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ORIGINAL PAPER

The effect of anticoagulants on venous thrombosis prevention after knee arthroscopy: a systematic review

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Abstract

Purpose Knee arthroscopy, with its unique advantages, has become a routine surgery and is widely carried out around the world. Venous thromboembolism (VTE) after knee arthroscopy is a potentially serious complication. This article analyzes the effects of anticoagulant therapy after knee arthroscopy.

Methods We used key words or entry terms without any limitations to search the PubMed, Embase, and Cochrane Library databases. Randomized controlled trials (RCTs) of drug prophylaxis for VTE after knee arthroscopy until November 2017 were included in our review.

Results This systematic review identified nine RCTs, consisting of 4290 patients, investigating drug prophylaxis in knee arthroscopy. There are three main drugs for preventing thrombosis after arthroscopic knee surgery: low-molecular-weight heparin (LMWH), rivaroxaban, and aspirin. Our study concluded that there is no difference in symptomatic VTE (excluding symptomatic distal DVT) risk during anticoagulant prophylaxis (RR, 0.98; 95% CI, 0.44–2.19; I^2 value = 0%; $P = 0.97$). Moreover, there was a lower incidence of symptomatic distal DVT (RR, 0.16; 95% CI, 0.06–0.45; I^2 value = 0%; $P = 0.0005$) in the anticoagulant group than in the control group.

Conclusions In our study, anticoagulant therapy after knee arthroscopy was ineffective. We recommend that anticoagulants not be provided routinely after knee arthroscopy.

Keywords Venous thromboembolism · Anticoagulant · Knee arthroscopy

Introduction

The American College of Chest Physicians guidance has recommended antithrombotic prophylaxis after total hip or knee arthroplasty [1]. These major orthopaedic procedures are associated with a particularly high risk of venous thromboembolism (VTE), and routine VTE prevention has been the standard of care for more than 20 years [2]. Without thromboprophylaxis, arthroscopic knee surgery carries a low-to-moderate risk of VTE [3]. The incidence of deep venous thrombosis (DVT) for arthroscopic knee surgery varies from 3.1 to 17.9%, and that of proximal DVT ranges from 0 to 4.9% [4]. More than 5 million arthroscopies are performed worldwide every year [3]. Arthroscopic knee surgery is one of the most common surgical procedures in traumatology and orthopaedics. In total, 3.5 million of these procedures are performed yearly worldwide [5].

The main thrombosis prevention drugs after knee arthroscopy according to our search are low-molecular-weight heparin (LMWH), rivaroxaban, and aspirin. However, vitamin K antagonists, such as warfarin, are used less frequently after arthroscopic surgery. Because routine thromboprophylaxis with a vitamin K antagonist requires the patient's condition to be monitored frequently; there may be delayed drug effects. Therefore, most vitamin K antagonists have been abandoned for the prevention of thrombosis in Europe [6]. For orthopaedic surgery,

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anticoagulant drugs also include ximelagatran [7]. However, its use after knee arthroscopy is also relatively rare.

Methods

Search strategy

We used "knee" AND ("arthroscopy" OR "arthroscopically" OR "arthroscopic") AND ("thromboembolism" OR "thromboprophylaxis" OR "thrombus" OR "thrombosis") for the search strategy. Three databases, PubMed, Embase, and the Cochrane Library, were searched without any limitations through November 23, 2017.

Selection criteria

The criteria for the included trials were as follows: (1) studies had an RCT design, and (2) patients underwent knee arthroscopy and were treated with anticoagulant drugs after surgery. The exclusion criteria were (1) case-control cohort studies, (2) one-armed RCTs with no control, and (3) studies from which data could not be extracted. We removed the duplicate studies first and then excluded the irrelevant studies by reading the topic and abstract. Finally, we read the full texts to determine the included studies.

Data extraction

Two researchers extracted data independently from the articles, including the first author, year of publication, details of the participants (sample size, age, etc.), comparators, study design, all-cause death, and outcome data, including symptomatic VTE events and symptomatic distal DVT events. A third researcher arbitrated when the two researchers disagreed.

Quality assessments

We used the Cochrane collaboration tool to evaluate the quality of nine studies. Two researchers assessed the quality of each study independently, and when the evaluation results were inconsistent, the third researcher's opinion was obtained. The risk of bias (selection bias, performance bias, detection bias, attrition bias, reporting bias, or other bias) in every study was determined to be "low risk of bias," "high risk of bias," or "unclear risk of bias."

Statistical analysis

Meta-analysis was conducted using Review Manager version 5.3 software (The Nordic Cochrane Centre, The Cochrane Collaboration) for data statistics. The heterogeneity between the studies was not significant (I^2 value < 50%), and we used the fixed-effect model for the analyses. Otherwise, we used the random-effects model. I^2 values of 75–100% indicate that the heterogeneity is high. I^2 values from 50 to 74.9% indicate moderate heterogeneity. I^2 values from 25 to 49.9% show low heterogeneity. I^2 values from 0 to 24.9% indicate no heterogeneity.

Results

Literature search and study characteristics

A total of 790 articles were found: 207 articles were from PubMed, 501 articles were from Embase, 80 articles were from the Cochrane Library, and two articles were from other sources (Fig. 1). By searching the literature, we found that thrombosis prevention measures after knee arthroscopy included mainly three drugs (LMWH, rivaroxaban, and aspirin) in nine RCTs (Table 1). The graph of the risk of bias for all of the included studies is shown in Fig. 2.

Efficacy of anticoagulants

All nine RCTs, which included 4290 patients, reported the efficacies of the anticoagulants. We used the random-effects model to combine the symptomatic VTE (excluding symptomatic distal DVT) data according to notable heterogeneity (I^2 value = 0%). Compared with that of the control group, the incidence of symptomatic VTE in the anticoagulant group was not significantly different (RR, 0.98; 95% confidence interval [CI], 0.44–2.19; $P = 0.97$, Fig. 2). Compared with that of the control group, the incidence of symptomatic VTE in the anticoagulant group was lower (RR, 0.16; 95% CI, 0.06–0.45; $P = 0.0005$, Fig. 3).

Discussion

Historically, knee arthroscopy is considered minor orthopaedic surgery, and symptomatic VTE after knee arthroscopy has been considered rare; however, the results of various studies are different. Knee arthroscopy is a minimally invasive treatment, and its post-operative anti-thrombosis treatment remains controversial and is different from that of total hip or total knee replacement surgeries, for which a consensus has been reached. Because the number of arthroscopic knee surgeries increases rapidly every year, it is necessary to determine the effects of anticoagulants after knee arthroscopy. Proximal DVT occurs when the common popliteal or femoral vein is included [12]. Distal DVT is DVT of the lower extremities. At present, there is considerable debate about the clinical relevance of distal VTE, and therapy is currently not recommended [16–20]. Based on the above reasons, we excluded distal DVT events from the symptomatic VTE events in this study.

Anticoagulants are widely used in patients undergoing total hip or total knee arthroplasty for post-operative venous

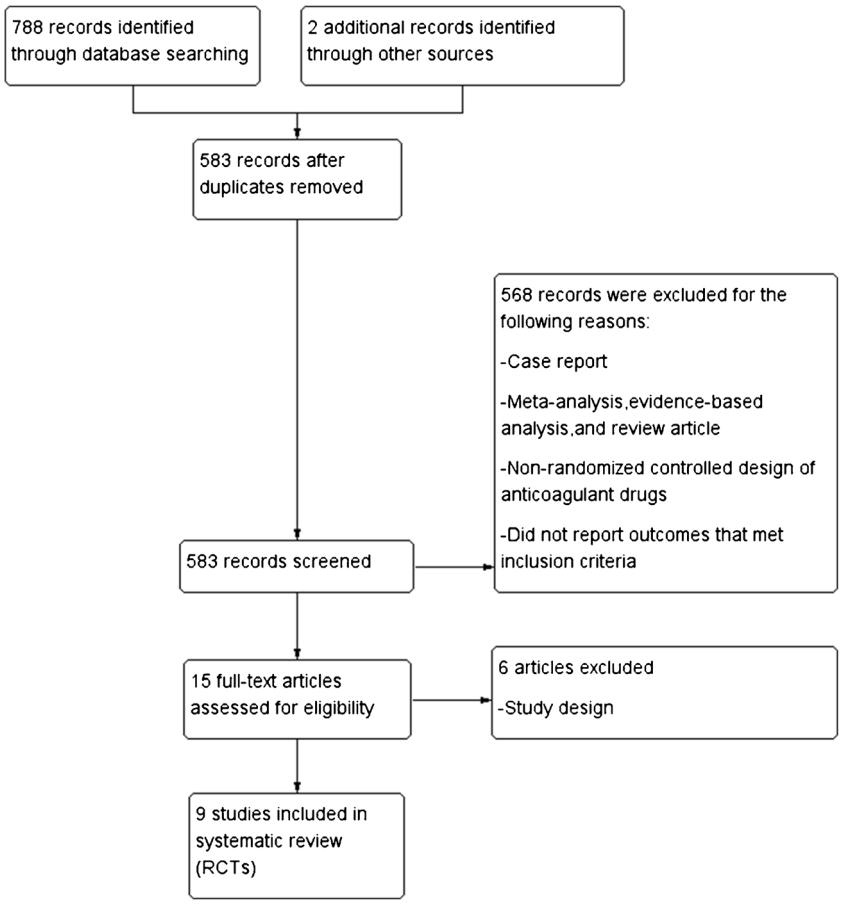

Fig. 1 Flowchart of the screened, excluded, and analyzed publications

thrombosis prevention. LMWH is a very common anticoagulant drug used after knee arthroscopy. A meta-analysis confirmed that the drug can prevent thrombotic events in a non-orthopaedic surgery group compared with a control group [21]. Rocha E et al. [22] considered LMWHs as the drugs of choice for VTE prevention in orthopaedic surgery. VTE (including DVT and pulmonary embolism (PE)) is a potentially life-threatening complication after orthopaedic surgery (including arthroscopic knee surgery). LMWH is the initial treatment of choice for acute DVT [23]. VTE incidence is 0~0.25% for adolescents after knee arthroscopy, and LMWH has been used to treat this complication successfully [24]. The latest medical evidence has proven that LMWH is not routinely required after knee arthroscopy [25]. This is consistent with the results of our research. The difference is that our research contains other anticoagulants, in addition to LMWH. Rivaroxaban is a highly selective drug, and factor Xa and prothrombin activity could be competitively inhibited by using it. After a literature search, we found that the number of articles reporting rivaroxaban used as an anticoagulant drug after arthroscopic knee surgery was rela-

Table 1 Study characteristics

Trial	Sample size	Age, years	Female (%)	Comparators	Study design	All-cause death
Roth, 1995 [[8]	122	NA	NA	LMWH vs NT	RCT	0
Wirth, 2001 [[9]	239	38.1	60 (25.1)	LMWH vs NT	RCT	0
Michot, 2002 [[10]	130	44.2	44 (33.8)	LMWH vs NT	RCT	0
Canata, 2003 [[11]	36	31.1	11 (30.6)	LMWH vs NT	RCT	0
Marlovits, 2007 [[12]	140	NA	58 (41.4)	LMWH vs PLA	RCT	0
Camporese, 2008 [[13]	1761	42.2	670 (38.0)	LMWH vs COM	RCT	0
Kaye, 2015 [[14]	170	44.4	66 (38.8)	ASP vs NT	RCT	0
Camporese, 2016 [[3]	241	45.4	79 (32.9)	RIV vs PLA	RCT	0
Van Adrichem, 2017 [[15]	1451	48.6	641 (44.2)	LMWH vs NT	RCT	0

NA, not available; *NT*, no treatment; *PLA*, placebo; *COM*, compression stockings; *LMWH*, low-molecular-weight heparin; *RIV*, rivaroxaban; *ASP*, aspirin

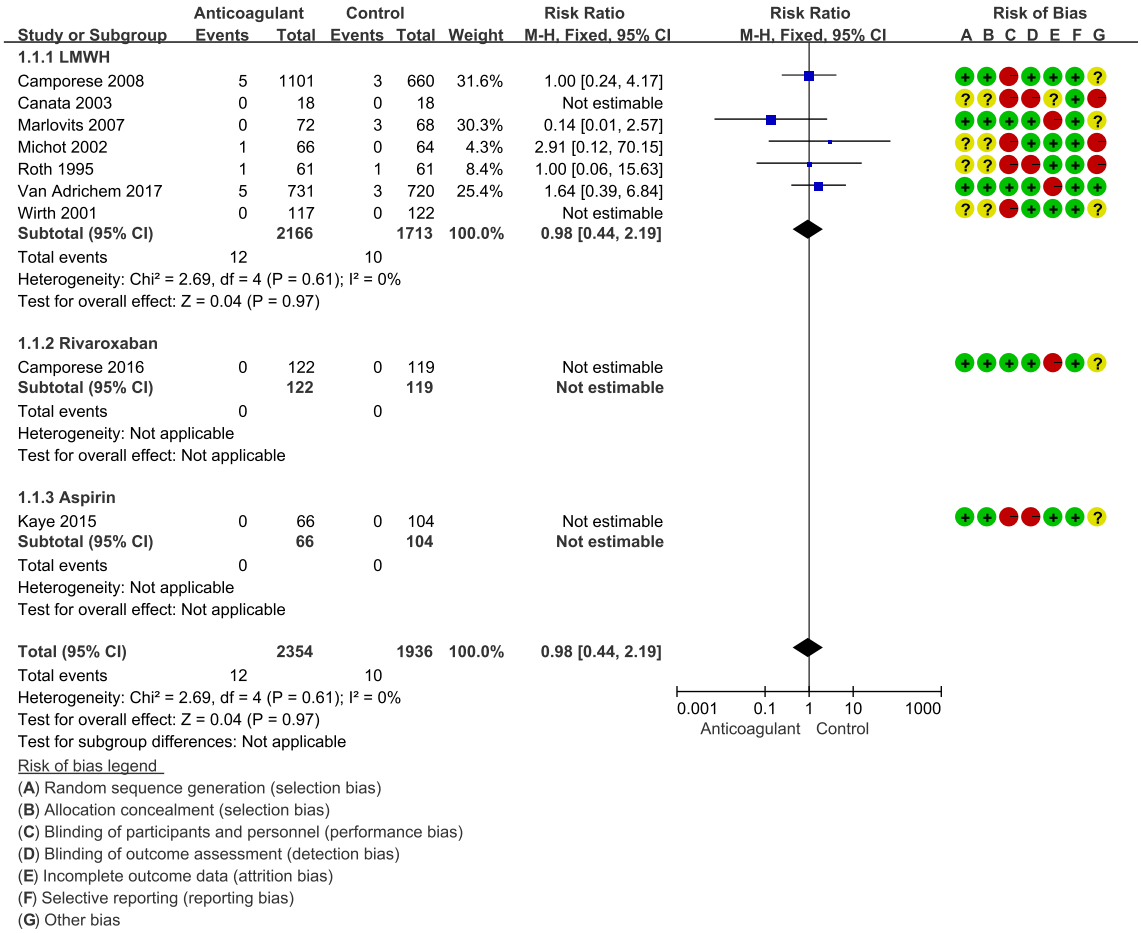

Fig. 2 Anticoagulant versus control. Symptomatic VTE (excluding symptomatic distal DVT) during follow-up. (+) indicates a low risk of bias; (−) indicates a high risk of bias; and (?) indicates an unclear risk of bias

tively low. Aspirin as an antiplatelet therapy was formerly thought to have no preventive effect on VTE, and many surgeons did not use it routinely for thromboprophylaxis after orthopaedic surgery, even for patients who were at substantial risk for VTE. However, aspirin has been used successfully for VTE prevention following orthopaedic surgery with the benefits of decreased cost, good efficacy, decreased bleeding risk, and easy administration when compared to LMWH [26, 27]. Currently, there are few studies on the efficacy of aspirin in reducing the occurrence rate of VTE following knee arthroscopy, and only one RCT [14] was found in our literature search.

The risk of developing symptomatic VTE after knee arthroscopy was relatively low in many previous studies (0.2% to 1.0%) [28, 29]. The 90-day incidence of symptomatic VTE after elective arthroscopic knee surgery was also relatively low, with a 0.17% incidence of symptomatic PE and a 0.25% incidence of symptomatic DVT [30]. However, in recent reports, its incidence is approximately 1.27%, and caution is needed after knee arthroscopy [31]. In the absence of thromboprophylaxis, the incidence of DVT (including symptomatic and asymptomatic) after knee arthroscopy was reported to be as high as 18% [32, 33]. Elective unilateral arthroscopic knee surgery performed without thromboprophylaxis was complicated by ipsilateral calf DVT in 7.8% of patients [34]. PE is a serious complication of knee arthroscopy, and there is limited information. The results of a large sample showed that there were 2.8 cases in every 10,000 knee arthroscopies [35]. Obviously, the risk of thrombosis after knee arthroscopy fluctuates greatly, and without prophylaxis, knee arthroscopy carries a low-to-moderate risk of VTE. After knee arthroscopy, patients would be best managed with the individual model of VTE risk assessment rather than the group model that is applied to knee and hip arthroplasty patients. The literature regarding the actual implementation of pharmacologic prophylaxis following arthroscopic knee surgery suggests that no consensus exists [36–40]. Our research showed that the incidence of symptomatic VTE could not be reduced by using anticoagulation therapy after arthroscopic knee surgery. There is no need for routine thrombosis prevention after arthroscopic knee surgery.

Strengths and limitations

This research has several strengths. On the one hand, it is the first systematic review of RCTs that explores the effects of anticoagulant use during arthroscopic knee surgery. We searched for as

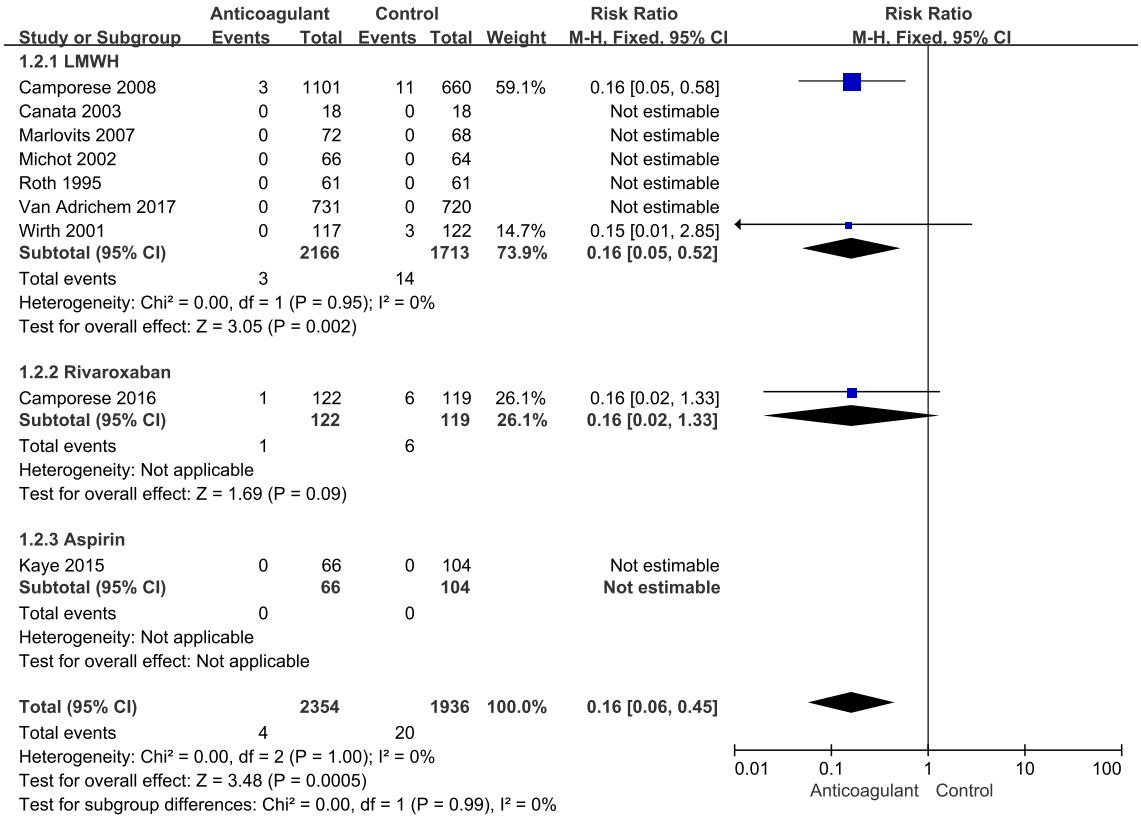

Fig. 3 Anticoagulant versus control. Symptomatic distal DVT during follow-up

many relevant RCTs in three major databases as possible. There were also several limitations of this study that cannot be ignored. That is, there were few RCTs examining anticoagulation prevention of venous thrombosis after knee arthroscopy, and there were not many types of anticoagulant drugs used in the RCTs. Further studies are needed to determine the effects of confounding factors, including the duration of medication, dosage of the drug, and type of surgery.

Conclusion

We conducted a systematic review and meta-analysis and found that the symptomatic VTE rate was not different when comparing anticoagulant and control groups. Therefore, anticoagulation therapy after knee arthroscopy is not effective.

Author contributions Conceived and designed the article: XBT and QX. Literature search and data extraction: HFH, YKS, and XTY. Analyzed the data: HFH and SSL. Wrote the paper: HFH, JLT, and LS. All of the authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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