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Original Research

Liver Disease Increases the Risk of Postoperative Complications in Patients Undergoing Aseptic Revision Total Hip and Knee Arthroplasty

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ABSTRACT

Background: Due to the multiorgan effects of liver disease, surgical patients with liver disease have an increased risk of perioperative complications. With revision total hip and knee arthroplasty surgeries increasing, it is important to determine the effects of liver disease in this patient population. The purpose of this study was to evaluate the impact of underlying liver disease on postoperative outcomes following revision total joint arthroplasty (TJA).

Methods: The National Surgical Quality Improvement Program database was used to identify patients undergoing aseptic revision TJA from 2006-2019 and group them based on liver disease. The presence of liver disease was assessed by calculating the Model for End-Stage Liver Disease–Sodium score. Patients with a Model for End-Stage Liver Disease–Sodium score of > 10 were classified as having underlying liver disease. In this analysis, differences in demographics, comorbidities, and postoperative complications were assessed.

Results: Of 7102 patients undergoing revision total hip arthroplasty, 11.6% of the patients had liver disease. Of 8378 patients undergoing revision total knee arthroplasty, 8.4% of the patients had liver disease. Following adjustment on multivariable regression analysis, patients with liver disease undergoing revision total hip arthroplasty or revision total knee arthroplasty had an increased risk of major complications, wound complications, septic complications, bleeding requiring transfusion, extended length of stay, and readmission compared to those without liver disease.

Conclusions: Patients with liver disease have an increased risk of complications following revision TJA. A multidisciplinary team approach should be employed for preoperative optimization and postoperative management of these vulnerable patients to improve outcomes and decrease the incidence and severity of complications.

Level of evidence: This is retrospective cohort study and is level 3 evidence.

Introduction

As the number of primary total joint arthroplasty (TJA) procedures continues to rise, the subsequent revision hip and knee burden will also increase [1]. Revision TJA procedures are more complex and are associated with longer operative times, increased complication rates, and worse outcomes when compared to primary TJA [2,3]. At the time of revision TJA, patients are typically older and have more comorbidities, putting them at higher risk of postoperative complications [3]. Preoperative vigilance for the presence of undiagnosed comorbidities and adequate preoperative optimization is critical to optimize a patient's risk profile and increase the likelihood of achieving a successful clinical outcome.

One comorbidity associated with higher complication rates following surgery is chronic liver disease (CLD) [4]. CLD and cirrhosis are estimated to affect about 1.5 billion people worldwide [5]. In the United States, the rising prevalence of nonalcoholic fatty liver disease related to obesity and diabetes has driven the adult prevalence of liver disease to be more than 30% [6]. Most cases of CLD are

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asymptomatic; even among patients in the United States with laboratory evidence of cirrhosis, nearly 70% report that they were previously unaware that they had CLD [7,8]. Annually in the United States, CLD results in 2.33 million disability-adjusted life years and 56,585 deaths [9,10]. The Model for End-Stage Liver Disease—Sodium (MELD-Na) score is 1 was to assess the severity of CLD based on the need for dialysis, and laboratory values including bilirubin, creatinine, international normalized ratio, and sodium [11].

CLD and cirrhosis are associated with higher complication rates and higher costs in patients undergoing elective primary TJA [12,13]. In this patient population, overall complications and death rates increased more than 3-fold and 4-fold, respectively [14]. What is unknown is the effect of CLD on surgical outcomes for patients undergoing revision TJA, which in certain circumstances are more urgent and cannot be performed on an elective basis. The purpose of this study was to use a national database to determine the effects of CLD on adverse outcomes following revision TJA. The authors hypothesize that CLD will be associated with increased rates of complications, readmissions, and length of stay. We anticipate greater complication rates for revision TJA given patients may be less optimized preoperatively.

Material and methods

This investigation used the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database, which includes data collected prospectively from more than 600 medical centers in the United States. The reliability of this database is maintained by auditing procedures, with <1.6% disagreement regarding collected variables [15]. Numerous preoperative, intraoperative, and postoperative variables are collected in this database. The utility of this national database for quality improvement in orthopaedic surgeries has been well documented in the literature [16].

Patient selection

Patients who underwent revision total hip arthroplasty (THA) and total knee arthroplasty (TKA) from 2006-2019 were identified using Current Procedural Terminology codes: 27134, 27137, and 27138 for revision THA (rTHA) and 27486 and 27487 for revision TKA (rTKA). Patients were excluded from this study if they had missing baseline demographic data (eg, gender or race), were aged less than 18 years, and had a diagnosis of periprosthetic joint infection. To limit confounding, only aseptic revision cases were included in the analysis by excluding cases with a primary diagnosis of prosthetic joint infection by the International Classification of Diseases, Ninth Revision and International Classification of Diseases, 10th Revision codes. After initial data collection, 7906 rTHA and 9310 rTKA patients met initial inclusion criteria. Exclusion criteria were applied and 804 rTHA and 932 rTKA patients were excluded, leaving 7102 rTHA and 8378 rTKA patients for final analysis.

Liver function assessment

Liver function was calculated from the MELD-Na score. Serum bilirubin and creatinine levels were measured in mg/dL. Sodium levels were measured in mmol/L. Any patient with missing preoperative serum creatinine, bilirubin, sodium levels, or international normalized ratio was excluded from this study. A MELD-Na score of > 10 was the threshold value for a diagnosis of CLD. This methodology was adapted from a 2019 study by Lu et al., which used the same MELD-Na score threshold to identify CLD in patients undergoing adult spinal deformity surgery [17]. MELD score < 10 has been associated with lower mortality for patients, with increasing mortality in groups with a score 10 and more [18]. Therefore, 2 patient groups were categorized in this study: patients with and without CLD.

Patient characteristics

Patients' baseline demographic information included age, gender, race, body mass index, American Society of Anesthesiologists score, smoking status, and functional status. Documented medical comorbidities included hypertension, current dialysis, congestive heart failure, chronic obstructive pulmonary disease, recent weight loss, chronic steroid usage, diabetes, bleeding disorders, preoperative transfusion requirement, and dyspnea. Anesthetic type used during surgery was also recorded.

Postoperative outcomes

Thirty-day outcomes were categorized into clinically relevant categories. These categories included wound (superficial or deep surgical site infection, organ or space infections, or wound dehiscence), cardiac (cardiac arrest or myocardial infarction), pulmonary (pneumonia, unplanned reintubation, or failure to wean off ventilator for >48 hours), renal (renal failure or insufficiency), thromboembolic (pulmonary embolism, deep vein thrombosis, or stroke), and septic (sepsis or septic shock). Complications were classified as major or minor in severity [19]. Postoperative transfusion requirement, reoperation, and readmission were also assessed. An extended length of stay was defined as more than 7 days based on previous literature [20].

Statistical analysis

Patients' demographic characteristics and preoperative comorbidities were analyzed with Pearson's Chi-squared tests and analysis of variance where appropriate to examine their association with CLD. To control for confounding variables, factors with P values < .20 were included in the multivariable regression models [21]. Postoperative complications were then reported as odds ratios (ORs) with 95% confidence intervals for the multivariable analysis results. A P value of < .05 was the value for statistical significance in all statistical tests. All statistical analyses were performed using IBM SPSS Statistics 28 (SPSS Inc., Armonk, NY).

Results

Overall, 7102 patients who underwent rTHA and 8378 patients who underwent rTKA were included in the analysis after applying the inclusion and exclusion criteria. A total of 823 (11.6%) patients undergoing rTHA and 703 (8.4%) patients undergoing rTKA had CLD. In both patient cohorts, those with CLD were more likely to be male (P < .001), older (P < .001), have an American Society of Anesthesiologists class of III or IV (P < .001), and have a dependent functional status (P < .001) (Table 1).

Comorbidities

Patients with liver disease undergoing revision TJA were more likely to have other medical comorbidities, including hypertension, current dialysis, congestive heart failure, chronic obstructive pulmonary disease, recent weight loss, diabetes, bleeding disorders, requirement for a preoperative transfusion, and dyspnea (P < .02 for all; Table 2). CLD patients were also more likely to receive general vs regional anesthesia (P < .01) (Table 2).

Table 1
Demographics and clinical characteristics among patients undergoing revision total hip and knee arthroplasty.

Demographics	Revision total hip arthroplasty			Revision total knee arthroplasty		
	No liver disease	Liver disease	*P* value	No liver disease	Liver disease	*P* value
Total patients, n	6279	823		7676	702	
Sex, n (%)			**<.001**[a]			**<.001**[a]
Female	3525 (56.1)	358 (43.5)		4682 (61.0)	300 (42.7)	
Male	2754 (43.9)	465 (56.5)		2994 (39.0)	402 (57.3)	
Race, n (%)			.447[a]			**<.001**[a]
White	5333 (84.9)	710 (86.3)		5843 (76.1)	571 (81.3)	
Black	552 (8.8)	71 (8.6)		1192 (15.5)	79 (11.3)	
Hispanic	277 (4.4)	24 (2.9)		482 (6.3)	26 (3.7)	
Native American	45 (0.7)	7 (0.9)		51 (0.7)	6 (0.9)	
Asian	61 (1.0)	10 (1.2)		70 (0.9)	9 (1.3)	
Native Hawaiian	11 (0.2)	1 (0.1)		38 (0.5)	11 (1.6)	
ASA, n (%)			**<.001**[a]			**<.001**[a]
I or II	2256 (36.0)	124 (15.1)		2848 (37.1)	134 (19.1)	
III or IV	4021 (64.0)	697 (84.9)		4821 (62.9)	568 (80.9)	
Smoker, n (%)	990 (15.8)	124 (15.1)	.604[a]	872 (11.4)	79 (11.3)	.932[a]
Dependent functional status, n (%)	537 (8.6)	128 (15.6)	**<.001**[a]	346 (4.5)	79 (11.4)	**<.001**[a]
Mean age, y (SD)	67.27 (12.40)	71.48 (12.72)	**<.001**[b]	65.53 (10.59)	69.49 (11.07)	**<.001**[b]
Mean BMI (SD)	29.57 (6.91)	28.51 (7.40)	**<.001**[b]	33.60 (7.45)	32.64 (7.61)	**.001**[b]

ASA, American Society of Anesthesiologists; SD, standard deviation; BMI, body mass index.
Bold signifies a *P*-value less than .05.
[a] Pearson's chi-squared test.
[b] Analysis of variance.

Postoperative complications

Tables 3 and 4 depict the results of a univariable and multivariable analysis, respectively, of postoperative complications in patients undergoing either revision THA or TKA. The multivariable analysis demonstrates that patients with CLD were at elevated risk for major complications following rTHA (OR 1.5; $P = .005$) and rTKA (OR 3.0; $P < .001$). Patients with CLD undergoing rTHA were more likely to require postoperative transfusion than those undergoing rTKA ($P < .001$). Wound complications were specifically increased in patients with CLD undergoing both rTKA ($P < .001$) and rTHA ($P = .002$).

Discussion

In this retrospective database study evaluating patients undergoing either revision THA or TKA, we found that MELD-Na score > 10 as a measure of CLD was an independent risk factor for postoperative complications including postoperative transfusion, wound complications, sepsis, readmission, and extended length of stay. Recent studies indicate the major complication rate for patients with CLD undergoing primary THA and TKA is 4.3% and 3.7%, respectively [22,23]. Major complication rates for rTHA in CLD patients were 8.6%, compared to 3.6% in patients without CLD. For rTKA, major complication rates for patients with liver disease were 9.5% compared to 2.1% for those without CLD. This affirms our hypothesis that CLD greatly increases the likelihood for adverse postoperative outcomes in these patients.

Previous studies have reviewed the effect of CLD on postoperative outcomes in both orthopaedic and nonorthopaedic patients [14,17,21,22,24-28]. Multiple studies have shown that CLD is an independent predictor for complications following surgery including liver and renal failure, bleeding, and infection

Table 2
Medical comorbidities and intraoperative variables among patients undergoing revision total hip and knee arthroplasty.

Comorbidities	Revision total hip arthroplasty			Revision total knee arthroplasty		
	No liver disease	Liver disease	*P* value[a]	No liver disease	Liver disease	*P* value[a]
Total patients, n	6279	823		7676	702	
Hypertension, n (%)	3865 (61.6)	646 (78.5)	**<.001**	5294 (69.0)	584 (83.2)	**<.001**
Dialysis, n (%)	4 (0.1)	60 (7.3)	**<.001**	5 (0.1)	40 (5.7)	**<.001**
CHF, n (%)	64 (1.0)	37 (4.5)	**<.001**	48 (0.6)	26 (3.7)	**<.001**
COPD, n (%)	451 (7.2)	80 (9.7)	**.009**	454 (5.9)	58 (8.3)	**.013**
Weight loss, n (%)	45 (0.7)	14 (1.7)	**.003**	33 (0.4)	8 (1.1)	**.010**
Steroid use, n (%)	462 (7.4)	60 (7.3)	.944	421 (5.5)	56 (8.0)	**.006**
Diabetes mellitus, n (%)	854 (13.6)	169 (20.5)	**<.001**	1673 (21.8)	211 (30.1)	**<.001**
Bleeding disorder, n (%)	398 (6.3)	126 (15.3)	**<.001**	348 (4.5)	112 (16.0)	**<.001**
Preoperative transfusion, n (%)	132 (2.1)	61 (7.4)	**<.001**	56 (0.7)	22 (3.1)	**<.001**
Dyspnea, n (%)			**<.001**			**<.001**
Moderate exertion	375 (6.0)	60 (7.3)		535 (7.0)	68 (9.7)	
At rest	28 (0.4)	13 (1.6)		19 (0.2)	7 (1.0)	
Anesthesia type, n (%)			**.005**			**<.001**
General	4882 (78.7)	697 (85.1)		4882 (64.9)	520 (74.5)	
Neuraxial	926 (14.9)	87 (10.6)		1834 (24.4)	123 (17.6)	
Regional	68 (1.1)	7 (0.9)		126 (1.7)	7 (1.0)	
MAC	326 (5.3)	28 (3.4)		661 (8.8)	46 (6.6)	

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; MAC, monitored anesthesia care.
Bold signifies a *P*-value less than .05.
[a] Pearson's chi-squared test.

Table 3
Univariable analysis of postoperative complications of patients following revision total hip and knee arthroplasty.

Complications	Revision total hip arthroplasty			Revision total knee arthroplasty		
	No liver disease	Liver disease	*P* value[a]	No liver disease	Liver disease	*P* value[a]
Total patients, n	6279	823		7676	702	
Major complication, n (%)[b]	227 (3.6)	71 (8.6)	**<.001**	159 (2.1)	67 (9.5)	**<.001**
Minor complication, n (%)[c]	347 (5.5)	69 (8.4)	**.001**	278 (3.6)	57 (8.1)	**<.001**
Death, n (%)	52 (0.8)	25 (3.0)	**<.001**	24 (0.3)	18 (2.6)	**<.001**
Wound complication, n (%)	281 (4.5)	57 (6.9)	**.002**	222 (2.9)	50 (7.1)	**<.001**
Cardiac complication, n (%)	54 (0.9)	10 (1.2)	.311	29 (0.4)	10 (1.4)	**<.001**
Pulmonary complication, n (%)	100 (1.6)	23 (2.8)	**.013**	57 (0.7)	20 (2.8)	**<.001**
Renal complication, n (%)	29 (0.5)	10 (1.2)	**.006**	22 (0.3)	10 (1.4)	**<.001**
Thromboembolic complication, n (%)	75 (1.2)	12 (1.5)	.518	105 (1.4)	13 (1.9)	.298
Sepsis complication, n (%)	104 (1.7)	34 (4.1)	**<.001**	72 (0.9)	44 (6.3)	**<.001**
Urinary tract infection, n (%)	100 (1.6)	24 (2.9)	**.006**	59 (0.8)	14 (2.0)	**<.001**
Postoperative transfusion, n (%)	1748 (27.8)	348 (42.3)	**<.001**	836 (10.9)	162 (23.1)	**<.001**
Extended length of stay (>7 d), n (%)	736 (11.7)	225 (27.4)	**<.001**	346 (4.5)	158 (22.5)	**<.001**
Reoperation, n (%)	426 (6.8)	76 (9.2)	**.034**	286 (3.7)	60 (8.6)	**<.001**
Readmission, n (%)	520 (10.6)	113 (17.7)	**<.001**	405 (6.7)	68 (12.8)	**<.001**

[a] Pearson's chi-squared test.
[b] Includes cardiac arrest, pulmonary embolism, myocardial infarction, unplanned intubation, sepsis, septic shock, acute renal failure, or mortality.
[c] Includes urinary tract infection, pneumonia, deep venous thrombosis, superficial surgical site infection, or deep surgical site infection.

[25,26]. For patients undergoing TJA, elevated rates of medical complications, prosthetic joint infections, instability, and reoperations are seen in patients with CLD [22,23,27,29]. This is the first study in the literature to evaluate the effect of CLD as measured by MELD-Na score > 10 on complication rates following revision TJA.

Among these complications, postoperative transfusion represents a specific complication that may be related to hepatic coagulopathy [30,31]. Previous studies have shown that patients with CLD undergoing orthopaedic surgery have an increased risk of transfusion, with a 34.6% risk of transfusion following spine surgery, which is similar to the risk found in our study [17]. Recent 90-day outcomes studies have estimated the risk for transfusion in cirrhotic patients at 3.4% for THA and 2.8% for TKA [22,23]. This study identified a transfusion rate of 42.3% for rTHA and 23.1% for rTKA in CLD patients. This compares to a transfusion rate of 27.8% for rTHA and 10.9% for rTKA in patients without CLD. The particularly high rate of transfusion in revision setting may be explained by the increase in the surgical exposure required for the procedure which, especially in the setting of hepatic coagulopathy, can increase blood loss. To minimize adverse events related to blood loss, careful surgical planning, use of tranexamic acid when permissible, meticulous hemostasis during surgical dissection, use of intraoperative blood salvage, and careful coordination with anesthesia both preoperatively and intraoperatively to optimize resuscitation are essential.

There was a significantly increased risk of wound complications in revision TJA procedures performed in patients with CLD. This is consistent with previous literature, which has demonstrated an increase in wound complications in primary TJA procedures in cirrhotic patients [12,23,25]. Wound complications from surgery in patients with CLD can be related to impaired immune system function and malnutrition associated with the disease, which can be as high as 80% [32,33]. Proper evaluation of the nutrition status of a patient with CLD is critical during the preoperative evaluation period when considering revision TJA, as malnutrition increases complications in revision arthroplasty [34]. An appropriate nutrition workup would include laboratory studies including albumin and a subsequent consult to nutrition services for a preoperative diet to optimize the patient [35]. Other strategies aimed to optimize wound healing including use of negative pressure wound therapy which has been shown to reduce the risks of wound complications in patients undergoing revision arthroplasty who are at a high risk for infection [36,37].

Table 4
Multivariable analysis of postoperative complications of patients following revision total hip and knee arthroplasty.

Complications	Revision total hip arthroplasty		Revision total knee arthroplasty	
	P value	Odds ratio (liver disease/no liver disease) (95% CI)	*P* value	Odds ratio (liver disease/no liver disease) (95% CI)
Major complication[a]	**.005**	1.548 (1.139-2.102)	**<.001**	2.960 (2.115-4.143)
Minor complication[b]	.194	1.212 (0.907-1.620)	**<.001**	1.902 (1.378-2.626)
Death	.073	1.657 (0.954-2.877)	**.004**	2.947 (1.400-6.203)
Wound complication	**.004**	1.587 (1.158-2.174)	**<.001**	2.287 (1.612-3.246)
Cardiac complication	.782	1.164 (0.438-2.873)	.492	1.345 (0.578-3.130)
Pulmonary complication	.844	1.051 (0.638-1.733)	**.007**	2.234 (1.250-3.992)
Renal complication	.063	2.040 (0.962-4.328)	**.002**	3.658 (1.611-8.308)
Sepsis complication	**.012**	1.740 (1.130-2.678)	**<.001**	4.627 (3.001-7.135)
Urinary tract infection	.107	1.486 (0.918-2.407)	.091	1.746 (0.916-3.331)
Postoperative transfusion	**<.001**	1.406 (1.191-1.659)	**<.001**	1.696 (1.368-2.103)
Extended length of stay (>7 d)	**<.001**	1.717 (1.406-2.096)	**<.001**	4.083 (3.211-5.191)
Reoperation	.114	1.249 (0.948-1.646)	**<.001**	2.052 (1.497-2.813)
Readmission	**.002**	1.464 (1.144-1.874)	**.013**	1.466 (1.084-1.984)

CI, confidence interval.
Bold signifies a *P*-value less than .05.
[a] Includes cardiac arrest, pulmonary embolism, myocardial infarction, unplanned intubation, sepsis, septic shock, acute renal failure, or mortality.
[b] Includes urinary tract infection, pneumonia, deep venous thrombosis, superficial surgical site infection, or deep surgical site infection.

This study has several important limitations. These include its retrospective nature and the limited amount of information available in the ACS-NSQIP database. The study is also limited by the possibility of incorrect or miscoded diagnoses [38,39]. The ACS-NSQIP database only includes 30-day short-term outcomes. Our results therefore may not be generalizable to long-term postoperative outcomes. We also cannot elucidate the nature of CLD for each cohort beyond the MELD-Na score. The MELD-Na score is an imperfect predictor of CLD, but it has been shown to be a reliable indicator in past studies [17,40,41]. Our use of Current Procedural Terminology codes to identify patients undergoing revision arthroplasty surgery also presents an inability to identify the reason for revision or whether the surgery was a single-component or multiple-component revision. Outcomes may differ based on the reason for revision, for example, both component revisions for aseptic loosening may differ in outcomes dramatically from polyethylene exchange for wear. Additionally, it is unknown whether the included patients were undergoing their first revision surgery or if this was a re-revision, which may be one factor that influences case complexity and postoperative outcomes. Despite these limitations, our study expands the current literature by demonstrating the postoperative risks and complications of revision TJA in patients with CLD as measured by the MELD-Na score.

Overall, the MELD-Na score represents a readily available tool that identifies patients with CLD who are at risk for complications following revision TJA. A thorough preoperative history, in conjunction with a complete blood count, comprehensive metabolic panel, and coagulation studies should be routinely acquired prior to revision surgery to appropriately identify CLD patients. Given the high prevalence of CLD in the United States, patients with suggestive findings preoperatively (hyponatremia, glucose abnormalities, transaminitis, elevated bilirubin, low albumin, and coagulative dysfunction) should undergo a thorough medical workup through primary care and subsequent subspecialist evaluation by gastroenterology and/or hepatology. The identification of CLD on preoperative evaluation should not be used to decrease access to care in this population. However, it may be used to identify higher risk patients, to counsel these patients, and encourage more robust preoperative medical optimization and implementation of perioperative and intraoperative strategies to mitigate their risk.

Conclusions

In this retrospective ACS-NSQIP database review of patients undergoing rTHA or rTKA, we found that MELD-Na score >10 as a proxy of CLD and is an independent risk factor for major complications, wound complications, sepsis, postoperative transfusion, readmission, and extended length of stay. Preoperative optimization and postoperative management of these patients should involve a multidisciplinary team so that patient outcomes can be improved by decreasing the incidence and severity of these complications. In patients with operative indications that allow for full optimization, we suggest a comprehensive laboratory workup to include complete blood count, comprehensive metabolic panel, coagulation studies, and albumin level and subsequent referral to primary care or gastroenterology prior to surgery.

Conflicts of interest

Jared Foran is a paid consultant for Zimmer Biomet; holds stock or stock options in ForCast Orthopedics; received research support from Zimmer Biomet; is in the medical/orthopaedic publications editorial/governing board of Editorial Board Journal of Arthroplasty.

Neil P Sheth is a paid consultant for Medacta, Smith & Nephew, and Zimmer; received publishing royalties, financial or material support, from Elsevier; is a committee member of AAOS Now, AAOS OrthoInfo, Eastern Orthopaedic Association, Arab Health Advisory Board, and Smith and Nephew Hip Advisory Board. The other authors disclose no conflicts of interest.

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CRediT authorship contribution statement

Matthew J. Kinnard: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Jordan S. Cohen:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Theodore Quan:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Jared R.H. Foran:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Neil P. Sheth:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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