1.19. PREVENTION: POSTOPERATIVE FACTORS

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QUESTION 1: Is early mobilization after orthopaedic procedures associated with an increased risk of wound drainage or surgical site infection/periprosthetic joint infection (SSI/PJI)?

RECOMMENDATION: Current literature reports no increased risk of wound drainage or SSI/PJI with early mobilization following orthopaedic procedures.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 94%, Disagree: 4%, Abstain: 2% (Super Majority, Strong Consensus)

RATIONALE

Persistent wound drainage after total joint arthroplasty (TJA) is defined as continued drainage from the surgical incision for greater than 72 hours, as this standard allows for earlier intervention and may thus limit adverse consequences [1]. Persistent drainage is an important sign that a surgical wound may become problematic [2,3].

Postoperative incisional drainage occurs in 1% to 10% of patients undergoing primary TJA [4–6]. While drainage requires close monitoring, the majority of cases resolve spontaneously without a need for surgical debridement [7]. Patients with a draining wound on postoperative days two to three should remain in the hospital for close clinical monitoring and they may initially be treated with compressive dry dressings because this typically involves superficial layers [2]. However, as persistent drainage for over 72 hours may represent more serious issues such as fat ischemia or a capsular defect, surgical intervention may be necessary to avoid infectious complications [2].

Physiotherapy, specifically knee range of motion, should be temporarily limited for 24 to 48 hours. Continuous passive motion should be avoided, or at least limited, as flexion past 40 degrees is known to reduce transcutaneous oxygen saturation about the incision following total knee arthroplasty (TKA) [8]. These limited range of motion parameters have shown no increased incidence of infection when compared to patients treated with complete immobilization [8].

Anticoagulation status should also be reviewed, and it is important to consider short-term cessation of anticoagulation. Hemostasis in the setting of orthopaedic procedures prevents hematoma formation and persistent drainage [2]. Patients treated with low-molecular weight heparin (LMWH) for prophylaxis against deep venous thrombosis have shown longer times to achieve a dry surgical wound, compared to those treated with aspirin and mechanical compression or Coumadin [7]. In light of this, it is prudent to temporarily stop anticoagulation with LMWH, or other chemical anticoagulation, but continue mechanical venous thromboembolism prophylaxis.

Based on the review of literature related to persistent wound drainage, we have found no evidence that links early mobilization of the patient with an increased risk of wound drainage and/or infection. Considering the fact that early ambulation of the patients in extremely useful to prevent complications such as venous thromboembolism and improve patient outcome, we still feel that early ambulation stands to benefit the patient while having minimal to no adverse effects.

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QUESTION 2: Is it necessary for a patient to postpone having an invasive dental procedure after total joint arthroplasty (TJA)?

RECOMMENDATION: In the absence of evidence, we recommend that non-urgent invasive dental procedures, if possible, be delayed until osseointegration of uncemented components are complete.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 82%, Disagree: 10%, Abstain: 8% (Super Majority, Strong Consensus)

RATIONALE

Hematogenous periprosthetic joint infection (PJI) occurs when bacteria are seeded to the prosthesis via the bloodstream from a distant anatomic source. It has been estimated that hematogenously-seeded infection may cause almost one third of all PJI cases [1]. In patients with joint prostheses in place, dental procedures have historically been considered a concern for producing a transient bacteremia that could potentially cause a hematogenously-seeded PJI [2,3]. Contributing to this concern are case reports in the literature that have attempted to link PJI temporally to dental procedures [4–12]. Such infections generally involve anaerobic organisms that could be expected to be part of the normal dental flora.

Given these concerns for possible hematogenous PJI from an oral source, questions have arisen regarding the value of antibiotic prophylaxis in joint arthroplasty patients undergoing dental procedures [13]. Both the American Academy of Orthopaedic Surgeons (AAOS) and the American Dental Association (ADA) have published guidelines with regard to such prophylaxis. The most recent of these, co-developed by the AAOS and the ADA, were issued in 2012 [14,15]. However, this latest guideline makes no definitive statement for or against antibiotic prophylaxis in arthroplasty patients prior to dental procedures. Overall recommendations indicate that there is limited evidence to support the practice of routine antibiotic prophylaxis for all dental patients with prosthetic implants and inconclusive evidence for or against the use of topical oral antimicrobials in these cases. There is a strong recommendation (unanimous consensus) for continued adequate oral hygiene in total joint replacement patients. More recently in 2016, the AAOS and ADA co-issued Appropriate Use Criteria for this topic [16]. The recommended actions seem to advocate an individualized approach for patients based upon the planned dental procedure, the immunocompromised status of the patient and the glycemic control of the patient, if the patient is diabetic. It can be argued that much of the conclusions of this latest report amount to nothing more than expert opinion/consensus.

A systematic review of the literature in this area yielded 90 individual studies, of which 9 [10,11,17–23] were felt to be adequate for inclusion. Six studies corresponded to a grade IV level of evidence, two studies to level III, and one study to level I. Methodological quality measurements showed an overall low quality of the included studies scoring a median of 6 (range 4 to 7) for case series studies [10,11,17–20]. The methodological quality of Berbari et al. [21], Skaar et al. [22] and Kao et al. [23] showed great heterogeneity in terms of study design and outcome assessment and mostly low methodological quality. Three of the studies were prospective in nature and the remaining were retrospective, six of them being case-series, two case-controlled and only one retrospective cohort study. All were conducted between 1980 and 2016, 7 were conducted among patients treated at a single institution, and 2 included data collected from research databases (Taiwan National Registry [23] and Medicare Registry [22]). None of the studies have suggested and/or been indicated to postpone having an invasive dental procedure after a TJA.

Accordingly, there is still limited evidence to stand for or against the use of antibiotic prophylaxis prior to a dental procedure in joint arthroplasty patients. Although some retrospective articles have associated extensive dental procedures with PJI [10,11] a prospective case-control study found that neither low-risk nor high-risk dental procedures were associated with PJI [21]. In that study, Berbari et.al., studied dental prophylaxis prospectively in 339 PJI patients with 339 control patients. They found that antibiotic prophylaxis prior to a surgical procedure conferred no benefit in terms of reducing the incidence of PJI. However, the authors admit that the numbers studied might not have been enough to detect a minor increase in PJI following dental procedures [21].

The issue of whether undergoing a dental procedure soon after TJA increases the risk of implant seeding and potential PJI has not been studied. To design a study that would examine this issue would be challenging. We speculate that the seeding of an implant is more likely to occur if the impant has not osseointegrated. Thus, in patients undergoing uncemented TJA, delaying the invasive non-urgent dental procedures may minimize the risk of seeding without exposing the patient to any risk.

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QUESTION 3: What is the role of prophylactic antibiotics for invasive procedures (dental, gastrointestinal (GI), urologic, etc.) in the presence of an arthroplasty to prevent subsequent periprosthetic joint infection (PJI)?

RECOMMENDATION: There is no role for routine prophylactic antibiotic administration prior to dental or genitourinary (GU) procedures. There is limited evidence that has shown certain GI procedures may be associated with a risk of subsequent PJI.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 64%, Disagree: 28%, Abstain: 8% (Super Majority, Weak Consensus)

RATIONALE

Dental Procedures

Transient bacteremia has been shown to occur following dental procedures [1,2]. There is a theoretical risk of hematogenous seeding of the prosthetic joint following transient bacteremia, however this is not necessarily borne out in the literature [3,4]. Further, there are two studies that show no difference in the rate of PJI between those patients who received antibiotic prophylaxis and those that did not. In a prospective case-control study of 339 patients, Berbari et al. showed that there was no statistically significant reduction in the rates of PJI in patients who received antibiotics prophylaxis [5]. In a large retrospective cohort study, Kao et al. identified 57,066 patients who had undergone dental treatment following total joint arthroplasty (TJA) and matched this cohort to patients who had undergone TJA and had not undergone dental procedures. The authors found no significant difference in the rate of PJI between the two group and, further, there was no difference in the rate of PJI for those who received antibiotics prophylaxis and those who did not [6]. With this evidence in mind, there is currently no evidence for routine antibiotic use for prophylaxis against PJI in patients undergoing dental procedures.

Genitourinary Procedures

GU procedures (including but not limited to) transurethral resection of the prostate (TURP), cystoscopy, urethral dilation, ureteral stenting and transrectal prostatic biopsy, have been shown to be associated with transient bacteremia [7–13] and there is a theoretical risk of seeding of the prosthetic joint via hematogenous spread. The literature regarding the subsequent development of PJI following GU procedures is limited. A number of case reports have documented PJI following TURP [14][15]. In a prospective, case-controlled study, Gupta et al. showed that there was no increased risk of PJI for patients undergoing GU procedures. They also noted that prophylactic antibiotics did not lower the rate of PJI, although it should be noted that a low percentage of patients in both the case and control groups received prophylactic antibiotics (1% and 2%, respectively) [16].

Gastrointestinal Procedures

GI procedures such as gastrointestinal endoscopy, colonoscopy and signmoidoscopy have been shown to produce transient bacteremia [17–19], most commonly in patients who are in an immunocompromised state [20,21]. There are several small-scale studies and case reports that have shown an association with PJI in patients following invasive gastrointestinal procedures [22–25]. Currently, there is only one single-center, case-control study which showed that esophago-gastro-dueodenoscopy with biopsy increased the risk of developing PJI (odds ratio (OR): 4, 95% confidence interval (CI) 1.5 to 10) [26]. While prophylactic antibiotics may be warranted in this situation and in high-risk patients, further investigation is needed to determine whether prophylactic antibiotics are necessary in all patients undergoing invasive gastrointestinal procedures, and whether their usage will successfully decrease the risk of PJI.

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QUESTION 4: Does the type of venous thromboembolic (VTE) prophylaxis influence the risk of surgical site infection/periprosthetic joint infection (SSI/PJI) in patients undergoing orthopaedic procedures?

RECOMMENDATION: Yes. In a majority of studies evaluating VTE prophylaxis in patients undergoing total joint arthroplasty (TJA), aspirin appears to result in a lower risk of SSI/PJI than anticoagulants (vitamin K antagonists, heparin-based products, factor Xa inhibitors and direct thrombin inhibitors).

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 80%, Disagree: 10%, Abstain: 10% (Super Majority, Strong Consensus)

RATIONALE

The risks versus benefits of VTE prophylactic agents in patients undergoing orthopaedic procedures, particularly TJA, remain controversial. Current Academy College of Chest Physicians (ACCP) guidelines recommend agreement with American Academy of Orthopaedic Surgeons (AAOS) guidelines for VTE prophylaxis and recommend pharmacologic prophylaxis over no prophylaxis, but do not provide support for or against any specific pharmacologic agent [1]. The most recent 2012 ACCP guidelines also recommend pharmacologic prophylaxis in all patients without a high risk of bleeding, but do not specify an agent [2,3]. Current commonly-used pharmacologic agents for prophylaxis following TJA include aspirin, vitamin K antagonists (i.e., warfarin), heparin-based anticoagulants (including low molecular weight heparins (LMWH), i.e., enoxaparin or dalteparin), direct oral anticoagulants (DOACs, i.e., rivaroxaban or apixaban) and direct thrombin inhibitors (DTIs, ie., dabigatran) [4].

Wound drainage, bleeding and hematoma formation have been associated with PJI [5,6]. Therefore, balance of thrombotic risk and bleeding risk becomes paramount in selection of the appropriate postoperative VTE prophylaxis.

A literature review was performed using the PubMed and Cochrane Database of Systematic Reviews. The Medical Subject Headings (MeSH) terms "venous thromboembolism," "prophylaxis," "arthroplasty" and "infection" were searched. Studies were identified to be related to VTE and arthroplasty based on their title and abstract. They were then reviewed and included if a reported outcome measure was PJI or SSI.

Low Molecular Weight Heparin

The 2012 ACCP guidelines suggest the use of LMWH for postoperative VTE prophylaxis due to extensive data supporting its efficacy and safety in medical literature [7]. However, there is conflicting evidence in the orthopaedic literature regarding the rate of complications with its use following TJA. Multiple studies in recent orthopaedic literature suggest that LMWH after TJA may result in increased SSI/PJI and wound complications.

Kulshrestha et al. [8] randomized patients undergoing primary total knee arthroplasty (TKA) to receive routine LMWH prophylaxis or risk stratification with the American Society of Anaesthesiologists (ASA) physical status score for standard risk and selective use of LMWH in high risk patients. They found that patients on LMWH had almost eight times the risk of wound complications compared with patients receiving ASA. Patel et al. [6] found that LMWH, compared with ASA and warfarin, was an independent risk factor for prolonged wound drainage following primary TJA. A prospective cohort study from the Global Orthopaedic Registry (GLORY) showed a significantly higher rate of SSIs in 1,561 patients receiving LMWH prophylaxis dosing (1.6% SSI) compared with 2,194 patients receiving therapeutic warfarin with or without bridging therapy (0.6% SSI) [9]. Burnett et al. [10] studied 290 patients undergoing TJA that received LMWH for 10 days postoperatively (3.4% required return to OR for wound complications). However, multiple other studies, including the RECORD 1-4 randomized control trials (RCTs) found no difference in SSI/PJI rates in patients undergoing TJA receiving either rivaroxaban or enoxaparin [11–14].

Factor Xa Inhibitors

There is conflicting evidence in current literature regarding rates of SSI and PJI in TJA patients receiving factor Xa inhibitors compared to other pharmacologic prophylaxis. Two recent meta-analyses of RCTs found no difference in SSI/PJI rates in TJA patients receiving rivaroxaban versus enoxaparin [11,15]. Multiple other retrospective studies have also found similar rates of PJI and superficial wound infections in patients receiving rivaroxaban and enoxaparin [7,16,17]. Agaba et al. [18] performed a retrospective review of 25,966 patients undergoing total hip arthroplasty (THA) receiving a single medication for VTE prophylaxis from the Humana National Healthcare Database between 2007 and 2016. 2.12% of patients received ASA, 26.15% enoxaparin, 46.25% warfarin, 1.3% apixaban, 3.37 fondaparinux and 20.81% rivaroxaban. They found that rivaroxaban had the lowest risk of PJI [18]. However, multiple studies have also found an increased risk of early SSI requiring reoperation following TJA with use of rivaroxaban compared to enoxaparin [19,20].

Direct Thrombin Inhibitors

Evidence regarding direct thrombin inhibitors is also unclear. Multiple studies have found that the use of dabigatran following TJA leads to prolonged wound drainage and increased risk of SSI/PJI. Gill et al. [21] found a 7% rate of reoperation for wound infection with dabigatran prophylaxis following TJA compared to 1% with a protocol of dalteparin while inpatient and ASA after discharge. Aquilina et al. [22] prospectively studied a cohort of 110 patients undergoing TJA and found mean of 6.6 days of wound drainage with dabigatran versus 3.4 days with ASA. Other studies have also found longer periods of wound drainage in patients receiving dabigatran prophylaxis compared with apixaban, enoxaparin and aspirin [23,24]. Bloch et al. [24] found a 20% wound drainage rate in TJA patients following introduction of use of dabigatran prophylaxis compared to 5% when using a multimodal regimen of LMWH while inpatient and ASA as outpatient. However, the RE-NOVATE (Clinical trial examining: “dabigatran etexilate compared with enoxaparin in prevention of VTE following THA”) and RE-NOVATE 2 RCTs compare dabigatran with enoxaparin for prophylaxis following THA and found no difference in wound infection rates [25].

Warfarin

Many recent studies have shown that SSI/PJI rates in TJA patients receiving warfarin prophylaxis are significantly higher than those receiving ASA prophylaxis. Sachs et al. [26] studied 785 patients treated without any pharmacologic prophylaxis compared with 957 patients treated with warfarin postoperatively and found similar VTE rates, but twice the infection rate in the warfarin group (0.6% vs.0.3%). Huang et al. [27] performed a single institution retrospective cohort study with 25,372 TJA patients receiving warfarin titrated to an international normalized ratio (INR) of 1.8 to 2.0 versus 4,898 TJA patients receiving ASA and found a 90-day postoperative PJI rate of 1.28% in the warfarin group compared to 0.22% in the ASA group. Other studies have also found prolonged wound drainage and significantly elevated PJI rates with warfarin compared with ASA following primary TJA [28–30]. However, Deirmengian et al. [31] found no difference in 90-day SSI rates in revision TJA patients receiving ASA versus warfarin, but found that ASA was more effective for VTE prevention. Comparing warfarin to other pharmacologic anticoagulation, evidence is less clear. As discussed above, Wang et al. [9] studied patients undergoing primary TJA from the Global Orthopaedic Registry and found significantly lower rates of superficial and deep infection in patients receiving warfarin prophylaxis compared with enoxaparin. Cafri et al. [32] found no significant difference in 90-day postoperative SSI rates between groups receiving ASA 325 mg once daily, fondaparinux 2.5 mg daily, LMWH 30 mg twice daily (BID) or 40 mg daily, and warfarin (goal INR 1.5 to 3.0) in a cohort of 30,499 patients from the Kaiser Permanente Total Joint Replacement Registry.

Aspirin

As discussed above, many studies have demonstrated lower SSI/PJI rates with ASA prophylaxis compared with warfarin prophylaxis. Other studies also demonstrate lower rates of infection and wound problems with ASA versus other anticoagulants. Kulshrestha et al. [8] randomized 450 TKA cases to either routine anticoagulation with 40 mg daily enoxaparin and 450 TKA cases to risk stratification and aspirin in low risk patients or enoxaparin in elevated risk patients. In patients receiving enoxaparin, there was nearly eight times the number of wound complications. Garfinkel et al. [33] found significantly higher rates of bleeding and wound complications with rivaroxaban compared with ASA.

Conclusion

The effects of specific anticoagulants on postoperative SSI and PJI remain uncertain. Rates of SSI/PJI with aspirin prophylaxis appear to be lower than rates with anticoagulation. Nevertheless, there is little level I evidence to support differences in risk of SSI/PJI between modes of pharmacologic VTE prophylaxis. Although many RCTs have been performed to evaluate the efficacy of various pharmacologic agents in prevention of VTE and their effects on other major complications such as bleeding and death, few report on the incidence of SSI and PJI in their treatment groups. Additionally, the definitions of SSI and PJI are heterogeneous across studies, making it difficult to compare infection rates. Finally, various dosages of the different pharmacologic agents need to be studied to determine their effect on SSI/PJI rates.

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