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Abstract

Background: Assessing patient's risk of infection is fundamental for prevention of periprosthetic joint infection (PJI) after total ankle arthroplasty (TAA). The Mayo Prosthetic Joint Infection Risk Score (Mayo Score) is based on data from total hip and knee arthroplasty and has not been validated for application for TAA.

Methods: A total of 405 consecutive TAA cases were followed for 6 months for PJI. Individual patients' Mayo Scores were calculated and analyzed with logistic regression and receiver operating characteristic (ROC) for predictability for PJI. A critical cut-off Mayo Score for patients at high risk of PJI was determined by best Youden index. Among the Mayo Score-defined high-risk patients, the contribution of different risk factors were compared between the PJI and non-PJI patients.

Results: There were 10 cases of PJI (2.5%) among the 405 cases within 6 months after TAA. Of the 405 patients, the Mayo Scores ranged between -4 and 13 (median 2; interquartile range 0-5). The average Mayo Score was 2.5 ± 3.4 in the non-PJI patients and 7.7 ± 3.1 in the PJI patients ($P < .001$). Logistic regression showed that the probability of PJI increased with higher Mayo Scores (odds ratio 1.48, 95% CI 1.23-1.78). All but 1 PJI patients had a Mayo Score >5 . The sensitivity and specificity were 90.0% and 84.3%, respectively, when a Mayo Score >5 was used as a criterion for high risk of PJI.

Conclusion: This study demonstrated that the Mayo Score could similarly predict PJI risk after TAA as in total hip and knee arthroplasty. Data analysis suggests that a Mayo Score >5 could be a criterion for identifying high-risk patients for PJI, although further validation with a large number of PJI cases is necessary.

Level of Evidence: Level II, developing diagnostic criteria with consecutive cases.

Keywords: arthroplasty, ankle, infection, risk factor, score

Introduction

Periprosthetic joint infection (PJI) can be a devastating and costly complication of arthroplasty.⁴⁴ Revision surgery for PJI leads to prolonged recovery, impaired joint function, and lower quality of life.⁶ Although there are contradicting projections of the trend of PJI incidence,^{7,9,33} the absolute number of PJI cases is bound to increase as joint replacement surgeries are increasingly performed.⁴² Measures have been introduced to reduce PJI, such as emphasizing antiseptic preparation of the surgical site, ultraclean/laminar air flow in operating room, and protective suits and hoods for surgeons but their effectiveness and cost are often subjects of debates.^{11,28}

Optimizing preoperative patient conditions is essential to prevent and manage PJI.³⁶ PJI is the result of bacterial contamination becoming infection due to lost balance between host resistance and bacteria's infectiousness.²⁶

Host resistance, an unquantifiable concept, can be weakened by PJI risk factors. Many of the PJI risk factors identified in the literature are the same as for surgical site infection, such as male gender, abnormal body mass index

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(BMI), smoking, diabetes mellitus, steroid use, rheumatoid arthritis, immunosuppression, prolonged operative time, and previous joint surgery.^{23,30,43,47} PJI risk factors are useful for assessing patients' conditions but would be even more helpful in clinical decision-making if they are converted into risk scores for quantitatively gauging the risk.¹⁰ A number of PJI risk factor scores/indexes have been developed in recent years.^{10,22,34,41} Most of them were based on literature reviews and retrospective analyses of PJI cases, which inherently had improper controls, missing data, or reduced sample sizes.²² Using the data of a prospective case-matched study, including 301 PJI cases following total hip and knee arthroplasty, Berbari et al⁵ established the following PJI risk factors: BMI, American Society of Anesthesiologists physical status classification score (ASA score), immunosuppression conditions, procedure time, and previous arthroplasty or other surgeries of the index joint. Rather than weighing the risk factors equally, the regression coefficients of the individual risk factors in a multivariate logistic regression model were approximated to points to constitute the Mayo Prosthetic Joint Infection Risk Score (henceforth Mayo Score).

Total ankle arthroplasty (TAA) is a reliable treatment option for end-stage ankle arthritis.⁸ Despite technical advances, the rate of PJI following TAA has been persistent. In a systematic review of 6977 TAA cases, PJI rates ranged from 3.0% to 4.8% from 2005 to 2012.¹ Compared with similar studies in hip and knee arthroplasty, analyses of PJI risk factor for TAA are often limited by the small number of PJI cases given fewer TAA performed overall.^{18,23} At the 2018 International Consensus Meeting on Musculoskeletal Infection, a group of foot and ankle surgeons unanimously agreed on the following PJI risk factors for TAA: inflammatory arthritis, prior ankle surgery, BMI <19, and peripheral vascular disease.³⁷ Otherwise, prospectively established PJI risk factors and scores specific to TAA are not available.

It is well known that medical implants themselves are a risk of surgical site infection.²⁰ The implanted foreign prostheses could induce neutrophil function deficiency and promote the formation of bacterial biofilm on their surfaces.¹⁶ The hypothesis of this study was that because hip, knee, and ankle arthroplasties share many PJI risks, the Mayo Score developed for hip and knee arthroplasty is applicable for stratifying PJI risk levels in TAA. This study calculated the Mayo Scores of a series of TAA cases for predictability of PJI risk, and a cut-off value for high-risk patients of PJI. Among the high-risk patients, the contributing risk factors were comparatively analyzed between PJI and non-PJI cases.

Materials and Methods

This study included consecutive TAA cases performed by one surgeon from October 2012 to January 2022, using the semiconstrained Trabecular Metal Total Ankle System

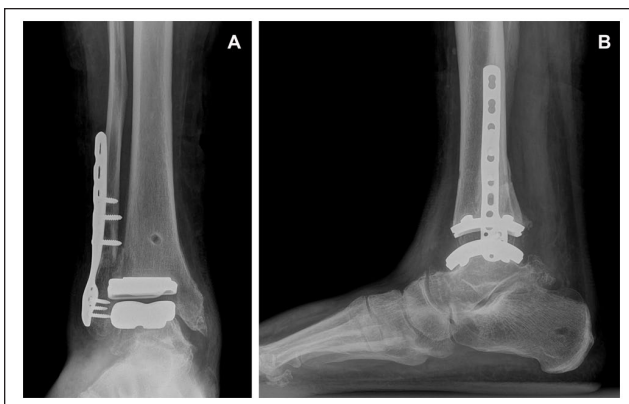


Figure 1. Postoperative radiographs of total ankle arthroplasty. (A) Anterior-posterior view and (B) lateral view of the implanted total ankle prosthesis (Trabecular Metal Total Ankle System; Zimmer Biomet).

(Zimmer Biomet, Warsaw, IN). The procedure features a lateral approach with distal fibular osteotomy and transection of the anterior inferior talofibular ligament, cementless implantation of total ankle prosthesis, fibular fixation, and ligament repair (Figure 1).^{24,40}

Patients with minimum follow-up of 6 months after TAA were included. PJI was diagnosed when one of the following criteria was met: (1) positive bacterial cultures of joint aspiration or (2) sinus tract/wound communicating with the joint or visualization of prosthesis through the wound. These major criteria were in line with PJI in hip and knee arthroplasty.³¹ All PJI cases were reviewed and confirmed by the operating senior surgeon.

The following patient information was collected: age, gender, indication for TAA, follow-up period, BMI, smoking, prior ankle arthroplasty and other surgeries, diagnosis of rheumatoid arthritis, diabetes, malignancy and chronic kidney disease, use of immunosuppressive drugs, ASA score (www.asahq.org), concurrent procedures, procedure time, results of wound bacterial culture if had PJI, interval between TAA and PJI diagnosis, and PJI management. The data were used to calculate the patient's Mayo Score.

A (baseline) Mayo Score sums points of the following risk factors: BMI, ASA score, immunosuppression conditions (including rheumatoid arthritis, use of systemic corticosteroids or immunosuppressive drugs, diabetes mellitus, presence of a malignancy and chronic kidney disease), procedure time, and previous arthroplasty or surgery of the index joint.⁵ In conversion of the Mayo Score for the current study, the ankle replaced knee and hip in the original study, as the index joint. The detail makeup of the Mayo Score is listed in Table 1. The minimum Mayo Scores is -5 and maximum is 19, with a higher Mayo Score indicative of greater PJI probability.

To identify critical risk factors of PJI, in this study, a risk factor constituting the Mayo Score was counted as a "major

Table 1. The Mayo Periprosthetic Joint Infection Risk Score (Baseline).⁵

Risk Factor	Mayo Score
BMI	
<25	0
25-39	-3
>40	0
Previous surgery	2
Previous TAA	3
Immunosuppression	3
ASA score	
1	0
2	1
3	3
4	9
Procedure time (h)	
<2	0
2-3	-2
3-4	-1
>4	2

Abbreviations: ASA, American Society of Anesthesiologists physical status classification score; BMI, body mass index; TAA, total ankle arthroplasty.

contributor” when its maximum value was assigned (for ASA, the maximum value was set at 3 as ASA score 4 is typically a contraindication of TAA). The major contributors in the high-risk group, as determined by the value of the Mayo Score, were compared between the PJI and non-PJI patients.

Statistical analysis: Data are expressed as mean $\pm$ SD or median (interquartile range [IQR]), where they are appropriate. The rates of PJI were calculated for the whole cohort as well as for those patients who were at high risk of PJI as determined by their Mayo Scores. The Mayo Scores of the PJI and non-PJI patients were compared with Mann-Whitney *U* test. Logistic regression was used to analyze the relationship between Mayo Scores and the occurrence of PJI following TAA. Overall evaluation of the logistic regression model included likelihood and Hosmer & Lemeshow tests. The model’s predictability was measured by the area under receiver operating characteristic (ROC) curves. Models are considered to have “reasonable” to “excellent” predictability when the area is 70% to 80% and 80% to 90%, respectively. An optimal cut-off of for the Mayo Score to stratify patients into high or low PJI risk was determined by using the best Youden index ($J_{\max}$, range from 0 to 1). For the patients at high risk of PJI, as determined by their Mayo Scores, comparison of the major contributing factors between the PJI and non-PJI groups was performed with Fisher exact test. The statistical analysis was conducted using MedCalc (version 20.009, MedCalc Software Ltd, Ostend, Belgium). $P < .05$ was set as significant.

Results

A total of 405 TAA cases (204 male patients and 201 female patients) were included in this retrospective study. Patients’ ages ranged from 23 to 86 years (median, 61; IQR 53-68).

Ten cases (2.5%) of PJI were identified, including 6 male and 4 female patients, with a median age of 59 years (range, 31-75). The average interval between TAA and PJI diagnosis was 83 (± 43) days. All PJI cases were confirmed by bacterial culture of ankle aspiration (Table 2). Of the PJI cases, 7 were for posttraumatic ankle osteoarthritis and 1 for end-stage primary ankle osteoarthritis. Two cases were revisions of failed TAA using implants different from the current series. One case was TAA performed for ankle osteoarthritis/deformity due to avascular necrosis of talus. PJI case 2 had multiple previous ankle procedures performed for congenital clubfoot, infection, and secondary avascular necrosis of the talus. After TAA, the ankle functioned well before it had increasing pain, warmth, and swelling at 6 months. Cultures of ankle joint aspiration were positive of *Propionibacterium acne*. The patient elected amputation over salvage given many years of suffering through multiple procedures since childhood. The PJI cases were treated with removal of distal fibular fixation (8/10), wound debridement and irrigation (9/10), placement of antibiotic beads (8/10), and exchange of polyethylene component (5/10). One case received negative-pressure wound application. In 1 case, peroneal brevis rotational muscle belly flap was used for wound coverage. One case was initially treated with exchange of polyethylene component, and eventually removed TAA prosthesis and replaced with a cement antibiotic spacer.

The Mayo Scores of these 405 patients ranged from -4 to 13, average 2.6 (± 3.5) and median 2 (IQR 0-5). For the non-PJI patients, the median Mayo Score was 5 (IQR 0-5), whereas it was 8 (IQR 7-10) for the PJI patients ($P < .0001$).

Logistic regression model showed that the odds of PJI occurrence increased by 48% (odds ratio 1.48, 95% CI 1.23-1.78) for every 1-point increase of Mayo Score (Figure 2). The model satisfied evaluations with likelihood test, Hosmer & Lemeshow test, and ROC under the curve area, which was 0.88 for the model’s discriminative ability for PJI risk in TAA (Table 3).

In this series, all but 1 PJI cases had a Mayo Score > 5 (Figure 3A). The ROC curve was well above the 45-degree dividing diagonal line (Figure 3B). The area under the ROC curve is 0.88. The optimal threshold with the maximal sum of sensitivity and specificity (Youden index), for high risk of PJI, was Mayo Score 5 (sensitivity 90.0% and specificity 84.3%; Youden index $J_{\max} = 0.74$; Figure 3C).

Of 405 TAA cases, 71 had a Mayo Score > 5 . Among them, there were 9 PJI cases ($PJI_{(ms>5)}$) and 62 non-PJI cases ($non-PJI_{(ms>5)}$). The patients with a Mayo Score > 5 had a PJI rate of 12.7%, in contrast to 0.3% for the patients with a Mayo Score ≤ 5 ($P < .001$).

Table 2. Details of PJI Cases.

Case	Age	Gender	Indication	Mayo Score	TAA to PJI Interval (d)	Bacteria	Treatment
1	43	F	OA, Talar AVN	9	39	Coagulase-negative staphylococci	I&D, poly exchange, antibiotic beads
2	31	M	Clubfoot, Talar AVN	6	180	<i>Propionibacterium acnes</i>	Amputation
3	59	M	PTOA	10	93	Enterobacter, <i>Streptococcus agalactiae</i>	I&D, poly exchange, antibiotic beads, muscle flap
4	75	M	PTOA	7	67	Serratia	I&D, removal of fibular fixation, antibiotic beads
5	58	F	PTOA	7	54	Enterobacter	I&D, antibiotic beads
6	68	M	OA	10	98	<i>Staphylococcus aureus</i>	I&D, removal of fibular fixation, antibiotic beads
7	45	F	PTOA	11	31	<i>Streptococcus agalactiae</i>	I&D, poly exchange, removal of fibular fixation, antibiotic beads
8	67	M	PTOA TAA revision	2	81	<i>Pseudomonas aeruginosa</i>	I&D, antibiotic beads
9	45	F	PTOA	13	115	Methicillin-resistant <i>S aureus</i>	I&D, poly exchange, removal of fibular fixation, antibiotic beads, external fixator, wound negative pressure suction
10	60	M	PTOA TAA revision	7	70	<i>Staphylococcus epidermidis</i>	I&D, removal of fibular fixation, total ankle explantation, cement antibiotic spacer

Abbreviations: AVN, avascular osteonecrosis; F, female; I&D, wound irrigation and debridement; M, male; OA, osteoarthritis; PJI, periprosthetic joint infection; PTOA, posttraumatic osteoarthritis; TAA, total ankle arthroplasty.

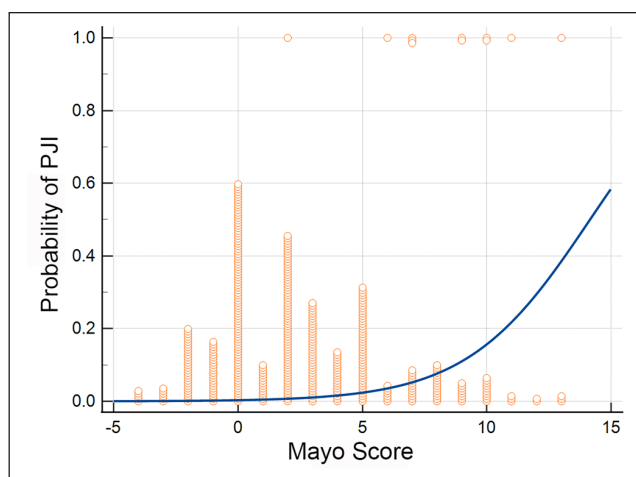


Figure 2. Logistic regression analysis of the occurrence of PJI and Mayo Score in 405 TAA cases. The probability of PJI increases as the patients' Mayo Scores are higher. In the figure, each case is represented by a circle, and the 405 cases are distributed across the x axis according to their Mayo Scores. Non-PJI cases are assigned 0 on the y axis, PJI cases are valued as 1 on the y axis, that is, the highest probability of infection. PJI, periprosthetic joint infection; TAA, total ankle arthroplasty.

A major contributing risk factor to the Mayo Score in both non-PJI_(ms>5) and PJI_(ms>5) groups was the history of previous ankle surgery (64% in non-PJI_(ms>5) and 9/9 in PJI_(ms>5))

patients; Table 4). ASA score was the second most common major contributor to the Mayo Score in the PJI_(ms>5) group (6/9), whereas it was a major contributor in 54% of non-PJI_(ms>5) patients. BMI, immunosuppression and surgical time, as a major Mayo Score contributor, presented in less than half of the 9 PJI_(ms>5) patients. In the non-PJI_(ms>5), immunosuppression and surgical time were the second and third most common major contributors to the Mayo Score (62% and 54%, respectively). However, the proportional distributions of the major contributors were not statistically different between the non-PJI_(ms>5) and PJI_(ms>5) groups.

Discussion

The diagnosis and reporting of TAA complications, including PJI, are still to be standardized diagnosed and reported in variable terms.²⁷ The diagnostic criteria of PJI after TAA are largely adapted from hip and knee arthroplasty and were applied for this study.² To emphasize PJI as a surgical complication, this study limited diagnosis of PJI within 6 months after TAA. Hematogenous PJI features a sudden onset of joint infection after the index arthroplasty being asymptomatic but the interval between arthroplasty and its diagnosis varies in clinical studies, from 30 days to 2 years.³ In many studies, the interval was set for at least 3 months after arthroplasty.^{38,46} Hematogenous PJI is associated with the frequency of bacteremia. No risk factors have been firmly

Table 3. Logistic Regression Results.

Logistic Regression	Coefficient	Standard Error	Wald Test	P
Mayo Score	0.39492	0.094575	17.4369	<.0001
Constant	-5.76384	0.81091	50.5223	<.0001
Model Evaluation	χ^2		df	P
Likelihood ratio test	21.766		1	<.0001
Hosmer & Lemeshow test	4.8071		8	.7780
ROC Curve Analysis				
Area under the ROC curve			0.884	
Standard error			0.0452	
95% CI			0.849-0.913	

Abbreviations: df, degrees of freedom; ROC, receiver operating characteristic.

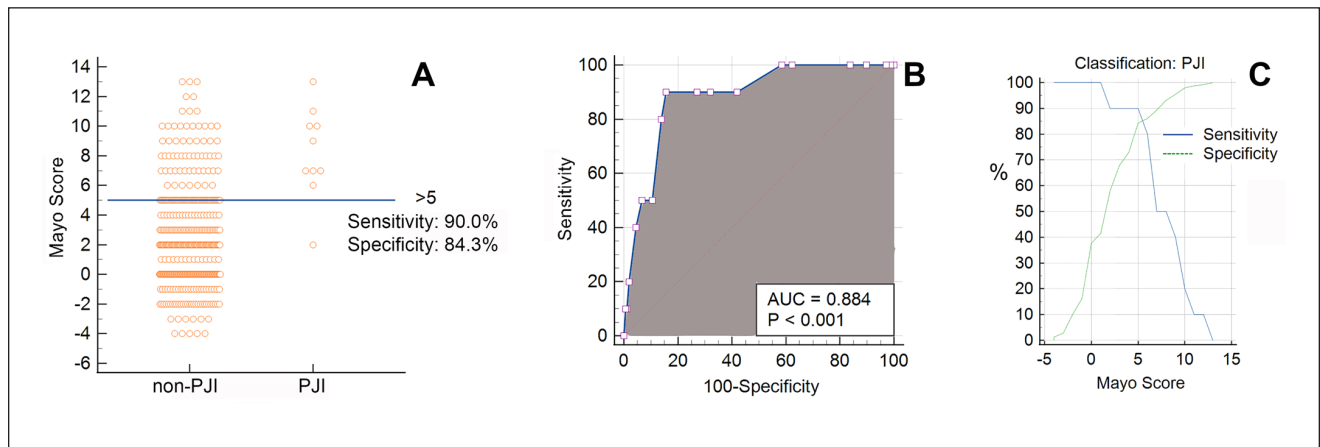


Figure 3. (A) Mayo Score distribution among non-PJI and PJI patients after TAA (n=405). Except for 1 case, PJI cases have a Mayo Score >5. The majority of non-PJI patients (84%) have a Mayo Score ≤5. (B) ROC analysis: the ROC curve is well above the diagonal line joining the point (0, 0) to (100, 100). The area under ROC curve is 0.88. (C) ROC analysis: Mayo Score >5 has the maximal sum of sensitivity (90.0%) and specificity (84.3%) and, therefore, is the selected cutoff value for high PJI risk. PJI, periprosthetic joint infection; ROC, receiver operating characteristic; TAA, total ankle arthroplasty.

Table 4. Major Contributors to the Mayo Scores of the Patients With a Mayo Score >5.

	Non-PJI, n (%) (n = 62)	PJI, n (n = 9)	P
BMI	29 (47)	4	.66
Prior ankle surgery	40 (65)	9	.08
Prior TAA	6 (10)	2	.35
Immunosuppression	39 (63)	3	.06
ASA	33 (53)	6	.73
Procedure time	32 (52)	3	.19

Abbreviations: ASA, American Society of Anesthesiologists physical status classification score; BMI, body mass index; non-PJI, without periprosthetic joint infection; PJI, periprosthetic joint infection; TAA, total ankle arthroplasty.

established for hematogenous PJI.^{14,38} Considering CDC guideline of surgical site infection and other studies,^{13,19,25} this study excluded hematogenous PJI beyond 6 months of TAA because it is more related to the presence of implants than the surgical procedure itself (i.e., TAA). Although hematogenous and recurrent PJI happens, the majority of PJI cases are attributed to bacterial contaminations from endogenous skin flora or exogenous sources during prosthesis implantation and wound healing, and these are the subject of this study.^{16,17}

The original Mayo Score model demonstrated a higher PJI risk with increased scores in a combined cohort of total hip and knee arthroplasty.⁵ As such, the Mayo Score was generalized for applications for both types of arthroplasties and is potentially applicable for TAA. In this series of 405

TAA cases, the patients with higher Mayo Scores similarly trended toward increased probability of PJI in a logistic regression model. The average Mayo Score of the PJI cases was more than 3 times that of the non-PJI group. The consistency of the Mayo Score application to hip and knee arthroplasty, and TAA for projection of PJI probability could be largely because these procedures have many PJI risk factors in common.^{23,32,39,42}

The risk factors constituting the Mayo Score have been identified in several previous TAA studies. For example, a history of previous ankle surgery and prolonged surgical time were confirmed as PJI risk factors for TAA in one case-controlled analysis.¹⁷ The risk factor of immunosuppression in the Mayo Score is a collection of several health conditions, such as rheumatoid arthritis, diabetes, malignancy, chronic kidney diseases, and use of immunosuppressive drugs. Some of them were individually considered as PJI risk factors by other TAA studies as well.^{1,32,35}

The results of ROC analysis suggest that a Mayo Score of 5 is a critical threshold for increased risk of PJI after TAA. All but 1 of the 10 PJI cases had a Mayo Score >5 . When the 405 TAA cases were stratified by Mayo Score of 5, the PJI rate in the patients with a Mayo Score >5 was more than 40 times higher than that of the patients with a Mayo Score ≤ 5 . Having a cutoff Mayo Score (>5) for high-risk patients (sensitivity 90.0%, specificity 84.3%) could benefit preoperative decision-making and conducting targeted, and therefore more efficient, PJI prevention.

Though it occurs at a low rate, PJI alone contributes to 80.6% of TAA failures.¹² The treatment of PJI following TAA is clinically challenging, with uncertain outcomes.^{21,32} To prevent PJI, one approach is preoperative risk stratification and mitigation.²⁹ Although no risk factor scores/indexes could precisely predict PJI or surgical site infection for a specific patient preoperatively, a criterion of Mayo Score >5 based on this study could identify those patients who are at high risk of PJI following TAA. For certain patients with a Mayo Score >5 , preoperative optimization may lower their PJI risk through addressing BMI and other immunosuppression conditions. In terms of surgical planning to lower the risk in vulnerable patients, procedures may be performed in stages, rather than concurrently, in order to shorten the TAA procedure time. Weighing the benefits and PJI risk of TAA, alternative therapies/procedures may be more appropriate for certain patients with a high Mayo Score. Studies have shown that for selected high-risk patients, intraoperative usage of vancomycin powder and diluted povidone-iodine solution reduced PJI risk by 27.8% after hip and knee arthroplasty,¹⁵ which could be similarly effective in high-risk patients for TAA.

The major contributing risk factors making up the Mayo Scores in the PJI_(ms >5) and non-PJI_(ms >5) cases showed no differences. It suggests that no individual PJI risk factors

are overwhelmingly decisive contribute to PJI in TAA. The PJI predictability of the Mayo Score lies in the aggregation of several PJI risk factors that sum up the host's resistance to bacterial infection after TAA.

This study is based on one surgeon's experience with PJI following TAA, using a single type of TAA implant. It ensures certain data uniformity but may not be representative of the diverse outcomes a multicenter study would have.⁴⁵ A limitation of this study is the few number of PJI cases, which has been a general shortcoming of studies on PJI in TAA.³⁷ Although the Mayo Score appears predictive of PJI in this TAA study, some differences between TAA and arthroplasties of hip and knee, from which the Mayo Score was derived, may contribute to the PJI in TAA. For example, knee and hip arthroplasties are commonly performed on primary osteoarthritic but TAA treats predominantly posttraumatic osteoarthritic, often preceded by previous ankle surgeries.^{4,39} TAA is also frequently performed concurrently with procedures addressing soft tissue balance and bony deformity. As a result, previous ankle surgery and prolonged procedure time were common contributing factors to PJI in this and other TAA studies.^{17,37} Additionally, a transfibular approach uniformly used in this study may also present a unique factor to the development, diagnosis, and management of PJI, as compared to TAA performed using an anterior approach.^{40,45} A future TAA-specific PJI risk score developed from a case-controlled prospective study would more precisely project the risk of PJI after TAA.

In summary, this study suggests the applicability of the Mayo Score for assessing PJI risk in TAA. For high-risk patients with a Mayo Score >5 , preoperative risk mitigation and proper TAA planning could potentially minimize PJI risk. Because of the limited number of PJI cases included in this study, these preliminary findings may require further validation.

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Ethical Approval

Ethical approval for this study was obtained from Mercy Medical Center Institutional Review Board (approval number 1648405).

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. ICMJE forms for all authors are available online.

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