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Factors That Affect Outcome Following Total Joint Arthroplasty: a Review of the Recent Literature

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Abstract
Purpose of Review It is well established that certain patient-specific risk factors affect outcomes following total joint arthroplasty. The goal of this paper is to summarize the latest data on several variables that have been investigated in the last 3 years and to characterize the effects these factors have on the success of hip and knee replacement.
Recent Findings Preoperative diagnoses of depression and anxiety, liver disease, hypoalbuminemia, vitamin D deficiency, and diabetes mellitus are associated with increased risk of postoperative complications and can lead to worse outcomes after joint replacement surgery.
Summary Recent investigations have clearly established a link between these patient-specific factors and poor outcomes after hip and knee arthroplasty, but future research is needed to determine best practices for stratifying and mitigating these risks for patients.

Keywords Total joint arthroplasty · Liver disease · Vitamin D deficiency · Depression · Hypoalbuminemia · Diabetes mellitus

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Introduction

The success of total joint arthroplasty over the last few decades has led to a dramatic increase in the number of joint replacements performed yearly throughout the world [1]. Despite its high rate of long-term success, minimizing post-operative complications after arthroplasty remains a challenge for surgeons. Failed total joint replacements are associated with a large burden both at the individual patient level and at the level of the broader healthcare system, making it critical for orthopedic surgeons to understand the factors that lead to unsatisfactory outcomes [2•]. As the demand for cost-effective care grows, patient selection and identification of modifiable risk factors have become increasingly important in order to minimize the burden of disease primarily for patients and secondarily for health care systems.

Decades of research have been devoted to the understanding of modifiable risk factors in the setting of joint replacement surgery, and it is clear that the determinants of outcomes following total joint arthroplasty are multifactorial. Some of the variables that have been shown to affect the outcome after total joint replacement include social and demographic characteristics, medical comorbidities, and surgical technique [3–7]. Areas of continued active research include the effect of intrinsic factors such as obesity [8–10], cardiovascular disease [11, 12], mental health disorders [13•, 14–17•, 18•, 19], hepatic disease [20, 21•, 22, 23•, 24], nutritional deficiencies [25–29•, 30], bone metabolic disease [31–37], and diabetes mellitus [38•, 39, 40], as well as external factors such as nicotine use [41, 42], recent corticosteroid injections [43–47], and discharge disposition [48, 49]. The goal of this article is to review the most recent literature, published within the last 3 years, regarding a selection of patient-specific factors that may influence

outcomes following total joint arthroplasty. We focus on the importance of mental health, liver disease, hypoalbuminemia, hypovitaminosis D, and diabetes management. However, we stress that these data are presented in the context of a wide range of other known factors affecting outcome after total joint replacement, as mentioned above that are not specifically discussed here.

Mental Health

Recent investigations have demonstrated that preoperative diagnoses of depression or anxiety play a role in determining both patient-reported outcomes and postoperative complications following total joint replacement surgery. In a prospective cohort study of 186 total knee arthroplasty patients at a single institution in Sweden, it was shown that patients with a preoperative diagnosis of anxiety or depression were six times more likely to report that they were not satisfied with the result of their operation at 4-year follow-up [$P < .001$; Table 1] [13•]. The overall rate of dissatisfaction in the entire cohort was 15%, which is consistent with previously reported data. Gold et al. utilized the California Healthcare Cost and Utilization Project database to show that after controlling for other comorbidities, a diagnosis of depression led to a 21% increase in 90-day readmission after total knee arthroplasty and a 24% increase in 90-day readmission after total hip arthroplasty [CI for TKA 1.13–1.29, $P < .001$; CI for THA 1.13–1.35, $P < .001$; Table 1] [14]. Another concurrent study based on a separate database, the Nationwide Inpatient Sample (NIS), demonstrated that a preoperative diagnosis of depression was linked to a higher risk of postoperative medical complications including anemia, infection, and pulmonary embolism [OR for anemia 1.14 with CI 1.09–1.17, $P < .001$; OR for infection 1.33 with CI 1.21–1.41, $P = .012$; OR for PE 1.20 with CI 1.14–1.25, $P = .005$; Table 1] [15]. These findings were again corroborated by a single institution's retrospective review of approximately 2000 patients, where a preoperative diagnosis of depression or anxiety was independently associated with a statistically significant increase in the rate of postoperative medical complications after hip and knee arthroplasty from 15.5% in the cohort with no mental health disorders to 29% in the patients with depression or anxiety [$P < .001$, Table 1] [16]. Using a different data set, the Medicare 5% national sample administrative database, Bozic et al. demonstrated an increase in the rate of early revision in patients with depression [RR for TKA 1.37 with CI 1.17–1.61, $P = .002$; RR for THA 1.89 with CI 1.63–2.20, $P < .001$; Table 1] [17•, 18•]. Interestingly, in addition to depression and anxiety alone, Klement et al. noted that the risk of complications following total joint arthroplasty is higher among patients with other psychiatric illnesses. In their retrospective review of the full Medicare database, the authors showed that patients with a diagnosis of depression, bipolar disorder, or schizophrenia had a twofold increase in the likelihood of knee extensor mechanism rupture, periprosthetic fracture, prosthetic join infection, and need for revision arthroplasty at minimum of 2-year follow-up [OR for extensor mechanism rupture 2.18 with CI 1.95–2.42, $P < .001$; OR for periprosthetic fracture 2.20 with CI 1.96–2.47, $P < .001$; OR for prosthetic joint infection 2.08 with CI 1.98–2.17, $P < .001$; OR for revision arthroplasty 2.01 with CI 1.88–2.15, $P < .001$; Table 1] [19].

These recent data indicate that psychiatric illness is correlated with worse patient-reported outcomes and an increase in medical and surgical complications after total joint arthroplasty. The retrospective nature of many of these studies limits our ability to comment on potential methods of improving the care of patients with anxiety and depression at the present time. Further study is needed to elucidate the biological mechanisms underlying these associations, as well as the effect that preoperative screening for and treatment of psychiatric disease may have on outcomes after total joint replacement surgery.

Liver Disease

As medical therapy continues to improve the life expectancy of patients with hepatitis C and cirrhosis, there is an increasing demand for total joint arthroplasty in this population [20, 21•]. However, despite the increase in lifespan associated with modern treatments, the negative effect that liver disease has on arthroplasty outcomes remains significant. In a matched-cohort review of 25,000 patients in the National Inpatient Sample database, hepatitis C was linked to an increased risk of overall perioperative medical complications after total knee, but not total hip arthroplasty [OR for medical complication after TKA 1.19 with CI 1.02–1.40, $P = .027$; Table 1] [20]. Data from the same sample demonstrated a significant increase in the risk of overall perioperative surgical complications following joint replacement surgery, including surgical site infection, hematoma, wound breakdown, and dislocation [OR for TKA 1.72 with CI 1.35–2.18, $P < .001$; OR for THA 1.85 with CI 1.42–2.41, $P < .001$; Table 1] [20]. It is important to note that this study focused on patients with a diagnosis of hepatitis C, not specifically cirrhosis, indicating that liver disease itself may increase complication rates even in the absence of cirrhosis. In addition, the authors grouped all complications together for analysis without reporting the rates of individual complications. Another single-institution retrospective study of 230 patients demonstrated an increased rate of early postoperative complications following total joint replacement in patients with cirrhosis. Within 90-days of the index arthroplasty procedure, patients with a diagnosis of cirrhosis had a higher rate of transfusion [$P < .001$], gastrointestinal

Table 1 Summary of the key findings in recent literature regarding factors affecting outcome following total joint arthroplasty

Publication	Topic	Variable	Result	95% confidence interval	*P* value
Ali et al. [13•]	Mental health	Preoperative diagnosis of anxiety or depression	(1) 6× risk of dissatisfaction with TKA at 4 years	NR	(1) $P < .001$
Gold et al. [14]	Mental health	Preoperative diagnosis of depression	(1) 21% increase in 90-day eadmission after TKA	(1) 1.13–1.29	(1) $P < .001$
			(2) 24% increase in 90-day readmission after THA	(2) 1.13–1.35	(2) $P < .001$
Browne et al. [15]	Mental health	Preoperative diagnosis of depression	(1) Increased risk of anemia (OR 1.14)	(1) 1.09–1.17	(1) $P < .001$
			(2) Increased risk of infection (OR 1.33)	(2) 1.21–1.41	(2) $P = .012$
			(3) Increased risk of PE (OR 1.20)	(3) 1.14–1.25	(3) $P = .005$
Rasouli et al. [16]	Mental health	Preoperative diagnosis of anxiety or depression	(1) 13.5% increase in overall complication rate after TJA	NR	(1) $P < .001$
Bozic et al. [17•][a]	Mental health	Preoperative diagnosis of depression	(1) Increased risk of revision TKA at 1-year (RR 1.37)	(1) 1.17–1.61	(1) $P = .002$
Bozic et al. [18•][b]	Mental health	Preoperative diagnosis of depression	(1) Increased risk of revision THA at 1 year (RR 1.89)	(1) 1.63–2.20	(1) $P < .001$
Klement et al. [19]	Mental health	Preoperative diagnosis of depression, bipolar disorder, or schizophrenia	(1) Increased risk of extensor mechanism rupture after TKA (OR 2.18)	(1) 1.95–2.42	(1) $P < .001$
			(2) Increased risk of periprosthetic fracture after TKA (OR 2.20)	(2) 1.96–2.47	(2) $P < .001$
			(3) Increased risk of PJI after TKA (OR 2.08)	(3) 1.98–2.17	(3) $P < .001$
			(4) Increased risk of revision TKA (OR 2.01)	(4) 1.88–2.15	(4) $P < .001$
Issa et al. [20]	Liver disease	Preoperative diagnosis of hepatitis C	(1) Increased risk of medical complication after TKA (OR 1.19)	(1) 1.02–1.40	(1) $P = .027$
			(2) Increased risk of surgical complication after TKA (OR 1.72)	(2) 1.35–2.18	(2) $P < .001$
			(3) Increased risk of surgical complication after THA (OR 1.85)	(3) 1.42–2.41	
Tiberi et al. [22]	Liver disease	Preoperative diagnosis of cirrhosis	(1) Increased risk of transfusion	(1) NR	(1) $P < .001$
			(2) Increased risk of GI bleeding	(2) NR	(2) $P = .04$
			(3) Increased risk of acute renal failure	(3) NR	(3) $P = .003$
			(4) Increased risk of THA dislocation	(4) NR	(4) $P = .01$
			(5) Increased risk of surgical site infection	(5) NR	(5) $P = .02$
			(6) Increased risk of need for revision surgery	(6) NR	(6) $P = .04$
			(7) Increased risk of medical complication after TJA in patients with MELD of 10 or greater (OR 3.16)	(7) 1.35–7.39	(7) $P < .001$
			(8) Increased risk of surgical complication after TJA in patients with MELD of 10 or greater (OR 4.75)	(8) 1.45–15.56	(8) $P < .001$
			(9) Increased risk of 1-year mortality in patients with MELD of 10 or greater (OR 4.1)	(9) 1.42–11.86	(9) $P < .001$
Jiang et al. [21•]	Liver disease	Preoperative diagnosis of cirrhosis	(1) Increased LOS after THA (5.7 versus 4.0 days) and TKA (4.4 versus 3.7 days)	(1) NR	(1) $P < .05$
			(2) Increased in-hospital mortality after THA (1.94 versus 0.2%) and TKA (0.41 versus 0.11%)	(2) NR	(2) $P < .05$
			(3) Increased risk of PJI (HR 2.42)	(3) 1.87–3.12	(3) $P < .001$
			(4) Increased risk of all-cause readmission after THA (HR 2.03) and TKA (HR 1.83)	(4) NR	(4) $P < .001$

Table 1 (continued)

Publication	Topic	Variable	Result	95% confidence interval	*P* value
Rozell et al. [23•]	Liver disease	Preoperative diagnosis of cirrhosis	(1) Increased risk of medical or surgical complication more than 24 h after surgery (OR 5.89)	(1) 1.05–33.07	(1) $P = .044$
Deleuran et al. [24]	Liver disease	Preoperative diagnosis of cirrhosis	(1) Increased risk of postoperative transfer to ICU (aOR 5.8)	(1) 1.3–25	(1) NR
			(2) Increased risk of PJI (aHR 2.1)	(2) 1.3–3.7	(2) NR
			(3) Increased risk of revision within 1-year (aHR 1.9)	(3) 1.1–3.3	(3) NR
			(4) Increased risk of hospital readmission (aOR 1.8)	(4) 1.3–2.4	(4) NR
			(5) Increased risk of 30-day mortality (aOR 3.9)	(5) 1.5–9.7	(5) NR
Kamath et al. [25]	Malnutrition	Preoperative albumin level less than 3.0 g/dL	(1) Increased risk of ICU admission if albumin less than 3.0 g/dL as compared to greater than 3.5 /dL (28 versus 3%)	(1) NR	(1) $P < .001$
Nelson et al. [26]	Malnutrition	Preoperative albumin level less than 3.5 g/dL	(1) Increased risk of deep surgical site infection after TKA (OR 3.64)	(1) 1.54–8.63	(1) $P = .003$
			(2) Increased risk of pneumonia after TKA (OR 3.55)	(2) 2.14–5.89	(2) $P < .001$
			(3) Increased risk of septic shock after TKA (OR 4.4)	(3) 1.74–11.09	(3) $P = .002$
			(4) Increased risk of cardiac arrest after TKA (3.74)	(4) 1.5–9.28	(4) $P = .005$
			(5) Increased risk of re-intubation after TKA (OR 2.24)	(5) 1.07–4.69	(5) $P = .003$
			(6) Increased risk of mortality after TKA (OR 3.17)	(6) 1.58–6.35	(6) $P = .001$
Walls et al. [27]	Malnutrition	Preoperative albumin level less than 3.5 g/dL	(1) Increased risk of composite major complication within 30-days of surgery after THA (OR 1.89)	(1) 1.29–2.76	(1) $P < .01$
			(2) Increased risk of deep surgical site infection after THA (OR 2.35)	(2) 1.12–4.91	(2) $P < .01$
			(3) Increased risk of pneumonia after THA (OR 2.41)	(3) 1.34–4.32	(3) $P < .01$
			(4) Increased risk of blood transfusion after THA (OR 1.82)	(4) 1.59–2.09	(4) $P < .01$
			(5) Increased risk of cardiopulmonary complication after THA (OR 1.66)	(5) 1.01–2.72	(5) $P < .01$
			(6) Increased risk of mortality after THA (OR 5.94)	(6) 3.07–11.48	(6) $P < .01$
Yi et al. [28]	Malnutrition	(1) Preoperative lymphocyte count less than 1500/mm3	(1) Increased rate of PJI after TJA with one or more markers of malnutrition	(1) NR	(1) $P = .003$
		(2) Preoperative serum albumin less than 3.5 g/dL	(2) Increased risk of acute postoperative infection after aseptic revision (OR 5.9)	(2) 1.32–26.06	(2) $P = .02$
		(3) Preoperative serum transferrin less than 200 mg/dL			
Bohl et al. [29•][c]	Malnutrition	Preoperative serum albumin less than 3.5 g/dL	(1) Increased risk of having a septic indication for revision TJA (RR 3.6)	(1) 3.2–4.1	(1) $P < .001$
			(2) Increased risk of acute post-operative infection after aseptic revision (RR 2.2)	(2) 1.3–3.5	(2) $P = .002$
Bohl et al. [30][d]	Malnutrition	Preoperative serum albumin less than 3.5 g/dL	(1) Increased risk of any complication (aRR 1.5)	(1) 1.2–1.7	(1) $P < .001$
			(2) Increased risk of major complication (aRR 1.4)	(2) 1.0–1.9	(2) $P = .042$
			(3) Increased risk of surgical site infection (aRR 2.0)	(3) 1.5–2.8	(3) $P < .001$

Table 1 (continued)

Publication	Topic	Variable	Result	95% confidence interval	*P* value
			(4) Increased risk of pneumonia (aRR 2.5)	4) 1.6–4.0	(4) $P < .001$
			(5) Increased risk of readmission (aRR 1.4)	5) 1.2–1.7	(5) $P < .001$
Jansen et al. [33]	Vitamin D	Preoperative serum vitamin D less than 40 ng/mL	(1) Lower pre-operative Knee Society Score compared to reference cohort with normal levels (51.5 vs 57.1)	(1) NR	(1) $P = .047$
			(2) Lower post-operative Knee Society Score compared to reference cohort with normal levels (74.6 versus 80.4)	(2) NR	(2) $P = .075$
Maniar et al. [34]	Vitamin D	Preoperative serum vitamin D less than 30 ng/mL	(1) Higher preoperative Western Ontario McMaster Osteoarthritis Index scores compared to reference cohort with normal levels (48.3 vs 42.3)	(1) NR	(1) $P = .04$
			(1) Equivalent postoperative Western Ontario McMaster Osteoarthritis Index scores between groups at 3 months with universal supplementation (17.6 vs 15.8)	(2) NR	(2) $P = .36$
Lavernia et al. [35]	Vitamin D	Preoperative serum vitamin D less than 30 ng/mL	(1) Lower preoperative Harris Hip Score compared to reference cohort with normal levels (43 vs 52)	(1) NR	(1) $P = .035$
			(2) Lower postoperative Harris Hip Score compared to reference cohort with normal levels (83 vs 92)		(2) $P = .002$
Maier et al. [36]	Vitamin D	Preoperative serum vitamin D less than 30 ng/mL	(1) Increased prevalence of hypovitaminosis D in patients underoing revision arthroplasty for septic indication as compared to primary elective arthroplasty (86% vs 65%)	(1) NR	(1) $P < .001$
Maier et al. [37]	Vitamin D	Preoperative serum vitamin D less than 20 ng/mL	(1) Increased mean length of stay as compared to reference cohort with normal levels (15.6 vs 11.3 days)	(1) NR	(1) $P = .014$
Yang et al. [38•]	Diabetes mellitus	Preoperative diagnosis of diabetes mellitus (any type/severity)	(1) Increased risk of deep infection (OR 1.61)	(1) 1.38–1.88	(1) $P < .001$
			(2) Increased risk of periprosthetic fracture (OR 1.89)	(2) 1.04–3.45	(2) $P = .04$
			(3) Increased risk of aseptic loosening (OR 9.36)	(3) 4.63–18.90	(3) $P < .001$
			(4) Worse Knee Society "function" sub-score (−5.86)	(4) −1.46 to −10.27	(4) $P < .001$
Adams et al. [39]	Diabetes mellitus	Preoperative diagnosis of diabetes mellitus with HbA1c greater/less than 7	(1) No difference in rate of revision in either diabetes group as compared to reference cohort without diabetes (OR 1.02)	(1) 0.68–1.54	(1) $P > .05$
			(2) No difference in rate of deep infection in either diabetes group as compared to reference cohort without diabetes (OR 0.55)	(2) 0.29–1.06	(2) $P > .05$
			(3) No difference in rate of DVT/PE in either diabetes group as compared to reference cohort without diabetes (OR 0.7)	(3) 0.43–1.13	(3) $P > .05$
Kremers et al. [40]	Diabetes mellitus	(1) Preoperative diagnosis of diabetes	(1) Increased risk of prosthetic joint infection within 1-year of elective, primary arthroplasty in patients with either diagnosis of diabetes or perioperative hyperglycemia (HR 1.55)	(1) 1.11–2.16	(1) NR
				(2) 0.87–1.74	(2) NR

Table 1 (continued)

Publication	Topic	Variable	Result	95% confidence interval	*P* value
		(2) Recorded perioperative hyperglycemia (blood glucose greater than 180 mg/dL within 1 week of surgery)	(2) No significantly increased risk of PJI in patients with diabetes/hyperglycemia after adjusting for BMI, ASA score, and operative time (HR 1.23)		
Bozic et al. [17•][a]	Diabetes mellitus	Preoperative diagnosis of diabetes mellitus	(1) No increase in risk of revision within 1 year of elective, primary TKA (HR 1.05)	(1) 0.93–1.19	(1) $P = .45$
Bozic et al. [18•][b]	Diabetes mellitus	Preoperative diagnosis of diabetes mellitus	(1) No increase in risk of revision within 1 year of elective primary THA (HR 1.05)	(1) 0.91–1.21	(1) $P = .51$

When multiple articles are listed with the same first author name and year of publication, each article is differentiated by a *superscript letter* in alphabetical order, in order of citation in the Reference section. (*OR* odds ratio, *aOR* adjusted odds ratio, *HR* hazard ratio, *aHR* adjusted hazard ratio, *RR* relative risk, *aRR* adjusted relative risk, *NR* not reported)

bleeding [$P = .04$], acute renal failure [$P = .003$], THA dislocation [$P = .01$], surgical site infection [$P = .02$], and need for revision surgery [$P = .04$] [22]. Cirrhotic patients also had a statistically greater length of stay, were more frequently discharged to nursing facilities, and had higher 90-day readmission rates. In addition, the authors found that a model for end-stage liver disease (MELD) score of 10 or greater increased the likelihood of any complication by three times [OR 2.99 with CI 1.28–7.00, $P = .001$; Table 1] and increased the likelihood of 1-year mortality by over 4-times [OR 4.10 with CI 1.42–11.86, $P < .001$; Table 1] [22]. A significant limitation of this study is that it did not control for comorbid diseases to isolate cirrhosis as an independent variable, but the authors contend that even a correlation between cirrhosis and complication risk is helpful when counseling patients preoperatively.

The relationship between cirrhosis and an increased risk of worse clinical outcomes after arthroplasty was confirmed by Jiang et al. in a retrospective review of the State Inpatient Database. Patients with cirrhosis had increased length of stay, increased risk of in-hospital mortality, greater risk of prosthetic joint infection, and higher rates of readmission and reoperation within 180-days of index surgery [Table 1] [21•]. In a multivariate analysis of this dataset, cirrhosis was shown to be an independent risk factor for prosthetic joint infection [HR 2.42 with CI 1.87–3.12, $P < .001$], as was a diagnosis of hepatitis C without cirrhosis [HR 2.33 with CI 1.97–2.76, $P < .001$] [21•]. In a prospective evaluation of 802 consecutive elective hip and knee arthroplasty patients, Rozell et al. identified several medical comorbidities that were associated with late complications following arthroplasty (defined as more than 24-h after surgery), of which cirrhosis carried the highest odds ratio of developing a medical or surgical complication [OR 5.89 with CI 1.05–33.07, $P = .044$; Table 1] [23•]. Another retrospective cohort study of primary hip and knee arthroplasty patients within the Danish National Patient Registry also supports a higher rate of medical and surgical complications within 1-year of surgery in patients with cirrhosis. Consistent with other studies, the rate of postoperative transfer to an intensive care service [aOR 5.8 with CI 1.3–25], prosthetic joint infection [aHR 2.1 with CI 1.3–3.7], revision surgery [aHR 1.9 with CI 1.1–3.3], hospital re-admission [aOR 1.8 with CI 1.3–2.4] and 30-day mortality [aOR 3.9 with CI 1.5–9.7] were significantly higher in the patients with a diagnosis of cirrhosis [Table 1] [24]. Interestingly, the analysis showed no difference in the rate of intra-operative complications between the cirrhotic group and the control group. The authors highlighted that 81% of patients with cirrhosis did not have any intra- or postoperative complications, as compared to 91% of the patients in the reference group [24].

Total joint arthroplasty in patients with liver disease is associated with an increased rate of both minor and major postoperative complications. This risk is present even in the absence of cirrhosis; however, end-stage liver disease does appear to heighten the risk of poor outcomes. How to minimize adverse events in this population remains an unanswered question, but it is important for surgeons to recognize the potential dangers of arthroplasty in patients with liver disease in order to counsel patients and plan appropriately for their postoperative care.

Hypoalbuminemia

Recently, markers of malnutrition, and particularly hypoalbuminemia, have been linked to adverse outcomes following total joint replacement surgery. For instance, in a prospectively gathered database of 1098 primary and revision arthroplasties, patients with hypoalbuminemia (serum albumin <3.0 g/dL) who underwent primary total joint arthroplasty had a 28.6%

rate of unplanned ICU admission in the immediate postoperative period, significantly higher than the rate in patients with serum albumin 3.5 g/dL or greater [$P < .001$; Table 1] [25]. In another study, Nelson et al. utilized the National Surgical Quality Improvement Program (NSQIP) database to explore the relationship between morbid obesity and hypoalbuminemia and their effect on outcomes following total joint replacement. The authors were able to show that while morbid obesity is associated with an increased risk of several minor complications including renal insufficiency [OR 2.47 with CI 1.27–4.29, $P < .001$] and superficial infection [OR 1.87 with CI 1.39–2.51, $P < .001$] after total knee arthroplasty, low serum albumin (less than 3.5 g/dL) carried a significantly higher and independent risk of major complications such as deep surgical site infection [OR 3.64 with CI 1.54–8.63, $P = .003$; Table 1], pneumonia [OR 3.55 with CI 2.14–5.89, $P < .001$; Table 1], septic shock [OR 4.4 with CI 1.74–11.09, $P = .002$; Table 1], cardiac arrest [OR 3.74 with CI 1.50–9.28, $P = .005$; Table 1], re-intubation [OR 2.24 with CI 1.07–4.69, $P = .033$; Table 1], and death [OR 3.17 with CI 1.58–6.35, $P = .001$; Table 1] [26]. The same group reported similar findings after total hip arthroplasty, with morbid obesity being independently associated with superficial surgical site infection [OR 2.02 with CI 1.36–3.02, $P < .01$] and the composite endpoint of "any infection" [OR 1.42 with CI 1.05–1.93, $P < .01$], but not associated with any of the major complications analyzed [27]. Hypoalbuminemia was, however, an independent risk factor for developing a major complication within 30-days of surgery [OR 1.89 with CI 1.29–2.76, $P < .01$; Table 1], including deep surgical site infection [OR 2.35 with CI 1.12–4.91, $P < .01$; Table 1], pneumonia [OR 2.41 with CI 1.34–4.32, $P < .01$; Table 1], blood transfusion [OR 1.82 with CI 1.59–2.09, $P < .01$; Table 1], cardiopulmonary complication [OR 1.66 with CI 1.01–2.72, $P < .01$; Table 1], and mortality [OR 5.94 with CI 3.07–11.48, $P < .01$; Table 1] [27].

The risk of postoperative surgical complication may also be elevated in malnourished patients who undergo revision arthroplasty. In a retrospective review of 375 consecutive aseptic revision arthroplasties, it was shown that having one or more laboratory markers suggestive of malnutrition increased the rate of postoperative prosthetic joint infection from 1 to 7% [$P = .003$; Table 1] [28]. The laboratory markers of malnutrition included in the analysis were total lymphocyte count less than 1500/mm^3, serum albumin less than 3.5 g/dL, or serum transferrin less than 200 mg/dL. Malnutrition was also independently associated with acute postoperative infection after an aseptic revision [OR 5.9 with CI 1.32–26.06, $P = .02$; Table 1] [28].

A different group confirmed these findings in a retrospective review of 4500 patients in the National Surgical Quality Improvement Program (NSQIP) database. In this cohort, patients with serum albumin less than 3.5 g/dL were over three times more likely to have a septic indication for revision than patients with normal albumin levels [RR 3.6 with CI 3.2–4.1; $P < .001$; Table 1] [29•]. The rate of prosthetic joint infection within 30 days of revision for aseptic indications was likewise two times higher in the group with hypoalbuminemia even after controlling for demographic differences and medical comorbidities [RR 2.2 with CI 1.3–3.5; $P = .002$; Table 1] [29•].

Bohl et al. also use the NSQIP database to analyze the impact of hypoalbuminia on complication rate after elective primary total joint arthroplasty and found higher rates of several complications in patients with serum albumin less than 3.5 g/dL including surgical site infection [aRR 2.0 with CI 1.5–2.8, $P < .001$; Table 1], pneumonia [aRR 2.5 with CI 1.6–4.0, $P < .001$; Table 1], and the composite endpoint of "serious complication" [aRR 1.4 with CI 1.0–1.9, $P = .042$; Table 1] [30].

Nutritional status is an intuitively important variable to consider in the pre-operative evaluation of surgical patients, and there is mounting scientific evidence to support its use for risk stratification. Most of the recent literature in this area uses hypoalbuminemia as a proxy for malnutrition, but low serum albumin can also be a marker of other chronic disease processes. Further research is necessary to clarify the impact of hypoalbuminemia—versus malnutrition specifically—on outcomes following total joint replacement, as well as the effectiveness of medical interventions to correct these abnormalities.

Hypovitaminosis D

Vitamin D is a critical hormone that has come to the forefront of medical research in recent years as we have learned more about its effects not only on bone growth and remodeling, but also on immune function and other metabolic pathways involved in the healing process [31]. A recent prospective analysis of 81 patients in the Northeastern USA undergoing elective orthopedic surgical procedures showed that approximately two-thirds of this adult population had low vitamin D levels (less than 30 ng/mL), highlighting the prevalence of hypovitaminosis D in the general orthopedic population [32]. There are several published reports of hypovitaminosis D being associated with a poor preoperative functional state in patients undergoing knee arthroplasty, but the effect of low vitamin D on postoperative function is less clear. Jansen and Haddad found that in a group of Caucasian patients undergoing elective primary knee arthroplasty, preoperative Knee Society Scores (KSS) were significantly lower in the vitamin D deficient group (less than 40 ng/mL) relative to the group with normal vitamin D levels [51.5 versus 57.1, $P = .047$, Table 1] [33]. Knee Society Scores were also lower in the vitamin D deficient group after knee replacement, but this difference was not statistically significant [74.6 versus 80.4, $P = .075$; Table 1] [33]. A similar review of 120 knee replacements by a single surgeon in India demonstrated that patients

with serum vitamin D levels less than 30 ng/mL had significantly higher preoperative Western Ontario and McMaster Osteoarthritis Index (WOMAC) scores than patients with serum vitamin D levels greater than 30 ng/mL [48.3 versus 42.3, $P = .04$; Table 1] [34]. All patients in this series were given vitamin D supplementation postoperatively, and at 3-month follow-up, there was no difference in WOMAC scores between the two groups. The authors of this study argued that preoperative correction of vitamin D deficiency is not necessary, as they demonstrated that similar functional outcomes can be achieved with postoperative supplementation only. Vitamin D insufficiency has also been linked to poor functional outcomes after hip replacement. Lavernia et al. retrospectively analyzed 60 consecutive patients who underwent elective primary total hip arthroplasty and found that patients with vitamin D levels less than 30 ng/mL had lower preoperative Harris Hip Scores (HHS) as compared to patients with vitamin D levels greater than 30 ng/mL [43 versus 52, $P = .035$; Table 1] [35]. The significant difference in HHS scores persisted at 11-month follow-up, with vitamin D insufficient patients having a mean HHS of 83 as compared to 92 in the normal vitamin D group [$P = .002$; Table 1] [35].

In addition to impacting function, hypovitaminosis D appears to play a role in other outcomes surrounding orthopedic procedures. A prospective study of 190 consecutive patients undergoing primary or revision hip, knee or shoulder arthroplasty in Germany demonstrated that vitamin D deficiency was prevalent in all groups and that vitamin D level was significantly lower in patients undergoing revision for prosthetic joint infection. Sixty-five percent of patients undergoing elective primary arthroplasty had vitamin D levels below 30 ng/mL as compared to 86% of patients undergoing revision for prosthetic joint infection [$P < .001$; Table 1] [36]. The patients who presented with a periprosthetic infection had a mean vitamin D level of 13.2 ng/mL, dramatically lower than the commonly accepted minimum normal threshold of 30 ng/mL. In a separate study, these authors reviewed the results of 1083 patients undergoing elective primary hip and knee arthroplasty and demonstrated that patients with serum 25-OH-D levels below 20 ng/mL had a 4-day increase in length of stay as compared to patients with vitamin D values above this level [15.6 versus 11.3 days, $P = .014$; Table 1] [37].

Vitamin D deficiency is widespread among the adult population undergoing elective orthopedic surgery in several northern-latitude regions, and the effect it has on outcomes after arthroplasty is becoming increasingly clear. The necessary vitamin D level for optimizing surgical results, as well as the ideal timing and regimen for supplementation has not yet been formalized, but current evidence suggests that correction of vitamin D levels at the time of surgery may have beneficial effects for patients undergoing total joint replacement.

Diabetes Mellitus

Diabetes mellitus is a known risk factor for postoperative complications following orthopedic surgery. For instance, in a recent systematic review and meta-analysis of 14 studies, Yang et al. showed that diabetic patients undergoing primary total knee arthroplasty were at increased risk of major and minor medical complications as well as lower Knee Society functional outcome sub-scores [Table 1] [38•]. However, risk stratification of diabetics in preparation for total joint arthroplasty has proved challenging. Adams et al. used the Kaiser Permanente Total Joint Replacement Registry to analyze the risk of revision arthroplasty, deep infection, or deep venous thrombosis in patients undergoing elective total knee arthroplasty. The authors evaluated the relative risk of developing each of these complications in well-controlled diabetics (HbA1c < 7) and poorly controlled diabetics (Hba1c > 7) as compared to a nondiabetic cohort, and they found no significantly increased risk in either group [OR for revision 1.02 with CI 0.68–1.54; OR for deep infection 0.55 with CI 0.29–1.06; OR for DVT/PE 0.7 with CI 0.43–1.13; Table 1] [39]. In a retrospective analysis of the Mayo Institutional Total Joint Registry identified over 20,000 patients operated on between 2002 and 2009, Kremers et al. showed a higher risk of prosthetic joint infection within 1-year of elective primary hip and knee arthroplasty in patients with either a diagnosis of diabetes or perioperative hyperglycemia defined as a single recorded blood glucose greater than 180 mg/dL within 1-week pre-/postoperatively [HR 1.55 with CI 1.11–2.16; Table 1] [40]. However, these effects did not remain statistically significant when adjusted for BMI, ASA score, and operative time. To make matters even more confusing, Bozic et al. queried the Medicare 5% database to examine the effect of 29 medical comorbidities on the rate of revision within 1-year of elective primary hip and knee replacements and found that simply a diagnosis of diabetes was not a risk factor for early revision in either total knee arthroplasty or total hip arthroplasty [HR for TKA 1.05 with CI 0.93–1.19, $P = .45$; HR for THA 1.05 with CI 0.91–1.21, $P = .51$; Table 1] [17•, 18•].

Thus, the effect of diabetes on the outcomes following total joint arthroplasty is clearly nuanced and likely result from specific manifestations of the disease. Although hemoglobin A1C has often been used as a marker of diabetes control for risk stratification prior to joint arthroplasty, it has not been solidly linked to an elevated risk of postoperative complications. Blood glucose levels in the acute perioperative period may be a useful marker of the risk of poor outcome. However, large prospective trials focusing on glucose control in the perioperative period are still needed in order to elucidate the effect of perioperative glucose control on outcomes.

Conclusion

Total joint arthroplasty is a highly successful intervention, conferring long-term functional benefits and pain relief to the majority of recipient patients. However, there are many factors that can contribute to adverse outcomes in some patient populations and these factors must be considered by the operating surgeon in order to optimize patients' postoperative results. Over the last 3 years, some of the areas of focus have included the optimization of preoperative mental health, liver function, nutritional status, vitamin D levels, and diabetes management. While these factors make up only a subset that may affect outcomes following total joint replacement, they represent current areas of research and deserve the attention of operating orthopedic surgeons in today's health care environment.

Compliance with ethical standards

Conflict of interest Both authors declare that they have no conflicts of interest.

Human and animal rights and informed consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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