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The Serum Neutrophil Gelatinase-Associated Lipocalin Predicts Early Acute Kidney Injury after Liver Transplantation

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ABSTRACT

Introduction: Acute kidney injury (AKI) following liver transplantation (LT) is a frequent complication and is associated with increased morbidity and mortality.
Aim: To investigate whether the levels of serum NGAL are able to predict early occurrence (within the first 48 hours) of the post-LT renal dysfunction.
Methods: The study was conducted on 50 recipients transplanted at the Fundeni Clinical Institute between May 2016 and June 2017. Serum NGAL and serum creatinine (sCr) were analyzed before LT, as well as 4 and 24 hours after graft reperfusion. In defining renal failure, the criteria of Kidney Disease Improving Global Outcome (KDIGO) were used. All patients received the same renal sparing regimen of immunosuppression.
Results: Twenty-four patients (48%) had early post-LT (<48 hours) renal dysfunction according to the KDIGO criteria. In the AKI group, there was a considerable increase in NGAL values at 4 hours after hepatic reperfusion in comparison with baseline values ($p<0.0001$), whereas in the group without AKI, the values of NGAL remained about the same ($p=0.18$). The single independent risk factor for early post-LT AKI occurrence was serum NGAL value 4 hours after hepatic reperfusion. The clinical utility of serum NGAL at 4 h after hepatic reperfusion for AKI prediction was excellent (AUROC 0.981, $p=0.0001$). Patients receiving a liver with a longer cold ischemia time (>6h) had a significantly higher NGAL serum levels at both 4 and 24h after reperfusion.
Conclusion: Early renal dysfunction following LT is frequent (48%) despite using a renal sparing immunosuppression regimen. Serum NGAL at 4 hours after hepatic reperfusion accurately predict AKI early, in the first 48 hours after LT.
Key words: biomarker, acute kidney injury, liver transplantation, Neutrophil gelatinase-associated lipocalin

INTRODUCTION

Liver transplantation is a life-saving therapy for patients with advanced liver disease, but can be accompanied by multiple postoperative complications. A common complication after liver transplantation is acute renal injury, associated with increased morbidity, mortality, costs, and length of hospitalization. The incidence of AKI is between 17% and 95%, depending on the criteria used in

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defining AKI (1,2). Patients with early acute renal injury after liver transplant have an increased risk of developing severe renal failure over the next 5 years, the need for renal dialysis being 18% at 5 years after LT (3,4). In O'Riordan et al. study, 30-day mortality in patients with AKI who required renal dialysis was 4 times higher compared with mortality in those without renal dysfunction (5). Multiple factors can predispose to AKI after LT, such as: pre-transplant renal dysfunction, high blood pressure and pre- and post-transplant diabetes, hepatitis C infection, graft quality, severity of liver disease, nephrotoxic drugs, especially the immunosuppression, pre-LT hypoalbuminemia, duration of the intraoperative vascular clamping, cold ischemia time, intraoperative transfusion requirement, perioperative hypotension and vasopressor support need, duration of surgery (6-16). Unlike other diseases, where new markers were discovered and used for diagnosis and staging, sCr remained the most common test in evaluating renal function. There are some drawbacks related to its use in the evaluation of renal function: it is influenced by diet, muscle mass, sex and age, has a low sensitivity to small changes in renal function and a considerable delay from kidney injury to its increasing.

Cirrhotic patients have a low creatinine formation from creatine, in muscle, as a consequence of decreased muscle mass (17), increased renal tubular creatinine secretion (18), increased volume distribution of sCr in cirrhosis and creatinine interference with increased bilirubin at the time of measurement (19). As a result, renal function is usually overestimated in these patients. The delay in diagnosing AKI implies missing a therapeutic opportunity, failure to correct the triggering factors, with an impact on the subsequent evolution of patients. Multiple markers of renal function have been studied in an attempt to identify a marker that is not influenced by muscle mass, diet, sex, race and increases much faster than creatinine after renal injury, some of them proving clinical utility (20,21). Neutrophil gelatinase-associated lipocalin (NGAL), also known as Lipocalin 2 or human neutrophil lipocalin, was first identified as a 25 kDa protein in the secondary granules of human neutrophils (22,23). Later, NGAL was localized in a number of human tissues, including trachea, lung, stomach, colon, and kidney (24). NGAL secretion from epithelial cells is induced by several pathological conditions (25) and was identified as the most rapidly induced protein in murine models of ischemic and nephrotoxic AKI (26). Its concentration increases several fold in both serum and urine within hours of the kidney insult. Human kidney biopsies also showed an accumulation of NGAL in cortical tubules in AKI patients. Accumulation was most pronounced in the most injured cells.

The purpose of the study was to investigate serum NGAL in detecting the early occurrence (within the first 48 hours) of post-LT renal dysfunction.

METHODS

The study was conducted on 50 liver transplant recipients at Fundeni Clinical Institute between May 2016 and June 2017. Exclusion criteria consisted of pediatric patients, pre-existing renal impairment (defined as serum creatinine > 1.5 mg/dl) and refusal to consent. All patients in the study group received a renal sparing immunosuppressive regimen consisting of basiliximab, tacrolimus and mycophenolate mofetil, as per institutional protocol. An analysis was conducted on their demographical data (age, gender, body mass index), lab reports (before LT, in the intra-operative stage, and on 4 consecutive days after the LT). Before the LT, 4 and 24 hours after the hepatic reperfusion, serum NGAL and sCr were analysed. The following intraoperative data was also recorded: requirement of blood products, the duration of the surgery, cold ischemia time, warm ischemia time, the presence or absence of the reperfusion syndrome, hemodynamic parameters (PICCO monitoring), the amount of vasopressor support. Serum NGAL levels were measured using the sandwich-type enzyme-linked immunosorbent assay kit (ELISA; BioVendor R&D, Czech Republic), which is commercially available, following manufacturer's instructions. The patients were split into two groups depending on the occurrence of the early (< 48 hours) renal dysfunction: with and without AKI. In defining renal failure, the criteria of Kidney Disease Improving Global Outcome (KDIGO) were used – see *Table 1* (27).

Statistical analysis

The demographic data of the two groups, with or without AKI, were comparatively analyzed, by using Fisher's exact test or Student t test. Depending on the data that were analyzed, the average and the standard deviation or the median and the interval of the values were calculated. The means of the pre-transplant parameters were compared with the post-surgery ones by using t test paired or t test unpaired, on a case by case basis. The ANOVA test was used to determine if the differences between the means of several sets of numerical data were statistically significant ($p < 0.05$). To determine if the differences between the medians of

Table 1 - The Kidney Disease Improving Global Outcome (KDIGO) classification (27)

Stage	Serum creatinine	Urine output
1	1.5-1.9 times baseline or ≥0.3 mg/dl (≥26.5 μmol/l) increase	< 0.5 ml/kg/h for 6-12 h
2	2.0-2.9 times baseline	<0.5 ml/kg/h for ≥12 h
3	3 times baseline or ≥ 4.0 mg/dl (≥ 353.6 μmol/l) increase or initiation of RRT or in patient <18 years a decrease in eGFR <35 ml/min/1.73 m²	<0.3 ml/kg/h for ≥24 h or anuria ≥12 h

RRT-renal replacement therapy, eGFR – estimated glomerular filtration rate

two sets of data were statistically significant, Mann-Whitney U test was used. The statistically significant parameters in the univariate analysis were analyzed through multivariate logistic regression. The AUROC (Area Under the Receiver Operating Characteristic curve) was used to determine the best cut off value of the analyzed parameters that predict post-LT AKI. The tests were considered statistically significant if $p < 0.05$.

RESULTS

The characteristics of the study group at inclusion are shown in *Table 2*. The etiology of hepatic cirrhosis in the analyzed cohort consisted of: HBV related cirrhosis in 27 (54%), HCV related cirrhosis in 11 (22%), alcoholic cirrhosis in 8 (16%) patients, while 8% of patients had other causes of cirrhosis; 15 (30%) patients also had associated hepatocellular carcinoma.

In an early post-LT phase (<48 hours) 24 patients (48%) had renal dysfunction according to the KDIGO criteria. Nineteen (38%) patients had AKI 1, two patients (4%) AKI 2 and three (6%) AKI 3. Three patients needed renal replacement therapy. *Table 3* presents the risk factors analyzed in association with or without occurrence of the post-LT AKI.

Table 2 - Baseline characteristics of the study group

Age(years)	50.98(±11.34)
Gender(males)	60%
Body mass index (kg/m²)	24.91(±4.46)
MELD score	17.48(±5.98)
Albumin(g/dl)	3.16(±0.63)
AST(U/l)	77.74(±44.07)
ALT(U/l)	53.6(±33.24)
Total bilirubin (mg/dl)	2.45(0.5-24.1)
INR	1.63(±0.38)
Creatinine(mg/dl)	0.82(±0.2)
Na (mmol/l)	135(±5.45)
Baseline NGAL (ng/ml)	44.1(±23.13)

MELD score - Model for End Stage Liver Disease score; AST- Aspartate aminotransferase; ALT- Alanine aminotransferase; INR-International Normalized Ratio; NGAL- Neutrophil gelatinase-associated lipocalin

There were no statistically significant differences between the two groups regarding the demographic data and the analyzed parameters, except for a higher values of cold ischemia time in the AKI group (p=0.02). There was a statistically significant difference between the values of NGAL within 4 and 24 hours after the hepatic reperfusion between the two groups (p<0.0001 and p<0.0001, respectively). In the AKI group, there was a considerable increase in NGAL values at 4 hours after hepatic reperfusion in comparison with baseline values (p<0.0001), whereas in the group without AKI, the values of NGAL remained about the same (p=0.18) (see *Fig. 1*).

The analysis by multivariate logistic regression found that the only independent risk factor for the post-LT occurrence of AKI was the value of serum NGAL at 4 hours after the hepatic reperfusion (p=0.001). The value of serum NGAL within 4 hours showed an excellent discriminatory ability to distinguish between

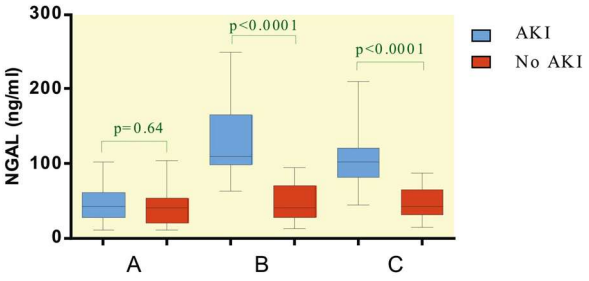

Figure 1 - NGAL (ng/ml) in pre-LT (A), 4 hours after hepatic reperfusion (B) and 24 hours after hepatic reperfusion (C) in the AKI group in comparison with the group without AKI

Table 3 - The risk factors analyzed for the occurrence of the post-LT AKI in the two groups

	With AKI (n=24)	Without AKI (n=26)	p value
Age (years)	53.71(±10.56)	47.69(±11.47)	0.06
Gender (males)	15(62.5%)	15(57.69%)	0.73
Body mass index (kg/m^2)	25.62(±4.46)	24.26(±4.47)	0.28
MELD score	17.96(±5.66)	17.04(±6.34)	0.59
Albumin (g/dl)	3.1(±0.53)	3.2(±0.71)	0.59
AST(U/l)	72.33(±46.62)	82.73(±41.87)	0.41
ALT(U/l)	46.65(±25.34)	59.65(±33.24)	0.2
Total bilirubin (mg/dl)	2.75(0.7-24.1)	2.25(0.5-8.6)	0.32
INR	1.64(±0.39)	1.62(±0.37)	0.87
Baseline creatinine(mg/dl)	0.84(±0.24)	0.8(±0.17)	0.52
Creatinine-4h (mg/dl)	0.89(±0.23)	0.76(±0.23)	0.063
Na (mmol/l)	135(±4.9)	134(±5.9)	0.31
Baseline NGAL (ng/ml)	45.68(±22.45)	42.64(±24.09)	0.64
NGAL-4h (ng/ml)	128.5(±45.28)	47.14(±24.31)	<0.0001
NGAL-24h (ng/ml)	108.5(±37.88)	47.52(±20.83)	<0.0001
Bleeding (ml)	4000(500-19000)	4000(500-14000)	0.96
Cold ischemia time (min)	530(±311.8)	226.5(±123.8)	0.02
Warm ischemia time (min)	45.38(±19.21)	43.31(±19.93)	0.7
Duration of LT (min)	461.7(±130.4)	455.8(±110.1)	0.86
Red blood cells transfusion (units)	2.5(0-18)	2.5(0-10)	0.78
Fresh frozen plasma transfusion(units)	1.45(0-19)	0.96(0-5)	0.56
Cardiac index l/min/m^2	4.07(±1.2)	4.27(±1.17)	0.57
Baseline lactate mmol/l	1.57(±0.58)	1.36(±0.35)	0.11
Lactate after hepatic reperfusion (mmol/l)	2.43(±1.7)	2.86(±1.82)	0.39

MELD score- Model for End Stage Liver Disease score, AST- Aspartate aminotransferase, ALT- Alanine aminotransferase, INR-International Normalized Ratio, NGAL- Neutrophil gelatinase-associated lipocalin, NGAL-4h and -24h- Neutrophil gelatinase-associated lipocalin at 4 and 24 hours after hepatic reperfusion, Creatinine-4h – serum creatinine at 4 hours after hepatic reperfusion.

patients who had early post-LT renal dysfunction (<48 hours) and those who did not (AUROC of 0.981, p=0.0001) (see *Fig. 2*). The corresponding cut-off value for NGAL at 4 hours after hepatic reperfusion was 85.26 ng/ml with 95.8% sensitivity and 93.33% specificity in diagnosing AKI in liver-transplanted patients. There was a significantly higher serum NGAL level at 4 hours (107.11 vs 66.71 ng/ml, p=0.003) and also at 24 hours (91.35 vs 57.67ng/ml, p=0.007) after reperfusion in patients that received grafts with a cold ischemia time >360 minutes.

DISCUSSION

Acute renal failure early after LT (<48 hours) is associated with short, as well as long term higher morbidity and mortality, increased costs and length of hospitalization. However, early therapeutic or preventive intervention is hampered by the lack of early effective prognostic factors. This underlines the importance of the early identification of at-risk individuals as well as the need of identifying preventive strategies. Furthermore, increasing evidence

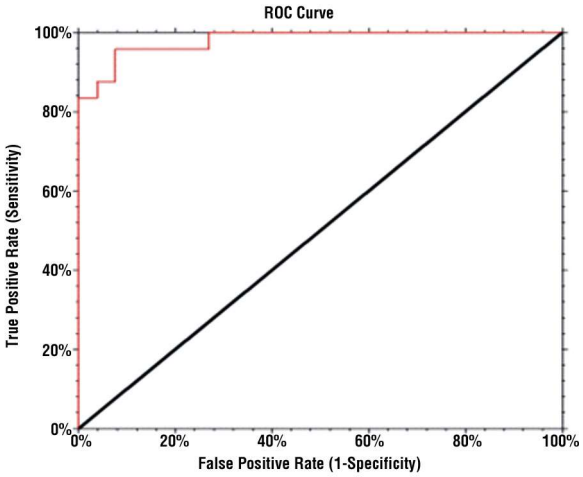

Figure 2 - ROC Curve for NGAL at 4 hours after hepatic reperfusion (AUROC of 0.981, p=0.0001)

supports the fact that even a relatively minor deterioration in renal function, not requiring RRT is associated with inferior patient and renal outcomes in the longer term (1,29). Many studies have attempted to determine risk factors for the development of post-LT renal dysfunction. Factors such as preoperative sCr, early severe graft dysfunction consequent to use of marginal grafts, postoperative sepsis, severe pre-transplant hyponatremia, low preoperative albumin, intraoperative blood loss and subsequent blood transfusion, cold ischemia time and warm ischemia time, hypovolemia and hepatic ischemia reperfusion injury have all been implicated in the development of renal dysfunction after LT (8,12,14,28,30). In our study, there were no statistically significant differences between the two groups regarding the demographic data and the analyzed parameters, except for a higher value of cold ischemia time and increased values of serum NGAL at 4 and 24 hours after hepatic reperfusion in the AKI group. The homogeneity of the studied group, exclusion of patients with pre-transplant renal dysfunction and a good perioperative management can contribute to these results. An increased cold ischemia time was associated with early acute renal injury after LT, similar to the findings reported by Zongyi Y. et al. (28). It was already proven that NGAL is directly released by ischemically damaged kidneys, independent of neutrophil activation. There was a strong correlation between NGAL staining intensity and cold ischemia time in kidney recipients (31). In liver transplant recipients we also demonstrated a significant increase in serum NGAL values at 4 and 24 hours after reperfusion in donors with cold ischemia times over 6 hours; thus, serum NGAL can be considered as an early marker of ischemia/reperfusion injury in both kidney and liver transplantation and consequently associated with higher rates of complications after LT (reperfusion syndrome, arterial and biliary complications, and prostaglandin requirements).

Pre-transplant renal dysfunction, as well as advanced liver insufficiency before LT reflected by a higher MELD score, have predictive value for developing AKI after LT. In our study, MELD score did not perform well for predicting AKI after LT (AUROC of 0.53) (data not shown); the same results have been obtained before by Hilmi I.A. et al. (13). This finding is in contrast to the study by Karapanagiotou et al. (32), in which these variables have been proven significant risk factors. However, unlike Karapanagiotouet al., we excluded patients with pre-transplant renal failure with high sCr (defined as serum creatinine > 1.5 mg/dl). Although a renal sparing immunosuppression protocol is used in our Transplant Centre (tacrolimus is introduced in the 5th postoperative day), AKI occurred early after LT in almost half of the analyzed patients. NGAL was identified as the most rapidly induced protein in murine models of ischemic and nephrotoxic AKI (26). Concentrations increased several fold in both serum and urine within hours of the insult. Human kidney biopsies also showed an accumulation of NGAL in cortical tubules in AKI patients. Accumulation was more pronounced in the most injured cells. Although initially the NGAL values were the same in the AKI and No AKI groups, at 4 and 24 hours after hepatic reperfusion they have significantly increased in AKI group. In our study NGAL at 4 hours after hepatic reperfusion predict early acute kidney injury (in the first 48 hours) after liver transplantation. Similar results were obtained by Portal AJ et al. (21). The limitations of our study are the small sample and the short follow up period for AKI. However, this is the first post-transplant study to analyze biomarkers for kidney dysfunction after LT in Romania.

CONCLUSIONS

Serum NGAL at 4 hours after hepatic reperfusion accurately predict AKI early, in the first 48 hours after LT. Given the frequency of the post-LT AKI, the costs, and the comorbidities that stem from it, measurement of serum NGAL at 4 hours after hepatic reperfusion is highly useful. We also conclude that serum NGAL at 4 and also 24 hours after LT can indicate higher rates of complications in donor livers with cold ischemia times longer than 6 hours. These findings can enable us to correct the modifiable factors and to improve the outcomes of our LT recipients.

Conflict of interests

The authors declare no conflict of interests.

REFERENCES

1. Barri YM, Sánchez EQ, Jennings LW, Melton LB, Hays S, Levy MF, et al. Acute kidney injury following liver transplantation: Definition and outcome. Liver Transpl. 2009;15(5):475-83.
2. Bilbao I, Charco R, Balsells J, Lazaro JL, Hidalgo E, Llopart L, et al. Risk factors for acute renal failure requiring dialysis after liver transplantation. Clin Transplant. 1998;12:123-129.
3. Herlenius G, Fistouris J, Olausson M, Felldin M, Bäckman L, Friman S. Early renal function post-liver transplantation is predictive of progressive chronic kidney disease. Scand J Gastroenterol. 2008; 43(3):344-9.
4. Ojo AO, Held PJ, Port FK, Wolfe RA, Leichtman AB, Young EW, et al.

Chronic renal failure after transplantation of a nonrenal organ. N Engl J Med. 2003;349(10):931-40.
5. O'Riordan A, Wong V, McQuillan R, McCormick PA, Hegarty JE, Watson AJ. Acute renal disease, as defined by the RIFLE criteria, post-liver transplantation. Am J Transplant 2007;7:168– 176.
6. Paramesh AS, Roayaie S, Doan Y, Schwartz ME, Emre S, Fishbein T, et al. Post-liver transplant acute renal failure: factors predicting development of end-stage renal disease. Clin Transplant. 2004;18: 94– 99.
7. Kendrick EA, McVicar JP, Kowdley KV, Bronner MP, Emond MJ, Alpers CE, et al. Renal disease in hepatitis C-positive liver transplant recipients. Transplantation 1997;63:1287–1293.
8. Cabezuelo JB, Ramírez P, Ríos A, Acosta F, Torres D, Sansano T, et al. Risk factors of acute renal failure after liver transplantation. Kidney Int. 2006;69(6):1073-80.
9. Yang GZ, Xue FS, Li HX. Assessing risk factors of acute kidney injury after liver transplantation. J Cancer Res Clin Oncol. 2017;143(12): 2635-2636.
10. Yalavarthy R, Edelstein CL, Teitelbaum I. Acute renal failure and chronic kidney disease following liver transplantation. HemodialInt 2007;11(Suppl 3):S7-S12.
11. Lima EQ, Zanetta DM, Castro I, Massarollo PC, Mies S, Machado MM, et al. Risk factors for development of acute renal failure after liver transplantation. Ren Fail. 2003;25(4):553-60.
12. Angeli P, Bezinover D, Biancofiore G, Bienholz A, Findlay J, Paugam BC, Reyntjens K, Sakai T, Saner FH, Tomescu D, Wagener G, Weiss E. Acute kidney injury in liver transplant candidates: a position paper on behalf of the Liver Intensive Care Group of Europe. Minerva Anestesiol 2017;83(1):88-101.
13. Hilmi IA, Damian D, Al-Khafaji A, Planinsic P, Boucek C, Sakai T, et al. Acute kidney injury following orthotopic liver transplantation: incidence, risk factors, and effects on patient and graft outcomes. Br J Anaesth. 2015;114(6):919-26.
14. Suehana Rahman, Brian R Davidson, Susan V Mallett. Early acute kidney injury after liver transplantation: Predisposing factors and clinical implications. World J Hepatol. 2017;9(18):823-832.
15. Wiedermann CJ, Wiedermann W, Joannidis M. Hypoalbuminemia and acute kidney injury: a meta-analysis of observational clinical studies. Intensive Care Med. 2010;36(10):1657-65.
16. Tudoroiu M-I, Constantin G, Pâslaru L, Iacob S, Gheorghe C, Popescu I, et al. The combination of serum cystatin c, urinary kidney injury molecule-1 and MELD plus score predicts early acute kidney injury after liver transplantation. Surg Gastroenterol Oncol. 2018;23:121–6.
17. Sherman DS, Fish DN, Teitelbaum I. Assessing renal function in cirrhotic patients: problems and pitfalls. American journal of kidney diseases. 2003;41(2):269–78.
18. Caregaro L, Menon F, Angeli P, Amodio P, Merkel C, Bortoluzzi A, et al. Limitations of serum creatinine level and creatinine clearance as filtration markers in cirrhosis. Archives of internal medicine. 1994; 154(2):201–5.
19. Spencer K. Analytical reviews in clinical biochemistry: the estimation of creatinine. Annals of clinical biochemistry. 1986;23(1):1–25.
20. Mȶrtensson J, Martling C-R, Bell M. Novel biomarkers of acute kidney injury and failure: clinical applicability. British journal of anaesthesia. 2012;109(6):843–50.
21. Portal AJ, McPhail MJ, Bruce M, Coltart I, Slack A, Sherwood R, et al. Neutrophil gelatinase—associated lipocalin predicts acute kidney injury in patients undergoing liver transplantation. Liver Transplantation. 2010;16(11):1257–66.
22. Kjeldsen L, Johnsen AH, Sengelov H, Borregaard N. Isolation and primary structure of NGAL, a novel protein associated with human neutrophil gelatinase. J Biol Chem. 1993;268:10425–32.
23. Xu SY, Carlson M, Engstrom A, Garcia R, Peterson CG, Venge P. Purification and characterization of a human neutrophil lipocalin (HNL) from the secondary granules of human neutrophils. Scand J Clin Lab Invest. 1994;54:365–76.
24. Cowland JB, Borregaard N. Molecular characterization and pattern of tissue expression of the gene for neutrophil gelatinaseassociated lipocalin from humans. Genomics. 1997;45:17–23.
25. Xu S, Venge P. Lipocalins as biochemical markers of disease. Biochim Biophys Acta. 2000;1482:298–307.
26. Mishra J, Ma Q, Prada A, Mitsnefes M, Zahedi K, Yang J, et al. Identification of neutrophil gelatinase-associated lipocalin as a novel early urinary biomarker for ischemic renal injury. J Am Soc Nephrol. 2003;14(10):2534–43.
27. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clinical Practice. 2012;120(4):c179–84.
28. Zongyi Y, Baifeng L, Funian Z, Hao L, Xin W. Risk factors of acute kidney injury after orthotopic liver transplantation in China. Scientific reports. 2017;7:41555.
29. Zand MS, Orloff MS, Abt P, Patel S, Tsoulfas G, Kashyap R, et al. High mortality in orthotopic liver transplant recipients who require hemodialysis. Clin Transplant. 2011;25(2):213-21.
30. Pawarode A, Fine D, Thuluvath P. Independent risk factors and natural history of renal dysfunction in liver transplant recipients. Liver Transpl. 2003;9(7):741-7.
31. Mishra J, Ma Q, Kelly C, Mitsnefes M, Mori K, Barasch J, Devarajan P. Kidney NGAL is a novel early marker of acute injury following transplantation. PediatrNephrol. 2006;21(6):856-63.
32. Karapanagiotou A, Kydona C, Dimitriadis C, Sgourou K, Giasnetsova T, Fouzas I, et al. Acute kidney injury after orthotopic liver transplantation. Transplant Proc. 2012; 44(9):2727–9.