Surgical Treatment of Inflammatory Abdominal Aortic Aneurysms: Outcome and Predictors Analysis

Edmond Nuellari, Edvin Prifti, Giampiero Esposito, Edmond Kapedani

Division of Cardiovascular Surgery, University Hospital Center of Tirana, Tirana, Albania

Humanitas Gavazzeni Clinic, Bergamo, Italy

ABSTRACT

Objectives: The aim of this study is to report our experience on the postoperative outcome of surgical treatment of inflammatory abdominal aortic aneurysm (IAAA).

Materials and Methods: Between 1997-2014, 35 patients with IAAA underwent surgery. The mean age was 63 +/- 18 years. Chronic renal failure was identified in 11 (31.4%) patients and confirmed ischemic heart disease in 15 (43%) patients. The mean aortic aneurysm diameter was 68 +/- 25 mm. The abdominal aorta was clamped above the renal arteries in 6 (17%) patients.

Results: The hospital mortality was 5.7% (2 patients). Three patients developed an aortic pseudoaneurysm and underwent a redo operation. Another patient developed a femoral anastomotic pseudoaneurysm 7 years after operation and he was treated surgically. The actuarial free-reoperation actuarial survival at 1, 5 and 7 years was 94%, 62% and 50% respectively. The Cox model revealed the delta ESR (p=0.002), ischemic heart disease (p=0.006) and renal failure (p=0.036) as strong predictors for poor overall outcome.

Conclusion: Early postoperative outcome in terms of mortality and morbidity seems acceptable, however patients with IAAA have an increased risk for reoperation due to pseudonaneurysm formation. Strong predictors for poor overall outcome seems to be the elevated erythrocyte sedimentation rate, ischemic heart disease and chronic renal failure.

Key Words: inflammatory aneurysm, aorta, surgery, abdominal, surgery.

1. INTRODUCTION

Inflammatory abdominal aortic aneurysms (IAAA), are characterized by marked thickness of the aortic wall, with dense perianeurysmal fibrosis involving adjacent organs (1, 2) such as inferior vena cava, ureters, and the third portion of the duodenum.

The prevalence of IAAA in autopsy material ranges between 2.5% and 10% of all aneurysms (3, 4). The IAAA is considered a distinct variant of AAA and accounts for 2% to 14% of all cases (5, 6). The first report of IAAA was by James in 1935, for a fatal case of uremia caused by inflammation and fibrosis (7). The first morphological definition of IAAA was provided by Walker et al (8) in 1972. The symptomatology and clinical findings of IAAA are not well established, and the epidemiological data are uncertain. The inflammatory process can be due to such conditions as syphilitic arterial disease, tuberculosis, giant cell arteritis and non specific infections, but the etiology of most IAAA cannot be established (4). Bacterial cultures from IAAA are usually negative (9). Some authors suggest that autoimmune mechanisms are involved in the pathogenesis of IAAA. However, Haug et al (10) in 150 consecutive patients undergoing surgery for IAAA revealed an IAAA in their first-degree relatives. The development of visceral organ complications in previously involved or uninvolved structures attributable to ongoing fibrosis after surgical intervention are well-known complications, but the impact of ongoing inflammation on longterm survival remains to be determined (11, 12).

The aim of this study is to report our 17 years experience on the early and late outcome of surgical treatment of IAAA and to evaluate the predictors for poor overall survival in this pool of patients.

2. MATERIALS AND METHODS

Between January 1997 and March 2014 total number of 430 consecutive patients underwent elective surgical repair for non-rupture abdominal aortic aneurysm. 35 patients (8.2 %) were classified as IAAA. Aneurysms were classified as inflammatory when macroscopic or microscopic findings such as gross computed tomography or intraoperative appearance of marked thickening of the aneurysm wall were observed with encasement of surrounding retroperitoneal organs, infiltrates of lymphocytes and plasma cells, endoarteritis obliterans, and fibrosis around nerve as previously described in the literature (8, 13, 14).

Basically the aneurysm was accepted as inflammatory if all of the following were present: (1) marked thickening of the aneurysm wall; (2) presence of periaortic fibrosis and...
inflammatory process involving adjacent organs; and (3) histopathologic evidence of inflammation at the biopsy material. Histologic confirmation was routinely obtained in all patients.

Patients’ characteristics are given in Table 1. The mean age of patients was 63 ± 18 years (range 43-78 years). Chronic renal failure with a creatinine level >2mg/dl was identified in 11 (31.4%) patients and confirmed ischemic heart disease in 15 (43%) patients. In patients with hydronephrosis, a ureteral stent was inserted before surgery. In these patients the intraoperative findings showed severe retroperitoneal fibrosis causing compression to the vena cava and ureters. Two patients had clinical evidence confirmed by color duplex scanning of deep venous thrombosis. 6 (17%) patients were asymptomatic.

| Variables                  | Nr (%)       |
|---------------------------|--------------|
| Total Nr of patients      | 35 (100%)    |
| Mean age (years)          | 63±18        |
| Range (years)             | 43-78        |
| Male, sex                 | 26 (74.2%)   |
| Smokers (>10 cigarette/die)| 17 (48.6%)   |
| History of aneurysm in family | 3 (8.6%)  |
| Hypertension              | 17 (48.6%)   |
| Dyslipidemia              | 10 (28.6%)   |
| Diabetes mellitus         | 6 (17%)      |
| Chronic renal failure     | 11 (31.4%)   |
| Peripheral arterial disease | 9 (25.7%)   |
| Ischemic heart disease    | 15 (43%)     |
| Cerebro-vascular disease  | 3 (8.6%)     |
| Chronic obstructive pulmonary disease | 6 (17%) |
| Elevated ESR              | 21 (60%)     |
| CRP in 15 patients (mg/dl)| 1.2 ± 0.8    |

Table 1. Preoperative patients characteristics. Legend: ESR – erythrocyte sedimentation rate, CRP – C reactive protein

Preoperative diagnostic. All patients underwent preoperative ultrasound tomography. Preoperative ultrasound tomography alone was performed in 4 (11%) patients and in none of them was an inflammatory process detected. Computed tomography was performed in the 31 (89%) patients and detected inflammatory aortic or retroperitoneal fibrosis in 27 (77%) patients with detection of the Mantle sign (9, 15) (Table 2). The mean maximal aneurysm diameter was 68 ± 25 mm (range 50-90mm).

Four patients underwent angiography and the inflammation process was demonstrated in only 1 (2.9%) patient, where the aneurismal wall seemed very thin and multiple ureteral stenosis was present. The overall preoperative diagnosis was achieved in 27 (77%) patients, while in the remaining, the intraoperative findings confirmed the diagnosis (13).

Intraoperative data. Transperitoneal standard median open laparotomy was the standard approach used in all cases. We exposed the proximal neck of the aneurysmal sac by upward mobilization of the left renal vein. The sites of the aortic calmping were choosed distant from the thickened parts of the aneurysmal wall or extensive fibrous adhesion to adjoining tissues and structures. The abdominal aorta was clamped above the renal arteries in 6 (17%) patients and below the renal arteries in 29 (83%) patients. The inferior clamp was employed at the common iliac arteries. Following the control of distal aorta, the aorta was clamped and the sac was opened at the right anterolateral aspect. The aneurysmatic segment was replaced with an appropriately sized Dacron tube graft in 21 (60%) patients, whereas in the remaining 14 (40%) patients, an aorto-bifemoral bypass operation was performed by using a bifurcated graft. The intraoperative data are given in Table 3.

| Variables                  | Nr (%)       |
|---------------------------|--------------|
| Abdominal pain            | 29 (83%)     |
| Lumbar pain               | 26 (74%)     |
| Weight loss               | 28 (80%)     |
| Tenderness in palpation   | 25 (71.4%)   |
| Fever                     | 22 (63%)     |
| Asymptomatic              | 6 (17%)      |
| Deep venous thrombosis    | 3 (8.6%)     |
| Aneurysm size >7cm        | 18 (51.4%)   |
| Mantle sign               | 27 (77%)     |
| Hydronephrosis            | 2 (5.7%)     |

Table 2. Preoperative symptoms

Intraoperative diagnosis was based on the characteristic appearance of an aorta encased in a thick white fibrotic tissue that appeared thick in all cases and especially in the anterior part of the aortic wall. In 7 (20%) patients the retroperitoneal fibrosis involved the ureters. In 29 (83%) patients specimens were obtained in the operating room and were sent to the laboratory to undergo histological examination. The main finding was fibrosis of the adventitia with lymphocyte and other plasma cell proliferation.

Follow-up. The first control visit was performed at one month after the operation. Patients underwent clinical examination by vascular surgeons and abdominal ultrasound examination at 3 months after the operation and annually thereafter. At 3 months after the surgical procedure the ESR rate was measured and compared with the preoperative value. The delta ESR was calculated according to the formula (preoperative ESR – postoperative ESR)
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Statistical analysis. Group statistics were expressed as mean ± SD. The relationship between preoperative and postoperative variables within the same group was assessed by the McNemar test. The multivariate Cox proportional regression (Statsoft 6-0) was performed to determine independent predictors. Long-term survival rates were calculated using the Kaplan-Meier method and the long rank test. Significance between data was considered achieved when p<0.05.

3. RESULTS

The hospital mortality was 5.7% (2 patients). One patient died on the 4th postoperative day due to myocardial infarction. The other patients developed renal failure requiring continuous veno-venous hemofiltration. He died in the 7th postoperative day due to multi organ failure.

Other complications included deep venous thromboses and pulmonary embolism in 1 (2.9%) patient and creatinine arose postoperatively in 9 (26%) patients. Table 4 demonstrate the perioperative (30-days) complications. The extensive retroperitoneal fibrosis caused technical difficulties and increased bleeding in some cases; 9 (26%) patients were transfused in the postoperative period receiving 4 blood units (range 3-5). In one patient the inferior vena cava was damaged and reconstructed. One patient underwent thromboembolectomy of the lower limb due to acute postoperative ischemia on the second postoperative day.

Three patients were lost during follow-up. One patient died from a pseudoaneurysm rupture 8 months after the operation without undergoing reoperation. At follow-up, ten patients died due to myocardial infarction, stroke, pneumonia, and neoplastic disease. (Table 5).

### Table 4. Perioperative and postoperative complications

| Complications           | Nr (%)  |
|-------------------------|---------|
| Cardiac                 |         |
| Arhythmias              | 10 (28.6%) |
| Ischemia                | 3 (8.6%)  |
| Pulmonary               |         |
| Pulmonary embolism      | 1 (2.9%)  |
| Vascular                |         |
| Acute limb ischemia     | 1 (2.9%)  |
| Deep vein thrombosis    | 1 (2.9%)  |
| Intestinal              |         |
| Prolonged paralytic ileus | 3 (8.6%) |
| Renal                   |         |
| Higher creatinine       | 9 (25.7%) |
| CVVHD                   | 1 (2.9%)  |
| Wound                   |         |
| Abdominal               | 1 (2.9%)  |
| Inguinal                | 1 (2.9%)  |

The Cox model revealed the delta ESR (p=0.002), ischemic heart disease (p=0.006) and renal failure (p=0.036) as strong predictors for poor overall outcome (Table 6). The advanced age was a predictor in the limits of significance (p=0.07).

### Table 6. Predictors for poor overall free reoperation survival

| Variables          | Beta    | Standard | t value | Wald | p value |
|--------------------|---------|----------|---------|------|---------|
| CAD                | -1.65   | 0.6      | -2.74   | 7.52 | 0.006   |
| Delta ESR          | -1.8    | 0.62     | 3       | 9    | 0.002   |
| CRF                | -1.7    | 0.81     | 2.1     | 4.4  | 0.036   |
| Age                | -1.22   | 0.74     | -1.75   | 3.4  | 0.07    |

4. DISCUSSION

The pathophysiology of the IAAA remains unclear. Some authors suggested that atherosclerotic aneurysm formation is the preceding phenomena, and that the inflammatory response is a secondary change(9). This hypothesis considers the IAAA as the end of an inflammatory process (4, 13). Other reports described the possible involvement of an autoimmune reaction (15). Patients with IAAA sometimes show serological autoimmune abnormalities; such as, the presence of auto-antibodies,
or the presence of systemic autoimmune disease (25). Many investigators suggested various theories like infective causes (viral, bacterial), or non specific arterial infections), autoimmunity, giant cell arteritis, vasa vasorum deficiency (4, 16-18). Various theories have been suggested including infected causes. Railo et al (3) found syphilitic arterial disease in 2 cases and tuberculosis in one case.

Most of the patients in our series were symptomatic. The large aneurysm size may be responsible for the presence of symptoms and signs. The pulsing mass, weight loss and elevated ESR level have been considered as a triad of IAAA. The intestinal tract or urethral obstruction due to diffuse retroperitoneal fibrosis might be present. However, preoperative recognition of IAAA requires a comprehensive examination and evaluation of the individual patient.

The sensitivity of computed tomography in our study was 87% and sensitivity of ultrasound examination 0%. Our experience confirms the findings of high sensitivity of computed tomography scanning and no sensitivity of the ultrasounds to the inflammatory nature of disease (3). Iino et al (19) showed 90% sensitivity for computed tomography. Computerized tomography is the most reliable diagnostic modality for IAAA. Therefore, computerized tomography images must be examined carefully before surgery to identify signs such as the mantle sign (8), which is a characteristic IAAA sign perceivable on computerized tomography images.

The transperitoneal approach was chosen in all patients. Because the anterior portion of the aorta is most affected by the inflammatory reaction, the retroperitoneal approach is thought to reduce risk for duodenal and left renal vein injury, as well as inferior vena cava injury and to gain proximal control more safely. In our series, the median laparotomy was demonstrated safe and effective.

The fibrotic process complicated surgical dissection and exposure of the aorta, however it does not seem to influence the results of surgery in terms of survival. Surgical injury to the adherent organs has been reported in 4.5% to 15% of cases (20). In one case in our series the inferior vena cava was injured and re-constructed with direct prolene suture. While performing adhesiolysis, it is important to avoid damage to the surrounding organs, particularly to the intestines (12). The proximal side of the inflammatory aneurysm normally extends to the lower border of the left renal vein. Similarly, in cases involving inflammatory aneurysm of the common iliac arteries, it is necessary to clamp the external iliac arteries, which are generally not inflamed, in order to perform minimal dissection.

The incidence of obstructive uropathy in IAAA is approximately 20% (6). In our series, the incidence of preoperative chronic renal failure was 31.5%, but only 2 patients presented with obstructive uropathy. 9 of them including the 2 patients with obstructive uropathy presented an increased creatinine level during the postoperative course. Despite the surgical intervention, the fibrotic process did not resolve or even progress in some patients. Therefore, we believe that postoperative persistence or progression of ureteral entrapment was the underlying cause of renal dysfunction. The postoperative renal failure in these patients was possibly due to the ureteral involvement.

Patients in this present series had acceptable short and long-term mortality rates which were quite comparable with those reported in the literature for non inflammatory AAA (21, 22).

Late evolution of periaortic fibrosis in IAAA is still controversial. Some reports showed regression after graft repair in almost all patients (9), whereas more recent studies have shown partial or no regression of the fibrotic process (5, 12, 15). Certainly, the length and the methods of follow-up vary among papers, and some observations are sporadic. In 4 patients requiring reoperation due to aortic pseudoaneurysm, signs of fibrotic process were evident in 3 of them, and not present in the last patient undergoing reoperation 6 years later after the first operation. We can be hypothesized that regression of fibrosis can take several years to complete, and that such a process is not necessarily related to normalization of the ESR, which occurs much earlier during the follow-up of these patients.

Interestingly in our series we found a high incidence of long term pseudoaneursymal formation rate. In our series, one patient developed an aortic pseudoaneurysm 8 months after operation and three patients developed an aortic pseudoaneurysm from 2 to 6 years after the operation. Another patient developed a femoral pseudoaneurysm. The overall pseudoaneurysm formation rate in our series was 14.2%. Different outcome have been reported in other series such as the Cleveland clinic experience (23), reporting a 0.4% rate of late graft complications was found, including three graft infections and only one femoral pseudoaneurysm formation. A significant differ-
ence, regarding pseudoaneurysm formation was found by Bonati et al (1), (3 out of 18 patients with IAAA) in a case-matched study comparing patients with IAAA and non-inflammatory abdominal aortic aneurysms with a similar incidence as in our series.

The higher incidence of pseudoaneurysm in our study raises the question of whether they have specific features predisposing to the development of this complication. Histopathologic changes of the aortic wall could play a pathogenetic role in the development of these complications. Flogistic infiltrates and endarteritis obliterans with subsequent ischemic aortic wall damage could induce arterial weakness leading to pseudoaneurysmal degeneration. The elastin depletion and collagen fiber alterations are more extensive in IAAAs inducing such wall weakness (24). It is likely that these or other unidentified defects affect the resistance of the aortic wall, predisposing to late anastomotic aneurysm development.

The predictors for poor overall outcome were similar to other reports (11, 21, 26). The elevated ESR level not reduced with >30% postoperatively demonstrated an ongoing inflammation inducing poor outcome. The presence of inflammation increases the probability of pseudoaneurysm formation requiring a reoperation with an increased mortality.

5. CONCLUSION

The presence of an abdominal aortic aneurysm in a patient with abdominal, back or pelvic pain, combined with elevated erythrocyte sedimentation levels, suggests an IAAA. Computed tomography should be the examination of choice. The early postoperative surgical outcome in terms of mortality and morbidity seems to be acceptable, however patients with IAAA have an increased risk for late reoperation especially due to pseudoaneurysm formation at the anastomotic sites. Larger series of IAAA with imaging follow-up are warranted to detect the true incidence of late graft pathology in this type of aneurysm and to confirm the tendency for pseudoaneurysms. Strong predictors for poor overall outcome, seems to be the elevated erythrocyte sedimentation rate not reduced significantly after the surgery, ischemic heart disease and chronic renal failure.

CONFLICT OF INTEREST: NONE DECLARED.

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