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Retrospective Cohort Study

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The Use of Preoperative CRP and ESR as Predictive Markers of Prosthetic Joint Infection in Primary Total Hip and Knee Arthroplasty

Andrew Hester, MD, Keenan Gibson, DO, Noah Embry, BS, Josiah Snowden, BS, Blake Campbell, BS and Russell Wagner, MD*

Department of Orthopedic Surgery, John Peter Smith Hospital, Fort Worth, TX 76104, USA

Abstract

Background: C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are inflammatory markers commonly used during the diagnosis and treatment of periprosthetic joint infection (PJI) in arthroplasty patients. The purpose of this study was to assess for a correlation between pre-operative CRP/ESR and post-operative development of PJI in patients undergoing primary total hip arthroplasty (THA) and total knee arthroplasty (TKA) and to assess modifiable and non-modifiable risk factors in patients with elevated preoperative inflammatory markers.

Methods: Retrospective review of 806 patients at a single institution who underwent THA (n = 291) and TKA (n = 515). CRP and ESR were obtained on all patients during the preoperative workup. Patient demographics, medical comorbidities, and occurrence of PJI were extracted. Positive CRP was set at any value > 0.3 mg/dL and positive ESR as any value > 30 mm/hr.

Results: In our study, we found no statistically significant correlation between pre-operative CRP or ESR and PJI. Although notably, we found that a higher proportion of patients with PJI had elevated preoperative CRP (70.6%) vs. those with normal CRP (29.4%).

Conclusions: This study is unable to validate the use of preoperative CRP/ESR as a predictive measure of PJI in primary THA/TKA. However, it does provide quantitative insight into the prevalence of elevated preoperative CRP/ESR in all patients prior to THA/TKA with a considerable proportion having modifiable risk factors. Since a large proportion of patients with elevated CRP/ESR didn't develop PJI, we do not recommend cancellation of THA/TKA unless there is an obvious modifiable risk factor that confers substantially heightened risk of PJI.

Keywords

Arthroplasty, Periprosthetic joint infection, ESR, CRP, Complications, Risk factors

Introduction

Total hip (THA) and total knee (TKA) arthroplasty are two of the most performed orthopaedic surgeries each year in the United States. Some of the more common complications include prosthetic joint infection (PJI), aseptic loosening, instability, dislocation, periprosthetic fracture, stiffness, chronic pain, and DVT/PE [1-4]. Currently, more than 400,000 THA and more than 700,000 TKA are performed each year with recent projections to increase to an estimated 635,000 THAs and 1,260,000 TKAs by year 2030 [5].

Despite advances, PJI remains one of the most common serious complications among all patients undergoing total joint arthroplasty (TJA) [6-10]. The overall incidence of PJI in THA and TKA is 1-2% and 2-3% respectively and it is increasing proportionately with the overall volume of TJA being performed nationwide [11]. It is estimated that PJI is responsible for 20% of all revision THA and 25% of all revision TKA [10]. In addition to the health burden of PJI to patients, the projected annual economic burden by 2030 is estimated to be $753.4 million for THA PJI and $1.1 billion for TKA PJI [12].

***Corresponding author:** Noah Embry, BS, Burnett School of Medicine at Texas Christian University, TCU Box 297085, Fort Worth, TX 76129, USA, Tel: 469-237-1001

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With the shift to value-based care and alternative payment models, it has become increasingly important to optimize patients prior to surgery to decrease the risk of postoperative complications [13-16]. Typical components of an optimization panel include history and physical exam, complete blood count, comprehensive metabolic panel, coagulation studies (PT/INR), electrocardiogram, body mass index (BMI), mental health screen, dental screen, nicotine screen, and alcohol and illicit drug use screen [15,16].

C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are commonly used, but nonspecific, markers for inflammation and infection in a wide variety of contexts throughout all fields of medicine [17-22]. Within the field of orthopaedic surgery, CRP and ESR are widely used to diagnose and track infection, including THA and TKA PJI. There has been a significant amount of literature on the use of CRP and ESR in the field of TJA, specifically for the diagnosis of PJI [23-27]. However, there is much less data focused on the use of preoperative CRP and ESR in the setting of primary TJA. Previous studies have found a correlation with elevated CRP and PJI, while others have found no correlation [6,28-31]. The purpose of this study is to further investigate any correlation that exists between preoperative CRP/ESR and PJI in primary THA and TKA. It also serves to assess risk factors among patients with elevated preoperative inflammatory markers to better understand overall incidence in this population of patients.

Materials and Methods

All patients who underwent primary total hip or total knee arthroplasty between 2016 and 2020 at John Peter Smith Hospital were identified and studied via a retrospective chart review. Patient characteristics, acute infections, labs, and past medical history were extracted from their medical records. Exclusion criteria included THA for femoral neck fracture, follow-up < 1 year, and federal inmates (due to minimal follow-up documentation). After excluding those patients, 806 patients were included in the final cohort for analysis. Minimum follow-up was 1 year. All surgeries were performed at a single institution (John Peter Smith Hospital, Fort Worth, TX) by one of two attending orthopaedic surgeons with fellowship training in adult reconstruction.

Baseline patient demographics, medical history, preoperative labs (CRP, ESR, urinalysis), and outcomes (prosthetic joint infection) were extracted from their medical records. Patient past medical history was used to assess the impact of documented obesity, smoking status, rheumatoid arthritis, liver disease, renal disease, HIV, and other conditions (DVT/PE, coagulopathy, stroke, transient ischemic attacks, coronary artery disease). For the purpose of an objective cutoff, positive CRP was set at any value > 0.3 mg/dL and ESR as any value > 30 mm/hr. PJI was defined using MSIS criteria.

A logistic regression was performed to assess the impact of ESR on positive CRP labs. To establish a full model, all items abstracted from the medical record underwent univariate pre-filtering. All available items were analyzed via univariate regression, and items with a p-value of 0.2 or lower were analyzed in our multivariate models. Backwards stepwise regression was used to construct parsimonious models. All testing across surgery type (i.e. Total Hip Arthroplasty and Total Knee Arthroplasty) was performed based on the data's distribution; where appropriate Wilcoxon-Mann-Whitney U test, chi square, or Fisher's exact test was used.

Approval through the North Texas Regional Institutional Review Board (IRB) was obtained for this chart review and thus informed consent was waivered by the IRB, approval number 1354130-2. All review of PHI in this study was HIPAA-compliant.

Results

Demographics and THA vs. TKA

A total of 806 patients underwent primary total hip (291) and total knee arthroplasty (515). Table 1 provides an overview of patient demographics and medical comorbidities distributed by surgery performed. There was a significant difference when comparing patient age (p-value < 0.0001) across the two surgery types, the median age in the THA group was 55 (IQR: 49 to 60), whereas the median age was 62 for patients undergoing a TKA (56-69). When assessing BMI across the two surgery types, there was a significant difference in proportion (p-value = 0.0001) and there were a larger proportion of patients who were obese undergoing a TKA (70.1%) when compared to those who had a THA (49.1%). Likewise, there was a significant difference (p-value < 0.0001) in patients who suffered avascular necrosis; there were zero patients suffering from avascular necrosis who underwent a TKA, and 22.3% of those who underwent THA had avascular necrosis. In total, there were 65 patients that developed avascular necrosis, two of whom had PJI. Similarly, there was a significantly lower (p-value = 0.0487) proportion of patients suffering from a PJIs who underwent a TKA (1.4%) when compared to those who underwent a THA (3.4%).

Patients who had a prior surgery make up a significantly greater proportion (p-value = 0.0001) of patients undergoing a TKA (22.1%) when compared to those undergoing a THA (11.4%). When assessing smoking status there was a significantly higher (p-value < 0.0001) proportion of patients who never smoked undergoing a TKA (61.9%) when compared to patients undergoing a THA (44.8%). There were significantly (p-value = 0.0009) more patients who suffered from diabetes mellitus undergoing a TKA (28.0%) when compared to those undergoing a THA (17.5%).

CRP and ESR distribution

The distribution of patient CRP and ESR results are detailed in Table 2. Overall, 49.9% of patients had no elevation in CRP (< 0.3 mg/dL) and 50.1% of patients had elevation in CRP (> 0.3 mg/dL). 82.8% of patients had no elevation in ESR (30 mm/hr or less) and 17.3% of patients had elevated ESR (> 30 mm/hr). 53.7% of patients had elevation of either CRP or ESR, 46.3% of patients had both normal CRP and ESR, and 13.7% of patients had elevation of both CRP and ESR. When assessing CRP and ESR elevation across the different lab results, there were no significant differences in PJI infection. Furthermore,

Table 1: Demographic distribution by surgery performed.

	Total Hip Arthroplasty N = 291	**Total Knee Arthroplasty N = 515**	**P-Value**
Median Age (IQR)[1]	55 (49-60)	62 (56-69)	< 0.0001
Gender[2]			
Female	161 (55.3%)	354 (68.7%)	0.0001
Male	130 (44.7%)	161 (31.3%)	
Body Mass Index[3]			
Underweight	5 (1.7%)	0 (0.0%)	< 0.0001
Normal	56 (19.2%)	44 (8.5%)	
Overweight	87 (29.9%)	110 (21.4%)	
Obese	143 (49.1%)	361 (70.1%)	
Avascular Necrosis[2]			
No	226 (77.7%)	515 (100.0%)	< 0.0001
Yes	65 (22.3%)	0 (0.0%)	
Positive Urinalysis[2]			
No	241 (82.8%)	424 (82.3%)	0.861
Yes	50 (17.2%)	91 (17.7%)	
Periprosthetic joint infection[2]			
No	281 (96.6%)	508 (98.6%)	0.0487
Yes	10 (3.4%)	7 (1.4%)	
Had Prior Surgery[2]			
No	257 (88.6%)	401 (77.9%)	0.0001
Yes	33 (11.4%)	114 (22.1%)	
Smoking Status[2]			
Former	90 (31.0%)	137 (26.6%)	< 0.0001
Never	130 (44.8%)	319 (61.9%)	
Current	70 (24.1%)	59 (11.5%)	
Diabetes Mellitus[2]			
No	240 (82.5%)	371 (72.0%)	0.0009
Yes	51 (17.5%)	144 (28.0%)	
Rheumatoid Arthritis[2]			
No	278 (95.5%)	501 (97.3%)	0.1851
Yes	13 (4.5%)	14 (2.7%)	
HIV[2]			
No	279 (95.9%)	503 (97.7%)	0.1502
Yes	12 (4.1%)	12 (2.3%)	
Renal Disease[2]			
No	264 (90.7%)	459 (89.1%)	0.4741
Yes	27 (9.3%)	56 (10.9%)	
Liver Disease[2]			
No	263 (90.4%)	470 (91.3%)	0.6744
Yes	28 (9.6%)	45 (8.7%)	
Congestive Heart Failure[2]			
No	270 (92.8%)	494 (95.9%)	0.0541
Yes	21 (7.2%)	21 (4.1%)	

Coagulation Condition[2]			
No	271 (93.1%)	486 (94.4%)	0.2486
Yes	20 (6.9%)	29 (5.6%)	
Positive CRP[2]			
Negative (lab of 0.3 or less)	132 (45.4%)	270 (52.4%)	0.054
Positive (lab greater than 0.3)	159 (54.6%)	245 (47.6%)	
Positive ESR[2]			
Negative (lab of 30 or less)	240 (82.5%)	427 (82.9%)	0.8743
Positive (lab greater than 30)	51 (17.5%)	88 (17.1%)	

[1]Wilcoxon-Mann-Whitney U test performed; [2]Chi Square was performed; [3]Fisher's Exact Test was performed

Table 2: Distribution of CRP and ESR elevation.

	Total Patient Population N = 806	**No PJI N = 789**	**PJI N = 17**	**P-Value**
Percent of Patients With Elevation of CRP				
Negative (lab of 0.3 or less)	402 (49.9%)	397 (50.3%)	5 (29.4%)	0.1392
Positive (lab greater than 0.3)	404 (50.1%)	392 (49.7%)	12 (70.6%)	
Percent of Patients With Elevation of ESR				
Negative (lab of 30 or less)	667 (82.8%)	667 (82.8%)	12 (58.8%)	0.1796
Positive (lab greater than 30)	139 (17.3%)	139 (17.3%)	5 (29.4%)	
Percent of Patients With Elevation of CRP or ESR				
Positive ESR or Positive CRP	373 (46.3%)	421 (52.2%)	5 (0.6%)	0.0557
Both ESR and CRP are Negative	433 (53.7%)	368 (45.7%)	12 (1.49%)	
Percent of Patients With Elevation of CRP and ESR				
Positive ESR and Positive CRP	696 (86.4%)	105 (13.0%)	5 (0.6%)	0.1586
Either ESR or CRP are Negative	110 (13.7%)	684 (84.9%)	12 (1.49%)	
Percent of Patients With Elevation of CRP but ESR is Negative				
Positive CRP and Negative ESR	294 (36.5%)	287 (35.6%)	7 (0.9%)	0.6841
CRP is Negative, and ESR can be positive/negative	512 (63.5%)	502 (62.3%)	10 (1.2%)	
Percent of Patients With Elevation of ESR but CRP is Negative				
Positive ESR and Negative CRP	29 (3.6%)	29 (3.6%)	0 (0.0%)	0.4208
ESR is Negative, and CRP can be positive/negative	777 (96.4%)	760 (94.3%)	17 (2.1%)	

Chi Square was performed

when combining ESR and CRP results there were no significant differences in PJI status across the combination labs.

Modifiable and non-modifiable risk factors

The distribution of modifiable and non-modifiable causative risk factors with associated elevations in CRP and/or ESR is detailed in Table 3. When assessing all potential causative risk factors (increased BMI, urinalysis, current smoking status, diabetes, rheumatoid arthritis, HIV, renal, liver, CHF, or coagulopathy), there were no significant differences across any combination of ESR and CRP labs. Elevations of ESR (p- value < 0.0001), and patients with positive CRP and negative ESR negative (p-value = 0.0132), were significantly associated with increased likelihood of having an unmodifiable risk factor (diabetes, rheumatoid arthritis, HIV, renal, liver, CHF, or coagulopathy). Similarly, elevations of ESR (p-value = 0.0039), along with positive CRP and negative ESR (p-value = 0.0051) were significantly associated with increased likelihood of having a modifiable risk factor (increased BMI, positive urinalysis, current smoking status).

Odds of PJI with elevated CRP and/or ESR

The full logistic model is presented in Table 4, and we found that a positive preoperative ESR significantly increases the odds of a positive preoperative CRP test (p-value < 0.0001). For each unit increase in ESR the odds of a positive CRP lab increase by a factor of 1.056 (95% CI: 1.040, 10.072). Additionally, the odds of a positive CRP was 1.973 times higher in patients who had a total hip arthroplasty when compared

Table 3: Distribution of CRP and ESR labs, by risk factors.

Potential Identifying Risk Factor: increased BMI, urinalysis, current smoking status, diabetes, rheumatoid arthritis, HIV, renal, liver, CHF, or coagulopathy.			
	Identifying Factor	**No Identifiying Factor**	**P-Value**
Percent of Patients With Elevation of CRP			
Negative (lab of 0.3 or less)	376 (46.7%)	26 (3.2%)	0.1093
Positive (lab greater than 0.3)	388 (48.1%)	16 (2.0%)	
Percent of Patients With Elevation of ESR			
Negative (lab of 30 or less)	633 (78.5%)	34 (4.2%)	0.7509
Positive (lab greater than 30)	131 (16.3%)	8 (1.0%)	
Percent of Patients With Elevation of CRP or ESR			
Positive ESR or Postive CRP	414 (51.4%)	19 (2.4%)	0.2574
Both ESR and CRP are Negative	350 (43.4%)	23 (2.9%)	
Percent of Patients With Elevation of CRP and ESR			
Positive ESR and Positive CRP	105 (13.0%)	5 (0.6%)	0.7354
Either ESR or CRP are Negative	659 (81.8%)	37 (4.6%)	
Percent of Patients With Elevation of CRP but ESR is Negative			
Positive CRP and Negative ESR	283 (35.1%)	11 (1.4%)	0.1549
CRP is Negative, and ESR can be positive/negative	481 (59.7%)	31 (3.9%)	
Percent of Patients With Elevation of ESR but CRP is Negative			
Positive ESR and Negative CRP	26 (3.2%)	3 (0.4%)	0.2052
ESR is Negative, and CRP can be positive/negative	738 (91.6%)	39 (4.8%)	
Unmodifiable Identifying Risk Factors: diabetes, rheumatoid arthritis, HIV, renal, liver, CHF, or coagulopathy			
	Identifying Factor	**No Identifiying Factor**	**P-Value**
Percent of Patients With Elevation of CRP			
Negative (lab of 0.3 or less)	178 (22.1%)	224 (27.8%)	0.4755
Positive (lab greater than 0.3)	189 (23.5%)	215 (26.7%)	
Percent of Patients With Elevation of ESR			
Negative (lab of 30 or less)	277 (34.4%)	390 (48.4%)	< 0.0001
Positive (lab greater than 30)	90 (11.2%)	49 (6.1%)	
Percent of Patients With Elevation of CRP or ESR			
Positive ESR or Positive CRP	207 (25.7%)	226 (28.0%)	0.1628
Both ESR and CRP are Negative	160 (19.9%)	213 (26.4%)	
Percent of Patients With Elevation of CRP and ESR			
Positive ESR and Positive CRP	72 (8.9%)	38 (4.7%)	< 0.0001
Either ESR or CRP are Negative	295 (36.6%)	401 (49.8%)	
Percent of Patients With Elevation of CRP but ESR is Negative			
Positive CRP and Negative ESR	117 (14.5%)	177 (22.0%)	0.0132
CRP is Negative, and ESR can be positive/negative	250 (31.0%)	262 (32.5%)	
Percent of Patients With Elevation of ESR but CRP is Negative			
Positive ESR and Negative CRP	18 (2.2%)	11 (1.4%)	0.0686
ESR is Negative, and CRP can be positive/negative	349 (43.3%)	428 (53.1%)	
Modifiable Identifying Risk Factors: increased BMI, urinalysis, or current smoking status,			
	Identifying Factor	**No Identifiying Factor**	**P-Value**
Percent of Patients With Elevation of CRP			

Negative (lab of 0.3 or less)	359 (44.5%)	43 (5.3%)	0.0039
Positive (lab greater than 0.3)	383 (47.5%)	21 (2.6%)	
Percent of Patients With Elevation of ESR			
Negative (lab of 30 or less)	616 (76.4%)	51 (6.3%)	0.4985
Positive (lab greater than 30)	126 (15.6%)	13 (1.6%)	
Percent of Patients With Elevation of CRP or ESR			
Positive ESR or Positive CRP	407 (50.5%)	26 (3.2%)	0.1022
Both ESR and CRP are Negative	335 (41.6%)	38 (4.7%)	
Percent of Patients With Elevation of CRP and ESR			
Positive ESR and Positive CRP	102 (12.7%)	8 (1.0%)	0.7804
Either ESR or CRP are Negative	640 (79.4%)	56 (6.9%)	
Percent of Patients With Elevation of CRP but ESR is Negative			
Positive CRP and Negative ESR	281 (34.9%)	13 (1.6%)	0.0051
CRP is Negative, and ESR can be positive/negative	461 (57.2%)	51 (6.3%)	
Percent of Patients With Elevation of ESR but CRP is Negative			
Positive ESR and Negative CRP	24 (3.0%)	5 (0.6%)	0.0592
ESR is Negative, and CRP can be positive/negative	718 (89.1%)	59 (7.3%)	

Chi Square was performed

Table 4: Full logistic model assessing positive C-reactive protein Labs.

	Crude Odds Ratio			Adjusted Odds Ratio		
	Estimate	**95% Confidence Interval**	**P-value**	**Estimate**	**95% Confidence Interval**	**P-value**
Erythrocyte Sedimentation Rate	1.057	(1.043, 1.072)	< 0.0001	1.056	(1.040, 1.072)	< 0.0001
Gender						
Female	1.684	(1.259, 2.253)	0.0004	1.063	(0.749, 1.509)	0.732
Male	Reference	Reference	Reference	Reference	Reference	Reference
Rheumatoid Arthritis						
Yes	6.036	(2.068, 17.612)	0.001	3.034	(0.873, 10.547)	0.0807
No	Reference	Reference	Reference	Reference	Reference	Reference
Procedure						
Total Hip Arthroplasty	1.311	(0.982, 1.750)	0.0664	1.973	(1.389, 2.803)	0.0001
Total Knee Arthroplasty	Reference	Reference	Reference	Reference	Reference	Reference
Periprosthetic joint infection						
Yes	2.442	(0.852, 6.995)	0.0964	1.641	(0.488, 5.519)	0.4235
No	Reference	Reference	Reference	Reference	Reference	Reference
Urinalysis						
Positive	1.543	(1.068, 2.231)	0.021	1.209	(0.794, 1.84)	0.3762
Negative	Reference	Reference	Reference	Reference	Reference	Reference
Smoking Status						
Former	0.695	(0.450, 1.073)	0.0397	0.54	(0.328, 0.888)	0.0116
Never	0.96	(0.648, 1.423)	0.3312	0.762	(0.482, 1.203)	0.8311
Current	Reference	Reference	Reference	Reference	Reference	Reference
Body Mass Index						
Underweight	0.478	(0.051, 4.446)	4.446	0.197	(0.015, 2.625)	0.1106
Normal	Reference	Reference	Reference	Reference	Reference	Reference

Overweight	0.906	(0.543, 1.511)	0.6108	0.977	(0.551, 1.732)	0.9197
Obese	2.906	(1.850, 4.565)	0.0006	4.102	(2.442, 6.89)	< 0.0001
Renal Disease						
Yes	1.207	(0.765, 1.904)	0.4186			
No	Reference	Reference	Reference			
Prior Surgery						
Yes	1.162	(0.812, 1.662)	0.4123			
No	Reference	Reference	Reference			
HIV						
Yes	1.187	(0.526, 2.683)	0.6795			
No	Reference	Reference	Reference			
Diabetes Mellitus						
Yes	0.885	(0.641, 1.223)	0.4594			
No	Reference	Reference	Reference			
Avascular Necrosis						
Yes	0.761	(0.455, 1.273)	0.2984			
No	Reference	Reference	Reference			
Revision						
Yes	1.134	(0.642, 2.001)	0.6647			
No	Reference	Reference	Reference			
Congestive Heart Failure						
Yes	0.695	(0.368, 1.315)	0.264			
No	Reference	Reference	Reference			
Coagulation Condition						
Yes	1.044	(0.586, 1.862)	0.8828			

to patients who had a total knee arthroplasty (95% CI: 1.389, 2.803; p-value = 0.0001). The odds of a positive CRP was 46% lower in patients who are former smokers, when compared to patients who currently smoke (95% CI: 0.328, 0.888; p-value = 0.0116). We also found that patients who were obese had a significantly (p-value < 0.0001) higher odds of having a positive CRP lab. The odds of an obese patient having a positive CRP lab were 4.102 times higher when compared to patients with a normal BMI (95% CI: 2.442, 6.89).

The results of the reduced model resulting from a stepwise regression are summarized by Table 5. The most parsimonious model consisted of ESR, procedure type, smoking status, and BMI. The odds of a positive CRP lab significantly (p-value < 0.0001) increases by 1.061 for each unit of ESR (95% CI: 1.046, 1.076). The odds of a positive CRP lab is 2.014 times higher (95% CI: 1.425, 2.845; p-value < 0.0001) in patients who underwent total hip arthroplasty, when compared to patients who underwent total knee arthroplasty. Furthermore, the odds of a positive CRP was 44.8% lower in patients who are former smokers, when compared to patients who currently smoke (95% CI: 0.336, 0.904; p-value = 0.0137). We also found that patients who were obese had a significantly (p-value < 0.0001) higher odds of having a positive CRP lab. The odds of an obese patient having a positive CRP lab were 4.203 times higher when compared to patients with a normal BMI (95% CI: 2.502, 7.059).

Discussion

To date, only a handful of studies have investigated preoperative ESR or CRP and the potential correlation with PJI. Results have been mixed; some studies have found a positive correlation while others have found no correlation [6,28-32]. Xu, et al. looked specifically at TKA in osteoarthritis patients. In their retrospective review of 3,376 cases, they found the overall prevalence of elevated preoperative inflammatory markers to be 4.1%. The rate of PJI was higher in patients with elevation of both CRP and ESR (12.5%) compared to either high (0.9%) or both normal groups (1.4%) [28]. In another retrospective review of 50 matched patients, Pfitzner, et al. found that the average preoperative CRP in the PJI group was 1.3 mg/dL vs. 0.4 mg/dL in the non-infected group. They recommend performing CRP on all patients before THA/TKA and suggest a threshold of 0.5 mg/dL in which you should perform further investigation as to a possible cause [29]. Although not specific to PJI, two additional studies have assessed preoperative CRP and outcomes in orthopaedic patients. In a study by Ghosh, et al. they found that patients with high preoperative CRP (> 3 mg/dL) may be at high risk of developing complications after postoperative day 14 and increased operative time [31]. Similarly, in a study by Ackland, et al. they found that in patients with higher preoperative CRP, there was an increase in delayed post-operative

Table 5: Reduced Logistic Model Assessing Positive C-Reactive Protein Labs.

	Estimate	95% Confidence Interval	P-Value
Erythrocyte Sedimentation Rate	1.061	(1.046, 1.076)	< 0.0001
Procedure			
Total Hip Arthroplasty	2.014	(1.425, 2.845)	< 0.0001
Total Knee Arthroplasty	Reference	Reference	Reference
Smoking Status			
Former	0.552	(0.336, 0.904)	0.0137
Never	0.773	(0.492, 1.215)	0.8103
Current	Reference	Reference	Reference
Body Mass Index			
Underweight	0.193	(0.015, 2.542)	0.1015
Normal	Reference	Reference	Reference
Overweight	1.028	(0.582, 1.817)	0.8377
Obese	4.203	(2.502, 7.059)	< 0.0001

complications and longer length of stay [32].

In a retrospective review of 351 TKAs, Godroy, et al. found no statistical difference between CRP or ESR and any complications. The overall number of infections in this group was 8, only 2 of which were considered deep infections [6]. Another study looked specifically at preoperative CRP on patients with femoral neck fracture before they underwent hemiarthroplasty. The overall infection rate was 4.85%. Their study did not validate the use of CRP levels or suggest a threshold that was predictive of pre-existing infection before performing a hemiarthroplasty for femoral neck fracture [30].

In our study, which is the second largest cohort to date that investigates preoperative inflammatory markers before primary TJA, we found no statistically significant correlation between pre-operative CRP or ESR and PJI. In total, 806 primary TJA cases were reviewed (515 TKA, 291 THA). The rate of PJI was 2.1%. We did find that a higher proportion of patients with PJI had elevated preoperative CRP (70.6%) versus those with normal CRP (29.4%); however, among patients without PJI, the preoperative CRP was still found to be elevated > 0.3 mg/dL in half of all patients (49.7%). ESR followed a different trend with only 29.4% of patients with PJI having an elevated preoperative ESR. Looking at the overall cohort, just over half of all patients with or without PJI had elevated preoperative CRP (50.1%), while only 17.3% of all patients had elevated ESR.

While our results regarding the correlation of preoperative CRP and ESR with PJI do not meet statistical significance, they do highlight an important finding. There is a large proportion of patients with elevated preoperative CRP and ESR that undergo primary TJA and most of them do not go on to develop a PJI. Given these findings, we investigated risk factors among our cohort of patients to see if there was a correlation. No study to date on the topic of TJA and preoperative CRP/ESR has investigated this. Among all patients with elevated preoperative CRP or ESR, we identified a potential risk factor in 95.6% of cases, with risk factors including increased BMI, positive urinalysis, current smoking status, diabetes mellitus, rheumatoid arthritis, HIV, renal disease, liver disease, CHF, and coagulopathy. Furthermore, 94.0% of the time, at least one modifiable risk factor was present, which we defined as increased BMI, positive urinalysis, and current smoking status. This finding can be explained by the fact that CRP/ESR are both non-specific inflammatory markers and, as such, are often elevated in patients with chronic disease which involves a systemic inflammatory response. A publication by Watson, et al. looked specifically at idiopathically elevated CRP and ESR in patients undergoing primary TKA. They found that higher BMI was correlated with higher levels of preoperative CRP and ESR [33]. Our study supports this same finding; patients with BMI in the obese category (> 30), were more likely to have elevated preoperative CRP level (OR 4.2, $p < 0.0001$). Lastly, data in Table 2 displays an interesting finding. Patients with elevation in CRP or ESR (Table 2) begins to closely approach statistical significance ($p = 0.0557$), indicating that pre-operative elevation in either CRP or ESR is sensitive for potential correlation with PJI. This highlights that there is value in obtaining these pre-operative labs despite the results not being statistically significant.

Even after identifying numerous potential inflammatory risk factors, there were still nearly 5% of cases in which there were no identifiable risk factors. This is potentially explained by the disease process of osteoarthritis itself inherently leading to an inflammatory response. A study by Takahashi investigated this, showing elevation of CRP in patients with generalized osteoarthritis and a positive correlation of elevated inflammatory markers with Kellgren-Lawrence scale of arthritis severity [34]. Similar findings were seen in a study that looked at CRP and ESR in patients with and without knee osteoarthritis. They found a positive correlation of elevated ESR and CRP with higher Kellgren-Lawrence grade in patients with knee osteoarthritis [35]. No literature, to our knowledge, has investigated this concept in hip osteoarthritis as both aforementioned studies were specific to knee osteoarthritis. In our study, we saw a slightly higher proportion of hip

arthritis patients with elevated preoperative labs than knee arthritis patients, as 54.6% of all patients who underwent THA had elevation in preoperative CRP, versus 47.6% of all TKA patients.

Weaknesses of our study include its retrospective nature and relatively low amount of total PJI (n = 17). To definitively identify a correlation with PJI, we would need thousands of patients in our cohort to investigate a highly substantial number of total PJIs. Despite this, our study does highlight the fact that there is a substantial number of patients that demonstrate elevated pre-op inflammatory markers, and most of them do not go on to develop PJI after primary TJA. Improved documentation in future studies could be helpful for increasing sample size and thus achieving a high statistical power. This study was unable to address the percentage of the time that a modifiable risk factor could have been addressed and resolved prior to surgery. This information was unable to be analyzed due to inconsistent documentation, which could be in part due to the retrospective nature of this study. A prospective analysis may have allowed the participating physicians to create a dataset as they operated for which patients' risk factors were able to be addressed. This information could be of clinical significance when compared to postoperative outcomes in this patient cohort versus those that were not able to have modifiable risk factors resolved prior to surgery. Future studies should aim at providing a high-powered study seeking a more definitive answer on this topic since the results thus far have been mixed, in addition to longer term follow-up and investigation into other complications (e.g., thromboembolic disease, stiffness, instability, and loosening).

Conclusions

This study is unable to validate the use of preoperative CRP/ESR as a predictive measure of future risk of PJI in primary TJA. However, it does provide quantitative insight into the prevalence of elevated preoperative inflammatory markers in all patients prior to TJA with a considerable proportion of patients having modifiable risk factors. Even then, there are still patients with elevated inflammatory markers and no known cause, which may be attributed to osteoarthritis itself. Because almost half of all patients studied were found to have elevated CRP/ESR, we cannot provide a firm recommendation in favor of or against the utility of obtaining these preoperative labs. Since there is such a large proportion of patients with elevated inflammatory markers that do not go on to develop PJI, we do not recommend cancellation of TJA unless there is an obvious identified modifiable risk factor that puts them at increased risk of PJI. Interestingly, we found that once we removed obesity as a modifiable risk factor, much of our data that was previously statistically significant became no longer significant. This shines important light onto the effect of obesity on elevation of inflammatory markers, especially CRP when ESR was negative. Lastly, we found that elevation in either CRP or ESR closely approached statistical significance for correlation with PJI, indicating perhaps some sensitivity for development of PJI. Our study does not refute the use of CRP/ESR in the setting of diagnosis and treatment of PJI after TJA, as this remains one of the gold standard biochemical markers.

Contributors

James-Michael Blackwell, MPH, Andrew Merwin, MD.

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