ORIGINAL ARTICLE

Symptomless Multi-Variable Apnea Prediction Index Assesses Obstructive Sleep Apnea Risk and Adverse Outcomes in Elective Surgery

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Study Objective: To validate that the symptomless Multi-Variable Apnea Prediction index (sMVAP) is associated with Obstructive Sleep Apnea (OSA) diagnosis and assess the relationship between sMVAP and adverse outcomes in patients having elective surgery. We also compare associations between Bariatric surgery, where preoperative screening for OSA risk is mandatory, and non-Bariatric surgery groups who are not screened routinely for OSA.

Methods: Using data from 40 432 elective inpatient surgeries, we used logistic regression to determine the relationship between sMVAP and previous OSA, current hypertension, and postoperative complications: extended length of stay (ELOS), intensive-care-unit-stay (ICU-stay), and respiratory complications (pulmonary embolism, acute respiratory distress syndrome, and/or aspiration pneumonia).

Results: Higher sMVAP was associated with increased likelihood of previous OSA, hypertension and all postoperative complications ($p < .0001$). The top sMVAP quintile had increased odds of postoperative complications compared to the bottom quintile. For ELOS, ICU-stay, and respiratory complications, respective odds ratios (95% CI) were: 1.83 (1.62, 2.07), 1.44 (1.32, 1.58), and 1.85 (1.37, 2.49). Compared against age-, gender- and BMI-matched patients having Bariatric surgery, sMVAP was more strongly associated with postoperative complications in non-Bariatric surgical groups, including: (1) ELOS (Orthopedics [$p < .0001$], Gastrointestinal [$p = .024$], Neurosurgery [$p = .016$], Spine [$p = .016$]); (2) ICU-stay (Orthopedics [$p = .0004$], Gastrointestinal [$p < .0001$], and Otorhinolaryngology [$p = .0102$]); and (3) respiratory complications (Orthopedics [$p = .037$] and Otorhinolaryngology [$p = .011$]).

Conclusions: OSA risk measured by sMVAP correlates with higher risk for select postoperative complications. Associations are stronger for non-Bariatric surgeries, where preoperative screening for OSA is not routinely performed. Thus, preoperative screening may reduce OSA-related risk for adverse postoperative outcomes.

Keywords: Obstructive Sleep Apnea, Postoperative Complications, Symptomless Multi-Variable Apnea Prediction, Elective Surgery, Obstructive Sleep Apnea Risk, Adverse Outcomes.

Statement of Significance

Most patients having elective surgery are not screened for obstructive sleep apnea (OSA), even though OSA is a risk factor for postoperative complications. The symptomless Multi-Variable Apnea Prediction index (sMVAP) is a simple OSA-risk-assessment tool using three routinely measured and well-established OSA risk factors: male gender, older age, and higher body mass index (BMI). We observe that sMVAP correlates with higher risk for OSA, hypertension, and select postoperative complications, particularly in non-Bariatric groups without routine preoperative screening for OSA. Future research should include a prospective evaluation of preoperative screening and treatment of OSA in sub-groups of surgical patients, to determine whether postoperative complications can be reduced, and whether any such reductions will decrease health care utilization and costs.

INTRODUCTION

Obstructive sleep apnea (OSA) is a major risk factor for postoperative complications.[1–6] Failure to identify and manage OSA perioperatively has been associated with death,[5,7] pulmonary,[1–4,8–10] cardiovascular,[1,3,4,8–10] and neurologic morbidities,[10] longer hospital stays,[1,4,9] increased health care utilization,[1,4,8–10] and medical litigation,[5,7] with plaintiffs receiving awards as high as 7.7 million dollars.[7] Despite this, over 75% of patients are not routinely screened for OSA before surgery.[11] Within our institution, Penn Medicine, third-party payers and Bariatric surgeons require screening sleep studies before Bariatric surgery, but such screening is not required before other surgeries. Guidelines also support such screening.[12]

Simple and efficient presurgical screening tools to assess OSA risk are necessary. Our group has validated such a tool, the “symptomless Multi-Variable Apnea Prediction” (sMVAP) index[13,14] to quantify OSA risk using three routinely measured and well-established OSA risk factors: male gender, older age, and higher body mass index (BMI).[15–17]

We examined associations between sMVAP and outcomes of surgery from a large retrospective sample of elective surgical procedures performed within the Penn Medicine hospital network. We assessed rates of serious respiratory complications following surgery[3] and examined length of stay and provider-level safety indicators that are tracked by the Medicare Patient Safety Monitoring System[18] and the Agency for Healthcare Research and Quality (AHRQ)[19]: postoperative pulmonary embolism (PE), aspiration pneumonia (AP), acute respiratory distress syndrome (ARDS), and admission to an intensive care unit (ICU). We hypothesized that higher sMVAP would be associated with increased likelihood of these postoperative complications. We also hypothesized that the association between sMVAP and increased risk of postoperative complications would be stronger in surgeries where OSA is not routinely identified and managed when compared to Bariatric surgery. Finally, as a validation of the sMVAP approach, we hypothesized that sMVAP would associate with previous diagnosis of OSA and hypertension, a known consequence of OSA.[20,21] To our knowledge, ours is the first study to evaluate the use of the sMVAP in a large database of multiple elective surgical specialties, including those with and without mandatory preoperative OSA screening.

METHODS

Data Source/IRB Approval

We retrieved data from Penn Medicine's Clinical Data Warehouse, the Penn Data Store.[22] We obtained data about elective, in-patient surgical procedures performed within the three major Penn Medicine network facilities, the Hospital of University of Pennsylvania (HUP), Pennsylvania Hospital (PAH) and Penn Presbyterian Medical Center (PPMC), between July 1, 2011 and June 30, 2014. This study was approved and exempted from consent requirements by the University of Pennsylvania's Institutional Review Board and complies with the Health Insurance Portability and Accountability Act.

Study Population and Surgical Categories

We identified 56 373 elective surgery patient records, including 1558 unique surgical procedure codes (1514 ICD-9 codes, 44 CPT codes). Supplementary online material contains details on extracted and derived variables.

Analyses included procedures requiring general anesthesia. We excluded obstetric procedures due to lack of data on confouding variables, including weight gain, parity, and gestational age. This resulted in 40 963 (73%) procedures. We also excluded 463 (1.1%) procedures for missing data, and 68 (0.2%) for data falling outside feasible ranges. The final dataset consisted of 40 432 surgical procedures grouped into 10 categories: Bariatric, Orthopedic, Cardiac, Gastrointestinal (GI), Genitourinary (GU), Neurological, Otorhinolaryngology/Oral-Maxillofacial/Ear-Nose-Throat (ORL), Pulmonary/Thoracic (PT), Spine, and Vascular. We categorized surgeries using validated, AHRQ-sponsored Clinical Classifications Software for Services and Procedures (CCSSP)[3,23] based on ICD-9 procedures. We grouped the 44 CPT codes based on author review and consensus (see Supplementary Table S1).

Study Outcomes

Primary analyses examined the relationship between the sMVAP and three postoperative complications: (1) "extended length of stay" (ELOS; a length of stay in the top 10% for a given surgical procedure); (2) "any time spent in the ICU" (ICU-stay); and (3) "post-surgical occurrence of any respiratory complications" (PE, ARDS and/or AP). Secondary analyses examined if associations between the sMVAP and postoperative complications differed between Bariatric and non-Bariatric surgery groups, matched for age, BMI and gender (see below). To confirm the sMVAP utility as a marker to estimate OSA risk, we determined the relationships between the sMVAP and a previous OSA diagnosis (validation) and a current diagnosis of hypertension.

Statistical Analysis

Additional details on outcome definitions and statistical methods are presented in the Supplementary Materials.

The sMVAP index is calculated as: sMVAP = $e^X/(1 + e^X)$, where $X = -10.784 + 0.203 \times (\text{BMI}) + 0.043 \times (\text{Age}) + 1.004 \times (\text{Gender}: 0 = \text{female}, 1 = \text{male})$.[13,14] The sMVAP ranges from 0 to 1, with higher values indicating higher OSA risk.[13,14] We used logistic regression to examine unadjusted associations, and conditional logistic regression to control for Hospital- and Surgical Subgroup-specific effects in our primary analyses. To provide clinically-relevant interpretations, first, we based analyses on sMVAP quintiles (five groups with equal numbers of patients). Second, we created five groups based on actual sMVAP values, with cutpoints at 0.2-increments (ie, 0.0–0.2, 0.2–0.4, 0.4–0.6, 0.6–0.8, and 0.8–1.0). Analyses of sMVAP categories in logistic regression models included assessment of differences between groups, and trend tests to determine if risk increased linearly with increasing values of sMVAP. Additionally, we analyzed continuous sMVAP using untransformed values to provide clinically-relevant interpretations. We used statistical significance threshold of $p < .05$ in analyses of relationships between the sMVAP and previous OSA or hypertension. Since we considered three post-surgical outcomes, we based significance for these analyses on a Bonferroni-corrected $p < .0167$.

To control for differences in covariates between Bariatric and non-Bariatric surgical in analyses comparing sMVAP effects, we conducted analyses within gender-, age- (±2.5 years) and BMI- (±1 kg/m^2)-matched subsets. Within the matched sample, we used logistic regression models to test for an interaction effect between sMVAP and surgical group for each postoperative complication, using $p < .05$ as significant evidence for a differential effect. We then assessed the effect of sMVAP within each surgical category separately. Results comparing Bariatric and Orthopedic surgery (which had the largest sample size) are presented in the main manuscript; results for other matched subgroups are presented in Supplementary Tables S7.1.1–S7.8.2. All analyses were conducted using Stata, Version 14 (StataCorp LP, College Station, TX) or SAS Version 9.4 (SAS Institute, Cary, NC).

RESULTS

Sample Characteristics

A total of 40 432 (71.8%) procedures fulfilled our inclusion criteria and were grouped into 10 surgical categories (Table 1). Orthopedic surgeries were the most prevalent, followed by GI, Cardiac, Spine, GU, Vascular, ORL, Neurosurgery, PT, and Bariatric. Table 2 details demographic information of the study population, overall and by sMVAP quintile. (see Supplementary Table S2 for demographics by sMVAP grouped in 0.2 unit increments.) The mean ± *SD* age and BMI were 59.0 ± 15.1 years and 30 ± 7.8 kg/m^2, respectively, with near-equal gender distribution.

Symptomless MVAP Associates With Previous Diagnosis of OSA and Current Status of Hypertension

We observed statistically significant associations between higher sMVAP index and both an increased likelihood of a previous OSA diagnosis and current hypertension in all analyses.

We first examined differences in sMVAP quintiles. As shown in Table 2, a larger prevalence of both previous OSA diagnosis and current hypertension was seen in higher sMVAP quintiles. OSA prevalence was highest (26.2%) in the top quintile, a group

Table 1—Distribution of Surgical Procedure Types and Hospital.

Surgical category	All hospitals	Hospital		
		HUP	PAH	PMC
Bariatric	1797 (4.4%)	982 (5.2%)	487 (4.2%)	328 (3.3%)
Orthopedic	9890 (24.5%)	1226 (6.4%)	3843 (33.3%)	4821 (49.1%)
Cardiac	5308 (13.1%)	3670 (19.2%)	355 (3.1%)	1283 (13.1%)
Gastrointestinal	5463 (13.5%)	3328 (17.4%)	398 (12.1%)	737 (7.5%)
Genitourinary	3785 (9.4%)	1662 (8.7%)	794 (6.9%)	1329 (13.5%)
Neurological	2152 (5.3%)	1485 (7.8%)	657 (5.7%)	10 (0.1%)
ORL	2728 (6.8%)	2131 (11.2%)	457 (4.0%)	140 (1.4%)
Pulmonary/Thoracic	1946 (4.8%)	1114 (5.8%)	301 (2.6%)	531 (5.4%)
Spine	4442 (11.0%)	1789 (9.4%)	2602 (22.6%)	51 (0.5%)
Vascular	2921 (7.2%)	1691 (8.9%)	634 (5.5%)	596 (6.1%)
Total surgical procedures	40 432 (100.0%)	19 078 (100.0%)	11 528 (100.0%)	9826 (100.0%)

HUP = Hospital of University of Pennsylvania; ORL = Otorhinolaryngology/Oral and Maxillofacial Surgery/Ear Nose Throat; PAH = Pennsylvania Hospital; PPMC = Penn Presbyterian Medical Center.

Table 2—Demographics and Surgical Adverse Outcome Measures in Included Procedures, Overall and by Symptomless Multi-Variable Apnea Prediction Quintile.

Outcome	Overall	sMVAP quintile						
		Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	p	p_{trend}
Age, y	59.0 ± 15.1	47.8 ± 16.1	59.1 ± 13.8	62.5 ± 12.9	64.3 ± 12.9	61.2 ± 13.4	<.0001	<.0001
Male, %	51.6	22.3	47.6	62.9	67.5	58	<.0001	<.0001
BMI, kg/m2	30.0 ± 7.8	22.8 ± 3.0	26.1 ± 3.3	28.5 ± 3.5	31.7 ± 3.9	40.9 ± 8.0	<.0001	<.0001
sMVAP[a]	0.24 ± 0.23	0.02 ± 0.01	0.08 ± 0.02	0.16 ± 0.03	0.29 ± 0.05	0.63 ± 0.18	<.0001	<.0001
Previous OSA, %	9.3	1.5	3.4	5.5	9.9	26.2	<.0001	<.0001
Current hypertension, %	54.5	25.1	47.6	58.6	67.6	73.7	<.0001	<.0001
Extended length of stay, %	7.4	5.8	6.9	7.3	7.3	9.8	<.0001	<.0001
Any stay in ICU, %	25.3	22	25.6	26.7	26.5	25.8	<0.0001	<.0001
Any respiratory complications, %	1.3	0.9	1.3	1.3	1.2	1.6	.0029	.0014

BMI = Body Mass Index; ICU = intensive care unit; OSA = Obstructive Sleep Apnea; sMVAP = Symptomless Multi-Variable Apnea Prediction. Any ICU-stay defined as Any Stay in Intensive Care Unit. Any respiratory complications defined as diagnosis of Pulmonary Embolus, Acute Respiratory Distress Syndrome, and/or Aspiration Pneumonia. Extended length of stay defined as a length of stay >90th percentile for given procedure code.
[a]sMVAP calculated as $e^x/(1 + e^x)$, where $x = -10.784 + (0.203 \times BMI) + (0.043 \times Age) + (1.004 \times Male)$.

that on average was older (61.2 ± 13.4 years), majority-male (58.0%) and morbidly obese (40.9 ± 8.0 kg/m^2). In contrast, only 1.5% in the bottom quintile had a previous OSA diagnosis, with subjects who are middle-aged (47.8 ± 16.1 years), primarily female (87.7%) and have normal BMI (22.8 ± 3.0 kg/m^2). While the top quintile is clearly driven by a high obesity level, increased previous OSA prevalence was seen in the 4th (9.9%) and 3rd (5.5%) quintiles, where obesity levels were more modest. Similar trends were found when sMVAP was grouped by increments of 0.2 units (see Supplementary Table S2).

This association was reflected in logistic regression analyses before (Supplementary Table S3) and after (Table 3) conditioning on hospital or surgical group-specific effects. In conditional analyses, the odds of a previous OSA diagnosis or current hypertension were both significantly different among sMVAP quintiles. Patients in the top quintile had a 16.8 times increased odds of previous OSA diagnosis (95% CI, 13.8–20.3; $p < .0001$) and an 8.4 times increased odds of current hypertension (95% CI, 7.82–9.08; $p < .0001$) compared to the bottom sMVAP quintile. We observed a significant linear trend for both measures, suggesting

Table 3—Adjusted[a] Relationship Between Symptomless Multi-Variable Apnea Prediction Quintiles and OSA, Hypertension, and Postoperative Complications.

Outcome	Previous OSA		Current hypertension		Extended length of stay		Any ICU-stay		Any respiratory complications	
	OR (95%CI)[b]	p[c]	OR (95%CI)[b]	p[c]	OR (95%CI)[b]	p[c]	OR (95%CI)[b]	p[c]	OR (95%CI)[b]	p[c]
ANOVA p[d]	<.0001		<.0001		<.0001		<.0001		.0012	
sMVAP quintile 1	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—	1.00 (reference)	—
sMVAP quintile 2	2.35 (1.89, 2.93)	<.0001	2.59 (2.42, 2.77)	<.0001	1.21 (1.06, 1.37)	.0041	1.17 (1.08, 1.28)	.0003	1.43 (1.06, 1.93)	.0204
sMVAP quintile 3	3.83 (3.12, 4.71)	<.0001	4.03 (3.76, 4.31)	<.0001	1.29 (1.14, 1.47)	<.0001	1.21 (1.11, 1.32)	<.0001	1.38 (1.02, 1.87)	.0384
sMVAP quintile 4	6.67 (5.48, 8.13)	<.0001	5.86 (5.47, 6.29)	<.0001	1.29 (1.13, 1.46)	.0001	1.16 (1.06, 1.27)	.0008	1.25 (0.91, 1.70)	.1643
sMVAP quintile 5	16.8 (13.8, 20.3)	<.0001	8.42 (7.82, 9.08)	<.0001	1.83 (1.62, 2.07)	<.0001	1.44 (1.32, 1.58)	<.0001	1.85 (1.37, 2.49)	<.0001
p for trend	<.0001		<.0001		<.0001		<.0001		.0014	
sMVAP quintile	2.00 (1.93, 2.07)		1.66 (1.64, 1.69)		1.14 (1.11, 1.17)		1.07 (1.05, 1.10)		1.11 (1.04, 1.19)	

CI = confidence interval; OR = odds ratio; ICU = Intensive Care Unit; OSA = Obstructive Sleep Apnea; sMVAP = Symptomless Multi-Variable Apnea Prediction. Any ICU-stay defined as Any Stay in Intensive Care Unit. Any respiratory complications defined as diagnosis of Pulmonary Embolus, Acute Respiratory Distress Syndrome, and/or Aspiration Pneumonia. Extended length of stay defined as a length of stay >90th percentile for given procedure code.
[a]Conditional logistic model controlled for Surgical Category and Hospital.
[b]Estimates presented as OR estimates (compared to Quintile 1) and 95% CI.
[c]*p*-value from logistic regression model comparing sMVAP groupings 2–5 versus group 1.
[d]Overall *p*-value testing whether there is any relationship between sMVAP Group and surgical outcome. *p*-value from regression model with group fit as an ordinal variable, examining the evidence for a linear change in risk across groups.

Table 4—Relationship Between Continuous Symptomless Multi-Variable Apnea Prediction and OSA, Hypertension and Postoperative Complications.

Outcome	sMVAP effect			
	Unconditional		Conditional[a]	
	OR (95% CI)[b]	p[c]	OR (95% CI)[b]	p[c]
Previous OSA	1.48 (1.46, 1.50)	<.0001	1.39 (1.37, 1.41)	<.0001
Current hypertension	1.33 (1.31, 1.34)	<.0001	1.35 (1.33, 1.36)	<.0001
Extended length of stay	1.09 (1.07, 1.11)	<.0001	1.10 (1.08, 1.12)	<.0001
Any ICU-stay	1.01 (1.00, 1.02)	.0185	1.06 (1.04, 1.07)	<.0001
Any respiratory complications	1.06 (1.02, 1.10)	.0015	1.08 (1.04, 1.12)	<.0001

CI = confidence interval; ICU = Intensive Care Unit; OR = Odds ratio; OSA = Obstructive Sleep Apnea sMVAP = Symptomless Multi-Variable Apnea Prediction. Any ICU-stay defined as Any Stay in Intensive Care Unit. Any respiratory complications defined as diagnosis of Pulmonary Embolus, Acute Respiratory Distress Syndrome, and/or Aspiration Pneumonia. Extended length of stay defined as a length of stay >90th percentile for given procedure code. Model adjusted for surgical category and hospital.
[a]Conditional logistic regression model controlled for effects of Surgical Category and Hospital (see Table 1).
[b]Estimates presented as OR and 95% CI, associated with a 0.1 unit increase in sMVAP.
[c]*p*-value from logistic regression model.

the higher risk for OSA or hypertension increased in a linear fashion across sMVAP quintiles. Similar patterns were observed when grouping sMVAP into 0.2 unit increments in unadjusted and conditional analyses (Supplementary Tables S4 and S5).

Based on similar analyses, Table 4 shows the associations between previous OSA diagnosis and current hypertension and continuous sMVAP. Conditional on hospital and surgical category-specific effects, a higher sMVAP was significantly associated with an increased odds of both measures. Specifically, a 0.1 unit increase in sMVAP was associated with a 1.39 times increased odds of previous OSA (95% CI, 1.37–1.41; $p < .0001$) and a 1.35 times increased odds of current hypertension (95% CI, 1.33–1.36; $p < .0001$). Similar results were seen using log-transformed values of sMVAP to control for the skewed distribution of sMVAP (see Supplementary Table S6).

Thus, strong associations exist between sMVAP values and both OSA diagnosis and hypertension. These results confirm sMVAP's utility as a marker for OSA and an index of hypertension risk.

Symptomless MVAP Is Associated With Increased Risk of Postoperative Complications

We observed significant associations between increases in sMVAP and increased risk of all three postoperative complications: (1) extended length of stay (ELOS); (2) ICU-stay; and (3) post-surgical occurrence of PE, ARDS and/or AP (respiratory complications).

We observed higher proportions of postoperative complications in higher sMVAP quintiles (Table 2) or 0.2 unit groupings (Supplementary Table S2). Results from conditional logistic regression models examining the increased likelihood of events across sMVAP quintiles are presented in Table 3. We found significantly higher proportions of all three outcomes in higher quintiles, compared to patients in the lowest quintile of sMVAP. Compared to patients in the bottom quintile of sMVAP, patients in the top quintile experienced a 1.83 times increased odds of extended length of stay (95% CI, 1.62–2.07; $p < .0001$), 1.44 times increased odds of ICU-stay (95% CI, 1.32–1.58; $p < .0001$), and 1.85 times increased odds of respiratory complications (95% CI, 1.37–2.49; $p < .0001$). All tests for linear trends were significant, suggesting a proportional increase in risk across sMVAP groupings. Similar results were seen in unconditional analyses based on sMVAP quintiles (Supplementary Table S3) and when examining sMVAP groupings of 0.2 units in unadjusted and conditional analyses (Supplementary Tables S4 and S5).

Associations between postoperative complications and continuous sMVAP are shown in Table 4. An 0.1 unit increase in sMVAP was associated with a 6%–10% increase in the odds of experiencing a postoperative complication. Specifically, the increases in odds of experiencing ELOS, increased ICU-stay and respiratory complications, with increased sMVAP were: 1.10 (95% CI, 1.08–1.12, $p < .001$), 1.06 (95% CI, 1.04–1.07, $p < .001$), and 1.08 (95% CI, 1.04–1.12, $p < .001$), respectively. Similar associations were seen in unconditional analyses (Supplementary Table S6).

Differential Associations Between Symptomless MVAP and Postoperative Complications in Non-Bariatric Versus Bariatric Surgery Groups

We next examined whether differences exist in the association between sMVAP and postoperative complications between Bariatric surgery (which requires pre-surgical OSA screening) and other surgical groups in sub-samples matched for age, gender, and BMI. When compared to Bariatric surgery, sMVAP was more strongly associated with postoperative complications in Orthopedic, GI, Neurosurgery, ORL, and Spine surgeries. We focus on Orthopedic surgery, which had the largest sample size and the most differences in associations between OSA risk factors and adverse outcomes (see Tables 5 and 6 for demographic comparisons and sMVAP associations, respectively). Comparisons between Bariatric and other surgical subgroups are presented in the Supplementary Tables S7.1.1–S7.8.2.

When examining differences between Bariatric surgery and Orthopedics, the sMVAP was more strongly associated with adverse postoperative outcomes in Orthopedics for all three outcomes. Matching for age, gender, and BMI resulted in a sample that was middle to older aged, morbidly obese and

Table 5—Summary of Demographics in Gender, Age, and BMI Matched Sub-Sample in Orthopedic Versus Bariatric Surgery Groups.

Variable	Bariatric surgery	Orthopedic surgery	p[a]
N	1057	1057	—
Age, years	52.1 ± 11.1	52.2 ± 11.1	.849
Male, %	26.7	26.7	—
BMI, kg/m^2	41.3 ± 8.8	41.2 ± 8.8	.863
sMVAP	0.52 ± 0.3	0.52 ± 0.3	.877
Previous OSA, %	**50.8**	**23.1**	**<.0001**
Current hypertension, %	63.0	63.1	.964
Extended length of stay, %	8.2	9.6	.256
Any ICU-stay, %	**5.4**	**14.3**	**<.0001**
Any respiratory complications, %	0.5	0.4	>.999

BMI = Body Mass Index; ICU = Intensive Care Unit; OSA = Obstructive Sleep Apnea; sMVAP = Symptomless Multi-Variable Apnea Prediction. Any ICU-stay defined as Any Stay in Intensive Care Unit. Any respiratory complications defined as diagnosis of Pulmonary Embolus, Acute Respiratory Distress Syndrome, and/or Aspiration Pneumonia. Extended Length of Stay defined as a length of stay >90th percentile for given procedure code. Significant results shown in bold.
[a]*p*-value from *t* test or Wilcoxon test (for continuous measures) and chi-squared or Fisher's exact test (for categorical measures).

Table 6—Examination of Differences in Symptomless Multi-Variable Apnea Prediction Associations in Orthopedic Versus Bariatric Surgery Groups.

Outcome	sMVAP effect[a]				
	Bariatric surgery		Orthopedic surgery		$p_{interaction}$[d]
	OR (95% CI)[b]	p[c]	OR (95% CI)[b]	p[c]	
Extended length of stay	1.00 (0.93, 1.08)	.9385	**1.23 (1.14, 1.34)**	**<.0001**	**<.0001**
Any ICU-stay	0.99 (0.90, 1.08)	.8045	**1.18 (1.11, 1.26)**	**<.0001**	**.0004**
Any respiratory complications	0.86 (0.64, 1.16)	.3343	1.96 (0.92, 4.20)	.0825	**.0369**

CI = confidence interval; ICU = Intensive Care Unit; OR = Odds ratio; sMVAP = Symptomless Multi-Variable Apnea Prediction. Any ICU-stay defined as Any Stay in Intensive Care Unit. Any respiratory complications defined as diagnosis of Pulmonary Embolus, Acute Respiratory Distress Syndrome and/or Aspiration Pneumonia. Extended length of stay defined as a length of stay >90th percentile for given procedure code. Significant results shown in bold.
[a]Model adjusted for hospital.
[b]Estimates presented as OR and 95% CI, associated with a 0.1 unit increase in sMVAP.
[c]*p*-value from logistic regression model testing within surgery group effect.
[d]*p*-value for interaction between surgical group and sMVAP.

majority female, with both groups having an average sMVAP index of 0.52 ± 0.30 (Table 5). Despite identical distribution of OSA risk factors, only 23.1% of patients having Orthopedic surgery had a previous diagnosis of OSA, compared to 50.8% of Bariatric patients ($p < .0001$). Moreover, the Orthopedic group had significantly higher proportion of any ICU-stay compared to the Bariatric group (14.3% vs. 5.4%, respectively, $p < .0001$; Table 5).

Similarly for postoperative outcomes, the sMVAP predicted adverse events in Orthopedic, but not Bariatric patients (Table 6). In Bariatric patients, who undergo routine preoperative screening and treatment of OSA, OSA risk was not associated with any of these complications. In Orthopedic patients, however, each 0.1 unit increase in sMVAP was associated with a 23% higher risk of extended length of stay ($OR_{Bariatric} = 1.00$ [95% CI, 0.93–1.08] vs. $OR_{Orthopedic} = 1.23$ [95% CI, 1.14–1.34]; $p < .001$), 18% higher risk of any ICU-stay ($OR_{Bariatric} = 0.99$ [95% CI, 0.90–1.08] vs. $OR_{Orthopedic} = 1.18$ [95% CI, 1.11–1.26]; $p = .0004$), and a borderline non-significant 96% higher odds of respiratory complications ($OR_{Bariatric} = 0.86$ [95% CI, 0.64–1.16) vs. $OR_{Orthopedic} = 1.96$ [95% CI, 0.92–4.20]; $p = .083$). Similar associations were observed when comparing sMVAP associations in Bariatric surgeries against other matched surgical groups. (see Supplementary Tables S7.1.1–S.7.8.1 for demographic comparisons and Supplementary Tables S7.1.2–S.7.8.2 for comparisons of sMVAP associations.)

Effect of Gender, Age and/or BMI on the Association of the Symptomless MVAP and Risk of Postoperative Complications

We examined the effect of sMVAP on predicting postoperative complications within strata defined by gender, age, and BMI (as well as associated interactions). For BMI and Age, we chose to rely on the observed distribution in our sample and split the population at the observed median values (28.0 kg/m^2 for BMI and 60.3 years for age); we also examined the effect of sMVAP in the four groups defined by the two binary variables.

In general, higher sMVAP was associated with increased risk of postoperative outcomes in all strata, suggesting that the sMVAP provides additional predictive information beyond simply knowing whether someone is younger/older or leaner/heavier. There was some evidence for interaction between the sMVAP and age/BMI strata, suggesting that while higher sMVAP is associated with higher risk of postoperative complications in both strata, the strength of this association may differ. For example, when stratifying by BMI, the sMVAP showed stronger associations with extended length of stay and any ICU-stay among those with BMI < 28 kg/m^2. Similarly, there was some evidence of a significantly stronger association with extended length of stay among those aged <60.3 years. Importantly, we note that while statistically significant, the overall magnitude of these differences were small, suggesting that the differences are not clinically important (see Table 7).

DISCUSSION

In this study, we found that when compared to patients in the lowest quintile and/or group of sMVAP values, patients undergoing elective surgery with sMVAP values in the highest quintile and/or group had significantly greater odds of experiencing postoperative complications, including extended length of stay, ICU-stay, and post-surgical serious respiratory complications (PE, ARDS, and/or AP). Second, when compared to age-, gender- and BMI-matched Bariatric surgery patients, specific non-Bariatric surgical groups demonstrated a stronger association between higher sMVAP and postoperative complications. Third, as noted by significant relationships with both OSA and hypertension diagnoses, we confirmed the sMVAP as a measure of OSA and, relatedly, cardiovascular risk.[20,21]

This is the first study to evaluate the use of the sMVAP, which requires three routinely measured clinical variables (age, gender, and BMI) to quantify OSA risk in elective surgery. In previous work,[14] our group demonstrated that the sMVAP is valid in commercial truck drivers as a screening tool to identify those who are at high, intermediate, or low risk for OSA,[16] in conjunction with confirmation of OSA by the gold-standard in-laboratory polysomnography (PSG). The strong association between sMVAP and OSA diagnosis in this analysis lends further support to the usefulness of sMVAP in delineating OSA risk.

Table 7—Relationship Between Continuous Symptomless Multi-Variable Apnea Prediction and Postoperative Complications in Gender, BMI, and Age Strata[a].

Outcome	Gender stratification				
	$p_{interaction}$[b]	Female		Male	
		OR (95% CI)[c]	p[d]	OR (95% CI)[c]	p[d]
Extended length of stay	.433	1.11 (1.08, 1.13)	**<.0001**	1.10 (1.08, 1.13)	**<.0001**
Any ICU-stay	.273	1.07 (1.05, 1.09)	**<.0001**	1.05 (1.04, 1.07)	**<.0001**
Any respiratory complications	.745	1.08 (1.02, 1.14)	**.005**	1.09 (1.03, 1.15)	**.002**
Outcome	**BMI stratification**				
	$p_{interaction}$[b]	BMI < 28.0 kg/m²		BMI ≥ 28.0 kg/m²	
		OR (95% CI)[c]	p[d]	OR (95% CI)[c]	p[d]
Extended length of stay	**.003**	1.27 (1.18, 1.37)	**<.0001**	1.14 (1.12, 1.16)	**<.0001**
Any ICU-stay	**<.0001**	1.20 (1.13, 1.27)	**<.0001**	1.09 (1.08, 1.11)	**<.0001**
Any respiratory complications	.186	1.19 (1.01, 1.40)	**.038**	1.13 (1.08, 1.19)	**<.0001**
Outcome	**Age stratification**				
	$p_{interaction}$[b]	Age < 60.3 y		Age ≥ 60.3 y	
		OR (95% CI)[c]	p[d]	OR (95% CI)[c]	p[d]
Extended length of stay	**.013**	1.11 (1.09, 1.14)	**<.0001**	1.07 (1.04, 1.09)	**<.0001**
Any ICU-stay	.701	1.05 (1.03, 1.07)	**<.0001**	1.03 (1.02, 1.05)	**.0002**
Any respiratory complications	.076	1.12 (1.05, 1.20)	**.001**	1.03 (0.98, 1.08)	.256
Outcome	**BMI and age stratification**				
	$p_{interaction}$[b,e]	BMI < 28.0 kg/m² and age < 60.3 y		BMI ≥ 28.0 kg/m² and age < 60.3 y	
		OR (95% CI)[c]	p[d]	OR (95% CI)[c]	p[d]
Extended length of stay	.388	1.21 (0.92, 1.60)	.173	1.13 (1.10, 1.17)	**<.0001**
Any ICU-stay	**.026**	1.07 (0.89, 1.29)	.477	1.06 (1.04, 1.09)	**<.0001**
Any respiratory complications	.203	1.72 (0.98, 3.30)	.102	1.16 (1.07, 1.25)	**.0004**
		BMI < 28.0 kg/m² and age ≥ 60.3 y		BMI ≥ 28.0 kg/m² and age ≥ 60.3 y	
		OR (95% CI)[c]	p[d]	OR (95% CI)[c]	p[d]
Extended length of stay		1.03 (0.94, 1.14)	.483	1.12 (1.09, 1.15)	**<.0001**
Any ICU-stay		1.02 (0.95, 1.10)	.552	1.10 (1.07, 1.12)	**<.0001**
Any respiratory complications		0.92 (0.75, 1.12)	.401	1.09 (1.01, 1.16)	**.019**

BMI = Body mass index; CI = confidence interval; ICU = Intensive Care Unit; OR = Odds ratio; sMVAP = Symptomless Multi-Variable Apnea Prediction. Any ICU-stay defined as Any Stay in Intensive Care Unit. Any respiratory complications defined as diagnosis of Pulmonary Embolus, Acute Respiratory Distress Syndrome and/or Aspiration Pneumonia. Extended length of stay defined as a length of stay >90th percentile for given procedure code. Conditional regression model controlling for surgical category and hospital. Significant results shown in bold.
[a]Age and BMI stratification based on a median split in the analysis sample.
[b]*p*-value for interaction term (sMVAP × stratification variable).
[c]Estimates presented as OR and 95% CI, associated with a 0.1 unit increase in sMVAP.
[d]*p*-value from logistic regression model.
[e]For combined BMI and Age stratification, $p_{interaction}$[e] represents the *p*-value for sMVAP by 4-group interaction variable for each of the three outcomes.

It is also important to consider associations with prior OSA diagnosis, as potentially supporting evidence for sMVAP associations as a marker of OSA related effects. In adjusted conditional models (data presented in Supplementary Table S8), we observed a strong association between previous OSA status and both current hypertension and extended length of stay. On the other hand, we did not see significant associations with previous OSA and either any ICU-stay or any respiratory complications. More detailed analysis is limited by the absence of information on potential perioperative treatments for OSA among these patients, as well as whether those with a diagnosis of OSA were currently being treated for the disorder. Future studies focused on OSA status and treatment during the perioperative period is warranted.

The observed association between sMVAP and all three postoperative complications is consistent with prior findings by Memtsoudis and colleagues[3] among >3 million lower extremity joint replacement and open abdominal surgeries. Conducted on the National Inpatient Sample (NIS), this prior study found that OSA patients were at increased risk for developing postoperative AP, ARDS and intubation/mechanical ventilation (a five-fold risk [lower extremity joint replacement] and two-fold risk [open abdominal surgeries]) compared to patients without OSA.[3] Furthermore, patients with OSA undergoing lower extremity joint replacement both developed and were at increased risk for PE compared to the abdominal surgery group.[3] Subjects with OSA who underwent joint replacement and developed postoperative respiratory complications were older-aged (63.1 years), male, and obese.[3]

Thus, the pathophysiology of OSA[15] can increase postoperative risk for respiratory compromise, including extended length of stay, ICU-stay, and overall rates of respiratory complications. However, indirectly, routine postoperative clinical conditions such as the use of general anesthetics, opioids, supine positioning, noise, surgical stress, pain, and frequent awakenings for postoperative clinical examination may also contribute to disrupted sleep architecture, exacerbated sleep fragmentation and intensify rebound in rapid eye movement (REM) sleep, which can further increase risk.[1,6,9,24] Together, both OSA and routine clinical conditions affecting sleep likely heighten risk for a range of postoperative complication.[1–6]

The Penn Bariatric surgery patients included in this study not only undergo routine preoperative OSA screening based on existing guidelines, but in addition, have implemented a meticulous team approach toward diagnosing, treatment, and perioperative management of OSA, that may in turn contribute to the reduction of adverse postoperative outcomes.[12] Specifically, given the known prevalence for OSA in their patient population,[12,25,26] perioperative OSA management strategies include: (1) requiring all Bariatric surgery patients to undergo a preoperative sleep study, (2) patients diagnosed with OSA who are not compliant to recommended Positive Airway Pressure (PAP) therapy are not taken to surgery, (3) a week prior to surgery, a list of patients who have OSA requiring PAP treatment is circulated to the multidisciplinary medical team, particularly respiratory therapists, to ensure PAP utilization starting in the recovery room and continued up to discharge from hospital, (4) postoperative pain management limits the use of patient controlled analgesia/narcotics to 24 hours, and favors intravenous nonsteroidal anti-inflammatory medications and, last (5) compliance to (PAP) is monitored via postoperative telephone follow-up and office visits at 10–14 days, 6 weeks, 3 months, 6 months, 1 year, and annually. We therefore hypothesized that the associations between OSA risk and postoperative complications would be lower in the Bariatric group compared to other surgical subgroups, who do not undergo routine preoperative OSA screening.

After matching for age, gender, and BMI, our results indicate that the sMVAP is associated with greater risk of post-surgical complications within specific non-Bariatric surgical specialties compared to effects in Bariatric surgery, including: (1) extended length of stay for Orthopedics, GI, Neurosurgery, and Spine, (2) ICU-stay in Orthopedics, GI, and ORL, and (3) respiratory complications for both Orthopedics and ORL. We note that only Orthopedic surgery, which was also the group with the highest number of procedures, showed significant differences for all three adverse postoperative outcomes compared to Bariatric surgery. However, Bariatric patients had a much higher prevalence of diagnosed OSA (51%) compared to Orthopedic patients (23%). This higher prevalence illustrates one potential benefit of pre-screening in the at-risk Orthopedic population, that is, the ability to identify a large number of patients with potentially undiagnosed OSA. Indeed, observations from the Longitudinal Assessment of Bariatric Surgery Consortium showed that OSA was independently associated with increased 30-day mortality, venous thromboembolism, and failed discharge from hospitalization; this included procedures of varying risk, which were completed by experienced surgeons.[26] Whether routine preoperative OSA screening (as is done before Bariatric surgery) may be effective in limiting the relationship between traditional OSA risk factors (ie, age, male gender, and obesity) and increased likelihood of postoperative complications requires further study. None-the-less, work by Penn Bariatrics suggests that it is logical that the benefits of rigorous preoperative screening and diagnosis for OSA followed by a tailored team approach toward ensuring compliance toward treatment postoperation, limiting risk of taking non-compliant patients to surgery and the overall perioperative and long-term management of the OSA patient may be effective in limiting the likelihood of select postoperative complications. Future studies should build on these results by formally examining the impact of designed screening and treatment programs, potentially within the framework of a randomized trial.

Over the next decade, studies project a 14% to 47% increase in surgical procedures within various specialties.[27] This increase includes a patient population that is older, and with increasing rates of obesity and OSA.[27,28] Indeed, a recent population based study comparing the prevalence of moderate to severe sleep disordered breathing using data from the Wisconsin Sleep Cohort Study/US National Health and Nutrition Examination Survey between 1994 and 2010 observed a 14% to 55% increase of OSA prevalence within subgroups analyzed by age, gender (most recently, 10%–17% among men and 3%–9% among women, 30–70 years old, respectively), and BMI.[28] Overall in our study, we observed that 9.3% of all surgical patients carried a diagnosis of OSA. This is similar to findings from data generated from other studies.[3,4,11,29] Memtsoudis and colleagues found that 8.4% of patients were identified as having OSA in a study amongst approximately half a million patients undergoing hip and knee arthroplasty from a proprietary database covering greater than 400 hospitals between the years 2006 and 2010[3]; however, these percentages are significantly higher than the study utilizing >3 million data from the NIS generated from 1998 to 2007[4] that observed up to 2.5% of patients who underwent orthopedic and abdominal surgery as having sleep apnea. A study by Singh and colleagues[11] observed that while up to 13% of 819 patients presenting for elective surgery had pre-existing OSA, this underestimated the true prevalence. When the remaining 708 patients underwent PSG screening, 31% were identified positive for a diagnosis of mild OSA, 21% for moderate OSA, and 17% had severe OSA; moreover, 92% of surgeons and 60% of anesthesiologists failed to diagnose those patients having moderate to severe OSA.[11] Similarly, Finkle and colleagues also observed that in a cohort of patients presenting for elective surgery, 81% out of 661 patients who screened high-risk for OSA utilizing the validated Apnea Risk Evaluation System questionnaire were not diagnosed with OSA; of which 82% of these high-risk patients were confirmed as having OSA following home sleep testing.[29] Thus, these data, together with known population-based estimates of prevalence (see above), indicate that there are substantial numbers of patients, who are having survery, have unrecognized obstructive sleep apnea.

The American Society of Anesthesiologists twice published guidelines recommending screening for OSA preoperatively and refering high-risk patients to a sleep specialist for diagnosis and treatment.[30,31] Although validated questionnaires, such as the STOP-Bang,[32] exist to screen for OSA in surgical patients, the pooled sensitivities and specificities of these questionnaires are low (approximately 60% to 70% and 40% to 60%, respectively, depending on the Apnea Hypopnea Index [AHI] categories).[33] Further, questionnaires that incorporate BMI in binary fashion (like the STOP-Bang,[32] which uses BMI >35 kg/m^2 rather than as a continuous variable [like the sMVAP]), may sacrifice discriminatory power. Another potential advantage of the sMVAP is its reliance on clinical risk factors that are easily avaiable. Future studies can look at the value of adding symptom data,[34,35] or compare how the sMVAP performs against existing tools like the STOP-Bang.

Given these results, we propose that future studies should prospectively explore a simple and effective two-stage presurgical screening model for OSA. First, patients presenting for elective surgery would be screened for OSA using the sMVAP. (Addition of symptom data, which was not available in this retrospective analysis, may further increase sensitivity.[34,35]) Based on the sMVAP index, patients could be grouped into three risk tiers. Those in the highest-risk tier would be presumed to have OSA and given empiric PAP therapy pre- and post-operatively. Those in the lowest-risk group would be presumed to be free of OSA. Those in the intermediate-risk tier would undergo confirmatory diagnostic testing with a home sleep study or full in-laboratory PSG.[16] The discriminatory power and cost-effectiveness of this approach deserves investigation in the population of patients undergoing elective surgeries.

Our study had some limitations. The sMVAP was validated in a population of commercial truck drivers who were primarily male (prevalent to this occupation), with an average age of 45.4 ± 11 years and BMI of 29.9 ± 5.2 kg/m^2. With the exception of gender, there were similarities to the overall demographic of age and BMI with our current study population. Nevertheless, future studies are necessary to more fully validate the sMVAP specifically in the elective surgical population. Additionally, given its retrospective design, one potential limitation of our study is confouding bias, from variables such as: differing proportions of high-risk procedures within surgical subgroups; more extensive pre-Bariatric screening for medical conditions other than OSA,[12,26] and more meticulous perioperative management of comorbidities.[26] These latter explanations,[26] highlight the potential benefit of robust screening and perioperative management of comorbidities, including OSA. Misclassification of OSA risk by sMVAP may also have occurred, as up to 20% of patients within a normal weight range may have OSA,[28] and ethnicity,[36] menopausal status, and craniofacial deformities or nasopharyngeal obstruction[16] were not measured and may impact OSA risk. We also did not control for comorbidities or adherence to PAP therapy. Also, information regarding the use of additional protocols to minimize risk, such as continuous monitoring of pulse oximetry, delayed extubation, empiric PAP use and the use of multimodal anesthesia, was not available.[30,31] Had these measures been in place, incuding PAP treatment, fewer complications would have been seen in OSA patients, making it harder to find a significant association between OSA risk and adverse events. Lastly, our study was based on data from one hospital network, and so may have limited generalizability.

CONCLUSIONS

In conclusion, in this retrospective analysis, a higher sMVAP index is associated with an increased risk of diagnosed OSA, current hypertension, and adverse postoperative complications, including extended length of stay, any ICU-stay, and respiratory complications. These associations are stronger in surgical subgroups that do not require preoperative screening and management of OSA, when compared against patients undergoing Bariatric surgery, a group routinely undergoing OSA preoperative screening and management in our hospital network. We acknowledge the limitations of this retrospective analysis; these results suggest the need for further research involving prospective studies. In particular, future studies should evaluate whether routine preoperative screening and treatment of OSA in patients such as those having Orthopedic surgery result in reductions in OSA-related postperative complications, and whether such reductions may lower health care utilization and costs.

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SUPPLEMENTARY MATERIALS

Supplementary materials are available at *SLEEP* online.

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DISCLOSURE STATEMENT

None declared.