International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 08-10-2019; Accepted: 10-11-2019
www.medicalsciencejournal.com
Volume 5; Issue 12; December 2019; Page No. 29-33

Clinical Assessment of Levels of Intestinal fatty acid binding protein (I-FABP) as a Marker for Acute Intestinal Ischemia in Patients from Bihar Region

Dr. Amarjit Kumar Raj[1], Dr. Manish Shah[2*], Dr Sanjay Kumar[3], Dr. Manish Mandal[4]

[1] Professor, Department of Surgical Gastroenterology, IGIMS (Indira Gandhi Institute of Medical Sciences), Patna, Bihar, India.

[2] Senior Resident, Department of Surgical Gastroenterology, Igims, Patna, India

[3] Associate Professor, Department of Surgical Gastroenterology, Igims, Patna, India

[4] Professor and Head, Department of Surgical Gastroenterology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India.

[*] Corresponding Author: Dr. Manish Shah

Abstract

Perioperative management of patients with peripheral vascular disease is challenging. Extensive atherosclerotic involvement of the vascular system including coronary, renal, mesenteric and cerebral vessels predisposes it to increased perioperative mortality and morbidity in the form of myocardial infarction, congestive heart failure and renal failure. Hence present study was planned to evaluate the Intestinal fatty acid binding protein (I-FABP) as a marker for acute intestinal ischemia in patients from Bihar region.

The present study was planned in Department of Gastrointestinal Surgery, Indira Gandhi Institute of Medical Sciences, Patna, Bihar. Total 20 cases of acute intestinal ischemia were enrolled in the present study as case patients. The more 20 patients without any complication were selected in control group patients. The study was conducted from May 2016 to Jan 2017.

The data generated from present study concludes that Intestinal ischemia is a surgical emergency and warrants immediate surgical intervention. Quicker diagnosis aided by serum I-FABP levels will enable us to intervene in such patients quickly reducing morbidity and mortality among patients.

I-FABP levels may be used to diagnose such fatal pathologies. Further studies with wider series are needed in order to investigate the diagnostic value of I-FABP in patients with abdominal pain.

Keywords: acute mesenteric ischemia, bowel ischemia, i-FABP, Bihar region, etc.

Introduction

Mesenteric ischemia is a medical condition in which injury to the small intestine occurs due to not enough blood supply. It can come on suddenly, known as acute mesenteric ischemia, or gradually, known as chronic mesenteric ischemia. The acute form of the disease often presents with sudden severe abdominal pain and is associated with a high risk of death. The chronic form typically presents more gradually with abdominal pain after eating, unintentional weight loss, vomiting, and fear of eating [1, 2].

Risk factors for acute mesenteric ischemia include atrial fibrillation, heart failure, chronic kidney failure, being prone to forming blood clots, and previous myocardial infarction. There are four mechanisms by which poor blood flow occurs: a blood clot from elsewhere getting lodged in an artery, a new blood clot forming in an artery, a blood clot forming in the superior mesenteric vein, and insufficient blood flow due to low blood pressure or spasms of arteries. Chronic disease is a risk factor for acute disease. The best method of diagnosis is angiography, with computed tomography (CT) being used when former is not available [1].

Treatment of acute ischemia may include stenting or medications to break down the clot provided at the site of obstruction by interventional radiology. Open surgery may also be used to remove or bypass the obstruction and may be required to remove any intestines that may have died. If not rapidly treated outcomes are often poor. Among those affected even with treatment the risk of death is 70% to 90% [3]. In those with chronic disease bypass surgery is the treatment of choice. Those who have thrombosis of the vein may be treated with anticoagulation such as heparin and warfarin, with surgery used if they do not improve [2].

Acute mesenteric ischemia affects about five per hundred thousand people per year in the developed world [4]. Chronic mesenteric ischemia affects about one per hundred thousand people [5]. Most people affected are over 60 years old. Rates are about equal in males and females of the same age [3]. Mesenteric ischemia was first described in 1895 [1].

Acute mesenteric ischemia (AMI) is a syndrome caused by inadequate blood flow through the mesenteric vessels, resulting in ischemia and eventual gangrene of the bowel wall. Although relatively rare, it is a potentially life-threatening condition. Broadly, AMI may be classified as either arterial or venous. AMI as arterial disease may be subdivided into nonocclusive mesenteric ischemia (NOMI) and occlusive mesenteric arterial ischemia (OMAI); OMAI may be further subdivided into acute mesenteric arterial embolism (AMAE) and acute mesenteric arterial thrombosis (AMAT). AMI as venous disease takes the form of mesenteric venous thrombosis (MVT).Thus, for practical purposes, AMI comprises four different primary clinical entities, as follows: NOMI, AMAE, AMAT&MVT.

The four types of AMI have somewhat different predisposing factors, clinical pictures, and prognoses. A secondary clinical entity of mesenteric ischemia occurs as a

consequence of mechanical obstruction (e.g., from internal hernia with strangulation, volvulus, or intussusception). Tumor compression, aortic dissection and post angiography thrombosis [6] are other reported causes. Occasionally, blunt trauma may cause isolated dissection of the superior mesenteric artery (SMA) and lead to intestinal infarction.

Because the four types of AMI share similarities and a final common pathway (i.e. bowel infarction and death, if not properly treated), they may usefully be discussed together.

In 1930, Cokkinis remarked, "Occlusion of the mesenteric vessels is apt to be regarded as one of those conditions of which the diagnosis is impossible, the prognosis is hopeless, and the treatment almost useless [7]." This quote indicates some of the extreme difficulties faced by physicians treating AMI. Symptoms are nonspecific initially, before evidence of peritonitis presents. Thus, diagnosis and treatment are often delayed until the disease is advanced [8-9]. Fortunately, since 1930, many advances (eg, in magnetic resonance imaging [MRI] and Doppler flowmetry [10]) have been made that allow earlier diagnosis and treatment. Whereas the prognosis remains grave for patients in whom the diagnosis is delayed until bowel infarction has already occurred, patients who receive the appropriate treatment in a timely manner are much more likely to recover [11].

Treatment options for acute thrombosis focus on surgical methods, which have changed little since the late 20th century. Some patients may be good candidates for percutaneous transluminal angioplasty with stenting [12]. Some authors recommend a trial of thrombolytic therapy if patients can be treated within 8 hours of presentation and do not have signs of bowel necrosis or peritonitis [13]. If no evidence of improvement is noted within 4 hours, patients should undergo exploration.

Mastery of the anatomy of the mesenteric vessels is the key to understanding and treating patients with mesenteric ischemia. However, the endless array of vascular variations can make this difficult. The celiac axis, the superior mesenteric artery SMA, and the inferior mesenteric artery (IMA) supply the foregut, midgut, and hindgut, respectively [14]. The celiac axis arises from the ventral surface of the aorta at the T12-L1 vertebral body. It courses anteroinferiorly before branching into the common hepatic, splenic, and left gastric arteries. The possible variations are too numerous to describe in this article.

The hepatic artery gives off the gastroduodenal artery, which branches further to the right gastroepiploic artery and the antero superior and postero superior pancreatico duodenal arteries. The right gastroepiploic artery communicates with the left gastroepiploic artery, which is an immediate branch of the splenic artery. The antero superior and postero superior pancreatico duodenal arteries communicate with the corresponding inferior branches from the SMA. The splenic artery gives off the left gastroepiploic artery, as well as the dorsal pancreatic artery, which supplies the body and tail of the pancreas and communicates with the antero superior pancreatico duodenal and gastroduodenal arteries and sometimes with the middle colic artery or SMA.

The left gastric artery, the third important branch of the celiac axis, communicates with the right gastric artery along the posterior aspect of the lesser curvature of the stomach. The celiac artery supplies most of the blood to the lower esophagus, stomach, duodenum, liver, pancreas, and spleen.

The SMA comes off the ventral aorta and supplies the midgut by giving off the inferior pancreaticoduodenal artery, middle colic, right colic, and jejunal and ileal branches. The inferior pancreatico duodenal artery gives rise to the corresponding anteroinferior and posteroinferior branches, which anastomose with their superior counterparts. This communication is an important connection that helps to maintain bowel perfusion in times of atherosclerosis of the mesenteric vessels. (For an illustration of a meandering artery, see the image below.)

Insufficient blood perfusion of the small bowel and colon may result from embolic or thrombotic arterial occlusion (AMAE or AMAT), thrombotic venous occlusion (ie, MVT), or nonocclusive processes such as vasospasm or low cardiac output (NOMI) [15-16]. Embolic phenomenon account for approximately 50% of all clinical cases, arterial thrombosis for about 25%, NOMI for roughly 20%, and MVT for fewer than 10%.Rarely, isolated spontaneous dissections of the SMA have been reported [17-18]. Whether the occlusion is arterial or venous, haemorrhagic infarction leading to perforation is the common pathologic pathway.

Injury severity is inversely proportional to the mesenteric blood flow and is influenced by the number of vessels involved, systemic mean blood pressure, duration of ischemia, and collateral circulation. The superior mesenteric vessels are involved more frequently than the inferior mesenteric vessels, with blockage of the latter often being silent because of better collateral circulation.

Damage to the affected bowel portion may range from reversible ischemia to transmural infarction with necrosis and perforation. The injury is complicated by reactive vasospasm in the SMA region after the initial occlusion. Arterial insufficiency causes tissue hypoxia, leading to initial bowel-wall spasm (see the image below). This leads to gut emptying by vomiting or diarrhea. Mucosal sloughing may cause bleeding into the gastrointestinal (GI) tract.

Fatty acid binding protein (FABP) is a small (12-15 kDa) intracellular protein that increases in conditions such as inflammation and ischemia. It plays a role in protecting cells from the side effects of fatty acids and increases in association with various pharmacological and pathophysiological effects, such as ischemia. Several types of FABP have been described immunologically, including heart, intestinal, liver, epidermal, muscle and adipocyte. Intestinal FABP (I-FABP) is located exclusively in gastric epithelial cells and intestinal mucosa. Recently, Vermeulen *et al*. reported that I-FABP levels increase significantly due to intestinal ischemia after aortic surgery.[19] Another study by Relja *et al*. showed that I-FABP and liver FABP (L-FABP) levels increase after abdominal trauma and are correlated with the severity of abdominal tissue injury in patients with polytrauma [20].

Perioperative management of patients with peripheral vascular disease is challenging. Extensive atherosclerotic involvement of the vascular system including coronary, renal, mesenteric and cerebral vessels predisposes it to increased perioperative mortality and morbidity in the form of myocardial infarction, congestive heart failure and renal

failure. Hence present study was planned to evaluate the Intestinal fatty acid binding protein (I-FABP) as a marker for acute intestinal ischemia in patients from Bihar region.

Methodology

The present study was conducted in Department of Surgical Gastroenterology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar. Total 20 cases of acute intestinal ischemia were enrolled in the present study as case patients. The-another 20 patients without any complication were selected in control group patients. The study was conducted from May 2016 to Jan 2017. Venous blood specimens (10 cc) were taken from patients who presented to the emergency department with abdominal pain in order to measure serum I-FABP levels. Serum specimens obtained by centrifugation at 3000 x g for 10 min were kept at -20ºC for a maximum of 6 months. Serum I-FABP levels were measured simultaneously at the end of the collection process. Human serum I-FABP levels from patients and healthy individuals were measured using a commercial ELISA (Enzy me Linked Immuno sorbent Assay kit; Hycult Biotech, the Netherlands) kit according to the manufacturer's instructions. Absorbance values were measured using a VERSA max tunable microplate reader (designed by Molecular Devices in California, USA) at a wavelength of 450 nm. Results were expressed as picograms/mL. Informed consents were taken from all the patients. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Results & Discussion

Extensive atherosclerotic disease should also increase vigilance towards other organ systems which may be hypoperfused. The development of symptomatic intestinal ischaemia after abdominal surgery in patients with atherosclerotic disease has been described [21]. The presumed mechanism is the division of vital collaterals during the surgical procedure. This sequence of events has been most frequently recognized after abdominal vascular surgery (e.g. aortic aneurysm or renal artery repair). Also there can be worsening of ischaemia in patients who have a pre-existing atherosclerosis of the mesenteric arteries. A high index of suspicion is therefore required in the presence of vague nonspecific clinical presentation. The risk factors for mesenteric artery ischaemia include age more than 65 years, cardiac arrhythmias, atherosclerosis, low cardiac output state, cardiac valvular disease and intra-abdominal malignancy [22-23]. The clinical presentation includes acute onset of severe abdominal pain if embolus is the cause. A gradual onset of pain which is visceral, poorly localized and classically out of proportion compared to findings on examination is however more common in the overall spectrum of mesenteric ischaemia. Nausea and vomiting are often present. Occult blood in rectum is seen in more than half of the cases. [23] Currently, there is no serum marker for establishing the diagnosis. The assay of intestinal fatty acid –binding protein (I-FABP), a marker of intestinal infarction, is not helpful in early diagnosis of the disease process [24]. D-dimer is a potential marker for early diagnosis. One study has reported 100% sensitivity but only 38% specificity for superior mesenteric artery thromboembolism [25].

Table 1: Demographic details of Age & Sex

Groups	Group A: Cases	Group B: Control
Cases of	Acute Intestinal Ischemia Cases	Control Cases
No. of Patients	20	20
Age and sex		
Sex		
Male	15	17
Female	5	3
Age		
0-20	0	0
21-40	5	3
41-60	4	6
61-80	9	6
81-100	2	5
Total	20	20

Table 2: Symptoms Observed

Groups	Group A: Cases	Group B: Control
Cases of	Acute Intestinal Ischemia Cases	Control Cases
No. of Patients	20	20
Distension of abdomen		
0-5	17	15
6-10	3	5
Fever		
Present	3	4
Absent	17	16
Malena		
Present	20	3
Absent	0	17
Guarding		
Present	16	14
Absent	4	6
Rigidity		

Present	11	2
Absent	9	18
Radiological diagnosis		
Positive	20	0
Negative	0	20

Table 3: Serum Parameters

Groups	Group A: Cases	Group B: Control
Cases of	Acute Intestinal Ischemia Cases	Control Cases
No. of Patients	20	20
TLC (cells/mm3)	1.28×10^3	1.14×10^3
Amylase (U/L)	51.9± 29.5	189.5 ± 48.2
Liapse (U/L)	52.6 ± 17.5	168.5 ± 21.4
Serum lactate(mg/dL)	36.5 ± 4.6	22.3 ± 5.6
Serum I-FABP(pg/mL)	589.6 ± 142.3	75.1 ± 38.5

Evennett *et al* [26]. reported that the most reliable plasma markers for intestinal ischemia are I-FABP, which is present in the mucosa of the small intestine, alpha-glutathione S - transferase, and D-lactate, which is released from bacteria in the intestinal lumen as a product of bacterial fermentation. Another study showed that an alpha-glutathione S-transferase level less than 4 ng/ml has a 100% negative predictive value in eliminating ischemic intestinal disease. The same study also showed that the increase in alpha GST levels had a negative predictive value of 92% in patients with suspected acute mesentery ischemia [27]. Bealer *et al*., [28] determined a diagnostic value of S100A8/A9 (calgranulin A/B) with 93% sensitivity and 54% specificity in patients with suspected acute appendicitis.

In a clinical study investigating the use of I-FABP as a marker in acute abdomen cases, Kanda *et al*., [29-31] enrolled a total of 96 individuals. Of these, 13 were diagnosed pre-surgically with ischemic intestinal disease (5 cases of mesenteric ischemia and 8 of strangulated hernia), 48 had a diagnosis of acute abdomen, and 35 served as healthy controls. This study also reported significantly high I-FABP values (>100 ng/mL) in 5 cases with mesenteric ischemia. Tölle *et al*., [32] reported elevated B-FABP in renal cell carcinoma patients and recommended that wider series be investigated to determine whether B-FABP could act as a tumor marker. Abdominal mass may cause ischemia, inflammation and intestinal membrane cell destruction, which do not typically lead to elevated FABP. These secondary causes may be assistant factors in these proteins being released into serum.

The exact point in time when the mesenteric ischemia occurs is often obscure in ICU patients since clinical signs of acute abdomen are frequently masked. I-FABP is abundant only at the tips of the villi of bowel mucosa and rapidly released into the circulation in case of severe mucosal ischemia [33-36]. It may be possible that I-FABP is not released when the ischemia of the bowel wall progresses and the mucosa does not recover, leading to false negative I-FABP test results. A similar case can be found in the study of Vermeulen Windsant *et al*, [33] where one patient with lethal mesenteric ischemia showed normalization of initially elevated I-FABP until day 4 after cardiac surgery. On the other hand, elevation of I-FABP over a short period of time may reflect transient mesenteric hypoperfusion and seems to not necessarily predict development of a transmural bowel necrosis, since regeneration of the bowel is possible when perfusion is restored. In the study of VermeulenWindsant *et al*., patients had serum I-FABP levels up to 2300 pg/ml (ELISA kit, Fa. HyCult) during open aortic surgery without developing mesenteric complications. Levels returned to normal until day one after surgery.

Conclusion

The data generated from present study concludes that Intestinal ischemia is a surgical emergency and warrants immediate surgical intervention. Quicker diagnosis aided by serum I-FABP levels will enable us to intervene in such patients quickly reducing morbidity and mortality among patients.

I-FABP levels may be used to diagnose such fatal pathologies. Further studies with wider series are needed in order to investigate the diagnostic value of I-FABP in patients with abdominal pain.

References

1. Bobadilla JL. "Mesenteric ischemia". The Surgical Clinics of North America. 2013; 93(4):925–40, ix. doi:10.1016/j.suc.2013.04.002. PMID 23885938.
2. Yelon Jay A. Geriatric Trauma and Critical Care (Aufl. 2014 ed.). New York: Springer Verlag, 2014, 182. ISBN 9781461485018. Archived from the original on 2017-09-08.
3. Britt LD. Acute care surgery (1st ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2012, 621. ISBN 9781608314287. Archived from the original on 2017-09-08.
4. Geoffrey D Rubin. CT and MR Angiography: Comprehensive Vascular Assessment. Lippincott Williams & Wilkins, 2012, 318. ISBN 9781469801834. Archived from the original on 2017-09-08.
5. Gustavo S Oderich. Mesenteric Vascular Disease: Current Therapy. Springer, 2014, 105. ISBN 9781493918478. Archived from the original on 2017-09-08.
6. Sachs SM, Morton JH, Schwartz SI. Acute mesenteric ischemia. Surgery. 1982 Oct. 92(4):646-53. [Medline].
7. Cokkinis AJ. Observations on the mesenteric circulation. J Anat. 1930;. 64:200-205. [Medline].
8. Mamode N, Pickford I, Leiberman P. Failure to improve outcome in acute mesenteric ischaemia: seven-year review. Eur J Surg. 1999;. 165(3):203-8. [Medline].
9. Alpern MB, Glazer GM, Francis IR. Ischemic or infarcted bowel: CT findings. Radiology. 1988; 166(1 Pt 1):149-52. [Medline].
10. Kim MY, Suh CH, Kim ST, Lee JH, Kong K, Lim TH, *et al*. Magnetic resonance imaging of bowel ischemia induced by ligation of superior mesenteric artery and vein in a cat model. J Comput Assist Tomogr. 2004; 28(2):187-92. [Medline].
11. Kozuch PL, Brandt LJ. Review article: diagnosis and management of mesenteric ischaemia with an emphasis on pharmacotherapy. Aliment Pharmacol Ther. 2005; 21(3):201-15. [Medline].

12. Aksu C, Demirpolat G, Oran I, Demirpolat G, Parildar M, Memis A. Stent implantation in chronic mesenteric ischemia. ActaRadiol. 2009; 50(6):610-6.
13. Schoots IG, Levi MM, Reekers JA, Lameris JS, van Gulik TM. Thrombolytic therapy for acute superior mesenteric artery occlusion. J VascInterv Radiol. 2005; Mar. 16(3):317-29.
14. Rosenblum JD, Boyle CM, Schwartz LB. The mesenteric circulation. Anatomy and physiology. Surg Clin North Am. 1997; 77(2):289-306.
15. Boley SJ. Circulatory responses to acute reduction of superior mesenteric arterial flow. Physiologist. 1969; 12:180.
16. Chang RW, Chang JB, Longo WE. Update in management of mesenteric ischemia. World J Gastroenterol. 2006; 12(20):3243-7.
17. Leung DA, Schneider E, Kubik-Huch R, Marincek B, Pfammatter T. Acute mesenteric ischemia caused by spontaneous isolated dissection of the superior mesenteric artery: treatment by percutaneous stent placement. EurRadiol. 2000; 10(12):1916-9. [Medline].
18. Miyamoto N, Sakurai Y, Hirokami M, Takahashi K, Nishimori H, Tsuji K, *et al*. Endovascular stent placement for isolated spontaneous dissection of the superior mesenteric artery: report of a case. Radiat Med. 2005; 23(7):520-4.
19. I C Vermeulen Windsant, *et al*., "Circulating intestinal fatty acid-binding protein as an early marker of intestinal necrosis after aortic surgery: a prospective observational cohort study," Annals of Surgery. 2012; 255(4):796–803.
20. Relja *et al*. • I-FABP AND L-FABP IN ABDOMINAL INJURY, ACAD EMERG MED, 2010, 17(7),www.aemj.org
21. Thomas JH, Blake K, Pierce GE, Hermreck AS, Seigel E. The clinical course of asymptomatic mesenteric arterial stenosis. J VascSurg.1998; 27:840-4.
22. McKinsey JF, Gewertz BL. Acute mesenteric ischemia. SurgClin North Am. 1997; 77:307-18.
23. Wadman M, Syk I, Elmstahl S. Survival after operation for ischemic bowel disease. Eur J Surg. 2000; 166:872-7.
24. Kanda T, Fujii H, Tani T, Murakami H, Suda T, Sakai Y, *et al*. Intestinal fatty acid-binding protein is a useful diagnostic marker for mesenteric infarction in humans. Gastroenterology. 1996; 110:339-43.
25. Acosta S, Nilsson TK, Bjorck M. Preliminary study of D-dimer as a possible marker of acute bowel ischaemia. Br J Surg. 2001; 88:385-8.
26. 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.
27. Delaney CP, O'Neill S, Manning F, Fitzpatrick JM, Gorey TF. Plasma concentrations of glutathione S-transferaseisoenzyme are raised in patients with intestinal ischaemia. Br J Surg. 1999; 86:1349-53. CrossRef
28. Bealer JF, Colgin M. S100A8/A9: a potential new diagnostic aid for acute appendicitis. AcadEmerg Med. 2010; 17:333-6.
29. Kanda T, Fujii H, Tani T, Murakami H, Suda T, Sakai Y, *et al*. Intestinal fatty acid-binding protein is a useful diagnostic marker for mesenteric infarction in humans. Gastroenterology. 1996; 110:339-43.
30. Kanda T, Nakatomi Y, Ishikawa H, Hitomi M, Matsubara Y, Ono T, *et al*. Intestinal fatty acid-binding protein as a sensitive marker of intestinal ischemia. Dig Dis Sci. 1992; 37:1362-7.
31. 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. 1995; 36:788-91.
32. Tölle A, Jung M, Lein M, Johannsen M, Miller K, Moch H, *et al*. Brain-type and liver-type fatty acid-binding proteins: new tumor markers for renal cancer? BMC Cancer. 2009; 9:248.
33. IC Vermeulen Windsant, *et al*. "Circulating intestinal fatty acid-binding protein as an early marker of intestinal necrosis after aortic surgery: a prospective observational cohort study," Annals of Surgery. 2012; 255(4):796–803.
34. A Camkıran, *et al*. "Clinical significance of intestinal type fatty acid binding protein in patients undergoing coronary artery bypass surgery," AnadoluKardiyolojiDergisi. 2011; 11(6):536–541.
35. DH Schellekens, J Grootjans, SA. Dello, *et al*., "Plasma intestinal fatty acid-binding protein levels correlate with morphologic epithelial intestinal damage in a human translational ischemia-reperfusion model," Journal of Clinical Gastroenterology. 2014; 48:253–260.
36. SJ Hanssen, *et al*., "Visceral injury and systemic inflammation in patients undergoing extracorporeal circulation during aortic surgery," Annals of Surgery. 2008; 248:117–125.