Mazurenko O. P., Tarabrin O. A. Acute renal failure in patients with implanted LVAD in the early postoperative period. Journal of Education, Health and Sport. 2023;47(1): 155-164. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2023.47.01.014
https://apcz.umk.pl/JEHS/article/view/47494
https://zenodo.org/record/10406577

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 17.07.2023 No. 32318.
Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).
Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 17.07.2023 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159.
Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

Received: 29.07.2023. Revised:21.08.2023. Accepted: 28.08.2023. Published: 29.08.2023.

UDC: 616.12–008.46:616.132–089.843–77–089–06–005.6/.7–084–039.72–089.5

Acute renal failure in patients with implanted LVAD in the early postoperative period

O. P. Mazurenko[1,2], O. A. Tarabrin[3]

[1]P. L. Shupyk National University of Health Care, Department of Anesthesiology and Intensive Care, Kyiv, Ukraine;
[2]Silesian Centre Heart Diseases, Department Cardiac anesthesiology SUM, ICU SCCS. Poland);
[3]International Humanitarian University, Department of Anesthesiology, Intensive Care and Emergency Medicine. Odesa, Ukraine

Abstract

AKI is one of the major complications in the cardiac surgery group of patients in the world. In patients with LVAD in the short postoperative period, the situation with such a complication as AKI is associated with the state of hemodynamics and fluctuations in the parameters of the hemostasis system.

The purpose of this scientific work is to analyze the state of the blood coagulation system and its response to therapy and complications in the early postoperative period in fifty patients with implanted devices for mechanical support of the left ventricle, left ventricle assist device, LVAD, in the Silesian Heart Disease, Poland. Patients were divided into two groups, a control group receiving classical anticoagulation targeted therapy (ATT), which included the most controlled monotherapy with heparin, after reaching the target values of

APTT, the addition and transition to monotherapy with warfarin until reaching the target INR and ASA, and the main, research group, who received an alternative ATT consisting of the previous one with the addition of P2Y12-receptor blockers and Xa-factors.

The results showed that the control group of patients with classical anticoagulant targeted therapy had greater mortality associated with AKI than the patients of the study group, and it was also demonstrated that the initially longer duration of surgery and intraoperative polyuria gave a greater percentage of AKI in the postoperative period.

The work was carried out within the framework of a bilateral agreement on scientific cooperation between the Department of Anesthesiology & Intensive Care at the National Medical Academy of Post-Graduate Education Named After P.L. Shupyk and the Silesian Center for Heart Diseases (Poland). This article is part of the analysis of the work on the analysis of the blood coagulation system in patients after implantation of the left ventricular mechanical circulatory support system with the analysis of such postoperative complication as acute kidney failure.

Keywords: left ventricle assist device (LVAD); anticoagulant targeted therapy (ATT); renal complications.

Introduction: The use of a device for mechanical support of the left ventricle, LVAD, as the only chance for patients with severe degrees of heart failure to live to heart transplantation on the waiting list, is recommended by the American and European Associations of Cardiology and Cardiac Surgery. The main complications after LVAD implantation include bleeding, thrombosis of the device, ischemic and hemorrhagic strokes, acute kidney damage, multiple organ failure, infections, etc. The timing of kidney complications after LVAD placement is classified as early (up to 30 days after implantation) or late (after 30 days until 3 years) [1-5]. Carrying out optimal therapy aimed at correcting the hemostasis system in such patients is an important component of intensive therapy, especially in the early postoperative period. This work analyzed the frequency of early adverse non-surgical events and complications in the postoperative period within 14 days after implantation of a left ventricular mechanical support device in fifty patients treated at SCCS over three years from 2016 to 2018, inclusive, aged 55± 13.5 years old, with a body mass index of 30.8±8.3 m2, with a left ventricular ejection fraction of 8–28%. Comparison of the analyzed survey results refers to qualitative and quantitative assessments of adverse events and complications in patients with different approaches to anticoagulation-targeted therapy.

Materials and methods. The study included 50 patients with various degrees of heart failure, all of whom had a device for mechanical support of the left ventricle of the heart installed, either planned or emergency. The average age of the patients was 52.8±1.7 years, with a predominance of patients older than 50 years (asymmetric type of distribution). The youngest patient was 19 years old, the oldest was 69 years old, Me=56.0 (1q: 47.0 3q: 62.0). The studied sample was characterized by a negative value of the asymmetry coefficient (As=-1.0 σAs=±0.3), the kurtosis coefficient had a positive value (k=0.4 σk=±0.6), the average BMI values were at the level of 26,1±0.9 kg/m2 (Me=25.0 (1q=21.7; 3q=30.7). Patients were divided into two groups (Table 1), the control group and the main study group. In the control group (21 patients), patients received monotherapy with heparin or warfarin or in combination with aspirin, due to the impossibility of switching to another stage of anticoagulant therapy. In the study group (29 patients), after controlled anticoagulant therapy with heparin, patients received warfarin up to a target value of 2.5 IU and then additionally received a blocker of blood coagulation Xa-factor and blockers of P2Y12 receptors. All patients were equally subjected to all possible analyses of the blood coagulation system after taking the medication.

In the control group of the study, 8 patients received heparin therapy in the first two weeks by continuous admission by the infusion pump with a rate from 6 to 11 Units/kg/h. (Me-9.05 Units/kg/hour), and 2 patients were on monotherapy with heparin until the end of their stay in the intensive care unit. Eleven patients during the first week and 7 patients during the second week received warfarin indirect anticoagulant in a dose of 1.5-7 mg/day (Me-3.45 mg/day).

As an alternative to the standard ATT, the following drugs were used: 5 patients received aspirin in doses of 1.4±0.7 mg/kg/day during the entire period; 3 patients during the first week and 5 patients during the second week received clopidogrel 1.3±0.8 mg/kg/day; nadroparin calcium (0.3-0.6 ml/ 2 times a day) and fondaparinux Na (2.5-5 mg/ 2 times a day).

The somatic condition of the patients corresponded to 6-14 points of the European System for assessing the risk of preoperative interventions, or 4-5\E. ASA. Depending on the status according to INTERMACS [6], Level 1 (cardiogenic shock) was observed in 15 patients, Level 2 (progressive circulatory failure) – in 6 patients, Level 3 – in 17 patients, Level 4 – in 10 patients, Level 5 – in 2 patients. Severe pretransplantation pulmonary hypertension (transpulmonary gradient ≥15 mmHg and/or pulmonary vascular resistance greater than 3 Wood Units) was detected in 8 patients. Fifteen patients were operated on in a

state of circulatory arrest with cardiopulmonary resuscitation, and ventricular fibrillation was noted in five patients.

The decision for renal replacement therapy was given are increase creatinine urinary acid and decrease GFR following KDIGO – Kidney Diseases Improving Global Output for patients with acute kidney injury [13].

Results. During the early postoperative period, in patients with different approaches to anticoagulant therapy, a rather diverse pattern of response to the therapy and, as a consequence, adverse events and complications were observed. The results showed that the control group of patients with classical anticoagulant therapy had greater mortality associated with AKI than the patients of the study group, and it was also demonstrated that the initially longer duration of surgery and intraoperative polyuria gave a greater percentage of AKI in the postoperative period.

The existing differences in the distribution of hemostasis indicators in the comparison groups are of considerable interest (Table 1). As can be seen from the above, normalization of the hemostasiogram was observed in both the control and main research groups, which was more pronounced in the main group.

The duration of surgical intervention in the main group did not differ significantly from the control group - 347.8±17.9 min and 459.3±57.4 min, respectively ($p>0.05$). During surgery, diuresis was higher in the control group (on average, 940.0±186.5 ml) than in the main group (704.5±82.5 ml). One of the patients in the control group received only warfarin as anticoagulant therapy, and he had the lowest levels of diuresis (200 ml) due to decompensation of chronic kidney injury. This patient later died.

Hemotransfusion was performed in 16 out of 29 patients of the main group (55.2%) in an average volume of 693.3±141.5 ml. ($p>0.05$). In the control group, Hemotransfusion was performed in 18 out of 21 patients (85.7%), with an average volume of 1140.0±222.0 ml ($p<0.05$). Thus, already at the intraoperative stage, the use of a polymodal scheme of anticoagulant therapy demonstrated certain advantages.

The volume of intraoperative infusion in the groups also differed. Thus, the patients of the main group received an average of 811.6±114.7 ml of crystalloids, and the control group - 656.5±87.1 ml. The existing differences are explained by the clinical situation, when censoring the sample with the removal of excesses, they are completely leveled - 760.6±85.8 ml versus 656.5±87.1 ml ($p>0.05$).

For an extended qualitative analysis of groups of patients, the analyzed data of intraoperative monitoring of patients are given in table No. 3, and in the ICU in table No. 3,

which makes clear the relationship of certain indicators to the postoperative state in the early postoperative period.

Table 1 - Comparison of groups of 50 patients with LVAD according to intraoperative management (N= 50)

Laboratory and other indicators of the intraoperative period	The control group of patients (n=21)			The examined group of patients (n=29)		
	n=6	n=1	n=14	n=6	n=20	n=3
Diuresis during the operation, ml	1160± 728,72	250	1312± 513,26	520± 396,6	652± 340,4	600± 355,5
Operation duration, minutes	468,33± 302,22	315	383,21± 123,78	311,66± 67,59	325± 80,86	260± 88,88

Data calculated in groups are statistically significant ($p<0.05$).

The analysis of the daily fluid balance showed that during the stay in the ICU, there was a decrease in the average daily balance from 9-11 ml/kg/day to 3-5 ml/kg/day. There is also an increase in the frequency of renal complications and the level of mortality in patients in whom the support of intra-aortic balloon counter pulsation (IABP) and extracorporeal membrane oxygenation (ECMO) was longer than the first two days of postoperative stay in the ICU (correlation +0.76, $p<0,05$).

The data after correction are statistically significantly different from the original ones, $p<0.05$.

As the study showed, in the first days of heparin therapy, one patient developed pronounced heparin-induced thrombocytopenia, which led to a change of strategy to alternative therapy with the use of calcium nadroparin. Subsequently, this patient had the case of extracorporeal renal replacement therapy in response to platelet conglomeration, which was evident only on a manual microscopic examination of the patient's blood morphology.

As shown in Table 2, 100% of patients who received heparin monotherapy developed acute renal failure in the postoperative period, which required the use of renal replacement therapy. In 2% of patients with heparin monotherapy, the postoperative period was complicated by the development of hemorrhagic stroke, liver failure, and aortic and right ventricular failure. As the study demonstrated, preliminary intraoperative data of a long duration of surgery affected the patient's renal complication, such as acute renal failure, which was not previously diagnosed. In total, in the control group of classical targeted anticoagulant therapy, the need for the use of extracorporeal support required 50% more patients than in the study during the entire short postoperative period. The percentage difference between the

need for hemodialysis and hemodiafiltration was not significant and depended more on the intensity of the increase in the symptoms of AKI.

Table 2 - Characteristics of complications in LVAD patients with different types of ACCT.

ACTT / Complication	*Heparin*	*Warfarin*	*Heparin+ Warfarin+ ASA*	*H/V/A+ P2Y12-bl.*	*H/V/A + anti-Xa.*	*H/V/A + P2Y12+ anti-Xa.*
Quantity of patients	12%	2%	28%	12%	40%	12%
AKI with CRRT:	10%	2%	4%	-	4%	0
HD-	2%	-	4%	-	4%	4%
HDF-						

The data are statistically significantly different from the original, $p<0.05$.

As shown in Table 3, timely acute renal replacement therapy (CRRT) in a short period helps to restore kidney function and further limit the manifestations of renal dysfunction.

Table 3 - Kidney function failures and disorders and CRRT in patients with LVAD

Indications \ Kind of CRRT	Hemodialysis	Hemodiafiltration
Duration of CRRT, day	2	10
Median of Creatinine in start\end of therapy CRRT, mmol/l.	294±24 /95±62	384 /100
Median of GFR in start\end of therapy CRRT, mmol/l. (ml/min1.72m²)	19±42 /56,2±12	18,2 />60
Median of 24-hour diuresis in start\end of therapy CRRT, ml.	346±640 /2516±1430	510 /3800
Median velocity of blood filtration in CRRT, ml\h.	105,1± 10,3	139
The quantity of CRRT-seat was useless during therapy	2,8 set/period	2,1 set/period
Quantity of CRRT-seat thrombosis during CRRT therapy	2	0

The data are statistically significantly different from the original, $p<0.05$.

According to the obtained data, in all patients, the level of creatinine in the blood decreased in comparison with the previous values, also, against the background of renal replacement therapy, an increase in the rate of glomerular filtration was noted. Continuous

renal replacement therapy was had by 43% of patients from the control group and 10% from the main research group.

Table 3 clearly demonstrates that in acute renal failure in patients using HDF, in contrast to HD, qualitatively fewer sets were used during the therapy period, the median recovery of diuresis was significantly higher and the number of thrombosis sets was also lower.

Discussion. As for the activity of the coagulation system according to ACT, it showed significant variability in both clinical groups. So, in the main group, the test corresponded to an average value of 123.8±3.7 units, and in the control group - 132.9±15.0 units. ($p>0.05$).

A similar situation was observed concerning the final creatinine level in the observation groups. So, in the main group, the creatinine content exceeded 2.7 ± 0.9, and in the control group, it reached 1.6 ± 1.5 units. ($p > 0.05$), which may be due to a higher percentage of AKI. The risk of death in the control group was 3.5 times higher than in the main group ($p < 0.05$).

After use in acute renal failure, renal replacement therapy in the main group compared to the control group was parametrically better, which requires explanation, although the discrepancy between the increase in the indicator after correction of anticoagulant therapy was more pronounced in the main group (Δ = + 140% versus + 58%).

Also, the analysis of this group of patients with daily fluid balance showed that during the stay in intensive care, there was a decrease in the average daily balance from 9-11 ml/kg/day to 3-5 ml/kg/day. There is also an increase in the incidence of renal complications and mortality rate in patients whose IABP and ECMO support was more intensive during the first two days of postoperative ICU stay (Δ = + 105% versus + 19%). Further analysis showed that, depending on the applied anesthetic support, the duration of the surgical intervention, the volume of blood transfusion, and postoperative renal complications of various structures are recorded in patients. Similar factors caused postoperative mortality. When looking for the most significant predictors, survival was defined as activated clotting time and lactate levels at the end of surgery.

The development of acute and chronic renal failure is quite common in patients with heart failure, especially in patients with implanted left ventricular mechanical support systems. INTERMACS reported that 876 of 7,286 (12%) LVAD-implanted patients developed acute renal failure requiring dialysis or hemofiltration. Also, in these patients, an increase in the concentration of creatinine in the serum more than 3 times compared to the

initial level or an increase in the concentration of creatinine above 5 mg/dL for more than 48 hours was noted [14]. There are also observational data describing the short-term effects of LVAD implantation on renal function, but insufficient data on long-term renal function outcomes. For example, a retrospective study of 220 patients showed [15] that in patients whose creatinine clearance improved by more than 50 ml/min. after LVAD implantation, the 30-day survival rate was 84%, while patients with lower creatinine levels had a 30-day survival rate of 66%. In our study, it was shown that the level of creatinine in the blood decreased in all patients compared to the previous values before the implantation of LVAD systems. During renal replacement therapy for patients who needed it, an increase in the rate of glomerular filtration and an improvement in central hemodynamics were noted, which was combined with a reduction in the doses of drugs used for adrenomimetic correction.

Conclusions:

1. The highest percentage of acute renal complications, in the form of bleeding and thromboembolic events, was observed in the control group of patients who received monotherapy with heparin or warfarin or their combination and correlated with right ventricular failure in 20% of cases and an increase in the diameter of the portal vein, which, when using modified ACTT, allowed reduce this indicator by 50%.

2. The study demonstrated that in acute renal failure in patients using HDF, in contrast to HD, qualitatively fewer sets were used during the therapy period, the median recovery of diuresis was significantly higher and the number of thrombosis sets was also lower.

3. Acute renal failure develops in patients with implanted LVADs in 40% of cases and requires GNST due to thrombosis of the proximal part of the tubules of the kidneys and a decrease in the perfusion pressure on the laminar blood flow of the mechanical circulatory support device. The use of an alternative ACCT scheme developed by us allows for reducing the frequency of development of this complication by 90%.

4. Regardless of the applied monitoring methods, the possibility of prediction of coagulation drive and serious complications related to blood coagulation function seems doubtful. There are advantages to multimodal anticoagulation therapy regimens, which require full monitoring of the main parameters of the coagulogram as often as possible.

References

1. Wever-Pinzon O, Drakos SG, Kfoury AG et al. Morbidity and mortality in heart transplant candidates supported with mechanical circulatory support: is reappraisal of the current Circulation. 2013 Jan 29;127(4) pp:452-62.

1. Akhter SA, Badami A, Murray M, et al. Hospital Readmissions After Continuous-Flow Left Ventricular Assist Device Implantation: Incidence, Causes, and Cost Analysis. Ann Thorac Surg. 2015 Sep;100(3) pp:884-9.

2. Slaughter MS, Pagani FD, McGee EC, et al. HeartWare Bridge to Transplant ADVANCE Trial Investigators. HeartWare ventricular assist system for bridge to transplant: combined results of the bridge to transplant and continued access protocol trial. J Heart Lung Transplant. 2013 Jul;32(7) pp:675-83.

3. Stulak JM, Davis ME, Haglund N, et al. Adverse events in contemporary continuous-flow left ventricular assist devices: A multi-institutional comparison shows significant differences. J Thorac Cardiovasc Surg. 2016 Jan;151(1) pp:177-89.

4. Harvey L, Holley C, Roy SS, et al. Stroke After Left Ventricular Assist Device Implantation: Outcomes in the Continuous-Flow Era. Ann Thorac Surg. 2015;100(2) pp:535-41.

5. Morgan JA, Brewer RJ, Nemeh HW, et al. Stroke while on long-term left ventricular assist device support: incidence, outcome, and predictors. ASAIO J. 2014 May-Jun;60(3) pp:284-9.

6. Xia Y, Stern D, Friedmann P, Goldstein D. Preoperative atrial fibrillation may not increase thromboembolic events in left ventricular assist device recipients on midterm follow-up. J Heart Lung Transplant. 2016;35(7) pp:906-12.

7. Najjar SS, Slaughter MS, Pagani FD, et al. HVAD Bridge to Transplant ADVANCE Trial Investigators. An analysis of pump thrombus events in patients in the HeartWare ADVANCE bridge to transplant and continued access protocol trial. J Heart Lung Transplant. 2014 Jan;33(1) pp:23-34.

8. Uriel N, Morrison KA, Garan AR, et al. Development of a novel echocardiography ramp test for speed optimization and diagnosis of device thrombosis in continuous-flow left ventricular assist devices: the Columbia ramp study. J Am Coll Cardiol. 2012 Oct 30; 60 (18) pp:1764-75.

9. Maltais S, Kilic A, Nathan S, et al. Prevention of HeartMate II Pump Thrombosis Through Clinical Management (PREVENT). J Heart Lung Transplant. 2016;35(4) pp:S161-S162.

10. Starling RC, Moazami N, Silvestry SC et al. Unexpected abrupt increase in left ventricular assist device thrombosis. N Engl J Med. 2014;370(1) pp:33-40.

11. Topkara VK, Kondareddy S, Malik F, et al. Infectious complications in patients with left ventricular assist device: etiology and outcomes in the continuous-flow era. Ann Thorac Surg. 2010 Oct;90(4) pp:1270-7.

12. https://kdigo.org/

13. Daniel W. Ross,1 Gerin R., et al. Left Ventricular Assist Devices and the Kidney. Clin J Am Soc Nephrol 13, 2018 pp: 348–355.

14. Bethany Roehm, Amanda R. Vest, and Daniel E. Weiner. Left Ventricular Assist Devices, Kidney Disease, and Dialysis. Am J Kidney Dis. 71(2) pp:257-266. 14/12/2017.