European Review for Medical and Pharmacological Sciences 2012; 16: 370-375

Pancreatic injury during AAA repair: a comparison between EVAR and open repair

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Abstract. – *Objectives:* **Enzymatic pancreatic injury (EPI) in abdominal aortic aneurysm (AAA) treatment has been scarcely studied in the literature. Aim of this work was to compare perioperative EPI in AAA patients treated by endovascular repair (EVAR) or open repair (OR).**

Methods: **Forty AAA patients consecutively treated with either EVAR (GI, 20 pts) or OR (GII, 20 pts) were prospectively evaluated in terms of epidemiology, comorbidities and technical details. Serum levels of amylase, lipase and pancreatic isoamylase were assessed before treatment (T0), before aortic clamping/endograft deployment (T1), 1, 2, and 6 hours after aortic declamping/endograft deployment (T2, T3, T4) and 24, 48, and 72 hours after the procedure (T5, T6, T7). GI and GII were compared by Mann Whitney test with significance set at $p < 0.05$.**

Results: **GI patients were significantly older and with higher frequency of preoperative renal insufficiency than GII ones ($p = 0.001$ and 0.047 respectively). Other characteristics were not significantly different.**

Pancreatic enzymes values at T0 were within normal parameters in all patients. Total serum amylase was significantly greater at T4 ($p = 0.003$), T5 ($p = 0.010$), T6 ($p = 0.003$), T7 ($p = 0.011$) and isoamylase at T3 ($p = 0.052$), T4 ($p = 0.037$), T5 ($p = 0.016$) and T6 ($p = 0.014$) in GII compared with GI. Amylase and isoamylase peak occurred 24 hours after the procedure. Lipase was significantly different in the two groups only in T4 ($p = 0.028$). No acute pancreatitis occurred in the whole study group.

Conclusions: **EVAR significantly reduces EPI compared with OR in the AAA treatment.**

Key Words:

Aortic aneurysm, Endograft, Pancreatic injury.

Introduction

Pancreatic injury, seen as increased serum concentrations of pancreatic enzymes, is a poorly studied aspect in the literature about abdominal aortic aneurysms (AAA). The pancreatic damage can range from subclinical paintings, characterized by increase in serum concentration of amylase, lipase and pancreatic isoamylase to clinical necrotizing pancreatitis.

In patients undergoing cardiac surgery with cardiopulmonary bypass, an acinar cell injury was detected in more than 25% of the patients[1].

The clinical presentation of an acute pancreatitis is a rare complication in AAA surgery, with a reported frequency ranging between 0.7% to 1.1%[2,3]. However, this complication is burdened with a high mortality rate (from 10% to 100%) according to the severity of pancreatitis[2], and may be secondary to pancreatic ischemia or perioperative ischemic injury of the pancreas[3].

There are no data available on pancreatic damage in patients undergoing aortic endovascular repair (EVAR), and only a single case of pancreatis has been reported to date[4].

The aim of our study was to determine and compare the enzymatic pancreatic injury (EPI) in patients treated for AAA with open repair (OR) and EVAR.

Materials and Methods

Forty non-randomized patients consecutively treated for AAA were prospectively included in the study between May 2009 and February 2010: 20 were submitted to EVAR (GI) and 20 to OR (GII).

In all patients, serum concentrations of total amylase, lipase and pancreatic isoamylase were assayed at admission (T0), before aortic clamping/release of aortic endograft (T1), 1, 2 and 6 hours after release of the aortic clamp/release of endograft (T2-T3-T4), in the first, second and

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third postoperative day (T5-T6-T7). Amylase activity was determined using a enzymatic colorimetric method (IFCC/EPS, in accordance with International Federation of Clinical Chemistry using as substrate the Etilidene-pnP-G7, Roche); pancreatic isoamylase activity was determined using enzymatic colorimetric inhibitor method through two monoclonal antibodies (Roche, Roche Diagnostic, Indianapolis, IN, USA); lipase activity was determinated by enzymatic colorimetric method (Roche, Roche Diagnostic, Indianapolis, IN, USA).

Serum levels of total amylase, lipase and pancreatic isoamylase of each patient were collected in a database with the patients' demographic characteristics (gender and age), cardiovascular risk factors (hypertension, diabetes mellitus, dyslipidemia, smoking), renal insufficiency (serum creatinine >1.5 mg/dl) and the anaesthesiology risk (ASA). The following chemistry parameters were also considered: glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), blood urea nitrogen (BUN), alkaline phosphatase and gamma-glutamyl transpeptidase. In GI, AAA treatment was considered according to the type of endograft (infrarenal and suprarenal fixation or fenestrated graft), to the use of proximal endograft ballooning and to the amount of contrast medium. In GII we have considered the type and time of aortic clamping (infrarenal, suprarenal and sub-diaphragmatic). We have finally considered the type of anaesthesia and postoperative complications.

Statistic Analysis

A descriptive assessment of the collected data was conducted. Mean and standard deviation were used for quantitative variables, the percentage for qualitative variables. The homogeneity of the two groups of treatment was assessed by Fischer's exact test and Mann-Whitney test.

The pancreatic enzyme response between GI and GII was then evaluated and compared; for comparing the means of pancreatic enzymes in the two groups, statistical analysis was performed using ANOVA.

Statistical significance was assigned to a p value < 0.05. The calculations were performed using SPSS for Windows software (version 13, SPSS Inc., Chicago, IL, USA).

Results

The two groups were homogeneous for all variables considered except for age and chronic renal failure (Table I). Patients in GI were older and with a higher incidence of renal failure than those of GII (GI vs. GII age = 76.60 ± 4.72 vs 68.10 ± 7.74, p = 0.001, CRF = 5 pts (25%) vs 0 pts (0%), p = 0.047).

Twelve endografts with infrarenal fixation (60%), 6 with suprarenal fixation (30%) and two fenestrated endografts (10%) were used in GI, with proximal juxtarenal aortic ballooning of the endograft in 50% of cases. In GII, clamping site was infrarenal in 15 patients (75%), suprarenal in 3 (15%), and supraceliac in 2 (10%).

Table I. Features of the patients in the two groups and statistical comparison.

Features of patients	GI (EVAR)	GII (OpenRepair)	*P*-value
Mean age (years)	76.60 ± 4.72	68.10 ± 7.74	0.001
Male	18 (90%)	18 (90%)	1.000
Hypertension	19 (95%)	16 (80%)	0.342
Diabetes	1 (5%)	3 (15%)	0.605
Altered lipid metabolism	13 (65%)	9 (45%)	0.341
Smoke	4 (20%)	9 (45%)	0.176
Alcohol	0 (0%)	1 (5%)	1.000
Cholelithiasis	1 (5%)	2 (10%)	1.000
Chronic renal failure (CRF)	5 (25%)	0 (0%)	0.047
Serum-glutamic oxaloacetic transaminase (GOT) (U/L)	17.65 ± 1.63	21.15 ± 8.00	0.121
Serum-glutamic pyruvic transaminase (GPT) (U/L)	20.15 ±1.60	20.30 ± 16.00	0.398
Alkaline phosphatase (U/L)	154.00 ± 54.31	156.00 ± 48.94	0.425
Gamma-glutamyl transpeptidase (γ-GT) (U/L)	29.50 ± 16.00	36.40 ± 19.00	0.329
Blood urea nitrogen (BUN) (mg/dL)	58.25 ± 33.44	56.00 ± 58.34	0.121
American Society of Anesthesiologists (ASA)[4]	2 (10%)	2 (10%)	1.000

Table II. Comparison of mean amylase serum levels in the two groups at the different intervals.

Intervals	Amylase GI (U/L)	Amylase GII (U/L)	*P*-value
T0	62.25	64.90	0.689
T1	52.35	59.60	0.238
T2	59.75	60.45	0.931
T3	63.20	69.85	0.525
T4	67.05	121.40	0.003
T5	64.75	151.65	0.010
T6	46.60	112.05	0.003
T7	41.00	82.00	0.011

GI = EVAR; GII = OR.

Spinal anaesthesia was used in all cases of GI but two, and general anaesthesia in all GII patients.

The values of pancreatic enzymes at T0 were within normal values in all patients studied. Total serum amylase was significantly increased in GII compared with GI at T4 (p = 0.003), T5 (p = 0.010), T6 (p = 0.003), T7 (p = 0.011) (Table II) (Figure 1). Pancreatic isoamylase was significantly increased at T3 (p = 0.052), T4 (p = 0.037), T5 (p = 0.016) and T6 (p = 0.014) (Table III) (Figure 2). Lipase was significantly different in the two groups only in T4 (p = 0.028) (Table IV) (Figure 3). The peak levels of amylase and pancreatic isoamylase were recorded 24 hours after OR.

In GI there was no significant difference in enzymatic response according to the amount of contrast medium. Clinical picture of acute pancreatitis did not occur in any patient. Mortality was 0% in both groups, with one case of acute myocardial ischemia in GII, and one case of renal function deterioration in GI.

Discussion

All patients included in the study had preoperative non-pathological serum pancreatic enzyme and had no clinical history of pancreatic disease or alcoholism. In patients treated with OR we ob-

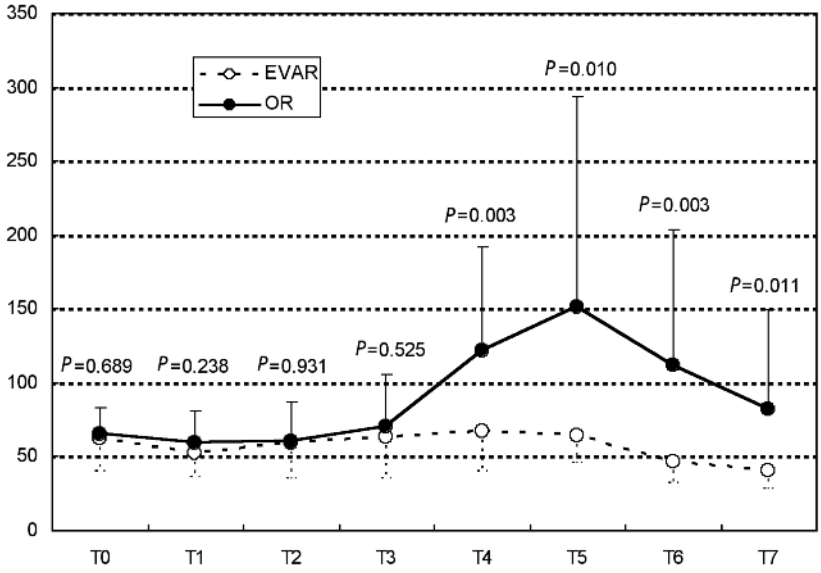

Figure 1. Statistical comparison of mean amylase serum levels in the two groups at the different intervals. (GI = EVAR; GII = OR).

Table III. Comparison of mean pancreatic isoamylase serum levels in the two groups at the different intervals.

Intervals	Pancreatic isoamylase GI (U/L)	Pancreatic isoamylase GII (U/L)	*P*-value
T0	32.95	32.60	0.932
T1	24.95	32.55	0.063
T2	31.65	39.50	0.167
T3	32.75	51.75	0.052
T4	33.75	58.50	0.037
T5	32.70	63.60	0.016
T6	30.00	51.40	0.014
T7	28.65	38.20	0.104

GI = EVAR; GII = OR.

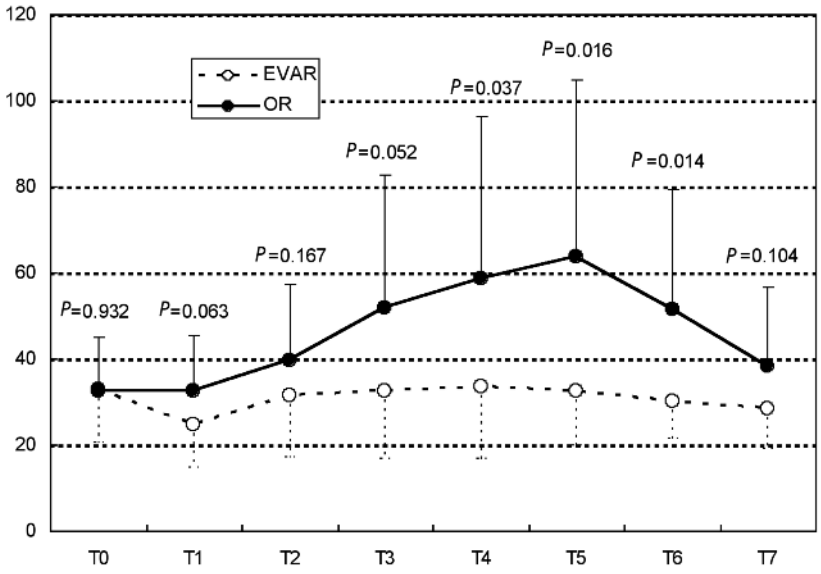

Figure 2. Statistical comparison of mean pancreatic isoamylase serum levels in the two groups at the different intervals. (GI = EVAR; GII = OR).

Table IV. Comparison of mean lipase serum levels in the two groups at the different intervals.

Intervals	Lipase GI (U/L)	Lipase GII (U/L)	*P*-value
T0	30.95	28.30	0.496
T1	26.20	35.20	0.173
T2	25.85	50.65	0.159
T3	27.95	49.35	0.149
T4	28.25	82.15	0.028
T5	26.50	47.10	0.099
T6	25.50	37.30	0.225
T7	26.60	31.20	0.560

GI = EVAR; GII = OR.

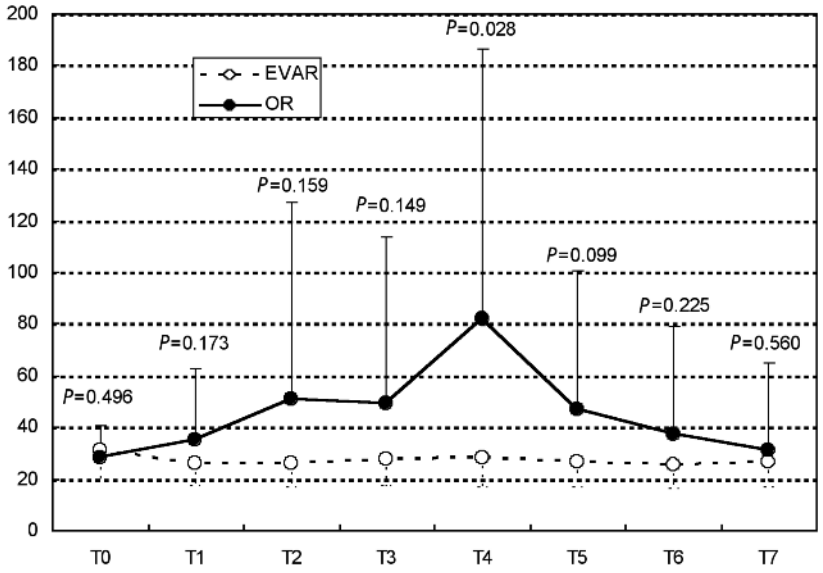

Figure 3. Statistical comparison of mean lipase serum levels in the two groups at the different intervals. (GI = EVAR; GII = OR).

served a significant increase in pancreatic amylase and isoamylase in comparison with patients treated with EVAR. In particular, amylase significantly increased in patients treated with OR from six hours after release of aortic clamp/release of endograft (T4) until 72 hours post-operatively. The peak of amylase was observed after 24 hours from treatment. Regarding pancreatic isoamylase, in patients treated with OR, there was a significant rise after only two hours from release of aortic clamp/release of endograft, which was maintained until 48 hours after treatment (T6). Regarding the pancreatic isoamylase, the peak of concentration was observed after 24 hours from treatment. These data may suggest that the pancreatic isoamylase represents an earlier marker of pancreatic injury. Pancreatic injury during AAA repair is a rare poorly studied complication in the literature: it may occur with a very wide range that varies from sub-clinical manifestations characterized by rising concentrations of serum amylase, lipase and isoamylase as far as acute necrotizing pancreatitis[5,6], which is diagnosed in some cases only at autopsy[2]. In the literature, cases of pancreatic injury are described associated with cardiac surgery[1,7,8] and gastrointestinal and biliary tract surgery[9,10].

Clinical experiences of acute pancreatitis are reported after OR in the treatment of AAA, but we have little data on the pancreatic enzyme response in the perioperative period[11]. In a previous study [11] we compared the pancreatic enzyme response in patients treated with OR for thoracoabdominal aortic aneurysm and infrarenal aortic aneurysm. In this last group (20 patients) no statistically significant changes in enzymes concentrations (amylase, lipase and pancreatic isoamylase) were observed, although an increase in pancreatic enzymes concentrations was seen 1, 2 and 6 hours after release of the aortic clamp in 2 of these patients. There are currently no published prospective studies comparing pancreatic enzyme response in patients treated for AAA with EVAR or OR. Our work is original in presenting different EPI data after different types of treatment. Higher EPI after OR are probably correlated with the greater invasiveness of this treatment. Only one case of acute pancreatitis after treatment is reported in the literature[4] in AAA patients treated with EVAR.

Several hypotheses explaining the onset of pancreatitis after surgical treatment of the abdominal aortic aneurysms are reported in the literature: pancreatic ischemic damage may occur following a perioperative visceral hypoperfusion or it can be secondary to the rotation of visceral vessels during isolation of pararenal aorta with an estimated frequency of up to 5%[12]. Another possible cause of acute pancreatitis after OR is atheroembolism, as reported already in 1957 by Probstein et al[13] and later confirmed by other observations[14]. Embolization may occur during aor-

tic clamping or for flow turbulence at the site of proximal aortic clamping. Another cause of postoperative acute pancreatitis may be an undetected biliary or pancreatic disease[2].

One hypothesis for pancreatic damage after EVAR is the effect of iodinated contrast medium. However, this hypothesis is not confirmed by a study showing no significant changes in amylase, lipase, C-reactive protein and leukocyte levels after injection or non injection of CT contrast medium in patients with severe acute pancreatitis[15].

In our study, inside each group, we have considered different types of intervention: in the group GI, the sovrarenal or infrarenal endograft fixation, while in the group GII the suprarenal, infrarenal or subdiaphragmatic aortic clamping.

None of the patients studied had symptoms of acute pancreatitis after treatment. Therefore the real clinical significance of EPI after treatment of an AAA remains undefined.

However, the fact that the OR is a possible cause for major EPI, may be an issue for preferring the EVAR in patients who require treatment for AAA and are carriers of a pancreatic disease.

Conclusions

This is the first prospective study of EPI after treatment of AAA with EVAR and OR. EVAR significantly reduces EPI compared with OR, on the basis of pancreatic enzymes increase in the first 72 hours after surgery. However, the real clinical significance of these observations remains undefined and requires further studies on larger series.

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