

Effects and safety of intraoperative intermittent pneumatic compression for preventing postoperative venous thromboembolism: a meta-analysis

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Abstract

Introduction: Intermittent pneumatic compression (IPC) has been used for venous thromboembolism (VTE) prevention. It is necessary to evaluate the effects and safety of intraoperative use of IPC devices in the prevention of VTE in surgical patients.

Material and methods: Two authors independently searched the PubMed, Cochrane Library, MEDLINE, Embase, China National Knowledge Infrastructure (CNKI), and Wanfang databases for randomized controlled trials (RCTs) and cohort studies on the use of IPC in surgical patients up to June 10, 2021. The Cochrane Collaborations risk of bias tool and the Newcastle-Ottawa Scale (NOS) were used for quality assessment. RevMan 5.3 software was used for statistical analyses.

Results: A total of 13 studies including seven RCTs and six retrospective cohort studies involving 6673 surgical patients were included; 1883 patients underwent IPC intervention. The synthesized RCT results indicated that IPC was beneficial to reduce the incidence of deep vein thrombosis (DVT) (RR = 0.30, 95% CI: 0.22–0.40, $p < 0.001$) and VTE (RR = 0.51, 95% CI: 0.27–0.95, $p = 0.03$). The synthesized results from retrospective cohort studies indicated that IPC is beneficial to reduce the incidence of DVT (RR = 0.63, 95% CI: 0.42–0.96, $p = 0.03$) and PE (RR = 0.34, 95% CI: 0.16–0.72, $p = 0.005$). No significant publication bias was found for any synthesized outcomes (all $p > 0.05$).

Conclusions: IPC seems to be safe and effective in the prevention and management of intraoperative VTE. Limited by study sample size, this conclusion still needs to be further confirmed by large-sample, multi-center, high-quality clinical studies.

Key words: intermittent pneumatic compression, surgery, venous thromboembolism, prevention, care.

Introduction

Venous thromboembolism (VTE) is a common yet potentially life-threatening complication during the perioperative period, including deep vein thrombosis (DVT) and pulmonary embolism (PE). According to previous reports [1, 2], there are more than 698,000 cases of symptomatic DVT and more than 434,000 cases of PE in Europe each year, resulting in more than 543,000 deaths. The incidence of VTE events in Asia is lower than that in European countries [3]. However, with the development of medical diagnostic methods and the strengthening of popula-

tion awareness, the incidence of VTE is increasing year by year [4, 5]. When a patient presents with DVT, the main manifestations are lower extremity swelling, pain, superficial vein dilation, elevated skin temperature, and restricted activity [6]. If not diagnosed and treated in time, fatal PE may occur, manifested as chest pain, cough, and dyspnea or even death [7]. Therefore, the prevention and treatment of VTE have become a major health problem of global medical workers.

The prevention and treatment of VTE in the perioperative period is of great significance to the prognosis of surgical patients. Intermittent pneumatic compression (IPC) devices use mechanical inflation to compress the veins of the lower limbs to promote blood circulation [8]. Several clinical studies [7, 9] have shown that IPC is beneficial to reduce the occurrence of perioperative VTE, promote rapid perioperative recovery, improve the quality of life, and reduce unexpected mortality. However, IPC is currently not widely used in surgery, and due to the limited sample size and different populations, the conclusions drawn by previous studies are different and inconsistent [10, 11]. Therefore, it is necessary to evaluate the preventive effect of IPC on perioperative VTE by using the method of meta-analysis, to provide evidence-based guidelines for the prevention and treatment of VTE in patients during surgery.

Material and methods

We aimed to perform and report this systematic review and meta-analysis in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [12].

Study search

We searched for randomized controlled trials (RCTs) and cohort studies related to the use of IPC in surgical patients, in databases including PubMed, Cochrane Library, MEDLINE, Embase, China National Knowledge Infrastructure (CNKI), and Wanfang. The search strategies were ((intermittent pneumatic compression) OR (IPC) OR (mechanical compression)) AND ((intraoperative) OR (surgery) OR (operation)) AND ((venous thrombosis) OR (thromboembolism) OR (deep vein thrombosis) OR (DVT) OR (VTE)). The search time limit is from the establishment of the database to June 10, 2021. The languages of reports were limited to Chinese and English. Additionally, we checked and reviewed the reference lists of associated RCTs and reviews to avoid missing any reports.

Literature inclusion and exclusion criteria

The inclusion criteria for this meta-analysis were as follows: The type of study was RCT or ret-

rospective cohort study on the application of IPC to patients undergoing surgery treatment. The populations of the study were patients ≥ 18 years of age. The intervention measures covered IPC and the control group, and the cycle and duration of IPC intervention were not limited. The article reported relevant outcome indicators such as the incidence of DVT and PE. The exclusion criteria for this meta-analysis were as follows: case reports, reviews, and observational studies were excluded; related data were incomplete or could not be obtained from contacting the corresponding authors of reports.

Data extraction

Two researchers independently read and screened the literature according to the inclusion and exclusion criteria. When the opinions were inconsistent, we held a discussion to reach a consensus or the third researcher decided whether to include the study. The content of the literature extraction included the setting, population, sample size, sampling and grouping methods, intervention measures, relevant outcome indicators and research conclusions.

Quality assessment of included studies

The Cochrane Collaborations risk of bias tool [13] was adopted by two authors independently to evaluate the quality and risk of bias of the included RCTs. Seven specific domains were examined in this tool: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other issues. Each domain was rated as low risk of bias, high risk of bias or unclear risk of bias according to the judgment criteria. Any disagreements were resolved by discussion and consensus. In addition, we used the Newcastle-Ottawa Scale (NOS) [14] to evaluate the quality of the cohort study. The scale included 8 items with a maximum score of 9 – the higher the score, the higher the quality of the study.

Statistical analysis

All the statistical analyses were conducted with RevMan 5.3 software. In this present meta-analysis, binary outcomes were presented as Mantel-Haenszel-style risk ratios (RR) with 95% confidence intervals (CI). Continuous outcomes were reported as mean differences (MDs). A fixed-effect model was applied in the cases of homogeneity (p -value of χ^2 test > 0.1 and $I^2 < 50\%$), whereas a random-effect model was used in cases of obvious heterogeneity (p -value of χ^2 test < 0.1 and $I^2 \geq 50\%$). Publication bias was evaluated using funnel

plots, and asymmetry was assessed by the Egger regression test. In this study, $p < 0.05$ was considered significant.

Results

Study selection

The flow chart of study selection is shown in Figure 1. The initial search identified 128 potentially relevant reports. Of these identified articles, 10 studies were excluded as duplicates. After viewing the titles and abstracts of the 118 remaining studies, the full texts of 41 reports were retrieved. Among them, 28 reports were excluded due to failure to meet the inclusion criteria. Finally, a total of 13 studies [15–27] including seven RCTs [15, 16, 21, 22, 25–27] and six retrospective cohort studies [17–20, 23, 24] were included in this meta-analysis.

Characteristics and quality of included studies

As presented in Table I, of the 13 studies [15–27] included in this meta-analysis, a total of 6673 surgical patients were included, and 1883 patients underwent IPC intervention. The types of surgery considered in this meta-analysis included joint replacement, neurosurgery, intracranial surgery, breast surgery, gastrointestinal surgery, and gynecological surgery. As shown in Tables II and III, the quality of the studies included in this meta-analysis were generally good. All studies described and compared baseline data such as age and gender of the two groups of patients; the baseline data between groups were relatively comparable.

Meta-analysis

The incidence of DVT in the 7 included RCTs [15, 16, 21, 22, 25–27] reported the incidence of DVT; there was no significant heterogeneity ($I^2 = 40\%$, $p = 0.13$) and a fixed model was applied for meta-analysis. As presented in Figure 2, the synthesized outcome indicated that IPC was beneficial to reduce the incidence of DVT (RR = 0.30, 95% CI: 0.22–0.40, $p < 0.001$).

The incidence of VTE in the 5 included RCTs [15, 16, 21, 26, 27] reported the incidence of VTE; there was significant heterogeneity ($I^2 = 61\%$, $p = 0.04$) and a random model was applied for meta-analysis. As presented in Figure 3, the synthesized outcome indicated that IPC was beneficial to reduce the incidence of VTE (RR = 0.51, 95% CI: 0.27–0.95, $p = 0.03$).

The incidence of DVT in the 6 included retrospective cohort studies [17–21, 23, 24] reported the incidence of DVT; there was no significant heterogeneity ($I^2 = 28\%$, $p = 0.23$) and a fixed model

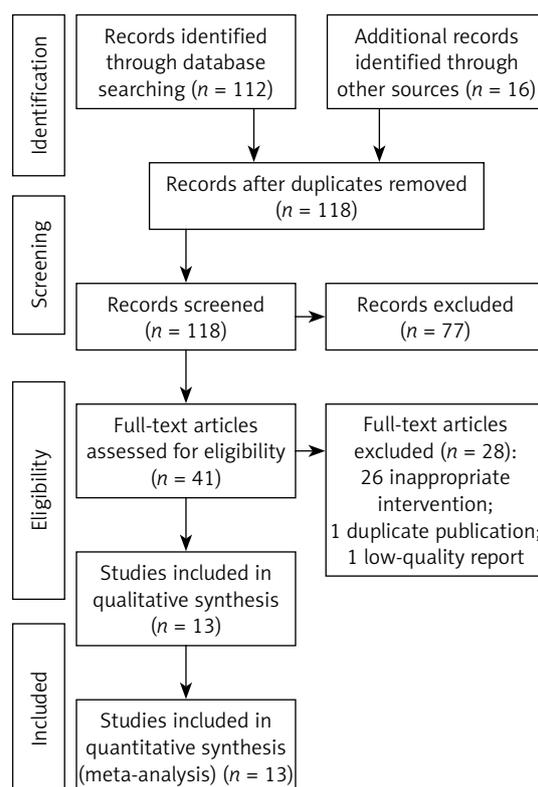


Figure 1. PRISMA flow diagram

was applied for meta-analysis. As presented in Figure 4, the synthesized outcome indicated that IPC was beneficial to reduce the incidence of DVT (RR = 0.63, 95% CI: 0.42–0.96, $p = 0.03$).

The incidence of PE in the 3 included retrospective cohort studies [18–20] reported the incidence of PE; there was no significant heterogeneity ($I^2 = 0\%$, $p = 0.89$) and a fixed model was applied for meta-analysis. As presented in Figure 5, the synthesized outcome indicated that IPC was beneficial to reduce the incidence of PE (RR = 0.34, 95% CI: 0.16–0.72, $p = 0.005$).

Publication bias

As presented in Figure 6, the dots were evenly distributed in the funnel plots for synthesized outcomes, and Egger regression tests indicated that there was no significant publication bias for all synthesized outcomes (all $p > 0.05$).

Discussions

IPC is currently one of the most widely used VTE physical preventive devices in clinical practice. Although it has been continuously studied in recent years, clinical medical staff still have doubts about its effectiveness and safety [28, 29]. Therefore, it is necessary to further update the evidence regarding the effectiveness and safety of IPC to guide the clinical practice. The results of this meta-analysis have shown that IPC is effective

Table 1. Characteristics of included RCTs

Study	Country	Population	Study design	Sample size		Intervention		Outcomes
				IPC group	Control group	IPC group	Control group	
Ebeling 2018	Germany	GBM	Retrospective cohort study	75	78	IPC + GCS	GCS	IPC/GCS: Before the operation starts to the time patients could get out of bed DVT, PE
Eisenring 2013	USA	Meningeal tumor surgery	Retrospective cohort study	242	482	IPC + GCS	GCS	IPC/GCS: Before the operation starts to the time patients could get out of bed DVT, PE, death
Frisius 2015	Germany	Neurosurgery	Retrospective cohort study	86	121	IPC + GCS	GCS	IPC/GCS: Before the operation starts to the time patients could get out of bed DVT, PE
Gao 2012	China	Gynecological surgery	RCT	52	54	IPC + GCS	GCS	IPC: Intraoperative and postoperative time that patients could get out of bed GCS: Before the operation starts to the time patients could get out of bed DVT, PLT, PT, APTT, TT, D-D
Gao 2018	China	Breast cancer surgery	RCT	127	124	IPC; IPC + GCS	Black control	IPC: After successful anesthesia to 48 h after surgery GCS: Before operation to 48 hours after operation DVT, PLT, PT, APTT, TT, D, D
Miao 2019	China	Laparoscopic gastrointestinal tumor surgery	Retrospective cohort study	100	100	IPC	GCS	IPC/GCS: Before the operation starts to the time patients could get out of bed DVT, PT, APTT
Prell 2018	Germany	Neurosurgery	RCT	41	53	IPC + GCS	GCS	IPC: Before the intraoperative fixed position to the end of the operation GCS: Before the operation to the 5th day after the operation DVT, PE
Sang 2018	China	Gynecological surgery	RCT	153	159	IPC + GCS	GCS	IPC: Before the start of the operation to 24 h after the operation GCS: Before the operation starts to the time patients could get out of bed DVT, PE
Tyagi 2018	USA	TKA, THA	Retrospective cohort study	390	2989	IPC	Black control	During the surgery VTE
Wang 2018	China	TKA, THA, HFS	Retrospective cohort study	51	61	IPC + GCS	GCS	IPC/GCS: Before the operation starts to the time patients could get out of bed DVT, femoral vein MBVF, PVBF, BFV
Wang 2019	China	Lung cancer patients undergoing video-assisted thoracoscopic surgery (VATS) lobectomy.	RCT	246	249	IPC	Black control	After induction of anesthesia and before patient positioning. DVT, Flow velocity of the femoral vein
Zhao 2015	China	TKA, THA	RCT	200	200	IPC	Black control	IPC: After successful anesthesia to the skin disinfection DVT, PE
Zhu 2019	China	TKA, THA	RCT	120	120	IPC + GCS	GCS	IPC/GCS: Before the operation starts to the time patients could get out of bed DVT, D-D

TKA – total knee replacement, THA – total hip replacement, GBM – glioblastoma, HFS – hip fracture surgery, GCS – graduated compression stockings, MBVF – myocardial blood volume fraction, PVBF – portal venous blood flow, BFV – blood flow volume, PLT – platelet count, PT – prothrombin time, APTT – activated partial thromboplastin time, TT – thrombin time, D-D – D-dimer.

Table II. Quality assessment of included RCTs

RCT	Sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective outcome reporting	Other bias
Gao 2012	Low risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
Gao 2018	Low risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
Prell 2018	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
Sang 2018	Low risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
Wang 2019	Low risk of bias	Low risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
Zhao 2015	Unclear risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias
Zhu 2019	Low risk of bias	Unclear risk of bias	High risk of bias	Unclear risk of bias	Low risk of bias	Low risk of bias	Low risk of bias

Table III. NOS quality evaluation of included retrospective cohort study

Study	Representativeness of exposure cohort	Selection of non-exposed cohort	Confirmation of exposure	No disease before inclusion	Comparability of exposed cohort and non-exposed cohort	Method of measuring results	Follow-up time	Completeness of follow-up	Total score
Ebeling 2018	1	1	1	1	1	1	1	1	8
Eisenring 2013	1	1	1	1	2	1	1	1	9
Frisius 2015	1	1	1	0	1	0	1	1	6
Miao 2019	1	1	1	1	1	1	0	1	7
Tyagi 2018	1	1	1	1	1	1	1	1	8
Wang 2018	1	1	1	1	2	1	1	1	9

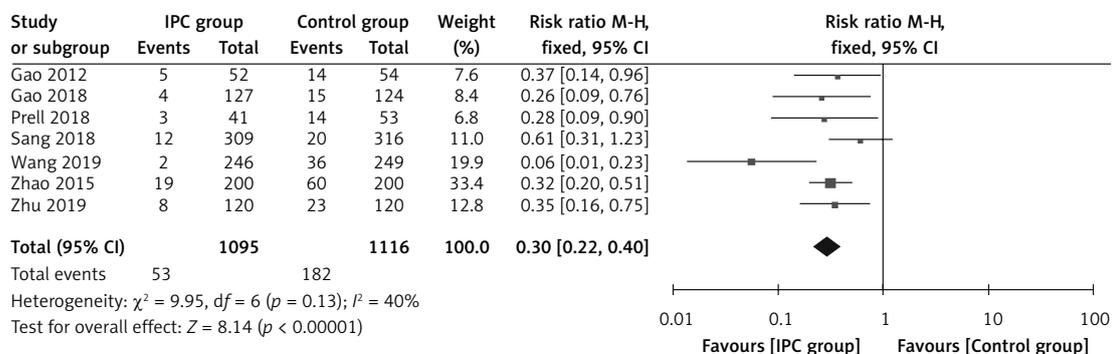


Figure 2. Forest plot for incidence of DVT in the included RCTs

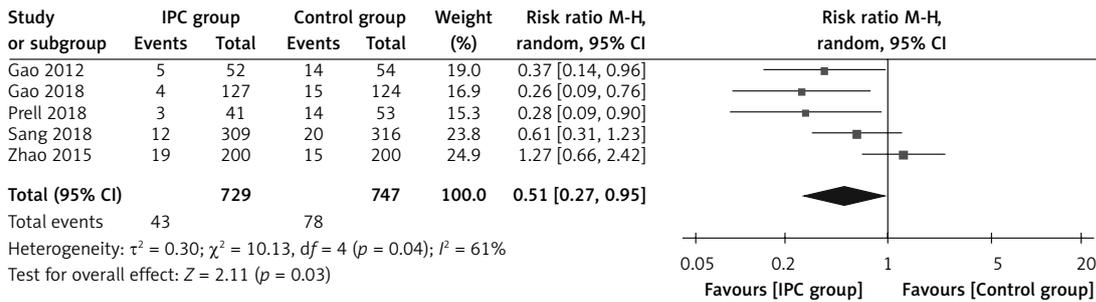


Figure 3. Forest plot for incidence of VTE in the included RCTs

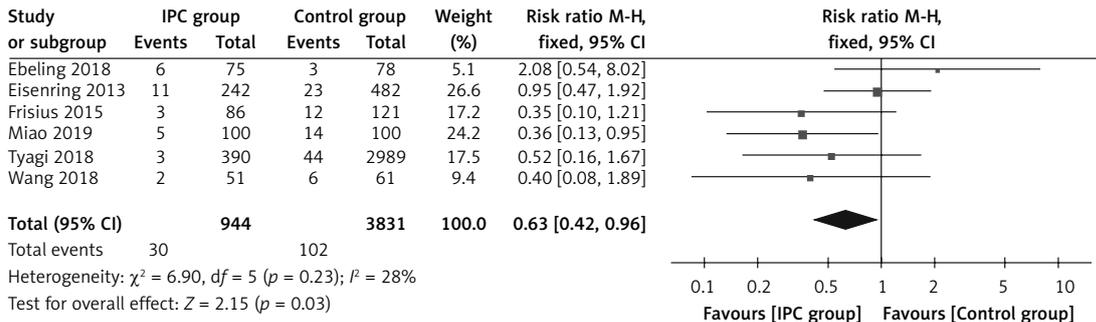


Figure 4. Forest plot for incidence of DVT in the included retrospective cohort studies

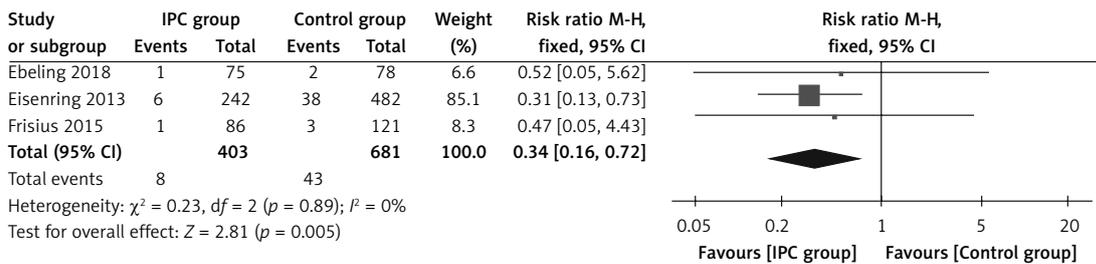


Figure 5. Forest plot for incidence of PE in the included retrospective cohort studies

tive to reduce the risk of DVT, VTE and PE in patients undergoing surgery.

Venous congestion, hypercoagulable state and vascular endothelial injury are recognized as the three major factors for the occurrence of VTE [30]. Surgical patients need to be immobilized for a long time. Surgical injury, the use of drugs such as anesthesia, muscle relaxation, and sedation during the operation put the patient in a high-risk state of thrombosis. Furthermore, intraoperative blood transfusion, hypothermia, laparoscopic pneumoperitoneum, lithotomy and the lying position greatly increase the risk of VTE [31, 32]. IPC is an effective method of thrombosis prevention, which can increase muscle contraction, promote lymphatic and venous blood circulation, and prevent partial accumulation of coagulation factors, thereby effectively preventing the occurrence of VTE. Both IPC and GCS are effective physical prevention methods for DVT [33–35]. Graduated compression stockings (GCS) are designed according to the principle of sequential decompression [36, 37]. The pressure at the ankle is the highest,

and it gradually decreases upwards along the legs, squeezing the veins of the lower extremities, speeding up the return of blood to the heart from the veins of the lower extremities, and reducing blood stasis to prevent dilation of the venous lumen [38, 39]. IPC mainly simulates the contraction and relaxation of lower extremity muscles through intermittent inflation and compression, and squeezes the veins of the lower extremities, thereby speeding up the blood flow of the veins of the lower extremities, avoiding blood pooling in the veins of the lower extremities, promoting venous blood return to the heart, and protecting the function of the venous valve, to achieve the purpose of preventing the occurrence of DVT [40–42].

With the aging of the population, the number of people at high risk of clinical VTE has increased sharply [43]. Therefore, IPC is often used in combination with drugs in order to improve safety. With the widespread use of drugs in clinics, bleeding has become a major clinical concern. This meta-analysis was unable to analyze the bleeding risk of IPC due to the lack of included data. Compared

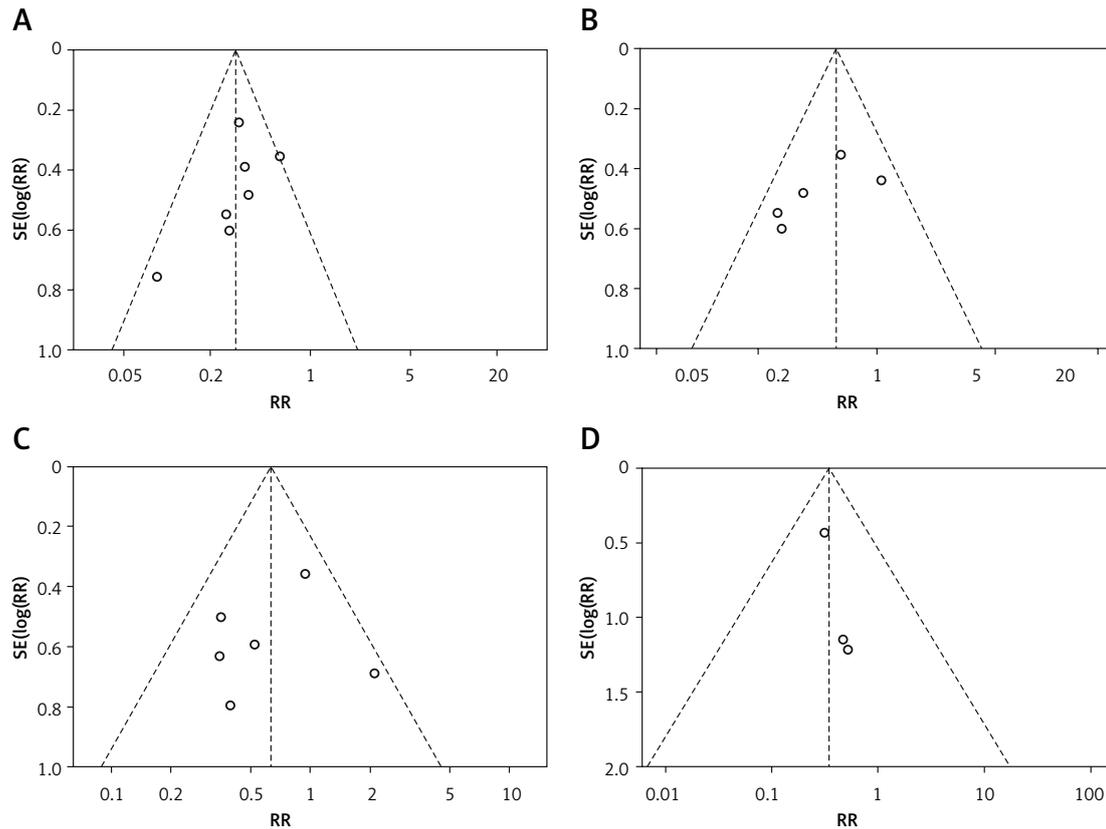


Figure 6. Funnel plots for synthesized outcomes: **A** – Funnel plot for the incidence of DVT in the included RCTs, **B** – Funnel plot for the incidence of VTE in the included RCTs, **C** – Funnel plot for the incidence of DVT in the included retrospective cohort studies, **D** – Funnel plot for the incidence of PE in the included retrospective cohort studies

with anticoagulants in previous studies [44, 45], IPC can reduce the incidence of bleeding events, but it is not yet possible to draw a certain conclusion on the incidence of major bleeding events and mortality [46]. This may be related to the insufficient number of studies and the different anticoagulants used in the research. Compared with IPC alone, studies have shown that IPC combined with low molecular weight heparin (LMWH) can reduce the incidence of bleeding events. The IPC combined anticoagulant group and the anticoagulant group alone cannot enable a certain conclusion to be drawn on the incidence of bleeding and major bleeding events [47]. It may be related to the heterogeneity between the studies and the insufficient number of studies. Therefore, the safety of use is subject to further analysis in follow-up research.

The results of previous studies [18, 48] are different from the results of this study, showing that intraoperative use of IPC will increase the incidence of postoperative DVT. The result may be due to the small sample size and the high risk of DVT in neurosurgery patients. Even if preventive measures are applied, the risk of DVT is still very high. Ultrasound is generally performed when the patient has symptoms after surgery, but a study

[49] showed that more than 50% of DVTs are invisible and asymptomatic. The reports included in this study come from different populations, and there is a certain degree of heterogeneity in the results, and most included studies did not assess the risk level of VTE during the operation before the preventive measures were given, and there may be insufficient prevention of high-risk patients. All these factors suggest that relevant specialized research is needed in the future to further confirm the effect of intraoperative IPC in surgical patients. At the same time, it is necessary to explore or develop intraoperative VTE risk assessment tools to provide a more scientific basis for the prevention of intraoperative VTE.

Several limitations in this present meta-analysis should be considered. Firstly, the literature included in this study comes from different populations, and there is a certain degree of heterogeneity in the results, and most included studies did not assess the risk level of VTE during the operation before the preventive measures were given, and there may be insufficient prevention of high-risk patients. Secondly, we could not perform subgroup analysis based on the types of surgical procedures limited by collected data; relevant specialized studies are needed in the future to further

confirm the effect of intraoperative IPC in surgical patients. Also, it is necessary to explore or develop intraoperative VTE risk assessment tools to provide a more scientific basis for the prevention of intraoperative VTE.

In conclusion, the results of this meta-analysis have shown that intraoperative IPC can effectively reduce the incidence of postoperative VTE, and it is worthy of promotion and use in clinical surgery. In view of the relatively small number of RCTs at present and certain clinical heterogeneity in the research population, interventions, and outcome indicators in this meta-analysis, the effectiveness and safety of IPC in surgery still need to be confirmed by multi-center and large-sample clinical studies, to provide reliable evidence-based guidelines for the preventions and management of VTE in surgical patients.

Conflict of interest

The authors declare no conflict of interest.

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