Arthroplasty Today 4 (2018) 340–342

Contents lists available at ScienceDirect

Arthroplasty Today

journal homepage: http://www.arthroplastytoday.org/

Original research

A dedicated anticoagulation clinic does not improve postoperative management of warfarin after total joint arthroplasty

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ARTICLE INFO

Article history:
Received 22 March 2018
Received in revised form
26 April 2018
Accepted 27 April 2018
Available online 12 June 2018

Keywords:
Total joint arthroplasty (TJA)
Periprosthetic joint infection (PJI)
International normalized ratio (INR)
Warfarin
Venous thromboembolism (VTE)
Pulmonary emboli (PE)

ABSTRACT

Background: Periprosthetic joint infections (PJIs) are devastating complications. Excessive anticoagulation with warfarin is an independent risk factor for PJIs. The use of a dedicated anticoagulation clinic to improve warfarin management has not been proven.
Methods: Between 2006 and 2014, we identified 92 patients who were placed on postoperative warfarin, and later developed PJI. These patients were compared to 313 patients who underwent total joint arthroplasty placed on warfarin without developing PJI. Patients were included if they had no history of a venous thromboembolic event, were warfarin naive, and enrolled in the anticoagulation clinic. A univariate analysis compared independent variables, and statistical analysis was performed using Student's t-test and Pearson chi-square test for continuous and categorical variables.
Results: Thirty-six PJI patients and 297 control patients met the inclusion criteria. The venous thromboembolism rate was 2.1%. At discharge, 82% of all patients were subtherapeutic. Patients were within their target international normalized ratio (INR) range 26.7% of the time. The mean INR in the initial postoperative period for the PJI group was 1.46 and 1.29 in the control group ($P < .001$). In the acute postoperative period, 13.3% of the knee PJI group were therapeutic or supratherapeutic compared with 3.5% in the knee control group ($P = .002$).
Conclusions: Despite utilization of a dedicated anticoagulation clinic, patients were only within their target INR range 27% of the time. Total knee arthroplasty patients who developed a PJI were more likely to be therapeutic or supratherapeutic in the initial postoperative period. Consequently, the risks associated with warfarin as a venous thromboembolism prophylaxis may outweigh the potential benefits.

Introduction

There are numerous venous thromboembolism (VTE) prophylaxis protocols currently in use after total joint arthroplasty (TJA) [1-4]. The purpose of these protocols is to reduce the risk of VTE, and consequently, fatal pulmonary emboli (PE) [5]. To date, no specific prophylactic agent or protocol has shown superiority in decreasing the overall incidence of fatal PE. This finding remains clinically important as recent evidence has shown excessive anticoagulation can increase the potential for wound complications including seromas and wound drainage after TJA, both of which are known risk factors for the development of a subsequent periprosthetic joint infection (PJI) [6-11].

This evidence, along with recent changes to the American College of Chest Physicians Guidelines ninth edition, has led to a dramatic shift in the preferred VTE prophylaxis protocols [12]. Warfarin, previously the favored VTE prophylactic agent following surgical procedures, is now less frequently used than aspirin, the more preferred VTE prophylactic agent in contemporary surgical practice [4].

One of the major problems associated with warfarin use is the challenge of monitoring and managing patients' international normalized ratios (INRs). Previous studies have shown that INR

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to https://doi.org/10.1016/j.artd.2018.04.004.

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https://doi.org/10.1016/j.artd.2018.04.004

levels after TJA frequently are not within the predetermined target range [13,14]. Studies have also shown that patients with an INR above the target range are more prone to developing a PJI [7].

At our institution, we implemented a dedicated anticoagulation clinic to help monitor and manage all patients on warfarin after TJA. Patients received warfarin education and were closely monitored throughout their entire prophylactic period to ensure that they were maintained within a targeted INR range. We hypothesized that by employing a dedicated anticoagulation clinic, we would be able to maintain our TJA patients within their target INR range. This would thereby prevent complications associated with excessive anticoagulation [7,10]. Hence, this study aimed to evaluate if a dedicated anticoagulation clinic could optimize warfarin management and maintain a targeted INR and reduce the risk of both subtherapeutic and supratherapeutic anticoagulation.

Material and methods

After institutional review board approval was obtained, a retrospective case-control study was performed at our institution from 2006 to 2014. Ninety-two TJA patients (53 TKAs, 39 THAs) who developed PJI were compared to 313 aseptic control TJA patients (161 TKAs, 152 THAs). The diagnosis of a PJI was made based on the Musculoskeletal Infection Society criteria with the patient having at least one positive major criteria or 3 of 5 minor criteria [15]. Patients were included if they had no history of a VTE, were warfarin naive, had their index procedure at our institution, were enrolled in the anticoagulation clinic, had a minimum of 2-year follow-up, and had their INR monitored by our anticoagulation clinic throughout their entire prophylactic period. Individual chart review of each medical record was performed to obtain relevant information to ensure each patient met the inclusion criteria. The PJI group was compared to a control group of patients that underwent the same procedure in the same time frame but did not develop a PJI after the index procedure.

Before surgery and enrollment in the anticoagulation clinic, all patients had a comprehensive evaluation and education by the anticoagulation clinic. The target INR for all patients was 2 to 2.5. Warfarin was started the night of surgery and continued for 2 weeks for patient who underwent total knee arthroplasty (TKA) and for 4 weeks for total hip arthroplasty (THA) patients. The INR was monitored daily while in the hospital and 2 to 3 times a week after discharge based on the discretion of the anticoagulation clinic. The acute postoperative period was defined as within 3 days of the procedure. Patients were classified as either subtherapeutic (INR < 2.0), therapeutic (INR, 2-2.5), or supratherapeutic (INR > 2.5) at each time point.

Statistical analysis

Univariate analysis was performed to compare 10 independent variables including age, sex, body mass index (BMI), hip or knee arthroplasty, diabetes, smoking status, end-stage renal disease, Charlson comorbidity score, and American Society of Anesthesiologists score to ensure that the 2 groups were similar. Statistical analysis was then performed using a Student's t-test and Pearson chi-square test for continuous and categorical variables, respectively. A *P*-value of less than .05 was considered statistically significant. Statistical analysis was performed with the statistical software packages SAS studio version 9.3 (SAS Institute, Cary, NC) and R version 3.1.2 [16]. A power analysis was performed to compare the 2 means of each group using a 2-sided equality test. It was determined that a minimum of 25 patients were needed to determine a significant INR difference of 0.2 between the 2 groups with an alpha error of 0.05. [17].

Table 1
Univariate analysis: PJI group compared with control group.

Variable	PJI group (N = 36)	Control group (N = 297)	*P*-value
Age (y)	68.6	67.8	.921
BMI (kg/m^2)	30.9	30.1	.3708
Male sex	52.7%	50.5%	.7667
Hip joint	33.3%	48.4%	.1584
Knee joint	66.7%	51.6%	.1584
Diabetes	12.1%	8.8%	.2671
Smoker	5.7%	3.3%	.3298
ESRD	4.7%	3.3%	.2544
ASA score	3.2	2.1	.0729
Charlson comorbidity score	2.4	2.0	.059

ASA, American Society of Anesthesiologists; ESRD, end-stage renal disease.

Results

After an extensive review of the medical charts, 297 control patients (153 TKA, 144 THA) and 36 PJI patients (24 TKA, 12 THA) met criteria for inclusion into the study. There were 7 clinically symptomatic VTEs, with an overall VTE rate of 2.1%; 3 in the TKA patients (zero were PJI and 3 were controls) and 4 in the THA patients (zero were PJI and 4 were controls), with no PEs in either group. The mean length of stay for all patients was 3 days (range, 1-11 days).

At the time of surgery, the mean age of the PJI group was 67.8 years, with 52.7% being male, and a mean BMI of 30.9 kg/m^2. The mean age of the control group was 67.8 years, with 50.5% being male, and a mean BMI of 30.1 kg/m^2. Univariate analysis showed no significant difference between the 2 groups with regards to the 10 independent variables reviewed (Table 1).

At the time of discharge, 86.1% of the PJI group and 86.2% of the control group remained subtherapeutic. After discharge, the PJI group was within their target INR range 21.5% of the time during the defined postoperative period, compared to 26.8% of the time in the control group. The mean INR in the acute postoperative period in the PJI group was 1.46 (standard deviation, 0.45) compared with 1.29 (standard deviation, 0.33) in the control group, which was significantly higher ($P < .001$). In the PJI group, 11.1% of patients were either therapeutic or supratherapeutic at the time of discharge compared with 2.9% in the control group ($P = .0021$). When differentiating between joints, TKA patients with PJI were therapeutic or supratherapeutic 13.3% of the time at discharge, compared with 3.5% in the control group, which was determined to be significant ($P = .0023$). However, in THA patients with PJI, only 4.2% were therapeutic or supratherapeutic compared with 2.4% in the control group, which was not significant ($P = .1592$).

Discussion

TJA is among the most successful surgical procedures in alleviating patient pain and improving function, yet is not without inherent risks [18,19]. Two of the most serious complications associated with TJA are thromboembolic events leading to potentially fatal PEs and PJIs [3,20]. Notably, PJIs have become a leading cause of failure in total knee arthroplasty [21]. Effective VTE prophylaxis is a difficult balance between avoiding complications of hypercoagulability and the known complications associated with excessive VTE prophylaxis [9].

Although no single VTE prophylactic agent has demonstrated superiority in preventing fatal PEs, it has been shown that more potent anticoagulants are associated with increased bleeding, wound complications, and all-cause mortality [5,10]. This knowledge has led to an increasing acceptance and usage of aspirin for VTE prophylaxis [1,4]. Warfarin is recognized as one of the potentially

more potent anticoagulants that has been associated with increased complications, but this may be due to the difficulty in managing and maintaining patients within their target INR range [2,22].

Since 2006, our institution has routinely used warfarin as the preferred VTE prophylactic agent after TJA. However, we have employed a dedicated anticoagulation clinic to aid in the challenges associated with monitoring and managing patients while on warfarin. Before this study, we assumed preoperative patient education and careful postoperative monitoring by a dedicated anticoagulation clinic would better maintain a patient's INR within the target range. With such monitoring, we could thereby optimize VTE prevention while minimizing the complications associated with excessive VTE prophylaxis.

The results of this study, however, contradicted our study hypothesis. Despite utilizing a dedicated anticoagulation clinic, the overwhelming majority of patients were outside their target INR range during their postoperative prophylactic period, being within range only 24% of the time. These data are consistent with other series that did not utilize an anticoagulation clinic [14]. In addition, we found that in the acute postoperative period, during which time patients are most prone to developing a VTE, over 86% of the patients were subtherapeutic. Our VTE rate of 2.1% was similar to the VTE rate in TJA populations treated without any VTE prophylaxis [23]. This suggests that while warfarin was used starting the evening of surgery, its efficacy in preventing VTE events remains questionable. However, we also know that hypercoagulable states shortly after TJA can predispose patients to a PJI, and we found that TKA patients who developed a PJI were more likely to be either therapeutic or supratherapeutic in the early postoperative period ($P = .0023$) [7].

This study is not without limitations. As a retrospective study, we cannot prove causality but rather only show associations between potential risk factors and complications. Although we evaluated several independent variables and performed a univariate analysis to ensure the 2 groups were similar, there are several other potential causes of infections that may not have been evaluated due to the retrospective nature of this study. Also, we only had 36 PJI patients to compare to 297 control patients. This was in part due to our strict inclusion criteria. As we only evaluated primary TJA patients who went onto develop a PJI, the majority of the PJI patients were excluded because they had their index procedure performed at an outside institution. As such they did not utilize our anticoagulation clinic at the time of their primary procedure. Despite these limitations, we feel that this study is able to highlight several important points.

First, despite our previous assumptions, we demonstrated that the utilization of a dedicated anticoagulation clinic does not adequately maintain patients' INR range within the target. Second, the vast majority of patients on warfarin in the acute postoperative period did not have adequate VTE prophylaxis based on our predetermined INR target, potentially predisposing them to an increased risk of VTE. Third, when total knee arthroplasty patients are either therapeutic or supratherapeutic in the acute postoperative period, they are more likely to develop a PJI.

Conclusions

Today's arthroplasty surgeon needs to weigh the risk-to-benefit ratio of VTE prophylaxis, recognizing the difficulties associated with monitoring and managing patients on certain medication such as warfarin. This study emphasizes that managing postoperative warfarin dosing and maintaining patients within a targeted INR range remains an ongoing clinical challenge. Despite utilization of a dedicated anticoagulation clinic at our institution, patients were only within their target INR range 27% of the time during the 2- to 4-week postoperative period. Total knee arthroplasty patients who developed a PJI were also more likely to be therapeutic or supratherapeutic in the initial postoperative period. Consequently, the risks associated with warfarin as a VTE prophylaxis may outweigh the potential benefits, especially with contemporary surgical techniques, mechanical VTE prophylaxis, early mobilization, and alternate chemoprophylaxis [24,25].

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