Heliyon 9 (2023) e22266

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

The effect of perioperative antithrombin supplementation on blood conservation and postoperative complications after cardiopulmonary bypass surgery: A systematic review, meta-analysis and trial sequential analysis

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ARTICLE INFO

Keywords:
CPB
Antithrombin
Blood loss
Blood transfusion
Morbidity

ABSTRACT

Study objective: Antithrombin (AT) activity is reduced during cardiopulmonary bypass (CPB) surgery. Guidelines has demonstrated that perioperative AT supplementation contributed to blood conservation and prevent perioperative thrombotic complications and target organ injury owing to its role in reducing thrombin generation. But these recommends is lack of support of meta-analysis in the guidelines. This meta-analysis aims to include all the relevant randomized controlled trails (RCT) on patients who experienced cardiac surgeries with CPB and investigate the effect of perioperative AT on blood conservation and complications after cardiac surgery.

Methods: Standard published RCTs were searched from bibliographic databases to identify all evidence reporting perioperative AT supplementation for patients undergoing cardiovascular surgeries. The primary outcome was postoperative blood loss, the secondary outcomes were blood component transfusion (red blood cell (RBC), fresh frozen plasma (FFP), platelet and autologous blood), postoperative morbidity and in hospital mortality. The relative risk (RR) for dichotomous outcomes and the standardized mean difference (SMD) for continuous outcomes were estimated using a random-effects model. Trial sequential analysis (TSA) was performed using TSA software 0.9.5.10.

Results: 13 RCTs with 996 participants undergoing different cardiovascular surgeries were included. Meta-analysis showed AT did not decrease postoperative blood loss (SMD -0.01, 95%CI -0.2 to 0.19). Subgroup analysis showed the effect of AT on postoperative blood loss was not associated with age, RCT type, surgery type, injection time of AT and AT deficiency. TSA further suggested that no additional studies were required for the stable result. Perioperative AT also did not reduce RBC ((SMD 0.10, 95%CI -0.66 to 0.85), (RR 0.99, 95%CI 0.83 to 1.19)), FFP ((SMD 0.11, 95%CI -0.19 to 0.41), (RR 1.30, 95%CI 0.90 to 1.87)), platelet (RR 1.10, 95%CI 0.83 to 1.46) and autologous blood (SMD 0.46, 95%CI -0.12 to 1.8504) transfusions. Perioperative AT significantly increased in hospital mortality (RR 2.53, 95%CI 1.02 to 6.28) and acute kidney injury (AKI) (RR 3.72, 95%CI 1.73 to 8.04) incidence. There was no significant difference in postoperative reexploration, thromboembolism, ECMO/IABP support, and stroke incidence between AT and non-AT group.

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https://doi.org/10.1016/j.heliyon.2023.e22266
Received 7 April 2023; Received in revised form 7 November 2023; Accepted 8 November 2023
Available online 13 November 2023

Conclusions: With the improvement of AT level and heparin sensitivity, perioperative AT has no significant effect on blood conservation. And it is noteworthy that the treatment increased in hospital mortality and the incidence of AKI after cardiac surgery.

1. Introduction

Cardiac surgery with CBP obviously activates thrombin which is a key enzyme in the

Pathophysiology of hemostasis that increases after CPB initiation and persists for several days postoperatively [1,2]. Consequently, patients can develop both hemorrhagic and thrombotic complications including myocardial infarction (MI), ischemic stroke, graft occlusion and venous thromboembolism [1].

AT is the major inhibitor of circulating thrombin in plasma, and its major effect is anticoagulation and anti-inflammatory [3,4]. During cardiac surgeries with CPB, AT concentration is significantly decreased [5,6]. And the concentration can be reduced to 40 %–60 % [7,8]. More importantly, low activity of AT is associated with an attenuated response to heparin, which leads to the heparin resistance [9–11]. It means that the activated clotting time (ACT) cannot be achieved to the targeted value for CPB after a standard dose of unfractionated heparin during surgery [12,13]. Investigators have found the incidence of heparin resistance among cardiac surgery patients came up to 13 % which was depended on the target ACT and heparin dose required and on whether patients have recently received heparin [14].

Failure to achieve an acceptable ACT for CPB is usually managed by additional heparin administration [15,16]. High heparin may increase the risk of postoperative bleeding [17]. And the exogenous RBC transfusion may be more needed. In order to restore heparin responsiveness, exogenous FFP or plasma-derived antithrombin concentrate is also required [18]. As heparin works by augmenting AT's anticoagulant effects [19] and AT concentration is significantly decreased during CPB, perioperative AT supplementation improves anticoagulation during CPB through increased heparin sensitivity and this in turn decreases consumption of coagulation factors during CPB and improves hemostasis.

The Society of Thoracic Surgeons and Society of Cardiovascular Anesthesiologists Blood Conservation has published clinical practice guidelines on AT administration. The guideline demonstrates that less bleeding and blood transfusion occur in patients whose hemostatic system is better preserved after the physiologic stresses of CPB [20]. Therefore, AT supplementation may reduce bleeding and provide a better hemostatic profile after CPB. The guideline displays AT concentrates on reducing plasma transfusion in patients with low AT level immediately before CPB as a Class I recommendation [20]. Another study also demonstrates an inverse relationship between AT III activity and adverse thromboembolic patient outcomes [21]. Thrombotic complications involving target organ injury may be related to microvascular thrombosis from a procoagulant postoperative environment, at least in part due to AT deficiency. It may be reasonable to add AT in patients at increased risk for end organ thrombotic complications after CPB [20]. While the effect of perioperative AT supplementation on blood conservation and postoperative complications were lack of evidence-based medical evidence support.

Some studies showed that AT significantly reduced postoperative bleeding [22,23] while others were not [24,25] and a few RCTs showed that postoperative bleeding was increased followed by AT administration [11,26]. A RCT published in 2022 demonstrated that AT administration did not show any advantage of AT over placebo group on safety outcomes and there were significantly more patients with AKI in the AT group [27]. Based on the aforementioned evidences, this study aimed to examine the available RCTs and evaluate the effect of perioperative AT supplementation on blood conservation and postoperative complications.

2. Methods

Initially in this meta-analysis addressing the intervention of anesthesia techniques was performed according the principles of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. The PRISMA check list was presented in Appendix 1. All the included studies were previous published RCTs thus no ethical approval and patient consent are required.

2.1. Search strategy

The Cochrane library, Pubmed and Embase electronic databases were searched for relevant published RCTs. The last retrieval was performed on 11 20, 2022. The search was performed to focus on the safety of perioperative AT supplementation. Search terms were applied to both subject headings and as keywords and restricted to human studies without language restriction. Manual retrieval was also performed for relevant papers, and the references of related reviews and included RCTs were further screened to obtain more appropriate studies. The search strategies can be found in Appendix 2.

2.2. Eligibility criteria

Related studies were included based on the following criteria: (1) subjects were patients who underwent cardiovascular surgeries with CPB; (2) randomized controlled trial (RCT); (3) patients were divided into AT and non-AT groups; (4) outcomes were perioperative blood loss, blood transfusion and adverse events. The exclusion criteria for this study included: (1) studies were involved with both AT and other medicines or chemical reagents (which could affect the outcomes); (2) data could not be used for statistical analysis;

(3) studies were not RCT.

2.3. Study identification

Search results including titles and abstracts were firstly independently reviewed by two investigators. Then the full texts of all those deemed potentially eligible were gathered and reviewed against the criteria by the same two reviewers. Full texts which met the eligibility criteria were agreed by all the investigators. Any disagreement on study identification was resolved through our discussion until a consensus was reached.

2.4. Data extraction and quality assessment

Two investigators searched literatures according to the above inclusion and exclusion criteria. The following data was extracted after eligible studies were included. The name of first author, year of publication, ages of the subjects, types of AT techniques, types of surgery, AT deficiency, case numbers, and relevant outcomes. Indicators at each time point were extracted when the data was longitudinal data. For data with different time points, value of the last time point was merged and was defined as the primary estimate. And values of each time point were also merged respectively. Quality assessment was conducted using the Cochrane evaluation system which includes 7 basic contents. All kinds of bias in studies were objectively and comprehensively evaluated. All disagreements were

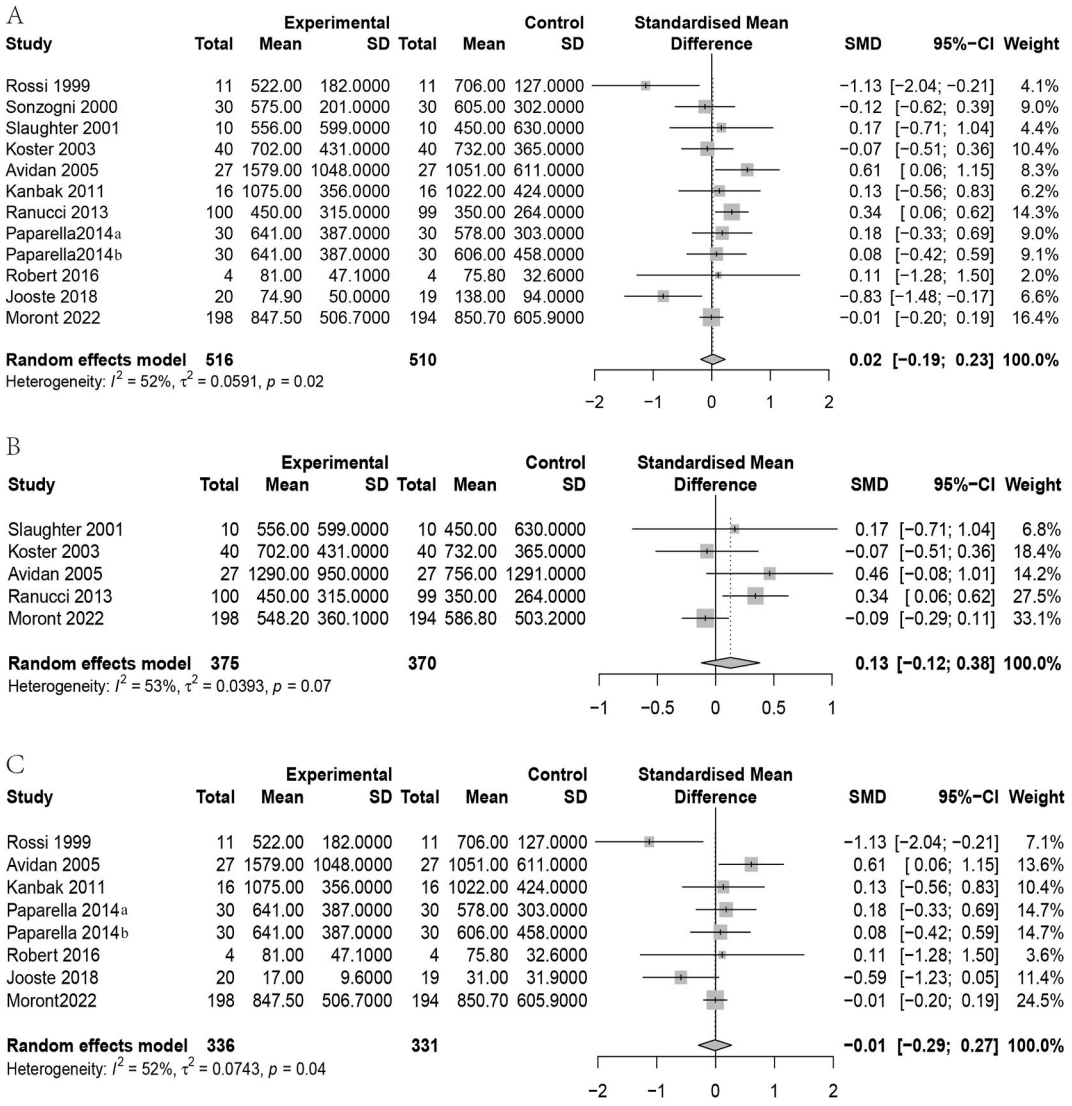


Fig. 1. Forest plots of AT on postoperative blood loss; A, Forest plot of AT on postoperative blood loss at the last time point; B, AT on postoperative blood loss at postoperative 12 h; C, AT on postoperative blood loss at postoperative 24 h

Table 1
Characteristics of the included studies.

Study	Sample size	RCT type	AT type	Injection time	AT dose	Age stratification	Surgery type	AT Deficiency	Blood loss	Transfusion requirement	Adverse events	Other conclusions
Rossi 1999	22	Single center	AT III	Before CPB	3000 U	Adult	CABG	Yes	PO 24 h Chest tube	Cell saver, RBC		
Sonzogni 2000	60	Single center	AT III	Before CPB	2000 U	Adult	CABG	Yes	PO Chest tube	FFP, RBC	Reexploration	A less RBC and FFP in AT III group
Slaughter 2001	20	Single center	AT III	After anesthesia induction	50 U/kg	Adult	CABG	No	PO 6 h, 12 h Chest tube	Not given	Death, Thromboembolism	A significant difference between 6 h and 12 h
Koster 2003	80	Single center	AT III	Before CPB	50 U/kg	Adult	CABG	No	PO 12 h Chest tube	RBC	Death, Thromboembolism	12 versus 14 U RBC were transfused in AT and control group
Avidan 2004	52	Multi center	RhAT	After randomization	75 U/kg	Adult	Not given	Yes	PO 24 h Chest tube	FFP, RBC, Platelet,	Death, Thromboembolism	Speed of bleeding was 82 versus 83 mL/h in AT and control group
Avidan 2005	54	Multi center	RhAT	After randomization	75 U/kg	Adult	Not given	Yes	PO 12 h, 24 h Chest tube	FFP, RBC, Platelet,	ECMO/IBP, Death, Thromboembolism	Rate of Hemorrhage (> 200 mL/h) was higher in AT group
Kanbak 2011	32	Single center	AT III	After anesthesia induction	1000 U	Adult	CABG	Yes	PO 24 h Chest tube	FFP, RBC		
Ranucci 2013	200	Single center	RhAT	After anesthesia induction	(120-actual AT activity) × weight (kg) × 0.8	Adult	GABG Isolated valve operation Coronary/ valve operation	No	PO 12 h Chest tube	FFP, RBC, Platelet	Death, Thromboembolism, Kidney injury, Stroke Reexploration	No significant difference on transfusion
Paparella 2014	90	Single center	RhAT	Postoperative in ICU	3000 U bolus+1000 U 8 h + 1000 U 16 h	Adult	CABG Valve repair/ replacement Thoracic aortic replacement	Yes	PO 24 h–48 h Chest tube	FFP, RBC, Platelet	ECMO/IBP, Death, Stroke, Kidney injury	
McCrindle 2015	17	Single center	RhAT	Before CPB	By preoperative AT level and patient weight	Infant	Congenital cardiac surgery	Yes	PO Chest tube	Not given	Thromboembolism	No significant difference on blood loss or transfusion
Robert 2016	8	Single center	RhAT	After anesthesia induction	(100-actual AT activity) × weight (kg) × 0.8	Infant	Congenital cardiac surgery	Yes	PO 24 h Chest tube	RBC	Reexploration	
Jooste 2018	39	Multi center	AT III	After anesthesia induction	(100-actual AT activity) × weight (kg)/1.4	Infant	Congenital cardiac surgery	Yes	PO 24 h Chest tube	FFP, RBC Platelet, Cryoprecipitate	ECMO/IBP, Reexploration Stroke	
Moront 2022	425	Multi center	AT III	After anesthesia induction	20 × weight (kg)/1.4	Adult	CABG Complex procedures Valve repair/ replacement	Yes	PO 12 h, 24 h Chest tube	Cell saver, FFP, RBC, Platelet, Cryoprecipitate	Death, Thromboembolism , Kidney injury, Reexploration	

AT, antithrombin; RhAT, recombined human antithrombin; PO, postoperative; RBC, red blood cell; FFP, fresh frozen plasma; ECMO, extracorporeal membrane oxygenation; IBP, Intra-aortic balloon refutation.

resolved through our discussion.

2.5. Outcomes

The primary outcome of the meta-analysis was the volume of postoperative blood loss and SMD was used as the summary measure for analysis. The secondly outcomes were blood component transfusion (RBC, FFP, platelet and autologous blood), postoperative morbidity and in hospital mortality. Both SMD and RR were used as the summary measures for analysis of the secondly outcomes.

2.6. Data analysis

The fixed or random effects model were used to combine the continuous and dichotomous data. Heterogeneity between RCTs was assessed via I^2 and χ^2Q statistics. Heterogeneity existence was defined as a P value < 0.05 or $I^2 > 25$ % [28]. When the outcomes were homogeneous ($I^2 < 50$ %), the fixed effects model was conducted. And, when there were significant heterogeneities existed between the studies ($I^2 > 50$ %), the random effects model was conducted.

We used sensitivity analysis and subgroup analysis to investigate the origin of existed heterogeneity. Sensitivity analysis was used to evaluate the stability of the pooled estimates. If a decrease in I^2 value was showed, it indicated that the origin of heterogeneity was found. The magnitude of the value represents the strength of the interpretable heterogeneity. The publication bias possibility was measured by funnel plot which was conducted by the effect size against the standard error of each trial. The Egger test was also used to examine publication bias and the P value < 0.1 was defined as a statistical significant difference of publication bias. Meta-analysis was performed using R software 4.0.3 and trial sequency analysis (TSA) was conducted using TSA software 0.9.5.10.

3. Results

3.1. Eligible studies

The flow chart of the article retrieval and the process of study selection is presented in Appendix Fig. 1. According to the pre-determined strategies, a total of 329 relevant studies were identified from PubMed, Cochrane library, Embase and references from other original article and meta-analysis. 110 studies were saved followed by removing the repeated citations. After browsing tittle and abstract, a total of 79 studies were excluded. A total of 14 studies were excluded due to the excluding criteria. And 4 studies were screened out following full-text reading. Finally, a total of 13 eligible studies were selected for this meta-analysis [11,22–27,29–34].

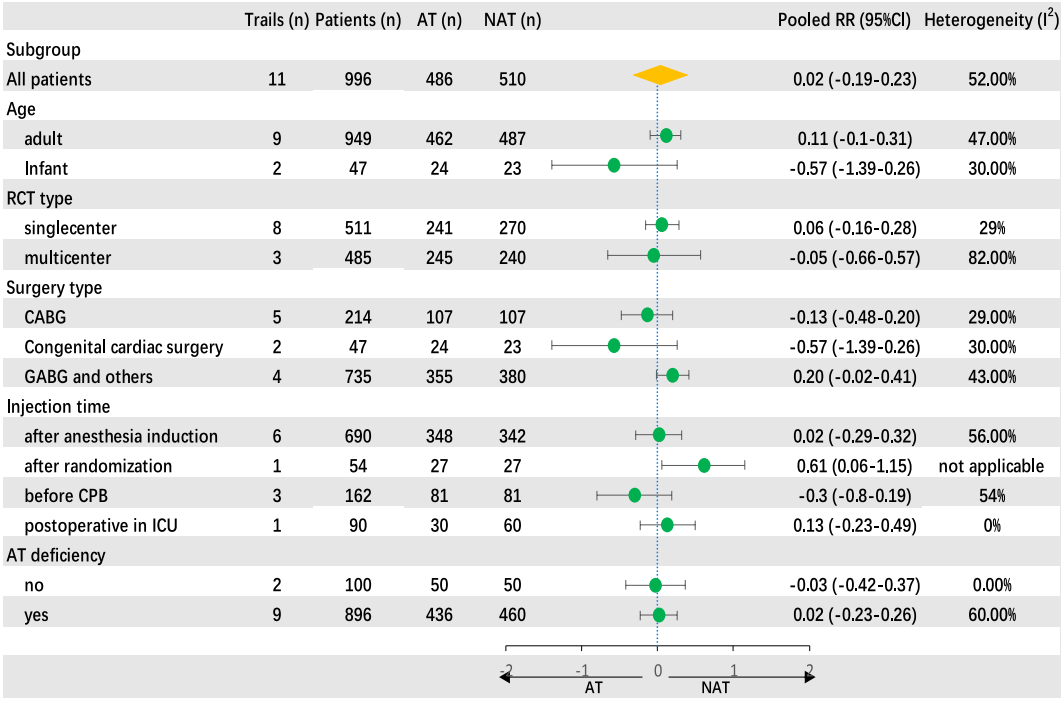
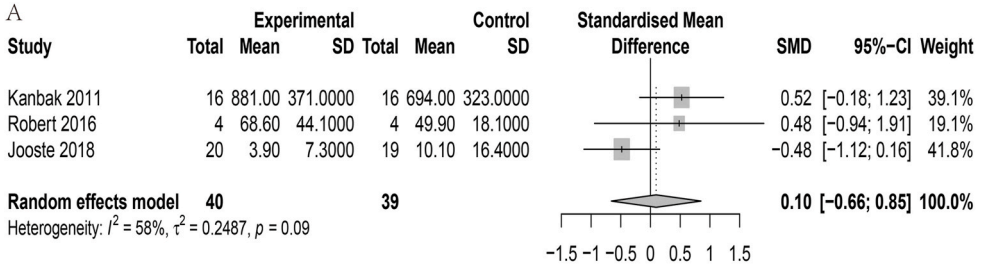


Fig. 2. Forest plot of subgroup analysis; pooled ES, pooled estimate (SMD).

A



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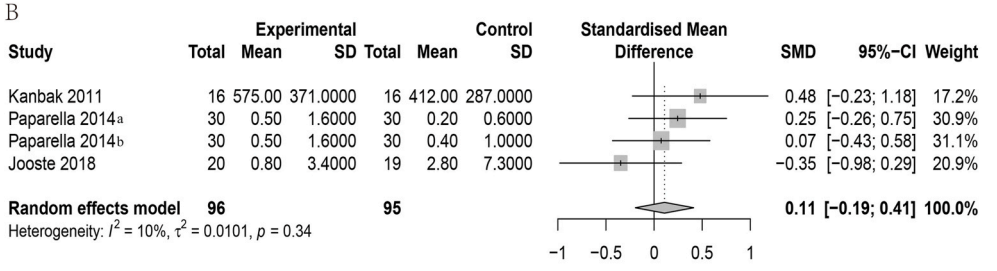

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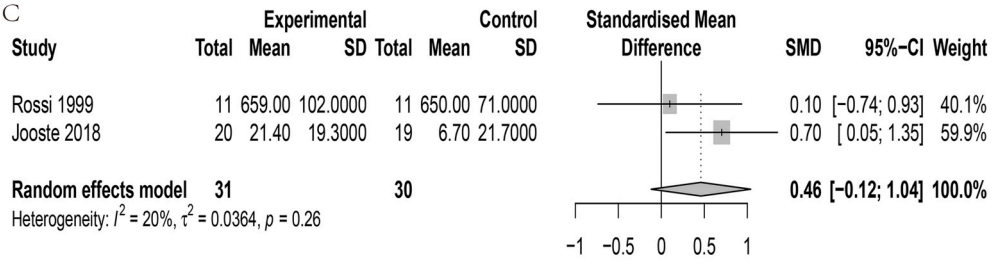

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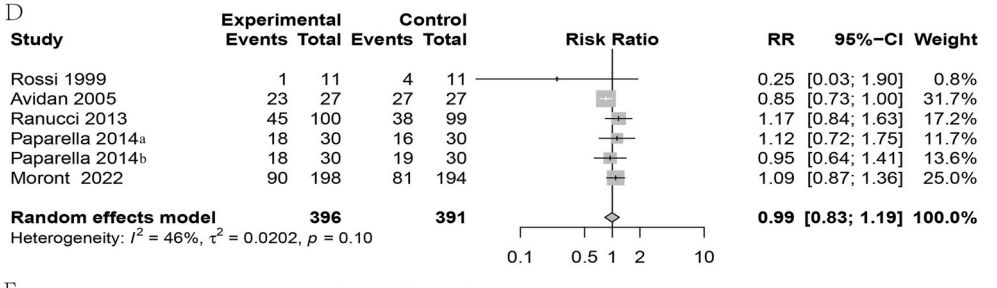

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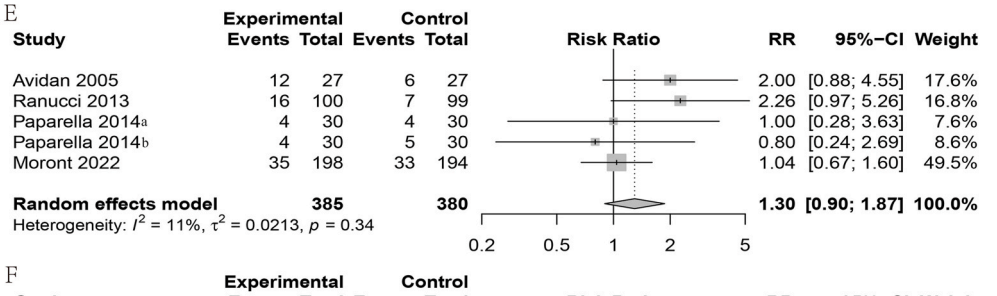

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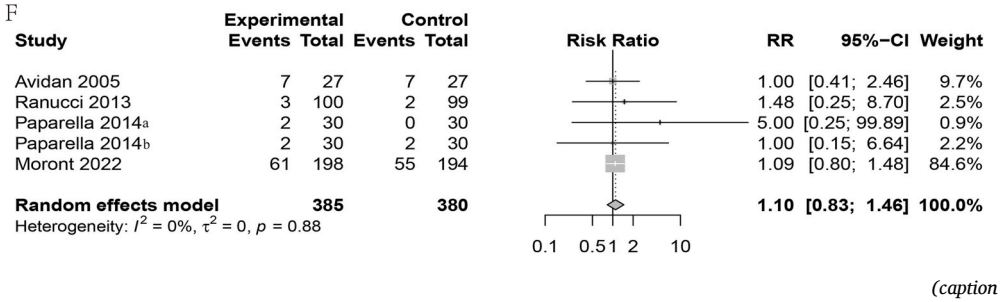

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Fig. 3. Forest plots of AT on blood component transfusion; A, Forest plot of AT on units of RBC transfusion; B, Forest plot of AT on units of FFP transfusion; C, Forest plot of AT on autologous blood transfusion; D, Forest plot of AT on incidence of RBC transfusion; E, Forest plot of AT on incidence of FFP transfusion; F, Forest plot of AT on incidence of platelet transfusion.

3.2. Study characteristics and quality assessments

Characteristics of the included studies are presented in Table 1. A total of 1099 participants were included in the review. Patients in most studies were infants or adults. According to the AT product types, AT was divided into ATIII and recombinant human antithrombin (RhAT). As shown in Appendix Fig. 2, only few methodological bias of the included studies was high, indicating that the qualities of the studies were relatively high.

3.3. Synthesis of results

3.3.1. Meta-analysis of primary outcome

Perioperative AT supplementation did not decrease postoperative blood loss compared with non-AT (SMD -0.01, 95%CI -0.2 to 0.19; I^2 52 %) according to the random effects model (Fig. 1A). There was no significant difference between AT and non-AT supplementation respectively at postoperative 12 h (SMD 0.13, 95%CI -0.12 to 0.38; I^2 53 %) and 24 h (SMD -0.01, 95%CI -0.29 to 0.27; I^2 52 %) (Fig. 1B and C).

3.3.1.1. Subgroup analysis. Based on patients' age, RCT type, surgery type, injection time and whether patients with AT deficiency, 5 subgroups were then established. There was no significant difference between AT and non-AT group both for adult (0.11 (−0.1-0.31)) and infant (−0.57 (−1.39-0.26)). Whether it is a single-center RCT (0.06 (−0.16-0.28)) or not (−0.05 (−0.66-0.57)) was not associated with the statistical difference of the pooled estimates. Surgery types (CABG, −0.13 (−0.48-0.20); congenital cardiac surgery, −0.57 (−1.39-0.26); GABG and other surgery, 0.20 (−0.02-0.41)) were not associated with postoperative blood loss. AT had no significant effect on postoperative blood loss in patients with AT deficiency (0.02 (−0.23-0.26)) or not (−0.03 (−0.42-0.37)). There was no statistical difference of AT on postoperative blood loss when AT was administrated after anesthesia induction (0.02 (−0.29-0.32)), before CPB (0.3 (−0.8-0.19)) and postoperative in ICU (0.13 (−0.23-0.49)). Interestingly, when AT was administrated after randomization, there was significant difference between AT and non-AT on postoperative blood loss (0.61 (0.06–1.15)), and there was only 1 study with this injection time (Fig. 2).

3.3.1.2. Sensitivity analysis. Sensitivity analysis showed the pooled estimates and 95%CIs for postoperative blood loss did not change significantly after each study's separately excluding. 95%CI crossed the invalid line and the absolute values of the 95%CI were not excessively large (Appendix Fig. 3A).

3.3.1.3. Publication bias. Deviations from symmetry was not showed in the funnel plots (Appendix Fig. 3B). P value of the Egger test was 0.446 which indicated that the funnel plot for postoperative blood loss was symmetry and there was no publication bias existed.

3.3.2. Meta-analysis of the secondary outcomes

Perioperative AT also did have significant influence on RBC transfusion ((SMD 0.10, 95%CI -0.66 to 0.85), (RR 0.99, 95%CI 0.83 to 1.19)) (Fig. 3A, D), FFP transfusion ((SMD 0.11, 95%CI -0.19 to 0.41), (RR 1.30, 95%CI 0.90 to 1.87)) (Fig. 3B, E), platelet transfusion (RR 1.10, 95%CI 0.83 to 1.46) (Fig. 3C) and autologous blood transfusion (SMD 0.46, 95%CI -0.12 to 1.8504) (Fig. 3F). Perioperative AT significantly increased in hospital mortality (RR 2.53, 95%CI 1.02 to 6.28) and acute kidney injury (RR 3.72, 95%CI 1.73 to 8.04). There was no significant difference in postoperative re-exploration (RR 1.81, 95 % CI 0.85 to 3.85), thromboembolism (RR 1.04, 95 % CI 0.28 to 3.80), ECMO/IABP support (RR 0.55, 95 % CI 0.09 to 3.28), and stroke (RR 0.73, 95 % CI 0.31 to 1.72) incidence between AT

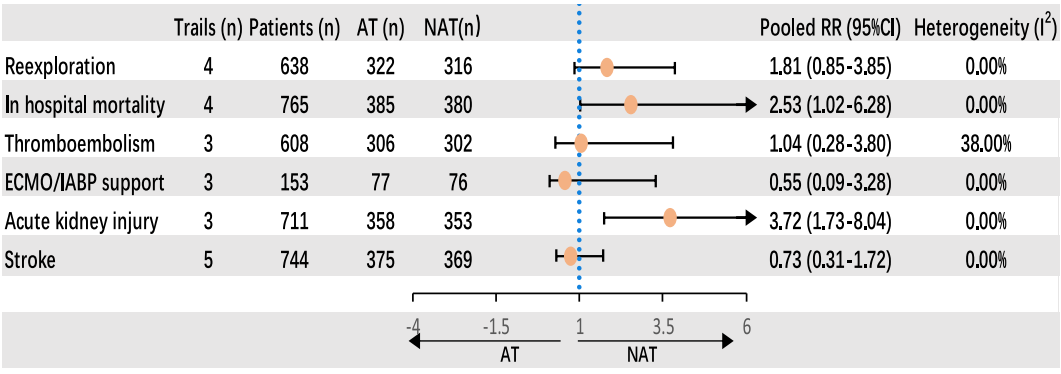

Fig. 4. Forest plots of AT on incidence of postoperative reexploration, thromboembolism, ECMO/IABP support, AKI and in hospital mortality.

and non-AT group (Fig. 4).

3.4. Trial sequential analysis

The effect mean difference is 135, type I error (α = 5 %), and type II error (β = 20 %) (power of 80 %) were used. The cumulative Z curve did not crosse the trial sequential monitoring boundary of AT for postoperative blood loss and crossed the line of the information value, further suggesting that no additional studies were required for a stable conclusion. The included studies for postoperative blood loss provide results with adequate statistical that AT administration did not have significant influence on postoperative blood loss compared with non-AT (Fig. 5).

4. Discussion

4.1. Summary of the evidences

The results of our meta-analysis provided evidences that perioperative AT did not influence postoperative blood loss and blood component transfusion significantly. Although no significant difference in postoperative re-exploration, thromboembolism, ECMO/IABP support, and stroke incidence between AT and non-AT group, but perioperative AT significantly increased in hospital mortality and acute kidney injury incidence. 13 RCTs with 996 participants were included in our meta-analysis. Heterogeneity analysis showed a moderate amount of statistical heterogeneity for postoperative blood loss ($I^2 = 52$ %) and units of RBC transfusion ($I^2 = 58$ %) and no statistical heterogeneity for the other outcomes ($I^2 < 25$ %). Several relevant subgroups were also established to find other results on postoperative blood loss. Based on 6 different standards, 6 subgroups were established and the results showed no statistic significant of AT on postoperative blood loss. When AT was administrated before CPB, there was significant difference between AT and non-AT on postoperative blood loss (0.61 (0.06–1.15)). As there was only 1 study with this injection time and the sample size of the study is relatively small, so this result may be not stable. Subsequently, we conducted sensitivity analysis and it showed that the stability of our result was high. Funnel plots did not show deviations from symmetry and the Egger's test indicated no publication bias was found. It is noteworthy that we found AT significantly increased in hospital mortality (RR 2.53, 95%CI 1.02 to 6.28) and the incidence of AKI (RR 3.72, 95%CI 1.73 to 8.04). The heterogeneity for the two outcomes were both 0 % and the sample size for the two results was 765 and 711. We believe these results should be arouse our attention in clinical practice because AT may be not safe enough for patients undergoing surgery with CPB.

During CPB, AT level is significantly decreased. Cofactor deficit might lead to an inadequate systemic anticoagulation during CPB and to the phenomena of consumptive coagulopathy due to excessive thrombin activation [35,36]. This may manifest with increased bleeding, the need for blood products, and prolonged surgical times. Moreover, low postoperative AT level increases the risk of thrombosis in vulnerable patients with shunts, indwelling central lines, surgical stress and low-flow cardiac output states post-CPB [37–39]. As AT has a biological half-life of 2.5 days, it may reduce postoperative blood loss and blood transfusion. Although in this meta-analysis we did not find perioperative AT contributed to postoperative blood loss and blood products transfusion, fortunately, it also did not increase postoperative bleeding and blood transfusion. This means it can be used in cardiac surgery without any stress on bleeding and blood components transfusion. In fact, AT has been approved for use in the setting of hereditary AT deficiency and has been extensively used in adult cardiac surgery patients requiring CPB with heparin resistance. For infants, AT may be more needed because infants and children with congenital cardiac disease are known to be at risk for AT deficiency [40,41]. AT has been proved to

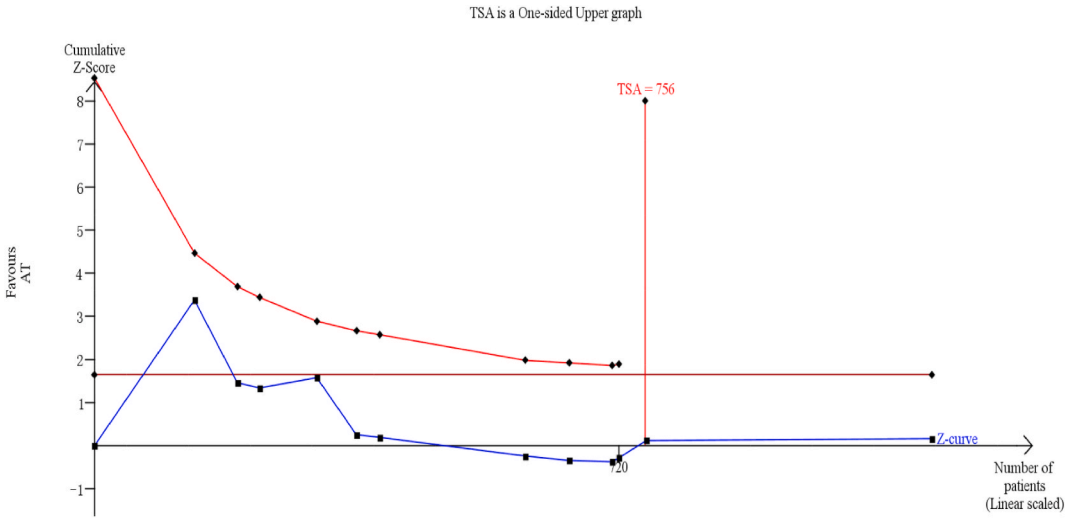

Fig. 5. TSA for AT on postoperative blood loss.

be effective on reduction of postoperative blood loss and transfusion for infants in one RCT [23]. Unfortunately, this meta-analysis did not illustrate this function of AT for infants. We predict the reason for this result is that the sample size is too small, therefore their result may be a false positive result. We are looking forward that more RCTs which are similar with the above research could be completed.

This meta-analysis demonstrated that there was no significant difference in postoperative thromboembolism and stroke incidence between AT and non-AT group. This was different from the positive function of AT on thromboembolic events according to the guideline. As there were not enough evidences for this conclusion, our results may provide evidence-based medicine evidences on the outcomes. Importantly, perioperative AT significantly increased in hospital mortality (RR 2.53, 95%CI 1.02 to 6.28) and AKI (RR 3.72, 95%CI 1.73 to 8.04) incidence. It seems that perioperative AT supplementation may be not safe enough for patients. The heterogeneity for the above two outcomes were both 0 % and the sample size for the two results was 765 and 711. Although some studies interpreted the theories for AKI such as the AT group has more advance aged and diabetes mellitus patients which is easier to develop AKI. Since the underlying mechanisms are multifactorial, these data must be interpreted with caution. At least detected from our results, perioperative AT supplementation may increase in hospital mortality and the incidence of AKI. Since mortality and AKI are both dichotomous data, we cannot rule out that there are false positive conclusions caused by insufficient sample size.

This meta-analysis showed postoperative blood loss was not significantly different between AT and NAT group. This means that AT is not related to postoperative bleeding because AT neither increased nor decreased postoperative volume of blood loss. In order to determine the accuracy of this result, we decided to perform the TSA for the evaluation of the analytical power of the data. The cumulative Z curve did not crosse the trial sequential monitoring boundary of AT for postoperative blood loss and crossed the line of the information value, further suggesting that no additional studies were required for a stable conclusion.

4.2. Limitations

Firstly, in the included studies, there were 6 RCTs with enouph sample size for target analysis. Although the primary outcome of their research was continuous data which did not need large sample size and risk of bias evaluation and the publication bias tests did not show a high risk, and the TSA indicated a stable result, some studies enrolled inadequate patients still contributes noise probably. Therefore, maximize the sample size and including more RCTs contributes to reduce the confidence interval. Secondly, there were several primary or secondary endpoints pre-designed. And this might potentially increase the overall type I error rate for all the outcomes which were under investigation. Thirdly, some grey literatures and clinical trial databases were not well searched. Although some conference abstracts from some medical conferences were searched, the full article still could not be identified and the relative data was not obtained for analysis.

5. Conclusions

Perioperative AT has no significant effect on blood conservation. Our research provided evidence-based medical evidence of AT on blood conservation and postoperative complications. And it is noteworthy that the treatment increased in hospital mortality and the incidence of AKI after cardiac surgery.

Ethical approval

Not applicable.

Funding

The authors have no sources of funding to declare for this manuscript.

Additional information

No additional information is available for this paper.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Tao Li: Writing – original draft, Project administration, Conceptualization. **FengShan Bo:** Writing – original draft, Project administration. **XiangRui Meng:** Software. **Di Wang:** Software, Data curation. **Jiahai Ma:** Software, Data curation. **Zhao Dai:** Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to give our thanks to our colleagues who supported us in the whole process of this paper work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e22266.

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