

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1.

Raw numbers of patients diagnosed with delirium for main groups and sub-group analysis

CCI	Incident Delirium Cases / N		
	Lighter Sedation	Heavier Sedation	Total
0	10/39	13/33	23/72
1	7/22	10/26	17/48
2	6/18	8/20	14/38
3	4/11	3/8	7/19
4	3/5	2/5	5/10
5	1/2	2/4	3/6
6	0/0	0/2	0/2
7	0/0	0/0	0/0
8	3/3	1/2	4/5
Overall	34/100	39/100	73/200

eTable 2:
Univariate analysis on associations between base line characteristics and incident post operative delirium in hospital

	Total (N = 200)	Delirium		p-value
		Yes (N=73)	No (N=127)	
		Mean (SD)		
Age	81.8 (7.7)	83.7 (7.2)	80.6 (7.8)	0.005
Charlson Comorbidity Score	1.5 (1.8)	2.1 (2.2)	1.5 (1.7)	0.06
		N (%)		
Charlson Comorbidity items:				
Myocardial Infarction	23 (11.5)	12 (16.4)	11 (8.7)	0.11
Congestive Heart Failure	23 (11.5)	10 (13.7)	13 (10.2)	0.49
Peripheral Vascular Disease	12 (6.0)	4 (5.5)	8 (6.3)	1.00
Chronic Obstructive Pulmonary Disease	32 (16.0)	15 (20.6)	17 (13.4)	0.23
Cerebrovascular Disease	32 (16.0)	13 (17.8)	19 (15.0)	0.69
Cancer				
Any Solid Tumor	18 (9.0)	6 (8.2)	12 (9.5)	1.00
Leukemia	2 (1.0)	2 (2.7)	0 (0.0)	0.13
Lymphoma	4 (2.0)	2 (2.7)	2 (1.6)	0.62
Metastatic Solid Tumor	3 (1.5)	2 (2.7)	1 (0.8)	0.56
Diabetes				
Overall	33 (16.5)	14 (19.2)	19 (15.0)	0.44
with End Organ Damage	9 (4.5)	4 (5.5)	5 (3.9)	0.73
Chronic Liver Disease				
Mild	2 (1.0)	0 (0.0)	2 (1.6)	0.53
Moderate or Severe	1 (0.5)	0 (0.0)	1 (0.8)	1.00
Chronic Kidney Disease	4 (2.0)	1 (1.4)	3 (2.4)	1.00
Dementia (N=199/72/127)	22 (11.1)	13 (18.1)	9 (7.1)	0.032
Type of Fracture				0.005
Femoral Neck	89 (44.5)	22 (30.1)	67 (52.8)	
Intertrochanteric	95 (47.5)	42 (57.5)	53 (41.7)	
Subtrochanteric	16 (8.0)	9 (12.3)	7 (5.5)	
Mini Mental Status Exam	24.3 (3.7)	23.0 (3.9)	25.0 (3.3)	0.0002
Geriatric Depression Score Overall N= 199/73/126	3.8 (3.5)	5.0 (3.8)	3.1 (3.1)	0.0005

eTable 3:
Intervention Effect Modification by CCI on Post Operative Incident Delirium Risk
CCI Truncated Values >2

Analysis of Maximum Likelihood Estimates							
Parameter	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
Age	0.02660	0.01682	2.4998	0.1139	1.027	0.994	1.061
MMSE score	-0.07282	0.03200	5.1789	0.0229	0.930	0.873	0.990
Fracture Type, Femoral Neck	-0.53302	0.26070	4.1801	0.0409	0.587	0.352	0.978
Geriatric Depression Scale score	0.07491	0.03015	6.1718	0.0130	1.078	1.016	1.143
Heavier Sedation	0.83129	0.38840	4.5809	0.0323	See eTable 3a below		
Charlson Comorbidity Score (CCI3), 0 to 3*	0.29340	0.15916	3.3983	0.0653			
CCI3 x Heavier Sedation	-0.45090	0.21609	4.3540	0.0369			

* CCI scores > 2 were coded as 3

eTable 3a.

Hazard Ratios for Heavier vs Lighter Sedation			
	Hazard Ratio	95% Confidence Limits	
At CCI3 = 0	2.296	1.073	4.916
At CCI3 = 1	1.463	0.888	2.411
At CCI3 = 2	0.932	0.550	1.580
At CCI3 = 3	0.594	0.262	1.343

**eTable 4:
Intervention Effect Modification by CCI on Post Operative Incident Delirium Risk
CCI Continuous Values**

Analysis of Maximum Likelihood Estimates							
Parameter	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
Age	0.03339	0.01759	3.6050	0.0576	1.034	0.999	1.070
MMSE score	-0.06153	0.03210	3.6754	0.0552	0.940	0.883	1.001
Fracture Type, Femoral Neck	-0.61849	0.26179	5.5817	0.0181	0.539	0.323	0.900
Geriatric Depression Scale score	0.06433	0.03077	4.3696	0.0366	1.066	1.004	1.133
Heavier Sedation	0.78879	0.33846	5.4315	0.0198	See eTable 4a below		
Charlson Comorbidity Score (CCI)	0.24163	0.09076	7.0875	0.0078			
CCI x Heavier Sedation	-0.33213	0.13292	6.2437	0.0125			

eTable 4a.

Hazard Ratios for Heavier vs Lighter Sedation			
	Hazard Ratio	95% Confidence Limits	
At CCI3 = 0	2.201	1.134	4.272
At CCI3 = 1	1.579	0.945	2.637
At CCI3 = 2	1.133	0.707	1.814
At CCI3 = 3	0.813	0.463	1.426
At CCI3 = 4	0.583	0.278	1.221
At CCI3 = 5	0.418	0.161	1.087
At CCI3 = 6	0.300	0.091	0.986
At CCI3 = 7	-	-	-
At CCI3 = 8	0.154	0.029	0.829

Note: Surgery date was not a significant confounder and adjustment for it did not make any difference in the model results. There was no difference in risks of incident delirium in hospital across the 4 anesthesiologists, stratified by intervention arms or with both arms combined. Further accounting for anesthesiologists in the Cox models did not change the main results on intervention effect or subgroup analyses on modification of intervention effect by CCI scores.

eFigure. Mini-Mental State Exam score and Delirium Rating Scale-Revised '98 severity score at baseline and postoperative days 1–5 in the lighter-sedation and heavier-sedation groups.

Upper Panel: Mini-Mental State Exam score with 95% confidence bands at baseline and postoperative days 1–5. Lower Panel: Delirium Rating Scale-Revised '98 severity score with 95% confidence bands at baseline and postoperative days 1–5. The difference in MMSE scores at postoperative day1 between group was not statistically significant (Wilcoxon $z=1.82$, $p=0.07$); the adjusted mean MMSE change from baseline to postoperative day 1 between groups was -0.96 (mixed effects model, $t=-2.01$, $p=0.04$). The difference in DRS severity scores at postoperative day1 between groups was statistically significant (Wilcoxon $z=-2.61$, $p=0.009$); the adjusted mean DRS severity score change from baseline to postoperative day1 between groups 1.27 (mixed effects model, $t=2.07$, $p=0.04$).



