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Comparation of intestinal fatty acid binding protein (I-FABP) level between pre- and post-surgery and its associated determinants in patients with microscopic otorhinolaryngology surgeries

Yuda Atmajaya[1], Mohammad Satriyo Wibowo[1], Prananda Surya Airlangga[1], Maulydia[1*], Prihatma Kriswidyatomo[1], Muhtarum Yusuf[1], Budi Utomo[1]

ABSTRACT

Introduction: Intestinal fatty acid binding protein (I-FABP) is expected could be used as predictor of tissue hypoperfusion. This study sought to compare the level of I-FABP between pre- and post-surgery and its associated determinants in patients with otorhinolaryngology surgeries using general anesthesia with controlled hypotension (CH) technique.

Methods: We did a cross-sectional study was conducted among patients that underwent elective surgeries at Dr. Soetomo in Surabaya, Indonesia. Those who underwent surgeries using general anesthesia with CH technique were recruited in the study. I-FABP levels were measured using ELISA 1 hour before the surgery and 30 minutes after general anesthesia ended. Fisher's exact test and Mann-Whitney test were used to determine the determinants associated with changes of I-FABP level between pre- and post-surgery.

Results: A total of 31 patients who underwent the surgeries with general anesthesia and CH technique were included in this study. The median of I-FABP level pre- and post-surgery was 0.639 ng/mL to 0.779 ng/mL, respectively suggesting there was a significant increase of I-FABP level after the CH technique ($p<0.001$). Gender and ASA score did not associate with I-FABP level changes pre- and post-surgery with p=0.333 and 0.060, respectively. Age, BMI did not associate with changes of I-FABP level between pre- and post-surgery ($p=0.747$ and $p=0.051$, respectively). Surgery duration, anesthesia duration, systolic, diastolic and MAP all also had no association with changes of the I-FABP level with p>0.05.

Conclusion: The levels of I-FABP increased significantly in post-surgery in patients with otorhinolaryngology surgeries using general anesthesia with CH. Further studies are warranted to confirm this result with bigger sample size.

Keywords: I-FABP, controlled hypotension, hypoperfusion, otorhinolaryngology.

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[1]Department of Anesthesiology and Reanimation, Faculty of Medicine, Universitas Airlangga - Dr Soetomo General Academic Hospital, Surabaya, 60132, Indonesia;

*Corresponding author:
Maulydia;
Department of Anesthesiology and Reanimation, Faculty of Medicine, Universitas Airlangga, Surabaya, 60132, Indonesia;
drmoly_sby@yahoo.com

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INTRODUCTION

General anesthesia is a common anesthetic technique used to make the operation easier for the operator, to provide patient comfort, and to prevent the patient from getting up or moving during the procedure.[1] In microscopic otorhinolaryngology surgeries, anesthesiologists should manage hemostasis because complicated bleeding tends to make visualization difficult.[2] There are several methods to reduce the amount of bleeding, including a 15-degree head elevation position, adrenaline infiltration at a dose of 1:50,000-1:200,000, and a controlled hypotension (CH).[3,4]

CH is one of the techniques applied in microscopic otorhinolaryngology surgeries to minimize the amount of bleeding, increase visualization of the operating field, shorten the duration of the operation, and reduce the risk of complications.[5] It is conducted by lowering systolic blood pressure to the range of 80-90 mmHg with mean arterial pressure (MAP) 50–65 mmHg, or reducing the MAP 20–30% from baseline.[6] Blood pressure, MAP, pulse oximetry, capnography, electrocardiograph (ECG), temperature, and urine production must all be monitored during CH technique. However, the CH technique has its own risks or complications that may occur to the patients.[7] Following surgery, complications such as renal hypoperfusion, thromboembolism, myocardial ischemia, and hyponatremia could occur.[8,9] The mortality rate from CH caused by organ ischemia is approximately 0.02–0.06%.[10] When the MAP is maintained at 40-50 mmHg, the brain, heart, liver, and kidneys have the ability to automatically regulate blood flow via intrinsic mechanisms of vascular smooth muscle, and vasodilators are produced in tissues.[10] However, there is a scarcity of data on gastrointestinal and skin hypoperfusion symptoms. When there is ischemia, the gastrointestinal mucosa, skin, and subcutaneous tissue are all extremely vulnerable.

Signs of tissue hypoperfusion could be indicated by a rising of the level of intestinal fatty acid binding protein (I-FABP). FABP is one of the intracellular proteins, with a low molecular weight of about 15 kDa, which plays an important role in the transport and metabolism of long-chain fatty acids. FABP family proteins can be used as tissue-specific injury markers based on the following FABP characteristics: (1) cytoplasmic soluble protein, (2) high tissue specificity, (3) tissue abundance, and (4) low molecular weight. Among the FABP family proteins, I-FABP is specific and abundant present in the epithelial cells of the mucosal lining of small intestinal tissues. I-FABP is also thought to be released rapidly into circulation right after the small intestinal mucosal tissue is injured.[11] This study was conducted to compare the level of I-FABP between pre- and post-surgery among patients underwent microscopic otorhinolaryngology surgeries with CH technique and to determine the plausible its associated determinants. Such biomarker is important since sensitive and specific biomarkers or predictors are critical to diagnosis dan prognosis of the diseases.[12-19]

METHODS

Study design and sample criteria

This study was a prospective observational analytic study to assess I-FABP levels in patients underwent microscopic otorhinolaryngology surgeries with CH technique. The study was conducted at the Integrated Surgery Center of Dr Soetomo General Academic Hospital in Surabaya Indonesia. The patients who underwent elective tympanoplasty, mastoidectomy, septoplasty, rhinoplasty, and functional endoscopic sinus surgery (FESS) were recruited. Patients 18–59 years old, underwent elective surgery with general anesthesia and had physical status with American Society of Anesthesiologists (ASA) I-II were included. We excluded all the patients with hypertension, pregnancy, anemia, diabetes mellitus, had a history of allergy to anesthetic drugs; had significant heart, liver, or kidney disorders; had a history of gastrointestinal disorders; a history of orthostatic hypotension, and a history of intracranial disease.

Data collection

Patients who met the inclusion criteria were recruited into the study. Preoperative I-FABP level was measured one hour before induction of anesthesia (defined as the baseline level). When the anesthesia process was about to begin, the initial values of MAP and Bispectral index were recorded in advance. General anesthesia was induced by administering fentanyl 1–2 mcg/kg IV, propofol 1–2 mg/kg IV, rocuronium 0.6–1.2 mg/kg IV, and pre oxygenated 100% FiO2 for five minutes. During maintenance of anesthesia, the patient was given the intraoperative analgesic fentanyl 1 mcg/kgBW intermittent intravenously. Inhaled gas isoflurane 1.2 Vol% FiO2 40% flow 3 lpm, tidal volume 8 ml/kg, frequency 16 x/minute with target $EtCO_2$ 35 and target SpO_2 >95%. MAP and Bispectral index were recorded every 15 minutes after induction of anesthesia. Techniques to minimize the amount of bleeding during surgery were carried out using head up 15 degree and controlled hypotension. The target MAP used was 60–70 mmHg during the controlled hypotension technique. If the MAP value is >70 mmHg, the anesthetic agent dose was increased by increasing the dose of inhaled gas and propofol bolus 0.25–0.50 mg/kg IV with a Bispectral index target of 40–60. If after the anesthetic dose was increased and there was a decrease in MAP <50 mmHg or systolic blood pressure <80 mmHg, then a 5–10 mg IV bolus of ephedrine was given. The next I-FABP level examination was performed 30 minutes after anesthesia/extubation. Demographic data such as gender, height, weight, and educational attainment were also collected.

ELISA examination of blood samples for I-FABP levels

Venous blood samples were collected and mixed for 10–20 minutes with EDTA or heparin as an anticoagulant. The samples were centrifuged at 2000–3000 RPM for 20 minutes. The supernatants were collected and then the I-FABP was measured using the Human Fatty Acid Binding Protein 2 ELISA Kit following the manufacturer's protocol (BT Lab, Birmingham, UK).

Statistical analysis

All demographic data were summarized using descriptive statistics. All ratio measurement data were presented as mean ± standard deviation. A paired difference test was used to assess the changes in I-FABP levels before and after the surgery. Since the data were not normally distributed, the Wilcoxon signed-rank test was used. The results were considered significant at $p<0.05$. SPSS software was used for all analyses (SPSS Inc., Chicago, IL, USA).

RESULTS

Characteristics of the patients

We included 31 patients who underwent the microscopic surgeries and the characteristics of the patients are presented in Table 1. There were 16 males and 15 females with the mean age were 31.7 years. The patients received canal wall up (CWU), canal wall down (CWD), septoplasty turbinoplasty, and FESS with mean surgery time was 184 minutes. The mean systolic, diastolic and the MAP during the surgeries was 96.6 mmHg, 57.5 mmHg and 70.5 mmHg, respectively.

Level of I-FABP pre- and post-surgery

We measured the level of I-FABP before and after the surgery for all the patients. The median of I-FABP before the surgery was 0.639 ng/mL while the mean of I-FABP post-surgery increased to 0.779 ng/mL. The levels of I-FABP pre- and post-surgery of the patients are presented in Table 1 and Figure 1. Our data suggested that there was significant increase of I-FABP levels after otorhinolaryngology surgeries using general anesthesia with CH.

Associated determinants with changes of I-FABP level pre- and post-surgery

Associated determinants with changes of I-FABP level between pre- and post-surgery were assessed including gender, age, BMI, anesthesia duration, MAP, systolic and diastolic blood pressure (Table 3 and Table 4). Our data suggested that gender and ASA score did not associate

Table 1. Characteristics of patients included in the study (*n*=31).

Characteristics	Frequency (%)
Gender	
Male	16 (51.6)
Female	15 (48.4)
ASA score	
ASA 1	12 (38.7)
ASA 2	19 (61.3)
Age (year), mean±SD	31.74±11.41
BMI (kg/m²), mean±SD	22.2±3.6
Surgery duration (minute), mean±SD	184.8±49.6
Anesthesia duration (minute), mean±SD	200±48.8
MAP (mmHg), mean±SD	70.5±2.1
Systolic (mmHg), mean±SD	96.6±3.9
Diastolic (mmHg), mean±SD	57.5±1.9

Table 2. The level of I-FABP before and after microscopic otorhinolaryngology surgeries with a controlled hypotension.

I-FABP level	Number of patients	Median (range), ng/mL	p-value
I-FABP Pre	31	0.639 (0.182 – 6.082)	<0.001
I-FABP Post	31	0.779 (0.192 – 7.088)	

Table 3. Determinants associated with changes of I-FABP level between pre- and post-surgery in patient with otorhinolaryngology surgeries.

Determinant	Frequency (%)	Changes of I-FABP		p-value*
		Increase	Decrease	
Gender				0.333
Male	16 (51.6)	4 (25.0)	12 (75.0)	
Female	15 (48.4)	1 (6.7)	14 (93.3)	
ASA score				0.060
ASA 1	12 (38.7)	4 (33.3)	8 (66.7)	
ASA 2	19 (61.3)	1 (5.3)	18 (94.7)	

*Analyzed using Fisher's exact test

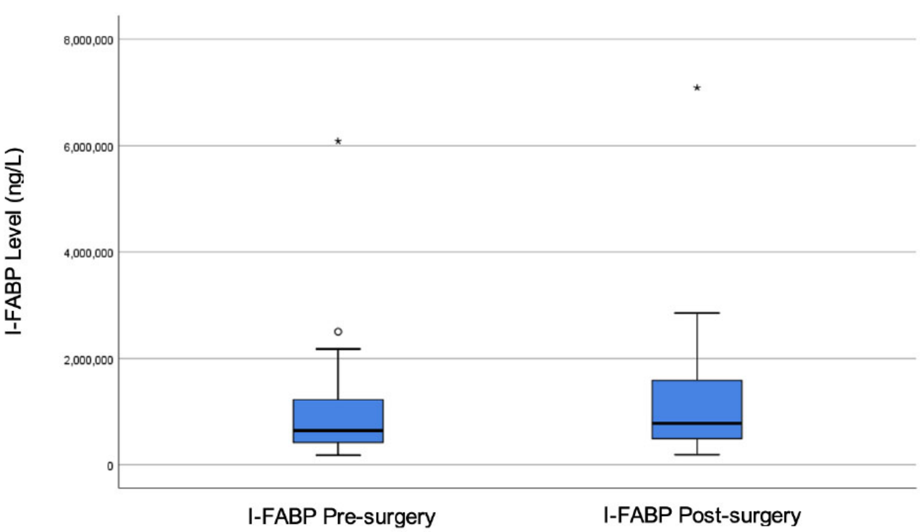

Figure 1. Comparation of I-FABP level between pre- and post-surgery in patient with otorhinolaryngology surgeries. The data are presented in ng/L.

with I-FABP level changes pre- and post-surgery with p=0.333 and p=0.060, respectively (Table 3).

Our data also suggested that age and BMI did not associate with changes of I-FABP level between pre- and post-surgery (p=0.747 and p=0.051, respectively) (Table 3). Nevertheless, the changes of I-FABP level were relatively different based on BMI; 25.2 and 21.7 for decreased and increased I-FABP level between pre- and post-surgery, respectively. Surgery duration and anesthesia duration also had no association with changes of the I-FABP level. Related to blood pressure, all systolic, diastolic and MAP all had no association with changes of the I-FABP level in the patients (Table 3).

DISCUSSION

CH could induce hypoxia by decreasing or suppressing microvascular autoregulation in vital organs and inhibiting the nervous system's autonomic effects. A countercurrent exchange mechanism, a hyperosmolar environment at the tips of the intestinal villi, explains the susceptibility of the mature enterocyte population to low blood flow and ischemic conditions. Reduced splanchnic perfusion could cause damage and loss of integrity of the epithelial cells.[20] This in particular due to oxidative stress and inflammation.[21] This epithelial dysfunction could cause increased GI permeability.[22] and loss of tight junction proteins.[23] Translocated bacteria may have increased permeability and translocation, and tight junction proteins are rapidly redistributed to effectively restore the intestinal barrier.[24,25]

We discovered an increase in I-FABP levels in 26 of the study samples after the CH in this study. These results are statistically significant, indicating a change in splanchnic perfusion. We found there was a change from the average value before anesthesia of 0.639 ng/mL to 0.779 ng/mL after the anesthesia (a p<0.001). This study's average I-FABP value was still within the normal range. According to a study, I-FABP was not found in the plasma of healthy individuals.[26] In a recent study of plasma I-FABP levels, the normal concentration of I-FABP in normal individuals was less than 2.0 ng/mL.[11] This means that I-FABP was released as a

Table 4. Determinants associated with changes of I-FABP level between pre- and post-surgery in patient with otorhinolaryngology surgeries (*n*=31).

Determinant	Mean±SD	Changes of I-FABP		*p*-value*
		Decrease (*n*=5)	Increase (*n*=16)	
Age (year)	31.7±11.4	30.00±9.6	32.08±11.8	0.747
BMI (kg/m^2)	22.2±3.6	25.2±3.3	21.7±3.5	0.051
Surgery duration (minute)	184.8±49.6	206.0±23.8	180.7±52.5	0.586
Anesthesia duration (minute)	200±48.8	222.0±24.6	195.7±51.4	0.390
MAP (mmHg)	70.5±2.1	70.8±2.8	70.5±1.8	0.766
Systolic (mmHg)	96.6±3.9	97.8±5.7	96.4±3.6	0.485
Diastolic (mmHg)	57.5±1.9	57.6±2.3	57.5±1.9	0.918

*Analyzed using Mann-Whitney test

result of hypoperfusion, but the level was still within normal ranges. Because of its location in the intestinal mucosal filling, I-FABP is extremely sensitive for the blood perfusion. A study found that when intestinal ischemia was limited to less than two hours, villi were affected while crypt cells were unaffected, and function could be quickly restored.[27] Since I-FABP is mainly expressed in villi and not in crypt cells, it is the first organ of the gut to be affected by hypoperfusion.[28] Decreased intestinal epithelial oxygenation can cause damage to the end of the intestinal villi.[21]

When assessing I-FABP as a clinical tissue injury marker, the proteins diffuse more quickly in interstitial space, then the endothelial cleft, and finally into the vascular space. These endothelial clefts vary in size, from large slits in the liver to smaller pores such as blood-brain barrier. As a result, the rate of protein diffusion into the circulation varies. Therefore, the appearance of this protein marker in plasma is influenced not only by the time of disease progression but also by size and its distribution.[29] I-FABP elevation was higher in acute conditions such as multi-trauma with and without abdominal trauma than in the general population. Patients with a MAP less than 70 mmHg had the higher I-FABP level than a normal MAP (70-100 mmHg) or higher (>100 mmHg). Patients with hemoglobin (Hb) less than 8 mg/dL had higher I-FABP than those with Hb greater than 8 mg/dL.[30] This suggests that an increase in I-FABP may be associated with shock or severe injury.[31]

In this study, we discovered a decrease in I-FABP levels in five cases. This can occur in patients who have issues with fat absorption. I-FABP is well known for its role in fatty acid metabolism. As demonstrated in mouse models, I-FABP is involved in signaling the presence of lipids in the diet.[32] A study found that there was a decrease in I-FABP levels in COVID-19 cases.[33] This is due to the modification of lipid metabolism in COVID-19 patients.[33] However, no lipid profile was examined in this study making this possibility is unable to be ruled out. Surprisingly, there was no significant relationship between the length of operation and I-FABP levels in this study. This may indicate that no tissue damage or hypoperfusion exists in the Splanchnic. The average length of operation in this study was approximately 195 minutes in the decreased I-FABP group and 210 minutes in the increased I-FABP group. This signifies that the patient's blood pressure was kept under control for more than two hours. Ischemia lasting more than two hours can cause intestinal damage in mice.[27] The sample characteristics in this study did not affect the increase in I-FABP.

There are several limitations to this study. First, the study did not control and evaluate the patients' gastrointestinal clinical symptoms; therefore, determining the occurrence of hypoperfusion in splanchnic was difficult. In addition, the use of a single measurement of hypoperfusion marker (I-FABP only), renders no other criterion for confirming the occurrence of splanchnic hypoperfusion. In addition, since lipid profiles were not examined in all patients, it study was unable to rule out the possibility of lipid absorption issues resulting in a decrease in I-FABP levels in some patients.

CONCLUSIONS

I-FABP levels increased significantly before and after controlled hypotension otorhinolaryngology surgery. However, this increase might not an indicative of tissue damages. Further study is needed to prove that tissue damage occurs as a result of controlled hypotension, particularly in the gastrointestinal system.

ETHICAL APPROVAL

Ethical approval was obtained from the Medical Research Ethics Committee of Dr Soetomo General Academic Hospital, Surabaya, Indonesia (050/KEPK/X/2022). All patients were given and signed an informed consent form.

COMPETING INTERESTS

The authors declare no competing interest.

GRANT INFORMATION

None.

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REFERENCES

1. Sabrina AM, Maulydia, Perdana RF, Fitriati M. Airway Foreign Bodies in Patients that Underwent Bronchoscopies with General Anesthesia in Dr. Soetomo General Academic Hospital Surabaya. Indones J Anesthesiol Reanim [Internet]. 2022;4(2):72–9. Available from: http://dx.doi.org/10.20473/ijar.v4i22022.72-79
2. Salinding A, Wahyudi W, Pradipta A. Anesthesia and Analgesia Management Profile for Airway Surgeries at Dr. Soetomo General Academic Hospital Surabaya. Indones J Anesthesiol Reanim [Internet]. 2022;4(2):98–

106. Available from: http://dx.doi.org/10.20473/ijar.v4i22022.98-106
3. Butterworth JF, Mackey DC, Wasnick JD. Morgan & Mikhail's clinical anesthesiology: McGraw-Hill New York; 2013.
4. Miller RD, Pardo MC. Preface [Internet]. Basics of Anesthesia. Elsevier; 2011. p. ix. Available from: http://dx.doi.org/10.1016/b978-1-4377-1614-6.00055-0
5. Gibson APA, Medina MM. The use of the controlled hypotension in otorhinolaryngology surgeries. Acta Médica Grupo Angeles. 2010;**8**(3):148-54.
6. Degoute C-S. Controlled Hypotension. Drugs [Internet]. 2007;67(7):1053–76. Available from: http://dx.doi.org/10.2165/00003495-200767070-00007
7. Lindop MJ. Complications And Morbidity Of Controlled Hypotension. Br J Anaesth [Internet]. 1975;47(7):799–803. Available from: http://dx.doi.org/10.1093/bja/47.7.799
8. Kohli HS, Bhaskaran MC, Muthukumar T, Thennarasu K, Sud K, Jha V, et al. Treatment-related acute renal failure in the elderly: a hospital-based prospective study. Nephrol Dial Transplant [Internet]. 2000;15(2):212–7. Available from: http://dx.doi.org/10.1093/ndt/15.2.212
9. Yun SH, Kim JH, Kim HJ. Comparison of the hemodynamic effects of nitroprusside and remifentanil for controlled hypotension during endoscopic sinus surgery. J Anesth [Internet]. 2014;29(1):35–9. Available from: http://dx.doi.org/10.1007/s00540-014-1856-0
10. Varol A, Basa S, Ozturk S. The role of controlled hypotension upon transfusion requirement during maxillary downfracture in double-jaw surgery. J Cranio-Maxillofacial Surg [Internet]. 2010;38(5):345–9. Available from: http://dx.doi.org/10.1016/j.jcms.2009.10.012
11. Kanda T, Fujii H, Fujita M, Sakai Y, Ono T, Hatakeyama K. Intestinal fatty acid binding protein is available for diagnosis of intestinal ischaemia: immunochemical analysis of two patients with ischaemic intestinal diseases. Gut [Internet]. 1995 May;36(5):788–91. Available from: https://pubmed.ncbi.nlm.nih.gov/7797132
12. Sarengat R, Islam MS, Ardhi MS. Correlation of neutrophil-to-lymphocyte ratio and clinical outcome of acute thrombotic stroke in patients with COVID-19. Narra J [Internet]. 2021;1(3). Available from: http://dx.doi.org/10.52225/narra.v1i3.50
13. Mahmud AA, Anu UH, Foysal KA, Hasan M, Sazib SM, Ragib AA, et al. Elevated serum malondialdehyde (MDA), insulin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and thyroid-stimulating hormone (TSH), and reduced antioxidant vitamins in polycystic ovarian syndrome patients. Narra J [Internet]. 2022;2(1). Available from: http://dx.doi.org/10.52225/narra.v2i1.56
14. Zahra Z, Ramadhani CT, Mamfaluti T, Pamungkas SR, Firdausa S. Association between depression and HbA1c levels in the elderly population with type 2 diabetes mellitus during COVID-19 pandemic. Narra J [Internet]. 2022;2(1). Available from: http://dx.doi.org/10.52225/narra.v2i1.51
15. Lorena C, Hamzah H, Maulydia M. Accuracy Comparison of Endotracheal Tube (ETT) Placement Using Chula Formula With Manubrium Sternal Joint (MSJ) Formula. Indones J Anesthesiol Reanim [Internet]. 2021;3(2):54. Available from: http://dx.doi.org/10.20473/ijar.v3i22021.54-61
16. Mudatsir M, Fajar JK, Wulandari L, Soegiarto G, Ilmawan M, Purnamasari Y, et al. Predictors of COVID-19 severity: a systematic review and meta-analysis. F1000Research [Internet]. 2020 Sep 9;9:1107. Available from: https://pubmed.ncbi.nlm.nih.gov/33163160
17. Harapan H, Fajar JK, Supriono S, Soegiarto G, Wulandari L, Seratin F, et al. The prevalence, predictors and outcomes of acute liver injury among patients with COVID-19: A systematic review and meta-analysis. Rev Med Virol [Internet]. 2021/10/13. 2022 May;32(3):e2304–e2304. Available from: https://pubmed.ncbi.nlm.nih.gov/34643006
18. Andrianto, Al-Farabi MJ, Nugraha RA, Marsudi BA, Azmi Y. Biomarkers of endothelial dysfunction and outcomes in coronavirus disease 2019 (COVID-19) patients: A systematic review and meta-analysis. Microvasc Res [Internet]. 2021/07/15. 2021 Nov;138:104224. Available from: https://pubmed.ncbi.nlm.nih.gov/34273359
19. Pramana Witarto A, Samarta Witarto B, Er Putra AJ, Pramudito SL, Rosyid AN. Serum Krebs von den Lungen-6 for Predicting the Severity of COVID-19 Lung Injury: A Systematic Review and Meta-Analysis. Iran Biomed J [Internet]. 2021 Nov 1;25(6):381–9. Available from: https://pubmed.ncbi.nlm.nih.gov/34641641
20. Derikx JPM, Vreugdenhil ACE, Van den Neucker AM, Grootjans J, van Bijnen AA, Damoiseaux JGMC, et al. A Pilot Study on the Noninvasive Evaluation of Intestinal Damage in Celiac Disease Using I-FABP and L-FABP. J Clin Gastroenterol [Internet]. 2009;43(8):727–33. Available from: http://dx.doi.org/10.1097/mcg.0b013e31819194b0
21. Grootjans J, Hodin CM, de Haan J, Derikx JPM, Rouschop KMA, Verheyen FK, et al. Level of Activation of the Unfolded Protein Response Correlates With Paneth Cell Apoptosis in Human Small Intestine Exposed to Ischemia/Reperfusion. Gastroenterology [Internet]. 2011;140(2):529-539.e3. Available from: http://dx.doi.org/10.1053/j.gastro.2010.10.040
22. Fink MP, Delude RL. Epithelial Barrier Dysfunction: A Unifying Theme to Explain the Pathogenesis of Multiple Organ Dysfunction at the Cellular Level. Crit Care Clin [Internet]. 2005;21(2):177–96. Available from: http://dx.doi.org/10.1016/j.ccc.2005.01.005
23. Thuijls G, Derikx JPM, Haan J-J de, Grootjans J, Bruïne A de, Masclee AAM, et al. Urine-based Detection of Intestinal Tight Junction Loss. J Clin Gastroenterol [Internet]. 2010;44(1):e14–9. Available from: http://dx.doi.org/10.1097/mcg.0b013e31819f5652
24. Berkes J, Viswanathan VK, Savkovic SD, Hecht G. Intestinal epithelial responses to enteric pathogens: effects on the tight junction barrier, ion transport, and inflammation. Gut [Internet]. 2003 Mar;52(3):439–51. Available from: https://pubmed.ncbi.nlm.nih.gov/12584232
25. Marchiando AM, Shen L, Graham WV, Edelblum KL, Duckworth CA, Guan Y, et al. The epithelial barrier is maintained by in vivo tight junction expansion during pathologic intestinal epithelial shedding. Gastroenterology [Internet]. 2011/01/13. 2011 Apr;140(4):1208-1218.e12182. Available from: https://pubmed.ncbi.nlm.nih.gov/21237166
26. Pelsers MMAL, Namiot Z, Kisielewski W, Namiot A, Januszkiewicz M, Hermens WT, et al. Intestinal-type and liver-type fatty acid-binding protein in the intestine. Tissue distribution and clinical utility. Clin Biochem [Internet]. 2003;36(7):529–35. Available from: http://dx.doi.org/10.1016/s0009-9120(03)00096-1
27. Robinson JW, Mirkovitch V. The recovery of function and microcirculation in small intestinal loops following ischaemia. Gut [Internet]. 1972 Oct;13(10):784–9. Available from: https://pubmed.ncbi.nlm.nih.gov/4263959
28. Lieberman JM, Sacchettini J, Marks C, Marks WH. Human intestinal fatty acid binding protein: Report of an assay with studies in normal volunteers and intestinal ischemia. Surgery [Internet]. 1997;121(3):335–42. Available from: http://dx.doi.org/10.1016/s0039-6060(97)90363-9
29. Hermens WT. Mechanisms of Protein Release from Injured Heart Muscle [Internet]. Developments in Cardiovascular Medicine. Springer Netherlands; 1998. p. 85–98. Available from: http://dx.doi.org/10.1007/978-94-017-2380-0_8
30. Timmermans K, Sir Ö, Kox M, Vaneker M, de Jong C, Gerretsen J, et al. Circulating iFABP Levels as a Marker of Intestinal Damage in Trauma Patients. Shock [Internet]. 2015;43(2):117–20. Available from: http://dx.doi.org/10.1097/shk.0000000000000284
31. Relja B, Szermutzky M, Henrich D, Maier M, De Haan J-J, Lubbers T, et al. Intestinal-FABP and Liver-FABP: Novel Markers for Severe Abdominal Injury. Acad Emerg Med [Internet]. 2010;17(7):729–35. Available from: http://dx.doi.org/10.1111/j.1553-2712.2010.00792.x
32. Lackey AI, Chen T, Zhou YX, Bottasso Arias NM, Doran JM, Zacharisen SM, et al. Mechanisms underlying reduced weight gain in intestinal fatty acid-binding protein (IFABP) null mice. Am J Physiol Gastrointest Liver Physiol [Internet]. 2020/01/06. 2020 Mar 1;318(3):G518–30. Available from: https://pubmed.ncbi.nlm.nih.gov/31905021
33. Guedj K, Uzzan M, Soudan D, Trichet C, Nicoletti A, Weiss E, et al. I-FABP is decreased in COVID-19 patients, independently of the prognosis. PLoS One [Internet]. 2021 Apr 15;16(4):e0249799–e0249799. Available from: https://pubmed.ncbi.nlm.nih.gov/33857216