The impact of graft surface area of polyester stentgrafts on post implantation syndrome after EVAR

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Abstract:

Background: Post-implantation syndrome (PIS) definition has been used to describe clinical and biochemical reflection of inflammatory response following endovascular aortic aneurysm repair (EVAR) with an incidence ranging from 14 to 60%. Polyester endograft materials have been considered as the most significant factor in PIS etiology. The aim of this study is to investigate the relationship between graft surface area and PIS following EVAR with polyester stentgrafts.

Methods: A retrospective study was undertaken including patiens undergoing elective EVAR between 2018 and 2020. Demographics, risk factors and blood test were analyzed. The calculation of the graft surface area (GSA) and extensions was undertaken with a mathematical formula (2π.r.h) for each patient separately. Overlap zone was subtracted from contralateral limbs length due to double layer stentgraft.

Results: Patients were divided in two groups according to the diagnosis of PIS; Group 1: PIS (-), Group 2: PIS (+). Age, gender distribution and co-morbidities were similar between groups. Pre-operative c-reactive proteine (CRP), White blood cells (WBCs) and neutrophil lymphocyte ratio were similar between groups. PIS was diagnosed in 15 of 33 patients (45.5%) (Group 2). GSA was calculated as 11,955 ± 4,146.38 mm^2 in Group 1 and 19,036.13 ± 8,821.51 mm^2 in Group 2; the difference between groups was significant (***p=0.009***). Post-operative mean WBC value was higher in group 2 (10,292.8 ± 2.23 vs 16,348.7 ± 4.94 ***p<0.001***). CRP also increased more in group 2 postoperatively and difference was significant (117.11 ± 41.66 vs 169.14 ± 42.05 ***p=0.001***). Postoperative Neutrophil Lymphocyte ratio was similar in both groups. Length of hospital (LOS) stay was longer in Group 2 (4.94 ± 0.99 days vs 6.53 ± 1.40 days ***p=0.002***). GSA was also correlated with LOS stay (***p=0.008***). All patients were discharged uneventfully, no in-hospital death and no major adverse cardiovascular event occured.

Conclusıons: Graft surface area may be related to PIS in patients undergoing EVAR with polyester stentgrafts. PIS seems to prolong hospitalization after EVAR.

INTRODUCTION

Post-implantation syndrome (PIS) definition has been used to describe clinical and biochemical reflection of inflammatory response following endovascular aortic aneurysm repair.[1,2] The reported incidence of PIS has been varying widely from 14 to 60%.[1-4] Basically, non infection-related fever and increase of inflamatory parameters (leucocyte count, C-reactive protein etc.) are major diagnostic features.[5]

The pathophysiology of PIS is still not clear. Many causative factors have been implicated such as the amount of contrast agent, the aneurysm size, the amount of the mural trombus in aneurysm sac, endograft material and the role of endothelium.[6,7,8,9]

In recent years, polyester endograft materials have been considered as the most significant causative factor in PIS etiology.[6,7,8,9,10,11] Following graft deployment, polyester material interacts with bloodstream, and activates inflammatory mediators. The aim of this study was to assess the hypothesis that wider contact surface may be associated with inreased inflammation and PIS.

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MATERIALS AND METHODS

In this retrospective study, all elective patiens having being treated with EVAR between 2018 and 2020 were included. The institutional ethics commitee approval was obtained. PIS was defined as the presence of fever (persisting body temperature > 38 °C lasting for more than 1 day during hospitalization), leukocytosis (White Blood Cell count > 12 000/mL) with negative blood culture results and high level of C-reactive Protein. A total of 33 EVAR patients were included in the

study. All patients' pre-operative and post-operative charts, physical examination data, pre-operative and post-operative hematologic inflammatory parameters (WBC, Neutrophil/Lymphocyte ratio, CRP), were analyzed and compared. Procedural data were reviewed and approximate graft surface area (GSA; main body and extensions) were calculated for each patient. Patients who had a fever > 38 °C consulted with infectious disease department and blood samples were collected for culture. All patients stayed one day in intensive care unit according to our clinical approach. Patient's hospital stay was calculated as total of intensive care unit and service stay.

The investigation of inflamatory parameters was undetaken at 7th postoperative day and 1st post-operative month. Surgical site infection was diagnosed in 3 patients and succesfuly treated with oral antibiotics and local dressing.

Procedure

All procedures were undertaken by the same operational team and under local anesthesia. Siemens Artis Zee Angiography Unit was used in all cases. Cardiovascular anesthesiologist provided monitarisation, sedation and blood pressure control. We administered standart prophilactic antibiotic regimen to each patients with cefazolin 1000 mg intravenously qid for the first 24 hours starting 30 minute pre-incision. Vascular access was achieved with open exposure of the common femoral arteries. EVAR was performed with polyester stentgrafts (20 Medtronic Endurant; Medtronic Vascular, Inc, Minneapolis, Minn, USA and 13 Anaconda endograft; Vascutek, Inchinnan, United Kingdom). Standart technique was used according to preoperative calculations and peroperative assessment in all cases.

Statistical Analyses

Statistical analyses were performed using SPSS 21 (IBM Corp., Armonk, NY, USA). A total of 33 patients were included in the statistical analysis. The numerical variables were investigated using visual (histograms, probability plots) and analytical (Shapiro-Wilk test) methods to determine whether or not they were normally distributed. Descriptive analyses of numerical variables were presented using mean, standard deviation, median, minimum, maximum, and interquartile range, while categorical variables were summarized by frequency and percentage. For the analyses of normally distributed numerical variables Student t test was used for comparison. Mann Whitney U test was used for non-normally distributed numerical variables. Chi-Square test and Fisher Exact test were used for the analyses of categorical variables. While investigating the associations between variables, the correlation coefficients and their significance were calculated using the Spearman test. A p-value of less than 0.05 was considered statistically significant.

Graft Surface Area (GSA) calculation

We calculated surface area of the grafts and extensions with a mathematical formula ($2\pi.r.h$) for each patient separately. Overlap zone (x) was subtracted from contralateral limbs length due to double layer stentgraft. (Figure 1)

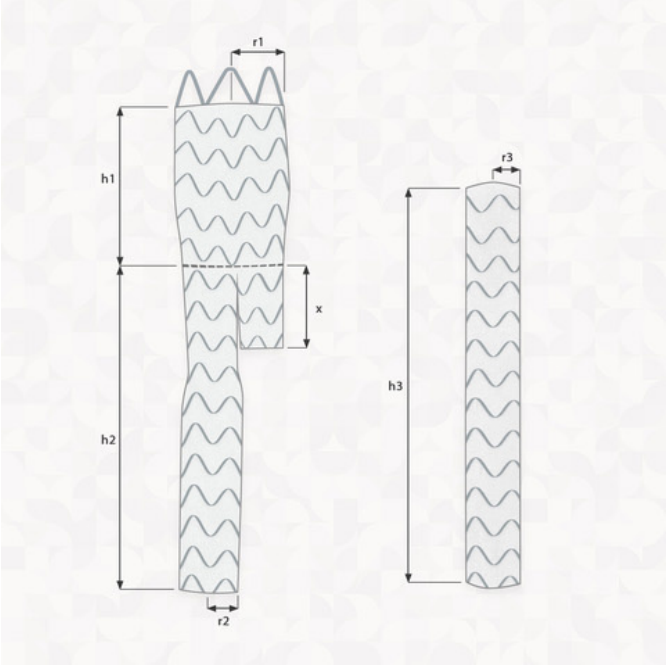

Figure 1. Diameters and lengths used for approximated graft surface area calculation (r:diameter, h: length, x: overlap zone).

RESULTS

PIS was diagnosed in 15 of 33 patients (45.5%). 26 patients (78.8%) were male and 7 patients (21.2%) were female. Mean age was 65.39 ± 14.28 years of age. Accompanying diseases and comorbidities are summarized in Table 1.

Endurant graft was used in 20 patients and Anaconda was used in 13. Calculated approximate GSA was 15,173.70 ± 7,433.31 mm^2. Mean volume of contrast agent was 146.33 ± 27.81 ml. No procedural complication occured in study population.

Patients were divided in two groups according to the diagnosis of PIS; Group 1: PIS (-), Group 2: PIS (+). Age and gender distribution were similar between groups. Diabetes mellitus, hypertension, peripheral arterial disease, coronary artery disease and chronic obstructive disease were also similar. (Table 1)

	Group 1	Group 2	P value
Age (y)	67,67 ± 11,19	62,67 ±17,29	0.562
Male Gender (%)	77.8%	80%	1
Diabetes Mellitus (%)	55.6%	53.3%	0.898
Hypertension (%)	77.8%	60%	0.448
Peripheral Arterial Disease (%)	38.8%	40%	0.672
Coronary Artery Disease (%)	22.2%	33.3%	0.137

Table 1. Preoperative characteristics of the patients.

	Group 1	Group 2	P value
Graft Surface Area (mm^2)	11 955,00 ± 4 146,38	19 036,13 ± 8821,51	0.009
White Blood Cell ($/mm^3$)	10 292 ± 2 231	16 348 ± 4 949	<0.001
C-Reactive Protein (mg/l)	117,11 ± 41,66	169,14 ± 42,05	0.001
Neutrophil-Lypmhocyte Ratio	7,58 ± 7,26	9,59 ± 9,39	0.138
Length of Hospital Stay (day)	4,94 ± 0,99	6,53 ± 1,40	0.002
Mean Maximum Temperature (°C)	36,41 ± 1,68	38,63 ± 1,17	0.036

Table 2. Graft Surface Area and postoperative results of the patients.

Pre-operative CRP, WBC and neutrophil lymphocyte ratio were similar between groups. The rate of PIS according in terms of stent graft system was similar (45% vs 46.1). Endurant graft was used in 9 patients Anaconda was used in 6 patients in Group 2.

GSA was calculated as 11,955 ± 4,146,38 mm^2 in Group 1 and 19,036,13 ± 8,821,51 mm^2 in Group 2 . The difference between groups was significant (***p=0.009***).

Post-operative mean WBC value was significantly higher in group 2 (10,292.8 ± 2.23 vs 16,348.7 ± 4.94 ***p<0.001***). CRP was increased more in group 2 postoperatively and difference was statistically significant (117.11 ± 41.66 vs 169.14 ± 42.05 ***p=0.001***). Postoperative Neutrophil Lymphocyte ratio was similar. Postoperative mean maximum forehead temperature was significantly different (36,41 ± 1,68 vs 38,63 ± 1,17 ***p=0.036***).

Length of hospital stay was found significantly longer in Group 2 (4,94 ± 0,99 vs 6,53 ± 1,40 ***p=0.002***). (Table 2) GSA was found significantly correlated with length of hospital stay (***p=0.008***).

All patients were discharged uneventfully, no in-hospital death and no major adverse cardiovascular event occured.

DISCUSSION

Since the introduction of EVAR in the current practise for AAA treatment, the incidence of post-operative fever and increase of inflamatory parameters has been reported in many publications.[2,4,10] In order to interpret those symptoms, this clinical condition has been accepted as a spesific kind of systemic inflamatory response and was defined as post-implantation syndrome. The incidence of PIS varies ranging from 14% to 60%.[2,3,10] The non-uniform definition and different graft types may account for this variation.

The inner layer of covered stent grafts becomes the new inner surface of the aorta which is exposed to the bloodstream. This contact activates leukocytes and platelets and promotes the release of inflammatory mediators such as cytokines and acute phase proteins. Different types of surface biomaterials may provoke different inflammatory responses. Previous studies showed that PIS occurs more common in those patients that are treated with EVAR using polyester covered stentgrafts.[6,7,8,9,13-15] Ito et al, compared polyester and ePTFE grafts and found that polyester grafts are significantly associated with PIS after elective EVAR.[7] Similary, Sartipy and collegues reported higher incidence of PIS and longer hospital stay in EVAR cases performed with polyester grafts.[8]

Polyester triggers higher release of inflammatory biomarkers (tumor necrosis factor-α, IL-6, IL-10, and CRP) than ePTFE in vitro.[12-14] Gerasimidis et al., reported also higher postoperative IL-8 levels in patients that were treated with polyester stentgraft than with PTFE.[15]

In this study, PIS was diagnosed in 45.5% of cases who underwent elective EVAR with polyester stentgraft. As mentioned above, contact between blood stream and graft surface is one of the potential causative factors of PIS. In this context, we hypothesized that wider graft surface area may be related with increased inflammation. Our results showed that higher GSA is significantly associated with PIS in patients being treated with polyester devices. No correlation was identified among GSA and WBC, NLR, CRP. Additionally, GSA was correlated with prolonged hospital stay.

The relationship between inflammation and blood prosthetic surface contact is well documented. Extracorporal circulation systems are the best known prosthetic surfaces interacting with bloodstream.[16] In the last two decades miniaturized cardiopulmonary bypass systems (CPB) have been popular for both minimal invasive cardiac surgery and to provide less harmful extracorporeal circuit. Nollert et al., reported marginal decrease of inflammation and coagulation disturbances with miniaturized CPB systems in comparison with standart CPB.[17]

Although PIS is frequently well-tolerated clinical condition the proven relationship between aortic aneurysm and aging population with multiple comorbidities may increase its impact on the outcomes following endovascular repair of aortic aneurysms.[11] In critically ill patients, uncontrolled inflammation may effect recovery process. However, in several large EVAR papers the association of adverse events with PIS has not been yet reported and still there is no consensus about the influence of PIS on clinical outcomes during follow-up. In this study, all patients were discharged uneventfully, no in-hospital death and no major adverse cardiovascular event occured.

In our series, patients that were diagnosed with PIS had a mean 1.59 day longer hospital stay. This may be a also socioeconomic issue except its clinical importance. In recent years, health management and economics have become one of the major determinants of success. In this context, prolonged length of hospital stay has been reported independent factor of increased treatment costs. [18-20] Hong and collegues compared percutanous EVAR (P-EVAR) with standart EVAR and found that P-EVAR had lower costs compared with standart

EVAR. The cost savings of P-EVAR was primarily driven by the cost differences in the length of hospitalization. On the other hand, length of hospital stay is well known risk factor for health care associated infection. This is a vicious circle which affects early outcomes and in-hospital death.[21]

Major limitations of this study are its retrospective design, the small sample size and the manual calculation of GSA. Future prospective studies are needed to understand pathophysiology of PIS and its clinical and economic impact on the EVAR patients.

CONCLUSION

Graft surface area may be related to PIS in patients undergoing EVAR with polyester stentgrafts. PIS seems to prolong hospitalization after EVAR.

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