Supplementary Online Content

Chan MTV, Wang CY, Seet E, et al; Postoperative Vascular Complications in Unrecognized Obstructive Sleep Apnea (POSA) Study Investigators. Association of unrecognized sleep apnea with postoperative cardiovascular events in patients undergoing major noncardiac surgery. *JAMA*. doi:10.1001/jama.2019.4783

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

eAppendix 1. Definitions of Respiratory Events During Sleep

ApneaLink Plus measurements

The following signals were recorded: respiratory flow (nasal pressure), breathing sounds (snore), respiratory effort, heart rate and oximetry.

Successful monitoring required at least 4 hours of recordings.

Parameters measured:

(1) Apnea event is defined as an episode of airflow reduction ≥ 90% from baseline for ≥ 10 seconds.

(2) Apnea index is the number of apnea events per hour of recording.

(3) Hypopnea event is defined as an episode of airflow reduction ≥ 30% from baseline for ≥ 10 seconds and associated with ≥ 3% oxyhemoglobin desaturation.

(4) Hypopnea index is the number of hypopnea events per hour of recording.

(5) Respiratory event index is the number of apnea and hypopnea events per hour of recording.

PULSOX-300i measurement

The following signals were recorded: pulse oximetry and heart rate.

Parameter measured:

Oxygen desaturation index is the number of events per hour of oximetry recording where oxyhemoglobin saturation decreased by ≥ 4% from baseline for ≥ 10 seconds.

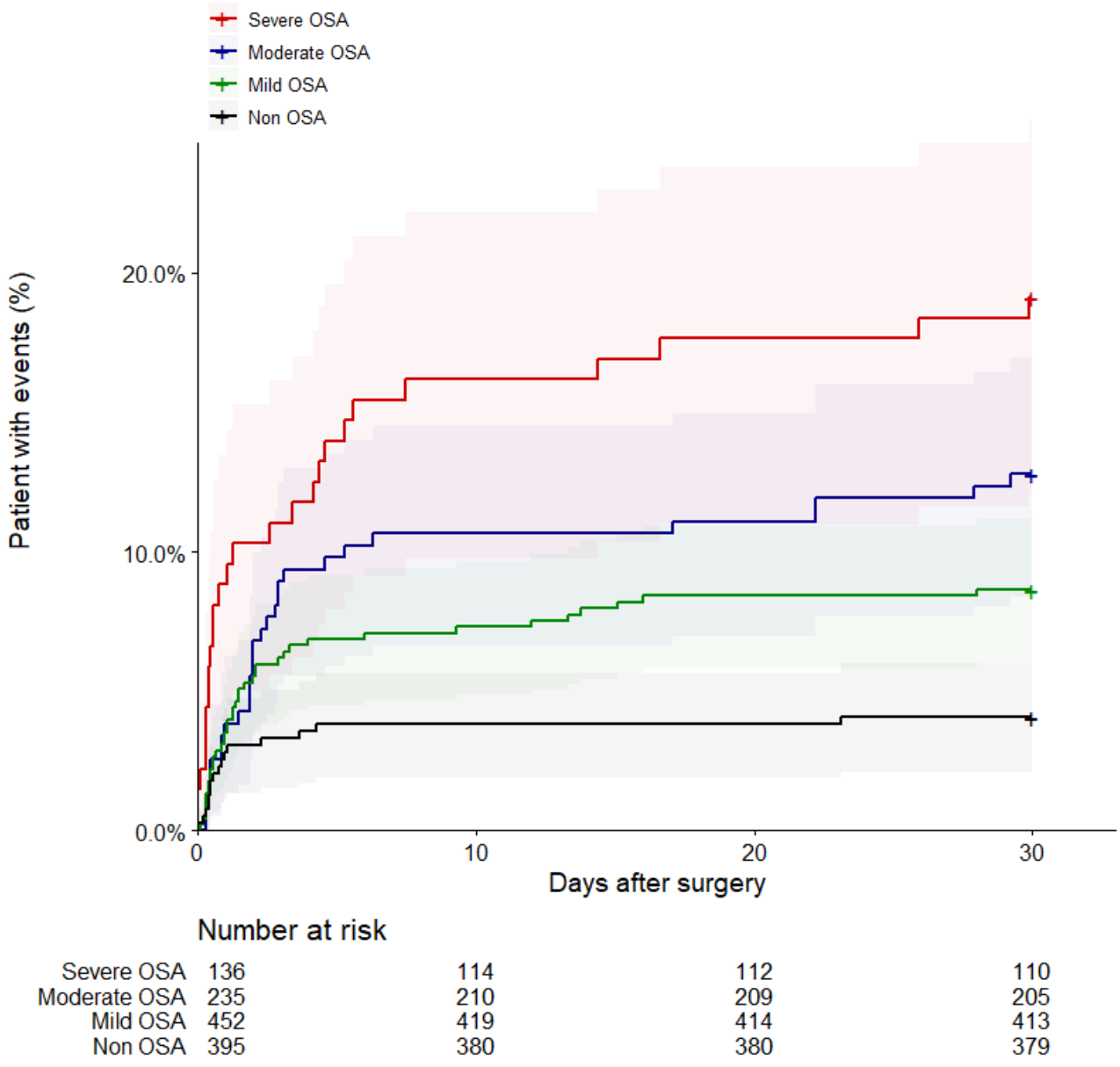
eAppendix 2. Outcome Definitions

Outcome	Definition
Cardiac death	Death attributable to a cardiovascular cause including deaths following myocardial infarction, cardiac arrest, revascularization procedure, pulmonary embolism, deep venous or arterial thrombosis, arrhythmias, stroke and congestive heart failure, or deaths due to an unknown cause.
Myocardial injury after noncardiac surgery	This is an elevated cardiac troponin value[a] within 30 days after surgery without evidence of a non-ischemic etiology, such as pulmonary embolism, sepsis, cardioversion, or known persistent elevated cardiac troponin values.
Myocardial infarction	The diagnosis of myocardial infarction requires any one of the following criterion: (1) Detection of a rise and/or fall of cardiac troponin values with at least one value above the 99th percentile upper reference limit and with at least one of the following: a. Symptoms of ischemia. b. New or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block. c. Development of pathological Q waves in the electrocardiogram. d. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. e. Identification of an intracoronary thrombus by angiography or autopsy. (2) Pathological Q waves with or without symptoms in the absence of non-ischemic causes. (3) Imaging evidence of a region of loss of viable myocardium that is thinned and fails to contract, in the absence of a non-ischemic cause. (4) Pathological findings of a prior myocardial infarction.
Non-fatal cardiac arrest	Nonfatal cardiac arrest is defined as successful resuscitation from ventricular fibrillation, ventricular tachycardia, asystole, or pulseless electrical activity.
Revascularization procedure	This is defined as percutaneous coronary intervention or coronary artery bypass graft surgery.
Pulmonary embolus	Any one of the following: (1) A high probability ventilation/perfusion lung scan; (2) An intraluminal filling defect of segmental or larger artery on a helical CT scan; (3) An intraluminal filling defect on pulmonary angiography; or (4) A positive diagnostic test for deep venous thrombosis (e.g., positive compression ultrasound) with either one of the following: a. low or intermediate probability ventilation/perfusion lung scan;

	b. subsegmental defects or technically inadequate study helical CT scan
Deep venous thrombosis	Any one of the following: (1) Non-compressibility of one or more venous segments on B mode compression ultrasonography; (2) Intraluminal filling defect on contrast enhanced computed tomography; (3) Persistent intraluminal filling defect on contrast venography.
New atrial fibrillation	Atrial fibrillation occurred after surgery with or without angina, heart failure, hypotension, requiring rate controlled drugs or cardioversion.
Stroke	Stroke is defined as a new focal neurological deficit thought to be vascular in origin with signs or symptoms that last > 24 hours or is leading to death.
Congestive heart failure	Any one of the clinical signs: elevated jugular venous pressure, respiratory crackles, or presence of S3 and At least one of radiographic features: vascular redistribution, interstitial edema, or alveolar pulmonary edema.
Pneumonia	Either crackles on physical examinations of chest with one of the followings: (1) purulent sputum or change in sputum characteristics, (2) positive blood culture or isolation of pathogen from transtracheal aspirate, bronchial brushing, or biopsy or chest radiography showing new or progressive infiltrate, consolidation, cavitation, or pleural effusion AND any of the following: (1) purulent sputum or change in sputum characteristics, (2) positive blood culture or isolation of pathogen from transtracheal aspirate, bronchial brushing, or biopsy (3) isolation of virus or detection of viral antigen from respiratory secretions, (4) diagnostic single antibody titer or fourfold increase in paired serum samples for pathogen, or (5) histopathologic evidence of pneumonia.
Infection/sepsis	Invasion of pathogenic organisms isolated from normally sterile tissue (including wound) or fluid or body cavity. Sepsis is defined by the presence of both infection and a systemic inflammatory response.

[a] Peak high-sensitivity cardiac troponin T concentration ≥65 ng/L or an absolute change of ≥5 ng/L when troponin T between 20 and 64 ng/L within 30 days after surgery

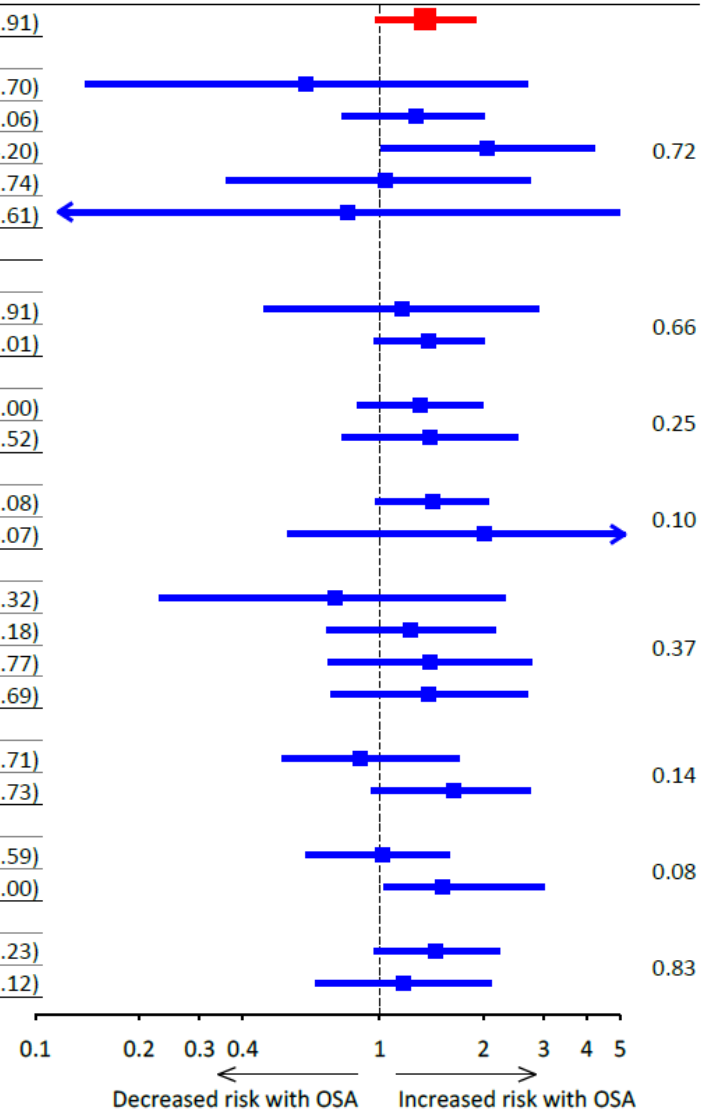
eFigure 1. Kaplan-Meier Estimates of Modified Primary Composite Outcome of Death, Myocardial Infarction, Congestive Heart Failure, Thromboembolism, New Atrial Fibrillation, and Stroke at 30 Days After Surgery



Shaded areas represent 95% confidence intervals
OSA indicates obstructive sleep apnea

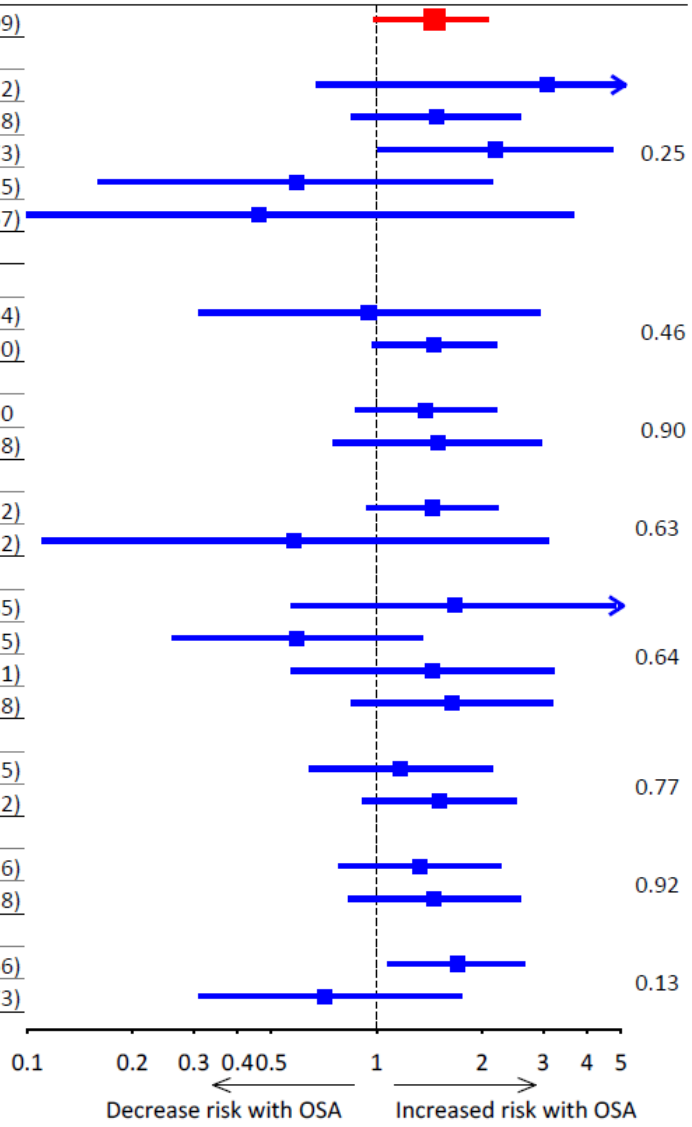
eFigure 2. Subgroup Analyses of Primary Outcome in Patients With Mild vs No Obstructive Sleep Apnea

	No OSA	Mild OSA	Adjusted hazard ratio (95% confidence intervals)	P value for interaction
	No. of patients with event/total no. of patients			
Overall	56/395	86/452	1.36 (0.97-1.91)	
Body mass index – kg/m^2				
< 18.5	5/20	3/16	0.61 (0.14-2.70)	
18.5 – 24.9	31/194	37/177	1.27 (0.78-2.06)	
25.0 – 29.9	11/119	32/169	2.06 (1.01-4.20)	0.72
30.0 – 34.9	6/44	12/69	1.04 (0.36-2.74)	
≥ 35.0	3/18	2/21	0.81 (0.12-5.61)	
Type of anesthesia				
General anesthesia				
No	8/81	13/101	1.16 (0.46-2.91)	0.66
Yes	48/314	73/351	1.39 (0.96-2.01)	
Regional or neuraxial block				
No	38/248	54/273	1.31 (0.86-2.00)	0.25
Yes	18/147	32/179	1.40 (0.78-2.52)	
Anesthetic agents				
Volatile-based	44/295	69/328	1.42 (0.97-2.08)	0.10
Propofol infusion	4/34	7/44	2.01 (0.54-8.07)	
Oxygen administration after surgery				
None	8/107	5/108	0.74 (0.23-2.32)	
One night	19/128	34/162	1.23 (0.70-2.18)	0.37
Two nights	14/89	22/100	1.40 (0.71-2.77)	
Three nights	15/71	25/82	1.39 (0.72-2.69)	
Postoperative opioid administration				
No	27/172	28/193	0.88 (0.52-1.71)	0.14
Yes	29/223	58/259	1.64 (0.95-2.73)	
Postoperative patient-controlled analgesia administration				
No	33/207	37/230	1.02 (0.61-1.59)	0.08
Yes	23/188	49/222	1.52 (1.03-3.00)	
Minimally invasive surgery				
No	35/274	58/312	1.46 (0.96-2.23)	0.83
Yes	21/121	28/140	1.17 (0.65-2.12)	



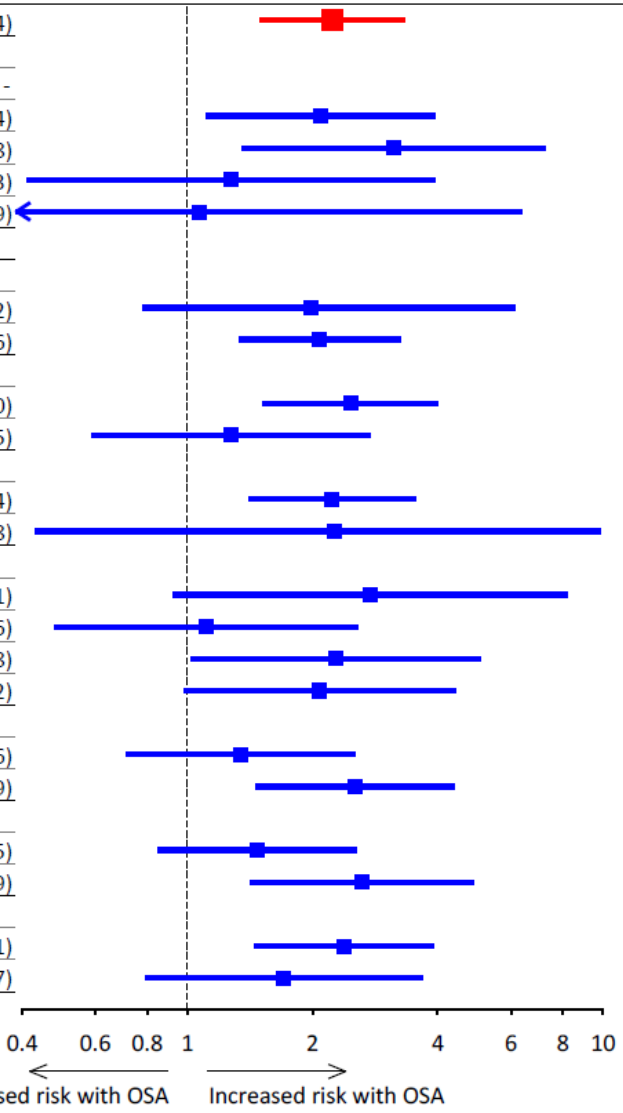
eFigure 3. Subgroup Analyses of Primary Outcome in Patients With Moderate vs No Obstructive Sleep Apnea

	No OSA	Moderate OSA	Adjusted hazard ratio (95% confidence intervals)	P value for interaction
	No. of patients with event/total no. of patients			
Overall	56/395	52/235	1.47 (0.98-2.09)	
Body mass index – kg/m				
< 18.5	5/20	3/5	3.07 (0.67-14.2)	
18.5 – 24.9	31/194	23/81	1.48 (0.85-2.58)	
25.0 – 29.9	11/119	18/87	2.18 (1.01-4.73)	0.25
30.0 – 34.9	6/44	5/35	0.59 (0.16-2.15)	
≥ 35.0	3/18	3/27	0.46 (0.10-3.67)	
Type of anesthesia				
General anesthesia				
No	8/81	5/52	0.95 (0.31-2.94)	0.46
Yes	48/314	47/183	1.46 (0.97-2.20)	
Regional or neuraxial block				
No	38/248	37/148	1.38 (0.87-2.20	0.90
Yes	18/147	15/87	1.50 (0.75-2.98)	
Anesthetic agents				
Volatile-based	44/295	42/171	1.45 (0.94-2.22)	0.63
Propofol infusion	4/34	3/26	0.58 (0.11-3.12)	
Oxygen administration after surgery				
None	8/107	6/47	1.67 (0.57-4.85)	
One night	19/128	10/73	0.59 (0.26-1.35)	0.64
Two nights	14/89	9/40	1.45 (0.57-3.21)	
Three nights	15/71	27/75	1.64 (0.85-3.18)	
Postoperative opioid administration				
No	27/172	19/84	1.17 (0.64-2.15)	0.77
Yes	29/223	33/151	1.51 (0.91-2.52)	
Postoperative patient-controlled analgesia administration				
No	33/207	25/104	1.33 (0.78-2.26)	0.92
Yes	23/188	27/131	1.46 (0.83-2.58)	
Minimally invasive surgery				
No	35/274	44/188	1.70 (1.08-2.66)	0.13
Yes	21/121	8/47	0.71 (0.31-1.73)	

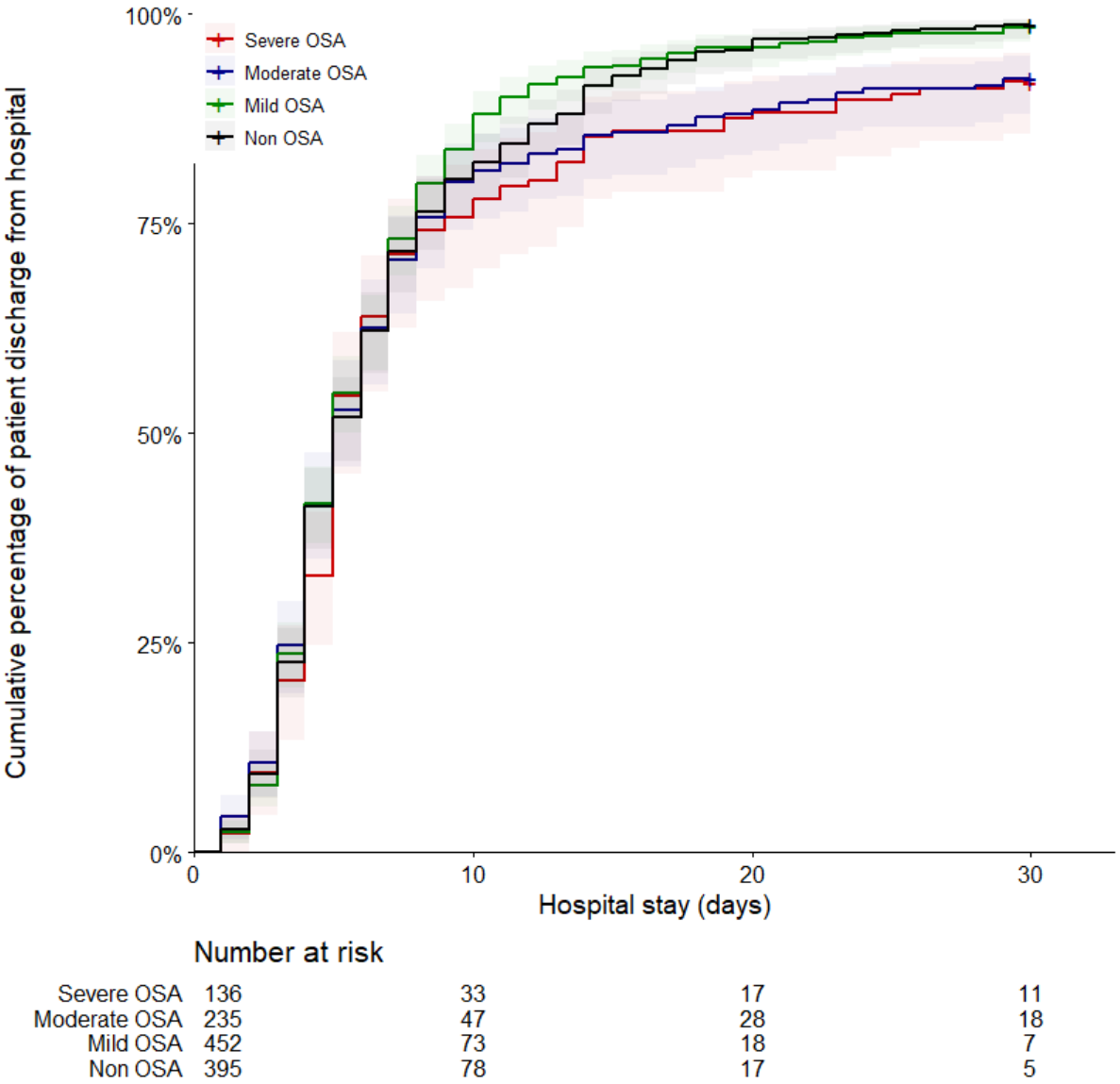


eFigure 4. Subgroup Analyses of Primary Outcome in Patients With Severe vs No Obstructive Sleep Apnea

	No OSA	Severe OSA	Adjusted hazard ratio (95% confidence intervals)	P value for interaction
	No. of patients with event/total no. of patients			
Overall	56/395	41/136	2.23 (1.49-3.34)	
Body mass index – kg/m				
< 18.5	5/20	-	-	
18.5 – 24.9	31/194	16/42	2.09 (1.11-3.94)	
25.0 – 29.9	11/119	12/42	3.13 (1.35-7.28)	0.80
30.0 – 34.9	6/44	9/31	1.27 (0.41-3.93)	
≥ 35.0	3/18	4/21	1.07 (0.18-6.39)	
Type of anesthesia				
General anesthesia				
No	8/81	8/33	1.98 (0.78-6.12)	0.66
Yes	48/314	33/103	2.08 (1.33-3.26)	
Regional or neuraxial block				
No	38/248	30/81	2.47 (1.52-4.00)	0.09
Yes	18/147	11/55	1.27 (0.59-2.75)	
Anesthetic agents				
Volatile-based	44/295	32/96	2.23 (1.41-3.54)	0.95
Propofol infusion	4/34	3/14	2.25 (0.43-9.88)	
Oxygen administration after surgery				
None	8/107	6/30	2.75 (0.92-8.21)	
One night	19/128	9/44	1.11 (0.48-2.56)	0.60
Two nights	14/89	11/29	2.27 (1.02-5.08)	
Three nights	15/71	15/33	2.08 (0.98-4.42)	
Postoperative opioid administration				
No	27/172	15/62	1.34 (0.71-2.56)	0.25
Yes	29/223	24/74	2.53 (1.46-4.39)	
Postoperative patient-controlled analgesia administration				
No	33/207	23/77	1.47 (0.85-2.55)	0.32
Yes	23/188	18/59	2.63 (1.42-4.89)	
Minimally invasive surgery				
No	35/274	31/99	2.38 (1.45-3.91)	0.87
Yes	21/121	10/37	1.70 (0.79-3.67)	



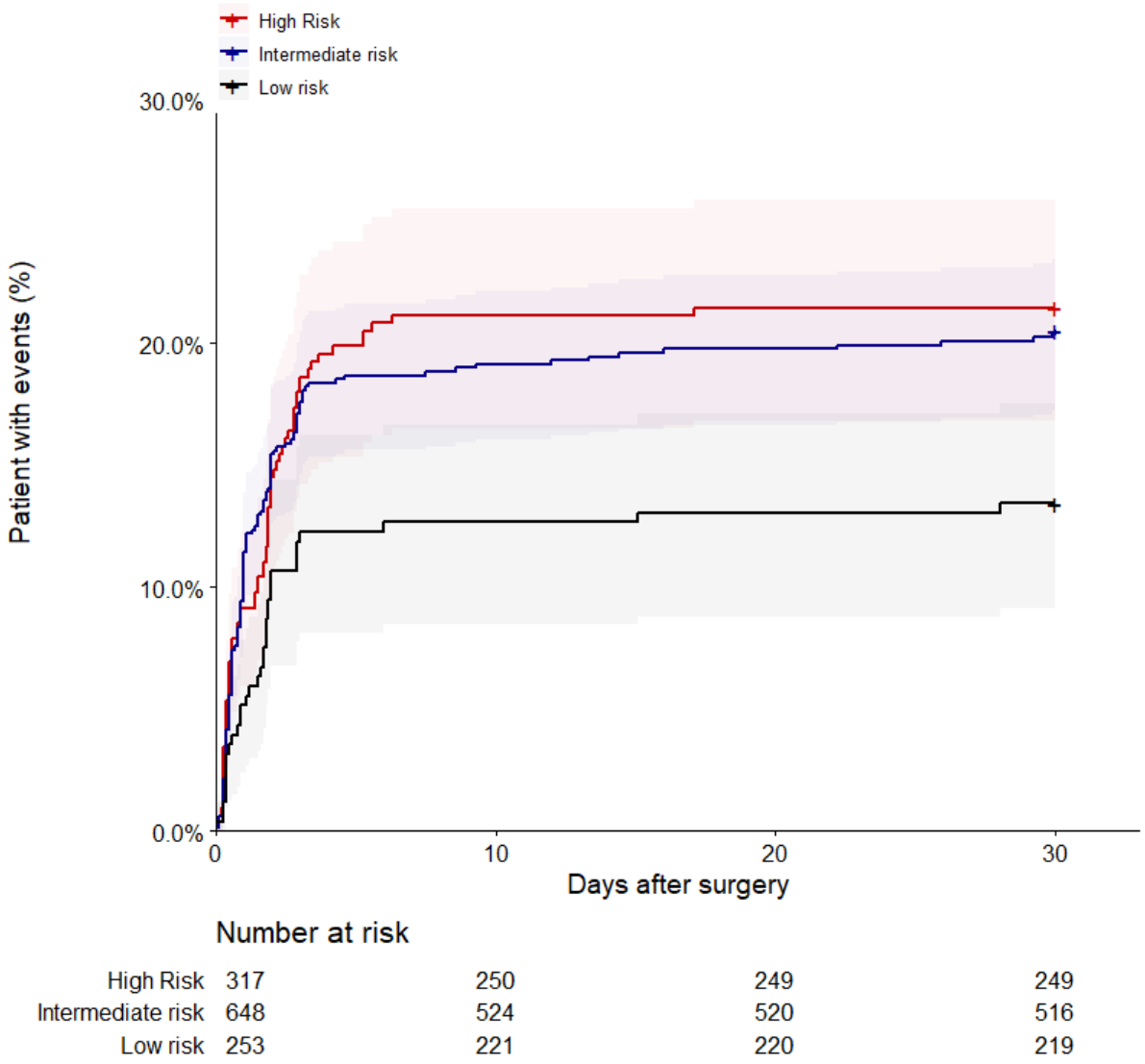
eFigure 5. Kaplan-Meier Estimates of Hospital Discharge



	Median (interquartile range) length of stay
Severe OSA	5.0 (4.0-8.0)
Moderate OSA	5.0 (4.0-8.0)
Mild OSA	5.0 (4.0-8.0)
Non OSA	5.0 (4.0-9.0)

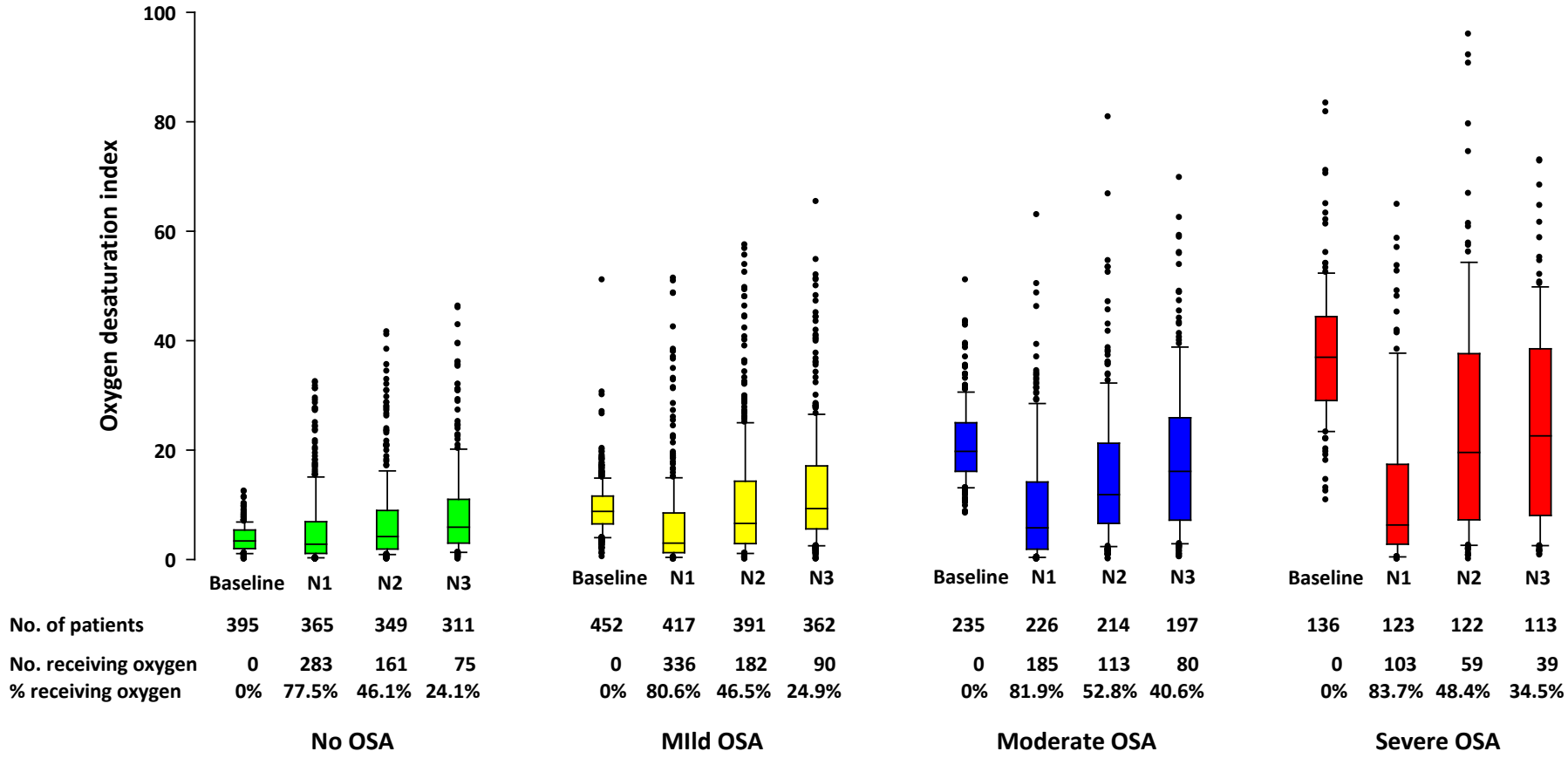
Shaded areas represent 95% confidence intervals

eFigure 6. Kaplan-Meier Estimates of 30-Day Postoperative Cardiovascular Events Based on the STOP-Bang Risk Score



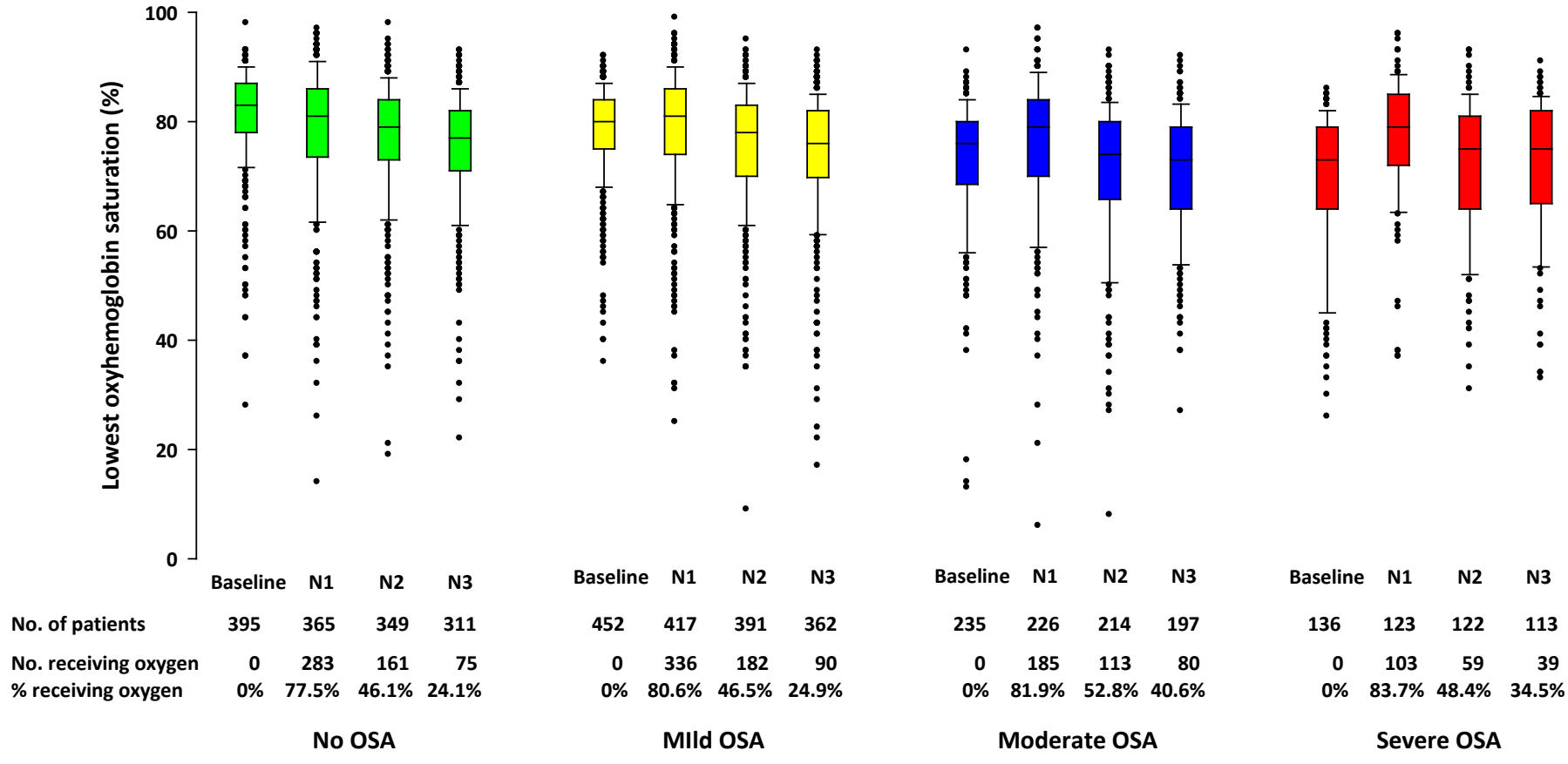
Shaded areas represent 95% confidence intervals

eFigure 7. Changes of Oxygen Desaturation Index Before and After Surgery in Patients With and Without Obstructive Sleep Apnea



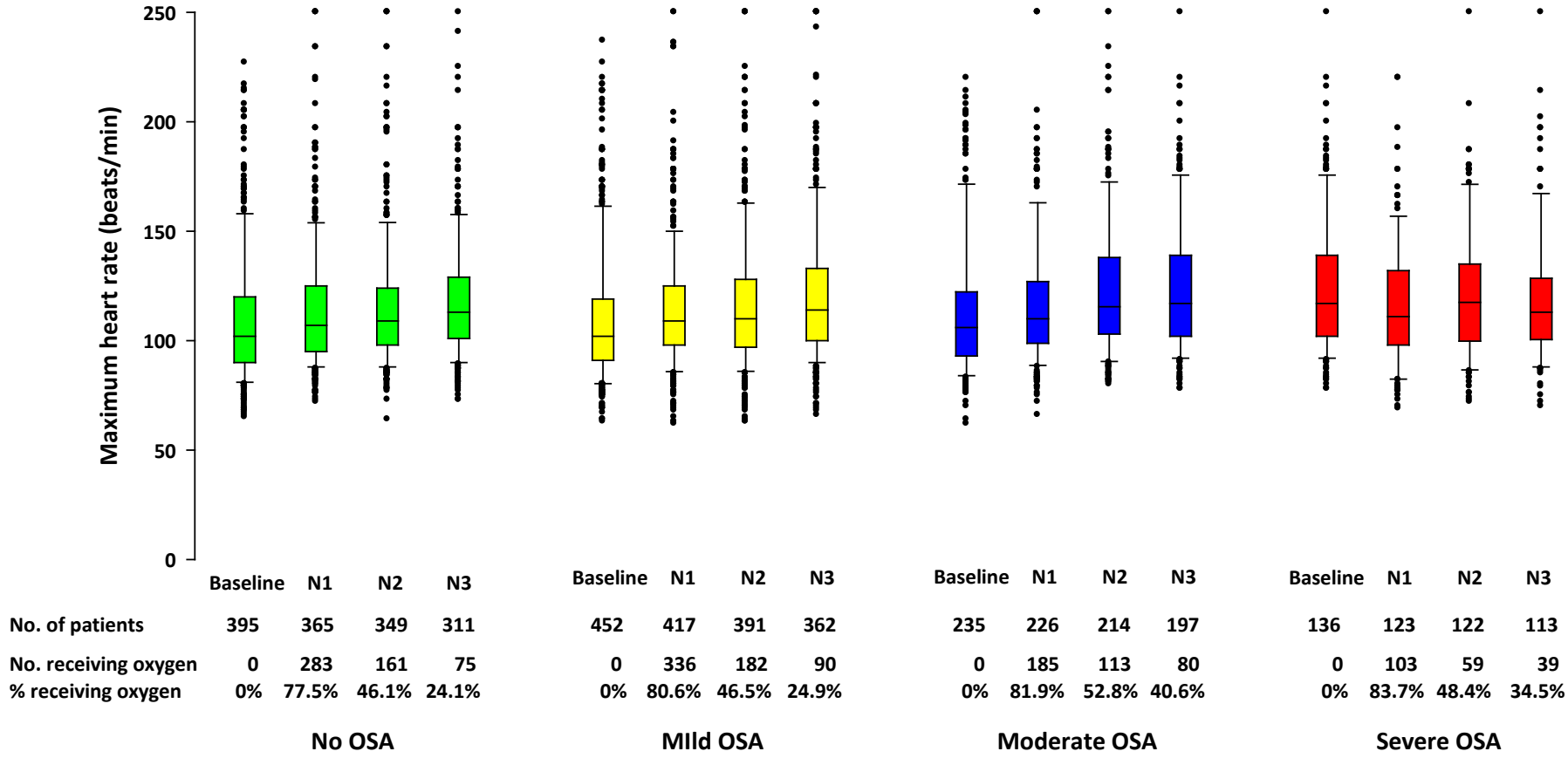
N1, N2 and N3 indicates the first, second and third night, respectively.
The horizontal line in each box represents the median value, and the top and bottom of the boxes are the interquartile range. The error bars indicate 95% confidence intervals, and the dots are outliers

eFigure 8. Lowest Oxyhemoglobin Saturation Before and After Surgery in Patients With and Without Obstructive Sleep Apnea



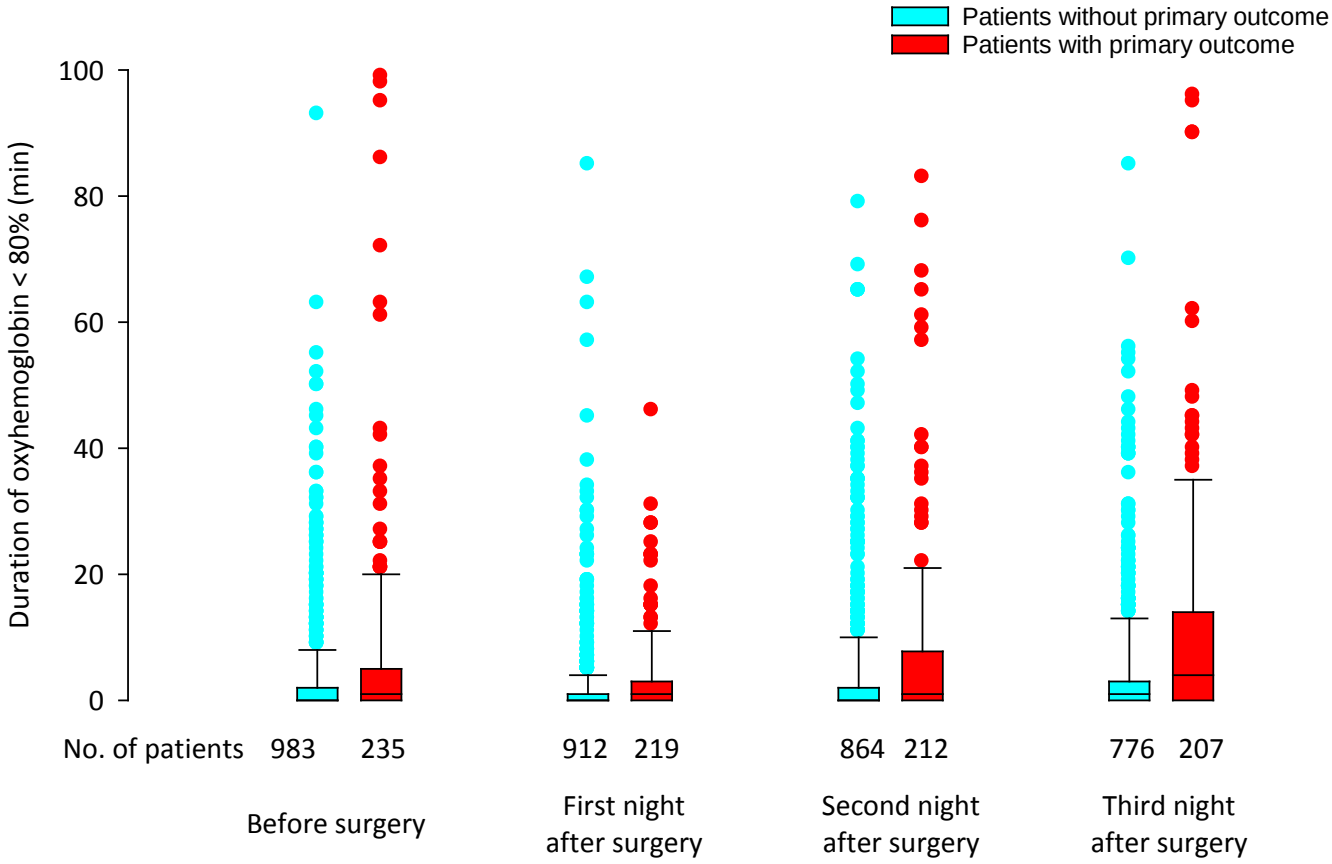
N1, N2 and N3 indicates the first, second and third night, respectively.
The horizontal line in each box represents the median value, and the top and bottom of the boxes are the interquartile range. The error bars indicate 95% confidence intervals, and the dots are outliers

eFigure 9. Highest Heart Rate Before and After Surgery in Patients With and Without Obstructive Sleep Apnea



N1, N2 and N3 indicates the first, second and third night, respectively.
The horizontal line in each box represents the median value, and the top and bottom of the boxes are the interquartile range. The error bars indicate 95% confidence intervals, and the dots are outliers

eFigure 10. Duration of Oxyhemoglobin Saturation <80% in Patients Who Did and Did Not Have the Primary Outcome



N1, N2 and N3 indicates the first, second and third night, respectively.
The horizontal line in each box represents the median value, and the top and bottom of the boxes are the interquartile range. The error bars indicate 95% confidence intervals, and the dots are outliers

eTable 1. Preoperative Sleep Study Results

	All patients	No OSA	Mild OSA	Moderate OSA	Severe OSA
No. of patients	1,218	395	452	235	136
	Means (SD)				
Sleep study before surgery, hours	79 (114)	69 (109)	88 (122)	79 (108)	82 (113)
Evaluation period, hours	9.4 (2.3)	9.5 (2.3)	9.4 (2.4)	9.1 (2.2)	9.4 (2.3)
Respiratory event index, events/h[a]	12.7 (13.8)	1.9 (1.4)	8.6 (2.7)	20.8 (4.5)	44.2 (12.0)
Apnea index, events/h[b]	6.6 (10.5)	0.7 (1.0)	3.5 (3.1)	9.8 (6.0)	28.4 (16.0)
Unclassified apnea	0.9 (4.1)	0.1 (0.4)	0.4 (1.1)	1.2 (2.4)	4.9 (10.9)
Obstructive apnea	4.7 (8.3)	0.5 (1.0)	2.6 (2.9)	7.0 (5.6)	19.9 (15.1)
Central apnea	0.8 (2.4)	0.1 (0.4)	0.4 (0.9)	1.4 (2.5)	3.2 (5.4)
Mixed apnea	0.1 (0.3)	0.0 (0.1)	0.0 (0.3)	0.1 (0.3)	0.3 (0.6
Hypopnea index, events/h[c]	6.2 (6.9)	1.2 (1.3)	5.2 (3.2)	10.7 (6.1)	15.9 (11.3)
Percent flow limited breaths without snoring	29.8 (15.7)	33.0 (17.6)	30.3 (14.8)	27.1 (13.7)	23.8 (13.6)
Percent flow limited breaths with snoring	2.2 (4.7)	1.1 (3.0)	1.9 (4.2)	3.7 (6.3)	4.0 (5.6)
Oxygen desaturation index, events/h[d]	12.9 (12.1)	3.8 (2.4)	9.2 (3.9)	20.9 (6.7)	37.7 (12.5)
Lowest SpO_2, %	77 (11)	81 (9)	78 (9)	73 (12)	69 (14)
Average SpO_2, %	95 (3)	95 (2)	94 (2)	93 (3)	95 (3)
Duration SpO_2 < 90%, min	28.4 (53.3)	10.7 (29.8)	20.1 (34.0)	42.6 (57.0)	83.1 (94.8)
Duration SpO_2 < 80%, min	4.0 (14.4)	0.9 (2.7)	2.2 (5.7)	6.1 (13.6)	12.2 (18.0)
Lowest pulse rate, beats/min	48 (12)	49 (12)	49 (11)	44 (13)	45 (12)
Average pulse rate, beats/min	69 (11)	69 (12)	68 (11)	68 (10)	70 (11)
Highest pulse rate, beats/min	112 (33)	110 (31)	111 (32)	116 (34)	118 (37)

Abbreviations: OSA, obstructive sleep apnea; SD, standard deviations; SpO_2, oxyhemoglobin saturation

[a] Respiratory event index is the number of apnea and hypopnea events per hour of recording.

[b] Apnea index is the number of apnea events (airflow reduction ≥ 90% from baseline for ≥ 10 seconds) per hour of recording.

[c] Hypopnea index is the number of hypopnea events (airflow reduction ≥ 30% from baseline for ≥ 10 seconds and associated with ≥ 3% oxyhemoglobin desaturation) per hour of recording.

[d] Oxygen desaturation index is the number of events per hour of oximetry recording (derived from the wristwatch) where oxyhemoglobin saturation decreased by ≥ 4% from baseline for ≥ 10 seconds.

eTable 2. Details of Anesthetic Administration

	All patients	No OSA	Mild OSA	Moderate OSA	Severe OSA	*P* values
No. of patients	1,218	395	452	235	136	
Regional block, no. (%)						0.82
Spinal anesthesia	286 (23.5)	83 (21.0)	108 (23.9)	59 (25.1)	36 (26.5)	
Epidural anesthesia	115 (9.4)	32(8.1)	48 (10.6)	24 (10.2)	11 (8.1)	
Nerve block	190 (15.6)	63 (15.9)	76 (16.8)	29 (12.3)	22 (16.2)	
General anesthesia, no. (%)	951 (78.1)	314 (79.5)	351 (77.7)	183 (77.9)	103 (75.7)	0.81
Anesthetic drug used						
Fentanyl, no. (%)	986 (81.0)	329 (83.3)	358 (79.2)	188 (80.0)	111 (81.6)	0.48
Dosage, μg/kg, mean (SD)	2.2 (2.3)	2.3 (2.6)	2.2 (2.3)	2.2 (2.2)	1.9 (1.9)	0.82
Morphine, no. (%)	711 (58.4)	248 (62.8)	251 (55.5)	132 (56.2)	80 (58.8)	0.16
Dosage, mg/kg, mean (SD)	0.11 (0.08)	0.11 (0.06)	0.10 (0.05)	0.12 (0.14)	0.09 (0.06)	0.27
Remifentanil, no. (%)	169 (13.9)	58 (14.7)	62 (13.7)	30 (12.8)	19 (14.0)	0.93
Propofol infusion, no. (%)	118 (9.7)	34 (8.6)	44 (9.7)	26 (11.1)	14 (10.3)	0.78
Targeted plasma concentration, μg/ml, mean (SD)	3.5 (0.7)	3.6 (0.8)	3.5 (0.6)	3.3 (0.6)	3.5 (0.7)	0.50
Inhalational anesthesia						0.80
Isoflurane, no. (%)	62 (7.0)	29 (9.8)	19 (5.8)	9 (5.3)	5 (5.2)	
Sevoflurane, no. (%)	608 (68.3)	201 (68.1)	226 (68.9)	109 (63.7)	72 (75.0)	
Desflurane, no. (%)	220 (24.7)	65 (22.0)	83 (25.3)	53 (31.0)	19 (19.8)	
End-tidal concentration, MAC-equivalents[a]), mean (SD)	0.94 (0.22)	0.95 (0.21)	0.94 (0.23)	0.93 (0.21)	0.93 (0.22)	0.27
Inspired oxygen concentration, %, mean (SD)	40.1 (7.5)	40.2 (7.3)	40.0 (7.6)	40.2 (7.2)	40.2 (8.1)	0.98
Core temperature at wound closure, °C, mean (SD)	36.1 (0.8)	36.1 (0.8)	36.2 (0.8)	36.0 (0.8)	36.1 (0.9)	0.06
Duration of anesthesia, hour, mean (SD)	3.8 (2.3)	3.9 (2.3)	3.7 (2.1)	3.7 (2.3)	3.9 (2.7)	0.55

Abbreviations: OSA, obstructive sleep apnea; SD, standard deviations

[a] MAC denotes minimum alveolar concentration and indicates the potency of volatile anesthetics.

eTable 3. Postoperative Analgesic Techniques

	All patients	No OSA	Mild OSA	Moderate OSA	Severe OSA	*P* values
No. of patients	1,218	395	452	235	136	
Postoperative use of opioid, no. (%)	707 (58)	223 (56.5)	259 (57.3)	151 (64.3)	74 (54.4)	0.17
Patient controlled analgesia of opioid, no. (%)	600 (49.3)	188 (47.6)	222 (49.1)	131 (55.7)	59 (43.4)	0.10
Non-steroidal anti-inflammatory drugs, no. (%)	675 (55.4)	206 (52.2)	267 (59.1)	131 (55.7)	71 (52.2)	0.19
Tramadol, no. (%)	681 (55.9)	231 (58.5)	252 (55.8)	125 (53.2)	73 (53.7)	0.56
Neuraxial block, no. (%)	130 (10.7)	33 (8.4)	50 (11.1)	29 (12.3)	18 (13.2)	0.27
Nerve block, no. (%)	77 (6.3)	23 (5.8)	32 (7.1)	12 (5.1)	10 (7.4)	0.70

Abbreviations: OSA, obstructive sleep apnea

eTable 4. Postoperative Troponin Measurements

	All patients	No OSA	Mild OSA	Moderate OSA	Severe OSA	*P* values
No. of patients	1,218	395	452	235	136	
No. of troponin measurements performed, No. (%)						0.75
4	963 (79.1)	306 (77.5)	363 (80.3)	183 (77.9)	111 (81.6)	
3	134 (11.0)	48 (12.2)	42 (9.3)	29 (12.3)	15 (11.0)	
2	62 (5.1)	17 (4.3)	24 (5.3)	16 (6.8)	5 (3.7)	
1	8 (0.7)	3 (0.8)	3 (0.7)	1 (0.4)	1 (0.7)	
0	51 (4.2)	21 (5.3)	20 (4.4)	6 (2.9)	4 (2.9)	

Abbreviation: OSA, obstructive sleep apnea

eTable 5. Preoperative Predictors for Postoperative Cardiovascular Events

Risk factors	No. event/Total no. (%)	Unadjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value	Population attributable risk (95% CI)
Age group						
45-64 y	56/433 (12.9)	Reference		Reference		15.6 (8.4-22.3)
65-74 y	98/513 (19.1)	1.52 (1.09-2.11)	0.01	1.45 (1.04-2.03)	0.03	
≥75 y	81/272 (29.8)	2.49 (1.77-3.51)	<0.001	2.30 (1.60-3.32)	<0.001	
Sex						
Female	69/490 (14.1)	Reference	<0.001	Reference	0.08	–
Male	166/728 (22.8)	1.70 (1.28-2.25)		1.30 (0.97-1.76)		
Ethnicity						
Malay	30/195 (15.4)	Reference		Reference		–
Caucasian	31/183 (16.9)	1.09 (0.66-1.80)	0.74	0.96 (0.56-1.66)	0.89	
Chinese	141/666 (21.2)	1.45 (0.98-2.15)	0.07	1.19 (0.78-1.84)	0.42	
Indian	32/161 (19.9)	1.31 (0.79-2.15)	0.29	1.61 (0.96-2.70)	0.07	
Hypertension						
No	23/181 (12.7)	Reference		Reference		–
Yes	212/1037 (20.4)	1.70 (1.10-2.61)	0.02	1.45 (0.93-2.26)	0.10	
Coronary artery disease						
No	150/887 (16.9)	Reference		Reference		–
Yes	85/331 (25.7)	1.58 (1.21-2.07)	0.001	1.11 (0.82-1.52)	0.50	
Congestive heart failure						
No	214/1158 (18.5)	Reference		Reference		–
Yes	21/60 (35.0)	2.22 (1.42-3.48)	<0.001	1.57 (0.96-2.57)	0.07	
Peripheral vascular disease						
No	193/1091 (17.7)	Reference		Reference		8.3 (3.5-12.9)
Yes	42/127 (33.1)	2.07 (1.48-2.89)	<0.001	1.59 (1.09-2.31)	0.02	
Stroke or transient ischemic attack						
No	184/1041 (17.7)	Reference		Reference		–
Yes	51/177 (28.8)	1.73 (1.27-2.36)	0.001	1.27 (0.91-1.76)	0.16	
Diabetes mellitus						
No	67/280 (23.9)	Reference		Reference		–
Yes	168/938 (17.9)	0.72 (0.54-0.96)	0.02	0.81 (0.60-1.11)	0.19	

Risk factors	No. event/Total no. (%)	Unadjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value	Population attributable risk (95% CI)
Chronic obstructive pulmonary disease						
No	218/1158 (18.8)	Reference		Reference		–
Yes	17/60 (28.3)	1.53 (0.94-2.51)	0.09	1.05 (0.62-1.77)	0.86	
Risk factors	No. event/Total no. (%)	Unadjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value	Population attributable risk (95% CI)
Renal impairment						
No	202/1147 (17.6)	Reference		Reference		8.7 (4.6-12.6)
Yes	33/71 (46.5)	3.54 (2.45-5.12)	<0.001	3.57 (2.40-5.30)	<0.001	
Current smokers						
No	210/1081 (19.4)	Reference		Reference		–
Yes	25/137 (18.2)	0.92 (0.61-1.39)	0.69	0.88 (0.57-1.35)	0.55	
Surgery for malignancy						
No	123/705 (17.4)	Reference		Reference		–
Yes	112/512 (21.9)	1.30 (1.00-1.67)	0.05	1.11 (0.74-1.66)	0.62	
Intraperitoneal surgery						
No	107/642 (16.7)	Reference		Reference		–
Yes	128/576 (22.2)	1.38 (1.07-1.79)	0.01	1.45 (0.99-2.13)	0.06	
Preoperative use of β blockers						
No	137/803 (17.1)	Reference		Reference		–
Yes	98/415 (23.6)	1.43 (1.11-1.86)	0.006	1.09 (0.82-1.44)	0.57	
Obstructive sleep apnea (OSA)						
No OSA	56/395 (14.2)	Reference		Reference		22.4 (14.9-29.9)
Mild OSA	86/452 (19.0)	1.37 (0.98-1.91)	0.07	1.36 (0.97-1.90)	0.08	
Moderate OSA	52/235 (22.1)	1.59 (1.09-2.32)	0.02	1.43 (0.98-2.09)	0.07	
Severe OSA	41/136 (30.1)	2.33 (1.55-3.48)	<0.001	2.04 (1.33-2.99)	0.001	

Abbreviations: HR, hazard ratios; CI, confidence intervals

eTable 6. Association Between Severity of Obstructive Sleep Apnea and Primary Outcome Stratified by Sites

Outcome	No. events/Total (%)	Unadjusted HR (95%CI)	*P* value	Adjusted HR (95%CI)	*P* value
Site 1					
No OSA	11/67 (16.4)	Reference		Reference	
Mild OSA	25/113 (22.1)	1.39 (0.69-2.83)	0.36	1.30 (0.64-2.66)	0.47
Moderate OSA	7/65 (10.8)	0.63 (0.24-1.61)	0.33	0.64 (0.25-1.65)	0.35
Severe OSA	8/34 (23.5)	1.49 (0.60-3.70)	0.39	1.31 (0.52-3.29)	0.57
Site 2					
No OSA	4/35 (11.4)	Reference		Reference	
Mild OSA	5/50 (10.0)	0.88 (0.24-3.26)	0.84	0.69 (0.18-2.67)	0.59
Moderate OSA	3/17 (17.6)	1.56 (0.35-6.98)	0.56	1.33 (0.26-6.85)	0.73
Severe OSA	1/16 (6.3)	0.55 (0.06-4.91)	0.59	0.62 (0.07-5.62)	0.67
Site 3					
No OSA	4/70 (5.7)	Reference		Reference	
Mild OSA	14/80 (17.5)	3.22 (1.06-9.79)	0.04	3.27 (1.07-10.04)	0.38
Moderate OSA	10/42 (23.8)	4.42 (1.39-14.11)	0.01	4.27 (1.33-13.68)	0.15
Severe OSA	8/26 (30.8)	6.11 (1.84-20.29)	0.003	5.72 (1.72-19.09)	0.005
Site 4					
No OSA	5/43 (11.6)	Reference		Reference	
Mild OSA	5/37 (13.5)	1.24 (0.36-4.28)	0.74	1.31 (0.37-4.64)	0.67
Moderate OSA	7/45 (15.6)	1.39 (0.44-4.39)	0.57	1.36 (0.41-4.53)	0.61
Severe OSA	5/16 (31.3)	3.03 (0.88-10.47)	0.08	3.39 (0.90-12.74)	0.07
Site 5					
No OSA	0/1 (0.0)	Reference		Reference	
Mild OSA	1/3 (33.3)	–	–	–	–
Moderate OSA	0/2 (0.0)	–	–	–	–
Severe OSA	1/6 (16.7)	–	–	–	–
Site 6					
No OSA	0/2 (0.0)	Reference		Reference	
Mild OSA	0/1 (0.0)	–	–	–	–
Moderate OSA	0/1 (0.0)	–	–	–	–
Severe OSA	0/0	–	–	–	–
Site 7					
No OSA	32/166 (19.3)	Reference		Reference	
Mild OSA	33/145 (22.8)	1.17 (0.72-1.91)	0.52	1.15 (0.71-1.88)	0.57
Moderate OSA	22/53 (41.5)	2.34 (1.36-4.02)	0.002	1.68 (0.96-2.94)	0.07
Severe OSA	15/39 (38.5)	2.30 (1.25-4.25)	0.008	1.96 (1.05-3.64)	0.03
Site 8					
No OSA	0/11 (0.0)	Reference		Reference	
Mild OSA	3/23 (13.0)	–	–	–	–
Moderate OSA	3/10 (30.0)	–	–	–	–
Severe OSA	4/5 (80.0)	–	–	–	–

eTable 7. Post hoc Analysis on the Association Between Severity of Obstructive Sleep Apnea and Modified Primary Outcome

	No. events/Total (%)	Unadjusted HR (95%CI)	*P* value	Adjusted HR (95%CI)	*P* value
Modified primary outcome[a]: cardiac death, myocardial infarction, congestive heart failure, thromboembolism, new atrial fibrillation and stroke					
No OSA	16/395 (4.1)	Reference		Reference	
Mild OSA	39/452 (8.6)	2.96 (0.95-8.07)	0.05	1.36 (0.97-1.90)	0.08
Moderate OSA	30/235 (12.8)	3.41 (1.20-9.71)	0.02	1.43 (0.98-2.09)	0.07
Severe OSA	26/136 (19.1)	3.82 (1.30-11.20)	0.003	2.04 (1.33-2.99)	0.001
Myocardial infarction					
No OSA	11/395 (2.8)	Reference		Reference	
Mild OSA	26/452 (5.8)	2.10 (1.04-4.25)	0.04	2.03 (1.00-4.12)	0.05
Moderate OSA	16/235 (6.8)	2.48 (1.15-5.33)	0.02	2.12 (0.98-4.57)	0.06
Severe OSA	14/136 (10.3)	3.85 (1.75-8.49)	0.001	3.20 (1.45-7.08)	0.004

Abbreviations: OSA, obstructive sleep apnea; CI, confidence intervals
[a]Myocardial injury replaced by myocardial infarction

eTable 8. STOP-Bang Risk Score in Patients With Different Severity of Obstructive Sleep Apnea

STOP-Bang Risk[a]	Severity of OSA based on apnea-hypopnea index			
	No OSA	Mild OSA	Moderate OSA	Severe OSA
Low risk, no. (%)	121 (30.6)	94 (20.8)	33 (14.0)	5 (3.7)
Moderate risk, no. (%)	217 (54.9)	260 57.5)	119 (50.6)	52 (38.2)
High risk, no. (%)[b]	57 (14.4)	98 (21.7)	83 (35.3)	79 (58.1)

[a] STOP-Bang denotes Snoring, Tiredness, Observed apnea, high blood Pressure, Body mass index, age, neck circumference, and gender. Scores range from 0 to 8; with a score of 0-2 indicating low risk; 3-4 moderate risk and 5-8 high risk.

[b] High STOP-Bang risk score predicted severe OSA with sensitivity and specificity of 58.1% and 78.0%, respectively, C-index 0.714 (95%CI: 0.670-0.758), $P < 0.001$.

eTable 9. Characteristics of Patients With STOP-Bang Risk Score

	Low risk	Intermediate risk	High risk	*P* value[a]
STOP-Bang score	0 – 2	3 – 4	5 – 8	
No. of patients	253	648	317	
(95%CI)	20.8 (18.6-23.1)	53.2 (50.4-56.0)	26.3 (23.6-28.6)	
Age group, no. (%)				0.93
45-64 y	94 (37.2)	226 (34.9)	113 (35.6)	
65-74 y	102 (40.3)	274 (42.3)	137 (43.2)	
≥75 y	57 (22.5)	148 (22.8)	67 (21.1)	
Male sex, no. (%)	49 (19.4)	413 (63.7)	266 (83.9)	<0.001
Race/ethnicity, no. (%)				<0.001
Chinese	121 (47.8)	380 (58.6)	165 (52.1)	
Malay	49 (19.4)	111 (17.1)	35 (11.0)	
White	33 (13.0)	76 (11.7)	74 (23.3)	
Indian	44 (17.4)	78 (12.0)	39 (12.3)	
Others[b]	6 (2.4)	3 (0.5)	4 (1.3)	
Patient fulfilling the entry criteria, no. (%)				
Hypertension	147 (58.1)	587 (90.6)	303 (95.6)	<0.001
Coronary artery disease	44 (17.4)	179 (27.6)	108 (34.1)	<0.001
Diabetes receiving insulin treatment	196 (77.5)	487 (75.2)	255 (80.4)	0.18
Stroke or transient ischemic attack	34 (13.4)	95 (14.7)	48 (15.1)	0.84
Current smoker	20 (7.9)	74 (11.4)	43 (13.6)	<0.001
Peripheral vascular disease	17 (6.7)	69 (10.6)	41 (12.9)	0.05
Preoperative creatinine concentration > 175 μmol/L	15 (5.9)	41 (6.3)	15 (4.7)	0.61
Congestive heart failure	15 (5.9)	31 (4.8)	14 (4.4)	0.69
Chronic pulmonary obstructive disease	8 (3.2)	26 (4.0)	26 (8.2)	0.006
Type of surgery, no. (%)				0.16
Intraperitoneal surgery	117 (46.2)	317 (48.9)	142 (44.8)	
Vascular surgery	26 (10.3)	98 (15.1)	45 (14.2)	
Major orthopedic surgery	83 (32.9)	172 (26.6)	109 (34.4)	
Others	26 (10.3)	160 (24.7)	23 (34.4)	
Cancer surgery, no. (%)	99 (39.1)	288 (44.4)	125 (39.6)	0.20
Minimally invasive surgery, no. (%)	46 (18.2)	204 (31.5)	95 (30.0)	<0.001
Preoperative medication, no. (%)				
Statin	153 (60.5)	464 (71.6)	237 (74.8)	0.001
ACE inhibitor or ARB	107 (42.3)	345 (53.2)	193 (60.9)	<0.001
β blocker	70 (27.7)	219 (33.8)	126 (39.7)	0.01
Aspirin	53 (20.9)	171 (26.4)	85 (26.8)	0.19
Clopidogrel	9 (3.6)	31 (4.8)	15 (4.7)	0.71
Anthropometric measurements, mean (SD)				
Body mass index, kg/m^2	24.7 (4.1)	26.2 (6)	29.5 (12.7)	<0.001
Neck circumference, cm	36.0 (2.8)	38.3 (3.0)	41.0 (3.4)	<0.001
Waist, cm	88.4 (11.9)	91.8 (11.8)	96.6 (13.4)	<0.001
Preoperative sleep study characteristics, median (IQR)				
Respiratory event index, events/h	5 (2-9)	8 (3-15)	15 (7-30.3)	
Oxygen desaturation index, events/h	6.5 (3.3-11.0)	8.2 (4.1-15.8)	14.7 (7-26.9)	
Epworth Sleepiness Scale score	4 (2-6)	4 (2-7)	5 (3-9)	

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; OSA, obstructive sleep apnea; CI, confidence intervals; SD, standard deviations; IQR, interquartile range

[a] *P* value for tests to determine imbalance among groups, continuous variables were compared using analysis of variance and categorical variables were compared using Pearson's χ^2 test.

[b] Other races/ethnicities included black and Arab.

[c] Other surgery included major urological, major hernia repair and spine surgery.

eTable 10. STOP-Bang Risk Score and Outcome

	No. events/Total (%)	Unadjusted HR or OR (95%CI)	*P* value	Adjusted HR or OR (95%CI)	*P* value
Primary outcome: cardiac death, myocardial injury, congestive heart failure, thromboembolism, new atrial fibrillation and stroke					
Low risk	34/253 (13.4)	Reference		Reference	
Intermediate risk	133/648 (20.5)	1.60 (1.10-2.33)	0.02	1.50 (1.00-2.18)	0.05
High risk	68/317 (21.5)	1.67 (1.11-2.52)	0.01	1.68 (1.11-2.54)	0.01
Post hoc analysis on the components of primary outcome					
Cardiac death					
Low risk	1/253 (0.4)	Reference		Reference	
Intermediate risk	12/648 (1.9)	4.71 (0.61-36.22)	0.14	3.57 (0.46-27.86)	0.22
High risk	4/317 (1.3)	3.21 (0.36-28.72)	0.30	2.54 (0.28-23.10)	0.41
Myocardial injury					
Low risk	30/240 (12.5)	Reference		Reference	
Intermediate risk	117/621 (18.8)	1.39 (0.91-2.11)	0.12	1.48 (0.99-2.21)	0.06
High risk	58/306 (19.0)	1.45 (0.92-2.31)	0.11	1.63 (1.06-2.54)	0.03
Congestive heart failure					
Low risk	2/253 (0.8)	Reference		Reference	
Intermediate risk	12/648 (1.9)	2.35 (0.53-10.49)	0.26	2.31 (0.48-9.83)	0.32
High risk	7/317 (2.2)	2.80 (0.58-13.47)	0.20	2.51 (0.51-12.38)	0.26
Thromboembolism					
Low risk	0/253 (0.0)	Reference		Reference	
Intermediate risk	6/648 (0.9)	-		-	
High risk	4/317 (1.3)	-		-	
New onset atrial fibrillation					
Low risk	5/253 (2.0)	Reference		Reference	
Intermediate risk	15/648 (2.3)	1.47 (0.49-4.43)	0.49	1.16 (0.46-3.18)	0.55
High risk	10/317 (3.2)	2.01 (0.63-6.41)	0.24	1.65 (0.56-4.83)	0.22
Stroke					
Low risk	0/253 (0.0)	Reference		Reference	
Intermediate risk	3/648 (0.5)	-		-	
High risk	2/317 (0.6)	-		-	
Secondary Outcomes					
Unplanned or readmission to ICU[a]					
Low risk	6/253 (2.4)	Reference		Reference	
Intermediate risk	41/648 (6.3)	2.78 (1.17-6.63)	0.02	2.69 (1.12-6.44)	0.03
High risk	21/317 (6.6)	2.92 (1.16-7.35)	0.02	2.86 (1.13-7.23)	0.03
Unplanned tracheal intubation or postoperative lung ventilation[a]					
Low risk	10/253 (4.0)	Reference		Reference	
Intermediate risk	52/648 (8.0)	2.12 (1.06-4.24)	0.03	2.06 (0.95-3.91)	0.07
High risk	19/317 (6.0)	1.55 (0.71-3.39)	0.27	1.50 (0.70-3.54)	0.28
Pneumonia					
Low risk	6/253 (2.4)	Reference		Reference	
Intermediate risk	21/648 (3.2)	1.37 (0.55-3.40)	0.50	1.28 (0.51-319)	0.60
High risk	9/317 (2.8)	1.20 (0.43-3.37)	0.73	1.06 (0.36-3.09)	0.92
Wound infection					
Low risk	12/253 (4.7)	Reference		Reference	
Intermediate risk	60/648 (9.3)	1.98 (1.07-3.69)	0.03	1.95 (1.05-3.64)	0.03
High risk	26/317 (8.2)	1.78 (0.90-3.52)	0.10	1.70 (0.86-3.37)	0.12

	No. events/Total (%)	Unadjusted HR or OR (95%CI)	*P* value	Adjusted HR or OR (95%CI)	*P* value
Other infections[b]					
Low risk	9/253 (3.6)	Reference		Reference	
Intermediate risk	44/648 (6.8)	1.93 (0.94-3.96)	0.07	1.84 (0.89-3.79)	0.10
High risk	17/317 (5.4)	1.52 (0.68-3.40)	0.31	1.35 (0.59-3.08)	0.48
	No. events/Total (%)	Unadjusted HR or OR (95%CI)	*P* value	Adjusted HR or OR (95%CI)	*P* value
Postoperative delirium					
Low risk	9 (3.6)	Reference		Reference	
Intermediate risk	30 (4.6)	1.27 (0.60-2.68)	0.53	1.23 (0.58-2.61)	0.59
High risk	16 (5.0)	1.43 (0.63-3.24)	0.39	1.46 (0.64-3.30)	0.37

Abbreviations: HR, hazard ratio; OR, odds ratio; OSA, obstructive sleep apnea; CI, confidence intervals; ICU, intensive care unit.

[a] Outcomes are expressed as odds ratios.

[b] Other infections included urinary tract, upper respiratory tract and central nervous system infection.

eTable 11. Postoperative Oxygen Administration

	All patients	No OSA	Mild OSA	Moderate OSA	Severe OSA	*P* value
No. of patients	1,218	395	452	235	136	
No. of nights with oxygen supplement, median (IQR)[a]	1 (1-2)	1 (0-2)	1 (1-2)	1 (1-3)	1 (1-2)	0.004
First night						
Patients receiving supplemental oxygen, No. (%)	907 (74.5)	283 (71.6)	336 (74.3)	185 (78.7)	103 (75.7)	0.26
Types of devices, No. (%)						0.15
Nasal cannula	600 (49.3)	189 (47.8)	229 (50.7)	119 (50.6)	63 (46.3)	
Simple facemask	220 (18.1)	73 (18.5)	82 (18.1)	41 (17.4)	24(17.6)	
Non-rebreathing mask	7 (0.6)	2 (0.5)	2 (0.4)	3 (1.3)	0 (0)	
Non-invasive ventilation devices[b]	63 (5.2)	9 (2.3)	21 (4.6)	20 (8.5)	13 (9.6)	
Duration of oxygen administration, hours, mean (SD)	12.4 (5.7)	12.4 (5.6)	11.9 (5.2)	13.0 (6.4)	12.8 (6.2)	0.12
Second night						
Patients receiving supplemental oxygen, No. (%)	515 (42.3)	161 (40.8)	182 (40.3)	113 (48.1)	59 (43.4)	0.22
Types of devices, No. (%)						0.004
Nasal cannula	407 (33.4)	131 (33.2)	157 (34.7)	80 (34.0)	39 (28.7)	
Simple facemask	59 (4.8)	15 (3.8)	13 (2.9)	22 (9.4)	9 (6.6)	
Non-rebreathing mask	13 (1.1)	6 (1.5)	2 (0.4)	3 (1.3)	2 (1.5)	
Non-invasive ventilation devices[b]	25 (2.1)	3 (0.8)	9 (2.0)	7 (3.0)	6 (4.4)	
Duration of oxygen administration, hours, mean (SD)	11.7 (5.8)	10.8 (5.0)	11.5 (5.4)	13.5 (7.0)	11.8 (5.8)	0.001
Third night						
Patients receiving supplemental oxygen,No. (%)	284 (23.3)	75 (19.0)	90 (19.9)	80 (34.0)	39 (28.7)	<0.001
Types of devices, No. (%)						<0.001
Nasal cannula	220 (18.1)	65 (16.5)	73 (16.2)	56 (23.8)	26 (19.1)	
Simple facemask	15 (1.2)	1 (0.3)	4 (0.9)	6 (2.6)	4 (2.9)	
Non-rebreathing mask	5 (0.4)	0 (0)	2 (0.4)	3 (1.3)	0 (0)	
Non-invasive ventilation devices[b]	15 (1.2)	1 (0.3)	4 (0.9)	6 (2.6)	4 (2.9)	
Duration of oxygen administration, hours, mean (SD)	11.4 (6.2)	10.8 (6.0)	11.4 (5.8)	12.0 (6.9)	11.1 (6.2)	0.65

Abbreviation: OSA, obstructive sleep apnea; IQR, interquartile range; SD, standard deviations

[a] Individual patient may use more than one oxygen delivering devices,

[b] Non-invasive ventilation devices include continuous positive airway pressure (CPAP), bilevel positive airway pressure (biPAP) ventilation

eTable 12. Changes of Oximetry and Heart Rate in Patients Who Did and Did Not Have the Primary Outcome

		Patients without primary outcome	Patients with primary outcome	*P* values
Oxygen administration, No. (%)				
Before surgery		—	—	
After surgery	Night 1	706 (71.8)	201 (85.5)	<0.001[a]
	Night 2	377 (38.4)	138 (58.7)	<0.001[a]
	Night 3	193 (19.6)	91 (38.7)	<0.001[a]
Duration of oxygen administered, hours, mean (95%CI)				0.37[b]
Before surgery				
After surgery	Night 1	13.4 (12.5-14.3)	12.1 (10.7-13.4)	
	Night 2	13.3 (12.3-14.3)	12.9 (11.3-14.2)	
	Night 3	11.6 (10.7-12.6)	11.5 (10.1-12.8)	
Oxygen desaturation index, events/h, mean (95%CI)				0.20[b]
Before surgery		12.6 (11.7-13.5)	15.6 (13.9-17.4)	
After surgery	Night 1	7.1 (6.4-7.8)	7.3 (6.0-8.7)	
	Night 2	12.2 (11.1-13.2)	12.2 (10.2-14.2)	
	Night 3	13.6 (12.6-14.6)	14.1 (12.3-16.0)	
Lowest oxyhemoglobin saturation, mean (95%CI)				0.15[b]
Before surgery		77.2 (76.4-78.0)	75.9 (74.4-77.5)	
After surgery	Night 1	78.4 (77.5-79.3)	76.7 (75.0-78.5)	
	Night 2	74.6 (73.7-75.5)	73.7 (71.9-75.4)	
	Night 3	73.3 (72.4-74.2)	73.4 (71.2-75.1)	
Highest heart rate* – beats/min, mean (95%CI)				0.78[b]
Before surgery		113 (110-115)	107 (102-112)	
After surgery	Night 1	114 (112-117)	116 (112-121)	
	Night 2	118 (115-120)	122 (117-126)	
	Night 3	121 (119-124)	123 (118-127)	
Duration of oxyhemoglobin saturation <90%, min, mean (95%CI)				0.88[b]
Before surgery		24.4 (20.6-28.1)	37.1 (29.9-44.3)	
After surgery	Night 1	20.4 (16.5-24.2)	19.5 (12.1-27.0)	
	Night 2	51.7 (44.4-59.0)	43.0 (28.9-57.2)	
	Night 3	51.7 (44.7-58.7)	51.0 (37.4-64.6)	
Duration of oxyhemoglobin saturation <80%, min, mean (95%CI)				<0.001[b]
Before surgery		2.9 (2.2-3.6)	6.9 (5.4-8.3)	
After surgery	Night 1	1.9 (1.3-2.4)	4.2 (3.1-5.4)	
	Night 2	4.0 (3.1-4.9)	8.0 (6.2-9.8)	
	Night 3	4.3 (3.4-5.1)	10.9 (9.3-12.5)	

Abbreviation: CI, confidence intervals
[a] Chi-square test
[b] General linear model