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Increased *Staphylococcus aureus* nasal carriage rates in Rheumatoid Arthritis patients on biologic therapy

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Abstract

Background: Rheumatoid arthritis patients are at increased risk for periprosthetic joint infection after arthroplasty. The reason is multifactorial. Nasal colonization with *Staphylococcus aureus* is a modifiable risk factor; carriage rates in RA patients is unknown. The goal of this study was to determine the *S. aureus* nasal carriage rates of RA patients on biologics, RA patients on traditional DMARDs, and osteoarthritis.

Methods: Consecutive patients with RA on biologics (+/- DMARDs), RA on non-biologic DMARDs, or OA were prospectively enrolled from April 2017 to May 2018 123 patients were determined necessary per group to show a difference in carriage rates. Patients underwent a nasal swab and answered questions to identify additional risk factors. *S. aureus* positive swabs were further categorized using Spa typing. Logistic regression evaluated the association with *S. aureus* colonization between the groups after controlling for known risk factors.

Results: RA patients on biologics, 70% of whom were on DMARDs, had statistically significant increase in *S. aureus* colonization (37%) compared to RA on DMARDs alone (24%), or OA (20%) $p = 0.01$ overall. After controlling for glucocorticoids, antibiotic use, recent hospitalization, and diabetes, RA on biologics had a significant increased risk of *S. aureus* nasal colonization (OR=1.80, 95% CI 1.00-3.22); $p=0.047$).

Conclusion: *S. aureus* colonization risk was increased for RA on biologics compared to RA not on biologics and OA. Nasal *S. aureus* carriage increases the risk of surgical site infection; this

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modifiable risk factor should be addressed prior to total joint arthroplasty for this higher risk patient group.

Keywords

S. aureus colonization; rheumatoid arthritis; osteoarthritis; biologics; tumor necrosis factor inhibitors (TNFi); periprosthetic joint infection

Introduction

Patients with rheumatoid arthritis (RA) are at increased risk of periprosthetic joint infection (PJI) and surgical site infection (SSI) after total joint arthroplasty, as compared to patients with osteoarthritis (OA)(1,2). The increased risk of infection is multifactorial and may relate to inherent immunologic dysregulation associated with the disease which may not be modifiable, while treatment with biologics disease modifying anti-rheumatic drugs (DMARDs) medications is a presumptive risk factor for surgical site infection, the association has been hard to define. Although biologics are routinely discontinued at the time of arthroplasty to mitigate the risk of infection, RA patients continue to have an increased risk of complication.

Nasal colonization with *S. aureus* has been identified as a significant risk factor for surgical site infection (3,4), but the prevalence of nasal colonization in patients with RA, and the factors that increase the risk of *S. aureus* colonization in patients with RA are not well established. In the general population, the prevalence of *S. aureus* colonization has been reported at 30% (5). In cross-sectional studies performed in rheumatology outpatient clinics, persistence of *S. aureus* colonization was shown to be greater in RA patients on tumor necrosis factor inhibitors (TNFi) compared to those not on a TNFi, especially if they were on combination TNFi plus MTX treatment, however the absolute rate of *S. aureus* colonization was similar to RA patients on DMARDs alone (6-8).

The purpose of this study was to determine if 1.) *S. aureus* colonization prevalence is different among RA patients on biologics, RA patients on traditional DMARDs, or OA, and 2.) Thereby identify an actionable risk factor for surgical site infection in patients with RA. We also assessed the relative prevalence of methicillin-susceptible (MSSA) and methicillin-resistant *S. aureus* (MRSA) in the study cohort as well as genetic variations in *S. aureus* in the study cohort and measured DNA sequence variation in the polymorphic region of *S. aureus* protein A as genetic marker for strain typing. Our hypothesis is that RA patients, both on or not on a biologic, would have a higher rate of *S. aureus* colonization than OA patients, and that treatment with a biologic medication would further increase the colonization rate.

Methods and Study Design

Patients

This study prospectively enrolled 369 adults 18 years of age diagnosed with either RA or OA in 3 equal groups of 123 patients based on an a priori power analysis to detect a relative difference of 20% among groups with 80% power. The 3 groups included: 1.) RA patients on biologics, who could also be on traditional DMARDs, 2.) RA patients not on biologics

but could be on traditional DMARDs, and 3.) lower extremity (hip and knee) OA patients. We included the oral small molecule tofacitinib among the biologics in light of the similar mechanism of action as a targeted therapy. For RA patients not on biologics, treatments could include DMARDs or alternative therapies. All patients were seen in outpatient clinics at a tertiary care orthopedic specialty hospital between April 2017 and May 2018. The RA cohort met the ACR 1987 or 2010 criteria for the diagnosis of RA (9,10). Patients in the OA group met 1991 ACR classification criteria for the diagnosis of OA. After inclusion criteria were verified, patients were concurrently enrolled into one of the three groups, assuring that one group did not enroll more than the others during each season to avoid the possibility of *S. aureus* carrier change with seasonal variation. Patients were excluded if they had systemic lupus erythematosus (SLE) or another autoimmune disease, active infection, or had received antibiotics within the month prior to recruitment. Demographic and clinical data, including age, sex, BMI, smoking history, prior hospitalizations, and medication history (including disease modifying anti-rheumatic drugs (DMARDs), biologics, and history of glucocorticoid use) was collected. The study was approved by our local Institutional Review Board.

Nasal swab Collection and Processing

Sterile cotton swabs (S/P® Brand CultureSwab Swab, Becton, Dickinson and Company, Cardinal Health, McGraw Park, IL) were used. Patients were instructed on how to perform a nasal swab using the Center for Disease Control's swabbing protocol and performed the nasal swab themselves in the presence of a research assistant. Patients then placed the swab into its sterile tube which was then immediately transferred to a 4.5-degree Celsius (range 2-8 °C) refrigerator. Swabs were stored in the refrigerator for no more than 14 days and were then sent for plating and evaluation at New York University, Division of Infectious Disease and Immunology lab. There, swabs were inoculated directly onto BBL ChromAgar/ChromID MRSA *Staph aureus* medium (Becton, Dickinson and Company, Cardinal Health, McGraw Park, IL) and incubated at 37°C for 48 h. Mauve colonies that grew only on ChromAgar plates and protein A were presumptively considered MSSA. Organisms that also grew on ChromID MRSA plates were presumptively identified as MRSA. Individual colonies were streaked onto sheep blood agar (5% on trypticase soy agar; Remel, Lenexa, KS) and incubated overnight at 37°C. The presence of the Protein A and methicillin-resistance genes was confirmed on all suspected *S. aureus* by polymerase chain reaction analysis of the *spa* and *mecA* genes, respectively (11,12).

Bacterial genotyping

The relatedness of *S. aureus* strains was determined by DNA sequence analysis of the protein A gene variable repeat region (*spa* typing) (12). *spa* types were used to identify multilocus sequence typing (MLST) clonal complexes, using the Ridom SpaServer database (available at: <http://spa.ridom.de/mlst.shtml>) (13).

Statistical analysis

An *a priori* power analysis determined 123 participants per group were needed to detect a relative difference of 20% *S. aureus* carriage among groups with 80% power. Mann-Whitney U and Chi-square tests were used to evaluate baseline differences between groups. A univariate analysis was initially performed and significant differences between the groups

were identified. An unadjusted subanalysis was also included to explore the association between groups and *S. aureus* carriage when OA was the reference group. A logistic regression controlling for age, BMI, diabetes, glucocorticoid use, antibiotics within 3 months, and hospitalization, was then used to evaluate the association between the 3 groups and *S. aureus* carriage. All statistical analyses were performed using SAS Software version 9.3 (SAS Institute, Cary, NC); statistical significance was defined as $p < 0.05$.

Results

Overall 369 patients were prospectively enrolled in the study and underwent nasal swab testing. The mean (standard deviation) age was 66 (SD 13.7), BMI 29 (SD 28.2), 78% were female, 7% had diabetes, 28% received antibiotics 31-90 days prior to the nasal swab, 24% had been hospitalized within the last year, and 18% were actively on glucocorticoids. Patients with osteoarthritis were more likely to have diabetes ($p=0.04$), to have been hospitalized in the last year ($p=0.0001$), and to have received antibiotics 31-90 days prior ($p=0.0001$) than patients in either RA group, whereas RA patients were more likely to be smokers ($p=0.009$), female ($p < 0.0001$), and to have received glucocorticoids ($p=0.02$) (Table 1). For RA patients on biologics, the most common were adalimumab (28%), etanercept (25.2%), abatacept (12.2%), and rituximab (12.2%) (Table 2). 86 (70%) of the biologics group were also on a traditional DMARD.

In the RA group not on biologics, 65% were on methotrexate, 16% on hydroxychloroquine, 11% on leflunomide, and 1.6% on sulfasalazine (Table 3).

S. aureus colonization and characteristics

In all three groups combined, 99 (26.83%) had a positive cultures for *S. aureus*. A univariate analysis was performed and demonstrated significant differences between the groups in *S. aureus* carriage. *S. aureus* carriage was most prevalent in RA patients on biologics (37%), followed by RA not on a biologic (24%), and OA (20%). For patients taking both biologics and traditional DMARDs combined, 35% grew *S. aureus*, of which 17% were MRSA. There was no difference in MRSA prevalence for those on combination therapy ($p=0.55$) compared to those on biologics alone. In an unadjusted sub analysis using OA as the reference group, there was no significant increase in *S. aureus* risk for RA (OR 1.2 (95% CI 0.66-2.2), while for RA+ biologics, the risk was increased OR 2.3(95%CI 1.3-4.0) (Table 4). After multivariate adjustment, the RA+ biologics group was found to have a significant increased odds of *S. aureus* colonization (OR=1.80, 95% CI 1.00-3.22); $p=0.047$) compared to the RA group not on biologics (Table 5). The OA group had a trend towards decreased odds of *S. aureus* growth when compared to the RA group; however this was not found to be statistically significant ($p=0.99$). Use of glucocorticoids, antibiotics, recent hospitalization, or diabetes did not influence the odds of *S. aureus* carriage in the multivariable regression analysis.

Overall, among 100 *S. aureus*-colonized patients, 8% were colonized by MRSA and 92% were colonized by MSSA. All isolates underwent PCR-sequencing of the staphylococcal protein A (*spa*) repeat region to determine the genetic relatedness of *S. aureus* isolates (12). This method, known as *spa* typing, is a front line DNA sequence-based typing method to

determine the genetic relatedness of *S. aureus* isolates. Sixty-eight different *spa* types were identified, with no one genotype accounting for more than 8% of the strains. The distribution of the four predominant *spa* clusters, based on the pattern of the repeat region, is similar to that recently described for MSSA in the United States (*spa* cluster frequencies: t002, 17%; t012, 16%; t008, 11%; t084, 8%)(14). Thus, genotypic diversity was high, consistent with the high proportion of MSSA in the study population and the high degree of genetic diversity associated with MSSA compared to MRSA strains (14). Comparison of *spa* type diversity among nasal isolates from 74 RA patients with those of 25 OA patients demonstrated that both groups were nonclonal and equally diverse. Thus, there was no evidence of clustering of *spa* types by diagnosis, and colonizations did not reflect dissemination of an outbreak strain, which could skew results.

Discussion:

This study demonstrates that patients with RA treated with biologics have an increased risk of *S. aureus* nasal colonization. While *S. aureus* carriage was most prevalent in patients with RA on biologics (37%), nasal *S. aureus* carriage was present in 24% of RA not on biologics, and 20% of patients with OA. RA treated with traditional DMARDs without biologic therapy was not an independent risk factor for *S. aureus* carriage, but treatment with biologics increased the risk of nasal *S. aureus* carriage by 80%. Moreover, those patients taking both biologics and traditional DMARDs have the same risk for *S. aureus* carriage as those on biologics alone; suggesting that the heightened risk of colonization is associated with use of biologic medications. While more patients with RA on biologics also received glucocorticoids, glucocorticoid use was not an independent risk factor for *S. aureus* carriage. It was surprising that OA patients were significantly more likely to have diabetes, to have received a prior antibiotic, and to have been hospitalized during the 3 months prior to obtaining the culture; nonetheless, fewer OA patients had positive *S. aureus* nasal carriage. Neither antibiotic use, hospitalization, nor diabetes were independent risk factors for *S. aureus* colonization.

S. aureus is the most common cause of overall hospital acquired infections (4,15-18), and is the most common pathogen identified in skin and soft tissue infection in patients with RA being treated with either TNFi or traditional DMARDs (4,18,19). In addition, where microbiologic diagnosis for septic arthritis including PJI was available, *S. aureus* was the most frequently reported organism in RA patients whether they were treated with TNFi (57%) or a traditional DMARDs (43%) (20). DMARDs and biologics are known to increase infection risk and are often in use by RA patients at the time of arthroplasty (21,22), but the association of DMARDs and biologics with surgical arthroplasty infections has not been directly established through randomized controlled trials performed in patients undergoing surgery (23,24). However, in a registry database study, the risk of septic arthritis including PJI was doubled for RA patients treated with TNFi, and a meta-analysis of surgical site infection in patients exposed to TNFi also showed an elevated infection risk (OR 2.47, 95% CI 1.66, 3.68) (20,25). However, a pharmaco-epidemiologic study using a large insurance database did not find an association between infliximab use and infection after arthroplasty (23). Altered immune function in active RA increases the risk of infection, and active RA at

the time of arthroplasty may contribute to increased risk of PJI infection in these patients (26,27).

While prior studies have not demonstrated a difference in *S. aureus* colonization for patients with RA overall, small numbers, or possibly inclusion of patients with less severe RA, may have prevented identification of medication-associated risks (7,8). However, in this study, neither recent hospitalization nor glucocorticoid use, surrogate measures for disease severity, influenced the risk of *S. aureus* carriage.

Only 8 of the 99 (8%) nasal swab colonized patients had MRSA. This is comparable to the results seen in earlier studies demonstrating a low frequency of MRSA colonization among individuals in the community (28). Indeed, community acquired (CA)-MRSA USA300 (*spa* type 1/t008, positive for staphylococcal cassette chromosome *mec* type IV [SCC*mec* IV], *pvl*, and the arginine catabolic mobile element [ACME]) was identified in isolates from 2% of patients in recent studies (29-31).

This study has certain limitations. Cultures were only obtained by nasal swab, as the association with surgical site infections is strongest with nares cultures; however, while the addition of other sites such as the throat or the surgical site might increase in culture yield, the increase is unlikely to be large (4, 32-34). Moreover, a difference in carriage would likely affect all three tested groups equally. In addition, patients performed the swabs, which might have introduced error, although they were instructed and observed by a member of the research team. While the low baseline colonization rate of 20% among OA patients might indicate our assay was not sensitive, this would indicate a higher rate among RA patients as the assay sensitivity would affect all groups equally. We were unable to analyze colonization risk differences between the biologics due to small number in each group. We also found little differences in genetic variation; however, this may be due to limitations in sample size as genetic associations require much larger samples. Finally, as with all observational studies, although we controlled for known risk factors, unmeasured confounders may also play a role.

We believe that our findings may have clinical impact in the perioperative care of RA patients. Decolonization of surgical patients may reduce risks of surgical site infection, but implementation of institutional programs to decolonize all perioperative patients empirically, or to screen and treat, can be cumbersome and have not been shown to be cost-effective (35). Common decolonization techniques include mupirocin and chlorhexidine at home, versus single-application treatment with a commercial iodine preparation just prior to incision. RA patients on biologics, who we have identified as higher risk of *S. aureus* colonization, as well as an increased baseline risk of infection, are a cohort which might benefit maximally from such a universal perioperative decolonization protocol.

In conclusion, this study demonstrates that patients with RA treated with biologics have an increased prevalence of *S. aureus* nasal colonization. Since nasal *S. aureus* carriage may play a role in the pathogenesis of surgical infections, our results help explain the increase in surgical infections in RA patients on TNF inhibitors, and support the use of decolonization

protocols in order to potentially decrease the increased risk of PJI seen in patients with RA undergoing joint replacement surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Ravi B, Croxford R, Hollands S, et al. Increased risk of complications following total joint arthroplasty in patients with rheumatoid arthritis. *Arthritis Rheumatol*. 2014;66(2):254–263. [PubMed: 24504797]
2. Schrama JC, Espehaug B, Hallan G, et al. Risk of revision for infection in primary total hip and knee arthroplasty in patients with rheumatoid arthritis compared with osteoarthritis: A prospective, population-based study on 108,786 hip and knee joint arthroplasties from the norwegian arthroplasty register. *Arthritis Care Res (Hoboken)*. 2010;62(4):473–479. [PubMed: 20391501]
3. Liu Z, Norman G, Iheozor-Ejiofor Z, Wong JK, Crosbie EJ, Wilson P. Nasal decontamination for the prevention of surgical site infection in staphylococcus aureus carriers. *Cochrane Database Syst Rev*. 2017;5:CD012462. [PubMed: 28516472]
4. Kluytmans JA, Mouton JW, Ijzerman EP, et al. Nasal carriage of staphylococcus aureus as a major risk factor for wound infections after cardiac surgery. *J Infect Dis*. 1995;171(1):216–219. [PubMed: 7798667]
5. Gorwitz RJ, Kruszon-Moran D, McAllister SK, et al. Changes in the prevalence of nasal colonization with staphylococcus aureus in the united states, 2001–2004. *J Infect Dis*. 2008;197(9):1226–1234. [PubMed: 18422434]
6. Bassetti S, Wasmer S, Hasler P, et al. Staphylococcus aureus in patients with rheumatoid arthritis under conventional and anti-tumor necrosis factor-alpha treatment. *J Rheumatol*. 2005;32(11):2125–2129. [PubMed: 16265689]
7. Albert G, Ricse M, Narvaez J, et al. Prevalence of nasal colonization with staphylococcus aureus in patients with rheumatoid arthritis. *Curr Rheumatol Rev*. 2018;14(1):78–83. [PubMed: 29057725]
8. Varley CD, Deodhar AA, Ehst BD, et al. Persistence of staphylococcus aureus colonization among individuals with immune-mediated inflammatory diseases treated with TNF-alpha inhibitor therapy. *Rheumatology (Oxford)*. 2014;53(2):332–337. [PubMed: 24173434]
9. Radner H, Neogi T, Smolen JS, Aletaha D. Performance of the 2010 ACR/EULAR classification criteria for rheumatoid arthritis: A systematic literature review. *Ann Rheum Dis*. 2014;73(1):114–123. [PubMed: 23592710]
10. Arnett FC, Edworthy SM, Bloch DA, et al. The american rheumatism association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum*. 1988;31(3):315–324. [PubMed: 3358796]
11. Herold BC, Immergluck LC, Maranan MC, et al. Community-acquired methicillin-resistant staphylococcus aureus in children with no identified predisposing risk. *JAMA*. 1998;279(8):593–598. [PubMed: 9486753]

12. Shopsis B, Gomez M, Montgomery SO, et al. Evaluation of protein A gene polymorphic region DNA sequencing for typing of staphylococcus aureus strains. *J Clin Microbiol.* 1999;37(11):3556–3563. [PubMed: 10523551]
13. Harmsen D, Claus H, Witte W, et al. Typing of methicillin-resistant staphylococcus aureus in a university hospital setting by using novel software for spa repeat determination and database management. *J Clin Microbiol.* 2003;41(12):5442–5448. [PubMed: 14662923]
14. Miko BA, Hafer CA, Lee CJ, et al. Molecular characterization of methicillin-susceptible staphylococcus aureus clinical isolates in the united states, 2004 to 2010. *J Clin Microbiol.* 2013;51(3):874–879. [PubMed: 23284029]
15. Ravi B, Croxford R, Hollands S, et al. Increased risk of complications following total joint arthroplasty in patients with rheumatoid arthritis. *Arthritis Rheumatol.* 2014;66(2):254–263. [PubMed: 24504797]
16. Doran MF, Crowson CS, Pond GR, O'Fallon WM, Gabriel SE. Frequency of infection in patients with rheumatoid arthritis compared with controls: A population-based study. *Arthritis Rheum.* 2002;46(9):2287–2293. [PubMed: 12355475]
17. von Eiff C, Becker K, Machka K, Stammer H, Peters G. Nasal carriage as a source of staphylococcus aureus bacteremia. study group. *N Engl J Med.* 2001;344(1):11–16. [PubMed: 11136954]
18. van Rijen M, Bonten M, Wenzel R, Kluytmans J. Mupirocin ointment for preventing staphylococcus aureus infections in nasal carriers. *Cochrane Database Syst Rev.* 2008; (4):CD006216. doi(4):CD06216.
19. Galloway JB, Mercer LK, Moseley A, et al. Risk of skin and soft tissue infections (including shingles) in patients exposed to anti-tumour necrosis factor therapy: Results from the british society for rheumatology biologics register. *Ann Rheum Dis.* 2013;72(2):229–234. [PubMed: 22532633]
20. Galloway JB, Hyrich KL, Mercer LK, et al. Risk of septic arthritis in patients with rheumatoid arthritis and the effect of anti-TNF therapy: Results from the british society for rheumatology biologics register. *Ann Rheum Dis.* 2011;70(10):1810–1814. [PubMed: 21784730]
21. Singh JA, Cameron C, Noorbaloochi S, et al. Risk of serious infection in biological treatment of patients with rheumatoid arthritis: A systematic review and meta-analysis. *Lancet.* 2015.
22. Goodman SM, Bykerk VP, DiCarlo E, et al. Flares in patients with rheumatoid arthritis after total hip and total knee arthroplasty: Rates, characteristics, and risk factors. *J Rheumatol.* 2018;45(5): 604–611. [PubMed: 29545451]
23. George MD, Baker JF, Hsu JY, et al. Perioperative timing of infliximab and the risk of serious infection after elective hip and knee arthroplasty. *Arthritis Care Res (Hoboken).* 2017;69(12): 1845–1854. [PubMed: 28129484]
24. Johnson BK, Goodman SM, Alexiades MM, Figgie MP, Demmer RT, Mandl LA. Patterns and associated risk of perioperative use of anti-tumor necrosis factor in patients with rheumatoid arthritis undergoing total knee replacement. *J Rheumatol.* 2013;40(5):617–623. [PubMed: 23547213]
25. Goodman SM, Menon I, Christos PJ, Smethurst R, Bykerk VP. Management of perioperative tumour necrosis factor alpha inhibitors in rheumatoid arthritis patients undergoing arthroplasty: A systematic review and meta-analysis. *Rheumatology (Oxford).* 2016;55(3):573–582. [PubMed: 26447162]
26. Au K, Reed G, Curtis JR, et al. High disease activity is associated with an increased risk of infection in patients with rheumatoid arthritis. *Ann Rheum Dis.* 2011;70(5):785–791. [PubMed: 21288960]
27. Goodman SM, Bykerk VP, DiCarlo E, et al. Flares in patients with rheumatoid arthritis after total hip and total knee arthroplasty: Rates, characteristics, and risk factors. *J Rheumatol.* 2018;45(5): 604–611. [PubMed: 29545451]
28. Gorwitz RJ, Kruszon-Moran D, McAllister SK, et al. Changes in the prevalence of nasal colonization with staphylococcus aureus in the united states, 2001–2004. *J Infect Dis.* 2008;197(9):1226–1234. [PubMed: 18422434]

29. Gorwitz RJ, Kruszon-Moran D, McAllister SK, et al. Changes in the prevalence of nasal colonization with staphylococcus aureus in the united states, 2001–2004. *J Infect Dis.* 2008;197(9):1226–1234. [PubMed: 18422434]
30. Shopsis B, Gomez M, Montgomery SO, et al. Evaluation of protein A gene polymorphic region DNA sequencing for typing of staphylococcus aureus strains. *J Clin Microbiol.* 1999;37(11):3556–3563. [PubMed: 10523551]
31. Harmsen D, Claus H, Witte W, et al. Typing of methicillin-resistant staphylococcus aureus in a university hospital setting by using novel software for spa repeat determination and database management. *J Clin Microbiol.* 2003;41(12):5442–5448. [PubMed: 14662923]
32. Antri K, Akkou M, Bouchiat C, et al. High levels of staphylococcus aureus and MRSA carriage in healthy population of algiers revealed by additional enrichment and multisite screening. *Eur J Clin Microbiol Infect Dis.* 2018.
33. Brown J, Li CS, Giordani M, et al. Swabbing surgical sites does not improve the detection of staphylococcus aureus carriage in high-risk surgical patients. *Surg Infect (Larchmt).* 2015;16(5):523–525. [PubMed: 26114763]
34. Young BC, Votintseva AA, Foster D, et al. Multi-site and nasal swabbing for carriage of staphylococcus aureus: What does a single nose swab predict? *J Hosp Infect.* 2017;96(3):232–237. [PubMed: 28246002]
35. Williams DM, Miller AO, Henry MW, Westrich GH, Ghomrawi HMK. Cost-effectiveness of staphylococcus aureus decolonization strategies in high-risk total joint arthroplasty patients. *J Arthroplasty.* 2017;32(9S):S91–S96. [PubMed: 28341280]

Table 1:

Characteristics of the cohort and differences between the groups

Variable	All Patients (n=369)	RA + Biologic (n=123)	RA no Biologic (n=123)	OA (n=123)	p-value
Age (Mean $\pm$ SD)	65.63 $\pm$ 13.77	59.15 $\pm$ 14.4	65.82 $\pm$ 13.86	71.91 $\pm$ 9.51	<0.0001
Sex: female, n (%)	289 (78.32)	108 (87.8)	106 (86.18)	75 (60.98)	<0.0001
BMI, kg/m ² (Mean $\pm$ SD)	28.17 $\pm$ 7.00	27.98 $\pm$ 7.12	26.36 $\pm$ 6.08	30.19 $\pm$ 7.25	<0.0001
Ethnicity, Hispanic or Latino, n (%)	27 (7.32)	8 (6.5)	14 (11.38)	5 (4.07)	-
Race, White, n (%)	294 (79.67)	87 (70.73)	97 (78.86)	110 (89.43)	-
Synthetic DMARDS n (%)					
Methotrexate	139 (37.67)	59 (47.97)	80 (65.04)	-	-
Leflunomide	30 (8.13)	17 (13.82)	13 (10.57)	-	-
Hydroxychloroquine	29 (7.86)	9 (7.32)	20 (16.26)	-	-
Sulfasalazine	3 (0.81)	1 (0.81)	2 (1.63)	-	-
Smoker (ever), n (%)	148 (40.11)	43 (34.96)	42 (34.15)	63 (51.22)	-
Smoker (current), n (%)	19 (12.84)	10 (23.26)	6 (14.29)	3 (4.76)	-
Diabetes, n (%)	27 (7.32)	6 (4.88)	6 (4.88)	15 (12.2)	0.04
Hospitalization in past year n (%)	89 (24.12)	22 (17.89)	14 (11.38)	53 (43.09)	<0.0001
Glucocorticoids, n (%)	67 (18.16)	32 (26.02)	18 (14.63)	17 (13.82)	0.02
Antibiotics in past 3 months, n (%)	104 (28.18)	29 (23.58)	21 (17.07)	54 (43.90)	<0.0001
Years since RA diagnosis (Mean $\pm$ SD)	11.55 $\pm$ 10.70	13.55 $\pm$ 11.01	9.55 $\pm$ 10.03	0	-
Years since OA diagnosis (Mean $\pm$ SD)	24.17 $\pm$ 176.99	0	0	25.54 $\pm$ 181.94	-
Positive <i>S. aureus</i> growth, n(%)	99 (26.83)	45 (36.59)	29 (23.58)	25 (20.33)	0.01

Table 2:

Biologic Use among RA patients

Biologic	Frequency (%)
Adalimumab	35 (28.5)
Etanercept	31 (25.2)
Abatacept	15 (12.2)
Rituximab	15 (12.2)
Tocilizumab	9 (7.3)
Infliximab	7 (5.7)
Golimumab	4 (3.3)
Tofacitinib	4 (3.3)
Certolizumab	2 (1.6)
Sarilumab	1 (1.0)

Table 3:

Synthetic DMARD Use in Patients with RA, RA + Biologics, and OA

Synthetic DMARDS n (%)	RA + Biologics	RA	OA
Methotrexate	59 (47.97)	80 (65.04)	0
Leflunomide	17 (13.82)	13 (10.57)	0
Hydroxychloroquine	9 (7.32)	20 (16.26)	0
Sulfasalazine	1 (0.81)	2 (1.63)	0

Table 4:

Unadjusted sub-analysis using OA as a reference group

Group	OR (Unadjusted)	p-value
OA vs. RA	1.2 (0.66-2.2)	0.54
OA vs. RA+B	2.3 (1.3-4.0)	0.01

Table 5:Multivariable Regression of the Risk of *S. aureus* colonization

Effect	OR		95% Wald Confidence Limits	p-value
OA vs. RA no biologics	0.99	0.50	1.96	0.98
RA + biologics vs. RA no biologics	1.80	1.01	3.22	0.047
Age	0.99	0.97	1.01	0.21
BMI	1.01	0.97	1.04	0.66
Sex (Male vs. Female)	0.80	0.43	1.50	0.49
Diabetes (Yes vs. No)	1.29	0.52	3.19	0.59
Glucocorticoids use (Yes vs. No)	0.79	0.42	1.48	0.46
Antibiotics in past 3 months (Yes vs. No)	0.88	0.50	1.56	0.66
Hospitalized in past year (yes vs. no)	0.82	0.44	1.53	0.52

Multivariable analysis controlling for age, BMI, Diabetes, Glucocorticoid use, antibiotics within 3 months, and hospitalization. Bold values indicate significant data.