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Supplemental material

Microsurgical clipping and endovascular management of unruptured anterior circulation aneurysms: how age, frailty, and comorbidity indexes influence outcomes

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Supplementary e-Table 1: Details of ICD-10 diagnostic and procedural codes

Diagnosis	ICD-10 codes (diagnostic and procedural)
Cerebral Unruptured aneurysm	I67.1
Endovascular management	'03VG3CZ','03VG3HZ','03VG3DZ','03VK3BZ','03VK3DZ','03VL3BZ','03VL3DZ','03VL3HZ','03LG3BZ','03LG3DZ','03LK3BZ','03LK3DZ','03LL3BZ','03LL3DZ','03VP3DZ','03VP3HZ','03VK4BZ','03VP4DZ','03P4HZ','03VQ3BZ','03VQ3DZ','03VQ3HZ','03VQ3ZZ','03VQ4BZ','03VQ4DZ','03VQ4HZ','03VQ4ZZ'
Open surgical clipping of aneurysm (anterior circulation)	03VG0CZ, 03VL0CZ, 03VK0CZ,03LK0CZ,03LGC0CZ,03LLOCZ
Wound complications, including CSF leak	T81.3,T81.30,T81.30XA,T81.30XD,T81.30XS,T81.31,T81.31XA,T81.31XD,T81.31XS,T81.32,T81.32XA,T81.32XD,T81.32XS, G97.0
Respiratory complications	J81.0,J80,J96.00,J96.90,J96.91,J96.92,J96.01,J96.02,J95.89,J95.859,T8.182XA,J18,J18.0,J18.1,J18.2,J18.8,J18.9
Acute Kidney Injury	N17.0,N17.1,N17.2,N17.8,N17.9
UTI	N39.0
Cardiac complications	I97.710, I97.790, I97.88, I97.89,I97.111,I97.121, I97.131,I97.191
Neurological complications	'G9751','G9761','E3601','E3612', G40
Sepsis and septic shock	A410,A4101,A4102,A411,A412,A413,A414,A415,A4150,A4151,A4152,A4153,A4159,A418,A4181,A4189,A419, T81.12, T81.12XA, T81.12XD, T81.12XS
Ventilation	5A1935Z, 5A1945Z, 5A1955Z
DVT	I82.2 (X)

Supplementary e-Table 2: Variables used for extraction of the Hospital Frailty Risk Score (HFRS)

ICD_Code	ICD_Description	Deficit_Category	Points
F00	Dementia in Alzheimer's disease	Memory & cognitive problems	7.1
G81	Hemiplegia	Cerebrovascular disease	4.4
G30	Alzheimer's disease	Memory & cognitive problems	4
I69	Sequelae of cerebrovascular disease (secondary codes)	Cerebrovascular disease	3.7
R29	Other symptoms and signs involving the nervous and musculoskeletal systems (R29.6 Tendency to fall)	Falls	3.6
N39	Other disorders of urinary system (includes urinary tract infection and urinary incontinence)	Urinary system	3.2
W19	Unspecified fall	Falls	3.2
S00	Superficial injury of head	Falls	3.2
F05	Delirium, not induced by alcohol and other psychoactive substances	Memory & cognitive problems	3.2
R31	Unspecified haematuria	Urinary system	3
B96	Other bacterial agents as the cause of diseases classified to other chapters (secondary code)	Acute Infection	2.9
R41	Other symptoms and signs involving cognitive functions and awareness	Memory & cognitive problems	2.7
R26	Abnormalities of gait and mobility	Mobility and transfer problems	2.6
R56	Convulsions, not elsewhere classified	Acute neurological	2.6
I67	Other cerebrovascular diseases	Cerebrovascular disease	2.6
R40	Somnolence, stupor and coma	Acute neurological	2.5
T83	Complications of genitourinary prosthetic devices, implants and grafts	Urinary system	2.4
S06	Intracranial injury	Cerebrovascular disease	2.4
E86	Volume depletion	Acute kidney injury/Dehydration	2.3

E87	Other disorders of fluid, electrolyte and acid-base balance	Electrolytes and Metabolic disorders	2.3
S42	Fracture of shoulder and upper arm	Fragility Fractures	2.3
M25	Other joint disorders, not elsewhere classified	Arthritis	2.3
R54	Senility	Memory & cognitive problems	2.2
F03	Unspecified dementia	Memory & cognitive problems	2.1
Z50	Care involving use of rehabilitation procedures	Mobility and transfer problems	2.1
W18	Other fall on same level	Falls	2.1
S80	Superficial injury of lower leg	Falls	2
L03	Cellulitis	Acute Infection	2
Z75	Problems related to medical facilities and other health care	Social vulnerability	2
F01	Vascular dementia	Memory & cognitive problems	2
H54	Blindness and low vision	Sensory loss	1.9
E53	Deficiency of other B group vitamins	Anaemia & haematinic deficiency	1.9
R55	Syncope and collapse	Hypotension / syncope	1.8
K59	Other functional intestinal disorders	Digestive tract functional disorders	1.8
S22	Fracture of rib(s), sternum and thoracic spine	Fragility Fractures	1.8
N17	Acute renal failure	Acute kidney injury/Dehydration	1.8
Z60	Problems related to social environment	Social vulnerability	1.8
G20	Parkinson's disease	Parkinsonism & tremor	1.8
B95	Streptococcus and staphylococcus as the cause of diseases classified to other chapters	Acute Infection	1.7
L89	Decubitus ulcer	Skin ulcer/pressure sore	1.7
Z22	Carrier of infectious disease	Hospital acquired complications or infections	1.7

R44	Other symptoms and signs involving general sensations and perceptions	Sensory loss	1.6
K26	Duodenal ulcer	Peptic ulcer	1.6
I95	Hypotension	Hypotension / syncope	1.6
N19	Unspecified renal failure	Chronic kidney disease	1.6
L97	Ulcer of lower limb, not elsewhere classified	Skin ulcer/pressure sore	1.6
A41	Other septicaemia	Acute Infection	1.6
X59	Exposure to unspecified factor	Other trauma (excl. fragility fractures)	1.5
J96	Respiratory failure, not elsewhere classified	Respiratory disease	1.5
G40	Epilepsy	Acute neurological	1.5
Z87	Personal history of other diseases and conditions	Social vulnerability	1.5
M19	Other arthrosis	Arthritis	1.5
S72	Fracture of femur	Fragility Fractures	1.4
E16	Other disorders of pancreatic internal secretion	Electrolytes and Metabolic disorders	1.4
R94	Abnormal results of function studies	Electrolytes and Metabolic disorders	1.4
M81	Osteoporosis without pathological fracture	Osteoporosis	1.4
S32	Fracture of lumbar spine and pelvis	Fragility Fractures	1.4
N18	Chronic renal failure	Chronic kidney disease	1.4
R33	Retention of urine	Urinary system	1.3
R69	Unknown and unspecified causes of morbidity	Uncertain diagnosis/Generally unwell	1.3
N28	Other disorders of kidney and ureter, not elsewhere classified	Chronic kidney disease	1.3
G45	Transient cerebral ischaemic attacks and related syndromes	Cerebrovascular disease	1.2
R45	Symptoms and signs involving emotional state	Depression and mood disorders	1.2
R32	Unspecified urinary incontinence	Urinary system	1.2
Y95	Nosocomial condition	Hospital acquired complications or infections	1.2

S09	Other and unspecified injuries of head	Falls	1.2
G31	Other degenerative diseases of nervous system, not elsewhere classified	Memory & cognitive problems	1.2
M79	Other soft tissue disorders, not elsewhere classified	Skin ulcer/pressure sore	1.1
A04	Other bacterial intestinal infections	Acute Infection	1.1
A09	Diarrhoea and gastroenteritis of presumed infectious origin	Acute Infection	1.1
J18	Pneumonia, organism unspecified	Acute Infection	1.1
W06	Fall involving bed	Falls	1.1
S01	Open wound of head	Falls	1.1
Z74	Problems related to care-provider dependency	Social vulnerability	1.1
R02	Gangrene, not elsewhere classified	Acute Infection	1
E55	Vitamin D deficiency	Osteoporosis	1
J69	Pneumonitis due to solids and liquids	Swallowing problems	1
Z93	Artificial opening status	Digestive tract functional disorders	1
R47	Speech disturbances, not elsewhere classified	Sensory loss	1
H91	Other hearing loss	Sensory loss	0.9
M41	Scoliosis	Arthritis	0.9
R63	Symptoms and signs concerning food and fluid intake	Uncertain diagnosis/Generally unwell	0.9
W10	Fall on and from stairs and steps	Falls	0.9
W01	Fall on same level from slipping, tripping and stumbling	Falls	0.9
E05	Thyrotoxicosis [hyperthyroidism]	Electrolytes and Metabolic disorders	0.9
U80	Agent resistant to penicillin and related antibiotics (secondary code only)	Hospital acquired complications or infections	0.8
M80	Osteoporosis with pathological fracture	Fragility Fractures	0.8
Z99	Dependence on enabling machines and devices, not elsewhere classified	Social vulnerability	0.8

I63	Cerebral Infarction	Cerebrovascular disease	0.8
R13	Dysphagia	Swallowing problems	0.8
K92	Other diseases of digestive system	Digestive tract functional disorders	0.8
R00	Abnormalities of heart beat	Atrial fibrillation	0.7
F10	Mental and behavioural disorders due to use of alcohol	Mental health/Mood	0.7
Y84	Other medical procedures as the cause of abnormal reaction of the patient, or of later complication, without mention of misadventure at the time of the procedure	Hospital acquired complications or infections	0.7
J22	Unspecified acute lower respiratory infection	Acute Infection	0.7
N20	Calculus of kidney and ureter	Urinary system	0.7
R79	Other abnormal findings of blood chemistry	Electrolytes and Metabolic disorders	0.6
Z73	Problems related to life-management difficulty	Social vulnerability	0.6
F32	Depressive episode	Depression and mood disorders	0.5
Z91	Personal history of risk-factors, not elsewhere classified	Social vulnerability	0.5
M48	Spinal stenosis (secondary code only)	Arthritis	0.5
S51	Open wound of forearm	Other trauma (excl. fragility fractures)	0.5
E83	Disorders of mineral metabolism	Electrolytes and Metabolic disorders	0.4
M15	Polyarthrosis	Arthritis	0.4
D64	Other anaemias	Anaemia & haematinic deficiency	0.4
L08	Other local infections of skin and subcutaneous tissue	Acute Infection	0.4
R11	Nausea and vomiting	Digestive tract functional disorders	0.3
K52	Other noninfective gastroenteritis and colitis	Digestive tract functional disorders	0.3
R50	3.6	Uncertain diagnosis/Generally unwell	0.1

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Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet*. 2018;391:1775-1782. © The authors, published with permission. CC BY 4.0 (<https://creativecommons.org/licenses/by/4.0/>).

Supplementary e-Table 3: Variables for extraction of the Neurovascular Comorbidity Index and Elixhauser Comorbidity Index

Neurovascular Comorbidity Index

Diagnosis (ICD-10)	Points given for each disorder
Neurological disorder	7
Renal insufficiency	6
GI bleeding	6
Paralysis	5
Acute MI	5
Electrolyte disorder	4
Weight loss	4
Metastatic cancer	4
Drug abuse	3
Arrhythmia	2
Coagulopathy	2
CVA	2
Psychosis	2
Alcoholism	1
Perivascular disease	1
Valvular disease	1
No comorbidities	0
Tobacco use	-1
Hypothyroidism	-1
Depression	-1
Hypercholesterolemia	-2

Reproduced from Newman WC, Neal DW, Hoh BL. A new comorbidities index for risk stratification for treatment of unruptured cerebral aneurysms. *J Neurosurg.* 2016;125(3):713-719. © AANS, published with permission.

Elixhauser Comorbidity Index

Comorbidity	Weight assigned
Neurological disorder	6
Renal insufficiency	5
Gastrointestinal bleeding	-
Paralysis	7
Acute MI	-
Electrolyte disorder	5
Weight loss	6
Metastatic cancer	12
Drug abuse	-7
Arrhythmia	5
Coagulopathy	3

CVA	-
Psychosis	0
Alcoholism	0
Perivascular disease	2
Valvular disease	-1
Tobacco use	-
Hypothyroidism	0
Depression	-
Hypercholesterolemia	-
Congestive heart failure	7
Dementia	-
Chronic pulmonary disease	3
Connective tissue disorder	0
Ulcer disease	-
Mild liver disease	11
Diabetes	0
Diabetes with end organ damage	0
Any solid tumor	4
Leukemia/Lymphoma	9
Moderate or severe liver disease	11
AIDS	0
Pulmonary circulation disorders	4
Hypertension	0
Obesity	-4
Anemia	-2

HCUP Elixhauser Comorbidity Software. Healthcare Cost and Utilization Project (HCUP). June 2107. Agency for Healthcare Research and Quality, Rockville, MD. <https://www.hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp>. Complete SAS code for extraction of the Elixhauser Index available for free at the above-mentioned link.

See also Elixhauser A, Steiner C, Harris R, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998;36(1):8-27; and Moore BJ, White S, Washington R, Coenen N, Elixhauser A. Identifying increased risk of readmission and in-hospital mortality using hospital administrative data: The AHRQ Elixhauser Comorbidity Index. *Med Care*. 2017;55(7):698-705.

Supplementary e-Table 4: Odds ratios computed using binary logistic regression analysis for clipping aneurysms after adjusting for potential confounders

Variables	Death in Hospital		Extended length of stay		Poor outcome		Any complication	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.204 (1.031-1.406)	0.01	0.991(0.973-1.009)	0.324	1.035(1.017-1.052)	<0.001	1.004(0.972-1.037)	0.817
Gender	0.240 (0.032-1.815)	0.167	0.96 (0.669-1.377)	0.823	1.310(0.944-1.818)	0.107	0.632(0.352-1.137)	0.126
Elixhauser comorbidity score	1.184 (0.982-1.428)	0.076	1.059 (1.023-1.096)	0.001	1.041 (1.008-1.074)	0.01	1.082(1.026-1.142)	0.04
Neurovascular comorbidity index	1.255(0.998-1.579)	0.156	1.105 (1.060-1.152)	<0.001	1.067(1.026-1.109)	0.001	0.981 (0.921-1.045)	0.547
Hospital Frailty Risk score	0.720(0.501-1.034)	0.075	1.185(1.113-1.261)	<0.001	1.171(1.102-1.244)	<0.001	1.313(1.208-1.426)	<0.001

Supplementary e-Table 5: Odds ratios computed for outcomes using binary logistic regression analysis for coiling aneurysms after adjusting for potential confounders

Variables	Death in Hospital		Extended length of stay		Poor outcome		Any complication	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.006(0.988-1.023)	0.526	1.001(0.998-1.004)	0.674	1.030 (1.026 - 1.035)	<0.001	1.009(1.002-1.016)	0.012
Gender	2.171 (1.342-3.511)	0.002	1.125 (1.045 - 1.210)	0.002	1.166(1.055-1.288)	0.107	1.079 (0.923-1.262)	0.338
Elixhauser comorbidity score	1.173(1.142-1.204)	<0.001	1.072(1.064-1.079)	<0.001	1.065(1.05-1.074)	0.01	1.046 (1.032-1.059)	<0.001
Neurovascular comorbidity index	1.050 (1.011-1.089)	0.01	1.083(1.072-1.093)	<0.001	1.069 (1.057 - 1.081)	0.001	1.046 (1.030-1.063)	<0.001
Hospital Frailty Risk score	1.041 (0.994-1.091)	0.086	1.229(1.212-1.247)	<0.001	1.247 (1.227 - 1.267)	<0.001	1.384 (1.355-1.414)	<0.001

Supplementary e-Table 6: Literature review of the various indexes along with online resources

Frailty Index	Description	URL
Rockwood Frailty scale	<p>Comprehensive geriatric assessment</p> <p>Dalhousie University, Halifax, Nova Scotia, Canada</p>	<p>https://www.cgakit.com/fr-1-rockwood-clinical-frailty-scale</p>
Fried Frailty index	<p>Unintentional weight loss Grip strength in lower quartile Self-reported exhaustion Slowness of the gait Low physical activity</p>	NA
Frailty Group Calculator	<p>The Frailty score (1-20) is calculated by multiplication of the weighted scores for the following four geriatric assessment variables: age, Charlson comorbidity index, Geriatric Nutritional Risk Index.</p> <p>University of Oslo, Norway</p>	<p>https://wide.shinyapps.io/app-frailty/</p>
Johns Hopkins adjusted clinical groups	<p>Johns Hopkins University</p> <p>A single score is generated which classifies categorically as Frail vs Non frail</p>	<p>https://www.johnshopkinsolutions.com/solution/frailty/</p>
Modified Frailty Index (mFI-11)	<p>This index was modelled by the variables in the NSQIP containing 11 variables.</p> <p>Diabetes Mellitus, Congestive Heart Failure, Hypertension, Stroke, Functional Status, Myocardial infraction, Vascular disease,</p>	<p>https://www.evidencio.com/models/show/1777</p>

	Neurological deficit, COPD, Pneumonia, Heart, Impaired sensorium Evidencio, Netherlands	
5 Factor modified frailty Index (mFI-5)	The original 11 factor modified frailty Index was later modified to 5 factors	N/A
Edmonton Frailty risk score	A simple tool consisting of 9 domains: Health status, functional performance, general health status, social support, medication use, nutrition, mood, continence and functional independence.	https://qxmd.com/calculate/calculator_595/edmonton-frail-scale
G8 Health Status Screening tool	The G-8 screening tool was initially used to identify elderly cancer patients by comprehensively geriatric assessment. Variables: Food Intake, Weight loss, Mobility, neuropsychological problems, BMI, Drugs, Health Status, Age. Evidencio, Netherlands	https://www.evidencio.com/models/show/1045
QFrailty Risk Calculator	This score was developed through the data across the General practitioners in UK. Developed in UK for the intent of predicting outcomes in geriatric patients. ClinRisk Ltd., UK	https://qfrailty.org/
Frailty Risk Calculator	This risk score evaluates the probability of mortality or being hospitalized within the next one year.	http://smartdata.cs.unibo.it/frailtycalc/

	<p>A logistic regression analysis was used utilizing 12 databases and 27 clinical variables.</p> <p>ALMA MATER STUDIORUM, University of Bologna, Italy.</p>	
Senior Health Calculator	<p>This is an online calculator which utilizes the following domains:</p> <p>Medical history (21 items) Functional status (22 items) Performance tests (4 items) Nutritional status (3 items)</p> <p>Beth Israel Medical center, USA</p>	<p>https://www.bidmc.org/research/research-by-department/medicine/gerontology/calculator</p>
CIRS-G	<p>Cumulative illness rating scale – Geriatric (CIRS-G)</p> <p>MD Calc, USA</p>	<p>https://www.mdcalc.com/cumulative-illness-rating-scale-geriatric-cirs-g#use-cases</p>