Research Square

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Low postoperative blood platelet count may be a risk factor for mortality in patients with acute type A aortic dissection

Guangyu Liu (liuguangyu@bjmu.edu.cn)
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital
https://orcid.org/0000-0002-6758-6590
Hongbai Wang
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital
Qipeng Luo
Peking University - Third School of Clinical Medicine: Peking University Third Hospital
Liang Cao
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital
Lijing Yang
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital
Cuntao Yu
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital
Fuxia Yan
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital
Su Yuan
Chinese Academy of Medical Sciences & Peking Union Medical College Fuwai Hospital

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Abstract

Background Mortality and complications remain high after Acute Type A Aortic Dissection (ATAAD) open surgery, which is associated with coagulation dysfunction. Platelets play an important role in the process of coagulation. This study was to explore the relationship between postoperative platelet counts and postoperative mortality in patients with ATAAD after open aortic repair surgery.

Methods Patients with ATAAD who underwent Total Arch Replacement and Frozen Elephant Trunk in Fuwai Hospital from 2011 to 2015 were selected in this study. The perioperative data were collected and sorted through the electronic clinical case system. Multivariate Logistic regression was used to analyze the risk factors for death within three years after surgery.

Results A total of 495 patients were included in the analysis. After correction with the confounding factors, postoperative platelets count remained as an independent factor that was associated with lower mortality (OR = 0.918, 95%CI 0.853-0.988, *P* = 0.023).

Conclusions The study indicated that decreased postoperative platelet count may lead to increased mortality, in patients with ATAAD underwent open aortic repair surgery.

Background

Aortic dissection is a relatively uncommon but potentially fatal condition. The incidence is approximately 2.6 to 3.5 per 100,000 population per year.[1-4] Surgery is the primary treatment for Acute Type A Aortic Dissection (ATAAD).[5] However, the incidence of surgical complications, such as postoperative cerebral infarction and reoperation for bleeding, is high. Thus, the perioperative mortality and long-term outcome remain dissatisfaction.[6-9]

One of the causes of poor prognosis is the perioperative abnormal coagulation function. Heparin is necessary for the use of extracorporeal circulation, and it may cause postoperative hemorrhage. Protamine can antagonize the effect of heparin, but it may inhibit platelet function.[10-12] Surgical trauma, which is unavoidable, is also an essential factor in coagulation disorders. When an injury such as surgery causes bleeding, platelets play a crucial role in hemostasis. On one hand after the occurrence of trauma, platelets quickly adhere to the wound, then gather into a group, and form a hemostatic embolus. On the other hand, platelets can activate, secrete, and interact with coagulation factors.[13, 14]

Above all, it was hypothesized that, in patients with ATAAD after open aortic repair, low platelet count may be associated to a poor prognosis. Therefore, we conducted a retrospective study to explore the relationship between postoperative platelet count and long-term prognosis in ATAAD.

Methods

Study Population

The study was approved by the ethics committee of research setting Hospital (Ethical approval number: 2017-877) and conducted under the guidance of the latest version of the Helsinki declaration[15]. Written informed consent from all patients for this study was waived. The authors conducted this retrospective observational study of all consecutive patients with ATAAD who underwent Total Arch Replacement and Frozen Elephant Trunk (TAR+FET) between January 2011 and December 2015. ATAAD was defined by observing an intimal flap separating 2 lumina in the ascending aorta that occurred within 14 days of symptom onset.[16] The TAR+FET surgical technique has been described previously in detail and is viewed as a standard therapy for ATAAD requiring repair of the aortic arch.[17] If the following techniques were used in the operation or the following conditions occurred, they will be excluded from this study: hybrid procedure or off-pump surgery, partial aortic arch replacement. Exclusion criteria: patients with missing data of perioperative period and of follow-up. This article follows the STROBE Statement[18].

Data acquisition

Demographic indicators were collected: age, gender, body mass index (BMI), history of hypertension, history of smoking, history of alcohol consumption, history of diabetes, history of chronic obstructive pulmonary disease (COPD), history of peripheral vascular disease, history of cerebrovascular disease. Preoperative blood pressure, preoperative cardiac ultrasonography, surgical history, and other preoperative conditions were also collected. Preoperative blood routine examinations such as hemoglobin (Hb), white blood cell counts (WBC), platelet counts were also recorded. In addition, intraoperative indicators should be collected, including lowest temperature during extracorporeal circulation, shutdown temperature of extracorporeal circulation, extracorporeal circulation duration and circulatory arrest duration. The data were collected and sorted through the electronic clinical case system of Fuwai Hospital.

Outcome indicators collected by assessors blinded to research design. The recorded outcome indicators include postoperative 3-year mortality, mortality in hospital, length of postoperative hospital stay, length of ICU stay. Other recorded outcomes included the rate of re-admission to the ICU, cardiovascular dysfunction, neurological complications, respiratory complications, and digestive complications. Neurological complications include cerebral infarction, cerebral hemorrhage, hemiparalysis, and paraplegia. Respiratory complications contained hydrothorax, pulmonary infection, respiratory insufficiency, and tracheal reintubation. Digestive systems complications contained postoperative liver insufficiency, gastrointestinal hemorrhage, intestinal obstruction, and acute pancreatitis. The diagnostic criteria of complications were listed in appendix table 1.

Statistical analysis

Patients were divided into two groups for comparison based on the outcome of follow-up for death or survival. Continuous variables were presented as mean ± standard deviation (SD), and Categorical variables were reported as counts (percentage). Time-to-event variables were presented as median (95% confidence interval of median). Differences between groups were assessed using the chi-square test or Fisher’s exact test for categorical variables, independent samples Student t-tests or Mann-Whitney U test for continuous variables. Time-to-event variables were estimated with the Kaplan-Meier method, and differences between groups were compared with the Log-Rank test. Two-sided *P* values of less than 0.05 were considered statistically significant.

Logistic regression was used to analyze the risk factors for death within three years after surgery. Death within three years after surgery was taken as the dependent variable, and all preoperative, intraoperative, postoperative indicators were put into single-factor regression analysis. Variables with *P* value < 0.1 were put into multi-factor regression equation. The backward stepwise method was adopted for the multi-factor logistic regression equation, that is, all factors were included in the equation at the beginning. Then, multi-factor regression is carried out step by step. During each step, when the *P*-value of a factor is not less than 0.1, the factor will be removed from the equation. Stata for Windows software version 16.0 was used for statistical analysis.

Results

Descriptive Statistics

All patients who underwent aortic dissection from 2011 to 2015 were screened. A total of 845 operation records were extracted from the database. Three hundred twenty-eight patients were excluded because the type of surgery did not meet the inclusion criteria. And, twenty-two patients were excluded due to the lack of postoperative platelet count or lost to follow-up. Hence, a total of 495 patients being included in the analysis. The screening process and result were shown in Figure 1.

Among all 495 patients, the mean age was 47.5 ± 10.7 years, 110 females and 385 males. All patients were followed up for more than three years after surgery. And the 3-year survival rate was 91.3%. In terms of preoperative indicators, there were no statistically significant differences between the two groups in BMI, time from onset to admission, preoperative complications, NYHA grading, preoperative ultrasound, preoperative WBC count, and HB count. However, there were statistical differences in gender, age, platelet count and other aspects between the two groups. The preoperative information of the patients was shown in Table 1.

Table 1. Preoperative and intraoperative variables of patients.

	Overall (n=495)	Survival (n = 452)	Death (n = 43)	*P* value
ler, male	385 (77.78%)	357 (78.98%)	28 (65.12%)	0.037
year	47.5±10.7	47.1±10.6	51.465±10.119	0.011
kg/m^2	25.57±3.951	25.64±4.026	24.86±3.000	0.300
from onset to admission, h	3 [1, 10]	3 [1, 10]	2 [1, 7]	0.369
ertension	364 (73.54%)	335 (74.12%)	29 (67.44%)	0.343
etes	10 (2.02%)	10 (2.21%)	0 (0%)	>0.999
pheral vascular disease	9 (1.82%)	9 (1.99%)	0 (0%)	>0.999
D	2 (0.40%)	2 (0.44%)	0 (0%)	>0.999
nic kidney disease	24 (4.85%)	21 (4.65%)	3 (6.98%)	0.454*
perative CNS disease	22 (4.44%)	21 (4.65%)	1 (2.33%)	0.710*
erlipidemia	80 (16.16%)	76 (16.81%)	4 (9.3%)	0.201
history of smoking	210 (42.42%)	192 (42.48%)	18 (41.86%)	0.938
history of drinking	25 (5.05%)	23 (5.09%)	2 (4.65%)	>0.999
ory of cardiovascular ery	35 (7.07%)	30 (6.64%)	5 (11.63%)	0.214*
perative pain	459 (92.73%)	417 (92.26%)	42 (97.67%)	0.350*
A grading: I	37 (7.47%)	33 (7.30%)	4 (9.3%)	0.437*
II	396 (80%)	364 (80.52%)	32 (74.42%)	
III	57 (11.52%)	51 (11.28%)	6 (13.95%)	
IV	5 (1.01%)	4 (0.88%)	1 (2.33%)	
, mmHg	106[96, 116.3]	106.7[96.67, 116.7]	100.7[93.33, 114]	0.091
F, %	60[58, 62]	60[58, 62]	60[59, 61]	0.8531
ventricular diameter, mm	51[47, 56]	51[47, 57]	49[44, 55]	0.082
cardial effusion	69 (13.94%)	62 (13.72%)	7 (16.28%)	0.643
perative WBC count, 10^9/L	10.90[8.220, 13.61]	10.83[8.165, 13.58]	11.39[8.490, 13.69]	0.448
perative PLT count, 10^9/L	169[134, 220]	171[137, 223]	147[114, 176]	<0.001
perative Hb count, g/L	132[116, 144]	132[116, 144]	128[117, 136]	0.165
rgency operation	285 (57.58%)	258 (57.08%)	27 (62.79%)	0.469
urrent CABG	48 (9.7%)	42 (9.29%)	6 (13.95%)	0.289*
urrent Aortic root surgery	148 (29.9%)	135 (29.87%)	13 (30.23%)	0.960
urrent mitral valve plastic placement	8 (1.62%)	8 (1.77%)	0 (0.00%)	>0.999
d loss, mL	900[600, 1200]	900 [600, 1200]	1000 [600, 1200]	0.311
blood cell infusion, unit	0 [0, 0]	0 [0, 0]	0 [0, 2]	0.003
en plasma infusion, mL	400[0, 600]	400 [0, 600]	400 [0, 800]	0.093
elet infusion, unit	2 [1, 2]	2 [1, 2]	2 [2, 2]	0.253
est temperature in CPB	18.3 [17.7, 20.2]	18.3 [17.7, 20.25]	18.3 [17.7, 19.6]	0.719
perature when CPB is ped	36.9 [36.6, 37.1]	36.9 [36.6, 37.1]	36.9 [36.6, 37.1]	0.514
iopulmonary bypass time,	186[158, 217]	186 [155, 216]	194 [171, 261]	0.022
ping time, min	22 [19, 26]	22 [19, 25]	22 [20, 27]	0.273

Data are presented as mean ± SD, number (%), or median [interquartile range].
BMI = Body mass index; COPD = Chronic obstructive pulmonary disease; CNS = Central nervous system; NYHA = New York Heart Association; MBP = Mean blood pressure; LVEF = Left ventricular ejection fraction; WBC = white blood cell; PLT = platelet; Hb = Hemoglobin; CABG = Coronary artery bypass grafting. *In these comparisons, Fisher's exact test was used.

However, intraoperative related indexes show no statistically significant differences between the two groups in intraoperative combined operation type, blood loss, plasma and platelet infusion volume and the clamping time. The *P* value of the two groups was less than 0.05 in the amount of red blood cell infusion and cardiopulmonary bypass (CPB) time, showing a statistical difference.

Among all enrolled patients, the in-hospital mortality rate was 8.28%. The median postoperative hospital stay was 12 days (IQR 9-16), and the median postoperative ICU stay was 48 hours (IQR 33-88). There were 18 patients (3.64%) who underwent reoperation for hemostasis after surgery, and 26 patients (5.25%) who underwent reoperation for other reasons. In terms of postoperative complications, there were 8 (1.62%) patients with cardiac dysfunction and 108 (21.82%) patients with central nervous system complications. The incidence of respiratory complications was 24.24%, and that of digestive complications was 33.74%. Postoperative data are shown in Table 2.

In the univariate Logistic regression analysis, preoperative and intraoperative factors were analyzed, and factors with *P*-value < 0.1 were included in multivariate Logistic regression. The result of univariate Logistic regression was shown in appendix table 2.

Table 2. Outcome results in patients.

	Overall (n=495)	Survival (n = 452)	Death (n = 43)	*P* value
In-hospital mortality	41 (8.28%)	0 (0.0%)	41 (95.35%)	< 0.001
Length of postoperative hospital, day	12 [9, 16]	12 [9, 16]	9 [4, 16]	0.001
Length of postoperative ICU stay, h	48 [33, 88]	48.5 [32, 88]	44 [35, 80]	0.5412
Reoperation for hemostasis	18 (3.64%)	13 (2.88%)	5 (11.63%)	0.003
Reoperation for other reasons	26 (5.25%)	18 (3.98%)	8 (18.60%)	<0.001*
Re-admission to ICU	19 (3.84%)	13 (2.88%)	6 (13.95%)	0.003
Postoperative cardiac insufficiency	8 (1.62%)	3 (0.66%)	5 (11.63%)	< 0.001*
Postoperative complications of the CNS	108 (21.82%)	84 (18.58%)	24 (55.81%)	< 0.001
Postoperative complications of respiratory system	120 (24.24%)	93 (20.58%)	27 (62.79%)	< 0.001
Postoperative complications of digestive systems	167 (33.74%)	141 (31.19%)	26 (60.47%)	< 0.001

Data are presented as number (%), or median [interquartile range].

ICU = Intensive care unit; CNS = Central nervous system. *In these comparisons, Fisher's exact test was used.

In the first step of multi-factor regression, a total of 13 factors were put into the regression, such as age, gender, CPB duration, RBC infusion, FFP infusion, postoperative platelet count, reoperation for hemostasis, reoperation for other reasons, readmission to ICU, postoperative cardiac insufficiency, postoperative CNS complications, postoperative complications of the respiratory system, postoperative infection. Backward-stepwise Logistic regression method was used in multivariate regression, and in every step, factors whose *P* value was not less than 0.1 were taken out of regression model. After correction with the confounding factors, postoperative platelets count remained as an independent factor that was associated with lower mortality (OR = 0.918, 95%CI 0.853-0.988, *P* = 0.023) (Table 3). Other factors remained in the Logistic regression model were gender (OR = 3.213, *P* = 0.005), CPB duration (OR = 1.008, *P* = 0.012), readmission to ICU (OR = 3.751, *P* = 0.041), postoperative cardiac insufficiency (OR = 13.614, *P* = 0.006) postoperative CNS complications (OR = 2.986, *P* = 0.004) and postoperative complications of the respiratory system (OR = 3.976, *P* < 0.001).

Table 3. Factors in association with postoperative death in follow up.

	Univariate analyses [a]		Multivariate analysis [b]	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value
je, year	1.040 (1.009, 1.072)	0.012	-	-
ender, male	2.013(1.034, 3.921)	0.040	3.213 (1.426, 7.240)	0.005
B duration, min	1.009 (1.003, 1.014)	0.002	1.008 (1.002, 1.015)	0.012
d blood cells infusion, U	1.200 (1.066, 1.351)	0.003	-	-
esh frozen plasma infusion, ml	1.001 (1.000, 1.001)	0.007	-	-
stoperative platelets count, *10^9/L	0.897 (0.837, 0.961)	0.002	0.918(0.853, 0.988)	0.023
operation for hemostasis	4.443 (1.504, 13.128)	0.007	-	-
operation for other reasons*	5.511 (2.238, 13.572)	<0.001	-	-
admission to ICU	5.476 (1.967, 15.245)	0.001	3.751 (1.055, 13.332)	0.041
stoperative cardiac insufficiency	19.693 (4.532, 85.572)	0.001	13.614 (2.124, 87.248)	0.006
stoperative complications of the NS	5.534 (2.898, 10.567)	<0.001	2.986 (1.411, 6.319)	0.004
stoperative complications of the spiratory system	6.514 (3.370, 12.592)	<0.001	3.976(1.860, 8.498)	<0.001
stoperative infection	2.206 (1.073, 3.826)	0.030	-	-

CPB = Cardiopulmonary bypass, ICU = Intensive care unit, CNS = Central nervous system. *Other postoperative operations other than postoperative hemostasis.

[a] Postoperative death was modeled as a function of a single factor in the univariate logistic regression analyses.

[b] Postoperative death was modeled as a function of several factors with a P value < 0.10 in the univariate analyses. Multivariate Logistic regression analysis was performed using a Backward stepwise procedure. Hosmer–Lemeshow test of goodness of fit of the model: $\chi2 = 1.98$, df = 6, $P = 0.922$

Discussion

The results of this study showed that in type A aortic dissection patients who were underwent open aortic repair surgery, low postoperative platelet count may be associated with increased 3-year mortality.

Although complication rate and mortality have declined as techniques have improved, patients’ outcomes remain to be improved. Hemostasis is a vital process in wound healing, which affects the length of hospitalization. In this process, the platelets play an important role. One aspect is that during surgery and CPB, large amounts of platelets are consumed, resulting in platelet count decrease. Another aspect which cannot be ignored is that, after acute aortic dissection, a large number of clots will form in the dissection, which will consume a large number of platelets

in human body. When platelet count is insufficient, postoperative wound hemostasis may be attenuated, resulting in poor prognosis.

There have been several studies that explored the association of platelets with postoperative outcomes after cardiac surgery. Ranucci[19] conducted PLATFORM study, which was a prospective cohort study, involving 490 cardiac surgery patients underwent extracorporeal circulation, and found that platelet function was significantly associated with the risk of massive hemorrhage after cardiac surgery. Some studies have also found that abnormal platelet function is associated with poor prognosis in patients after cardiac surgery.[20] In addition, when fibrinogen or platelets were transfused into the body of patients with progressive hemorrhage after cardiac surgery, it is found that they can significantly improve the functions of blood coagulation and platelet, thereby reduce the amount of blood loss.[21] A meta-analysis of 1720 patients who underwent coronary bypass surgery found that postoperative platelet transfusion was associated with poor prognosis, but platelet transfusion might be a surrogate marker of sicker patients to some extent, rather than the direct cause of adverse factors.[22]

Several previous studies have explored the relationship between platelets and prognosis in patients underwent aortic dissection. Chen[23] found that in patients with acute type A aortic dissection, platelet count, lymphocyte to Neutrophil ratio and lymphocyte to monocyte ratio may predict postoperative death of patients. Although the multi-factor prediction model is not of statistical significance, he believed that combined use of the three in multifactor analysis was necessary. Otherwise, there was no statistical significance. Sbarouni[24] observed 120 consecutive patients with ATAAD, and found that the ratio of platelet to lymphocyte was associated with mortality, and the best critical value was 159, which showed a sensitivity of 53% and a specificity of 86%. These two studies suggest that the platelet counts may be associated with prognosis, but not be an independent risk factor.

There are some limitations in present study. Platelet counts instead of platelet function tests was used. There are several methods to measure platelet function, such as light transmission platelets aggregation, lumiaggregometry and impedance platelet aggregation.[25-27] Currently, there is no widely used laboratory test method to measure platelet function[28]. The platelet count used in this study is more widely used in clinical practice, making the results of the study more generally applicable. On the other side, the research was a retrospective study. Prospective studies are needed to verify the findings.

Conclusions

The study indicated that decreased postoperative platelet count may lead to increased mortality, in patients with ATAAD underwent open aortic repair surgery. It is necessary to infuse ATAAD patients with platelets in this type of surgery to maintain a high platelet count.

List Of Abbreviations

ATAAD: Acute Type A Aortic Dissection

TAR+FET: Total Arch Replacement and Frozen Elephant Trunk

BMI: body mass index

COPD: chronic obstructive pulmonary disease

WBC: white blood cell

HB: hemoglobin

ICU: intensive care unit

CPB: Cardiopulmonary bypass

RBC: Red blood cell

FFP: fresh frozen plasma

CNS: Central nervous system

Declarations

Ethics approval

The study was approved by the ethics committee of research setting Hospital (Ethical approval number: 2017-877). Written informed consent from all patients for this study was waived.

Consent for publication

Not applicable.

Availability of data and materials

Due to the policy of management, raw data and material are not available.

Reasonable requests for access to the datasets used and/or analyzed during this study can be made to the corresponding author.

Competing interests

Nil.

Funding

Nil

Authors' contributions

Conceptualization, Guangyu Liu; Methodology and Formal analysis, Qipeng Luo and Guangyu Liu; Investigation, Qipeng Luo and Guangyu Liu; Data curation: Hongbai Wang, Lijing Yang, Cuntao Yu and Guangyu Liu; Writing, Guangyu Liu and Su Yuan; Project administration: Su Yuan and Fuxia Yan. All authors have read and approved the manuscript.

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Figures

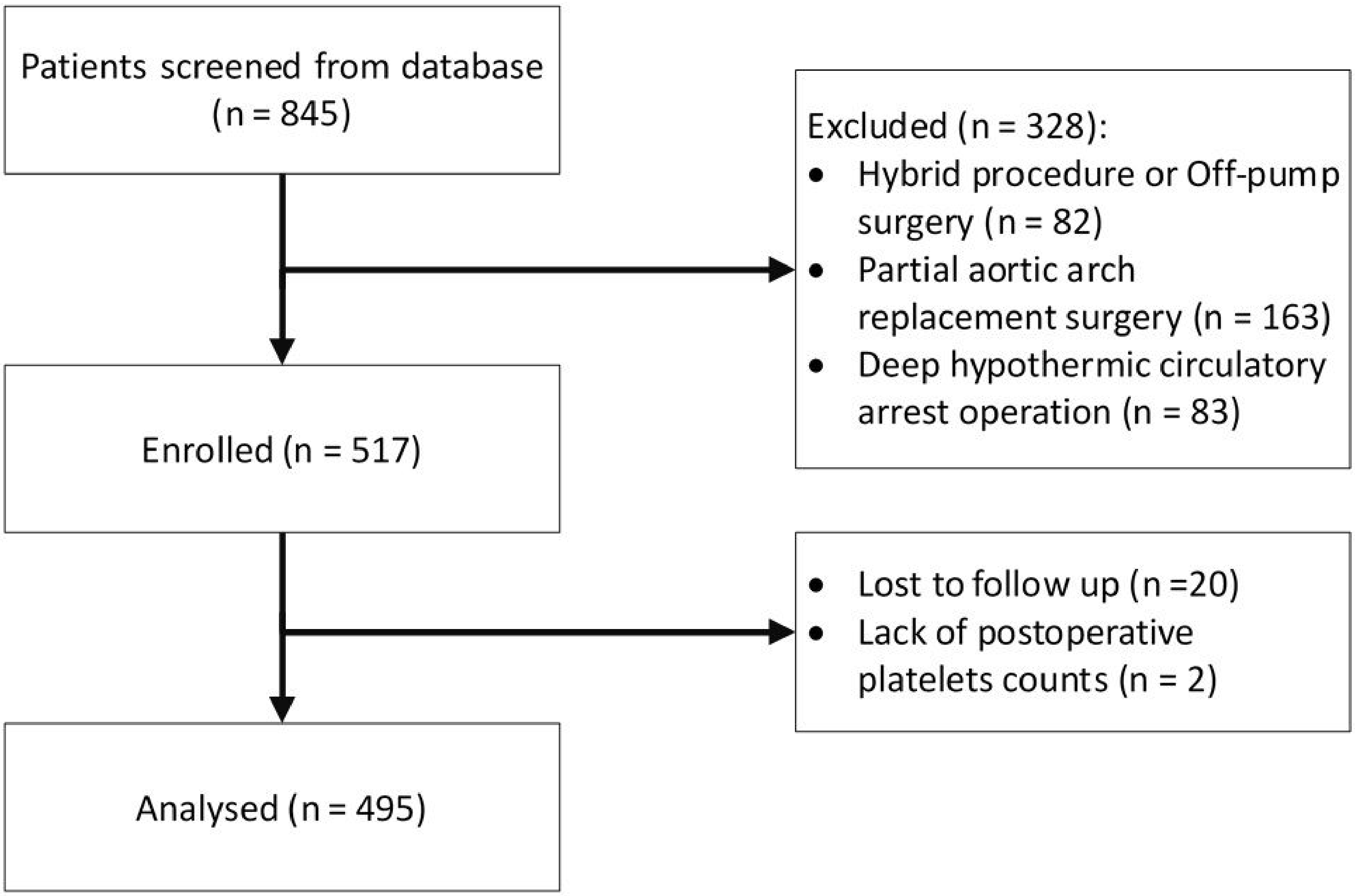

Figure 1

Research Flowchart.

Supplementary Files

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