Clinical significance of intestinal type fatty acid binding protein in patients undergoing coronary artery bypass surgery

Koroner arter baypas cerrahisi geçiren hastalarda intestinal tipteki yağ asitini bağlayan proteinin klinik önemi

Aynur Camkıran, Aslı Dönmez[1], Derya Aldemir, Rauf Agah İşgüzar, Bahadır Gültekin***

From Departments of Anesthesiology, *Biochemistry, and **Cardiovascular Surgery, Faculty of Medicine, Başkent University, Ankara
[1]Clinic of Anesthesiology, Türkiye Yüksek İhtisas Training and Research Hospital, Ankara-*Turkey*

Abstract

Objective: The aim of this study was to determine whether serum levels of intestinal type fatty acid binding protein (I-FABP) are related to intestinal ischemia in patients undergoing coronary bypass surgery.
Methods: The study was planned as prospective, observational. Elective coronary artery bypass candidate patients between ages of 50 and 70 were consecutively included in the study. Thirty-five patients scheduled for cardiopulmonary bypass (CPB) were identified as the CPB group and 16 patients not scheduled for CPB were identified as the off-pump coronary artery bypass surgery (OPCAB) group. The variables between and within the groups were analyzed with Student's t, Mann-Whitney U, Friedman and Wilcoxon tests respectively.
Results: In both CPB and OPCAB groups, I-FABP level at the end of the operation was significantly higher than that noted at the beginning of the operation ($p<0.005$). In the CPB group, there was a significant drop in I-FABP from the end of the operation to each of the postoperative time points (12th hour and 24th hour) (respectively $p<0.001$, $p<0.001$). In the OPCAB group, the I-FABP levels at both postoperative time points were lower than that at the end of the operation ($p<0.001$), and the level at 24-hour post-surgery was significantly lower than at both the end-of-operation I-FABP value ($p<0.001$) and the 12-hour post-surgery I-FABP value.
Conclusion: Since we have not observed any intestinal ischemia through our research, slight changes of I-FABP measurements make us believe that I-FABP would be a valuable way to monitor for intestinal ischemia in patients who undergo cardiac surgery.
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Key words: Coronary artery bypass grafting surgery, intestinal ischemia, intestinal fatty acid binding protein

ÖZET

Amaç: Çalışmamızın amacı, kardiyopulmoner baypas (KPB) uygulanan ve uygulanmayan (OPCAB) hastalarda intestinal iskemi ile intestinal yağ asidi bağlayıcı protein (I-FABP) arasında ilişki olup olmadığını belirlemektir.
Yöntemler: Çalışma prospektif, gözlemsel olarak planlandı. Elektif koroner arter baypas greftleme cerrahisi uygulanacak 50-70 yaşları arasında hastalar ardışık olarak çalışmaya alındı. Kardiyopulmoner baypas uygulanan 35 hasta birinci grup (CPB), uygulanmayan 16 hasta ikinci grup (OPCAB) olarak kabul edildi. Gruplar arası ve grup içi karşılaştırmalar Student's t, Mann-Whitney U, Friedman ve Wilcoxon testleri ile analiz edildi.
Bulgular: Kardiyopulmoner baypas uygulanan grubun I-FABP düzeylerinde operasyon sonunda, başlangıca göre anlamlı yükselme olurken ($p<0.005$), postoperatif 12. ve 24. saatlerde operasyon bitişine göre anlamlı düşme görüldü (sırasıyla $p<0.001$, $p<0.001$). Kardiyopulmoner baypas uygulanmayan grupta ise operasyon sonunda operasyon başlangıcına göre yükselme görülürken ($p<0.001$), postoperatif 24. saatte operasyon başlangıcına göre anlamlı düşme görüldü ($p<0.001$). Her iki grubun I-FABP düzeyleri cerrahi bitiminde preoperatif değerlere göre anlamlı şekilde yükseldi.
Sonuç: Çalışmamız sırasında hiçbir hastamızda intestinal iskemi görülmezken, I-FABP düzeylerindeki değişiklik bize açık kalp cerrahisi geçiren hastalarda intestinal iskemi monitörizasyonunda I-FABP'nin kullanılabileceğini düşündürdü. *(Anadolu Kardiyol Derg 2011; 11: 536-41)*
Anahtar kelimeler: Koroner arter baypas cerrahisi, intestinal iskemi, intestinal yağ asidi bağlayıcı protein

Address for Correspondence/Yazışma Adresi: Dr. Aynur Camkıran, Department of Anesthesiology, Faculty of Medicine, Başkent University, Fevzi Çakmak Cad. 10 Sok. No:45, Bahçelievler, Ankara-*Turkey* Phone: +90 312 212 68 68/1172-74 Fax: +90 312 223 73 33 E-mail: acamkiran@gmail.com

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Introduction

Intra-abdominal complications after cardiac surgery with patients on cardiopulmonary bypass (CPB) are rare, with an incidence ranging from 0.3% to 2%, but result in a significantly high mortality rate (11-59%) (1). Complications such as bleeding in the lower and upper gastrointestinal system (GIS), gastroesophagitis, colitis, intestinal ischemia, pancreatitis, liver failure, cholecystitis, peptic ulcer perforation, diverticulitis, intestinal occlusion and/or combinations of these occur. These problems are associated with high mortality and are considered to account for approximately 15% of all postoperative deaths (1, 2). Intestinal ischemia is a potentially catastrophic abdominal emergency. In clinical practice, the definitive diagnosis of acute intestinal ischemia is notoriously difficult, and often delayed. Symptoms of pain are often out of proportion to clinical signs such as peritonitis, and when the latter develops it usually indicates full-thickness infarction (3).

Changes in systemic perfusion occur during CPB and these changes affect gastrointestinal perfusion. Furthermore, preoperative hypotension, prolonged CPB, use of vasoconstrictor agents, arrhythmia, hemorrhage, preexisting vascular diseases and/or combinations of these can also cause organ damage by lowering mucosal perfusion (4). Off-pump coronary artery bypass surgery (OPCAB) eliminates negative effects of CPB. This technique is considered to reduce the systemic inflammatory response and allow more appropriate physiological conditions for organ systems (5). OPCAB has recently gained popularity because it reduces morbidity and has positive effects on major organ systems (6). It has been reported by many series that off-pump surgery reduces the need for early systemic vasoconstrictor or inotropic requirement. This may contribute to improved organ function, particularly in critically ill patients. Therefore, OPCAB has recently gained popularity for being a method that is physiologically more appropriate for maintaining the functional integrity of major organ systems and reducing morbidity. Studies on the effects of OPCAB have reported decreased need for systemic vasoconstrictors and inotropes after surgery (7, 8). However, although it is believed that OPCAB decreases inflammatory response several reports indicate that this has not been clinically proven (2, 7, 8).

Intestinal fatty acid binding protein (I-FABP) is a protein that is only present in the *villus* tips of intestinal mucosa and is not present in the circulation under normal conditions. I-FABP is strongly correlated with severity of intestinal ischemia (9). However, there are no data on the IFAP levels in patients undergoing coronary artery bypass surgery (CABG).

The aim of our study was to determine whether serum levels of I-FABP are related to intestinal ischemia in patients undergoing CABG.

Methods

Study design and patients

Fifty-one consecutive American Society of Anesthesiology risk grade 3 patients aged 50 to 70 years who were scheduled to undergo elective CABG surgery were included in the prospective and observational study. Thirty-five patients scheduled for CPB were identified as the CPB group and 16 patients not scheduled for CPB were identified as the OPCAB group. The exclusion criteria were history of organ failure (hepatic, renal), need for valve surgery in the same session as CABG surgery, chest pain, and ejection fraction (EF) <40%.

The study was approved by Başkent University Institutional Review Board (KA 07/133, 31.07.007) and supported by Başkent University Research Fund. All participants gave signed consent.

Study protocol

The following were recorded for each patient: cardiac rhythm, EF value, position in the NYHA classification, smoking habits, history of previous abdominal surgery, history of mesenteric or peripheral embolism, diabetes mellitus, hypertension, peptic ulcer, myocardial infarct, endocarditis, cerebrovascular event, history of chronic lung disease, and times of cardiac catheterization. Diazepam (Diazem®), famotidin HCl (Famodin®) and midazolam (Dormicum®) were used as premedication.

Once inside the operating room, patients were monitored with 5-lead electrocardiogram, noninvasive blood pressure monitoring, and pulse oximetry. Anesthesia was induced with midazolam (Dormicum®) 0.02-0.05 mg/kg intravenous (i.v.), etomidate (Hypnomidate®) 0.2-0.3 mg/kg i.v., fentanyl (Fentanyl®) 500 µg i.v., and vecuronium bromide (Norcuron®) 0.1 mg/kg i.v. Isoflurane (Forane®) at a concentration of 0.8-1% and 10 µg/kg/h fentanyl were used for maintenance anesthesia. After induction, invasive blood pressure was monitored by placing a 20G catheter in the right radial artery. Ultrasonography-guided cannulation of the right internal jugular vein was performed. The stomach was decompressed using a nasogastric tube. A urinary catheter was placed and intra-abdominal pressure (IAP) was measured. This was done by attaching a three-way connector to the end of the transurethral catheter, injecting 25 mL of sterile saline solution into the bladder through one port, and then measuring IAP by attaching a manometer to the other available port. Intra-abdominal pressure was measured with the patient in supine position and at the end of expiration, and the mid-axillary line was accepted as the zero point (9). This measurement was taken at four time points: beginning of surgery, end of surgery, 12-hour postoperatively, 24-hour postoperatively.

Operative techniques

Each patient in the CPB group received a bolus of 250 mg sodium thiopental (Pentotal®), 3 mg midazolam, 500 mg methylprednisolone (Prednol®) and 10 mg vecuronium bromide at the beginning of the operation as our clinics routine protocol. During the warm-up period, another bolus of the same drugs/doses except methylprednisolone was administered. A membrane oxygenator (Cobe® Optima® XP™ Hollow Fiber Membrane Oxygenator, Sorin Biomedical, Italy) was used during CPB. In all cases, our clinical protocol for standard CPB surgery and standard perfusion techniques were used. Cardiopulmonary bypass was adjusted at a perfusion rate of 50-70 mL/kg/min and mean arterial pressures (MAP) 55-65 mmHg with nonpulsatile flow. Crystalloid cardioplegia solution was used at the aortic cross-clamp stage.

Blood samples

Blood samples for arterial blood gas measurements and determination of serum I-FABP levels and IAP measurements were obtained at the beginning of surgery, end of surgery, and at 12 and 24 hour postoperatively. Time of extubation and length of intensive care unit (ICU) stay were determined based on the cardiovascular surgeon's routine protocol. All blood samples were collected into ice-cold tubes containing EDTA and centrifuged for 20 min. Plasma was drawn off and stored at -80°C until the time of analysis. Plasma samples were analyzed at 1:2 dilutions using an enzyme-linked immunosorbent assay kit (Hycult Biotechnology, Catalog No: HK406, Uden, the Netherlands). Results were expressed as pg/mL. No result was derived for samples that were below the analytic sensitivity.

Statistical analysis

Data analysis was done using SPSS software (SPSS version 15; SPSS, Inc, Chicago, IL). The both groups results for continuous variables with normal distribution were analyzed using Student's t-test for independent samples, and results for continuous variables with non-normal distribution were analyzed using the Mann-Whitney U test. Repeated laboratory measurements and differences between serum levels of IFAB-P and IAP within groups were analyzed using the Friedman test, Wilcoxon sign test was performed to analyze within group differences between 2 periods measurements. Categorical variables were compared using Chi-square test. A p value <0.05 was accepted as statistically significant.

Results

Basal characteristics

Demographic characteristics such as co-existing diseases, age and gender of the patients are shown at Table 1. The EF values were similar for the CPB group and OPCAB (p=0.806). Duration of surgery was significantly longer for the CPB group (p<0.001). There were no significant differences between the groups with respect to length of hospital stay or duration of intubation. The OPCAB group had a significantly shorter ICU stay.

There were no differences between the two groups with respect to changes in systolic, diastolic, and mean blood pressures during the surgery. The mean number of bypass grafts placed in the CPB group was significantly higher than that for the OPCAB group (p<0.001).

Table 2 lists rates of hypotension, fever, infection, neurological complication, postoperative atrial fibrillation, postoperative first oral intake and defecation of the patients in both groups. There were no complaints of abdominal distension or abdominal pain postoperatively in either group. None of the patients developed sepsis and none required the use of an intra-aortic balloon pump. The incidence of atrial fibrillation was statistically higher in the CPB group (p=0.043). One patient in each group required revision to control bleeding in the postoperative period. Mean time, first postoperative oral intake was significantly shorter in the OPCAB group (p<0.011). There was no statistical difference between the groups with respect to first defecation after surgery.

IFAB-P and IAB values during peri-operative period

Table 3 shows significant changes in IFAB-P of CPB and OPCAB groups through the beginning of the operation, at the end of the operation, at the 12th postoperative hour, and at the 24th postoperative hour (p=0.008 and p=0.002 for trend, respectively). Significant differences among the mean values of the CPB and OPCAB groups were observed at different time intervals. In both CPB and OPCAB groups, I-FABP level at the end of

Table 1. Demographic, clinical and perioperative characteristics of the patients

Variables	CPB (n=35)	OPCAB (n=16)	p*
Age, years	60.4±6.0 60 (50-72)	60.1±8.6 59 (42-72)	0.907
Gender, M, n (%)	27 (77)	12 (75)	1.000
Diabetes mellitus, n (%)	8 (22.9)	5 (31.3)	0.730
Hypertension, n (%)	22 (62.9)	13 (81.3)	0.189
Syncope, n (%)	1 (2.9)	1 (6.3)	0.533
Peptic ulcer, n (%)	3 (8.6)	3 (18.8)	0.363
Cigarette smoking, n (%)			0.331
Active smoker	12 (34.3)	9 (56.2)	
Ex-smoker	9 (25.7)	3 (18.8)	
Never smoked	14 (40.0)	4 (25.0)	
Myocardial infarction within the previous two months, n (%)	14 (40.0)	7 (43.8)	0.801
History of abdominal surgery, n (%)	6 (17.1)	5 (31.3)	0.288
Duration of the operation, min	229.7±37.2 240 (160-315)	162.5±43.4 172 (75-225)	<0.001
Aortic cross-clamp duration, min	40.2±13.5 41 (15-75)	-	-
CBP duration, min	73.5±16.1 72 (49-121)	-	-
Duration of extubation, hours	11.5±3.9 11 (5-20)	9.7±3.2 9.7 (5-18)	0.099
Duration of ICU stay, days	2.5±1.0 2 (1-5)	1.6±0.5 2 (1-2)	<0.001
Duration of hospital stay, days	9.5±2.7 8 (6-17)	8.9±2.6 8 (6-15)	0.240

Data are expressed as mean±standard deviation (median, minimum-maximum) values and number (percentage)
*unpaired Student's t-test, Mann-Whitney U and Chi-square tests
CPB - cardiopulmonary bypass, ICU - intensive care unit, M - male, OPCAB - off-pump coronary bypass surgery

the operation (1338.9±958.21 pg/ml, 1056.7±593.28 pg/ml respectively) was significantly higher than that noted at the beginning of the operation (1168.7±927.83 pg/ml, 774.6±406.22 pg/ml, $p<0.05$ for both respectively). In the CPB group, there was a significant drop in I-FABP from the end of the operation to each of the postoperative time points (12 hour and 24 hour, 1012.9±697.77 pg/ml and 967.4±676.79 pg/ml, $p<0.01$ and $p<0.01$, respectively). In the OPCAB group, the I-FABP levels at both postoperative time points were lower than that at the end of the operation (1056.7±593.28 pg/ml, $p<0.05$), and the level at 24 hour post-surgery (667.9±362.7 pg/ml, $p<0.01$) was significantly lower than both the end-of-operation I-FABP value and the 12-h I-FABP value (882.3±429.85 pg/ml, $p<0.01$).

Table 4 summarizes the results for intra-abdominal pressure values of CPB and OPCAB groups at the beginning of the operation, at the end of the operation, at the 12th postoperative hour, at the 24th postoperative hour and p values. There were no significant differences within or between the groups with respect to IAP at the 4 time points assessed (beginning of operation, end of the operation, 12 and 24 hour post-surgery).

Discussion

Our study demonstrated that I-FABP levels, a strong indicator of intestinal ischemia, was elevated at the end of surgery in both CPB and OPCAB groups. The levels of I-FABP had dropped, however, by 12 hour postoperatively in both groups. We observed no significant difference among the IAP levels recorded at the 4 different time points in both groups.

Although GIS complications are rare in patients who undergo CPB, the reported mortality rates associated with these problems are high (11-59%) (1). In the critical care setting, the development of intestinal ischemia carries with it a mortality of between 67% and 80% (3). In our study, we investigated 51 patients who underwent heart surgery with or without CPB, and none developed clinical intestinal ischemia.

Despite variations among studies in the literature, an extensive list of risk factors for development of GIS complications after coronary artery bypass graft surgery has been identified (1, 2, 4): advanced age, decreased EF or congestive heart failure, renal failure, emergency surgery, reoperation, heart valve surgery or combined heart surgeries, heart transplantation, CPB or cross-clamp duration, non-pulsatile flow and hypothermia. Mangi et al. (10) retrospectively analyzed findings of 8709 consecutive patients who had undergone heart operation and developed GIS complications. They identified chronic obstructive lung disease, need for intra-aortic balloon counter-pulsation, diabetes mellitus, prior cerebrovascular accident, atrial fibrillation, renal insufficiency with a creatinine of >1.3 mg/dl, peripheral vascular disease, hypertension, and prior myocardial infarction as risk factors for GIS complications after CABG surgery.

Until recently, there has been considerable disagreement in the literature about GIS complications in cardiac surgical patients (11-13). Spotnitz et al. (14) reported that there is a direct

Table 2. Postoperative variables

Variables	CBP (n=35)	OPCAB (n=16)	p*
Hypotension, n (%)	1 (5.7)	-	1.000
Fever, n (%)	11 (31.4)	6 (37.5)	0.670
Infection, n (%)	1 (2.9)	3 (18.8)	0.086
Neurological complication, n (%)	1 (2.9)	-	1.000
Postoperative atrial fibrillation, n (%)	8 (23.5)	-	0.043
Postoperative first oral intake, hour	14.3±3.95 13 (9-24)	11.0±4.00 11 (5-18)	0.011
Postoperative first defecation, day	3.5±1 3 (1-6)	3.5±1 3 (2-5)	0.700

Data are expressed as mean±standard deviation (median, minimum-maximum) values and number (percentage)
*unpaired Student's t-test, Mann-Whitney U and Chi-square tests
CPB - cardiopulmonary bypass, OPCAB - off-pump coronary bypass surgery

Table 3. Perioperative dynamics in I-FABP values

I-FABP, pg/ml	CPB	OPCAB
At the beginning of the operation	1168.7±927.83 822 (152.1-4138.7)	774.6±406.22 668 (202.1-1563.6)
At the end of the operation	1338.9±958.21** 981 (98.6-3517.8)	1056.7±593.28** 705 (408.2-2226.1)
At the 12th postoperative hour	1012.9±697.77$^{\#}$ 857 (58.9-2837.4)	882.3±429.85 771 (402.9-1906.6)
At the 24th postoperative hour	967.4±676.79$^{\#}$ 729 (35.9-2320.7)	667.9±362.70$^{\#,\Delta}$ 460 (280.6-1347.4)
Chi-square*	11.700	14.486
p*	0.008	0.002

Data are expressed as mean±standard deviation (median, minimum-maximum values)
*Friedman test for repeated measurements
Wilcoxon sign rank test: for comparison with preoperative value - * *-$p<0.05$, $^{\#}$-$p<0.01$; for comparison with 12th postoperative hour-
$^{\Delta}$-$p<0.01$
CPB - cardiopulmonary bypass, I-FABP - intestinal type fatty acid binding protein, OPCAB - off-pump coronary bypass surgery

Table 4. Perioperative dynamics in IAP values

IAP, mmHg	CPB	OPCAB
At the beginning of the operation	9.9±4.18 10 (2-21)	11.7±4.89 12 (4-20)
At the end of the operation	11.7±6.28 11 (3-33)	11.5±3.11 12 (6-17)
At the 12th postoperative hour	10.0±5.24 9 (1-25)	10.0±4.34 10 (2-18)
At the 24th postoperative hour	10.1±4.20 10 (5-19)	10.5±2.47 11 (6-13)
Chi-square*	2.097	1.936
p*	0.552	0.586

Data are expressed as mean±standard deviation (median, minimum-maximum values)
* Friedman test for repeated measurements
CPB - cardiopulmonary bypass, IAP - intraabdominal pressure, OPCAB - off-pump coronary bypass surgery

relationship between CPB and GIS complications, and that, in particular, the frequency of GIS bleeding rises with CPB. In contrast, Christenson et al. (11) argued that there is no significant difference between CPB and development of GIS complications. Although there are different views, it is generally accepted that visceral vasoconstriction during CPB contributes to the development of GIS complications. Some of the studies have shown that heart surgery without CPB provides more myocardial and renal protection and generates minimal inflammatory response compared to heart surgery with CPB (15-17). As expected, we noted longer duration of surgery and higher number of grafts placed in our CPB group than in our OPCAB group. Still, none of our patients developed GIS complications. Longer operative time can lead to differences in laboratory values in the early postoperative period in patients who undergo CPB. According to the literature, in addition to duration of surgery, CPB, number of grafts, duration of CPB, and perfusion of organs during CPB, are the main determinants for development of GIS complications in patients who undergo heart surgery (1, 2, 4). The number of subjects in our study (51) was relatively low. In addition, we excluded patients who had preoperative risk factors and we ensured sufficient perfusion intraoperatively. Supporting our hypothesis, all these factors suggest why we observed no GIS complication in either study group.

It has been reported that development of GIS complications in cardiac surgery is linked with postoperative mechanical ventilation, duration of stay in the ICU, and duration of hospital stay (12). There were no differences between our study groups concerning time to extubation or time of hospital stay. The CPB group had a longer mean ICU stay and yet there were no clinical GIS complications in either group. Patients who undergo CPB at our hospital are kept in the ICU for extended hemodynamic follow-up due to the risk of postoperative atrial fibrillation. We believe that this longer period of close monitoring and support may be the reason of the absence of any GIS complications in our CPB group.

Neither of the groups in our study had issues with abdominal distension, abdominal pain or sepsis, and none required intra-aortic balloon placement. These are considered predictors for the development of GIS complications in cardiac surgery (1, 2, 11). GIS complications are rarely observed, it is less probable to observe GIS complication at our small group either.

Although there is no information in the literature on times to first oral intake and first defecation after heart surgery, it is assumed that these would be prolonged by reduced splanchnic perfusion. We noted no significant difference between our CPB and OPCAB patients with respect to first defecation, even though time to first oral intake was longer in the CPB group. The latter can be influenced by longer time to extubation, but there was also no difference between our groups with respect to this interval.

The importance of IAP level is well-known with respect to GIS complications. LeRoith et al. (18) reported reduced splanchnic blood flow in relation with a rise in IAP. They found that the rise in pressure had multiple effects that reduced vascular flow: i) direct mechanical pressure on the splanchnic vein, ii) triggering of myogenic reflexes within the walls of the splanchnic vein, and iii) mesenteric vasoconstriction due to release of vasoactive hormones. The hepatic perfusion and microvascular blood flow are all affected by elevated IAP (19, 20). Increased IAP can reduce mesenteric blood flow (20), and thereby reduce arterial perfusion (19) and venous flow in the stomach, duodenum, small intestine, pancreas and spleen. The resulting intestinal ischemia creates free oxygen radicals. It has been proposed that this release may be responsible for the damage that occurs to distal organs in the setting of increased IAP. However, we observed no such rise in either of our patient groups. This probably helps to explain the lack of GIS complications in our patients, and is also in line with the mild clinical changes we observed. If our patients had shown clinically significant rises in laboratory values (aspartate aminotransferase, bilirubin, etc.), we would have also seen altered IAP.

Another parameter that can be used as an indicator of intestinal ischemia is I-FABP, which is characterized by being an early indicator. Sonnino et al. (9) reported that peritoneal fluid levels of I-FABP, a protein that is only present in the *villus* tips of intestinal mucosa and is not present in the circulation under normal conditions, is strongly correlated with severity of intestinal ischemia (3). It has been shown that functional and structural changes in intestinal mucosa begin with the short-term (5-15 min) disappearance of superior mesenteric artery flow, and then gradually become more severe with time. Other research has shown that, especially after 30 min of the ischemia, the epithelial cells in the *villi* are damaged and decrease in number, thus increasing intestinal wall permeability (21-24). Loss of epithelial cells from intestinal *villi* is correlated with plasma and urinary levels of I-FABP. In both patient groups in our study. At the end of the surgery, we observed significantly higher I-FABP levels than the baseline levels, but I-FABP levels decreased postoperatively. Although we did not observe this link in our study, changes in I-FABP can be associated with negative effects of CPB on the GIS. In fact, I-FABP is considered a more sensitive indicator of the development of intestinal ischemia than IAP during follow-up of patients undergoing cardiac surgery.

We focused on intestinal ischemia and related indicators (particularly I-FABP) in patients who have undergone CPB. We summarize the results of as follows: No GIS complications occurred in either our CPB group or OPCAB group. No changes in IAP were observed within or between the groups. Serum levels of I-FABP were significantly elevated at the end of the surgery compared to preoperative values, but these levels dropped again within 12-hours.

Study limitations

There is a need for large studies to evaluate the early marker determine effect of CBP on the GIS. Our study is the first clinical trial of the use of I-FABP in patients undergoing CABG. We investigated only 51 patients who underwent heart surgery with or without CPB, and none developed clinical intestinal ischemia.

Conclusion

Since we have not observed any intestinal ischemia through our research, slight changes of I-FABP measurements make us believe that I-FABP would be a valuable way to monitor for intestinal ischemia in patients who undergo cardiac surgery. In addition, with its increase and decrease, I-FABP may allow diagnosis of continuing or recurring intestinal ischemia after cardiac surgery and therefore may permit more timely initiation of specific treatment strategies.

Conflict of interest: None declared.

References

1. D' Ancona G, Baillot R, Poirier B, Dagenais F, de Ibarra JI, Bauset R, et al. Determinants of gastrointestinal complications in cardiac surgery. Tex Heart Inst J 2003; 30: 280-5.
2. Hessel EA 2nd. Abdominal organ injury after cardiac surgery. Semin Cardiothorac Vasc Anesth 2004; 8: 243-63.
3. Evennett NJ, Petrov MS, Mittal A, Windsor JA. Systematic review and pooled estimates for the diagnostic accuracy of serological markers for intestinal ischemia. World J Surg 2009; 33: 1374-83.
4. Sakorafas George H, Tsitos Gregory G. Intraabdominal complications after cardiac surgery. Eur J Surg 1999; 165: 820-7.
5. Matata BM, Sosnowski AW, Galinanes M. Off-pump bypass graft operation significantly reduces oxidative stress and inflammation. Ann Thorac Surg 2000; 69: 785-91.
6. Plomondon ME, Cleveland JC Jr, Ludwig ST, Grunwald GK, Kiefe CI, Grover FL, et al. Off-pump coronary artery bypass is associated with improved risk-adjusted outcomes. Ann Thorac Surg 2001; 72: 114-9.
7. Schulze C, Conrad N, Schütz A, Egi K, Reichenspurner H, Reichart B, et al. Reduced expression of systemic proinflammatory cytokines after off-pump versus conventional coronary artery bypass grafting. Thorac Cardiovasc Surg 2000; 48: 364-9.
8. Ascione R, Caputo M, Angelini GD. Off-pump coronary artery bypass grafting: not a flash in the pan. Ann Thorac Surg 2003; 75: 306-13.
9. Sonnino R, Ereso G, Arcuni J, Franson R. Human intestinal fatty acid binding protein in peritoneal fluid is a marker of intestinal ischemia. Transplant Proc 2000; 32: 1280.
10. Mangi AA, Christison-Lagay ER, Torchiana DF, Warshaw AL, Berger DL. Gastrointestinal complications in patients undergoing heart operation: an analysis of 8709 consecutive cardiac surgical patients. Ann Surg 2005; 241: 895-901.
11. Christenson JT, Schmuziger M, Maurice J, Simonet F, Velebit V. Gastrointestinal complications after coronary artery bypass grafting. J Thorac Cardiovasc Surg 1994; 108: 899-906.
12. Perugini RA, Orr RK, Porter D, Dumas EM, Maini BS. Gastrointestinal complications following cardiac surgery. An analysis of 1477 cardiac surgery patients. Arch Surg 1997; 132: 352-7.
13. Zacharias A, Schwann TA, Parenteau GL, Riordan CJ, Durham SJ, Engoren M, et al. Predictors of gastrointestinal complications in cardiac surgery. Tex Heart Inst J 2000; 27: 93-9.
14. Spotnitz WD, Sanders RP, Hanks JB, Nolan SP, Tribble CG, Bergin JD, et al. General surgical complications can be predicted after cardiopulmonary bypass. Ann Surg 1995; 221: 489-96.
15. Ascione R, Lloyd CT, Gomes WJ, Caputo M, Bryan AJ, Angelini GD. Beating versus arrested heart revascularization: evaluation of myocardial function in a prospective randomized study. Eur J Cardiothorac Surg 1999; 15: 685-90.
16. Ascione R, Lloyd CT, Underwood MJ, Lotto AA, Pitsis AA, Angelini GD. Inflammatory response after coronary revascularization with or without cardiopulmonary bypass. Ann Thorac Surg 2000; 69: 1198-204.
17. Ömeroğlu SN, Kıralı K, Güler M, Toker ME, İpek G, Işık O, et al. Midterm angiographic assessment of coronary artery bypass grafting without cardiopulmonary bypass. Ann Thorac Surg 2000; 70: 844-9.
18. Le Roith D, Bark H, Nyska M, Glick SM. The effect of abdominal pressure on plasma antidiuretic hormone levels in the dog. J Surg Res 1982; 32: 65-9.
19. Caldwell CB, Ricotta JJ. Changes in visceral blood flow with elevated intra-abdominal pressure. J Surg Res 1987; 43: 14-20.
20. Diebel LN, Wilson RF, Dulchavsky SA, Saxe J. Effect of increased intra-abdominal pressure on hepatic arterial, portal venous, and hepatic microcirculatory blood flow. J Trauma 1992; 33: 279-82.
21. Parks DA, Grogaard B, Granger DN. Comparison of partial and complete arterial occlusion models for studying intestinal ischemia. Surgery 1982; 92: 896-901.
22. Semenza GL. Cellular and molecular dissection of reperfusion injury: ROS within and without. Circ Res 2000; 86: 117-8.
23. Puyana JC, Soller BR, Zhang S, Heard SO. Continuous measurement of gut pH with near-infrared spectroscopy during hemorrhagic shock. J Trauma 1999; 46: 9-15.
24. Crissinger KD, Granger DN. Mucosal injury induced by ischemia and reperfusion in the piglet intestine: influences of age and feeding. Gastroenterology 1989; 97: 920-6.