

Rheumatoid arthritis patients undergoing total hip and knee arthroplasty have better in-hospital outcomes compared with non-rheumatoid arthritis patients

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Abstract

Objective

Rheumatoid arthritis (RA) is known to be associated with multiple comorbidities and, therefore, overall management is critical for those patients undergoing elective major orthopaedic surgeries, such as total hip arthroplasty (THA) and total knee arthroplasty (TKA). The purpose of this study was to compare in-hospital outcomes of elective THA and TKA between patients with and without RA in the US during the last decade. We hypothesised that patients with RA would have similar perioperative outcomes after elective THA and TKA.

Methods

Clinical data were derived from the US Nationwide Inpatient Sample (NIS) between 2000 and 2009. Patients who underwent elective THA and TKA were identified. Data regarding patient- and healthcare system-related characteristics, comorbidities, in-hospital complications, and mortality were retrieved. In-hospital outcomes of the procedures were compared between patients with and without RA.

Results

Comparison between patients with and without RA showed that patients with RA had significantly lower overall in-hospital complication rates following THA and TKA, and lower in-hospital mortality rate following THA. Patients with RA undergoing THA and TKA had decreased risk of overall in-hospital complications compared to those without RA.

Conclusion

Contrary to our hypothesis, perioperative outcomes of elective THA and TKA in patients with RA were better than those in patients without RA. These results may indicate that patient selection and pre- and perioperative management of patients with RA undergoing elective THA and TKA were well conducted in the US during the last decade.

Key words

rheumatoid arthritis, total hip arthroplasty, total knee arthroplasty, elective surgery, complication, mortality, Nationwide Inpatient Sample

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Introduction

Although widespread use of potent disease-modifying drugs and biologic therapy has improved the outlook for patients with rheumatoid arthritis (RA) (1), orthopaedic surgery maintains a significant role in the management of end-stage joints (2). Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are among the major orthopaedic surgeries for patients with RA. The need for THA and TKA has been a severe long-term consequence for patients with RA (3).

RA is known to be associated with a multitude of comorbidities and has the potential to deteriorate different organ systems (4). Cardiovascular disease, pulmonary disease, and osteoporosis are the well-known comorbidities for patients with RA. Drug treatment for RA has improved markedly and decreased the risk of comorbidities such as cardiovascular disease (5, 6). However, such medications are also associated with certain comorbidities. Furthermore, immunosuppressive agents can increase the risk of postoperative infection (2). Therefore, decisions regarding management of medications must be made in the perioperative period, balancing the RA disease activity and the negative effects of medication therapy (2).

Patients with RA undergoing major surgical procedures such as THA and TKA require careful preoperative assessment for optimal outcomes and fewer adverse events (2). The purpose of this study was to compare in-hospital outcomes of elective THA and TKA procedures between patients with RA and without RA, using population-based national hospital discharge data collected for the Nationwide Inpatient Sample (NIS) during the last decade. In addition, the risks of RA for those outcomes were analysed with the use of logistic regression. We hypothesised that patients with RA would have similar perioperative outcomes as compared to those without RA after elective THA and TKA.

Materials and methods

Data source

The NIS is the largest all-payer inpatient care database in the US and contains data from approximately 8 mil-

lion hospital stays from 1,000 hospitals each year. These data comprise a 20% stratified sample of all US community hospitals (7). Each entry in the database represents a single hospitalisation record. Records in the NIS database include discharge and hospital information, which was used to generate national estimates in this analysis. The Nationwide Inpatient Sample is publicly available and contains no personal identifying information; therefore, this study was exempt from institutional review board approval.

Patient selection

Our study samples were retrospectively obtained from the NIS between 2000 and 2009, using codes from the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM). Patients aged ≥ 18 who underwent primary THA (81.51), and primary TKA (81.54) were included in this study. ATYPE 3 (code for elective admission) was included to exclude confounding cases such as fracture cases. The data of these patients were then sorted according to the presence (714.0, 714.1, 714.2) and absence of RA.

Patient- and healthcare system-related characteristics and patient outcomes

Patient age, gender, race, comorbidities, hospital size, hospital teaching status, hospital region, payer information, complications, mortality, and disposition of patients were extracted from the NIS. Patients were categorised into the following four groups according to age: "18–44 years," "45–64 years," "65–84 years," and "older than 84 years." Patients were also categorised according to race as "white," "black," "Hispanic," "others," and "not stated." Comorbidity was assessed using the Elixhauser method, which is a well-established technique for identifying comorbidities from administrative databases (8). Elixhauser comorbidity index includes a set of 30 medical comorbidities. A diagnosis of RA was excluded in this study. Total comorbidity score was determined for each case by adding 1 point per comorbidity. Hospital size (bed number) was categorised into "small," "medium," and "large", while hospital teaching sta-

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Competing interests: none declared.

tus was categorised into “non-teaching” and “teaching.” Hospital census region was categorised into “Northeast,” “Midwest,” “South,” and “West,” and the payer information was categorised into “Medicare,” “Medicaid,” “private,” and “others.” In-hospital complications were obtained using the following ICD-9-CM codes: neurologic complications (997.00–997.09); respiratory complications (518.4, 518.5, 518.81–518.84, 997.3); cardiac complications (410, 997.1); gastrointestinal complications (535.0, 570, 575.0, 577.0, 997.4); urinary and renal complications (584, 997.5); pulmonary embolism (415.1); wound-related complications including infection, dehiscence, seroma, and haematoma (998.1, 998.3, 998.5, 998.83, 999.3). Four-digit and 5-digit codes were included under the respective 3-digit and 4-digit codes. Disposition of patients was categorised into “routine,” “transfer to short-term hospital,” “other transfers,” “home health care,” “died in hospital,” and “other.” Other transfers include skilled nursing facility, intermediate care, and any other type of facility.

Data analysis

To calculate national estimates using the NIS, discharge weights supplied by the Federal Agency for Healthcare Research and Quality (AHRQ) were applied. Categorical patient data were retrieved. The *t*-test was used to compare the means of continuous variables between the 2 groups. Characteristics between the 2 groups were assessed using χ^2 tests for equality of proportion or Fisher’s exact test. Logistic regression models were used to determine the contribution of RA on perioperative outcomes, controlling for age, gender, race, Elixhauser Comorbidity Score, hospital size, hospital teaching status, hospital region, payer information and complications. Statistical analyses were performed with R v. 2.15.1 (Free Software Foundation’s GNU General Public License). Because of the large sample size, a *p*-value of 0.001 was used to define significant differences.

Results

Between 2000 and 2009, there were 1,802,382 patients aged ≥ 18 who under-

Table IA. Patient demographics of patients ≥ 18 who underwent elective THA between 2000 and 2009.

	RA		Non-RA		<i>p</i> -value
	WF	%	WF	%	
Total number of cases	50689		1751693		
Mean age (yr) (SD)	63.4 (13.1)		65.2 (12.9)		<0.001
Mean Elixhauser Comorbidity score*	1.54		1.50		0.001
Age					<0.001
18–44	4345	8.6%	111243	6.4%	
45–64	20550	40.5%	666973	38.1%	
65–84	24630	48.6%	902571	51.5%	
≥ 85	1164	2.3%	70906	4.0%	
Gender					<0.001
Male	12620	24.9%	773698	44.2%	
Female	38069	75.1%	977925	55.8%	
Race					<0.001
White	29919	59.0%	1086741	62.0%	
Black	3331	6.6%	77106	4.4%	
Hispanic	2085	4.1%	28424	1.6%	
Others	1125	2.2%	34966	2.0%	
Not stated	14229	28.1%	524456	29.9%	
Elixhauser Comorbidity score*					<0.001
0	11422	22.5%	403600	23.0%	
1	16153	31.9%	578366	33.0%	
2	12820	25.3%	428786	24.5%	
3	6538	12.9%	218858	12.5%	
4 or more	3756	7.4%	122084	7.0%	
Hospital size					<0.001
Small	6500	12.8%	258379	14.8%	
Medium	12240	24.1%	418660	23.9%	
Large	31838	62.8%	1070970	61.1%	
No information	111	0.2%	3684	0.2%	
Hospital teaching status					<0.001
Non-teaching	24742	48.8%	888059	50.7%	
Teaching	25837	51.0%	859951	49.1%	
No information	110	0.2%	3683	0.2%	
Hospital region					<0.001
Northeast	11329	22.4%	422316	24.1%	
Midwest	14220	28.1%	519551	29.7%	
South	19353	38.2%	594593	33.9%	
West	5787	11.4%	215233	12.3%	
Payer information					<0.001
Medicare	29015	57.2%	940459	53.7%	
Medicaid	2415	4.8%	49579	2.8%	
Private	17793	35.1%	705694	40.3%	
Others	1397	2.8%	53320	3.0%	

RA: rheumatoid arthritis; THA: total hip arthroplasty; WF: weighted frequency; *Diagnosis of RA is excluded.

went elective THA, and 3,815,319 patients aged ≥ 18 who underwent elective TKA. Among them, 50,689 patients for THA and 121,349 patients for TKA had a diagnosis of RA (Table IA, IB). The mean age of patients with and without RA undergoing THA procedures was 63.4 and 65.2 years, respectively, and, that undergoing TKA was 64.3 and 66.8 years. The mean Elixhauser comorbidity score excluding a diagnosis of RA was not significantly different between patients with and without RA for both THA and TKA.

Overall in-hospital complication rates of both THA and TKA were signifi-

cantly lower in patients with RA than in those without RA (THA: 4.8% vs. 6.3%; TKA: 4.9% vs. 6.2%, respectively; $p < 0.001$) (Table IIA, IIB). The in-hospital mortality rate of THA was significantly lower in patients with RA than in those without RA (THA: 0.05% vs. 0.15%; $p < 0.001$) (Table IIA). There was no significant difference between those patients for the in-hospital mortality of TKA; however, the rate in patients with RA decreased from 0.12% (2000–2004) to 0.05% (2005–2009). Regression analysis revealed that the presence of RA was associated with the decreased risk of in-hospital overall

Table I B. Patient demographics of patients ≥ 18 who underwent elective TKA between 2000 and 2009.

	RA		Non-RA		<i>p</i> -value
	WF	%	WF	%	
Total number of cases	121349		3693970		
Mean age (yr) (SD)	64.3 (11.2)		66.8 (10.5)		<0.001
Mean Elixhauser Comorbidity score*	1.72		1.72		0.753
Age					<0.001
18-44	5506	4.5%	69285	1.9%	
45-64	53370	44.0%	1404031	38.0%	
65-84	60398	49.8%	2113703	57.2%	
≥ 85	2075	1.7%	106185	2.9%	
Gender					<0.001
Male	26144	21.5%	1350803	36.6%	
Female	95200	78.5%	2342162	63.4%	
Race					<0.001
White	70710	58.3%	2266771	61.4%	
Black	8976	7.4%	174494	4.7%	
Hispanic	4841	4.0%	101026	2.7%	
Others	3154	2.6%	85988	2.3%	
Not stated	33668	27.7%	1065691	28.8%	
Elixhauser Comorbidity score*					<0.001
0	21402	17.6%	631414	17.1%	
1	37581	31.0%	1151850	31.2%	
2	32057	26.4%	1003190	27.2%	
3	18660	15.4%	563726	15.3%	
4 or more	11649	9.6%	343026	9.3%	
Hospital size					<0.001
Small	17032	14.0%	549734	14.9%	
Medium	29878	24.6%	921620	24.9%	
Large	74033	61.0%	2212983	59.9%	
No information	406	0.3%	9633	0.3%	
Hospital teaching status					<0.001
Non-teaching	65546	54.0%	2097439	56.8%	
Teaching	55397	45.7%	1586897	43.0%	
No information	406	0.3%	9634	0.3%	
Hospital region					<0.001
Northeast	23097	19.0%	717187	19.4%	
Midwest	35474	29.2%	1145026	31.0%	
South	49822	41.1%	1419181	38.4%	
West	12955	10.7%	411812	11.1%	
Payer information					<0.001
Medicare	70151	57.8%	2123240	57.5%	
Medicaid	4948	4.1%	84770	2.3%	
Private	42751	35.2%	1347100	36.5%	
Others	3338	2.8%	131743	3.6%	

RA: rheumatoid arthritis; TKA: total knee arthroplasty; WF: weighted frequency. *Diagnosis of RA is excluded.

complications (THA: OR, 0.62; 95% confidence interval (CI) 0.55–0.69; $p < 0.001$) (TKA: OR, 0.67; 95% CI 0.62–0.73; $p < 0.001$) (Table IIIA, IIIB), respiratory complications, cardiac complications, gastrointestinal complications, urinary and renal complications, and pulmonary embolism. Regression analysis revealed that the presence of RA was not associated with the increased risk of in-hospital mortality.

Discussion

This study demonstrated that patients with RA had significantly lower overall in-hospital complication rates of elec-

tive THA and TKA, and lower in-hospital mortality rate of THA than those without RA. Patients with RA undergoing elective THA and TKA had decreased risk of overall in-hospital complications compared to those without RA. Furthermore, the mean Elixhauser comorbidity score of patients with RA was not significantly different from that of patients without RA, undergoing those procedures.

Patients with RA are at an increased risk of developing a number of comorbid conditions. Certain comorbidities are causally associated with RA disease activity and many others are related to its

treatment (4). For example, RA disease activity related comorbidities include cardiovascular disease, pulmonary disease, and osteoporosis (9–11). Immunosuppression drugs such as disease-modifying drugs and biologics have many associated risks of comorbidities, ranging from liver disease to chest and other infections (4, 12–14). Non-steroidal anti-inflammatory drugs are a major risk factor for a range of bowel and liver problems (15–17). Therefore, preoperative assessment of existing comorbidities in patients with RA is critical for optimal outcomes when undergoing major surgeries such as THA and TKA (2). Elixhauser comorbidity score includes 29 comorbidities, excluding RA, and we believe this score reflects patient comorbidity condition adequately. Our result may suggest that patient selection for elective THA and TKA procedures was well conducted.

RA has been reported to be a risk factor for more adverse postoperative events (18); therefore, careful evaluation of comorbidities and management of medications are necessary for preoperative assessment. Anesthesia should be consulted when instability of upper cervical spine is found, to avoid manipulation of the neck and neurologic complications at the time of intubation if general endotracheal anesthesia is utilised (2). Provocation of cardiac ischaemia by stress testing can be useful in predicting perioperative cardiac risk (19). Decisions regarding management of medications must be made in the perioperative period (2). RA is typically treated with immunosuppressive agents, including systematic corticosteroids, methotrexate, and biologic agents. Such management should be adjusted to reach a desirable balance between the negative effect of active RA and flare on postoperative rehabilitation regimens, as well as the increase in infection risk of RA compared with the clear infection risk attributable to biologic and synthetic disease-modifying therapy (2, 20). For example, the American Rheumatology Association recommends that biologic therapy should be stopped 1 to 4 weeks before surgery (21). In this study, despite similar comorbidity score, most adverse events were significantly lower

Table II A. In-hospital outcomes of patients ≥ 18 who underwent elective THA.

	RA (n=50689)		Non-RA (n=1751693)		p-value
	WF	%	WF	%	
Complications					
Neurologic	44	0.1%	1460	0.1%	0.999
Respiratory	387	0.8%	19959	1.1%	<0.001
Cardiac	387	0.8%	18359	1.0%	<0.001
Gastrointestinal	310	0.6%	15418	0.9%	<0.001
Urinary and renal	551	1.1%	28258	1.6%	<0.001
Pulmonary embolism	87	0.2%	3776	0.2%	0.119
Wound-related complications	688	1.4%	23165	1.3%	0.999
Overall complications	2454	4.8%	110395	6.3%	<0.001
Disposition status					
Routine	10761	21.2%	413000	23.6%	<0.001
Transfer to short-term hospital	444	0.9%	15574	0.9%	0.774
Other transfers	24496	48.3%	748321	42.7%	<0.001
Home health care	14712	29.0%	565281	32.3%	<0.001
Died in hospital	27	0.05%	2555	0.15%	<0.001
Other	10	0.02%	739	0.04%	<0.001

Table II B. In-hospital outcomes of patients ≥ 18 who underwent elective TKA.

	RA (n=121349)		Non-RA (n=3693970)		p-value
	WF	%	WF	%	
Complications					
Neurologic	45	0.0%	1826	0.0%	0.065
Respiratory	1126	0.9%	48012	1.3%	<0.001
Cardiac	1111	0.9%	38438	1.0%	<0.001
Gastrointestinal	566	0.5%	25031	0.7%	<0.001
Urinary and renal	1198	1.0%	57030	1.5%	<0.001
Pulmonary embolism	443	0.4%	17255	0.5%	<0.001
Wound-related complications	1471	1.2%	40753	1.1%	<0.001
Overall complications	5960	4.9%	228345	6.2%	<0.001
Disposition status					
Routine	27410	22.6%	919429	24.9%	<0.001
Transfer to short-term hospital	1081	0.9%	31418	0.9%	0.137
Other transfers	54507	44.9%	1528486	41.4%	<0.001
Home health care	37676	31.0%	1192040	32.3%	<0.001
Died in hospital	91	0.07%	3992	0.11%	0.002
Other	25	0.02%	1472	0.04%	0.002

RA: rheumatoid arthritis; TKA: total knee arthroplasty; WF: weighted frequency.

in patients with RA than in those without RA and patients with RA had decreased risk of those events. Rheumatologists are frequently involved in the care of patients with RA in addition to the regular perioperative team (22), which might lead to this excellent result.

Most of the recent studies did not find a difference when comparing patients with RA operated for THA and TKA to those without RA for 30 days or 90 days mortality (22-26). Although the current study only includes in-hospital events, the mortality rate in patients with RA who underwent THA was significantly lower than that in patients without RA. This was not the case with TKA; how-

ever, the rate of TKA between 2005-2009 (0.05%) was lower than that between 2000-2004 (0.12%). This also may indicate improved perioperative care for patients with RA.

Recently, Stundner *et al.* performed studies determining differences in the risk of perioperative adverse events in THA and TKA procedures between patients with and without RA using another US nationwide database (22, 26). Their results showed that the adverse outcomes are similar between those patients for TKA and higher in patients with RA for THA. Although the criteria for complications are different, their studies include patients with urgent or

emergent admission. Those patients usually undergo the procedures for the treatment of fracture, particularly for THA. Preoperative management of those patients is not well prepared and perioperative adverse events may increase. In contrast, the current study includes only elective cases and those patients have enough time for careful preoperative management of their comorbidities and medications; therefore, our result may indicate that pre- and perioperative management of patients with RA undergoing elective THA and TKA were well conducted.

Our study is limited by several factors inherent to retrospective analysis of large administrative databases. Data entry may be subject to an element of coding or reporting bias; however, reporting should not vary substantially over time within the database. The accuracy of RA diagnoses within administrative databases has been controversial; however, the co-existence of the arthroplasty codes may increase the accuracy of identification (22). Although the results can be affected by other diseases, such as other inflammatory diseases or haemophilia, the proportion of patients with such diseases in both groups is low (*e.g.* the proportion of patients with haemophilia is less than 0.1% for both groups). Therefore, the bias associated with the inclusion of other diseases should be minimal. We did not use patients' drug consumption in the database. The drug information in the database would likely not be representative of the patients' long-term medication intake, as immunosuppressive medication is frequently altered or temporarily discontinued during admission for surgery (26). In addition, our data are limited to in-hospital events and the adverse events may be underestimating the true incidence; therefore, making it difficult to discuss the adverse events in detail, such as wound infection and mortality. However, we believe that these data provide a valuable information of in-hospital outcomes associated with elective THA and TKA procedures in patients with RA in the US during the last decade.

In conclusion, perioperative outcomes of elective THA and TKA in patients

Table III A. Regression modeling predicting influence of RA on in-hospital outcomes of patients ≥ 18 who underwent elective THA*.

Outcome variables	RA OR (95% CI)	p-value
Neurologic	0.39 (0.12, 1.21)	0.104
Respiratory	0.47 (0.36, 0.62)	<0.001
Cardiac	0.59 (0.45, 0.77)	<0.001
Gastrointestinal	0.67 (0.50, 0.90)	0.008
Urinary and renal	0.50 (0.40, 0.62)	<0.001
Pulmonary embolism	0.36 (0.19, 0.67)	0.001
Wound-related complications	0.91 (0.74, 1.11)	0.349
Overall complications	0.62 (0.55, 0.69)	<0.001
Died in hospital**	0.44 (0.16, 1.21)	0.111

Table III B. Regression modeling predicting influence of RA on in-hospital outcomes of patients ≥ 18 who underwent elective TKA*.

Outcome variables	RA OR (95% CI)	p-value
Neurologic	0.48 (0.20, 1.17)	0.105
Respiratory	0.59 (0.51, 0.69)	<0.001
Cardiac	0.75 (0.64, 0.88)	<0.001
Gastrointestinal	0.68 (0.53, 0.87)	0.002
Urinary and renal	0.49 (0.42, 0.57)	<0.001
Pulmonary embolism	0.45 (0.35, 0.57)	<0.001
Wound-related complications	1.07 (0.91, 1.25)	0.433
Overall complications	0.67 (0.62, 0.73)	<0.001
Died in hospital**	0.97 (0.55, 1.73)	0.927

RA: Rheumatoid arthritis; TKA: Total knee arthroplasty; OR: Odds ratio.

*Model adjusted for age, gender, race, Elixhauser Comorbidity Score, hospital size, hospital teaching status, hospital region, payer information; **Model adjusted for age, gender, race, Elixhauser Comorbidity Score, hospital size, hospital teaching status, hospital region, payer information, complications.

with RA were better than those in patients without RA. These results may indicate that patient selection and pre- and perioperative management of patients with RA undergoing elective THA and TKA were well conducted in the US during the last decade.

References

- PINCUS T, SOKKA T, KAUTIAINEN H: Patients seen for standard rheumatoid arthritis care have significantly better articular, radiographic, laboratory, and functional status in 2000 than in 1985. *Arthritis Rheum* 2005; 52: 1009-19.
- GOODMAN SM: Rheumatoid arthritis: preoperative evaluation for total hip and total knee replacement surgery. *J Clin Rheumatol* 2013; 19: 187-92.
- KHAN NA, SOKKA T: Declining needs for total joint replacements for rheumatoid arthritis. *Arthritis Res Ther* 2011; 13: 130.
- GULLICK NJ, SCOTT DL: Co-morbidities in established rheumatoid arthritis. *Best Pract Res Clin Rheumatol* 2011; 25: 469-83.
- DIXON WG, WATSON KD, LUNT M *et al.*: Reduction in the incidence of myocardial infarction in patients with rheumatoid arthritis who respond to anti-tumor necrosis factor alpha therapy: results from the British Society for Rheumatology Biologics Register. *Arthritis Rheum* 2007; 56: 2905-12.
- GREENBERG JD, KREMER JM, CURTIS JR *et al.*: Tumour necrosis factor antagonist use and associated risk reduction of cardiovascular events among patients with rheumatoid arthritis. *Ann Rheum Dis* 2011; 70: 576-82.
- HCUP Databases. Healthcare Cost and Utilization Project (HCUP). 2000-2009. Agency for Healthcare Research and Quality, Rockville, MD. <http://www.hcup-us.ahrq.gov/databases.jsp>
- ELIXHAUSER A, STEINER C, HARRIS DR *et al.*: Comorbidity measures for use with administrative data. *Medical care* 1998; 36: 8-27.
- SALMON JE, ROMAN MJ: Subclinical atherosclerosis in rheumatoid arthritis and systemic lupus erythematosus. *Am J Med* 2008; 121: S3-8.
- PAPPAS DA, GILES JT, CONNORS G *et al.*: Respiratory symptoms and disease characteristics as predictors of pulmonary function abnormalities in patients with rheumatoid arthritis: an observational cohort study. *Arthritis Res Ther* 2010; 12: R104.
- DUNCAN H, FROST HM, VILLANUEVA AR *et al.*: The osteoporosis of rheumatoid arthritis. *Arthritis Rheum* 1965; 8: 943-54.
- CURTIS JR, BEUKELMAN T, ONOFREI A *et al.*: Elevated liver enzyme tests among patients with rheumatoid arthritis or psoriatic arthritis treated with methotrexate and/or leflunomide. *Ann Rheum Dis* 2010; 69: 43-7.
- JU JH, KIM SI, LEE JH *et al.*: Risk of interstitial lung disease associated with leflunomide treatment in Korean patients with rheumatoid arthritis. *Arthritis Rheum* 2007; 56: 2094-6.
- DORAN MF, CROWSON CS, POND GR *et al.*: Frequency of infection in patients with rheumatoid arthritis compared with controls: a population-based study. *Arthritis Rheum* 2002; 46: 2287-93.
- FRIES JF, MILLER SR, SPITZE PW *et al.*: Toward an epidemiology of gastropathy associated with nonsteroidal antiinflammatory drug use. *Gastroenterology* 1989; 96: 647-55.
- FRIES JF, MURTAGH KN, BENNETT M *et al.*: The rise and decline of nonsteroidal antiinflammatory drug-associated gastropathy in rheumatoid arthritis. *Arthritis Rheum* 2004; 50: 2433-40.
- BJORNSSON E, JERLSTAD P, BERGQVIST A *et al.*: Fulminant drug-induced hepatic failure leading to death or liver transplantation in Sweden. *Scand J Gastroenterol* 2005; 40: 1095-101.
- SOOHOO NF, FARNG E, LIEBERMAN JR *et al.*: Factors that predict short-term complication rates after total hip arthroplasty. *Clin Orthop Relat Res* 2010; 468: 2363-71.
- FLEISHER LA, BACKMAN JA, BROWN KA *et al.*: 2009 ACCF/AHA focused update on perioperative beta blockade incorporated into the ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for non-cardiac surgery: a report of the American college of cardiology foundation/American heart association task force on practice guidelines. *Circulation* 2009; 120: e169-276.
- 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: 785-91.
- SAAG KG, TENG GG, PATKAR NM *et al.*: American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum* 2008; 59: 762-84.
- STUNDNER O, DANNINGER T, CHIU YL *et al.*: Rheumatoid arthritis vs osteoarthritis in patients receiving total knee arthroplasty: perioperative outcomes. *J Arthroplasty* 2014; 29: 308-13.
- SINGH JA, KUNDUKULAM J, RIDDLE DL *et al.*: Early postoperative mortality following joint arthroplasty: a systematic review. *J Rheumatol* 2011; 38: 1507-13.
- DOMSIC RT, LINGALA B, KRISHNAN E: Systemic lupus erythematosus, rheumatoid arthritis, and postarthroplasty mortality: a cross-sectional analysis from the nationwide inpatient sample. *J Rheumatol* 2010; 37: 1467-72.
- BOZIC KJ, LAU E, KURTZ S *et al.*: Patient-related risk factors for periprosthetic joint infection and postoperative mortality following total hip arthroplasty in Medicare patients. *J Bone Joint Surg Am* 2012; 94: 794-800.
- STUDNER O, CHIU YL, SUN X *et al.*: Perioperative outcomes in patients with rheumatoid versus osteoarthritis for total hip arthroplasty: a population-based study. *Clin Exp Rheumatol* 2013; 31: 889-95.
- CANCIENNE JM, WERNER BC, BROWNE JA: Complications after TKA in patients with hemophilia or Von Willebrand's disease. *J Arthroplasty* 2015; 30: 2285-9.