Journal of Cardiothoracic and Vascular Anesthesia 39 (2025) 3387–3394

Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Original Article

Urinary Liver-Type Fatty Acid Binding Protein as a Postoperative Marker of Acute Kidney Injury in Patients Undergoing Endovascular Aortic Aneurysm Repair

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Objective: To evaluate the role of urinary liver-type fatty acid binding protein (L-FABP) in early detection of acute kidney injury (AKI) after endovascular aortic aneurysm repair (EVAR) for abdominal aortic aneurysm (AAA).
Design: Prospective, observational, multicenter study.
Setting: Four university hospitals from January 2024 to June 2024.
Participants: Fifty-nine hospitalized patients with AAA.
Interventions: Patients undergoing EVAR were included. Demographic data, comorbidities, and renal function data were recorded at baseline and after intervention. L-FABP data were collected at baseline and at 6 hours and 24 hours after surgery.

This work was supported by #NEXTGENERATIONEU (NGEU) and funded by the Ministry of University and Research, National Recovery and Resilience Plan, Project MNESYS (PE0000006) – A Multiscale Integrated Approach to the Study of the Nervous System in Health and Disease (DN. 1553 11.10.2022).
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https://doi.org/10.1053/j.jvca.2025.08.020

Measurements and Main Results: The cohort had a mean age of 70.2 ± 7.3 years and was predominantly male (84.7%). Positive L-FABP results were observed in 24.1% of patients at 6 hours post-EVAR and in 23.7% at 24 hours post-EVAR. A positive L-FABP status at both time points was significantly associated with elevated postoperative serum creatinine (SCr) and reduced estimated glomerular filtration rate (eGFR) ($p \leq 0.015$), reduced urine output ($p = 0.009$ and $p < 0.001$), and shorter hospital length of stay (LOS) ($p = 0.004$ and $p = 0.013$). Multivariable logistic regression analysis fully confirmed these associations. Predictive models incorporating L-FABP achieved high accuracy for identifying patients with reduced diuresis (up to 86.1%). Additionally, L-FABP at 6 hours and 24 hours predicted LOS, whereas SCr and eGFR values did not.
Conclusion: Urinary L-FABP is emerging as a sensitive biomarker for AKI in patients undergoing EVAR.

Key Words: acute kidney injury; abdominal aortic aneurysms; biomarkers; endovascular aortic aneurysm repair; liver–type fatty–acid–binding protein

ENDOVASCULAR AORTIC ANEURYSM REPAIR (EVAR) has become the preferred treatment modality for patients with abdominal aortic aneurysm (AAA) with suitable anatomy. Several clinical trials have demonstrated superior midterm outcomes, including reduced mortality and morbidity, in both low-risk and high-risk patients compared to open surgical repair.[1-4]

Acute kidney injury (AKI) is one of the most frequent complications following EVAR, with an incidence ranging from 2.9% to 18%.[5] Post-EVAR AKI is multifactorial disorder attributed primarily to contrast-induced nephrotoxicity, prolonged duration of procedure, perioperative reduction in hemoglobin level, and receipt of transfusions.[6] Unfortunately, the development of AKI following EVAR is associated with an increased risk of progression to chronic kidney disease (CKD), greater morbidity and mortality, and higher healthcare costs.[6] The term "contrast-associated AKI" has replaced "contrast-induced nephropathy" as a more accurate diagnostic term, referring to any instance of AKI. According to the Kidney Disease Improving Global Outcomes (KDIGO) criteria, AKI is defined as: (1) an increase in serum creatinine (SCr) concentration of ≥0.3 mg/dL within 48 hours; (2) an increase in SCr to 1.5 times baseline, which is known or presumed to have occurred within the previous 7 days; and (3) urine output <0.5 mL/kg/hour for 6 hours.[7]

Recently, several urinary biomarkers, including urinary liver-type fatty acid binding protein (L-FABP), have been investigated for the early detection of kidney injury, particularly in the settings of cardiac surgery and transcatheter aortic valve implantation.[8-10] L-FABP is a 14-kDa protein expressed in proximal tubular epithelial cells that acts as a carrier for short-chain fatty acids to mitochondria and peroxisomes for β-oxidation.[11] Unlike the other biomarkers, L-FABP is more closely associated with tubular dysfunction rather than glomerular impairment, and it is detected in urine only during tubular injury.[12]

The aim of this prospective study was to evaluate the role of urinary L-FABP in the early detection of post-EVAR AKI, assessing its correlation with postoperative SCr, estimated glomerular filtration rate (eGFR), urine output, and hospital length of stay (LOS).

Methods

Study Population

In the framework of a prospective observational cohort study, adult patients with AAA undergoing elective EVAR were consecutively enrolled from January to June 2024. Patients in end-stage renal failure, undergoing emergency procedures, or dying within 24 hours after surgery were excluded. The study was carried out in the Department of Vascular Surgery of 4 Italian university hospitals. Demographic, clinical, and microbiological data were collected at 4 time points: baseline, end of the surgical procedure, and at 6 hours and 24 hours after surgery.

Study Protocol

This study was approved by the hospital review board and regional ethics committee (Comitato Etico Unico Regionale for Basilicata, CE 37/2024, 20240028191). Written informed consent was obtained from all participants by investigators trained in good clinical practice and in accordance with the Declaration of Helsinki guidelines. At admission, demographic characteristics (age, sex, and body mass index [BMI]) and comorbidities (hypertension, dyslipidemia, diabetes, chronic obstructive pulmonary disease, coronary artery disease, and smoking status) were recorded in a specific database using Microsoft Excel for Mac. All data were anonymized.

To analyze the kinetics of urinary L-FABP, we used an immunochromatographic test enabling semi-quantitative measurement (Appendix A, Figure S1), using 100 μL of urine per sample. L-FABP levels were measured within 15 minutes after the sample was added to the test cassette. In urine specimens, the protein reacts with a gold colloid anti-human L-FABP mouse monoclonal antibody, forming an antigen-antibody complex. This complex moves through the membrane via capillary action and interacts with the anti-human L-FABP mouse monoclonal antibody on the test line, producing a visible burgundy coloration. The L-FABP concentration range was assessed by comparing the color intensity of the test line to the color blocks on the reference card. A normal result corresponds to an L-FABP level <12.5 ng/mL, while abnormal results are categorized as an L-FABP level between 12.5 ng/mL and 100 ng/mL (weakly positive), and a level ≥100 ng/mL (strongly positive). Renal function data (SCr, eGFR [calculated according to the MDRD 186 study equation formula], and diuresis) were assessed at baseline and at the end of the intervention. L-FABP was measured at baseline and at 6 hours and 24 hours after surgery. The duration of surgery and information on the contrast agent used (type and amount)

were collected as well. At discharge, the LOS was recorded for each patient.

Statistical Analysis

Descriptive data are expressed as frequency and percentage for categorical variables. Continuous data are reported as mean ± SD (normally distributed data) or as median and interquartile range (non-normally distributed data). The Shapiro-Wilk test was performed to assess normality. Group comparisons were performed using the independent *t* test or the Mann-Whitney *U* test (continuous variables) and the χ^2 test or Fisher exact test (categorical data). Based on SCr, eGFR, and L-FABP values, binary variables were created using cut-off values of 1.2 mg/dL, 60 mL/min/1.73m^2, and 12.5 ng/mL, respectively. The relationship between L-FABP status (positive/negative) at 6 hours and 24 hours after surgery and clinical variables were tested by multivariable logistic regression analysis, adjusted for traditional and nontraditional confounding factors (age, sex, BMI, diabetes, contrast agent, SCr, and eGFR values). Receiver operating characteristic (ROC) curve analysis was performed to evaluate the accuracy of the models.

The level of uncertainty around each estimate was expressed through a 95% confidence interval (CI). A p value ≤0.05 was considered statistically significant. All statistical analyses were carried out using SPSS Statistics version 29 (IBM).

Results

Characteristics of the Study Cohort

Fifty-nine hospitalized patients were included in the study. The main demographic, clinical, and baseline characteristics of the study cohort are reported in Table 1. The study cohort had a mean age of 70.2 ± 7.3 years, with a BMI of 27.4 ± 4.0 kg/m^2, and was predominantly male (84.7%). The median baseline and postoperative SCr concentrations were 0.91 (IQR, 0.80-1.12) mg/dL and 1.02 (IQR, 0.83-1.53) mg/dL, respectively. Likewise, the median baseline eGFR was 71.3 (IQR, 59.3-85.1) mL/min/1.73 m^2, and the postoperative eGFR was 70.7 (IQR, 40.8-91.3) mL/min/1.73 m^2.

At baseline, 9 patients (15.3%) had a positive urinary L-FABP concentration. Following the intervention, 14 patients (24.1%) had a positive L-FABP, at 6 hours postprocedure, whereas this percentage decreased slightly to 23.7% after 24 hours. As for the prevalent comorbidities, 84.7% of patients had hypertension, 59.3% had dyslipidemia, and 23.7% had diabetes. Furthermore, 35.6% of the patients were current smokers, and 22.0% (n =13) had diminished diuresis. The median hospital LOS for the entire cohort was 5 days (IQR, 4-7 days).

Comparison of the Basal, 6-Hour, and 24-Hour L-FABP Groups

A direct assessment of baseline L-FABP results revealed slightly higher basal SCr and lower basal eGFR in the negative patients compared to the positive patients (Table 2). Conversely, a face-to-face comparison of 6-hour L-FABP groups revealed a worse renal function profile in positive patients than in negative ones (Table 3). 6-hour L-FABP positive patients were also older and with a longer LOS (Table 3). The same

Table 1
Demographic and clinical data of the whole cohort (N = 59)

Variable	Value
Age, y, mean ± SD	70.2 ± 7.3
Male sex, n (%)	50 (84.7)
BMI, kg/m^2, mean ± SD	27.4 ± 4.0
Hypertension, n (%)	50 (84.7)
Dyslipidemia, n (%)	35 (59.3)
Diabetes, n (%)	14 (23.7)
Current smoker, n (%)	21 (35.6)
Past smoker, n (%)	20 (33.9)
COPD, n (%)	13 (22.0)
CAD, n (%)	16 (27.1)
Baseline SCr, mg/dL, median (IQR)	0.91 (0.80-1.12)
Postoperative SCr, mg/dL, median (IQR)	1.02 (0.83-1.53)
High postoperative SCr (≥1.2 mg/dL), n (%)	25 (42.4)
Baseline eGFR,mL/min/1.73 m^2, median (IQR)	71.3 (59.3-85.1)
Postoperative eGFR,mL/min/1.73 m^2, median (IQR)	70.7 (40.8-91.3)
Low postoperative eGFR (<60 mL/min/1.73 m^2), n (%)	25 (42.4)
Contrast agent, mL, median (IQR)	120 (9-171)
Baseline positive L-FABP, n (%)	9 (15.3)
6 hours postoperative positive L-FABP, n (%)*	14 (24.1)
24 hours postoperative positive L-FABP, n (%)	14 (23.7)
Reduced diuresis (<0.5 mL/24 h), n (%)	13 (22.0)
Hospital LOS, d, median (IQR)	5 (4-7)
Hospital LOS (≥7 d), n (%)	16 (27.1)

Abbreviations: BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; L-FABP, liver-type fatty acid binding protein; LOS, length of stay; SCr. serum creatinine.

* 1 is missing.

Table 2
Comparison of basal L-FABP groups

Variable	Basal L-FABP		p value
	Negative (N = 50)	Positive (N = 9)	
Age, y, mean ± SD	70.1 ± 6.6	71.2 ± 10.6	0.758
Male sex, n (%)	43 (86.0)	7 (77.8)	0.615
BMI, kg/m^2, mean ± SD	27.3 ± 3.8	27.5 ± 5.4	0.934
Hypertension, n (%)	41 (82.0)	9 (100.0)	0.329
Dyslipidemia, n (%)	30 (60.0)	5 (55.6)	1.000
Diabetes, n (%)	13 (26.0)	1 (11.1)	0.671
Baseline SCr, mg/dL, median (IQR)	0.99 (0.83-1.17)	0.83 (0.72-0.98)	**0.031**
High preop SCr (≥1.2 mg/dL), n (%)	7 (14.0)	0 (0.0)	0.581
Baseline eGFR, mL/min/1.73m^2, median (IQR)	69.9 (59.2-83.8)	91.7 (69.2-107.9)	**0.037**
Low preop eGFR (<60 mL/min/1.73m^2), n (%)	14 (28.0)	1 (11.1)	0.424

Bold type indicates statistical significance.

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; IQR, interquartile range; L-FABP, liver-type fatty acid binding protein; SCr, serum creatinine; SD, standard deviation.

Table 3
Comparison of 6-hour L-FABP groups

Variable	6-hour L-FABP*		
	Negative (N = 44)	Positive (N = 14)	p value
Age, y, mean ± SD	69.1 ± 7.4	73.4 ± 6.1	**0.036**
Male sex, n (%)	39 (88.6)	10 (71.4)	0.198
BMI, kg/m^2, mean ± SD	27.8 ± 4.4	26.3 ± 2.0	0.079
Hypertension, n (%)	36 (81.8)	13 (92.9)	0.431
Dyslipidemia, n (%)	26 (59.1)	9 (64.3)	0.766
Diabetes, n (%)	12 (27.3)	2 (14.3)	0.480
Baseline SCr, mg/dL, median (IQR)	0.91 (0.81-1.15)	0.93 (0.77-1.12)	0.429
Postop SCr, mg/dL, median (IQR)	0.97 (0.82-1.27)	1.71 (1.21-2.18)	**0.011**
High postop SCr (≥1.2 mg/dL), n (%)	14 (31.8)	11 (78.6)	**0.004**
Baseline eGFR, mL/min/1.73 m^2, median (IQR)	71.2 (58.2-84.2)	71.3 (60.1-96.2)	0.490
Postop eGFR, mL/min/1.73 m^2, median (IQR)	75.5 (55.9-92.0)	34.3 (28.3-64.5)	**0.004**
Low postop eGFR (<60 mL/min/1.73 m^2), n (%)	14 (31.8)	11 (78.6)	**0.015**
Contrast agent, mL, median (IQR)	117.5 (87.8-161.5)	147.0 (84.5-197.5)	0.283
Reduced diuresis (<0.5 mL/24 hours), n (%)	6 (13.6)	7 (50.0)	**0.009**
Hospital LOS, d, median (IQR)	5.0 (3.8-6.0)	7.0 (6.0-8.0)	**0.010**
Hospital LOS ≥7 d, n (%)	7 (15.9)	8 (57.1)	**0.004**

Bold type indicates statistical significance.
Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; IQR, interquartile range; L-FABP, liver-type fatty acid binding protein; LOS, length of stay; SCr, serum creatinine; SD, standard deviation.
* 1 is missing.

analysis carried out according to 24-hour L-FABP provided similar results (Table 4) and also revealed a between-group difference in contrast agents. Both the 6-hour and 24-hour L-FABP−positive groups had a higher percentage of patients with altered postoperative SCr levels (78.6% and 71.4%, respectively) compared to the 6-hour and 24-hour L-FABP−negative groups (31.8% and 33.3%, respectively; p ≤ 0.015) (Appendix A, Figure S2).

The association between urinary L-FABP concentration at 6 hours postsurgery and postoperative SCr level was further investigated by multivariable logistic regression analysis. This analysis, adjusted for potential confounders including age, sex, BMI, baseline SCr, and contrast agent dose, revealed that patients with altered 6-hour L-FABP had an approximately 8-fold higher risk of high postsurgery SCr (≥1.2 mg/dL) (odds ratio [OR]: 8.3; 95% CI: 1.7-40.5; p = 0.009; Table 5).

This strong association also was confirmed when investigating the relationship between 24-hour L-FABP and high postoperative SCr (OR: 5.0; 95% CI: 1.11-22.4; p = 0.036). Similar to SCr, a higher percentage of patients with altered

Table 4
Comparison of 24-hour L-FABP groups

Variable	24-hour L-FABP		
	Negative (N = 45)	Positive (N = 14)	p value
Age, y, mean ± SD	69.0 ± 6.9	74.1 ± 7.3	**0.031**
Male sex, n (%)	38 (84.4)	12 (85.7)	0.908
BMI, kg/m^2, mean ± SD	27.5 ± 4.4	27.0 ± 2.8	0.623
Hypertension, n (%)	38 (84.4)	12 (85.7)	1.000
Dyslipidemia, n (%)	27 (60.0)	8 (57.1)	1.000
Diabetes, n (%)	12 (26.7)	2 (14.3)	0.482
Baseline SCr, mg/dL, median (IQR)	0.90 (0.79-1.11)	1.10 (0.83-1.16)	0.387
Postop SCr, mg/dL, median (IQR)	0.97 (0.81-1.27)	1.71 (1.15-2.07)	**0.005**
High postop SCr (≥1.2 mg/dL), n (%)	15 (33.3)	10 (71.4)	**0.015**
Baseline eGFR, mL/min/1.73 m^2, median (IQR)	72.6 (58.6-85.7)	66.7 (60.0-86.8)	0.735
Postop eGFR, mL/min/1.73 m^2, median (IQR)	75.5 (54.9-92.7)	34.7 (30.6-67.7)	**0.004**
Low postop eGFR (<60 mL/min/1.73 m^2), n (%)	15 (33.3)	10 (71.4)	**0.015**
Contrast agent, mL, median (IQR)	114.0 (80.0-155.0)	162.5 (111.3-208.0)	**0.018**
Reduced diuresis (<0.5 mL/24 h), n (%)	3 (6.7)	10 (71.4)	**<0.001**
Hospital LOS, days, median (IQR)	5 (4-6)	7 (6-7)	**0.042**
Hospital LOS ≥7 d, n (%)	8 (17.8)	8 (57.1)	**0.013**

Bold type indicates statistical significance.
Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; IQR, interquartile range; L-FABP, liver-type fatty acid binding protein; LOS, length of stay; SCr, serum creatinine; SD, standard deviation.

Table 5
Multivariable logistic regression analysis of postsurgery SCr and eGFR

Variable (units of increase)	OR	95% CI	p value
Postsurgery creatinine ≥1.2 mg/dL			
6-hour L-FABP (0: negative; 1: positive)	8.3	1.7-40.5	**0.009**
24-hour L-FABP (0: negative; 1: positive)	5.0	1.1-22.4	**0.036**
Postsurgery eGFR <60 mL/min/1.73 m^2			
6-hour L-FABP (0: negative; 1: positive)	41.2	4.3-398.2	**0.001**
24-hour L-FABP (0: negative; 1: positive)	9.5	1.7-54.6	**0.012**

Adjusted model: age, sex, body mass index, contrast agent, baseline SCr, and baseline eGFR.
Bold type indicates statistical significance.
Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; L-FABP, liver-type fatty acid binding protein; OR, odds ratio.

postoperative eGFR was observed in both the 6-hour and 24-hour positive L-FABP groups (78.6% and 71.4%, respectively) compared to the negative groups (31.8% and 33.3%, respectively; p ≤ 0.015; Appendix A, Figure S3). The relationship between 6-hour L-FABP and 24-hour L-FABP with postsurgery eGFR values was fully confirmed in multivariable logistic regression analyses (OR: 41.2; 95% CI: 4.3-398.2; p = 0.001 and OR: 9.5; 95% CI: 1.7-54.6; p = 0.012, respectively; Table 5).

Furthermore, there was a greater prevalence of patients with diminished diuresis in the 6-hour and 24-hour L-FABP−positive groups (50% and 71.4%) compared to the negative groups (13.6% and 6.7%; p = 0.009 and p <0.001; Appendix A, Figure S4), and again these associations were fully confirmed in multivariable logistic regression analyses (Table 6), after also adjusting for postoperative SCr ≥1.2 mg/dL and postoperative eGFR <60 mL/min/1.73 m^2 (data not shown).

Of note, the models described in Table 6 had an accuracy in predicting reduced diuresis of 79.3% (95% CI, 0.65-0.94; p < 0.001) and 86.1% (95% CI, 0.73-0.996; p < 0.001) (Figure 1).

Positive L-FABP at 6 hours and 24 hours also was associated with longer hospitalization (≥7 days), as shown in Appendix A, Figure S5. Specifically, 57.1% of patients with positive L-FABP at both time points experienced prolonged hospital LOS, compared to 15.9% (p = 0.004) and 17.8% (p = 0.013) in the L-FABP−negative group. To assess the extent to which 6-hour and 24-hour L-FABP predicted a longer hospital LOS compared with postoperative creatinine ≥1.2 mg/dL and postoperative eGFR <60 mL/min/1.73 m^2 and other risk factors, we constructed 2 multivariable logistic regression models including these 2 indicators of renal function (Table 7). In both models, 6-hour and 24-hour L-FABP significantly predicted a longer hospital LOS, whereas postoperative creatinine and eGFR values did not.

Table 6
Multivariable logistic regression analysis of altered diuresis (<0.5 mL/24 hours)

Variable (units of increase)	OR	95% CI	p value
6-hour L-FABP (0: negative; 1: positive)	7.9	1.7-37.2	**0.009**
24-hour L-FABP (0: negative; 1: positive)	47.8	6.8-336.9	**<0.001**

Adjusted model: age, sex, body mass index, and diabetes.
Bold type indicates statistical significance.
Abbreviations: CI, confidence interval; L-FABP, liver-type fatty acid binding protein; OR, odds ratio.

Additional Analysis

In an additional analysis, we studied the relationship between 24-hour L-FABP status and contrast agent dose. Correlation analysis initially revealed a positive significant association (r = 0.38; p = 0.003). This association was further examined by logistic regression analysis. A crude analysis revealed that for each 5-unit increase in contrast agent dose, a 1.08% increase in the odds of patients with altered 24-hour L-FABP was observed (OR: 1.08; 95% CI: 1.02-1.14; p = 0.013). In the same analysis adjusted for traditional confounders such as age, sex, and BMI, a significant association remained (OR: 1.07; 95% CI: 1.01-1.15; p= 0.028).

Discussion

Patients undergoing vascular procedures are at an increased risk of experiencing postoperative AKI.[13] The incidence of postoperative AKI requiring dialysis ranges from 5% to 15%, with preoperative renal impairment and severity of atherosclerotic disease as notable predictors of its occurrence.[14,15] Recent studies have identified several additional risk factors for AKI, including age >75 years (OR: 1.58; 95% CI: 1.11-2.26), treated hypertension (OR: 1.87; 95% CI: 1.28-2.74), hyperlipidemia, preoperative SCr level >150 mmol/L (OR: 2.75; 95% CI, 1.69-4.50), diabetes (OR: 1.67; 95% CI: 1.01-2.77), liver disease, BMI, high-risk surgery, symptomatic AAA (OR: 1.77; 95% CI: 1.24-2.52), supra/juxta AAA-related renal issues (OR: 2.17; 95% CI: 1.32-3.57), and chronic obstructive pulmonary disease (OR: 2.08; 95% CI: 1.45-2.97), and smoking.[16]

Compared to open AAA repair, EVAR is associated with lower rates of postoperative renal complications. The Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial, along with subsequent registry analyses, have narrowed this estimation to a range of 0.6% to 1.1%.[1,2,4,17] Patients developing postoperative AKI have an estimated 5-year survival rate of ∼53.5%, whereas those who require hemodialysis have an estimated 3-year survival rate of ∼22.8%.[17-20] According to the most widely accepted theories, the underlying pathophysiology is thought to involve medullary hypoxemia secondary to renal vasoconstriction, driven by alterations in nitric oxide and endothelin concentrations, as well as by the direct cytotoxic effects of the contrast medium.[5]

Following endovascular procedures, the search for the “holy grail” of renal biomarkers is ongoing. In the context of AKI, biomarkers are essential for early detection, diagnosis, prognosis, and monitoring of the disease. Different types of biomarkers can be identified based on their function. Functional biomarkers, such as SCr and blood urea nitrogen, reflect renal function. Damage biomarkers, on the other hand, provide insight into kidney injury. Remarkable examples include neutrophil gelatinase-associated lipocalin (NGAL), which is one of the earliest markers to rise in response to kidney tubule cells

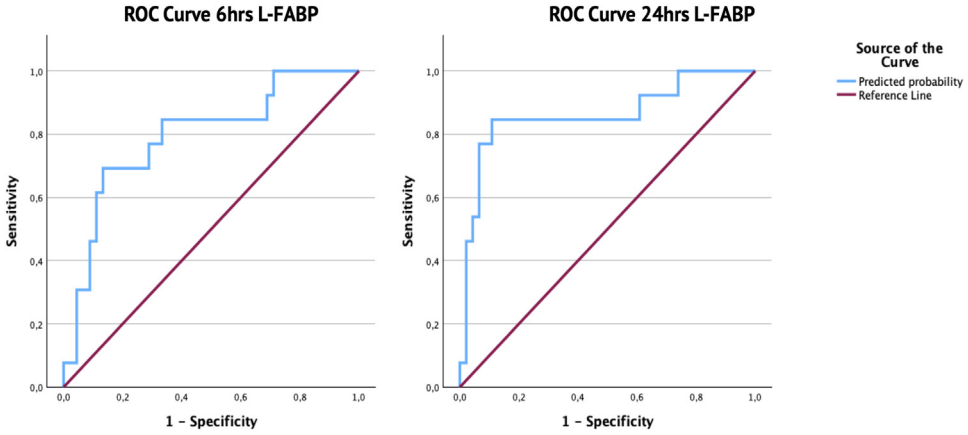

Fig 1. Receiver operating characteristic (ROC) curve analysis of the prognostic accuracy of models reported in Table 6 to discriminate patients with and without reduced diuresis (<0.5 mL/24 hours). The area under the ROC curve (AUC) was 0.793 (ie, 79.3%) and 0.861 (ie, 86.1%), respectively.

after injury and is measurable in the urine; interleukin 18, a cytokine up-regulated in response to inflammation and injury, particularly in the kidneys; cystatin C, a protein filtered by the kidneys and reabsorbed, providing an early indication of reduced eGFR; and L-FABP, which is elevated in the urine following renal injury. However, the presence of underlying pathologies poses additional challenges in differential diagnosis, as these conditions can alter both baseline biomarker excretion and performance. Endre et al[21] highlighted that cystatin C and kidney injury molecule 1 (KIM-1) levels are affected by hypovolemia. On the other hand, SCr responds more slowly following the onset of AKI and is of low sensitivity in patients with poor renal function or low muscle mass.[22] According to Li et al,[23] NGAL may be a more accurate early biomarker of contrast-induced nephropathy compared to SCr and eGFR in patients undergoing EVAR. Nonetheless, elevated NGAL levels may be detected in urine owing to other clinical factors, such as malignancy, urinary tract infections, medical treatments, and sepsis.[24] Unlike the other biomarkers, L-FABP is expressed in proximal tubular epithelial cells, where it is critically involved in lipid homeostasis. Specifically, it prevents the accumulation of intracellular free fatty acids (FFAs), promotes FA metabolism, and regulates gene expression involved in FA metabolism, thereby preventing FFA oxidation. In fact, FFAs are highly susceptible to oxidation, leading to oxidative stress in cells, which contributes to the development of numerous diseases.[25,26] L-FABP also has a significant role in the early diagnosis and management of AKI related to EVAR, although its clinical effectiveness has not yet been thoroughly assessed in vascular surgery.

Table 7
Multivariable logistic regression analysis of hospitalization (≥7 days)

Variable (units of increase)	OR	95% CI	p value
6-hour L-FABP (0: negative; 1: positive)	5.4	1.1-25.3	**0.033**
24-hour L-FABP (0: negative; 1: positive)	4.7	1.1-20.4	**0.039**

Adjusted model: age, sex, body mass index, postop serum creatinine, and postoperative estimated glomerular filtration rate.
Bold type indicates statistical significance.
Abbreviations: CI, confidence interval; L-FABP, liver-type fatty acid binding protein; OR, odds ratio.

The present analysis shows that L-FABP is a valuable biomarker for the early detection of AKI, providing an easy bedside point-of-care test that confirms, in real time, the trends of other validated biomarkers while using urine samples instead of blood. In this study, patients with positive L-FABP status at both 6 hours and 24 hours postsurgery had a worse renal function profile compared to patients with negative status. Furthermore, L-FABP not only correlated clearly with the other renal biomarkers considered (SCr and eGFR), but also proved to be a reliable marker, as 51 out of 58 patients maintained the same L-FABP status at both 6 hours and 24 hours postsurgery (data not shown). Significant associations were found between elevated L-FABP levels at both time points and an increased incidence of altered diuresis in patients. Specifically, reduced diuresis was observed in 50% of patients at 6 hours and in 71.4% at 24 hours in the L-FABP−positive groups, compared to just 13.6% and 6.7% in the respective L-FABP−negative groups, representing highly statistically meaningful differences ($p = 0.009$ and $p < 0.001$). The robustness of these associations was further validated through multivariable logistic regression analysis adjusted for potential confounders, such as postoperative creatinine level ≥1.2 mg/dL and eGFR <60 mL/min/1.73 m^2. Of note, the predictive model detailed in Table 6 demonstrated impressive accuracy in predicting reduced diuresis, achieving 79.3% accuracy (sensitivity: 69.2%; specificity: 86.7%) and 86.1% accuracy (sensitivity: 84.6%; specificity: 89.1%), respectively. These results align with data from several studies in the literature. Portilla et al[27] reported that in children undergoing cardiopulmonary bypass, L-FABP level at 4 hours is an independent risk factor for AKI, with an area under the receiver operating characteristic curve (AUC) of 81.0% (sensitivity: 71.4%; specificity: 68.4%), whereas Ferguson et al[28] found that in hospitalized patients with established AKI, the AUC of urinary L-FABP for AKI prediction was 93% (sensitivity: 83%; specificity: 90%). Furthermore, in a study of the early prediction of AKI after endovascular stent graft repair of aortic aneurysm, Ueta et al[29] reported an AUC of 87% for L-FABP (the 2- to 6-hour

postsurgical value), with a sensitivity and specificity of 83%. In our study, patients received hydration according to internal protocols: 0.5 mL/kg/hour for patients with an ejection fraction <40% and 1 mL/kg/hour for those with an ejection fraction >40%. No further diuretic treatments or new therapies were initiated during the observation period; therefore, L-FABP levels are not affected by urine volume.

To further investigate the potential of L-FABP, the present study considered the clinical endpoint of hospital LOS. Most of the patients (57.1%) had a longer hospital LOS (≥7 days) both at 6 hours and 24 hours in the L-FABP−positive groups, compared to 15.9% (p = 0.004) and 17.8% (p = 0.013) in the L-FABP−negative groups. These findings were fully confirmed by multivariable logistic regression models, including postoperative SCr ≥1.2 mg/dL and postoperative eGFR <60 mL/min/1.73 m^2 , indicating that L-FABP at both 6 hours and 24 hours predicted a longer hospital LOS, while SCr and eGFR did not.

Recent national surveys indicate that contrast agent is recognized as the primary cause of nephropathy in 6.7% of cases, posing a particularly significant risk for patients with reduced eGFR.[1] Despite the short-term ramifications, notably related to the nephrotoxic effects of contrast agents, such factors as a past medical history of cardiovascular diseases, the use of medical imaging contrast, aortic cross-clamping time, and intraoperative hemodynamic instability contribute to renal injury[18-20] Nevertheless, the exact mechanism by which contrast agents induce kidney injury remains unclear. Therefore, early AKI detection using L-FABP can improve outcomes.

Notwithstanding certain limitations, including the relatively small sample size and the possibility of residual confounding, no previous studies have investigated these associations and achieved robust results like those presented here or have emphasized the role of L-FABP with such a substantial impact on clinical practice. Connolly et al[30] studied L-FABP in acute renal damage caused by contrast agents during percutaneous coronary intervention and found a significant increase in L-FABP excretion at 1, 2, and 4 hours after the procedure in patients who developed contrast nephropathy.

Taken together, the present findings support L-FABP's potential as a valuable biomarker for the early detection of patients at risk for postoperative renal impairment. Early identification could facilitate timely and targeted interventions, potentially slowing the progression of renal insufficiency and improving overall patient outcomes.

Conclusions

Urinary L-FABP is emerging as a sensitive biomarker for AKI in patients undergoing EVAR. Given its strong association with postoperative renal dysfunction and clinical outcomes, L-FABP could serve as a valuable prognostic tool in this setting. Its clinical implementation should be considered, although further studies are needed to confirm these findings.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Domenico Abelardo: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Pasquale Raimondo:** Writing – original draft. **Cristina Santonocito:** Writing – original draft. **Alessio Barile:** Writing – original draft, Data curation. **Mauro D'Amora:** Data curation. **Andrea Esposito:** Data curation. **Martina Maria Giambra:** Data curation. **Maria Grazia Lumia:** Data curation. **Giovanni Mastrangelo:** Data curation. **Danilo Menna:** Data curation. **Francesco Murgolo:** Data curation. **Angelo Pascarella:** Data curation. **Rosetta Salvatore:** Data curation. **Rosaria Vignale:** Data curation. **Sergio Zacà:** Data curation. **Gianluca Paternoster:** Writing – review & editing, Supervision, Conceptualization.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2025.08.020.

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