JSES International 7 (2023) 601–606

Contents lists available at ScienceDirect

JSES International

journal homepage: www.jsesinternational.org

Abnormal preoperative leukocyte counts and postoperative complications following total shoulder arthroplasty

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ARTICLE INFO

Keywords:
Total shoulder arthroplasty
Reverse shoulder arthroplasty
Leukopenia
Leukocytosis
Postoperative complications
Readmission

Level of evidence: Level III; Retrospective Cohort Comparison Using Large Database; Prognosis Study

Background: Total shoulder arthroplasty (TSA) has become the mainstay of treatment for degenerative glenohumeral arthritis, proximal humerus fracture, and rotator cuff arthropathy. The expanding indications for reverse TSA have increased the overall demand for TSA. This necessitates higher quality preoperative testing and risk stratification. White blood cell counts can be obtained from routine preoperative complete blood count testing. The association between abnormal preoperative white blood cell counts and postoperative complications has not been extensively studied. The purpose of this study was to investigate the association between abnormal preoperative leukocyte counts and 30-day postoperative complications following TSA.

Methods: The American College of Surgeons National Surgical Quality Improvement Program database was queried for all patients who underwent TSA between 2015-2020. Patient demographics, comorbidities, surgical characteristics, and 30-day postoperative complication data were collected. Multivariate logistic regression was used to identify postoperative complications associated with preoperative leukopenia and leukocytosis.

Results: In this study, 23,341 patients were included: 20,791 (89.1%) were in the normal cohort, 1307 (5.6%) were in the leukopenia cohort, and 1243 (5.3%) were in the leukocytosis cohort. Preoperative leukopenia was significantly associated with higher rates of bleeding transfusions ($P = .011$), deep vein thrombosis ($P = .037$), and non–home discharge ($P = .041$). After controlling for significant patient variables, preoperative leukopenia was independently associated with higher rates of bleeding transfusions (odds ratios [OR] 1.55, 95% confidence intervals [CI] 1.08-2.23; $P = .017$) and deep vein thrombosis (OR 2.26, 95% CI 1.07-4.78; $P = .033$). Preoperative leukocytosis was significantly associated with higher rates of pneumonia ($P < .001$), pulmonary embolism ($P = .004$), bleeding transfusions ($P < .001$), sepsis ($P = .007$), septic shock ($P < .001$), readmission ($P < .001$), and non–home discharge ($P < .001$). After controlling for significant patient variables, preoperative leukocytosis was independently associated with higher rates of pneumonia (OR 2.20, 95% CI 1.30-3.75; $P = .004$), pulmonary embolism (OR 2.43, 95% CI 1.17-5.04; $P = .017$), bleeding transfusions (OR 2.00, 95% CI 1.46-2.72; $P < .001$), sepsis (OR 2.95, 95% CI 1.20-7.25; $P = .018$), septic shock (OR 4.91, 95% CI 1.38-17.53; $P = .014$), readmission (OR 1.36, 95% CI 1.03-1.79; $P = .030$), and non–home discharge (OR 1.61, 95% CI 1.35-1.92; $P < .001$).

Conclusion: Preoperative leukopenia is independently associated with higher rates of deep vein thrombosis within 30 days following TSA. Preoperative leukocytosis is independently associated with higher rates of pneumonia, pulmonary embolism, bleeding transfusion, sepsis, septic shock, readmission, and non–home discharge within 30 days following TSA. Understanding the predictive value of abnormal preoperative lab values will aid in perioperative risk stratification and minimize postoperative complications.

Over the past decade, total shoulder arthroplasty (TSA) has become the mainstay of treatment for degenerative glenohumeral arthritis, proximal humerus fracture, and rotator cuff arthropathy.[7,12,13,18] The number of primary TSAs performed each year is projected to reach at least 37,000 by the year 2040 due to the

Institutional review board approval was not required for this study.

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https://doi.org/10.1016/j.jseint.2023.03.001

expanding indications for reverse TSA.[16] A significant contribution to this increase will be from the treatment of fracture-related cases in patients over 80 years of age.[14,16,23] However, there is also growing demand for TSA in younger patients, with a projected increase of 333.3% from 2011 to 2030 for patients under 55 years of age.[22,26] With increasing demand regardless of age, higher quality preoperative risk stratification will help to optimize outcomes in a diverse patient population with a potentially higher incidence of medical comorbidities.

The preoperative evaluation can typically include routine laboratory tests such as the complete blood count (CBC), metabolic panels, and coagulation studies. Previous studies have reported on the predictive value of preoperative hematocrit levels prior to TSA. These studies reported that patients with anemia, based on the preoperative hematocrit, were at increased risk for blood transfusion and postoperative complication.[4,15,21] Studies have also reported on the predictive value of other preoperative lab results, including the international normalized ratio and blood urea nitrogen, and their associated postoperative complications after TSA.[6,24]

White blood cell (WBC) count is a component of the CBC that has not been extensively studied in relation to postoperative complications. WBCs are involved in immune system function and can be indicative of the body's inflammatory response to various etiologies.[25] Studies investigating the postoperative complications associated with preoperative leukocytosis are limited to cardiac and vascular surgery.[2,5,9,19] Within the realm of orthopedic surgery, studies on leukocyte counts are limited to postoperative leukocytosis following total hip (THA) and knee arthroplasty (TKA).[10,11]

The purpose of this study was to investigate the association between abnormal preoperative leukocyte counts and 30-day postoperative complications following TSA. We hypothesized that preoperative leukopenia and leukocytosis are associated with higher rates of infectious complications and readmission following TSA.

Methods

The authors queried the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database for all patients who underwent TSA between 2015-2020. This study was deemed exempt from approval by our university's institutional review board, as the NSQIP database is fully deidentified. Data in the NSQIP database is obtained from over 600 hospitals in the United States and is collected by trained surgical clinical reviewers. The data is periodically audited to maintain high fidelity.

The current procedural terminology code 23472 was used to identify patients who underwent TSA, both anatomic and reverse, from 2015 to 2020. The exclusion criteria inherent to the NSQIP database excludes all cases for patients younger than 18 years of age or TSA performed for cases classified as trauma. Cases were also excluded if any of the following variables had missing information: height/weight, discharge destination, American Society of Anesthesiologists (ASA) classification, functional health status, readmission status, and preoperative leukocyte counts.

Variables collected in this study included patient demographics, comorbidities, preoperative laboratory values, and 30-day postoperative complication data. Patient demographics included gender, body mass index (BMI), age, smoking status, functional health status, ASA classification, and preoperative steroid use. Preoperative comorbidities included insulin-dependent and non−insulin-dependent diabetes, severe chronic obstructive pulmonary disease (COPD), congestive heart failure, hypertension, disseminated cancer, open wound/wound infection, bleeding disorders, and transfusion prior to surgery. Preoperative laboratory values included leukocyte counts and hematocrit. Complications that occurred within 30 days postoperatively were included in the analysis. These complications included pneumonia, superficial incisional surgical site infection (SSI), deep incisional SSI, organ/space SSI, wound dehiscence, reintubation, pulmonary embolism, ventilator >48 hours, urinary tract infection, stroke, cardiac arrest, myocardial infarction, bleeding transfusion, deep vein thrombosis, sepsis, septic shock, readmission, reoperation, and non−home discharge.

The initial pool of patients was divided into three cohorts based on preoperative leukocyte counts: leukopenia, normal, and leukocytosis. Patients in the leukopenia cohort had leukocyte counts <4500. Patients in the normal cohort had leukocyte counts between 4500 and 11,000. Patients in the leukocytosis cohort had leukocyte counts >11,000.

A total of 27,050 patients underwent primary TSA in the NSQIP from 2015-2020. Cases were excluded as follows: 152 for missing height/weight, 11 for missing discharge destination, 29 for missing ASA classification, 227 for missing functional health status prior to surgery, 2 for missing 30-day readmission status, and 3288 for missing preoperative leukocyte counts. Of the 23,341 patients remaining after exclusion criteria, 20,791 (89.1%) were in the normal cohort, 1307 (5.6%) were in the leukopenia cohort, and 1243 (5.3%) were in the leukocytosis cohort.

All statistical analyses were conducted using SPSS Software version 26.0 (IBM Corp., Armonk, NY, USA). Patient demographics and comorbidities were compared between cohorts using bivariate analysis. Multivariate logistic regression, adjusted for all significantly associated patient demographics and comorbidities, was used to identify associations between preoperative leukopenia or leukocytosis and postoperative complications. Odds ratios (OR) were reported with 95% confidence intervals (CI). The level of statistical significance was set at $P < .05$.

Results

Patient demographics and comorbidities that were significantly associated with preoperative leukopenia were age between 40-64 ($P < .001$), BMI between 18.5-29.9 ($P < .001$), ASA classification 1-2 ($P < .001$), chronic steroid use ($P = .005$), bleeding disorders ($P = .017$), and preoperative anemia ($P < .001$) (Table I). Compared to the normal cohort, the leukopenia cohort had lower rates of current smoking status ($P < .001$), COPD ($P < .001$), and hypertension ($P < .001$). Patient demographics and comorbidities that were significantly associated with preoperative leukocytosis were age between 18-39 ($P = .006$), BMI <18.5 ($P < .001$) or BMI >35.0 ($P < .001$), female sex ($P < .001$), dependent functional status ($P < .001$), ASA classification ≥3 ($P < .001$), insulin-dependent ($P < .001$) and non−insulin-dependent diabetes ($P < .001$), current smoking status ($P < .001$), COPD ($P < .001$), hypertension ($P < .001$), disseminated cancer ($P < .001$), chronic steroid use ($P < .001$), bleeding disorders ($P = .006$), transfusion prior to surgery ($P < .001$), and preoperative anemia ($P < .001$).

Bivariate analysis was used to determine postoperative complications associated with preoperative leukopenia and preoperative leukocytosis (Table II). The 30-day postoperative complications that were significantly associated with leukopenia were bleeding transfusions ($P = .011$), deep vein thrombosis ($P = .037$), and non−home discharge ($P = .041$). The 30-day postoperative complications that were significantly associated with leukocytosis were pneumonia ($P < .001$), pulmonary embolism ($P = .004$), bleeding transfusions ($P < .001$), sepsis ($P = .007$), septic shock ($P < .001$), readmission ($P < .001$), and non−home discharge ($P < .001$).

After adjusting for all significantly associated patient variables, multivariate logistic regression identified the 30-day postoperative

Table I
Patient characteristics for patients who underwent TSA with normal preoperative leukocyte count, preoperative leukopenia, and preoperative leukocytosis.

Characteristic	Normal		Leukopenia			Leukocytosis		
	Number	Percent	Number	Percent	*P* value	Number	Percent	*P* value
Total	20,791	100.0%	1307	100.0%		1243	100.0%	
Age					**.007**			**.006**
18-39	94	0.5%	6	0.5%		12	1.0%	
40-64	5487	26.4%	405	31.0%		360	29.0%	
65-74	8747	42.1%	537	41.1%		477	38.4%	
≥75	6463	31.1%	359	27.5%		394	31.7%	
Body mass index (kg/m^2)					**<.001**			**<.001**
<18.5	136	0.7%	16	1.2%		19	1.5%	
18.5-29.9	9879	47.5%	774	59.2%		518	41.7%	
30.0-34.9	5586	26.9%	295	22.6%		323	26.0%	
35.0-39.9	2969	14.3%	131	10.0%		204	16.4%	
≥40.0	2221	10.7%	91	7.0%		179	14.4%	
Gender					.878			**<.001**
Female	11,599	55.8%	732	56.0%		804	64.7%	
Male	9192	44.2%	575	44.0%		439	35.3%	
Functional status					.930			**<.001**
Independent	20,354	97.9%	1280	97.9%		1189	95.7%	
Dependent	437	2.1%	27	2.1%		54	4.3%	
ASA classification					**<.001**			**<.001**
1-2	8679	41.7%	608	46.5%		395	31.8%	
≥3	12,112	58.3%	699	53.5%		848	68.2%	
Diabetes mellitus					.211			**<.001**
No	16,981	81.7%	1142	87.4%		908	73.0%	
Noninsulin	2736	13.2%	104	8.0%		226	18.2%	
Insulin	1074	5.2%	61	4.7%		109	8.8%	
Current smoker					**<.001**			**<.001**
No	18,710	90.0%	1233	94.3%		997	80.2%	
Yes	2081	10.0%	74	5.7%		246	19.8%	
COPD					**<.001**			**<.001**
No	19,386	93.2%	1250	95.6%		1083	87.1%	
Yes	1405	6.8%	57	4.4%		160	12.9%	
Congestive heart failure					.881			.195
No	20,655	99.3%	1298	99.3%		1231	99.0%	
Yes	136	0.7%	9	0.7%		12	1.0%	
Hypertension					**<.001**			**<.001**
No	6799	32.7%	540	41.3%		321	25.8%	
Yes	13,992	67.3%	767	58.7%		922	74.2%	
Disseminated cancer					.479			**<.001**
No	20,747	99.8%	1303	99.7%		1232	99.1%	
Yes	44	0.2%	4	0.3%		11	0.9%	
Open wound/wound infection					.216			.057
No	20,714	99.6%	1305	99.8%		1234	99.3%	
Yes	77	0.4%	2	0.2%		9	0.7%	
Chronic steroid use					**.005**			**<.001**
No	19,840	95.4%	1225	93.7%		1094	88.0%	
Yes	951	4.6%	82	6.3%		149	12.0%	
Bleeding disorders					**.017**			**.006**
No	20,269	97.5%	1260	96.4%		1196	96.2%	
Yes	522	2.5%	47	3.6%		47	3.8%	
Transfusion prior to surgery					.325			**<.001**
No	20,748	99.8%	1306	99.9%		1231	99.0%	
Yes	43	0.2%	1	0.1%		12	1.0%	
Anemia (male Hct < 39, female Hct < 36)					**<.001**			**<.001**
No	17,229	82.9%	964	73.8%		937	75.4%	
Yes	3537	17.0%	342	26.2%		304	24.5%	

ASA, American Society of Anesthesiologists; *COPD*, chronic obstructive pulmonary disease; *TSA*, total shoulder arthroplasty.
Bold *P* values indicate statistical significance with $P < .05$.

complications associated with preoperative leukopenia and leukocytosis (Table III). Multivariate analysis found preoperative leukopenia to be independently associated with higher rates of deep vein thrombosis (OR 2.28, 95% CI 1.08-4.84; $P = .031$). Multivariate analysis also identified preoperative leukocytosis to be independently associated with higher rates of pneumonia (OR 2.14, 95% CI 1.26-3.77; $P = .005$), pulmonary embolism (OR 2.40, 95% CI 1.15-4.99; $P = .019$), bleeding transfusions (OR 1.78, 95% CI 1.29-2.44; $P < .001$), sepsis (OR 2.80, 95% CI 1.13-6.93; $P = .026$), septic shock (OR 4.70, 95% CI 1.29-17.10; $P = .019$), readmission (OR 1.33, 95% CI 1.01-1.75; $P = .046$), and non–home discharge (OR 1.55, 95% CI 1.30-1.85; $P < .001$).

Discussion

In this study, we reported on 30-day postoperative complications associated with preoperative leukopenia and preoperative leukocytosis in patients who underwent TSA from 2015-2020 using a large national database. Our analysis included 23,341 patients, of whom 20,791 (89.1%) had normal preoperative leukocyte counts,

Table II
Bivariate analysis of 30-day postoperative complications in patients with normal preoperative leukocyte count, preoperative leukopenia, and preoperative leukocytosis.

Complication	Normal		Leukopenia			Leukocytosis		
	Number	Percent	Number	Percent	*P* value	Number	Percent	*P* value
Pneumonia	102	0.49%	4	0.31%	.353	17	1.37%	**<.001**
Superficial incisional SSI	57	0.27%	3	0.23%	.764	4	0.32%	.756
Deep incisional SSI	12	0.06%	1	0.08%	.786	1	0.08%	.75
Organ/Space SSI	45	0.22%	3	0.23%	.921	5	0.40%	.188
Wound dehiscence	14	0.07%	2	0.15%	.277	0	0.00%	–
Reintubation	41	0.20%	1	0.08%	.349	5	0.40%	.132
Pulmonary embolism	53	0.25%	2	0.15%	.478	9	0.72%	**.004**
Ventilator >48 hours	23	0.11%	0	0.00%	–	3	0.24%	.204
Urinary tract infection	150	0.72%	8	0.61%	.649	12	0.97%	.33
Stroke	19	0.09%	0	0.00%	–	2	0.16%	.446
Cardiac arrest	13	0.06%	0	0.00%	–	0	0.00%	–
Myocardial infarction	61	0.29%	2	0.15%	.346	3	0.24%	.741
Bleeding transfusions	357	1.72%	35	2.68%	**.011**	54	4.34%	**<.001**
Deep vein thrombosis	58	0.28%	8	0.61%	**.037**	3	0.24%	.806
Sepsis	30	0.14%	1	0.08%	.532	6	0.48%	**.007**
Septic shock	8	0.04%	0	0.00%	–	4	0.32%	**<.001**
Readmission	609	2.93%	36	2.75%	.716	61	4.91%	**<.001**
Reoperation	281	1.35%	18	1.38%	.938	21	1.69%	.321
Non–home discharge	1803	8.67%	92	7.04%	**.041**	198	15.93%	**<.001**

SSI, surgical site infection.
Bold *P* values indicate statistical significance with $P < .05$.

Table III
Multivariate analysis of 30-day postoperative complications in patients with preoperative leukopenia and preoperative leukocytosis, adjusted for significantly associated patient demographics/comorbidities.

Complication	Leukopenia			Leukocytosis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Pneumonia	0.62	0.23-1.70	.354	2.14	1.26-3.77	**.005**
Pulmonary embolism	0.64	0.15-2.64	.531	2.40	1.15-4.99	**.019**
Bleeding transfusions	1.15	0.80-1.65	.456	1.78	1.29-2.44	**<.001**
Deep vein thrombosis	2.28	1.08-4.84	**.031**	0.71	0.22-2.32	.573
Sepsis	0.54	0.07-4.02	.550	2.80	1.13-6.93	**.026**
Septic shock	–	–	–	4.70	1.29-17.10	**.019**
Readmission	0.95	0.67-1.34	.768	1.33	1.01-1.75	**.046**
Non–home discharge	0.79	0.63-1.00	.134	1.55	1.30-1.85	**<.001**

OR, odds ratio; *CI*, confidence interval.
Bold *P* values indicate statistical significance with $P < .05$.

1307 (5.6%) had preoperative leukopenia, and 1243 (5.3%) had preoperative leukocytosis. Through bivariate analysis, we identified preoperative leukopenia to be significantly associated with bleeding transfusions, deep vein thrombosis, and non–home discharge. We also identified preoperative leukocytosis to be significantly associated with pneumonia, pulmonary embolism, bleeding transfusions, sepsis, septic shock, readmission, and non–home discharge. After controlling for significant patient demographics and comorbidities, we identified preoperative leukopenia to be independently associated with higher rates of deep vein thrombosis. We also identified preoperative leukocytosis to be independently associated with higher rates of pneumonia, pulmonary embolism, bleeding transfusions, sepsis, septic shock, readmission, and non–home discharge.

In recent years, TSA has gained increasing popularity as the treatment of choice for degenerative diseases of the shoulder.[17] The incidence of TSA performed each year has increased substantially, with a concomitant decrease in the incidence of hemiarthroplasty.[7] The indications for reverse TSA have also expanded to include proximal humerus fractures, posttraumatic reconstruction, and failed prior arthroplasty.[26] Consequently, the increase in the annual incidence of TSA is projected to greatly outpace that of total hip (THA) and knee arthroplasty (TKA). From 2017 to 2025, there is a projected 235% increase in annual volume, compared to 47% and 22% for THA and TKA, respectively.[26] Given this increasing demand, higher quality preoperative risk stratification based on preoperative lab testing may help to minimize adverse outcomes.

With the overall increase in surgical volume for TSA, outpatient TSA has also been gaining popularity. Several studies have reported that outpatient TSA can be a safe, cost-effective alternative to inpatient TSA in appropriately selected patients.[1,8,20] While there is currently no established algorithm for patient selection for outpatient TSA, the results of our study may suggest the utility of preoperative CBC as a screening tool for patient selection.

Routine preoperative and postoperative laboratory tests for arthroplasty can include CBCs, metabolic panels, and coagulation studies. There is no clear consensus on the utility of routine perioperative laboratory tests for THA, TKA, or TSA. A recent study by Angerame et al suggested that routine perioperative testing may not be necessary in all patients undergoing THA and TKA. Angerame et al concluded that medical comorbidities and abnormal preoperative lab tests should guide the decision to obtain postoperative lab testing.[3] However, their conclusion was solely based on whether abnormal labs led to actionable medical interventions. Hence, their study does acknowledge that abnormal preoperative labs can still predict adverse outcomes.

More specifically, studies investigating WBC count in arthroplasty are limited to the postoperative periods for THA and TKA.[10,11] These studies are also limited to leukocytosis and do not investigate leukopenia. Similar studies investigating WBC count have not been done for TSA, and therefore, this study can help address the paucity of literature.

Our study investigated leukopenia and leukocytosis as categorical variables, with the leukopenia cohort having leukocyte counts <4500 and the leukocytosis cohort having leukocyte counts >11,000. Although the degree of leukocytosis may indicate the severity of the disease, only 0.7% of the included patients had leukocyte counts greater than 15,000. Therefore, we did not assess leukocytosis as a continuous variable and maintained it as categorical.

Our study identified preoperative leukopenia to be an independent risk factor for deep vein thrombosis following TSA. Patients with preoperative leukopenia had significantly higher rates

of chronic steroid use and bleeding disorders preoperatively. Our study also identified preoperative leukocytosis to be an independent risk factor for pneumonia, pulmonary embolism, bleeding transfusion, sepsis, septic shock, readmission, and non–home discharge following TSA. Patients with preoperative leukocytosis had significantly higher rates of dependent functional status, ASA $\geq$3, diabetes mellitus, current smoking status, COPD, hypertension, disseminated cancer, chronic steroid use, bleeding disorders, and transfusions preoperatively. The common comorbidities between the cohorts were chronic steroid use and bleeding disorders. Chronic steroid use has been shown to be an independent risk factor for postoperative complications following TSA.[17] However, this was controlled for in our multivariate analysis.

Of note, while preoperative leukocytosis was associated with sepsis and septic shock, it was not associated with SSI. This may be the result of preexisting infection during the preoperative period that was unrecognized. Alternatively, due to the expanded indications of TSA to include proximal humerus fracture, the preoperative period may have been limited in managing an existing infection. Regardless of the cause, physicians should be aware of the higher risk of postoperative sepsis and septic shock when managing patients with preoperative leukocytosis.

The findings of our study suggest that patients with preoperative leukocytosis tend to be sicker, with more medical comorbidities. These patients are at greater risk for postoperative complications that may require rehospitalization, leading to increased medical costs and decreased patient satisfaction. Therefore, these patients may require a higher level of postoperative care with a more thorough work-up for possible complications. Our findings also suggest that patients with preoperative leukocytosis may not be proper candidates for outpatient TSA, given the increased risk for many complications.

Of the NSQIP database, one key limitation is that postoperative complication data is only collected up to 30 days postoperatively. Therefore, complications that occur outside of the 30-day postoperative period are not available. Another limitation is that the database is not able to determine the etiology of the abnormal WBC count. Therefore, we were unable to determine whether abnormal leukocyte counts were acute or chronic in nature. However, we attempted to account for this by including significant patient variables in our multivariate analysis. Future studies are needed to compare complication rates between acute vs. chronic leukocytosis, as acute leukocytosis may be a modifiable risk factor in the preoperative period. Additionally, the NSQIP database does not account for relevant operative variables such as experience of the surgeon, institution where the procedure was performed, and postoperative rehabilitation. Regardless of these limitations, this is the first study to investigate postoperative complications associated with preoperative leukopenia and preoperative leukocytosis in patients undergoing TSA. Moreover, we used a large national database that included 23,341 cases of TSA over a 6-year period.

Conclusion

Preoperative leukopenia is independently associated with higher rates of deep vein thrombosis following TSA. Preoperative leukocytosis is independently associated with higher rates of pneumonia, pulmonary embolism, bleeding transfusion, sepsis, septic shock, readmission, and non–home discharge. As indications for TSA continue to expand, the patient population grows to include patients who are older and have more chronic comorbidities. Understanding the predictive value of abnormal preoperative lab values will aid in perioperative risk stratification and minimize postoperative complications.

Disclaimers:

Funding: No funding was disclosed by the authors.
Conflicts of interest: The authors, their immediate families, and any research foundation with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

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