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Preoperative Comorbidities as Potential Risk Factors for Venous Thromboembolism after Joint Arthroplasty: A Systematic Review and Meta-Analysis of Cohort and Case-Control Studies

Zeng Yi, MD, Shen Bin, MD, PhD, Yang Jing, MD, Zhou Zongke, MD, Kang Pengde, MD, Pei Fuxing, MD

Department of Orthopaedic Surgery, West China Hospital, West China Medical School, Sichuan University, Chengdu, Sichuan Province, China

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ABSTRACT

The purpose of this study was to examine the effect of preoperative comorbidities on the risk of VTE after joint arthroplasty surgery. Of 2235 citations identified for screening, 16 studies reporting 7,395,847 patients were eligible. The results showed that patients with cardiovascular disease, previous VTE history, neurologic disease and high anesthetic ASA rating had significantly higher VTE risk than those with no such preexisting medical comorbidities after joint arthroplasty. The presence of respiratory disease, urinary and kidney disease, coronary artery disease, endocrine disease, cancer and malignant disease, hematological disease and comorbidities index did not increase the risk of VTE in our study. The data suggest that risk assessment of patients may further reduce the overall incidence of DVT and PE from VTE prophylaxis.

Venous thromboembolism (VTE) is a very serious adverse event after joint arthroplasty surgery (JAS) occasionally resulting in death or long or short-term morbidity [1–3]. In patients without prophylactic therapy, the incidence of postoperative VTE varies from 0.9% to 57% after hip arthroplasty and from 1.5% to 85% after knee arthroplasty, which is particularly high compared with other orthopedic surgery [4]. Although prophylactic anticoagulant therapy against VTE has been routinely used in recent decades, previously reported incidences of VTE have not yet declined noticeably, which are approximately 1.4% to 6% after hip arthroplasty and 16% to 27% after knee arthroplasty [5,6].

Several risk factors exist for VTE, such as advanced age, female gender, high BMI, bilateral surgery, smoking and prolonged immobility [7–10]. However, information regarding comorbidities as risk factors for VTE after JAS is lacking. With the population aging around the world, patients undergoing JAS have a high comorbidity load, which is associated with a higher postoperative complication rate [7,11,12]. According to the literature, some authors reported that preoperative comorbidities increased the risk of postoperative VTE after JAS [8,9,13]. However, the samples of those studies were small and lacked high-level clinical evidence. To our knowledge, no systematic review or meta-analysis has been published on this matter.

In order to examine the effect of preoperative comorbidities on the risk of VTE after JAS, we therefore carried out this systematic review and meta-analysis of cohort and case-control studies. The comorbidities were classified into 11 categories: cardiovascular disease, respiratory disease, urinary and kidney disease, coronary artery disease, endocrine disease, cancer and malignant disease, previous VTE history, neurologic disease, hematological disease, anesthetic ASA rating and Charlson comorbidity index/score. For each comorbidity, odd ratios (OR) or relative ratios (RR) were extracted from included studies and pooled together to determine whether those preoperative comorbidities increase the risk of postoperative VTE after JAS.

Materials and Methods

Searching

We searched electronic databases including PubMed (1966 to Mar 2013), CENTRAL (Cochrane Controlled Trials Register; issue 2, 2008), Web of Science (1994 to Mar 2013), Embase (1984 to Mar 2013), and Chinese CNKI database (1979 to Mar 2013). The search strategy employed used a combination of Medical Subject Headings and keywords, along with their corresponding Chinese translations for the CNKI database. Details of the search strategy may be found in the appendix. We identified all relevant studies and searched reference lists of review articles to identify other potentially eligible studies. There was no limitation on language or publication status. For consideration of VTE routine prophylaxis after JAS in recent decades, we only included studies published after 2000.

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Reprint requests: Bin Shen, MD, PhD, Department of Orthopaedics, West China Hospital, Sichuan University, 37# Guoxue Road, Chengdu 610041, People's Republic of China.

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Selection Criteria

Studies were included if they were cohort studies or case-control studies investigating the incidence and predictors of VTE after JAS. After exclusion of duplicates, two reviewers (ZY, HY) performed an initial title and abstract screening of articles to discard those which were clearly ineligible. Then two reviewers (SB, YJ) independently examined the full article to assess the studies for eligibility for inclusion, with disagreement resolved by discussion.

Validity Assessment

Two reviewers (ZZK, KPD) rated the quality of the eligible studies independently. Study quality was judged by using the Newcastle-Ottawa quality assessment scale. We assessed included studies based on three aspects: the selection of the study groups (0–4 points), the comparability of the groups (0–2 points), and the ascertainment of either the exposure or outcome of interest (0–3 points). The maximum total score was 9.

Data Extraction

After studies included, we extracted details from each article as follows: (1) sample size, patient's age and gender, type of surgery, follow-up duration, location of study, article design. (2) The strategy of postoperative VTE prophylaxis, the method of VTE diagnosis and VTE incidence rate. (3) We categorized patients according to the presence of given conditions at the time of surgery. Comorbidities from each category were pooled together separately for assessment and OR or RR values were pooled separately for statistical purposes. If necessary, we attempted to contact the author of the original report to obtain further details.

Quantitative Data Synthesis

All outcomes in this study were dichotomous variables. The ORs and RRs indicating the risk of VTE for each comorbidity were extracted along with their 95% confidence intervals (CI). Chi-square test was used to assess the heterogeneity of included studies. We adopted a *P*-value of ≤ 0.1 or an $I^2 > 50\%$ as evidence of heterogeneity. Depending on the heterogeneity, meta-analysis was performed using fixed effect or random effect models. When there was no statistical evidence of heterogeneity, a fixed effect model was adopted; otherwise, a random effect model was chosen. The statistical analysis was performed by STATA 11.0 software with the updated commands METAN and METABIAS. A two-sided *P* value less than 0.05 was regarded as significant for all analyses.

Results

Flow of Included Studies

Fig. 1 shows details of study identification, inclusion and exclusion. The primary search strategy initially yielded 2235 articles. After scanning the titles and abstracts, reading the full text and tracing relevant references, we included 16 articles with 7,395,847 patients in this meta-analysis [14–20,8,21–28]. Among these 16 articles, 4 articles were case-control studies [14,15,17,20], and 12 articles were cohort studies; one of these was a prospective study [20], while 15 articles were retrospective studies. All the 16 articles were published after 2000, including 8 articles published after 2010.

Study Characteristics and Quality

Table 1 summarized the characteristics of the included studies. The studies were undertaken in USA, Canada, Thailand, Australia, Denmark, Switzerland, Korea and Taiwan in the past 12 years. 2 articles assessed VTE risk factors after total ankle arthroplasty (TAA) and shoulder arthroplasty [18,24], 14 articles assessed either total hip arthroplasty (THA), total knee arthroplasty (TKA) or both. Follow-up time ranged from 7 days to 1 year.

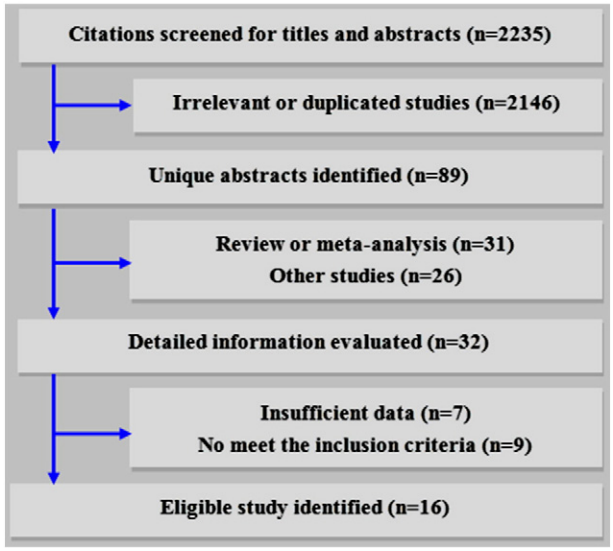

Fig. 1. Flow of study identification, inclusion, and exclusion.

Table 2 summarized the VTE perioperative prophylaxis strategy, the method for VTE diagnosis and VTE incidence rate in each article. Low molecular weight heparin (LMWH) was used routinely for VTE prophylaxis in 9 articles [14–17,20,22,24,25,28], warfarin was used in 3 articles [14,15,23], heparin was used in 3 articles [14,15,23] and aspirin was used in 2 articles [14,28]. No patients received thromboprophylactic agents in 1 article [21] and thromboprophylactic strategy was unclear in 5 articles [18,19,8,26,27]. Doppler venous ultrasound, ventilation-perfusion scan, angiography and helical CT scan were mostly used for VTE diagnosis from the included studies. According to Newcastle-Ottawa quality assessment scale, 2 studies [19,26] scored 7 points and the rest scored 8 points, which meant the included studies had high quality (Table 3).

Meta-Analysis Result of Comorbidities on the Risk of VTE

The results of meta-analysis are showed in Table 4. Figs. 2 and 3 showed the pooled OR and RR meta-analysis results, respectively.

Cardiovascular Disease

A total of 6 studies [16,17,19,22,23,25] provided data on VTE incidence rate after JAS for patients with cardiovascular disease versus no cardiovascular disease. 112,643 patients were included and 17,125 patients had cardiovascular disease preoperatively. Among them, 4026 patients had hypertension, 677 had valve disease, 439 had arrhythmia, 157 had chronic heart failure, 19 had myocardial infarction, and 11,807 had underlying heart disease. 3 studies reported OR values [17,19,23] and the others reported RR values. We performed meta-analysis for OR value, and there was significant heterogeneity among 3 studies ($P = 0.075$, $I^2 = 47.7\%$). Random-effects meta-analysis showed that patients with cardiovascular disease had significantly higher VTE risk than those with no cardiovascular disease after JAS (pooled OR = 1.44, 95%CI 1.09–1.89). For the RR value, there was no evidence of statistical heterogeneity between 3 studies and fixed-effects model was used ($P = 0.893$, $I^2 = 0.00\%$). The meta-analysis showed cardiovascular disease increased the risk of VTE after JAS by 1.37 times (pooled RR = 1.37, 95%CI 1.17–1.60), which had statistical significance.