FABP1, FABP2 and FABP3

Subjects: Biochemistry & Molecular Biology

Contributor: Shabarni Gaffar , A Sayyidatina Aathirah

Fatty-acid-binding proteins (FABPs) are a class of low-molecular-weight intracellular proteins that play a role as a transporter by binding to hydrophobic ligands, typically fatty acids, with different affinities, and are involved in the metabolism of these fatty acids (FAs). These hydrophobic ligands include, but are not limited to, saturated fatty acids, monounsaturated fatty acids (MUFAs), polyunsaturated fatty acids (PUFAs), eicosanoids, and other lipids. FABPs have been shown to be important in modulating lipid metabolism, gene regulation, and signal transmission. They have been thought of as the key mediators in the metabolic and inflammatory processes.

FABPs biomarkers overexpression

1. FABP1/L-FABP

L-FABP is extensively expressed in the liver (hepatocyte cytoplasm) and has been found in other tissues, like kidneys (renal tubules and proximal tubules), intestines (enterocytes), lungs, stomach, and pancreas [1][2][3]. L-FABP is believed to be capable of binding two ligands concurrently via two separate binding sites (low and high affinity); it can also bind molecules that have the potential to be cytotoxic, such as heme groups, apart from fatty acids [1][2].

In a study of infants with necrotizing enterocolitis (NEC), Benkoe et al. (2014) discovered a substantial rise in serum levels of I-FABP, L-FABP, and IL-8 (interleukin-8). Through their research, there were 15 infants with NEC involved and they were grouped into two groups based on different treatments, namely, medical NEC and surgical NEC. They measured the levels of I-FABP and L-FABP using ELISA and compared them with the level of IL-8 as a proinflammatory chemokine. The study has shown that all three have the ability to detect NEC, indicating that they could be potential biomarkers for the disease. Although the highest ratio between infants in the control group and infants with NEC was shown by IL-8 compared to both FABPs, they concluded that IL-8 is considered to be superior to I-FABP, its diagnostic ability is similar to L-FABP, and IL-8 is more significant as a biomarker for NEC [4]. However, the population tested in this study is still considered insufficiently representative, and further research with a larger population is needed to support the results of this study.

Furthermore, in multiple investigations, L-FABP has been investigated as a potential biomarker for liver and kidney injury [5][6][7][8][9]. It is thought to be a potential biomarker for acute kidney injury (AKI) [10][11]. Naruse et al. (2018) conducted a study on a population of 1273, which was divided into 224 patients with AKI and 1049 non-AKI. They collected urine and blood samples and measured the level of L-FABP using a latex-enhanced immunoturbidimetric assay. The results of this study reported that the combination of L-FABP and NT-proBNP measurements as the

early detection of AKI in patients provides better prediction. However, this study has limitations because the treatments in this study were not controlled or randomized, so the administration of different treatment strategies to patients may affect the evaluation, and the observation of its effects on the progression of AKI in patients becomes difficult. Nonetheless, multivariate logistic analyses performed with a variety of factors showed that this study has good significance and validity for AKI [12]. It has also been observed that L-FABP can distinguish between AKI and acute-on-chronic liver failure (ACLF) in cirrhotic patients. A study by Graupera et al. (2017) revealed that L-FABP has the potential to be applied as a biomarker for detecting liver injury caused by cirrhosis, as L-FABP levels were observed to be greater in individuals with cirrhosis compared to healthy subjects [13]. Through the research conducted by Belcher et al. (2014), testing was performed on 188 patients with cirrhosis and AKI by measuring L-FABP and other biomarker levels. The measurement of L-FABP in the study used anti-human L-FABP antibodies that have been developed and the ELISA method. The study concluded that L-FABP, along with three other biomarkers (NGAL/Neutrophil gelatinase-associated lipocalin, IL-18/Interleukin-18, and albumin), has a good and efficient ability to differentiate patients with progressive AKI and cirrhosis. Although this study has comprehensively observed each biomarker, it cannot standardize the treatments performed by patients, so the effect of treatment response on biomarker levels cannot be ascertained and assessed [14]. A similar study by Juanola et al. (2021) also indicates the potential of L-FABP as a biomarker of complications for patients with decompensated cirrhosis. This study was based on 444 patients with decompensated cirrhosis, and L-FABP measurements were performed using the Human L-FABP ELISA kit based on plasma and urine samples. The results of the study showed that L-FABP can predict the mortality rate and detect ACLF in patients with decompensated cirrhosis. However, there is still a need for further studies regarding the contribution of L-FABP in the development of ACLF which was not obtained through this study [15]. Furthermore, some researchers have suggested that L-FABP could be used as a biomarker for graft failure in kidney transplant recipients [3][16].

L-FABP was found to be useful in detecting hepatocyte injury in individuals having a liver resection, according to Van De Poll et al. (2007). Through this research, they studied ten patients undergoing liver resection and took arterial blood samples before and after the operation to measure the level of L-FABP. The number of test populations in the study is still too small to represent and strengthen the test results, but, through this study, a hypothesis was obtained regarding the participation of L-FABP in inflammation in the intestines and liver; thus, they concluded that L-FABP is referred to as an important biomarker in measuring patient plasma because of its role in systemic inflammation [17]. Based on the considerable increase in blood serum L-FABP levels in patients with acute hepatocellular damage, Pelsers et al. (2002) state that L-FABP can be used as a biomarker for diagnosing acute hepatocellular damage and sensitive liver transplant patients. The study was conducted on 21 liver transplant recipients; the criteria of the subjects were patients who had experienced acute hepatocellular rejection several times during the post-transplantation recovery process at the hospital. The results showed that L-FABP was as good as, or even better than, a-GST for early detection and had a significantly high level in liver transplant patients with acute hepatocellular damage. Although the number of patients studied was not sufficient to represent the research results and further research is needed on this finding, this study has been a good guide in the discovery of this hypothesis [18]. According to a study by Karvellas et al. (2017), serum L-FABP levels were measured in 198 patients with APAP-ALF using ELISA. It has been reported that serum L-FABP levels rise in patients with

acetaminophen-induced acute liver failure (APAP-ALF). Because an increase in serum L-FABP levels is related to an increased risk of patient mortality, L-FABP is suspected of having the capacity to discriminate between survivors and non-survivors in patients with APAP-ALF. This study is comprehensive and able to present the role and contribution of L-FABP in APAP-ALF quite clearly, making it a strong foundation to support the research data [19].

A substantial rise in serum levels of L-FABP was found in chronic hepatitis C (CHC) patients with liver injury compared to CHC patients without liver injury. According to Akbal et al. (2013), L-FABP had an 80% sensitivity and 100% specificity in diagnosing liver injury in CHC patients. In this study, testing was performed on 42 patients, consisting of 20 healthy controls and 22 patients with CHC. The results showed a strong correlation between the level of L-FABP and the level of hepatitis C virus (HCV) RNA, alanine aminotransferase, and hepatic inflammation. However, further research on these findings is needed, especially in the case of normal alanine aminotransferase and higher HCV RNA levels [20].

Other research has suggested that L-FABP, together with I-FABP, could be used as a marker to detect severe abdominal injuries in patients who have suffered numerous traumas. The study discovered an increase in both FABP levels in patients with multiple traumas compared to healthy subjects, which is associated with the severity of abdominal injury in patients. In this study, L-FABP and I-FABP levels were measured in blood samples from 102 patients with multiple traumas and 30 healthy subjects using ELISA. Although the results of the study showed good significance, future clinical research with a larger test population is needed to validate the potential of L-FABP and I-FABP as detectors of severe abdominal trauma in patients [21].

2. FABP2/I-FABP

I-FABP is expressed in stomach and intestinal epithelial cells and can be quantified in the form of plasma (I-FABPp) and urine (I-FABPu) [1][22]. I-FABP co-expresses with L-FABP and Il-FABP in the small intestine but is distributed differently. L-FABP is predominantly expressed in the proximal region, while Il-FABP is predominantly expressed in the distal region. I-FABP, on the other hand, is distributed throughout the intestine but is most abundant in the distal part [1]. I-FABP also plays an important role in the uptake of dietary fatty acids in enterocytes [23].

As mentioned before, in a study conducted by Benkoe et al. (2014), I-FABP was revealed as one of the relevant biomarkers for identifying NEC, and, although I-FABP has the lowest value among the three, they found the potential of I-FABP to differentiate between infants with surgical NEC and medical NEC to be in accordance with the increased level of I-FABP, but this increase did not reach statistical significance [4]. However, several additional papers have also suggested I-FABP's potential as a biomarker for NEC. In a study by Schurink et al. (2014), plasma I-FABP and urine I-FABP levels were evaluated in infants suspected of having NEC. In this study, measurements and analysis of I-FABP levels were conducted on urine and plasma samples from 37 infants with NEC using the ELISA method. The results of the study showed that both plasma I-FABP and urine I-FABP are significantly correlated with NEC and have the potential to develop a diagnostic method for infants with suspected NEC through the measurement of I-FABP. The study reports a strong correlation between urine I-FABP and other

conventional NEC biomarkers such as IL-6, WBC, and lactate. They hypothesized that NEC occurs due to ischemia of the upper villi, which leads to enterocyte damage and the subsequent release of I-FABP into the bloodstream. This is what connects I-FABP with lactate in the early stages of NEC. The test population size is still considered insufficient to represent and explain the participation of I-FABP in NEC onset, so further research is needed regarding the potential of I-FABP as a biomarker for NEC [22]. These findings are supported by Abdel Haie et al. (2017), which has a similar report about this hypothesis. This study was conducted on 160 preterm neonates who were less than 35 weeks old and weighed less than 2000 g. After the observation period, 18 of them developed NEC (group 1), while the remaining 10 were used as healthy controls (group 2). The I-FABP levels were measured in both groups using an ELISA kit. The results of the study showed an increase in I-FABP levels in neonates with NEC compared to healthy neonates. This increase in I-FABP levels was found to be correlated with the severity of NEC (stage 1, stage 2, and stage 3). Therefore, the researchers hypothesized that measuring I-FABP could be an early detection method for neonates with NEC. The statistical analysis also indicated that serum I-FABP has high specificity and sensitivity as a biomarker. However, the number of subjects tested was considered relatively low, and further research with a larger sample size focusing on the ability of I-FABP to differentiate the severity levels in neonates with NEC is needed to confirm the findings of this study [24][25].

Another study by El-Abd Ahmed et al. (2020) also supports the finding. In this study, plasma and urine I-FABP levels were analyzed by using ELISA on 55 neonates with NEC and 23 healthy neonates as controls. Through the study, it was reported that there is a different role between plasma I-FABP and urine I-FABP. Plasma I-FABP has been discovered as a potential detector of surgical NEC for early diagnosis, whereas urine I-FABP has been discovered as a marker that differentiates between Bell's stage II and Bell's stage III in NEC cases. The statistical analysis also mentioned that urine I-FABP has better specificity compared to plasma I-FABP, while both have the same sensitivity. This study provides deeper findings regarding the potential of I-FABP as a biomarker for NEC by conducting testing and comparing plasma and urine I-FABP in differentiating NEC stages [25]. The role of I-FABP in the pathogenicity of NEC has not been widely discussed. This could be a suggestion for further research so that the hypothesis regarding the potential of I-FABP as a biomarker for NEC can be supported by more comprehensive knowledge.

I-FABP has also been reported to detect intestinal ischemia based on several works of literature. Niewold et al. (2004) discovered that I-FABP levels rose in pigs with intestinal ischemia [26]. In their investigation of the involvement of I-FABP and D-lactate in intestinal ischemia, Shi et al. (2015) discovered a significant rise of the concentration levels of I-FABP and D-lactate. A total of 272 patients with severe abdominal pain symptoms had their blood samples taken to measure the levels of I-FABP and D-lactate using an ELISA kit. Among these patients, there were 39 patients diagnosed with intestinal ischemia and 233 patients who did not have ischemia. When enterocytes are damaged, I-FABP, a low-molecular-weight intracellular protein, is found exclusively in the small intestine and, consequently, released and circulated, resulting in a rise in I-FABP levels. The sensitivity and specificity of I-FABP have been reported to be 90.0% and 86.7%, respectively, for the detection of acute intestinal ischemia. Although I-FABP has the highest sensitivity compared to other biomarkers, its specificity is still lower than that of D-lactate, which has the highest value among other biomarkers. Therefore, the application of I-FABP as a single biomarker may not be recommended and combining it with D-lactate may provide better predictive results

[27]. Another study has found comparable results in terms of I-FABP's potential as a biomarker for acute intestinal ischemia, particularly in patients with small bowel ischemia. The analysis and measurement of I-FABP levels in 40 patients with symptoms of acute intestinal ischemia using an ELISA kit showed that I-FABP has a sensitivity and specificity of 95.7% and 88%, respectively. This study concluded that I-FABP is a novel biomarker that is fast, sensitive, specific, and cost-effective for intestinal/bowel ischemia. However, this study did not perform a comparative analysis with other biomarkers, so the application of I-FABP as a single biomarker for early detection and diagnosis cannot be confirmed based solely on these findings [28]. Camara-Lemarroy et al. (2021) similarly reported high serum I-FABP and D-lactate concentrations in individuals with acute ischemic stroke (AIS), confirming I-FABP's potential as a promising biomarker. In this study, 61 patients with acute ischemic stroke were tested for I-FABP levels using an ELISA kit. Among them, 20 patients had small-vessel disease, 20 patients had cardioembolic stroke, 21 patients had atherosclerosis, and 20 healthy patients were included as controls. The study considered the factors causing acute ischemic stroke as testing variations and hypothesized the possibility of intestinal mucosa/barrier damage in patients with acute ischemic stroke. However, this study has not been able to directly prove the occurrence of intestinal injury in patients with acute ischemic stroke. Therefore, further research with a larger number of test subjects is needed to validate these findings and investigate the mechanisms and correlation of I-FABP with acute ischemic stroke clinically [29].

A study by Vermeulen et al. (2012) also discovered that I-FABP has the potential to be applied as an early detection biomarker for intestinal necrosis in post-aortic surgery patients by measuring the circulating level of I-FABP. The testing in this study involved 96 patients who had undergone aortic surgery, classified into three groups: OR-TAA(A) (open repair of a thoracic or thoracoabdominal aortic aneurysm), AAA (open infrarenal or juxtarenal abdominal aortic aneurysm repair), and EVAR (endovascular aneurysm repair) with 55, 25, and 16 patients, respectively. The I-FABP level measurement was performed using an ELISA kit. The measurement results showed the potential of I-FABP in detecting intestinal injury in patients with open aortic repair, and no intestinal injury was detected in patients with EVAR. Further research with a larger population of patients is needed to test the ability of I-FABP to detect lethal postoperative intestinal injury to confirm the hypothesis in this study [30]. Another finding from Relja et al. (2010) also reported that I-FABP has the potential to be used as a marker for severe abdominal injury along with L-FABP, as previously mentioned [21].

3. FABP3/H-FABP

H-FABP is broadly expressed in numerous organs such as the brain, lungs, testis, and renal cortex. However, it is mainly expressed in skeletal muscle and the heart [1][31][32]. When there is muscle injury, H-FABP is involved in the transfer and metabolism of fatty acids and will be released into the circulation at the site of injury [31][32][33]. H-FABP is a small protein that regulates myocardial fatty acid metabolism, which is expressed in cardiomyocytes. Its expression concentration increases in acute ischemic stroke and acute myocardial injury (MI) conditions [34]. Additionally, H-FABP is exclusively expressed in neurons. While H-FABP is hardly noticeable in the brain during embryonic development, its expression increases gradually from birth until it reaches adulthood [35].

H-FABP has been associated with patients with chest pain, as mentioned in several studies. Bivona et al. (2018) conducted research on H-FABP and found that it can be used as a novel marker for acute coronary syndrome (ACS). A study found that individuals with acute coronary syndrome (ACS) had considerably greater levels of H-FABP expression than healthy controls. According to the study, H-FABP has the capacity to predict the risk of major adverse cardiovascular events (MACEs) in ACS patients [34]. Reddy et al. (2016) reported similar findings; through their study involving 88 patients with ACS and non-ACS, H-FABP had better sensitivity while its specificity was lower than hs-TropT. Therefore, the combination of hs-TropT and H-FABP can provide a more precise prediction for ACS than their separate use [36].

H-FABP is also referred to as a novel marker for the early detection of myocardial infarction. Collinson et al. (2014) compared the diagnostic accuracy between H-FABP and troponin for patients with myocardial infarction and they discovered that H-FABP can be used as a marker for diagnosing myocardial infarction. However, cardiac troponin is considered a better marker in terms of sensitivity. Combining both markers is believed to optimize the diagnostic method for myocardial infarction for patients with symptoms, such as chest pain. This study involved 850 randomized patients, and, after testing, 68 of them were diagnosed with myocardial infarction. The test results reported that the detection ability of H-FABP is lower than troponin, but the combination of both can increase diagnostic sensitivity. Therefore, H-FABP is not recommended as a single biomarker because its specificity is lower than that of troponin. Nevertheless, this study has reported comprehensive findings on the potential of H-FABP as a myocardial infarction biomarker, and the test subject scale is sufficient to represent the reported findings [37]. This statement is supported by Vupputuri et al. (2015), which reported that H-FABP is a biomarker with high sensitivity and has the potential to be developed for the acute myocardial injury (AMI) early detection biomarker and can even be used for patients with unstable angina. This study involved 54 patients with acute chest pain by measuring the level of H-FABP and other biomarkers using a latex-enhanced immunoturbidimetric assay. The test results showed that H-FABP has a greater sensitivity compared to other biomarkers, making it a better choice for early detection. Therefore, combining H-FABP as the early detection biomarker and cardiac troponin as the late detection marker can potentially develop an optimal method for diagnosing myocardial injury [38].

Pyati et al. (2015) stated that H-FABP can be applied as the early detector of myocardial injury and is even considered a better early detector for acute myocardial injury due to its sensitivity and specificity in patients with chest pain within 3–6 h of symptom onset compared to CK-MB and myoglobin. This study involved 40 patients with AMI and 40 healthy controls, with CK-MB, myoglobin, and H-FABP levels measured using immunoturbidimetric, immunoinhibition, and chemiluminescence immunoassay methods, respectively. The test results showed that H-FABP had the highest PPV (positive predictive value), NPV (negative predictive value), specificity, and sensitivity compared to the other two biomarkers in detecting patients with AMI. Although this study has provided significant data and comprehensive methods, the number of patients tested is considered insufficient. Further testing with a larger sample size will be able to confirm the findings of this study [39]. Agnello et al. (2017) also reported that H-FABP can detect chest pain in patients more sensitively within one hour of symptom onset compared to cardiac troponin. This study involved 28 patients with AMI and 28 patients with non-AMI who experienced chest pain within an hour of the onset of pain. The measurement of H-FABP and hs-TnI (cardiac troponin) in the patient's blood samples was performed using an immunoturbidimetric assay. However, the specificity of H-FABP is still lower than

hs-TnI. Therefore, the application of H-FABP as a single marker is still considered inadequate. In addition, this study used a very small sample size, so the validity of these findings cannot be confirmed until further testing is conducted with a more sufficient population size. Nevertheless, the ability of H-FABP to detect AMI in patients with chest pain within an hour is a great potential that can prevent fatal conditions from occurring in patients and provide an opportunity for faster treatment if the development of H-FABP as a biomarker can be further studied [40]. In addition, H-FABP is also mentioned as a novel biomarker that has the ability to predict the diagnosis and prognosis of peripheral arterial disease (PAD), by measuring H-FABP and other biomarkers in 1200 patients with PAD and non-PAD using ELISA. The test results reported that H-FABP and N-terminal pro-B-type natriuretic peptide have the best predictive ability among other biomarkers. H-FABP is strongly associated with the severity of PAD and shows the strongest correlation with PAD and CLI (critical limb ischemia) with sensitivity and specificity values of 91% and 100%, respectively [41]. This is due to its high expression in PAD patients with a history of coronary arterial disease (CAD) or diabetes mellitus, as H-FABP is released and circulates when skeletal muscle injury occurs [42].

In addition to its potential as a biomarker for myocardial injury and peripheral arterial disease, H-FABP is also being studied as a novel biomarker for Alzheimer's disease (AD). Guo et al. (2013) found that combining H-FABP and VEGF in cerebrospinal fluid (CSF) with previously discovered markers, namely, $A\beta_{1–42}$, tTau, and $pTau_{181}$, is an optimal early diagnostic method for AD. The study involved 149 patients with mild cognitive impairment (MCI), 69 patients with AD dementia, and 92 controls. The test results showed that H-FABP and VEGF (vascular endothelial growth factor) were able to detect AD dementia, and H-FABP was said to be capable of predicting the progression of MCI into AD in patients, but the specificity and sensitivity of FABP were lower than those of VEGF. They reported that optimal detection was achieved when H-FABP and VEGF were combined with the three established markers, resulting in an increase in specificity and sensitivity to 86% and 83%, respectively. This study did not analyze the relationship between H-FABP and VEGF and cardiovascular risk in AD patients. Further research to analyze the impact of cardiovascular risk on AD patients may be needed to better understand the correlation between H-FABP and AD pathology [43]. Sepe et al. (2018) also reported that H-FABP is related to the accumulation pathway of α-Syn and the deregulation of dopaminergic pathways in synucleinopathy, and found that the expression level of H-FABP is associated with α-Syn aggregation in synucleinopathy [44]. However, this mechanism is still not clearly understood and requires further research.

References

1. Furuhashi, M.; Hotamisligil, G.S. Fatty Acid-Binding Proteins: Role in Metabolic Diseases and Potential as Drug Targets. Nat. Rev. Drug Discov. 2008, 7, 489–503.
2. Wang, G.Q.; Bonkovsky, H.L.; De Lemos, A.; Burczynski, F.J. Recent Insights into the Biological Functions of Liver Fatty Acid Binding Protein 1. J. Lipid Res. 2015, 56, 2238–2247.

3. Malyszko, J.; Lukaszyk, E.; Glowinska, I.; Durlik, M. Biomarkers of Delayed Graft Function as a Form of Acute Kidney Injury in Kidney Transplantation. Sci. Rep. 2015, 5, 11684.
4. Benkoe, T.M.; Mechtler, T.P.; Weninger, M.; Pones, M.; Rebhandl, W.; Kasper, D.C. Serum Levels of Interleukin-8 and Gut-Associated Biomarkers in Diagnosing Necrotizing Enterocolitis in Preterm Infants. J. Pediatr. Surg. 2014, 49, 1446–1451.
5. Yanishi, M.; Kinoshita, H. Urinary L-Type Fatty Acid-Binding Protein Is a Predictor of Cisplatin-Induced Acute Kidney Injury. BMC Nephrol. 2022, 23, 125.
6. Eguchi, A.; Hasegawa, H.; Iwasa, M.; Tamai, Y.; Ohata, K.; Oikawa, T.; Sugaya, T.; Takei, Y. Serum Liver-Type Fatty Acid–Binding Protein Is a Possible Prognostic Factor in Human Chronic Liver Diseases From Chronic Hepatitis to Liver Cirrhosis and Hepatocellular Carcinoma. Hepatol. Commun. 2019, 3, 825–837.
7. Sunayama, T.; Matsue, Y.; Yatsu, S.; Dotare, T.; Ishiwata, S.; Suda, S.; Kato, T.; Hiki, M.; Kasai, T.; Minamino, T. Prognostic implication of tubular injury defined by urinary liver-type fatty acid binding protein in patients with acute heart failure. J. Am. Coll. Cardiol. 2021, 77, 731.
8. Gokcen, P.; Cakmak, E.; Adali, G.; Dogan, H.O.; Yildiz, S.N.; Ozturk, O.; Doganay, H.L.; Ozdil, K. Liver Fatty Acid Binding Protein: Is It an Early Diagnostic and Prognostic Marker in Liver Damage? Med. Sci. Discov. 2021, 8, 213–218.
9. Obata, Y.; Kamijo-Ikemori, A.; Inoue, S. Clinical Utility of Urinary Biomarkers for Prediction of Acute Kidney Injury and Chronic Renal Dysfunction after Open Abdominal Aortic Aneurysm Repair. Int. J. Nephrol. Renovasc. Dis. 2021, 14, 371–384.
10. Alge, J.L.; Arthur, J.M. Biomarkers of AKI: A Review of Mechanistic Relevance and Potential Therapeutic Implications. Clin. J. Am. Soc. Nephrol. 2015, 10, 147–155.
11. Malhotra, R.; Siew, E.D. Biomarkers for the Early Detection and Prognosis of Acute Kidney Injury. Clin. J. Am. Soc. Nephrol. 2017, 12, 149–173.
12. Naruse, H.; Ishii, J.; Takahashi, H.; Kitagawa, F.; Nishimura, H.; Kawai, H.; Muramatsu, T.; Harada, M.; Yamada, A.; Motoyama, S.; et al. Predicting Acute Kidney Injury Using Urinary Liver-Type Fatty-Acid Binding Protein and Serum N-Terminal pro-B-Type Natriuretic Peptide Levels in Patients Treated at Medical Cardiac Intensive Care Units. Crit. Care 2018, 22, 197.
13. Graupera, I.; Coll, M.; Pose, E.; Elia, C.; Piano, S.; Solà, E.; Blaya, D.; Huelin, P.; Solé, C.; Moreira, R.; et al. Adipocyte Fatty-Acid Binding Protein Is Overexpressed in Cirrhosis and Correlates with Clinical Outcomes. Sci. Rep. 2017, 7, 1829.
14. Belcher, J.M.; Sanyal, A.J.; Peixoto, A.J.; Perazella, M.A.; Lim, J.; Thiessen-Philbrook, H.; Ansari, N.; Coca, S.G.; Garcia-Tsao, G.; Parikh, C.R. Kidney Biomarkers and Differential Diagnosis of Patients with Cirrhosis and Acute Kidney Injury. Hepatology 2014, 60, 622–632.

15. Juanola, A.; Graupera, I.; Elia, C.; Piano, S.; Solé, C.; Carol, M.; Pérez-Guasch, M.; Bassegoda, O.; Escudé, L.; Rubio, A.B.; et al. Urinary L-FABP Is a Promising Prognostic Biomarker of ACLF and Mortality in Patients with Decompensated Cirrhosis. J. Hepatol. 2022, 76, 107–114.
16. Yepes-Calderón, M.; Sotomayor, C.G.; Pena, M.; Eisenga, M.F.; Gans, R.O.B.; Berger, S.P.; Moers, C.; Sugaya, T.; Doekharan, D.; Navis, G.J.; et al. Urinary Liver-Type Fatty Acid-Binding Protein Is Independently Associated with Graft Failure in Outpatient Kidney Transplant Recipients. Am. J. Transplant. 2021, 21, 1535–1544.
17. Van De Poll, M.C.G.; Derikx, J.P.M.; Buurman, W.A.; Peters, W.H.M.; Roelofs, H.M.J.; Wigmore, S.J.; Dejong, C.H.C. Liver Manipulation Causes Hepatocyte Injury and Precedes Systemic Inflammation in Patients Undergoing Liver Resection. World J. Surg. 2007, 31, 2033–2038.
18. Pelsers, M.M.A.L.; Morovat, A.; Alexander, G.J.M.; Hermens, W.T.; Trull, A.K.; Glatz, J.F.C. Liver Fatty Acid-Binding Protein as a Sensitive Serum Marker of Acute Hepatocellular Damage in Liver Transplant Recipients. Clin. Chem. 2002, 48, 2055–2057.
19. Karvellas, C.J.; Speiser, J.L.; Tremblay, M.; Lee, W.M.; Rose, C.F. Elevated FABP1 Serum Levels Are Associated with Poorer Survival in Acetaminophen-Induced Acute Liver Failure. Hepatology 2017, 65, 938–949.
20. Akbal, E.; Köklü, S.; Koçak, E.; Çakal, B.; Güneş, F.; Başar, Ö.; Tuna, Y.; Şenes, M. Liver Fatty Acid-Binding Protein Is A Diagnostic Marker to Detect Liver Injury Due to Chronic Hepatitis C Infection. Arch. Med. Res. 2013, 44, 34–38.
21. Relja, B.; Szermutzky, M.; Henrich, D.; Maier, M.; De Haan, J.J.; Lubbers, T.; Buurman, W.A.; Marzi, I. Intestinal-FABP and Liver-FABP: Novel Markers for Severe Abdominal Injury. Acad. Emerg. Med. 2010, 17, 729–735.
22. Schurink, M.; Scholten, I.G.H.; Kooi, E.M.W.; Hulzebos, C.V.; Kox, R.G.; Groen, H.; Heineman, E.; Bos, A.F.; Hulscher, J.B.F. Intestinal Fatty Acid-Binding Protein in Neonates with Imminent Necrotizing Enterocolitis. Neonatology 2014, 106, 49–54.
23. Gajda, A.M.; Storch, J. Enterocyte Fatty Acid-Binding Proteins (FABPs): Different Functions of Liver and Intestinal FABPs in the Intestine. Prostaglandins Leukot. Essent. Fat. Acids 2015, 93, 9–16.
24. Abdel-Haie, O.M.; Behiry, E.G.; Abd Almonaem, E.R.; Ahmad, E.S.; Assar, E.H. Predictive and Diagnostic Value of Serum Intestinal Fatty Acid Binding Protein in Neonatal Necrotizing Enterocolitis (Case Series). Ann. Med. Surg. 2017, 21, 9–13.
25. El-Abd Ahmed, A.; Hassan, M.H.; Abo-Halawa, N.; Abdel-Razik, G.M.; Moubarak, F.A.; Sakhr, H.M. Lactate and Intestinal Fatty Acid Binding Protein as Essential Biomarkers in Neonates with Necrotizing Enterocolitis: Ultrasonographic and Surgical Considerations. Pediatr. Neonatol. 2020, 61, 481–489.

26. Niewold, T.A.; Meinen, M.; van der Meulen, J. Plasma Intestinal Fatty Acid Binding Protein (I-FABP) Concentrations Increase Following Intestinal Ischemia in Pigs. Res. Vet. Sci. 2004, 77, 89–91.
27. Shi, H.; Wu, B.; Wan, J.; Liu, W.; Su, B. The Role of Serum Intestinal Fatty Acid Binding Protein Levels and D-Lactate Levels in the Diagnosis of Acute Intestinal Ischemia. Clin. Res. Hepatol. Gastroenterol. 2015, 39, 373–378.
28. Girish, T.U.; Hegde, A. Intestinal Fatty Acid Binding Protein (I-FABP) as a Marker for Acute Intestinal Ischemia. Int. Surg. J. 2019, 6, 374–380.
29. Camara-Lemarroy, C.R.; Escobedo-Zúñiga, N.; Guzmán-de la Garza, F.J.; Castro-Garza, J.; Vargas-Villarreal, J.; Góngora-Rivera, F. D-Lactate and Intestinal Fatty Acid-Binding Protein Are Elevated in Serum in Patients with Acute Ischemic Stroke. Acta Neurol. Belg. 2021, 121, 87–93.
30. Vermeulen Windsant, I.C.; Hellenthal, F.A.; Derikx, J.P.M.; Prins, M.H.; Buurman, W.A.; Jacobs, M.J.; Schurink, G.W.H. Circulating Intestinal Fatty Acid-Binding Protein as an Early Marker of Intestinal Necrosis after Aortic Surgery: A Prospective Observational Cohort Study. Ann. Surg. 2012, 255, 796–803.
31. Smathers, R.L.; Petersen, D.R. The Human Fatty Acid-Binding Protein Family: Evolutionary Divergences and Functions. Hum. Genom. 2011, 5, 170–191.
32. Varrone, F.; Gargano, B.; Carullo, P.; Di Silvestre, D.; De Palma, A.; Grasso, L.; Di Somma, C.; Mauri, P.; Benazzi, L.; Franzone, A.; et al. The Circulating Level of FABP3 Is an Indirect Biomarker of MicroRNA-1. J. Am. Coll. Cardiol. 2013, 61, 88–95.
33. Burch, P.M.; Hall, D.G.; Walker, E.G.; Bracken, W.; Giovanelli, R.; Goldstein, R.; Higgs, R.E.; King, N.M.P.; Lane, P.; Sauer, J.M.; et al. Evaluation of the Relative Performance of Drug-Induced Skeletal Muscle Injury Biomarkers in Rats. Toxicol. Sci. 2016, 150, 247–256.
34. Bivona, G.; Agnello, L.; Bellia, C.; Lo Sasso, B.; Ciaccio, M. Diagnostic and Prognostic Value of H-FABP in Acute Coronary Syndrome: Still Evidence to Bring. Clin. Biochem. 2018, 58, 1–4.
35. Mita, R.; Beaulieu, M.J.; Field, C.; Godbout, R. Brain Fatty Acid-Binding Protein and ω-3/ω-6 Fatty Acids. J. Biol. Chem. 2010, 285, 37005–37015.
36. Reddy, L.L.; Shah, S.A.V.; Dherai, A.J.; Ponde, C.K.; Ashavaid, T.F. Troponin T and Heart Type Fatty Acid Binding Protein (h-Fabp) as Biomarkers in Patients Presenting with Chest Pain. Indian J. Clin. Biochem. 2016, 31, 87–92.
37. Collinson, P.; Gaze, D.; Goodacre, S. Comparison of Contemporary Troponin Assays with the Novel Biomarkers, Heart Fatty Acid Binding Protein and Copeptin, for the Early Confirmation or Exclusion of Myocardial Infarction in Patients Presenting to the Emergency Department with Chest Pain. Heart 2014, 100, 140–145.

38. Vupputuri, A.; Sekhar, S.; Krishnan, S.; Venugopal, K.; Natarajan, K.U. Heart-Type Fatty Acid-Binding Protein (H-FABP) as an Early Diagnostic Biomarker in Patients with Acute Chest Pain. Indian Heart J. 2015, 67, 538–542.
39. Pyati, A.K.; Devaranavadagi, B.B.; Sajjannar, S.L.; Nikam, S.V.; Shannawaz, M.; Sudharani. Heart-Type Fatty Acid Binding Protein: A Better Cardiac Biomarker than CK-MB and Myoglobin in the Early Diagnosis of Acute Myocardial Infarction. J. Clin. Diagn. Res. 2015, 9, BC08.
40. Agnello, L.; Bivona, G.; Novo, G.; Scazzone, C.; Muratore, R.; Levantino, P.; Bellia, C.; Lo Sasso, B.; Ciaccio, M. Heart-Type Fatty Acid Binding Protein Is a Sensitive Biomarker for Early AMI Detection in Troponin Negative Patients: A Pilot Study. Scand. J. Clin. Lab. Investig. 2017, 77, 428–432.
41. Jain, S.; Khan, H.; Afxentiou, S.; Abdin, R.; Harlock, J.; Narang, T.; Wheatcroft, M.; Hussain, M.; Singh, K.; Qadura, M. Status of Cardiac Markers in Patients With Peripheral Arterial Disease and Critical Limb Ischemia. J. Vasc. Surg. 2018, 68, e68–e69.
42. Syed, M.H.; Zamzam, A.; Khan, H.; Singh, K.; Forbes, T.L.; Rotstein, O.; Abdin, R.; Eikelboom, J.; Qadura, M. Fatty Acid Binding Protein 3 Is Associated with Peripheral Arterial Disease. JVS Vasc. Sci. 2020, 1, 168–175.
43. Guo, L.H.; Alexopoulos, P.; Perneczky, R. Heart-Type Fatty Acid Binding Protein and Vascular Endothelial Growth Factor: Cerebrospinal Fluid Biomarker Candidates for Alzheimer’s Disease. Eur. Arch. Psychiatry Clin. Neurosci. 2013, 263, 553–560.
44. Sepe, F.N.; Chiasserini, D.; Parnetti, L. Role of FABP3 as Biomarker in Alzheimer’s Disease and Synucleinopathies. Future Neurol. 2018, 13, 199–207.