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Complications - Infection

BMI is a Better Predictor of Periprosthetic Joint Infection Risk Than Local Measures of Adipose Tissue After TKA

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ABSTRACT

Background: Both body mass index (BMI) and local measures of adiposity at the surgical site have been identified as independent risk factors for periprosthetic joint infection (PJI) (periprosthetic joint infection) after total knee arthroplasty (TKA). We aimed to 1) evaluate previously used measures of assessing knee adiposity and 2) determine the best measure for predicting both surgical duration and PJI after TKA.
Methods: We performed a multicentre retrospective review of 4745 patients who underwent primary TKA between January 2013 and December 2016. Patient demographic information, surgical duration and postoperative infection status within one year were obtained. Preoperative weight-bearing AP and lateral x-rays were analyzed to determine prepatellar adipose thickness, bony width of the tibial plateau, and total soft tissue knee width. The knee adipose index (KAI) was calculated from the ratio of bone to total knee width.
Results: We observed substantial variability in both local measures of adiposity compared with BMI. Neither measure of local knee adipose showed a significant correlation with PJI risk. By contrast, there was a strong correlation between PJI risk and BMI >35 (odds ratio 2.9, 95% CI 1.4-6.1). Surgical duration increased with both BMI and measures of local adipose tissue (KAI and prepatellar fat thickness).
Conclusion: Local adipose deposition varies greatly for any given BMI. In this study, BMI was a better predictor of PJI after TKA than local measures of knee adipose tissue.

Obesity is a risk factor for poor outcomes after total knee arthroplasty (TKA), particularly periprosthetic joint infection (PJI) [1,2]. The risk is independent of the comorbidities that typically accompany obesity such as diabetes mellitus and the metabolic syndrome, resulting in greater health care costs and increased morbidity and mortality for patients [3]. Proposed mechanisms include poor vascularity of adipose tissue, larger incisions, widened dissection, increased retraction, lower tissue oxygenation, increased dead space after wound closure, and increased surgical duration in obese patients [4–7].

Obesity is typically defined by body mass index (BMI). This measure is used to quantify obesity in the general population; however, it does not provide information on body composition (muscle versus adipose) or the distribution of adipose deposition in an individual which may be relevant to PJI risk after TKA. These perceived pitfalls of BMI have led to development of different methods to quantify adiposity at the knee joint, such as a ratio of the prepatellar thickness (PPT) to the thickness of the patella [8]; PPT and pretubercular thickness (PTT) [9]; and a ratio of the amount of soft tissue to bone at the knee joint on a lateral radiograph [10]. These measures of "local" knee adiposity have been associated with PJI risk after TKA; however, it is unclear if this association is stronger than that of BMI [1,11]. This inconsistency highlights the ambiguity surrounding the importance of "central" versus "local" adiposity at the surgical site as a risk for development of complications after TKA. In general surgical studies, central obesity has been touted as being an important risk factor for infection; however, it is unknown whether that is because of the adverse metabolic effects of central obesity, or because of the effects of local fat at the surgical site [12].

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The aim of this study was to investigate BMI and local knee adiposity as predictors of PJI and surgical duration to clarify which measure of obesity has the stronger association. As current methods for measuring local adiposity at the knee are often time-consuming and complex, we also investigated a novel, more user-friendly method, the knee adipose index (KAI).

Materials and Methods

Study Design and Setting

We conducted a multicentre, retrospective review of 4745 consecutive patients undergoing primary TKA between January 2013 and December 2016, at three tertiary referral hospitals. Individual review of patient electronic records including clinical notes, laboratory results, and radiographs was performed. Supplemental data on all 4745 patients was obtained from the New Zealand National Joint Registry and the national Surgical Site Infection surveillance program.

Study Subjects

Inclusion criteria were patients undergoing a primary TKA, with acceptable preoperative AP and lateral knee X-ray radiographs taken within one year (weight-bearing, leg within the film area, not supine and/or Rosenberg) before TKA, with at least 1 year of clinical follow-up ($n = 4560$). Of the 4745 patients who received a primary TKA during the study period, 185 were excluded because of inadequate preoperative radiographs.

PJI was defined using MSIS criteria within one year of primary TKA [13]. Criteria include the presence of a draining sinus tract or 2 positive cultures, or the presence of any 3 of the following minor criteria: elevated ESR and CRP, elevated synovial white blood cell count or positive leukocyte esterase, elevated synovial fluid polymorphonuclear neutrophil percentage, positive histological diagnosis, and a single positive culture.

Variables

Knee Adipose Index

The width of the tibia was measured at the tibial plateau on anteroposterior (AP) radiograph with a line drawn parallel to the joint line, excluding osteophytes (Fig. 1A). On the medial side, the edge of the medial tibial plateau was determined either by a clear cortical margin beneath the osteophyte or by a tangent that was projected from the metaphysis immediately below the osteophyte to the level of the joint line. On the lateral side, a similar method was used to determine the lateral edge. Where there was a recess immediately below the osteophyte, this was used as the tangent point and the edge was then taken at the level of the plateau where this intersected. The width of the leg was then measured to determine the medial and lateral soft tissue aspects at the level of the tibial plateau. A horizontal line coincident to the line determining the width of the tibia was drawn from the medial edge of the soft tissue to the lateral edge of the soft tissue (Fig. 1A). This gave the total thickness of the leg. The total thickness of the leg was divided by the width of the tibial plateau to obtain the KAI. By using a ratio of soft tissue to bone, magnification and body size are controlled for to determine the relative amount of fat at the surgical site.

Prepatellar Fat

We modified the previously reported method of Watts et al. to assess prepatellar fat thickness [9]. The lateral radiographs were inverted to better visualize the boundaries of soft tissue and bone. There were no radiographs in which the edge of the soft tissue was out of field. The length of the articular surface of the patella was measured by a line from the superior aspect to the inferior aspect, excluding osteophytes (Fig. 1B). The center of this line was determined by dividing this value in two. A line perpendicular to the patellar articular surface was made at the level of the center from the superficial border of the patella to the skin. This allowed the measurement of the prepatellar soft tissue thickness at the surgical site.

Patient Characteristics: Age, Sex, BMI, ASA Score, SSI Risk Index

Retrospective chart review allowed determination of patient characteristics: age, sex, height, weight, ASA score, and SSI risk index. The patient height and weight data were used to calculate BMI, using the formula BMI = weight (kg)/height $(m)^2$. The measures BMI, KAI, and prepatellar fat were analyzed both as continuous and categorical variables.

The SSI risk index was analyzed, which is a scoring measure that predicts the patient's risk of developing an SSI [14]. The risk index was calculated using the patient's ASA score (1 point for ASA >2) and the duration of the operation (1 point for greater than 2 hours).

Surgical Duration

The surgical duration (skin to skin minutes) for surgeons that performed >50 TKAs during the study period were included, with surgeries performed by trainees in part or in whole excluded ($n = 430$). For each surgeon, the average surgical duration for "non-

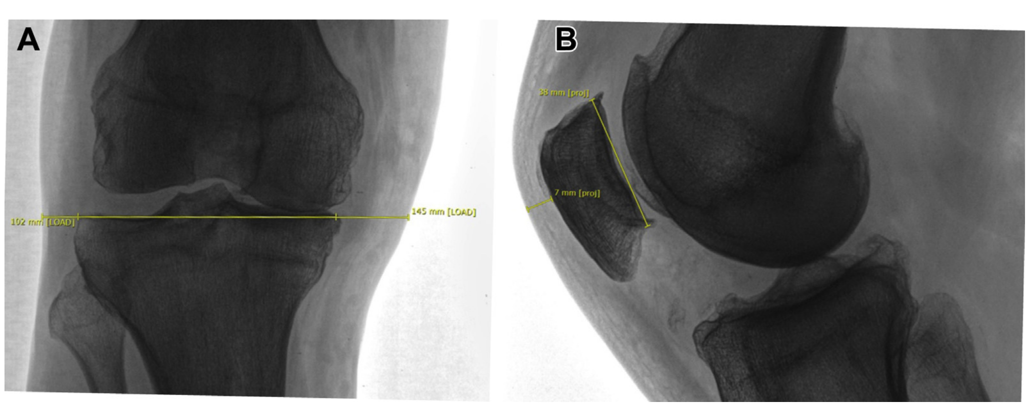

Fig. 1. (A) AP radiograph with example measurements of tibial bone width and total knee thickness. Tibial bone width is measured by a line at the tibial plateau. Total knee thickness is measured by a line at the same level, between the medial and lateral soft tissue boundaries. These measurements were used to calculate knee adipose index (KAI). (B) Lateral radiograph with example measurements of the length of the articular surface of the patella, and the prepatellar fat. The midpoint of the articular surface of the patella was used as a reference point for where to take the prepatellar fat measurement. This was then taken from the superficial border of the patella to the edge of the soft tissue boundary.

obese" patients (bottom 40% of BMI, KAI, and pre-patellar fat, respectively) was used as the baseline, and compared with the surgical duration for larger patients (top 10% of BMI, KAI, and pre-patellar fat). Individual surgeon results were then averaged to find the mean difference from the baseline for each of the 3 measures.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics Version 25. Q-Q plots and histograms were produced to assess continuous variables for normality. Univariate analysis of *P*-values was carried out using Student's t-tests for continuous variables and chi-square test of independence or Fisher's exact test for categorical variables. Statistical significance was defined at $P < .05$. Variables that were found to be significant on univariate analysis were forced into a multivariable binary logistic regression model and results were expressed as odds ratios (OR) with 95% confidence intervals.

Results

Demographics

Of the 4745 TKAs performed during the study period, 31 developed subsequent PJI giving a PJI rate at one year of 0.65% (Table 1). There were slightly more females than males in the study population, with a mean prepatellar fat measurement of 10 mm, a mean KAI of 1.71, and a mean BMI of 32 kg/m^2. The mean surgical duration was 89.8 minutes.

On univariate analysis, hospital, gender, ASA score, SSI risk index, and elevated BMI were all associated with PJI ($P < .05$, Table 2). No association was seen between the development of subsequent PJI and local adiposity as measured by either KAI or prepatellar fat. On multivariate analysis, a BMI >35 was strongly associated with subsequent PJI (odds ratio 2.9, 95% CI 1.41-6.09, Table 3). Other factors that were associated with PJI included male sex (adjusted OR = 3.02, $P = .005$ and an SSI risk index of 1 (adjusted OR = 2.50, $P = .022$).

Table 1
Baseline Patient and Surgical Demographics.

Number of Primary TKA	n = 4745
Number of Deep Infections	n = 31
Hospital	
Hospital A	2203
Hospital B	1033
Hospital C	1509
Age	
Mean (range), years	68.33 (15-96)
Gender	
Male	2091
Female	2654
ASA Score	
1	307
2	2909
3	1442
4	28
NR	59
SSI Risk Index	
0	2514
1	1486
2	278
BMI	
Mean (range), kg/m^2	32.12 (15-65)
Surgical Duration	
Mean (range), minutes	89.79 (26-359)
Surgeon Level	
Trainee	430
Consultant	4315

BMI, body mass index; TKA, total knee arthroplasty.

The average surgical duration increased in patients with higher KAI, prepatellar fat, and BMI (Fig. 3). The strongest association was seen with BMI, with an increase of +16.5 minutes for the patients in the top 10% of BMI compared with patients in the baseline bottom 40% of BMI. The mean increase for prepatellar fat and KAI was +3.7 and +6.7 minutes, respectively.

Pearson correlation analysis of the aforementioned measures revealed KAI interobserver reliability of 0.94 and intraobserver reliability of 0.99 (Table 4). PPT measurement interobserver reliability was 0.75 and intraobserver reliability was 0.99. Pearson correlation analysis was also performed on previously reported measures of local adipose, and in most cases was not as high as previously reported in the literature.

Discussion

This study found BMI was more strongly associated with subsequent PJI risk than measures of local knee adipose tissue (KAI and

Table 2
Univariate Analysis of Patient and Surgical Factors for PJI.

Patient and Surgical Factors	n	PJI			*P* Value
		Yes	No	%	
Hospital					.049
Hospital A	2203	8	2195	0.36%	
Hospital B	1033	11	1022	1.06%	
Hospital C	1509	12	1497	0.80%	
Age					.37
Mean ± SD	68.33 ± 9.47	66.81 ± 9.58	68.34 ± 9.47		
Gender					.008
Male	2091	21	2070	1.00%	
Female	2654	10	2644	0.38%	
ASA Score					.023
1	307	0	307	0.00%	
2	2909	14	2895	0.48%	
3	1442	17	1425	1.18%	
4	28	0	28	0.00%	
SSI Risk Index					.011
0	2514	10	2504	0.40%	
1	1486	18	1468	1.21%	
2	278	3	275	1.08%	
Prepatellar Fat					
Continuous					
Mean ± SD	10.05 ± 5.29	10.71 ± 6.80	10.05 ± 5.28		.486
Categorical					
0-5	698	6	692	0.86%	.335
6-10	2241	15	2226	0.67%	
11-15	985	3	982	0.30%	
16-20	392	5	387	1.28%	
>20	228	2	226	0.88%	
KAI					
Continuous					
Mean ± SD	1.71 ± 0.27	1.61 ± 0.23	1.72 ± 0.28		.029
Categorical					
1-1.4	472	4	468	0.85%	.272
>1.4-1.6	1452	14	1438	0.96%	
>1.6-1.8	1079	7	1072	0.65%	
>1.8-2.0	837	5	832	0.60%	
>2.0	720	1	719	0.14%	
BMI					.056
Continuous					
Mean ± SD	32.12 ± 6.56	34.35 ± 8.09	32.10 ± 6.54		
Categorical					
≤35	3221	15	3206	0.47%	.003
>35	1240	16	1224	1.29%	
Surgical Duration	89.79	94.64	89.75		.381
Surgeon Level					.757
Trainee	430	3	427	0.70%	
Consultant	4315	28	4287	0.65%	

ASA, American Society of Anesthesiologists; BMI, body mass index; PJI, periprosthetic joint infection.
P value significant at .05.

Table 3
Multivariate Analysis of Patient and Surgical Factors for PJI.

Patient Factor	OR (95% CI)	*P* Value
Hospital		
Hospital A	Reference	
Hospital B	2.61 (1.04-6.54)	.041
Hospital C	2.21 (0.89-5.50)	.087
Gender		
Female	Reference	
Male	3.02 (1.40-6.51)	.005
SSI Risk Index		
0	Reference	
1	2.50 (1.14-5.49)	.022
2	2.10 (0.55-7.98)	.276
BMI		
Categorical		
≤35	Reference	
>35	2.93 (1.41-6.09)	.004

OR, odds ratio; BMI, body mass index.

prepatellar fat thickness) after TKA. In addition, we found BMI to be strongly associated with increased surgical duration after TKA. The association between BMI and PJI risk after TKA is well documented in the literature, including in meta-analyses [1,11]. However, although we found the PJI risk to be greater in patients with high BMI (1.3% with BMI >35 vs 0.46% with BMI <35), there was no statistically significant association between PJI risk and prepatellar fat or KAI score. A potential explanation for this finding may be that the systemic effects of obesity are more important to PJI risk, as patients with central obesity are known to be at higher risk for metabolic syndrome [15]. Furthermore, obesity is postulated to induce a chronic low-level inflammatory state which compromises immune function [15]. Our findings, consistent with findings in both orthopedic and general surgical literature, suggest such systemic effects of obesity may be more important in PJI risk than local adipose tissue at the knee [4–7].

Our findings contrast with previous smaller studies reporting local adipose tissue at the surgical site to be an independent risk factor for PJI after TKA. In a case-control study of 572 patients, Wagner et al. [8] used a prepatellar fat thickness ratio (PFTR) to assess local adiposity. They identified infection rates of 1.5% for PFTR of <1 and 5% for PFTR >1. All patients who developed infections were obese, so there is no data on infection rates for obese vs nonobese patients in this study. The overall infection rate was 2.3% for this group.

Watts et al. conducted a case-control study of 1689 obese patients (BMI range 40-58 kg/m^2) [9]. They took absolute measurements of prepatellar and PTT, and assessed risk of early reoperation for wound complications and infection after primary TKA. Of the 58 patients requiring early reoperation, both PPT and PTT were greater than that of case-matched controls. They identified PPT ≥15 mm and PTT ≥ 25 mm to increase risk of complications by 2x and 1.6x, respectively. When considering BMI as a risk factor, there was no difference between the group of BMI 40-49.9 and BMI >50.

Yu et al. [10] conducted a case-control study of 374 patients. They used the periarticular soft tissue index (PASTI) for the femur and tibia to assess a ratio of fat to bone at the knee and used this to predict risk of minor and major complications after TKA. Minor complications were any clinical intervention that was directly related to the surgical wound, including office debridement and antibiotics without operative intervention. Major complications were return to the operating theater for periprosthetic infection and wound dehiscence. They identified no difference in both minor and major complications for nonobese vs obese patients. They identified PASTI >3 to increase the risk of minor complications (20.9% vs 6.4% for tibial, and 15.3% vs 7.2% for femoral), but to have no significant difference in risk of major complications. PASTI was not significant when analyzed as a continuous variable.

As these studies were of a case-control design, particularly the work of Wagner et al. [8] and Watts et al. [9], they are most applicable to an obese population. Our study both included patients who were not obese, and also included infections in patients that were not obese in a large population of 4745 patients. As we analyzed a greater range and number of patients, our results may be more representative of the risk of PJI after TKA for the general population, without bias toward a select population of obese individuals. This is important when considering the use of factors such as BMI and measures of local adiposity in prediction of PJI risk in clinical practice.

We did not observe a significant relationship between infection risk and PPT (Fig. 2B). This contrast with the findings of Watts et al. [9] in which PPT >15 was a significant predictor for infection after TKA. Prepatellar fat is not standardized to body size and magnification, and therefore may be inaccurate as a measure of local adiposity. Furthermore, many previously discussed methods of measuring local adiposity at the knee are complex and time-consuming. We chose to investigate KAI as it is both simple and quick to perform, and controls for magnification due to it being a ratio of bone to fat.

We found BMI, KAI, and PPT were all associated with increased surgical duration of TKA (Fig. 3). This can be explained by increased difficulty with exposure, retraction, visualization, and limb positioning in obese patients. Surprisingly, high BMI was associated with the greatest increase, with an average difference of +16.5 minutes in skin to skin operating time between patients in the top 10% of BMI

Table 4
Pearson Correlation Analysis of Interobserver and Intraobserver Reliability for Different Methods.

Method	Reported Interobserver Reliability	Measured Interobserver Reliability	Reported Intraobserver Reliability	Measured Intraobserver Reliability
KAI	-	0.94	-	0.99
Prepatellar thickness	-	0.75	-	0.99
Tibial PASTI Yu et al. 2018 [10]	0.98	0.63	0.97	0.93
Femoral PASTI Yu et al. 2018 [10]	0.98	0.46	0.98	0.62
PFTR Wagner et al. 2018 [8]	0.95	0.65	Not reported	0.85
PPT Watts et al. 2016 [9]	0.92	0.52	0.95	0.90
PTT Watts et al. 2016 [9]	0.96	0.72	0.98	0.99

KAI, knee adipose index; PASTI, periarticular soft tissue index; PFTR, prepatellar fat thickness ratio; PPT, prepatellar thickness; PTT, pretubercular thickness.

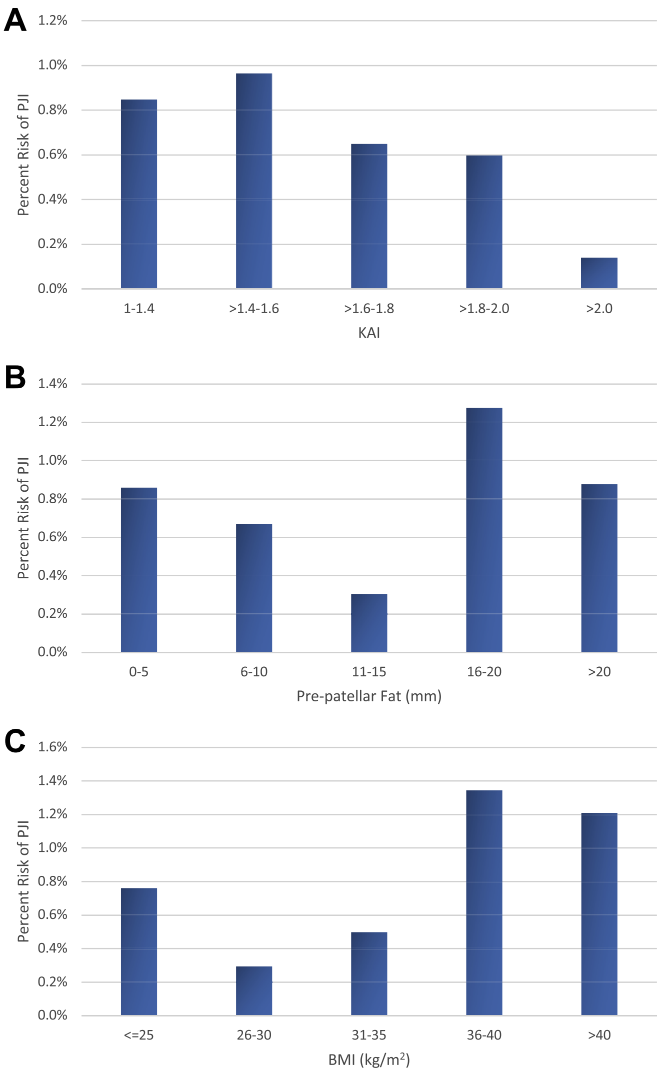

Fig. 2. Relationship between risk of PJI with increasing levels of KAI (A), prepatellar fat (B), and BMI (C). BMI, body mass index; KAI, knee adipose index.

compared with those in the baseline bottom 40%. This compares with +6.7 minutes for KAI and +3.7 minutes for PPT. These findings are of relevance as increased surgical duration increases the period that bacterial contamination can occur, potentially altering PJI risk [16,17]. Evidence thus far on surgical duration in obese patients undergoing unilateral TKA is limited, and has not conclusively identified a trend. Two studies have identified no correlation, whereas 4 other studies have identified that surgical duration was increased in their study populations [18–23].

This study had a number of limitations. First, PJI is a relatively rare outcome and has a low incidence after primary TKA. However, this is the largest such study on this topic, and contrasts with previous smaller studies using case-control matching. If a variable is to have value in risk stratification for PJI it must be supported by large cohort studies such as this, and our findings support the continued use of BMI over local measures of adiposity. Second, we chose a PJI cutoff of one year after TKA, and late PJI may also be associated with obesity. However, those late PJIs are less relevant when evaluating perioperative risk, as most PJIs due to bacteria introduced during surgery occur within one year [24]. Similar to previous studies measuring local adiposity, variations in measurement and x-ray technique may occur. However, we followed a standardized measurement protocol, and used only weight-bearing radiographs in which the legs were within the film and the soft-tissue boundaries were well-defined. Furthermore, this is the first study to perform intra- and inter-observability assessment of the other various measures of local adiposity, and the KAI and pre-patellar fat measurements used in this study were of similar caliber to other previously reported methods.

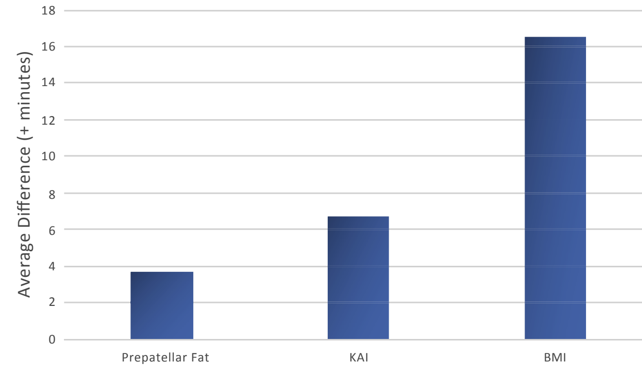

Fig. 3. Graph showing the average increase in surgical duration from the baseline for KAI, prepatellar fat, and BMI. Baseline was determined by the average surgical duration for nonobese patients (bottom 40% of BMI, KAI, and PPF). This was compared with the average surgical duration for larger patients (top 10% of BMI, KAI, and PPF), to find the average difference for each of the three measures. BMI, body mass index; KAI, knee adipose index; PPF, pre-patellar fat.

Conclusion

Local adipose deposition varies greatly for any given BMI. In this study, BMI was a better predictor of PJI after TKA than local measures of knee adipose tissue.

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