Perioperative outcomes in patients with rheumatoid *versus* osteoarthritis for total hip arthroplasty: a population-based study

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Abstract

Objective

Little is known about perioperative outcomes among the subset of patients undergoing total hip arthroplasty (THA) for a diagnosis of rheumatoid arthritis (RA) rather than osteoarthritis (OA). We sought to 1) identify the prevalence of RA in patients undergoing THA, 2) compare their demographics to those being operated on for OA, 3) determine differences in perioperative outcomes and 4) analyse if RA represents an independent risk factor for complications, mortality, utilisation of resources, increased length of stay and cost.

Methods

Entries of patients who underwent elective THA between 2006 and 2010 were identified in a national database and subgrouped according to presence of a concurrent diagnosis of RA. Differences in demographics and perioperative outcomes were analysed.

Results

We identified 157,775 entries for patients who underwent THA between 2006 and 2010. RA was present in 3.42% (n=5,400). Patients in the group RA were on average younger [RA: 63.94 years vs. OA: 65.64 years; p<0.0001] and more likely female [RA: 75.47% vs. OA: 56.09%; p<0.0001]. While mortality was not statistically different, perioperative pulmonary and infectious complications occurred more frequently in RA patients. Compared with OA, multivariate logistic regression revealed higher overall odds for complications [OR=1.15 (CI 1.05;1.25), p=0.0037], need for mechanical ventilation [OR=1.42 (CI 1.01;2.00), p=0.0414], transfusion [OR=1.35 (CI 1.26;1.44), p<0.0001], prolonged hospitalisation [OR=1.16 (CI 1.08;1.23), p<0.0001] and increased hospital charges [OR=1.17 (CI 1.09;1.26), p<0.0001].

Conclusion

In THA patients suffering from RA, perioperative risk for complications and utilization of health care resources continues to be increased compared to OA patients.

Key words

hip arthroplasty, hip replacement, rheumatoid arthritis, osteoarthritis, complications

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Received on January 15, 2013; accepted in revised form on May 27, 2013.

Funding: this work was supported with funds from the Hospital for Special Surgery, Department of Anesthesiology (Stavros G. Memtsoudis. Contribution of Dr Mazumdar, Ms Chiu and Ms Sun on this project was supported in part by funds from the Clinical Translational Science Center (CTSC), National Center for Advancing Translational Sciences (NCATS) grant no. UL1-RR024996 and Center for Education, Research, and Therapeutics (CERTs), Agency for Healthcare Research and Quality (AHRQ) grant no. U18 HSO16-75. The content is solely the responsibility of the authors and does not necessarily represent the official views of the funding sources NCATS and AHRQ based in Rockville, MD, USA.

Competing interests: none declared.

Introduction

Total hip arthroplasty (THA) is one of the most frequently performed orthopedic procedures. While the vast majority of patients undergoes this surgery for a diagnosis of osteoarthritis (OA), approximately three percent of patients are known to suffer from chronic rheumatoid arthritis (RA). A substantial fraction of patients will develop hip involvement during the course of their disease (1, 2). The widespread use of potent disease-modifying anti-rheumatic drugs (DMARDs) evoked fundamental improvements in treatment, improved overall function and quality of life (3) while decreasing joint damage by erosive disease (4), and made lower extremity arthroplasty abdicable in many cases (5). Yet, progressive joint destruction can prevail in a subgroup of patients, ultimately necessitating hip replacement. In a recent study by Pantos *et al*., the authors reported a hip or knee replacement incidence of 4.3% among 750 patients with RA. Longer disease duration and failure to respond to medical treatment were associated with a higher likelihood to undergo joint replacement (6). In contrast to osteoarthritis, RA is regarded a systemic disease, producing synovitis and cartilage destruction as well as an increased cardiac mortality (7). Moreover, a strong association with pulmonary disease exists (8). RA influences the occurrence of perioperative complications and, historically, perioperative mortality (9, 10). Widespread use of DMARDs, in particular methotrexate and more recently the potent biologic tumour necrosis factor inhibitors (TNFi) has been linked to a decrease in overall cardiac events in RA patients (11, 12). There is no evidence that the incidence of pulmonary disease has similarly decreased, however, perhaps it relates to the known strong etiologic association between smoking and RA (13). Infection is also of heightened concern, particularly in TNFi treated patients (14). Considering these characteristics, one cannot extrapolate data on perioperative outcomes from studies performed prior to the widespread use of biologics. Available studies are additionally limited by the fact that they include a heterogenic population of patients suffering from a variety of rheumatoid conditions and undergoing lower extremity joint arthroplasties in general, or total knee arthroplasty only (9, 15, 16). Moreover, most available studies concentrate on long-term outcomes and mortality profiles after THA in RA patients. We sought to study perioperative outcomes by using a population-based approach. Utilising recent data from approximately 400 hospitals the United States we evaluated and compared multiple outcomes of patients undergoing THA with or without a diagnosis of RA using the principles of comparative effectiveness research. We hypothesised that patients suffering from RA would exhibit higher rates and risk of major in-hospital complications and mortality.

Methods

Data files for the time period between years 2006 and 2010 were obtained from Premier Perspective, Inc. (Charlotte, North Carolina), an administrative database containing discharge information from approximately 400 acute care hospitals located throughout the United States (17). Data included is compliant with the Health Insurance Portability and Accountability Act (18). The data undergoes rigorous quality assurance and data validation checks performed by the provider prior to distribution. This assures accuracy of entries. Our Institutional Review Board exempted this project from requirement for consent as the data presented is sufficiently de-identified.

Study sample

We searched the database for entries indicating the performance of primary hip arthroplasty by using the International Classification of Diseases - 9th revision - Clinical Modification (ICD-9-CM) procedure code (81.51). The entries were separated into two groups according to underlying pathology, OA or RA.

Demographic variables

The following patient and health care-related characteristics, grouped by underlying disease, were calculated and compared between groups: age (con-

tinuously and categorised), sex, race, admission type, type of anesthesia (general, neuraxial, combined neuraxial-general, unknown), hospital size, hospital location and hospital teaching status. Using the method described by Deyo *et al*. (19), prevalence of individual pre-existing comorbidities as well as the overall comorbidity burden was assessed and compared between groups.

Complication variables

The incidence of major complications was calculated and compared between groups after identifying cases that had listed ICD-9-CM codes consistent with such diagnoses (Appendix 1). Further, the incidence of in-hospital and 30-day mortality was computed. The complications analysed included pulmonary embolism, deep vein thrombosis, cerebrovascular events, pulmonary compromise, sepsis, cardiac complication (treating myocardial infarction and other cardiac complications as separate entities), pneumonia, all other infectious complications, acute renal failure, and gastrointestinal complications as well as in-hospital mortality. Moreover, the incidence of mechanical ventilation and transfusion of blood products was recorded using ICD-9 and billing codes (see Appendix 1). In addition, we analysed overall hospital charges and length of stay. For the regression analysis, the latter two were dichotomised based on the 75th percentile; entries above the 75th percentile were defined as increased hospital charges or prolonged hospitalisation, respectively.

Statistical analysis

We aimed at determining if the presence of RA in patients undergoing total hip arthroplasty is associated with differences in perioperative outcomes. All statistical analyses were carried out using SAS version 9.2 (SAS Institute, Cary, NC). For modeling purposes and descriptive analyses, the SAS procedures SURVEYMEANS, SURVEYFREQ, SURVEYREG and SURVEYLOGISTIC were utilised.

Weighted means and percentages were described for continuous and categorical variables, respectively. For variables that had a skewed distribution, median and interquartile range was estimated. For continuous variables, 95% confidence intervals (CI) were shown as a measure of variability. Chi-Square test was performed to evaluate the association of two categorical variables. Two-sample *t*-test or Wilcoxon Ranked sum test were used to compare means for a continuous variable between more than two groups.

Multivariate regression analysis

Binary outcomes of incidence of complications, mechanical ventilation, use of blood product transfusion, prolonged length of hospital stay and increased hospital charges (as defined above) were defined. For the purpose of the evaluation of major complications, a combined outcome variable was created including following complications: pulmonary embolism, deep venous thrombosis, cerebrovascular event, pulmonary compromise, sepsis, cardiac complications including myocardial infarction, pneumonia, all other infections, acute renal failure, gastrointestinal complications, and in-hospital mortality. For each outcome, logistic regression was used to evaluate its association with the type of arthritis while controlling for age, sex,

Appendix 1. ICD-9-CM diagnosis codes for major complications.

Complications	ICD-9-CM diagnosis codes
Device Related Complication	996.xx
Wound infection	998.5x
Pulmonary Embolism	415.1
ARDS	518.5
Deep Vein Thrombosis	451.1, 451.2, 451.8, 451.9, 453.2, 453.4, 453.8, 453.9
Cerebrovascular Event	433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, 997.02
Pulmonary Compromise	514, 518.4, 518.5, 518.81, 518.82
Cardiac (Non-myocardial Infarction)	426.0, 427.41, 427.42, 429.4, 997.1, 427.4, 427.3, 427.31, 427.32
Pneumonia	481, 482.00- 482.99, 483 ,485 , 486, 507.0, 997.31, 997.39
Wound Complication	998.3, 998.30, 998.31, 998.32, 997.4, 997.5, 998.33, 998.83, 998.12, 998.13, 998.6, 998.51, 729.92
All Infections	590.1, 590.10, 590.11,590.8 ,590.81, 590.2, 590.9, 595.0, 595.9, 599.0, 567.0
	480, 480.0, 480.1, 480.2, 480.8, 480.9, 481, 482.0, 482.1, 482.2, 482.3, 482.30, 482.31, 482.32, 482.39, 482.4, 482.40, 482.41, 482.42, 482.49, 482.5, 482.8, 482.81, 482.82, 482.83, 482.84, 482.89, 482.9, 483, 483.0, 483.1, 483.8, 485, 486, 487, 997.31,
	038, 038.0, 038.1, 038.10, 038.11, 038.12, 038.19, 038.2, 038.3, 038.4, 038.40, 038.41, 038.42, 038.43, 038.44, 038.49, 038.8, 038.9, 790.7,
	998.0, 958.4, 998.5, 998.59, 998.89, 785, 785.50, 785.52, 785.59, 999.39, 999.31, 999.3
Acute Renal Failure	584, 584.5, 584.9
Gastrointestinal Complication	997.4, 560.1, 560.81, 560.9, 536.2, 537.3
Acute Myocardial Infarction	410.XX
Mechanical Ventilation	93.90, 96.7, 96.70, 96.71, 96.72,
(CPT Code)	94002, 94656, 94003, 94657
Blood Transfusion	99.0, 99.01, 99.02, 99.03, 99.04, 99.05, 99.06, 99.07, 99.08, 99.09,
(HCPCS codes)	P9010, P9011, P9012, P9016, P9017, P9019, P9020, P9021, P9022, P9023, P9031, P9032, P9033, P9034, P9035, P9036, P9037, P9038, P9039, P9040

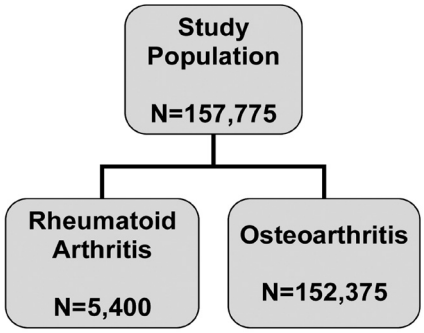

Fig. 1. The flow chart depicts the study population and subgroup distribution.

race, admission type, type of anesthesia, hospital size, hospital teaching status, hospital location and year. Additionally, individual regressions were fit comparing various outcomes between the first (2006) and last (2010) year of observation, adjusting for all other covariates. Adjusted odds ratios, 95% CI and *p*-values were reported. A test of model discrimination using the C-statistic and a test of model calibration using the Hosmer-Lemeshow (H-L) test were performed for each model (20). The conventional threshold of statistical significance (*i.e.* two-sided *p*-value <0.05) was used to determine significance of variables. 95% CIs of estimates were reported to provide readers additional information on the significance of the findings. The value inflation factor (VIF) for multicollinearity (VIF <10, representing a conventional criterion for absence of multicollinearity) was evaluated. Validation of the final models was accomplished using C-statistics (21) (area under the receiver-operating characteristic curve). The latter was applied to measure the level of model discrimination between observed data at different levels of outcome (22).

Table I. Detailed are patient and health care system related characteristics, grouped by underlying pathology.

		Characteristics		
Variable	Category	Rheumatoid arthritis	Osteoarthritis	*p*-value
Number =		5.400	152.375	–
% of total		3.42%	96.58%	–
Average Comorbidity Index (CI)		1.48 (1.45.1.51)	0.49 (0.49, 0.50)	<0.0001
Type of anesthesia (%)				
	Neuraxial	6.34	7.35	<0.0001
	General	58.09	54.24	
	Neuraxial + General	9.93	9.72	
	Unknown	25.63	28,7	
Average Age (years) (CI)		63.94 (63.54,64.34)	65.64 (65.57,65.71)	<0.0001
Age Group	</=44	8.33	4.08	<0.0001
	45-54	13.87	14.67	
	55-64	25.61	26.22	
	65-74	28.02	28.85	
	>/=75	24.18	26.19	
Gender	Female	75.47	56.09	<0.0001
	Male	24.53	43.91	
Race	White	68.35	73.49	<0.0001
	Black	8.71	5.57	
	Other	3.93	1.69	
	Missing	19.02	19.25	
Admission Type	Emergent	6.16	2.36	<0.0001
	Urgent	4.10	3.36	
	Routine	89.27	93.98	
	Other	0.12	0.05	
	Missing	0.36	0.25	
Payor	Commercial	34.92	41.55	<0.0001
	Medicaid	4.42	2.22	
	Medicare	58.44	53.42	
	Uninsured	0.54	0.68	
	Missing	1.69	2.12	
Hospital size (Bed number)	≤299	33.51	35.85	0.0039
	300-499	42.67	41.64	
	≥500	23.82	22.51	
Hospital Location	Rural	4.19	4.11	0.6924
	Urban	95.81	95.89	
Hospital Teaching Status	Non-teaching	76.16	75.71	0.3884
	Teaching	23.84	24.29	

Results

We identified 157,775 entries for patients who underwent THA between 2006 and 2010 with a diagnosis of either RA or OA as underlying pathology. 3.42% (n=5,400) of patients had a diagnosis of RA (see Figure 1 for group distribution). Table I details the patient and healthcare system related demographic parameters for both groups.

Patients in the group OA were on average older than those in the RA group [RA: 63.94 years (95% C.I.= (63.54,64.34)) *vs*. OA: 65.64 years (95% C.I.= (65.57,65.71)); *p*<0.0001], and the proportion of female patients was higher among RA patients [RA: 75.47% *vs*. OA: 56.09%; *p*<0.0001]. More patients in the OA group underwent their surgery under neuraxial anesthesia. Table II depicts the prevalence of the individual comorbidities among the groups. Patients in the RA group tended to have higher rates of pulmonary disease.

The incidence of in-hospital mortality (RA: 0.19% *vs*. OA: 0.11%; *p*=0.1465) and 30-day mortality (RA: 0.21% *vs*. OA: 0.14%; *p*=0.2448) tended to be higher in the RA group, but the difference between groups did not reach statistical significance. However, a number of complications occurred significantly more frequently in patients with a diagnosis of RA: deep vein thrombosis, pulmonary compromise, sepsis, pneumonia, other infectious complications and acute renal failure. Please refer to Table

III for a list of individual complication incidence rates. The combined rates of complications studied were 14.05% in the RA group and 12.70% in the OA group, respectively (p=0.010). Further, patients in the RA group required blood product transfusion significantly more frequently (RA: 30.81% *vs*. OA: 22.98%; p<0.0001), had elevated requirement for mechanical ventilation (RA: 0.87% *vs*. OA: 0.60%; p=0.0237), and , on average, had longer lengths of hospitalisation (RA: 3.86 (95 % C.I.= (3.77, 3.94)) days *vs*. OA: 3.51 (95% C.I= (3.50, 3.52)) days; p<0.0001) as well as higher hospital charges (RA: 49,821 (95% C.I.=(49056, 50586)) USD *vs*. OA: 47,110 (95% C.I.= (49684, 47235)) USD; p<0.0001). In Table IV, the results of the multivariate logistic regression are presented. For patients in the RA group, the analysis revealed increased adjusted odds for all studied outcomes when compared with OA: occurrence of perioperative complications [OR=1.15 (CI 1.05;1.25), p=0.0037], need for mechanical ventilation [OR=1.42 (CI 1.01;2.00), p=0.0428] and transfusion [OR=1.35 (CI 1.26;1.44), P<0.0001], prolonged hospitalisation [OR=1.16 (CI 1.08;1.23), p<0.0001] and increased hospital charges [OR=1.18 (CI 1.20;1.27), p<0.0001]. While the OR for cumulative complications (1.00 (CI 0.95, 1.06), p=0.90) and mechanical ventilation (1.20 (CI 0.92, 1.57), p=0.18) indicates no significant difference between the years of 2006 and 2010, patients exhibited significantly lower ORs for transfusion (0.78 (CI 0.75, 0.82), p<0.0001) as well as for length of stay exceeding the 75th percentile (0.43 (0.42, 0.45), p<0.0001), but a considerably higher OR for increased hospital charges (2.54 (2.43, 2.66), p<0.0001) towards the end of the observation period.

Multicollinearity was found absent (VIF <10). The C-statistics were 0.7, 0.7, 0.7, 0.6, 0.6 for cumulative complications, mechanical ventilation, transfusion, prolonged hospitalisation, and increased hospital charges, respectively.

Table II. Listed are the prevalences of preexisting comorbidities among patients, grouped by underlying pathology.

	Comorbidities		
	Rheumatoid arthritis (%)	Osteoarthritis (%)	p-value
Myocardial infarction	3.58	3.62	0.8821
Peripheral vascular disease	2.09	1.85	0.2812
Cerebrovascular disease	0.25	0.21	0.6426
Renal disease	0.09	0.05	0.4356
COPD	17.35	13.14	<0.0001
Uncomplicated diabetes mellitus	12.77	12.98	0.6873
Complicated diabetes mellitus	0.81	0.75	0.6493
Cancer	1.85	1.88	0.8935

Table III. Listed are the incidences of complications, use of blood product transfusion and mechanical ventilation as well as median length of stay and hospital charges, grouped by underlying pathology.

	Rheumatoid arthritis (%)	Osteoarthritis (%)	p-value
In-hospital mortality (%)	0.19	0.11	0.4165
30-day mortality (%)	0.21	0.14	0.2448
Pulmonary embolism (%)	0.28	0.23	0.5178
Deep vein thrombosis (%)	0.57	0.36	0.0284
Cerebrovascular event (%)	0.19	0.13	0.3423
Pulmonary compromise (%)	1.00	0.60	0.0008
Sepsis	0.40	0.14	<0.0001
Cardiac (non-MI) (%)	5.84	6.36	0.1735
Pneumonia (%)	1.21	0.80	0.0036
All other infections (%)	6.32	4.38	<0.0001
Acute renal failure (%)	2.14	1.52	0.0019
Gastrointestinal complication (%)	0.97	0.96	0.9583
Acute myocardial infarction (%)	0.30	0.29	0.879
Blood transfusion (%)	30.81	22.98	<0.0001
Mechanical ventilation (%)	0.87	0.60	0.0237
Length of stay (mean and CI)	3.86 (3.74, 3.94)	3.51 (3.0, 3.52)	<0.0001
Hospital charges (mean and CI)	49.821 (49.056, 50,586)	47.110 (46.984, 47.235)	<0.0001

Discussion

In this study comparing the outcomes of patients with OA and RA undergoing primary hip arthroplasty, we found higher rates of perioperative complications in patients with RA when compared to those with no such diagnosis. Moreover, the presence of this diagnosis was independently associated with higher adjusted odds for requirement of mechanical ventilation, transfusion, prolonged hospitalisation and increased hospital costs. RA was not associated with increased post-arthroplasty mortality.

Patients in the RA group were on average younger and more likely female, consistent with the usual age and sex distribution of RA (23).

Several possible causes for the increased risk of complications come into consideration. On the one hand, RA is known to be associated with a multitude of comorbidities and has the potential to deteriorate different organ systems (24). Although regional anesthesia and extremity surgery may not confer a high risk for pulmonary complications, more patients in the RA group underwent surgery under general anesthesia, permitting underlying pulmonary disease to become clinically relevant after surgery, and potentially contributing to the increase in prolonged mechanical ventilation reported here. Furthermore, drugs administered for treatment of RA, including steroids and biologics like TNFi, are known to be associated with infection in the perioperative period (25, 26), methotrexate and TNFis might evoke pulmonary interstitial disease leading to pulmonary compromise (27). Concerning 30-day mortality,

Table IV. Results from the multivariate regression.

			Cumulative Complications (C-statistics = 0.7)		Mechanical Ventilation (C-statistics = 0.7)		Transfusion (C-statistics = 0.7)		Length of stay >75th percentile (C-statistics = 0.6)		Hospital charges >75th percentile (C-statistics = 0.6)	
Category	Comparison	ref.	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*
Underlying pathology	RA	OA	1.15 (1.05, 1.25)	0.0037	1.42 (1.01, 2.00)	0.0428	1.35 (1.26, 1.44)	<0.0001	1.16 (1.08, 1.23)	<0.0001	1.18 (1.20, 1.27)	<0.0001

odds ratios and 95% confidence intervals (CI); reference = 1. RA: rheumatoid arthritis; OA: osteoarthritis; cumulative complications comprise following events: pulmonary embolism, deep venous thrombosis, cerebrovascular event, pulmonary compromise, sepsis, cardiac complications including myocardial infarction, pneumonia, all other infections, acute renal failure, gastrointestinal complications and in-hospital mortality.

most contemporary studies did not find a difference when comparing patients operated for RA to those with OA (15, 28, 29). Similarly, in a recent systematic review by Singh *et al*. outlining demographic and surgical factors associated with increased 30- and 90-day mortality after total joint arthroplasty, RA was not associated with increased rates of this outcome (10).

Anaemia is common in RA, and may be multifactorial. Iron deficiency anaemia caused by chronic non-steroidal (NSAID) use, bone marrow suppression due to medications, and the anemia of chronic disease all may contribute to the increase in transfusions we demonstrated (30).

The observed increases in both length of stay and hospital cost seen in the RA group *versus* the OA group is likely attributable to the increase in significant postoperative complications in the RA group and their associated costs of treatment. Along with significant postoperative wound-related complications, prior authors demonstrated longer length of stays in RA patients undergoing hip or knee arthroplasty is positively correlated with female gender and non-white ethnicity. Both were significantly more prevalent in the RA group in our study. A positive rheumatoid factor was shown to predict an increase in LOS by nearly three days (31). While the odds ratio for length of stay exceeding the 75th percentile is lower towards the end of our observation period, indicating lower likelihood for extended stay, risk for increased cost is higher.

Our study is limited by a number of factors inherent to population-based database analysis. First, we are not able to determine the exact criteria used to diagnose RA, the duration of the disease. While patients requiring surgical treatment of the joint destruction they incurred are likely subject to a longer and/or more intense disease course, their comorbidity burden is known to increase at the same time. We did in part account for the potentially elevated risk of "sicker" patients by adjusting for comorbidity load in the multivariate regression analysis. Apart from death within 30 days, post-discharge events cannot be taken into account because only events occurring during the index admission, in which the surgery was performed, are captured. Further, we were not able to capture intra- and perioperative events like anesthetic complications, blood loss and medication intake, including drugs administered for rheumatoid arthritis, infection, anticoagulants or cardioprotective agents. Although present in the database, it is not easily possible to obtain data on drug consumption, because the information only includes the immediate perioperative time frame. As immunosuppressive medication is frequently altered or temporarily discontinued during this time, the information would likely not be representative of the patients' long-term medication intake. However, the outcomes are evaluated in a "real-world" setting, consistent with the standards of comparative effectiveness research. Finally, comorbidities and complications were identified using ICD-9-CM codes (Appendix 1). Despite rigorous quality checks by the vendor of the database, there is a possibility that inconsistencies and coding errors occurred. Likely, the potential influence exerted by this effect is relatively low because the whole data collection process is exposed to the same coding bias.

In conclusion, while perioperative complications, especially those affecting the pulmonary system among patients with RA undergoing THA are increased, they have no increase in mortality compared to OA. Although widespread use of potent DMARDs is known to improve overall functional status, decrease the need for arthroplasty, and improve cardiac risk, there is no effect on pulmonary disease and infection risk may even be increased. The increase in pulmonary compromise, pneumonia, requirement for mechanical ventilation, infection and sepsis, without an increase in cardiac complications may reflect this trend.

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