Osteoarthritis and Cartilage 24 (2016) 1718–1726

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Evaluation of three co-morbidity measures to predict mortality in patients undergoing total joint arthroplasty

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ARTICLE INFO

Article history:
Received 29 September 2015
Accepted 9 May 2016

Keywords:
Joint arthroplasty
Mortality
Co-morbidity
RxRisk-V
Charlson
Elixhauser

SUMMARY

Objective: To evaluate the 90 days and 1 year mortality predictive ability of the RxRisk-V, Charlson, and Elixhauser co-morbidity measures in total hip arthroplasty (THA) and total knee arthroplasty (TKA) patients.

Method: A retrospective study of 11,848 THAs and 18,972 TKAs (2001–2002) was conducted. Death within 90 days and 1 year of the surgery were the main endpoints. Co-morbidity measures were calculated using either medication or hospitalisation history. Logistic regression models were employed and discrimination and calibration were assessed. Specifically, models with unweighted and weighted measure scores, models with the specific conditions, and a model combining conditions identified by all measures were assessed.

Results: In THAs, the best performing prediction models included co-morbidities from all three measures (90 days: $c = 0.84$, $P = 0.284$, 1 year: $c = 0.79$, $P = 0.158$). Individually, the model with Charlson conditions performed best at 90 days mortality ($c = 0.80$, $P = 0.777$) and the Charlson and Elixhauser performed similarly at 1 year (both $c = 0.77$, $P > 0.05$). In TKAs, the best performing prediction model included co-morbidities from all measures (90 days: $c = 0.82$, $P = 0.349$, 1 year: $c = 0.78$, $P = 0.873$). Individually, the model with Elixhauser conditions performed best with 90 days mortality ($c = 0.79$, $P = 0.435$) and all performed similarly at 1 year ($c = 0.74$–0.75, all $P > 0.05$).

Conclusions: A combined model with co-morbidities identified by the Elixhauser, Charlson, and RxRisk-V was the best mortality prediction model. The RxRisk-V did not perform as well as the others. Because of the Elixhauser and Charlson's similar performance we suggest basing the choice of measurement use on factors such as the need of specific conditions and modelling limitations.

Background

The incidence of joint arthroplasty has dramatically increased in the past couple of decades[1–4]. Along with the increase in incidence, a change in patient profiles has also been observed[5–9]. Patients with several co-morbid conditions, which would have precluded them from having joint arthroplasty in the past, are now undergoing these procedures. The number of co-morbid conditions in patients undergoing elective arthroplasty has even doubled in certain countries[5,6]. Further, not only has the prevalence of many conditions like diabetes, obesity, rheumatologic conditions, renal disease, heart disease, and depression[10–14] increased in this patient population, the conditions have also been implicated in higher risk of post-arthroplasty mortality[15–22]. Seemingly contradictory, the rates of mortality after total joint arthroplasty surgery have reportedly decreased in patients over the last few years[6,17,23,24]. This is likely due to a patient selection bias with healthier patients more likely to be selected for surgery[24,25]. These patients typically having a lower overall mortality risk after the first 30 days after surgery than the general population. This highlights the need to determine whether co-morbidities in a joint arthroplasty population affect mortality in a similar fashion as they do in the general

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http://dx.doi.org/10.1016/j.joca.2016.05.006
1063-4584/

population and ascertaining which co-morbidity measure performs best in this patient population.

There are several well established measures to capture both the co-morbidity burden and specific co-morbid conditions in large cohorts of patients using existing secondary data such as claims data[26]. In orthopaedics the Charlson[27] and Elixhauser[28] measures are regularly used to identify specific conditions and co-morbidity burden of patients using diagnostic codes of inpatient encounters. There is substantial evidence that both are good predictors of death in total joint arthroplasty patients and useful for case-mix adjustments for mortality[29]. Additionally, both the Charlson and Elixhauser have been evaluated as predictors of infection and revision in cohorts of joint arthroplasty patients[10,30,31]. However, less commonly used in orthopaedics are pharmacy based co-morbidity measures. The RxRisk-V[32] is one of the most commonly used pharmacy based measures used in health services and pharmacoepidemiological research and there has been no validation of whether it is a good predictor of death in a cohort of joint arthroplasty patients. The RxRisk-V has, however, been evaluated as a predictor of infection and revision with satisfactory results in this patient population[30,31]. Identifying the best performing co-morbidity measures for mortality prediction and case-mix adjustments will assure better confounding adjustment in large cohort analysis of joint arthroplasty patients. Additionally, having alternative measures can give researchers latitude when conducing analysis to leverage their datasets (e.g., encounters or pharmacy) of preference or availability and also understand the shortcomings of the measures in comparison to others.

In this study, we compared the performance of a medication prescription based co-morbidity measure in predicting 90 days and 1 year mortality after total joint arthroplasty to the more commonly used inpatient diagnoses based measures. Specifically, we evaluated the predictive ability of the RxRisk-V[32], Charlson[27], and Elixhauser[28] co-morbidity measures with 90 days and 1 year mortality. We evaluated the unweighted and weighted measure scores, models with the specific conditions, and a model combining conditions identified by all measures. Unweighted scores are simple counts of conditions and weighted scores use an algorithm to calculate the scores accounting for the severity of the conditions a patient has.

Methods

Study design, setting, and sample

A retrospective study was conducted on a cohort of patients who underwent total hip arthroplasty (THA) and total knee arthroplasty (TKA) procedures between 2001 and 2012 and that were subsidized by the Australian Government Department of Veterans' Affairs (DVA). De-identified administrative inpatient encounter information and prescription medicine (inpatient and outpatient) data for this captured population was obtained.

The sample included adults (≥18 years old) who had all health services subsidized by the DVA, and underwent primary unilateral THA and TKA procedures. Using International Classification of Disease, 10th Revision, Australian Modification (ICD-10-AM) codes, THA (4931800) and TKA procedures (4951800, 4952100, 4952102, 4952400) were identified. Only patients with primary diagnoses associated with elective primary arthroplasty procedures were included.

Co-morbidity measures and data sources

The RxRisk-V[32], which evolved from the Chronic Disease Score, is a co-morbidity prescription based measure that uses patients' medication history to determine the prevalence of 45 conditions[33]. In this study a modified RxRisk-V was used with 42 conditions, the conditions ostomy, neurogenic bladder, and urinary incontinency were excluded. This measure is predictive of cost of care[32,33] and mortality[34–36] in different patient samples and using both inpatient and outpatient pharmacy data[34,36]. The sum of the co-morbidities identified by this measure was considered the unweighted RxRisk-V score and the weighted score was based on the weighting algorithm published by Johnson *et al.*[34].

The Charlson co-morbidity measure uses inpatient hospitalisations for a set period of time to calculate a score based on the presence of 17 conditions[27,37]. The Charlson measure was originally developed to predict and assist with case-mix adjustment of mortality, but has been applied to several other outcomes, including some surgical outcomes[38,39]. The Charlson is the most commonly used co-morbidity algorithm in orthopaedic studies[40], and several adaptations exist. In this study we used the Quan *et al.*'s ICD-10-AM algorithm to identify the conditions[37]. The sum of the conditions identified by the Charlson co-morbidity measure was the unweighted Charlson score and the weighted score was based on the original weights proposed by Charlson *et al.*[27]

The Elixhauser co-morbidity measure, like the Charlson, also uses inpatient hospitalisations during a specific period to identify co-morbidities. The most commonly used form of this measure identifies the presence of 30 conditions and has been evaluated as a predictor of need for blood transfusions, length of stay, and mortality[37,41]. This measure was developed by the Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project and is widely used in health services research[28,42]. The sum of conditions identified by the Elixhauser was considered the unweighted Elixhauser score and the weighted score was calculated using weights proposed by van Walraven *et al.*[41].

The RxRisk-V and Charlson have six common co-morbidities, the Elixhauser and RxRisk-V have 10 common co-morbidities, and the Charlson and Elixhauser have 12 in common. Combined these measures identify 64 co-morbidities.

Using the DVA administrative databases all inpatient hospitalisations and prescription medicine history were accessed for the study. The database contains details of all prescription medications, medical, allied health services and hospitalisations provided to veterans for which DVA pays a subsidy. In the dataset, medications are coded according to the Anatomic, Therapeutic and Chemical Classification (ATC), and the Pharmaceutical Benefits Schedule (PBS) item codes. Hospitalisations are coded according to the ICD-10-AM. The DVA also maintains a client file, which contains information on gender, date of birth, date of death, and family status for a treatment population that in September 2011 was 242,000 people. In this study, the 12 months period preceding the discharge date of the arthroplasty procedure was used to ascertain the co-morbidities according to the two diagnoses based co-morbidity algorithms and the 12 months period preceding the admission date of the arthroplasty was used for the medication based algorithm. The arthroplasty procedure hospitalisation was included in the calculation of the diagnostic co-morbidity indices (ICD-10-AM adapted Charlson and Elixhauser).

Outcome

Ninety days and 1 year post-operative mortality was the main endpoint of this study. Date of death was obtained from the client file maintained by the DVA on its membership and time to death was calculated from the index date of the joint arthroplasty.

Covariates

Age, gender and primary diagnosis for the procedure were included in all models as covariates.

Table I
Characteristics of the sample undergoing total hip and knee arthroplasty and mortality crude incidence within 90 days and 1 year, 2001–2012

		THA		TKA	
		N	(%)	*N*	(%)
Total		11,848	100.0	18,972	100.0
Age, median (IQR), years		80.9	76.4–84.4	79.8	74.7–83.5
Gender	Female	5898	49.8	9047	47.7
	Male	5950	50.2	9925	52.3
THA diagnosis (ICD-10-AM)	Other primary coxarthrosis (M161)	9648	81.4	–	–
	Coxarthrosis unspecified (M169)	1109	9.4	–	–
	Other	1091	9.2	–	–
TKA diagnosis (ICD-10-AM)	Other primary gonarthrosis (M171)	–	–	16,329	86.1
	Gonarthrosis unspecified (M179)	–	–	1437	7.6
	Other	–	–	1092	5.8
Elixhauser unweighted score (median, IQR)		0.0	0–1	0.0	0–1
Elixhauser unweighted score	None	6087	51.4	9910	52.2
	1 and 2	4333	36.6	7034	37.1
	≥3	1428	12.1	2028	10.7
Elixhauser weighted score (median, IQR)		0.0	0–4	0.0	0–3
Elixhauser weighted score	≤0	8162	68.9	13,810	72.8
	Between 1 and 6	2378	20.1	3510	18.5
	≥7	1308	11.0	1652	8.7
Charlson unweighted score (median, IQR)		0.0	0–1	0.0	0–1
Charlson unweighted score	None	8529	72.0	13,917	73.4
	1 and 2	2946	24.9	4628	24.4
	≥3	373	3.1	427	2.3
Charlson weighted score (median, IQR)		0.0	0–1	0.0	0–1
Charlson weighted score	0	8529	72.0	13,917	73.4
	1 and 2	2472	20.9	3913	20.6
	≥3	847	7.1	1142	6.0
RxRisk-V unweighted score (median, IQR)		6.0	3–8	6.0	3–8
RxRisk-V unweighted score	None	1466	12.4	3290	17.3
	1 and 2	747	6.3	938	4.9
	3–4	2041	17.2	2785	14.7
	5–6	2888	24.4	4398	23.2
	≥7	4706	39.7	7561	39.9
RxRisk-V weighted score (median, IQR)		5.0	2–8	4.0	1–8
RxRisk-V weighted score	≤0	2022	17.1	4092	21.6
	Between 1 and 6	5650	47.7	8341	44.0
	≥7	4176	35.2	6539	34.5
Death within 90 days		112	0.9	95	0.5
Death within 1 year		360	3.1	380	2.0

IQR = Interquartile range. THA = Total hip arthroplasty. TKA = Total knee arthroplasty. ICD-10-AM = International Classifications of Disease, 10th Revision, Australian Modification.

Table II
Associations of co-morbidity measures and THA with 90 days and 1 year mortality. Odds ratios, 95% confidence intervals, discrimination (*c* statistic), calibration (HLGOF Chi-square test *P* value)

Models	90 Days*			1 Year*		
	OR (95% CI)	*C* Statistic	HLGOF	OR (95% CI)	*C* Statistic	HLGOF
Base (model 1)	–	0.69	0.525	–	0.69	0.936
Unweighted co-morbidity scores						
Elixhauser (model 2)	1.49 (1.36–1.63)	0.77	0.338	1.45 (1.37–1.54)	0.75	0.204
Charlson (model 3)	1.86 (1.63–2.13)	0.78	0.576	1.80 (1.65–1.96)	0.76	0.420
RxRisk-V (model 4)	1.13 (1.06–1.19)	0.72	0.615	1.12 (1.09–1.16)	0.72	0.213
Weighted co-morbidity scores						
Elixhauser (model 5)	1.13 (1.10–1.16)	0.77	0.194	1.12 (1.10–1.14)	0.75	0.134
Charlson (model 6)	1.42 (1.31–1.55)	0.76	0.561	1.45 (1.37–1.53)	0.75	0.150
RxRisk-V (model 7)	1.08 (1.04–1.12)	0.72	0.548	1.09 (1.07–1.11)	0.72	0.291
Specific conditions within each measure†						
Elixhauser (model 8)	–	0.79	0.356	–	0.77	0.051
Charlson (model 9)	–	0.80	0.777	–	0.77	0.544
RxRisk-V (model 10)	–	0.78	0.439	–	0.74	0.353
Combined Elixhauser, Charlson, and RxRisk-V (model 11)	–	0.84	0.284	–	0.79	0.158

OR = Odds ratio. CI = Confidence intervals.
* All models include age, gender, and primary diagnosis.
† See Table III for models with specific conditions.

Table III
Adjusted odds of 90 days and 1 year mortality in THA patients by specific co-morbidity measure conditions

Co-morbidity measure conditions	90 Days*	1 Year*
	OR (95% CI)	OR (95% CI)
Elixhauser (model 8)		
Metastatic cancer	**20.1 (4.13–97.8)**	**6.67 (3.00–14.8)**
Liver disease	**8.43 (1.80–39.5)**	**4.94 (1.57–15.6)**
Congestive heart failure	**3.82 (2.31–6.33)**	**2.71 (1.93–3.80)**
Hypertension complicated	**3.67 (0.77–17.5)**	**5.84 (2.10–16.3)**
Cardiac arrhythmia	**2.14 (1.40–3.28)**	**1.37 (1.05–1.77)**
Coagulopathy	2.39 (0.97–5.86)	–
Blood loss anaemia	2.24 (0.70–7.13)	**2.54 (1.18–5.47)**
Depression	1.99 (0.78–5.10)	–
Deficiency anaemia	1.91 (0.78–4.70)	–
Valvular disease	1.78 (0.92–3.43)	1.56 (1.00–2.43)
Diabetes uncomplicated	1.70 (0.93–3.11)	–
Renal failure	1.63 (0.90–2.96)	**2.05 (1.43–2.93)**
Solid tumor without metastasis	0.22 (0.05–1.01)	1.54 (0.91–2.61)
Lymphoma	–	**3.74 (1.41–9.89)**
Rheumatoid arthritis/collagen	–	**3.13 (1.84–5.32)**
Other neurological disorders	–	**2.88 (1.67–4.98)**
Diabetes complicated	–	**1.66 (1.18–2.34)**
Drug abuse	–	4.24 (0.53–33.9)
Fluid and electrolyte disorders		1.27 (0.92–1.75)
Charlson (model 9)		
Moderate/severe liver disease	**12.1 (2.13–69.0)**	**3.96 (0.72–21.9)**
Metastatic solid tumor	**8.04 (2.74–23.6)**	**5.72 (2.75–11.9)**
Myocardial infarction	**5.15 (3.08–8.61)**	**2.88 (1.98–4.18)**
Congestive heart failure	**3.94 (2.40–6.47)**	**2.79 (2.01–3.87)**
Dementia	**3.19 (1.53–6.63)**	**2.97 (1.86–4.73)**
Renal disease	**2.07 (1.14–3.76)**	**2.32 (1.62–3.34)**
Diabetes without chronic complications	1.53 (0.85–2.74)	–
Any malignancy	–	**2.64 (1.62–4.29)**
Rheumatic disease	–	**2.47 (1.32–4.61)**
Diabetes with chronic complications	–	**1.67 (1.18–2.37)**
Cerebrovascular disease	–	1.51 (0.92–2.48)
Peripheral vascular disease	–	1.43 (0.89–2.30)
RxRisk-V (model 10)		
Psychotic illness	**3.78 (1.83–7.81)**	**2.47 (1.51–4.02)**
Congestive heart failure	**2.78 (1.78–4.34)**	**1.91 (1.47–2.48)**
Liver failure	**1.98 (1.06–3.71)**	1.40 (0.93–2.10)
IHD angina	**1.65 (1.04–2.62)**	**1.45 (1.09–1.93)**
Malnutrition	5.04 (0.63–40.0)	–
Migraine	3.98 (0.51–30.8)	–
End stage renal disease	2.41 (0.85–6.84)	2.98 (1.68–5.31)
Parkinson's	2.13 (0.84–5.43)	–
Hypertension	1.42 (0.96–2.11)	–
GORD	1.37 (0.92–2.05)	–
Inflammation pain	0.72 (0.49–1.06)	–
Chronic airway disease	0.68 (0.42–1.09)	–
Epilepsy	0.26 (0.06–1.06)	1.36 (0.89–2.08)
Hyperkalaemia	–	**9.77 (2.06–46.4)**
Diabetes	–	**1.48 (1.05–2.09)**
Transplant	–	6.38 (0.46–88.7)
Psoriasis	–	2.30 (0.86–6.12)
Osteoporosis Pagets	–	1.29 (0.94–1.76)
Steroid responsive diseases	–	1.29 (0.99–1.67)
Hyperlipidaemia	–	0.88 (0.70–1.11)
Combined Elixhauser, Charlson, and RxRisk-V conditions (model 11)		
Metastatic cancer	**21.9 (4.74–101.4)**	**7.65 (3.47–16.9)**
Myocardial infarction	**4.96 (2.97–8.28)**	**2.73 (1.88–3.95)**
Dementia	**3.19 (1.58–4.00)**	**2.56 (1.61–4.05)**
Psychoses	**2.76 (1.26–5.92)**	**1.73 (1.03–2.91)**
Moderate/severe liver disease	**2.17 (1.18–4.00)**	1.35 (0.90–2.04)
Cardiac arrhythmia	**2.14 (1.41–3.25)**	**1.32 (1.03–1.69)**
Congestive heart failure	**1.84 (1.17–2.91)**	**1.60 (1.22–2.09)**
Renal disease	1.75 (1.00–3.09)	**2.37 (1.72–3.27)**
Hyperkalaemia	6.80 (0.73–63.3)	–
Migraine	4.37 (0.54–35.1)	3.16 (0.72–14.0)
Parkinson's	2.35 (0.91–6.09)	–
Anaemia	2.06 (0.84–5.03)	–
Blood loss anaemia	2.04 (0.65–6.45)	**2.56 (1.20–5.47)**
Valvular disease	1.66 (0.85–3.22)	1.53 (0.98–2.39)
IHD angina	1.40 (0.88–2.24)	**1.34 (1.01–1.77)**
GORD	1.24 (0.83–1.86)	–
Chronic airway disease	0.64 (0.39–1.05)	–
Solid tumor without metastasis	0.24 (0.05–1.06)	1.57 (0.93–2.65)
Epilepsy	0.21 (0.05–0.87)	–
Lymphoma	–	**3.68 (1.40–9.71)**
Rheumatoid arthritis	–	**3.43 (2.03–5.82)**
Psoriasis	–	**2.77 (1.05–7.30)**
Other neurological disorders	–	**2.41 (1.38–4.18)**
Diabetes with chronic complications	–	**1.55 (1.10–2.20)**
Peptic ulcer	–	0.45 (0.13–1.48)

GORD = Gastro-oesophageal reflux disease. IHD = Ischemic heart disease. OR = Odds ratio. CI = Confidence intervals.
Bold values are statistically significant.
* All models adjusted for age, gender, and primary diagnosis.

Statistical analysis

Analyses were conducted for hips and knees separately. Frequencies, proportions, median and interquartile ranges (IQRs) were used to describe the hip and knee cohorts. Both co-morbidity burden (i.e., unweighted or weighted co-morbidity scores) and specific co-morbid conditions were evaluated. Logistic regression models were used to construct the base model (model 1), and evaluate the association of death with unweighted co-morbidity scores (models 2–4), weighted co-morbidity scores (models 5–7), as well as specific co-morbidity conditions as determined by each measure (models 8–11). The unweighted and weighted co-morbidity scores for measures were modelled as continuous (per 1 unit increments). When modelling co-morbidity conditions from each of the three measures (models 8–10) and the one combined measures (model 11), a model was initially created with all non-collinear (tolerance > 0.10) conditions and covariates. Subsequently, variables not associated with the outcome ($P > 0.20$) were removed from the model manually and model fit was evaluated. A backward elimination model (with a $P < 0.20$ for variable keep) was then created for comparison to the manually fitted model. Logistic regression model performance was evaluated based on its discrimination ability (*c* statistic) and its calibration (comparison of predicted event probability with observed for specific risk groups of equal sizes using the Hosmer and Lemeshow Goodness of Fit (HLGOF) test). *c* Statistics between 0.6 and 0.85 are typical in prognostic models[43] and models with values in this range were deemed to have acceptable discriminative ability in this study. All tests were two sided and alpha = 0.05 was considered statistically significant. SAS 9.4 (SAS Institute, Cary, NC, USA) was used for all analysis.

Results

A sample of 11,848 THA and 18,972 TKA patients were included in the study. The THA patients median age was 80.9 years (IQR = 76.4–84.4) while the TKAs patients' was 79.8 (IQR = 74.7–83.5). The sample had slightly more men (50.2% THAs and 52.3% in TKAs), Table I.

THA co-morbidities and associations with death

The RxRisk-V measure identified the highest proportion of patients with multiple co-morbidities (81.3%, $N = 9635$ had three or more). Using the Elixhauser (12.1%, $N = 1428$) and Charlson (3.1%, $N = 373$) measures, less patients were considered to have more three

or more co-morbidities (Table I). In the THA sample, 112 (0.9%) deaths occurred within 90 days of the surgery and 360 (3.1%) within 1 year.

In all models evaluating co-morbidity burden the higher the co-morbidity score, weighted or unweighted, the higher the odds of either 90 days or 1 year mortality, Table II. All models had moderate to good discrimination (all $c > 0.72$), but models with the specific co-morbidity conditions, and not scores, had better discrimination ($c = 0.74–0.84$) compared to models with scores ($c = 0.72–0.76$). All models had acceptable predictive ability ($P > 0.051$). The model with combined conditions from all measures (model 11) performed best in predicting death both within 90 days ($c = 0.84$, $P = 0.284$) and 1 year ($c = 0.79$, $P = 0.151$). The Charlson model with specific conditions (model 9, $c = 0.80$, $P = 0.777$) was the second best performing model for mortality within 90 days, followed by the model with the Elixhauser conditions (model 8, $c = 0.79$, $P = 0.356$). For mortality within 1 year, the Charlson (model 8) and Elixhauser (model 9) measures performed similarly (both $c = 0.77$, $P > 0.05$). See Table III for the complete description of co-morbidities measures' associations with mortality. For the co-morbidity unweighted and weighted score models, the unweighted Charlson score (model 3) was the best predictor of death within 90 days ($c = 0.78$, $P = 0.576$) and 1 year ($c = 0.76$, $P = 0.420$).

TKA co-morbidities and associations with death

According to the RxRisk-V algorithm, 77.8% ($N = 14,744$) of patients had three or more co-morbidities. Using the Elixhauser (10.7%, $N = 2028$) and Charlson (2.3%, $N = 427$) measures less patients had three or more co-morbidities, Table I. In the TKA sample, there were 95 (0.5%) deaths within 90 days and 380 (2.0%) deaths within 1 year of the index procedure.

The increasing number of co-morbidities, measured by all algorithms, was associated with higher odds of death, Table IV. All models had moderate to good discrimination ability ($c = 0.73–0.82$), but models with specific co-morbidity conditions had better discrimination ($c = 0.75–0.82$) compared to models with unweighted and weighted co-morbidity scores ($c = 0.73–0.78$). All models had acceptable predictive ability ($P > 0.088$). The model with combined conditions from all measures (model 11) performed best in predicting death within 90 days ($c = 0.82$, $P = 0.349$) and 1 year ($c = 0.78$, $P = 0.873$); see Table V for the complete description of co-morbidities associated with higher mortality. For mortality within 90 days, the second best performing model was the one with conditions identified by the Elixhauser measure (model 8, $c = 0.79$, $P = 0.435$). For mortality within 1 year the Charlson unweighted score (model 3), Elixhauser conditions (model 8), Charlson conditions (model 9), and RxRisk-V conditions (model 10) performed similarly (all $c = 0.75$, $P > 0.05$).

Discussion

In this elderly cohort of patients undergoing total joint arthroplasty we found that a comprehensive model with co-morbidities identified by the combination of conditions from Elixhauser, Charlson, and RxRisk-V was the best mortality prediction model, for both mortality periods evaluated for both THAs and TKAs. However, small differences were observed when evaluating the specific measures. In the THA cohort, the Charlson performed best for mortality prediction within 90 days, but for the 1 year prediction the Charlson and Elixhauser performed similarly. In the TKA cohort, the Elixhauser performed best for mortality prediction within 90 days, but within 1 year all three measures performed similarly. Generally, the RxRisk-V did not perform as well as the diagnosis based measures with the lowest discrimination in all evaluations. Additionally, models with unweighted and weighted scores (i.e., models 2–7) did not perform as well as the ones with the ones with specific co-morbid conditions (i.e., models 8–10).

While the predictive ability of a prescription based co-morbidity measure for mortality had not been evaluated before in a joint arthroplasty cohort it had been evaluated in other patient populations[34,39,44,45]. Johnson *et al.* validated the use of the RxRisk-V in predicting mortality in two patient populations[34]. In patients with congestive heart failure, the RxRisk-V measure had acceptable discriminatory ability ($c = 0.65–0.69$) and in a patients taking non-steroidal anti-inflammatory drugs (NSAIDs) it had good discriminatory ability ($c = 0.77–0.79$)[34]. Lu *et al.* reported that the unweighted RxRisk-V ($c = 0.70$) and weighted RxRisk-V ($c = 0.73$) did not perform as well as most of the Charlson adaptations ($c = 0.76$) in a cohort of Australian veterans[44]. Schneeweiss *et al.* compared the performance of the RxRisk-V predecessor, the chronic disease

Table IV
Associations of co-morbidity measures and TKA with 90 days and 1 year mortality. Odds ratios, 95% confidence intervals, discrimination (*c* statistic), calibration (HLGOF Chi-square test *P* value)

Models	90 Days*			1 Year*		
	OR (95% CI)	*C* Statistic	HLGOF	OR (95% CI)	*C* Statistic	HLGOF
Base (model 1)	–	0.69	0.635	–	0.70	0.310
Unweighted co-morbidity scores						
Elixhauser (model 2)	1.60 (1.45–1.77)	0.78	0.795	1.41 (1.33–1.49)	0.74	0.877
Charlson (model 3)	1.83 (1.57–2.13)	0.76	0.643	1.69 (1.55–1.85)	0.75	0.495
RxRisk-V (model 4)	1.20 (1.13–1.28)	0.75	0.747	1.13 (1.10–1.16)	0.73	0.141
Weighted co-morbidity scores						
Elixhauser (model 5)	1.14 (1.11–1.17)	0.77	0.554	1.11 (1.09–1.13)	0.74	0.609
Charlson (model 6)	1.43 (1.30–1.57)	0.75	0.626	1.37 (1.30–1.45)	0.74	0.088
RxRisk-V (model 7)	1.12 (1.08–1.17)	0.74	0.949	1.10 (1.08–1.12)	0.74	0.778
Specific conditions within each measure†						
Elixhauser (model 8)	–	0.79‡	0.435	–	0.75	0.858
Charlson (model 9)	–	0.75‡	0.981	–	0.75	0.310
RxRisk-V (model 10)	–	0.78‡	0.207	–	0.75	0.201
Combined Elixhauser, Charlson, and RxRisk-V (model 11)	–	0.82‡	0.349	–	0.78	0.873

OR = Odds ratio. CI = Confidence intervals.
* All include age, gender, and primary diagnosis unless otherwise specified.
† See Table V for models with specific conditions.
‡ Model was better fit with age and primary diagnoses.

Table V
Adjusted odds of 90 days and 1 year mortality in TKA patients by specific Co-morbidity measure conditions

Co-morbidity measure conditions	90 Days*	1 Year*
	OR (95% CI)	OR (95% CI)
Elixhauser (model 8)		
Drug abuse	**14.5 (1.47–143.6)**	–
Metastatic cancer	**8.09 (1.76–37.1)**	**6.02 (2.25–16.1)**
Congestive heart failure	**3.03 (1.74–5.29)**	**2.80 (2.03–3.86)**
Deficiency anaemia	**2.86 (1.10–7.40)**	1.61 (0.85–3.05)
Pulmonary circulation disorders	**2.75 (1.25–6.05)**	–
Fluid and electrolyte disorders	**2.19 (1.30–3.71)**	1.34 (0.96–1.86)
Cardiac arrhythmia	**2.03 (1.28–3.22)**	**1.72 (1.35–2.18)**
Other neurological disorders	2.56 (0.96–6.79)	1.62 (0.84–3.11)
Obesity	2.18 (0.86–5.51)	–
Coagulopathy	2.16 (0.73–6.38)	–
Peripheral vascular disorders	1.77 (0.77–4.09)	–
Valvular disease	1.72 (0.82–3.57)	**1.70 (1.10–2.63)**
Hypertension uncomplicated	1.54 (0.99–2.39)	1.25 (0.99–1.57)
Paralysis	–	**2.93 (1.38–6.19)**
Renal failure	–	**1.84 (1.28–2.66)**
Hypothyroidism	–	2.13 (0.83–5.45)
Rheumatoid arthritis/collagen	–	1.77 (0.98–3.18)
Charlson (model 9)		
Myocardial infarction	**4.28 (2.30–7.96)**	**2.17 (1.44–3.28)**
Congestive heart failure	**3.78 (2.14–6.66)**	**3.17 (2.29–4.38)**
Cerebrovascular disease	**2.68 (1.20–6.01)**	**2.94 (1.93–4.49)**
Renal disease	**2.04 (1.04–3.98)**	**2.01 (1.39–2.93)**
Mild liver disease	5.58 (0.71–43.7)	**4.11 (1.17–14.5)**
Metastatic solid tumor	4.75 (0.83–27.3)	**3.53 (1.20–10.4)**
Any malignancy	2.21 (0.74–6.60)	**2.10 (1.19–3.72)**
Peripheral vascular disease	1.99 (0.88–4.50)	1.46 (0.88–2.42)
Dementia	–	**3.21 (1.93–5.34)**
Rheumatic disease	–	1.84 (1.00–3.39)
RxRisk-V (model 10)		
Hyperkalaemia	**17.7 (3.86–81.1)**	–
Psychotic illness	**2.87 (1.23–6.71)**	**2.51 (1.55–4.07)**
Congestive heart failure	**2.42 (1.55–3.80)**	**1.87 (1.46–2.41)**
Antiplatelets	**2.06 (1.34–3.19)**	**1.42 (1.13–1.77)**
IHD hypertension	**1.70 (1.12–2.59)**	**1.24 (1.00–1.54)**
Benign prostatic hyperplasia	1.96 (0.97–3.95)	–
Chronic airways disease	1.49 (0.96–2.31)	**1.28 (1.01–1.62)**
Gout	1.48 (0.89–2.47)	**1.41 (1.08–1.85)**
Anticoagulation	1.35 (0.88–2.07)	–
Hyperlipidaemia	0.71 (0.46–1.10)	0.81 (0.65–1.02)
End stage renal disease	–	**2.37 (1.39–4.03)**
Arrhythmia	–	**1.51 (1.15–1.98)**
Inflammation pain	–	**1.26 (1.01–1.57)**
Malignancies	–	1.43 (0.93–2.19)
Liver failure	–	1.38 (0.89–2.13)
Epilepsy	–	1.33 (0.86–2.05)
Allergies	–	0.82 (0.62–1.08)
Combined Charlson, Elixhauser, and RxRisk-V conditions (model 11)		
Hyperkalaemia	**16.2 (3.31–79.0)**	**4.98 (1.30–19.1)**
Metastatic cancer	**11.7 (2.58–62.6)**	**5.34 (1.92–14.9)**
Myocardial infarction	**3.81 (2.08–6.97)**	**2.23 (1.49–3.33)**
Pulmonary circulation disorder	**3.10 (1.42–6.77)**	–
Deficiency anaemia	**3.01 (1.16–7.79)**	–
Obese	**2.56 (1.02–6.41)**	–
Arrhythmia	**2.07 (1.33–3.21)**	**1.75 (1.39–2.19)**
Congestive heart failure	**1.97 (1.24–3.14)**	**1.83 (1.43–2.34)**
Antiplatelets	**1.83 (1.17–2.86)**	1.25 (1.00–1.57)
IHD hypertension	**1.71 (1.12–2.61)**	1.20 (0.97–1.49)
Drug abuse	10.9 (0.95–124)	–
Other neurological disorders	2.52 (0.92–6.86)	–
Cerebrovascular disease	2.09 (0.90–4.85)	**2.72 (1.78–4.15)**
Valvular disease	1.99 (0.97–4.07)	**1.89 (1.23–2.90)**
Benign prostatic hyperplasia	1.81 (0.89–3.71)	–
Chronic airways disease	1.45 (0.93–2.27)	1.27 (1.00–1.62)
Gout	1.43 (0.85–2.39)	1.31 (1.00–1.73)
Hyperlipidaemia	0.65 (0.41–1.02)	0.76 (0.60–0.96)
Dementia		**2.53 (1.54–4.16)**
Psychosis		**2.24 (1.36–3.69)**
Renal disease		**1.87 (1.35–2.60)**
Any malignancy		**1.55 (1.07–2.26)**
Inflammation pain		**1.37 (1.09–1.71)**
Mild liver disease		2.90 (0.80–10.6)
Smoke cessation		2.24 (0.67–7.49)
Glaucoma		1.15 (0.85–1.57)
Steroid responsive disorders		1.12 (0.87–1.44)
Allergies		0.84 (0.63–1.12)
Psoriasis		0.46 (0.06–3.37)
Alcohol abuse		0.35 (0.08–1.57)

IHD = Ischemic heart disease. OR = Odds ratio. CI = Confidence intervals.
Bold values are statistically significant.
* All models adjusted for age and primary diagnosis.

score measure, to various Charlson measure adaptations and found that while it performed satisfactorily ($c = 0.72–0.74$) in predicting mortality, it was not superior to most Charlson adaptations ($c = 0.74–0.77$)[45]. These findings are similar to ours that while the RxRisk-V can contribute to the case-mix adjustment in a joint arthroplasty population satisfactorily, it does not perform as well as the individual conditions identified by the Elixhauser and Charlson measures, either weighted or unweighted. This is likely due to the inclusion of conditions in the RxRisk-V score that may not be as severe as the ones captured by the diagnostic based measures using hospitalisation records. Having information on a more complete history of patient's co-morbidities, as offered by the RxRisk-V, may be useful in the performance of outcomes related to resource utilisation but mortality seems to be better predicted by hospitalisation events using diagnostic codes.

The Charlson and Elixhauser co-morbidity measures have been extensively compared in general patient populations and there is consensus that the Elixhauser measure, with the conditions included as individual covariates in the model, is the best predictor of mortality after 30 days[29,46]. In the orthopaedic surgical population, the Elixhauser measure has also been found to be the better predictor of in-hospital death after orthopaedic surgery[47]. However, in total joint arthroplasty patients there is no consensus as to which co-morbidity measure is the best in regards to mortality prediction. In a sample of almost 250,000 US Medicare surgical patients between 1985 and 1989, Melfi *et al.* reported that the unweighted co-morbidity score at the time of surgery was the best performer ($c = 0.82$) in predicting short term death in comparison to the Charlson weighted score ($c = 0.65$), which performed very poorly in comparison to the other measures ($c = 0.65–0.82$)[48]. More recently, when Mnatzaganian *et al.* evaluated some of these measures in a smaller cohort of 819 Australian men, they reported that the Charlson weighted score ($c = 0.88$) performed better in the 1 year mortality prediction than the Elixhauser conditions ($c = 0.86$), but similarly to our results the differences were small between the co-morbidity measures ($c = 0.76–0.88$)[46]. In our study, in patients undergoing either THAs or TKAs, the combination of conditions from all three evaluated measures was superior in predicting death but small differences were found in predictive performance between the best performing measure and others. We found the models with specific conditions performed the best, followed by the Charlson unweighted score for hips for 90 days and 1 year, and knees for 1 year estimates.

While the 90 days mortality rate of this cohort (THA: 0.9%, TKA: 0.5%) is within the range of other large cohorts (THA range: 0.29–1.3%[16,17,19,20,49], TKA range: 0.35–0.7%[13,20,25]) the 1 year mortality rate (3% in THAs and 2.1% in TKAs) is substantially higher (1.2–1.8% in THAs and 0.9–1.5% in TKAs)[20,50]. This difference in

mortality rates is likely due to the older age of the cohort included in this study. While our analyses were adjusted for age and therefore the impact of co-morbidity measures should be independent of age, it is possible that residual confounding exits and limits the representativeness of our findings to similar elderly cohorts of patients. Another limitation of our study was our susceptibility to the common problems of administrative data, which include coding errors, missing data, and underreporting of certain conditions depending on the setting[51–53]. These were possibilities, but we have no reason to believe that these errors would be differential in the groups evaluated and therefore do not expect this to affect our overall findings. Finally, because of the data availability only inpatient records were used ascertain co-morbidities with the Charlson and Elixhauser measures, this may have resulted in a lower discriminatory ability than if outpatient data was also used.[26]

Because the Australian DVA pays for all the services received by the patients included in this study it is likely that full records of the cohort's activity in regards to their hospitalisations and pharmacy utilisation were available. The likelihood of missing data or cohort attrition was extremely low. A strength of our study is our evaluation of several co-morbidity measures and adaptations of these measures in our large cohort of patients with a large number of events. Our large cohort size also allowed us to evaluate both a THA and TKA cohort of patients separately and therefore determine procedure specific estimates, which is important since the co-morbidity profile of these patient cohorts are slightly different and the incidence of mortality is 35–45% lower in TKA patients. Additionally, we were able to examine the robustness of our estimates over two time periods including the shorter time frame of 90 days mortality, which is the most commonly reported and scrutinized outcome of joint arthroplasty surgery.

This study validates the Elixhauser and Charlson, and RxRisk-V co-morbidity measures as acceptable mortality predictors in THA and TKA patient cohorts. However, individually, the Charlson performed slightly better than the Elixhauser, which performed better than the RxRisk-V. These findings are important as no consensus as to which co-morbidity measure is best in regards to mortality prediction exists for a total joint arthroplasty cohort. The similar performance of the diagnoses measures indicates that the choice of which to use when conducing mortality prediction, case-mix adjustment, and other important mortality analysis in total joint arthroplasty patients should be the Elixhauser and Charlson. To determine the choice between the two measures factors such specific conditions in each measure and possible modelling limitations due to the differential number of conditions in each measure should be considered.

Authors' contributions

Conception and design: MCSI, NLP, EER, SEG.
Acquisition of data: MCSI, NLP, EER.
Analysis and interpretation of data: MCSI, NLP, EER, SEG.
Drafting and revising manuscript: MCSI.
Final approval: MCSI, NLP, EER, SEG.

Conflict of interest

None of the authors have any conflict of interest.

Role of the funding source

This work was supported by an Australian Government National Health and Medical Research Council (NHMRC) Centre of Research Excellence in Post-Marketing Surveillance of Medicines and Medical Devices grant (GNT1040938). Nicole L. Pratt is supported by an NHMRC Early Career Fellowship (GNT1035889). No financial support or other benefits from commercial sources was received by any of the authors for the work reported on in the manuscript.

Acknowledgements

We acknowledge the provision of data for this study by the Australian Government DVA. The DVA reviewed the manuscript to be submitted for publication but played no role in the analysis or interpretation of the data or in the preparation of this manuscript.

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