

Does postimplantation syndrome due to endovascular aneurysm repair increase mortality rate?

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Abstract

Aim: Postimplantation syndrome diagnosed by high levels of white blood cell and c-reactive protein or fever is an inflammatory clinical finding after endovascular aneurysm repair. We aimed to analyze whether it can increase mortality rate or not.

Material and Methods: A literature search was performed in electronic database, Pubmed, without date limitation. Trials that compare the rate of mortality between patients with postimplantation syndrome and controls were included. Date of articles and numbers of death in each groups were noted. The results of studies were evaluated by random or fixed effect model according to heterogeneity. Statistical analysis was performed by using *Jamovi* software.

Results: After the database search, we attained in all 358 articles. After overview of titles and abstracts, we included 5 articles in the meta-analysis which contained 1283 patients and abided by inclusion criteria. In analysis, it was observed that there was no significant difference for mortality between patients with postimplantation syndrome and controls (OR: 0.27, 95% CI -0.27-0.81 and p=0.33. Studies included in the analysis were not heterogeneous ($I^2=6.63\%$). Possible publication bias was found ($\tau^2:0.0$). The weight of one of five studies with regard to results of analysis was 57.7%.

Conclusion: We concluded that postimplantation syndrome cannot increase mortality, though it's high development rate after endovascular aneurysm repair.

Keywords: Endovascular aneurysm repair; mortality; postimplantation syndrome

INTRODUCTION

Endovascular aneurysm repair (EVAR), the important advance for treatment of abdominal aortic aneurysm (AAA) was first performed by Parodi et al. (1) in 1991. It was reported as an alternative method on poor candidate patients for conventional surgical treatment because of medical comorbidities.

EVAR is usually performed through the lumen of the common femoral artery under local or general anesthesia (2). Folded and compressed graft components are inserted within a delivery sheath. EVAR has been found superior than open surgical aneurysm repair according to 30 day mortality, early postoperative outcomes and quality of life, in the current meta-analysis in literature (3,4). Though, EVAR can cause endograft and systemic complications. Postimplantation syndrome (PIS) is one of those complications which we may predict its development with preoperative biomarkers such as leucocyte, fibrinogen and thrombocyte (5).

Hastaoglu et al. (6) found early mortality rate as 10.7% and late mortality rate as 28.5% for EVAR. However, the fatal risk of PIS, simply defined as systemic inflammatory response after EVAR, is not clearly known. Therefore we aimed to analyze whether PIS increases mortality rate after EVAR or not.

MATERIAL and METHODS

Search strategy

We performed the database searching in accordance with the guideline of *Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA)* (7). We used the electronic database search to determine whether PIS can increase the mortality rate after EVAR or not. Two authors (S.O and İ.Ö.) searched database until 25.01.2019. There was no limitation for publication date. PubMed was used as electronic database and we didn't performed manual search.

Keywords or combinations of them (*endovascular aneurysm repair, postimplantation syndrome, EVAR, TEVAR and*

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inflammatory response) were used for searching. Searching was limited to English language only and the articles in other languages were excluded. The methods of studies were not limited but only the studies which compare patients with PIS and no PIS.

Study selection

The studies, regardless of the sample size, included were retrospective or prospective clinical studies. Inclusion criteria were: (i) clinical study, (ii) endovascular abdominal or thoracic aortic aneurysm repair, (iii) article in English. Exclusion criteria were: (i) experimental studies or case series (ii) articles in other than English language, and (iii) open surgical aneurysm repair. The articles, associated with the issue of our review but not containing the knowledge about the rates of death, were also excluded. Articles containing data with figures, not numerical values, were excluded.

Data extraction

Two reviewers (S.Ö. and İ.Ö.) independently extracted data from relevant studies. We extracted publication information (first author's name, publication year, sample size, number of patients with PIS and also with no-PIS, and death rates in each group). Disagreement was resolved by two authors (H.Y. and B.Ş.). The number of patients who died because of PIS and sample size of groups with PIS and without PIS were recorded as data.

Statistical analysis

The meta-analysis program, Jamovi®, was used for statistical analysis. The Odds ratio (OR) and 95% confidence interval (CI) was used for analysis. The heterogeneity was evaluated with the statistics of I^2 . Heterogeneity was accepted as significant if $I^2 \geq 25\%$ and heterogeneity was evaluated with the analysis of moderators. Meta-analysis was applied by using fixed or random effect models. We performed random effect model in the presence of heterogeneity ($I^2 > 25\%$) and fixed effect model in absence of heterogeneity ($I^2 < 25\%$). Publication bias was evaluated with Begg test.

RESULTS

Records identified through database searching were 358. After duplicates were removed, 235 records remained. Unrelated records ($n=84$) were excluded after screening. Full-text of 151 articles was assessed for eligibility and 146 of them were excluded because of absence of detailed data. 5 articles, summarized in Table 1, were included to quantitative synthesis (8-12). Flow diagram of database searching was shown in Figure 1. Demographical features of studies were summarized in Table 1. The ratio of development of PIS was 29.46% (378 cases of 1283). The mortality rate was 6.61% for PIS and 5.63% for non-PIS.

Table 1. Summary of studies

	Year	PIS (+) n	Total n	Definition of PIS	Design	Evaluated risk factors	Mortality rate	Weights of studies in analysis (%)
Kwon et al	2016	64 (31.37%)	204	Temperature $>38^{\circ}\text{C}$ WBC $>12,000/\text{mm}^3$, Negative culture results	Retrospective	HT, CAD, COPD, Smoking, CVA, DM, Hyperlipidemia, cancer, CRF	22.54%	57.7
Gorla et al.	2016	21 (15.78%)	133	Temperature $>38^{\circ}\text{C}$, WBC $>12.0/\text{nl}$, CRP $>10 \text{ mg/dl}$ Negative blood culture	Retrospective	HT, DM, Smoking	5.26%	3.48
Nano et al.	2014	24 (20.33%)	118	Temperature $\geq 38^{\circ}\text{C}$, WBC $\geq 12,000/\text{mm}^3$, Negative culture results	Retrospective	Not available	6.77%	12.86
Arnaoutoglou et al	2016	65 (35.71%)	182	Temperature $>38^{\circ}\text{C}$, WBC count $>12,000/\mu\text{L}$, Negative blood culture	Prospective	HT, CAD, COPD, Smoking, CHF, DM, Hyperlipidemia	2.19%	5.61
Zhu et al	2018	204 (31.57%)	646	Temperature $>38^{\circ}\text{C}$, WBC count $>12,000/\mu\text{L}$, Negative blood culture	Retrospective	HT, CAD, COPD, Smoking, DM, Stroke	1.7%	20.36

PIS: Postimplantation syndrome, WBC: White Blood Cell, CRP: C-Reactive Protein, HT: Hypertension, CAD: Coronary Artery Disease, COPD: Chronic Obstructive Disease, CHF: Congestive Heart Failure, DM: Diabetes Mellitus, CVA: Cerebro Vascular Accident, CRF: Chronic Renal Failure

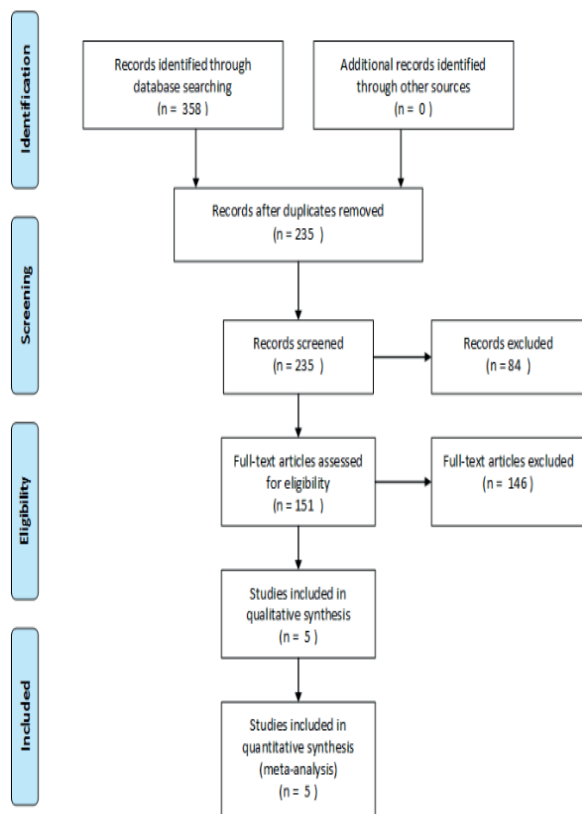


Figure 1. Flow diagram of database search

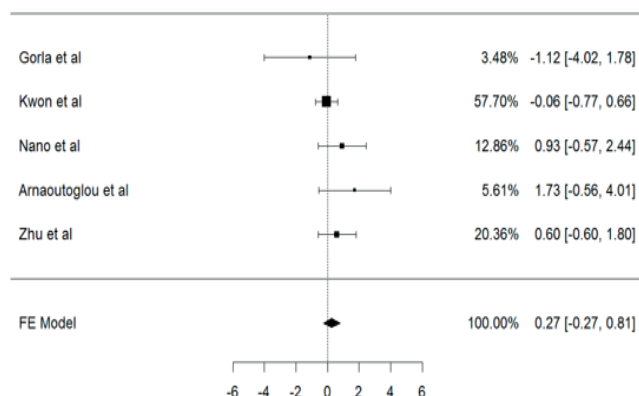


Figure 2. Forest plot of analysis

The weights of studies due to result of analysis were shown in Table 1.

Analysis results of four studies according to fixed effect model were OR: 0.27, 95% CI -0.27-0.81 and $p=0.33$. There was no significant difference between patients with PIS and controls ($p>0.05$). Effect size was not observed as heterogeneous for studies ($Q(df: 4.28, p:0.369, I^2:6.6\%)$). Results were summarized with forest plot in Figure 2. The result of evaluation of publication bias was significant ($\tau^2=0.0$). The funnel plot was shown in Figure 3. The possible number of studies that we might miss out during database search (*fail-safe N*) is 0 according to Rosenberg and Rosenthal approach and 5 according to Orwin approach.

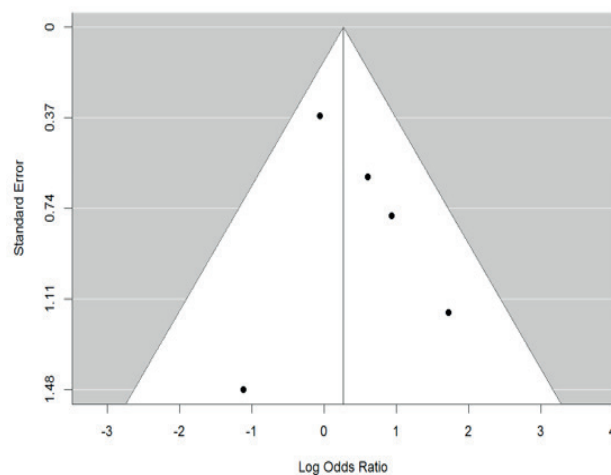


Figure 3. Funnel plot of analysis

DISCUSSION

In our analysis, we found no difference between patients with or without PIS for mortality rate, though PIS is a common and serious complication of EVAR.

Mortality rate was ranging 1.7-22.54% in five studies (8-12). Nano et al. (11) and Arnaoutoglou et al. (8) found the mortality rate for PIS greater than control group. However, Kwon et al. (10), the trial which has the biggest weight in the results of analysis had found the rates similar in both groups.

Five adverse clinical outcomes were described in literature. Those are: prolonged hospital stay and/or readmission, renal dysfunction, cardiovascular events, endoleaks and quality of life. While five studies (10,11,13-15) have found that PIS effected the hospital stay/readmission, in a prospective trial performed by Moulakakis et al. (16) there was no difference at clinical outcomes related to PIS and also there was no readmission to hospital. And also in this trial authors have found no difference for postoperative renal dysfunction between PIS and non-PIS groups after EVAR. Chang et al. (17) aimed to study the inflammatory and coagulopathic response to endovascular repair of thoracoabdominal aortic aneurysm and to evaluate the effect of the response on postoperative renal function. And they demonstrated that patients with renal insufficiency had significantly larger changes in WBC and platelet count. All patients had significant increases in NGAL after stent-graft insertion. Six patients had increased cystatin C after stent-graft insertion, with a greater rise in those with postoperative renal insufficiency. In this trial, while IL-6 and d-dimer levels markedly increased at all patients after repair, protein C and Factor V levels uniformly decreased.

Arnaoutoglou et al. (15) studied the relationship between postoperative s-CRP, PIS, maximum temperature smoking and all adverse events (cardiovascular events, acute renal failure, readmission and death). And they demonstrated them as independent predictors of all adverse events by multiple logistic regression analysis. On the contrary,

Kwon et al. (10) determined the long term survival and clinical outcomes as similar for patients with or without PIS.

On the other hand 3 studies showed no correlation between endoleaks and PIS (8,11,18). And only one study investigated the correlation of PIS with quality of life. Nano et al. (11) found that PIS limited the daily physical activities following EVAR at 1 month.

In our analysis, rate of PIS development was between 15.78% and 35.71% in five studies included the analysis. This ratio was 13-60% in literature (16,19). When we compare the PIS incidence and mortality rate, Zhu et al. (12) found the least mortality rate (1.7%) in contrast with the greater PIS incidence (31.57%). And Arnaoutoglou et al. (8) have obtained similar results like Zhu et al. (12) Both mortality rate and PIS incidence were greater in only Kwon et al.'s (11) study (22.54% v.s 31.37%).

LIMITATIONS

The primary limitation of our analysis was the limited articles about PIS. In addition to limited articles, mortality rates were not provided as a outcome variable in most of them. The selected article language as only English was the other limitation.

CONCLUSION

We observed that PIS has not increased the possibility of mortality, though high occurrence degree in different trials after EVAR. However, there is no standard or compromised definition and diagnostic criteria. Therefore our results need support with larger trials performed under compromised diagnosis.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: Ethics committee approval was not required as the study was conducted electronically.

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