysis prevents activation of the coagulation cascade in the blood, resulting in slowing of cardiac remodeling and coordination of the cardio-renal syndrome.
4. Regular use of Alteplase as antithrombotic therapy in patients undergoing regular hemodialysis prevents exacerbation of heart remodeling and, as a result, relatively reduces the risk of death from heart failure.

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