The Journal of Arthroplasty 30 (2015) 902–907

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Prevention of Periprosthetic Joint Infection

Maryam Rezapoor, MS, Javad Parvizi, MD, FRCS

The Rothman Institute at Thomas Jefferson University Hospital, Philadelphia, Pennsylvania

ARTICLE INFO

Article history:
Received 4 February 2015
Accepted 9 February 2015

Keywords:
prosthetic joint infection
arthroplasty
prevention
optimization
strategies

ABSTRACT

Periprosthetic joint infection (PJI) has moved into the first place as the cause of failure following total knee arthroplasty (TKA). Recent studies have shown that PJI results in higher mortality in patients than many cancers. The economic burden of treating PJI is likely to exceed $1 billion this year in the US. Thus, it is paramount that all efforts are invested to prevent this dreaded complication after total joint arthroplasty (TJA). This article summarizes some of the most effective and proven strategies for prevention of PJI. It is hoped that the article will be of benefit to the readers of the journal.

A recent editorial in the New England Journal of Medicine compared infection with cancer and drew many parallels between the two [1]. The article, while insightful, highlighted a sobering fact that we, as orthopedic surgeons, are becoming more familiar with as our patients fall victim to this terrible complication following TJA. A recent study by Berend et al demonstrated that 7% of patients die between the first and second stages of exchange arthroplasty performed for treatment of PJI [2]. A study from our institution observed that the five year mortality rate for patients with PJI was higher than for breast cancer, melanoma, Hodgkin's lymphoma, and many other cancers [3]. Over the last decade or so, the orthopedic community has become more involved in the management of PJI as the number of patients presenting with this terrible complication continues to rise [4]. In a recent unofficial survey of orthopedic surgeons, PJI was declared as the most worrisome complication of TJA. The fear of infection is also very real for the patients who undergo this otherwise successful surgical procedure. It is abundantly clear that if we are to reverse the rising burden of PJI and the psychological and economic costs associated with this complication, better strategies for its prevention need to be devised. The Centers for Disease Control (CDC) has recognized the rising problem of infection in general and PJI in particular, leading the organization to revisit the guidelines for Prevention of Surgical Site Infection. The massive effort of the CDC has culminated in an evidence-based recommendation that may soon be made public. The CDC workgroup recognized an obvious lack of evidence for many treatment practices that we have in place and the urgent need for (re) examining some of these strategies. A recent development related to the issue of PJI was the meeting of the International Consensus Meeting Group (ICG) on Periprosthetic Joint Infection. The ICG, being aware of the lack of evidence supporting some of the practices for management of PJI, convened a group of experts whose intention was to standardize practices across the globe in an effort to reduce the burden of PJI [5]. This article will highlight some of the effective strategies that are either proven, through studies; or deemed, through expert opinion, to be effective in reducing the surgical site infections (SSI) and PJI.

Optimization of Host

TJA is an elective surgery with an inherited flexibility that enables one to medically optimize the patients prior to surgery, thus reducing the risk of developing infection.

Active Systemic or Local Infection

The presence of active infection, either local or systemic, predisposes patients to developing PJI after TJA [6,7]. Presence of septicemia, septic arthritis, or presence of active local cutaneous, subcutaneous, or deep tissue infection can lead to the hematogenous or direct seeding of the prosthesis [8,9]. Thus, TJA as an elective surgery should be delayed until all possible sources of infection are eradicated; a six-month minimum interval between an active septic arthritis and elective arthroplasty has been recommended [10].

History of Previous Surgery

A prior open surgical procedure can make the local wound environment susceptible to SSI or PJI following TJA [11]. In a matched study of patients undergoing TKA, Peersman et al compared infected with non-

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 http://dx.doi.org/10.1016/j.arth.2015.02.044.

Reprint requests: Javad Parvizi, MD, FRCS, Rothman Institute of Orthopaedics at Thomas Jefferson University Hospital, 925 Chestnut Street, Philadelphia PA 19107.
E-mail address: research@rothmaninstitute.com (J. Parvizi).

http://dx.doi.org/10.1016/j.arth.2015.02.044
0883-5403/

infected patients and reported that prior surgery in the affected joint was a significant risk factor ($P < 0.0001$) for developing PJI [12]. The ICG recommended that documenting a patient's surgical history and analyzing the local wound environment should be considered for possible modification of the operative approaches and techniques [8,11].

Immunosuppressive Medications

Multiple studies have shown that there is a higher incidence of postoperative infection in patients with rheumatoid arthritis and other inflammatory conditions [13,14]. Although patients with inflammatory arthritis have an inherent immunosuppressive state, the fact that many of these patients also receive corticosteroids and disease-modifying anti-rheumatic drugs (DMARDs), places them at high risk for developing infection following surgical procedures, in particular TJA [15–17]. Continuing to use the disease-modifying agents prior to TJA can lead to higher incidence of SSI and PJI [17]. Berbari et al have also developed PJI and SSI risk stratification models that list immunosuppressive medicine as a significant risk factor (hazard ratio 1.96, 95% confidence interval [CI] 1.37–2.82) for PJI [18]. The ICG also recommended that DMARDs should be stopped prior to performing elective TJA. They also presented an individualized cessation schedule for different immunosuppressive agents (see Table 1) [10].

Uncontrolled Diabetes Mellitus

There is ample evidence that links uncontrolled diabetes with subsequent SSI, especially PJI [19,20]. Thus, patients with diabetes or hyperglycemia may benefit from preoperative optimization. Despite the lack of definitive evidence, a fasting glucose level >180 mg/dl or 10 mmol/l and HbA1C >7% are considered potential indicators of uncontrolled diabetes [21,22]. The CDC has also recommended a fasting glucose level of >200 mmol/l as an indicator of uncontrolled diabetes. The ICG recommended that the perioperative glucose level of patients undergoing TJA should be kept below 180 mg/dl (10 mmol/l) and the HbA1C level should be lower than 7% [10].

Chronic Diseases

Chronic conditions such as liver disease, chronic renal failure, chronic anemia, and others are known to increase the risk of infection in a patient undergoing TJA [23,24]. The exact reason for the increased risk for infection and other complications in patients with chronic conditions is not known but may be multifactorial. The higher incidence of malnutrition and low number of platelets or non-functioning platelets may place these patients at higher risk for bleeding and wound-related complications. In addition, these patients are likely to suffer from anemia of chronic disease, that increases their chance of needing allogeneic blood transfusion, with all its adverse effects [25,26]. Patients with other conditions such as the human immunodeficiency virus (HIV) infection are also deemed to be at higher risk of developing SSI, if their underlying conditions are not well treated or controlled [27]. Thus, all efforts should be made to optimize patients with chronic conditions prior to elective arthroplasty in an attempt to reduce the risk of SSI.

Table 1
The Recommendation of the International Consensus Group for Halting Various Anti-Inflammatory Agents Prior to Total Joint Arthroplasty.

Timing	Half Life	Medication
Continue therapy including the surgery day	1–2 month	Hydroxychroquine
Hold at least 1.5 week before	4.3 days	Biological Response Modifiers Etanercept
Hold 3 weeks prior	8–10 days	Infliximab
Hold 1 month prior	12–14 days	Golimumab
		Tocilizumab
		Abatacept
		Adalimumab
		Certolizumab
Hold 6 weeks prior	~2 weeks	Leflunomide
Hold 2 month prior	21 days	Rituximab
Discontinue 1 week prior	2–17 hours	NSAIDs
		Gout agents:
	1–2 hours	Allopurinol
	26–32 hours	Colchicine
	26–32 hours	Probenecid
	5 hours	Sulfasalazine
	7.6 hours	Azathioprine
	0.7–5.8 hours	Methotrexate[a]

Reproduced with permission from Parvizi et al.
[a] Continue therapy 2 weeks after surgery. Patients with renal dysfunction, hold 2 weeks prior to surgery.

Malnutrition

Malnutrition is strongly associated with multiple adverse outcomes following TJA. Resulting complications include prolonged hospitalization [28], delayed wound healing [29], persistent wound drainage, and subsequent susceptibility to infection [30,31]. Different parameters have been reported as measurements of nutritional status such as the level of serum albumin (normal 3.5–5.0 g/dl), serum transferrin (normal 204–360 mg/dl), serum prealbumin (normal 15–35 mg/dl), and total lymphocyte count (800–2000/mm^3) [10]. The threshold for the above tests, which would indicate malnutrition, has not been determined. However, derangement in any of these parameters is thought to potentially result in a protracted postoperative course and a higher complication rate [32]. Gherini et al studied the correlation between nutritional status and postoperative complications. Compared with albumin and total lymphocyte count, only preoperative serum transferrin levels showed significant correlation in predicting delayed wound-healing [29]. On the other hand, Lavernia et al defined an albumin level <34 g/l and total lymphocyte <1200 cells/ml as predictors of postoperative adverse outcomes [28]. Prior to elective arthroplasty, patients thought to be malnourished, especially obese patients, should have their nutritional status checked. Although important, the methods of preoperative treatment of malnutrition have not been determined yet.

Morbid Obesity

Patients with obesity have been shown to be at higher risk for all complications including SSI and PJI [33–35]. The reason for this phenomenon may relate to increased operative time, greater need for allogeneic blood transfusion, and the presence of other comorbidities such as diabetes in the obese [36–38]. Although the optimal threshold for body mass index (BMI) for patients undergoing elective arthroplasty has not been determined, a workgroup convened by the American Association of Hip and Knee Surgeons stated that elective arthroplasty in patients with a BMI >40 kg/m^2 may place these patients at an unacceptable risk for developing complications [39]. An exception may apply to patients with considerable muscle mass in whom the BMI may be paradoxically elevated [10].

Depression

Depression can directly affect the cells of the immune system and can lead to higher susceptibility to infectious disease and poorer recovery from infection [40,41]. Depression induces overproduction of proinflammatory cytokines, including IL-6, which modulates the secretion of corticotropin-releasing hormone (CRH), followed by elevated levels of plasma ACTH and cortisol; elevated levels of ACTH and cortisol inhibit certain aspects of immune responses [40]. Depression may also be associated with other infection risk factors such as malnutrition and subsequent need for allogeneic blood transfusion [42]. Because patients with depression are at a higher risk for developing PJI [43], elective arthroplasty in these patients may be delayed until their underlying affective disorder is better controlled.