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Comorbidity indices in orthopaedic surgery: a narrative review focused on hip and knee arthroplasty

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- Comorbidity indices currently used to estimate negative postoperative outcomes in orthopaedic surgery were originally developed among non-orthopaedic patient populations.

- While current indices were initially intended to predict short-term mortality, they have since been used for other purposes as well.

- As the rate of hip and knee arthroplasty steadily rises, understanding the magnitude of the effect of comorbid disease on postoperative outcomes has become increasingly more important.

- Currently, the ASA classification is the most commonly used comorbidity measure and is systematically recorded by the majority of national arthroplasty registries.

- Consideration should be given to developing an updated, standardized approach for comorbidity assessment and reporting in orthopaedic surgery, especially within the setting of elective hip and knee arthroplasty.

Introduction

Total joint arthroplasty is a common surgical procedure worldwide, with more than 1 million total hip arthroplasties (THAs) performed globally each year and several countries reporting nearly 100,000 annual total knee arthroplasties (TKAs).[1,2] By 2030, it is projected that the annual procedure volume for primary THA and TKA in the United States alone will grow by 71% and 85% respectively, totalling an estimated 635,000 primary THAs and nearly 1.26 million primary TKAs.[3] Additional reports within the field of lower limb arthroplasty agree with this continued growth in procedure volume around the world.[1,4–6] While the majority of patients experience improved postoperative pain and function without adverse events, there remains a risk of complications, particularly for patients with multiple comorbidities. Comorbidity is generally defined as the presence of more than one distinct disease or medical condition in a single individual.[7] Diagnoses such as diabetes,[8] respiratory disease,[8] chronic kidney disease,[9] and depression[10] have all been associated with adverse clinical outcomes, including infection,[8] extended hospital stay,[9] and mortality,[10] after arthroplasty. This information is vital to orthopaedic surgeons when determining best practices for patient management, as it impacts the long-term health of the patient. Estimating the magnitude of the effect these diagnoses have on outcomes can significantly aid clinical decision-making, yet there is no uniform comorbidity reporting method within the area of hip and knee reconstruction to standardize their assessment. The utility of such comorbidity assessments may aid in appropriate risk stratification of patients not only for preoperative optimization but for reimbursement purposes.

Currently, comorbidity measurement in orthopaedics relies on indices originally intended for patient populations in other specialties. Two of the most commonly used comorbidity indices include the Charlson Comorbidity Index (CCI)[11] and the Elixhauser Comorbidity Measure (ECM).[12] Charlson et al[11] developed the CCI for estimating risk of mortality in non-surgical patients.[11] The Elixhauser Comorbidity Measure was created for use with administrative data to estimate adverse outcomes in the setting of acute care.[12] These comorbidity indices provide a systematic method to predict the risk of various outcomes in the presence of comorbid disease and have also been used to control for confounding in multiple studies.[13,14] Though originally intended to predict mortality, these tools have been helpful in elucidating outcomes for patients with

Table 1. Summary of comorbidity indices used in orthopaedic surgery

Comorbidity measure:	ASA Physical Status Classification	Charlson Comorbidity Index (CCI)	Age-Adjusted Charlson (ACCI)	Modified Charlson (mCCI)**	Elixhauser Comorbidity Measure (ECM)	Weighted Elixhauser	Modified Frailty Index (mFI)	5-Factor modified Frailty (mFI-5)	RxRisk-V
Year of publication	1941	1987	1994	2017	1998	2009	2013	2018	2003
Author(s)	Saklad[15]	Charlson et al[11]	Charlson et al[42]	Lakomkin et al[44]	Elixhauser et al[12]	van Walraven et al[55]	Velanovich et al[58]	Subramaniam et al[61]	Sloan et al[63]
Original study population	Decision by members of the ASA to classify a patient **based solely on physical state**.	604 patients admitted to **the internal medicine** service at New York Hospital-Cornell Medical Center in 1984.	218 patients who underwent elective **general surgery** between 1982 and 1985.	6,121 **revision hip arthroplasty** patients between 2006 and 2013.	1,779,167 patients admitted to an **acute care** hospital in 1992.	228,565 **adult hospitalizations** at The Ottawa Hospital, Canada between 1996 and 2007.	971,434 **surgical inpatients across all surgical specialties** between 2005 and 2009.	Clinical data for patients **across surgical specialties** contained within the NSQIP database in 2012.	126,075 **veteran users of VHA services** (Northwest Network) in 1998.
Type of data	Clinical	Clinical	Clinical	ACS NSQIP Clinical data	Administrative	Administrative	ACS NSQIP Clinical data	ACS NSQIP Clinical data	Veteran Health Administrative Data
Predicted outcome(s) in arthroplasty	3-month revision/ reoperation, 6-month mortality, 6-month Oxford Scores, 2-year revision, length of stay, health-related quality of life, any adverse event	Hospital readmission, length of stay, EQ visual analogue scale	5-year mortality	Mortality, major and minor complications, length of stay, blood transfusion, and any adverse event	Length of stay, postoperative complications, discharge disposition, and EQ-5D index	90-day readmission	30-day morbidity, mortality, readmission, and reoperation	30-day mortality, postoperative complications, readmission, and surgical site infection	90-day and 1-year mortality, 1-year and 5-year revision, and infection
Number of variables	N/A	19	19	10	30	21	11	5	45
Single summary score?	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No

Notes. ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; ASA, American Society of Anesthesiologists; EQ, European Quality of Life; EQ-5D, European Quality of Life Five Dimensions; VHA, Veterans Health Administration.

**Reflects information for the mCCI used in orthopaedics by Lakomkin et al.[44]

varying degrees of comorbidity. Further validation is also needed for both specific patient populations and specific outcomes (e.g. readmission, reoperation). However, no standardized system of comorbidity reporting currently exists in orthopaedic surgery, specifically for patients undergoing hip and knee arthroplasty.

Therefore, the purpose of this study was to review the comorbidity indices currently used in arthroplasty research to better understand their properties and potentially highlight the need for a consistent, data-driven approach for standardized comorbidity assessment and reporting in arthroplasty-related research. Specifically, we assessed the development and validation of: (1) the American Society of Anesthesiologists Physical Status (ASA-PS) Classification; (2) the Charlson Comorbidity Index; (3) the Age-adjusted Charlson Comorbidity Index; (4) the Modified Charlson Comorbidity Index; (5) the Elixhauser Comorbidity Measure; (6) the Weighted Elixhauser Comorbidity Measure; (7) the modified Frailty Index; (8) the 5-Factor modified Frailty Index; and (9) the RxRisk-V (Table 1).

American Society of Anesthesiologists Physical Status Classification

In 1941, members of the American Society of Anesthesiologists developed the ASA Physical Status Classification for the assessment of a patient's preoperative condition.[15–18] This classification system contained seven categories which described overall health status, ranging from no systemic disturbance (Class 1) to moribund (Class 7). Though it allowed statistics regarding preoperative health, type of operation, and outcome to be recorded, it was not intended to provide a prediction of postoperative outcomes.[15,18] Upon its development, Dripps et al[19] revised the classification system, giving rise to the current model comprising six classes and a separate designation for emergency procedures (Table 2).[17,19] Currently, the ASA classification is the most commonly used comorbidity measure and is systematically recorded by the majority of national and regional arthroplasty registries, including the National Joint Registry in England, Wales, Northern Ireland, the Isle of Man, and the States of Guernsey, as well as the Swedish, Finnish, and Norwegian Arthroplasty Registers, and several others.[20] As arthroplasty registries constitute a major source for hip and knee arthroplasty outcomes, the widespread use of the ASA class is undeniable.

In the setting of arthroplasty, ASA-PS class has been widely utilized. Joshi et al[21] examined the relationship between ASA-PS class and length of stay (LOS). Among a cohort of 245 patients who underwent THA and TKA, the ASA-PS class had a positive correlation with postoperative LOS ($p < 0.01$).[21]

Table 2. The American Society of Anesthesiologists Physical Status Classification

Revised ASA Physical Status Classification (Dripps et al)[19]

PS Class 1:	no systemic condition	ASA I:	normal, healthy patient
PS Class 2:	moderate systemic condition (pre-existent or caused by the condition being treated by the operation)	ASA II:	mild systemic condition
PS Class 3:	severe systemic condition	ASA III:	severe systemic condition
PS Class 4:	extreme systemic disorders, eminent threat to life regardless of the type of treatment	ASA IV:	severe systemic condition that is a constant threat to life
PS Class 5:	class 1 or 2 patients undergoing an emergency operation	ASA V:	moribund, not expected to survive without the operation
PS Class 6:	class 3 or 4 patients undergoing an emergency operation	ASA VI:	declared brain-dead, organs are being removed for donor purposes
PS Class 7:	moribund, not expected to survive 24 hours with or without the operation	*E	emergency operation

Notes. ASA, American Society of Anesthesiologists; PS, physical status.

*E: may be added to indicate an emergency operation.

Source: Adapted from Fitz-Henry.[15–17,19]

Additional work by Hooper et al[22] investigated the relationship between the ASA class and six-month mortality, six-month Oxford Hip and Knee Scores, and two-year revision among 22,600 THA patients and 18,434 TKA patients.[22] Among the THA cohort, Hooper and colleagues reported a statistically significant difference in the six-month mortality rate between patients with an ASA class of 1 (0.12%, 95% confidence interval [CI]: 0.03–0.30, $p < 0.001$) and patients with an ASA class of 4 (10.06%, 5.96–15.62, $p < 0.001$).[22] Higher ASA class was also associated with lower Oxford Hip Scores (ASA Class 1: 42.1±0.3, 95% CI: 41.6–42.6; ASA class 4: 35.2±2.1, 95% CI: 31.1–39.2, $p = 0.005$), indicating worse outcome with higher comorbidity burden.[22] Investigators also noted statistically significant differences in the two-year revision rate between ASA classes 1 and 3 only when controlling for age and sex (hazard ratio[HR] = 1.39, 95% CI: 1.04–1.95, $p = 0.015$).[22] While there were no differences between ASA classes with respect to early revision among the TKA cohort, higher ASA class was associated with increased six-month mortality rate (ASA Class 1: 0.12%, 95% CI: 0.01–0.43; ASA Class 4: 2.44%, 95% CI: 0.30–8.53, $p < 0.05$).[22]

Ferguson et al[23] evaluated the relationship between ASA class and three-month revision and reoperation among patients found in the Geneva and Swedish Hip Arthroplasty Registers. In this study, investigators reported that higher ASA score had a statistically significant association with increased risk of both revision (ASA Class 3 and 4: HR = 3.3, 95% CI: 2.6–4.0, $p < 0.001$) and reoperation (ASA class 3 and 4: HR = 3.2, 95% CI: 2.3–4.3, $p = 0.001$).[23]

Further investigation by Teni et al[24] examined the relationship between ASA class and postoperative health-related quality of life among patients who underwent THA and were registered in the Swedish Hip Arthroplasty Register. Teni and colleagues reported that ASA class was predictive of health-related quality of life after adjusting for demographic, clinical, and patient-reported outcomes, as a decline in quality of life was consistently observed with increasing ASA class.[24]

Ondeck et al[14] assessed the discriminative ability of the ASA-PS classification when predicting any adverse event following THA. The system was tested in a cohort of 64,792 patients and had an area under the curve (AUC) of 0.584 (95% CI: 0.578–0.589), where AUC is equivalent to the concordance probability (c-statistic).[14] Additional investigation by Silman et al[25] evaluated the relationship between the ASA-PS class and one-year mortality among 418,916 primary THAs identified within all international arthroplasty registries containing ASA-PS class and mortality data. Investigators reported that increased ASA-PS score was associated with a statistically significant increase in risk of mortality within one year following THA (ASA class 1: 0.18%, 95% CI: 0.12–0.25 vs. ASA class 4: 8.9%, 95% CI: 6.7–12).[25] Silman and colleagues also noted variation in the distribution of ASA class between registries.[25]

Although the ASA-PS classification has been commonly used within the arthroplasty literature, the method of classifying patients in this system remains relatively unspecific and subjective, leading to variability across studies.[17] Similar to the Charnley classification, which divides patients into three categories based on severity of conditions that affect mobility (e.g. A: single joint arthropathy and no comorbidity; B: two joints in need of arthroplasty; C: multiple joints in need of arthroplasty or severe medical impairment),[26] this system relies on clinical perception of the significance of disease. Recognizing that severity of diagnosis may not always be assessed retrospectively, such risk models are not ideal for research which collect data via medical chart review.[26] However, since 2015, more recent studies have included scoring examples alongside the ASA score; thereby decreasing interobserver variability among both anaesthesiologists and non-anaesthesiologist physicians and allowing for improved grade assignment.[27,28]

Charlson Comorbidity Index

The Charlson Comorbidity Index (CCI) was originally developed by Charlson et al[11] in 1987 with the intention of creating a system of classification for comorbid diseases that may affect the short-term risk of mortality for patients in prospective studies.[11] The initial cohort for this index was composed of 604 patients admitted to the internal medicine service during a one-month period at New York Hospital-Cornell Medical Center in 1984. For each patient, comorbidities were recorded and assigned a weight at the time of admission.[11,29] The weight of each comorbid condition was then added to provide a total comorbidity score ranging from 0 to 37, with a higher score indicating a larger quantity or worse severity of disease.[11,30] Overall, the original CCI identified 19 comorbidities that demonstrated an effect on in-hospital and one-year mortality (Table 3).[11] Subsequent studies have often combined any tumour, leukaemia, and lymphoma into a single category of any malignancy, yielding a total of 17 comorbid conditions.[30–32]

Following its development, the Charlson Index was adapted to include International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes.[30,31] A study conducted by Deyo et al[31] identified ICD-9-CM codes which corresponded to the comorbid diseases in the initial index, and matched those codes with the relevant comorbidities. This change allowed the CCI to be used in studies where physical examination of each patient was not possible. Another study conducted by Romano et al[30] revised the ICD-9-CM diagnosis definitions of the CCI, broadening the strict code assignments implemented by Deyo et al.[30,31,33,34] Investigators noted similar relative risks when the index was used within homogeneous data; however, the relative risks differed among heterogeneous data.[13,30]

Additional work conducted by Quan et al[35] in 2011 sought to update the original Charlson Index based on data among a cohort of 55,929 patients up to one year following hospital admission. In this study, five of the 17 Charlson comorbidities no longer had an association with mortality during this timeframe.[35] Therefore, they evaluated an adapted Charlson Index model which included only 12 comorbid conditions.[35] Quan and colleagues reported that the adapted index demonstrated similar discrimination to the original CCI for in-hospital mortality, 30-day mortality, and one-year mortality (Quan-adapted CCI: c-statistic = 0.882, 0.884, 0.897, respectively; original CCI: c-statistic = 0.884, 0.886, 0.899, respectively).[35]

Further work conducted by Brusselaers and Lagergren[36] explored additional ICD-adaptations of the CCI, and highlighted the utility of the Royal College of Surgeons (RCS) Charlson Score. This version of the score removed peptic ulcer disease and grouped similar diseases regardless of severity, ultimately encompassing 14 categories.[36] The method of weighting in the original Charlson Index has been a point of controversy, with some investigators believing the addition of risk ratios performed by Charlson and colleagues was erroneous.[37,38] The RCS adaptation of the index eliminated the use of weights within the scoring system and instead counted the number of diagnoses (e.g. 0, 1, 2, or ≥ 3).[36] Authors noted that while the RCS Charlson Score is appropriate for use in registry-based research and relatively easy to use, it may underestimate the effect of malignancy, AIDS, and moderate liver disease. This deficiency would make it less effective when evaluating the impact of comorbid disease among certain patient populations.[36]

Since its development, several studies have elaborated on the utility of the Charlson Index within orthopaedics. Voskuijl et al[39] analysed the efficacy of the CCI as a predictive tool for readmission, adverse events, transfusion risk, and mortality in a sample of 30,126 orthopaedic surgeries performed between 2008 and 2011. In the arthroplasty cohort, every point increase in CCI score added an additional 0.45% (95% CI: 0.0023–0.0066, p < 0.001) and 0.11% (95% CI: 0.000027–0.0022, p < 0.044) risk for readmission and transfusion, respectively.[39] The index did not predict postoperative adverse events or mortality after arthroplasty; however, CCI score was positively associated

Table 3. Variables of the original and modified Charlson Comorbidity Indices

Charlson Comorbidity Index (CCI)*	Modified CCI (mCCI)**
Conditions with assigned weight of 1	**Conditions with assigned weight of 1**
Cerebrovascular disease	Chronic obstructive pulmonary disease
Chronic pulmonary disease	Congestive heart failure
Congestive heart failure	Diabetes mellitus
Connective tissue disease	Peripheral vascular disease or pain at rest
Dementia	Myocardial infarction
Diabetes mellitus	Transient ischemic attack or stroke
Mild liver disease	
Myocardial infarct	
Peripheral vascular disease	
Ulcer disease	
Conditions with assigned weight of 2	**Conditions with assigned weight of 2**
Any tumour	Hemiplegia
Diabetes with end organ damage	Renal failure
Hemiplegia	
Leukaemia	
Lymphoma	
Moderate or severe renal disease	
Conditions with assigned weight of 3	**Conditions with assigned weight of 3**
Moderate or severe liver disease	Ascites or oesophageal varices (indicate liver disease)
Conditions with assigned weight of 6	**Conditions with assigned weight of 6**
AIDS	Disseminated cancer
Metastatic solid tumour	

Notes. AIDS, Acquired Immunodeficiency Syndrome.

*The original CCI by Charlson et al.[11]

**The mCCI used in orthopaedics by Lakomkin et al.[44]

with mortality following shoulder, trauma, and oncologic surgeries.[39] These findings indicated that the utility of the index may vary across orthopaedic subspecialties and procedures.

Melfi et al[40] tested the validity of the adapted CCI in patients who underwent TKA between 1985 and 1989. This study analysed the ability of the index to predict hospital LOS among a total of 249,744 patients and 30-day mortality among 238,999 patients.[40] When estimating LOS, the adapted index had a coefficient of determination (R^2) of 0.175 in comparison to the baseline of no index ($R^2 = 0.174$), indicating that CCI was not useful in predicting LOS after knee arthroplasty.[13,40] Regarding the ability to predict 30-day mortality, the index had a c-statistic of 0.653 which was only a slight improvement from the baseline model of no index (c-statistic = 0.645).[13,40] Melfi et al[40] suggested that in studies using administrative data, it may be more appropriate to use a comorbidity index that was originally developed based on administrative data rather than an index that was initially developed with clinical data and later adapted.[40]

Additional work conducted by Greene et al[41] investigated the influence of the Charlson Index on patient-reported outcome measures (PROMs) in the setting of THA. In this study, investigators evaluated the impact of the CCI on the EQ-5D index, EQ visual analogue scale (VAS), pain VAS, and satisfaction VAS among a cohort of 22,263 patients in the Swedish National Patient Register who underwent THA between 2002 and 2007.[41] Greene and colleagues reported the CCI had minimal impact on the postoperative EQ-5D index (ß = −0.023, 95% CI: −0.035 to −0.011, p < 0.001) and the postoperative EQ VAS (ß = −3.407, 95% CI: −4.400 to −2.414, p < 0.001) regardless of timeframe.[41] Investigators noted the CCI did not influence the pain VAS or the satisfaction VAS.[41] Greene and colleagues cited the index's original purpose of predicting mortality and hospitalization as a plausible explanation for the CCI's negligible influence on PROMs.[41]

Age-adjusted Charlson Comorbidity Index

Following the initial study, Charlson et al[42] validated a model that incorporated age and comorbidity into a single prognostic variable. This risk model used the original CCI and added one point to the overall comorbidity score for every decade of age over 40 years.[11,42] The age-adjusted CCI (ACCI) was tested within a cohort of 218 patients who underwent elective general surgery between July 1982 and September 1985. Using the proportional hazards model, this study showed the combined age-comorbidity index was highly predictive of mortality within five years (each age-comorbidity unit: relative risk = 1.45, 95% CI: 1.25–1.68, p < 0.0001).[42]

Within orthopaedic studies, the ACCI has been evaluated for its ability to predict five-year mortality following hip fracture surgery.[43] Jiang et al[43] assessed the age-adjusted CCI among 1,057 patients aged 60 years and older who received surgical treatment between January 2007 and December 2009.[43] A multiple regression model including ACCI, age, gender, and fracture pattern demonstrated satisfactory predictive ability (c-statistic = 0.68),[43] where a c-statistic of 1, 0.70, and 0.50 indicated predictive ability that was perfect, good, and no better than chance, respectively. The five-year survival was 89.3%, 62.1%, and 41.8% for patients with an age-comorbidity score of ≤ 3, 4 to 5, and ≥ 6, respectively.[43] The odds ratio for an ACCI score of 4 or 5 was 6.23 (95% CI: 3.12–14.46, p < 0.001), while the odds ratio for an ACCI score ≥ 6 was 13.57 (95% CI: 6.72–31.84, p < 0.001),[43] indicating a higher age-comorbidity score was associated with a statistically significant increase in risk of mortality. According to these findings, the age-adjusted Charlson Index shows promise of satisfactory predictive ability for five-year survival after hip fracture surgery,[43] yet additional information regarding the predictive power of this index for other outcomes is limited.

Modified Charlson Comorbidity Index

Additional studies have given rise to what is now known as the modified Charlson Comorbidity index (mCCI).[14,44–46] Lakomkin et al[44] used a modified CCI with comorbidities found in the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database among a cohort of 6,121 patients who underwent revision hip arthroplasty between 2006 and 2013 (Table 3). Similar to the age-adjusted Charlson, one point was added to the overall comorbidity score for every decade of age over 40 years.[11,42,44] Using this mCCI, higher index scores were associated with increased mortality (OR = 1.89, 95% CI: 1.64–2.18, p < 0.001), major (OR = 1.12, 95% CI: 1.05–1.20, p = 0.001) and minor (OR = 1.53, 95% CI: 1.39–1.69, p < 0.001) complications, increased LOS (OR = 1.32, 95% CI: 1.26–1.39, p < 0.001), and blood transfusions (OR = 1.14, 95% CI: 1.09–1.20, p < 0.001).[44]

Assessing the predictive power of the modified Charlson Index, Ondeck et al[14] investigated the performance of the index among 64,792 THA patients identified using NSQIP data. An analysis of the discriminative ability of the index for any adverse event showed the mCCI had an AUC of 0.534 (95% CI: 0.529–0.539), performing more poorly than both the ASA (AUC 0.584, 95% CI: 0.578–0.589) and the modified Frailty Index (mFI) (AUC 0.567, 95% CI: 0.561–0.573).[14]

Although it has become more commonly used within the literature, these findings suggest that the mCCI has

poor discriminative power for adverse events in orthopaedic studies relative to other available indices.[14,46] Additionally, Shultz et al[47] have highlighted changes within the NSQIP database that have resulted in missing information with respect to variables included in the mCCI. Unavailable data could limit the use of this index in the future.

Elixhauser Comorbidity Measure

In 1997, Elixhauser et al[12] used the 1992 California State-wide Inpatient Database to identify a cohort of 1,779,167 patients who had had an inpatient stay in one of 438 hospitals.[12] Investigators then used univariate and multivariate analyses to identify relevant comorbidities. Heterogenous conditions were divided (e.g. alcohol and drug use), and diagnoses that had more significant associations when combined were grouped as one (e.g. hypertension and complicated hypertension).[12] The authors also noted the inclusion of a diagnosis-related group (DRG) assignment screen, which eliminated comorbidities related to the principal diagnosis and allowed the measure to be used when investigating various diseases without requiring further refinement of the index.[12] In total, 30 comorbid diagnoses were included in the original index. Rather than utilizing weights to yield a summary score,

each comorbidity in the original ECM was treated as a dichotomous variable (e.g. present or not present) (Table 4). This model was then tested within one group containing patients with various reasons for admission and ten other sub-groups in which patients had the same reason for admission.[12] In all groups, comorbidities were associated with notable increases in hospital charges, LOS, and mortality.[12] Among patients with various reasons for hospitalization, the ECM showed ten comorbid conditions (metastatic cancer, paralysis, other neurological disorders, lymphoma, AIDS, congestive heart failure, coagulopathy, pulmonary circulation disorders, fluid and electrolyte disorders, and weight loss) consistently increased hospital charges by at least 25% or risk of mortality by at least 50%.[12]

Building on this work, Quan et al[32] developed an ECM model with updated ICD-9-CM coding as well as an ECM model that incorporated ICD-10-CM codes. Investigators identified 56,585 patients (ICD-9-CM data) and 58,805 patients (ICD-10-CM data) within the 2001 and 2002 Calgary Health Region Discharge Database, respectively.[32] Both models were assessed for the ability to predict in-hospital mortality and compared to the original Elixhauser measure. The ECM model using enhanced ICD-9-CM coding had a c-statistic of 0.878, while the model

Table 4. Variables of the Elixhauser Comorbidity Measure (ECM), ACS NSQIP Surgical Risk Calculator, and modified Frailty Index (mFI)

Elixhauser Comorbidity Measure

Congestive heart failure	Diabetes (uncomplicated)	Coagulopathy
*Cardiac arrhythmias	Diabetes (complicated)	Obesity
Valvular disease	Hypothyroidism	Weight loss
Pulmonary circulation disorders	Renal failure	Fluid/electrolyte disorders
Peripheral vascular disorders	Liver disease	Blood loss anaemia
Hypertension (combined)	Peptic ulcer disease (excluding bleeding)	Deficiency anaemia
Hypertension – uncomplicated	AIDS/HIV infection	Alcohol abuse
Hypertension – complicated	Lymphoma	Drug abuse
Paralysis	Metastatic cancer	Psychoses
Other neurologic disorders	Solid tumour without metastasis	Depression
Chronic pulmonary disease	Rheumatoid arthritis/collagen vascular diseases	

ACS NSQIP Surgical Risk Calculator

Age group	System sepsis (48 hours preop.)	Dyspnea
Sex	Ventilator dependent	Current smoker within 1 year
Functional status	Disseminated cancer	History of COPD
Emergency case	Diabetes	Dialysis
ASA Class	Hypertension requiring medication	Acute renal failure
Steroid use for chronic condition	Previous cardiac event	BMI class
Ascites (30 days preop.)	Congestive heart failure (30 days preop.)	CPT-specific linear risk

Modified Frailty Index

‡ Diabetes mellitus	Cerebrovascular problems
‡ Congestive heart disease	History of stroke
Hypertension requiring medication	Clouding or delirium
Myocardial infarction	Respiratory problems, ‡ COPD
Cardiac problems	‡ Decreased peripheral pulses
	‡ Functional status

Notes. AIDS, Acquired Immunodeficiency Syndrome; ACS NSQIP, American College of Surgeons National Quality Improvement Program; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; BMI, body mass index; CPT, Current Procedural Terminology; HIV, Human Immunodeficiency Virus.

‡Included in the 5-Factor modified Frailty Index (mFI-5).

*Included in the original ECM but removed in subsequent versions.

using ICD-10-CM codes had a c-statistic of 0.870.[32] Both models demonstrated improved predictive ability in comparison to the original ECM (c-statistic = 0.868).[32] A study conducted by Fortin et al[48] validated the Elixhauser model with enhanced ICD-9-CM coding among 3,273,298 patients within the Cerner Health Facts® US Database who received care between 2002 and 2011. In this study, the model showed strong discrimination when predicting in-hospital and one-year mortality (c-statistic = 0.887, 95% CI: 0.885–0.889, p < 0.0001, and c-statistic = 0.884, 95% CI: 0.883–0.886, p < 0.0001, respectively).[48] Databases sponsored by the Agency for Healthcare Research and Quality (AHRQ), such as the National and State Inpatient Sample databases within the Healthcare Cost and Utilization Project (HCUP), have afforded the feasibility of extended research utilizing administrative data. The specific ICD codes used for the calculation of the ECM, CCI, and other classification tools are provided within the coder R package.[49]

In orthopaedic studies, the Elixhauser measure has demonstrated better discriminative ability for postoperative complications, LOS, and discharge to a facility.[50] Ondeck et al[50] evaluated the predictive ability of the ECM among 68,680 THA patients identified in the 2013 National Inpatient Sample. The ECM had an AUC of 0.739 (95% CI: 0.728–0.750) and 0.647 (95% CI: 0.643–0.652) when estimating LOS and discharge to a facility, respectively.[50] This performance was better than that of both the CCI (AUC 0.642, 95% CI: 0.631–0.655 and AUC 0.589, 95% CI: 0.585–0.594, respectively) and the modified Frailty Index (AUC 0.618, 95% CI: 0.607–0.630 and AUC 0.605, 95% CI: 0.600–0.609, respectively).[50] The ECM also showed increased discrimination relative to the CCI and mFI with respect to the occurrence of the Centers for Medicare & Medicaid Services procedure-specific complication measures for elective primary THA and TKA.[50]

In an aforementioned study conducted by Greene et al,[41] investigators examined the influence of the Elixhauser measure on PROMs among a cohort of 22,263 patients in the setting of THA. Here, Greene and colleagues observed minimal impact of the Elixhauser measure on the postoperative EQ-5D index (ß = –0.010, 95% CI: –0.015 to –0.004, p < 0.001) and the postoperative EQ VAS (ß = –0.886, 95% CI: –1.353 to –0.420, p < 0.001).[41] Unlike the CCI, the Elixhauser measure had a small influence on the pain VAS (ß = 0.522, 95% CI: 0.091–0.954, p = 0.018) and the satisfaction VAS (ß = 0.628, 95% CI: 0.141–1.116, p = 0.012).[41]

Many studies have indicated that the ECM has strong discriminative ability.[12,51–53] The Elixhauser measure has demonstrated increased predictive ability over the original CCI. However, despite its usefulness, the ECM consists of a large number of variables and does not allow for the formation of one summary score.[11,12]

Weighted Elixhauser Comorbidity Measure

Attempts have been made to modify the original ECM to include a system of weights.[54,55] Van Walraven et al[55] developed and validated a weighted ECM among adult patients who were admitted to Ottawa Hospital between January 1996 and September 2007. Investigators determined the association of the Elixhauser comorbidities with in-hospital mortality. Twenty-one comorbidity groups had a statistically significant association with in-hospital mortality after adjusting for all other comorbidity categories and were therefore identified as independently associated with in-hospital death. A scoring system was formed by dividing each regression coefficient by the smallest regression coefficient in the risk model and rounding to the nearest integer.[55,56] This method demonstrated the strength of each comorbidity's association with the outcome. The weights were summed and yielded an overall comorbidity score, with a possible range of –19 to +89.[55] The weighted ECM (c-statistic = 0.763, 95% CI: 0.759–0.766) had similar discriminative ability to that of the original (c-statistic = 0.760, 95% CI: 0.756–0.764) and increased discrimination in comparison to the CCI (c-statistic = 0.745, 95% CI: 0.742–0.749).[55] While the weighted Elixhauser measure demonstrated good predictive ability, it should be noted that the method of weight formation for this model was similar to the controversial manner of weighting in the original Charlson Index mentioned previously.[37,38] Van Walraven and colleagues also suggested that comorbidities associated with a decreased risk of in-hospital mortality (i.e. a negative score) may be the result of bias in coding and may not provide an accurate reflection of the condition itself.[55] Here, authors point out that patients with severe disease are less likely to have minor conditions coded, while healthy patients are more likely to have these conditions coded.[55]

Few studies have evaluated this measure within the setting of arthroplasty. Goltz et al[56] investigated the ability of the weighted Elixhauser measure to predict 90-day readmission following THA and TKA. Investigators identified 14 comorbidities associated with the outcome and calculated weights as described by van Walraven et al.[55,56] Among a validation cohort consisting of 2,005 patients who underwent THA or TKA, the weighted ECM (AUC 0.656, 95% CI: 0.60–0.71) did not show significant loss in predictive ability compared to the unweighted model (AUC 0.665).[56]

While there is evidence that adapting the ECM to provide a single score may be beneficial, additional studies show there is currently no consensus on the method of calculating weights or on which of the original Elixhauser variables should be included for risk estimation.[54–56] A study conducted by Gagne et al[57] combined the Elixhauser measure with the Charlson Index by grouping

similar comorbidity variables between the two indices. This model encompassed 37 conditions and incorporated weights by dividing the regression coefficient by 0.3 and rounding to the nearest integer.[54,57] When assessed for predictive ability of 30-day mortality, investigators reported increased discrimination of the combined index (c-statistic = 0.860, 95% CI: 0.854–0.866) in comparison with both the Charlson Index (c-statistic = 0.839, 95% CI: 0.836–0.849) and the van Walraven-weighted ECM (c-statistic = 0.836, 95% CI: 0.834–0.847).[57] Still it is worth noting the weights for both the weighted ECM and the combined measure were initially developed to predict mortality. This may present limitations when predicting other postoperative outcomes.[54,56]

Modified Frailty Index

Another common risk tool is the modified Frailty Index.[58] Velanovich et al[58] developed this index to predict 30-day morbidity and mortality across all surgical specialties. Investigators identified 11 variables which overlapped between the Canadian Study of Health and Aging Frailty Index (CSHA-FI) and the preoperative variables from the NSQIP (Table 4).[58] The total number of items present for a given patient was divided by 11, which provided an index value ranging between 0 and 1.[58] Investigators also stratified operations based on work relative value units (RVUs) to control for level of complexity. Using the mFI among 971,434 surgical inpatients, each unit increase in index value was associated with an increased risk of 30-day mortality and morbidity within all surgical specialties.[58]

Runner et al[59] examined the mFI for its ability to predict 30-day mortality, postoperative complications, readmission, and reoperation among 90,260 patients identified in the NSQIP database who underwent primary TKA.[59] Among patients who had 0 to 4 of the 11 possible variables, risk of 30-day mortality doubled with increasing index value (OR = 2.10, 95% CI: 1.73–2.55, p < 0.001).[59] There was no association between index value and deep vein thrombosis (DVT) (OR = 1.05, 95% CI: 0.96–1.15, p = 0.255); however, increasing mFI was significantly associated with higher rates of any complication (OR = 1.22, 95% CI: 1.19–1.25, p < 0.001), surgical site infection (SSI) (OR = 1.24, 95% CI: 1.13–1.36, p < 0.001), wound dehiscence (OR = 1.43, 95% CI: 1.24–1.65, p < 0.001), myocardial infarction (MI) (OR = 2.15, 95% CI: 1.89–2.44, p < 0.001), pulmonary embolism (PE)/pneumonia (OR = 1.79, 95% CI: 1.58–2.02, p < 0.001), and acute renal failure (OR = 2.30, 95% CI: 1.78–2.98, p < 0.001).[59] The modified Frailty Index also had statistically significant associations with both 30-day readmission and reoperation (OR = 8.71, 95% CI: 2.11–35.98, *p* = 0.003 and OR = 3.32, 95% CI: 1.36–8.11, p = 0.009, respectively).[59]

Further work by Bellamy et al[60] performed similar tests using the index among 51,582 patients identified in the NSQIP database who underwent primary THA. Increasing mFI was associated with increased risk of 30-day mortality (OR = 2.45, 95% CI: 2.08–2.88, p < 0.001), readmission (OR = 1.43, 95% CI: 1.23–1.65, p < 0.001), and reoperation (OR = 1.36, 95% CI: 1.27–1.47, p < 0.001).[59,60] Higher index value was also associated with higher rates of the complications mentioned by Runner et al;[59] however, unlike the TKA cohort, increasing index score was associated with a higher risk of DVT (OR = 1.25, 95% CI: 1.08–1.46, p = 0.0035).[59,60] The mFI also demonstrated a stronger association with 30-day readmission (OR = 14.72, 95% CI: 6.95–31.18, p < 0.001) and reoperation (OR = 6.52, 95% CI: 2.48–17.13, p < 0.001) than the ASA-PS classification.[60]

Contradicting these findings, a study by Ondeck et al[14] showed the mFI demonstrated poorer performance than the ASA classification among THA patients. In this study, investigators evaluated the ability of the mFI to predict adverse events among 64,792 patients who underwent THA. Upon analysis, the modified Frailty Index had an AUC of 0.567 (95% CI: 0.561–0.573), while the ASA classification had an AUC of 0.584 (95% CI: 0.578–0.589).[14]

5-Factor modified Frailty Index

By 2015, only five of the 11 variables used within the 11-Factor mFI (mFI-11) remained in the NSQIP data.[61,62] Therefore, Subramaniam et al[61] used the remaining factors (Table 4), forming the 5-Factor mFI (mFI-5), and compared its predictive ability for mortality, complications, and 30-day readmission with that of the mFI-11.[61] Comparison of the two indices was conducted using 2012 NSQIP data and revealed similar c-statistics for mortality (c-statistic = 0.905 for both), complications (c-statistic = 0.788 for both), and readmission (c-statistic = 0.688 for mFI-5, c-statistic = 0.687 for mFI-11).[61] Within orthopaedic surgery, both indices showed good to strong predictive ability for mortality (c-statistic = 0.908 for mFI-5, c-statistic = 0.909 for mFI-11), complications (c-statistic = 0.765 for mFI-5, c-statistic = 0.766 for mFI-11), and 30-day readmission (c-statistic = 0.707 for mFI-5, c-statistic = 0.706 for mFI-11).[61]

In the setting of arthroplasty, Traven et al[62] used the five-factor modified Frailty Index among 140,158 THA patients and 226,398 TKA patients within the NSQIP database between 2005 and 2016. Within the THA cohort, each unit increase in mFI-5 value was significantly associated with increased risk of 30-day mortality (OR = 1.491, 95% CI: 1.283–1.732, p < 0.001), readmission (OR = 1.285, 95% CI: 1.232–1.341, p < 0.001), any complication (OR = 1.254, 95% CI: 1.209–1.302, p < 0.001), and SSI (OR = 1.209, 95% CI: 1.118–1.308, p < 0.001).[62] Among TKA

patients, every increasing unit of mFI-5 was associated with increased risk of 30-day mortality (OR = 1.569, 95% CI: 1.340–1.838, p < 0.001), readmission (OR = 1.249, 95% CI: 1.206–1.293, p < 0.001), any complication (OR = 1.175, 95% CI: 1.140–1.211, p < 0.001), and deep SSI (OR = 1.438, 95% CI: 1.233–1.677, p < 0.001).[62] As seen with the modified CCI, changes in available NSQIP data have affected the utility of the modified Frailty Index. While the 5-Factor mFI has demonstrated comparable predictive ability to that of the original, the possibility of continued changes in available data should be considered.

RxRisk-V

Inconsistent availability of diagnostic data prompted Sloan et al[63] to develop the RxRisk. This risk measure was initially adapted from the Chronic Disease Score with the intention of identifying comorbid conditions and predicting healthcare spending among the Veterans Health Administration (VHA) population.[63] Since its creation, the RxRisk-V has become a commonly used pharmacy-based measure when attempting to understand the burden of disease.[63–66] To form this tool, National Drug Codes (NDCs) were translated into drug names and routes of administration using the Multum Lexicon.[63] This information was then mapped to VHA product names and drug classes. Investigators defined 45 RxRisk-V categories using information regarding the drugs and drug classes, with each category representing a single comorbidity.[63] The use of a drug by a patient could therefore be deemed as the presence of the associated comorbid condition.

Subsequent studies have modified the original RxRisk-V to include a varying number of comorbidity categories.[64,67–69] Pratt et al[67] developed an updated model of the RxRisk-V by mapping the index to codes from the Anatomical Therapeutic Chemical (ATC) classification system. The adapted RxRisk-V included a total of 46 categories.[67] Investigators examined an unweighted model, in which the score was calculated as the number of relevant comorbidity categories for a given patient.[67] An additional model incorporated a weighting system based on the odds ratio of each comorbidity category determined using logistic regression.[67] The predictive ability of the RxRisk-V models for one-year mortality was then assessed among 135,406 veterans within the Australian Government's Department of Veteran's Affairs (DVA) administrative claims database.[67] Pratt and colleagues reported increased predictive ability of the weighted RxRisk-V model (c-statistic = 0.786, 95% CI: 0.782–0.789, p < 0.0001) over the unweighted index (c-statistic = 0.751, 95% CI: 0.747–0.754, p < 0.0001).[67] Both indices were better predictors of one-year mortality than a base model including age and gender (c-statistic: 0.738, 95% CI: 0.734–0.742).[67] When validated among a cohort of 303,135 patients, the weighted RxRisk-V model

demonstrated strong predictive ability of one-year mortality (c-statistic = 0.833, 95% CI: 0.829–0.837, p < 0.0001).[67]

Inacio et al[64] evaluated the RxRisk-V for its ability to predict 90-day and one-year mortality among 11,848 THA patients and 18,972 TKA patients who underwent a hip or knee arthroplasty procedure between 2001 and 2012 that was subsidized by the Australian Government Department of Veterans' Affairs.[64] Among the THA cohort, the RxRisk-V had a c-statistic of 0.72 for both outcomes.[64] This was only slightly better than the base model which did not include comorbidity assessment and had a c-statistic of 0.69 for both outcomes.[64] Among TKA patients, the RxRisk-V had a c-statistic of 0.75 and 0.73 for 90-day and one-year mortality, respectively, while the baseline model had a c-statistic of 0.69 and 0.70 for the respective outcomes.[64]

Another study by Inacio et al[66] investigated the ability of the RxRisk-V to predict the risk of revision one year and five years following THA and TKA within the aforementioned cohorts. Among THA patients, the RxRisk-V had satisfactory predictive ability for both one-year revision (c-statistic = 0.61) and five-year revision (c-statistic = 0.60).[66] The RxRisk-V also showed satisfactory predictive ability among the TKA cohort, with a c-statistic of 0.62 and 0.63 for revision after one year and five years, respectively.[66]

Inacio et al[65] also evaluated the ability for the RxRisk-V to predict postoperative infections following total joint arthroplasty. Among the previously described cohorts of arthroplasty patients, this study showed the RxRisk-V did not have high predictive ability for estimating infection (c-statistic = 0.57).[65]

Overall, the RxRisk-V provides an alternative method of measuring comorbidities which may be beneficial in the absence of complete diagnostic information. However, within orthopaedic studies, this risk measure has not demonstrated high predictive ability among arthroplasty patients.[64–66]

Conclusion

The presence of comorbid disease can have a substantial impact on patient mortality, postoperative complications, use of hospital resources, and reimbursement. Several comorbidity measures currently exist to estimate the risk of various clinical outcomes in the face of these conditions. Inconsistent performance and sparse validation of comorbidity indices to predict revision, reoperation, patient-reported outcomes (e.g. Oxford Hip and Knee Scores, EQ-5D index), and mortality in orthopaedic literature indicate a need for an improved method of predicting risks, especially within elective THA and TKA studies. Future research should explore the development of a standardized comorbidity measure that is tailored for use among the specific patient population in orthopaedics (e.g. arthroplasty).

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