INTRODUCTION

Obstructive sleep apnoea (OSA) is characterised by repetitive episodes of complete or partial upper airway obstruction with periods of apnoea during sleep,[1] resulting in intermittent hypoxia and fragmented sleep patterns. This triggers a systemic inflammatory response resulting in long-term cardiorespiratory complications.[2] Rising levels of obesity have contributed to a 15-fold increase in the global prevalence of OSA over the last two decades.[3] In particular, obesity amongst Asian patients is associated with more obesity-related diseases at a lower body mass index (BMI) than their Caucasian counterparts. As a result, the Ministry of Health of Singapore
redefined its BMI guidelines, with severe obesity defined as a BMI \geq 32.5 \text{ kg/m}^2.\textsuperscript{[4]} It is estimated that one in six Singaporeans has some degree of OSA due to the rising levels of obesity compounded by the inherent craniofacial features of the local Chinese population.\textsuperscript{[5,6]}

In 2014, the American Society of Anesthesiologists (ASA) guidelines proposed preoperative identification of patients with OSA and initiation of continuous positive airway pressure (CPAP) therapy as the effects of anaesthesia and analgesia predispose these patients to episodes of airway obstruction with delayed awakening response to the ensuing hypoxia and hypercarbia; thus, increasing postoperative cardiorespiratory complications.\textsuperscript{[7]} However, this has resulted in unintended consequences of increased cost and postponement of surgery to facilitate the formal diagnosis of OSA via a polysomnography (PSG).

Prevalence of undiagnosed OSA can be as high as 24.5% in the surgical population and the management of obese patients with undiagnosed OSA has always been a challenge to clinicians.\textsuperscript{[8]} There is a justified concern of cardiopulmonary complications, including the increased sensitivity to opioids and anaesthetic agents resulting in a delayed appropriate respiratory response; cardiovascular complications associated with hypoxia, hypercarbia and increased sympathetic stimulation; and the increased risk of a difficult airway should an endotracheal intubation be required. Yet, there are no specific guidelines on the management of patients with possible undiagnosed OSA.

Hence, we examined the effectiveness of CPAP therapy retrospectively in reducing postoperative cardiorespiratory complications in obese patients undiagnosed with OSA by addressing the following objectives: first, to investigate the prevalence of postoperative cardiorespiratory complications amongst an obese Asian population presenting for elective noncardiac surgery; and second, to evaluate the efficacy of perioperative CPAP therapy in reducing cardiorespiratory complications.

**METHODS**

A retrospective study of elective surgical patients on the ‘Fast-track OSA’ pathway at a tertiary teaching hospital was conducted between March 2017 and December 2019. Waiver of informed consent was obtained from the SingHealth Institutional Research Board (CIRB 2019/2701).

Patients who were more than 17 years of age undergoing elective noncardiac surgery with a BMI >32 kg/m\(^2\) and deemed at risk of moderate to severe OSA were included. OSA risk was based on the STOP BANG Questionnaire\textsuperscript{[1]} (STOP-BANG \geq 3) or the Ear Nose and Throat (ENT) Sleep Clinic assessment, the referral having been triggered by the operating surgeon or the STOP BANG Questionnaire score.

At the ENT Sleep clinic, patients were assessed for OSA risk based on clinical findings such as high BMI, micrognathia, tonsillar hypertrophy, long uvula, low-lying soft palate, large tongue size and outpatient nasoendoscopic airway assessment, including static upper airway narrowing and identifying the site of airway collapsibility on performing Mueller’s manoeuvre with the nostrils pinched. A positive result on Mueller’s manoeuvre would suggest the presence of OSA but a negative result would not imply a low risk of OSA (L-OSA). These patients were divided into low or high risk of moderate to severe OSA after consultation at the clinic. The exclusion criteria were known OSA patients on CPAP therapy.

Subsequently, patients deemed at high risk of moderate to severe OSA were counselled and offered CPAP therapy as well as PSG pre- or postoperatively. Those who agreed to CPAP therapy (C-OSA) utilised it 1 day to 2 weeks prior to surgery until they were discharged. CPAP settings were individualised to each patient’s requirements via an automated optimising feedback mechanism on the machine that adjusted pressure levels between 4 and 20 cmH\(_2\)O, as assessed by the respiratory therapist. Patients deemed to be at high risk of OSA based on the STOP BANG Questionnaire and who did not undergo the ENT Sleep Clinic assessment but refused CPAP therapy (R-OSA) due to time or financial constraints proceeded with surgery. Most patients refused PSG due to time or financial constraints. Patients deemed to be at L-OSA were also included in the analysis [Figure 1]. Individualised anaesthetic management [Table 1] was administered by the assigned anaesthetist.

C-OSA and R-OSA patients were monitored in the postanaesthesia care unit (PACU) for up to 4 h postoperatively before being discharged. CPAP therapy was instituted as instructed by the anaesthetist or surgeon for the C-OSA group. For the R-CPAP group, oxygen (either via nasal cannula or Hudson’s mask) was administered at the discretion of the anaesthetist, surgeon or PACU nurse. Disposition after PACU discharge was at the discretion of the
surgeon or anaesthetist, with the application of CPAP therapy in the (i) high dependency (HD) unit where patients were monitored continuously with close nursing supervision or (ii) general ward (GW) with routine monitoring at hourly to six hourly intervals. All nursing staff in GW and HD unit were trained to manage OSA patients on CPAP therapy.

Ambulatory C-OSA patients were started on CPAP therapy 1 day to 2 weeks prior to surgery and postoperatively and were discharged from PACU to the Day Surgery Unit before being discharged home. They did not receive CPAP therapy postoperatively. All in-patients received supplemental oxygen, if indicated, for at least the first 24 postoperative hours to maintain an oxygen saturation (SpO₂) of ≥95%. If pulse oximetry recorded SpO₂ levels below the preoperative reference level despite the administration of oxygen, the patient would be upgraded to a higher level of care. Patients who remained intubated postoperatively were sent directly to the surgical intensive care unit (SICU), bypassing PACU. Mechanical ventilation was only possible in the SICU.

Preoperative CPAP therapy compliance was assessed via the report generated from the CPAP therapy machine, and it was defined as ≥4 h of usage per night as an average over the duration of the machine loan. Patients were deemed compliant with postoperative CPAP therapy when they used ≥4 h per night as an average over all the nights observed.

Data collection was implemented through review of the anaesthetic chart, electronic clinical notes and the discharge summary. The following data was collected: demographic data, ASA physical status, type of surgery and anaesthesia, postoperative disposition immediately after surgery, length of hospital stay and postoperative complications. Cardiac complications included myocardial ischaemia/infarct, cardiogenic pulmonary oedema and arrhythmias. Pulmonary complications included oxygen desaturation/hypoxia, atelectasis, aspiration, pneumonia and respiratory failure. Step-up care was defined as higher level of care beyond the GW, where there was continuous telemetry and SpO₂ monitoring with a higher nurse-to-patient ratio.

We estimated that a minimal sample size of 208 patients would be required for a dichotomous endpoint, two independent sample study with a primary postoperative cardiovascular complication rate of 30% versus 14%,[9] assuming 5% type 1 error and 80% power.

Statistical analysis was performed using International Business Machines Statistical Package for the Social Sciences (IBM SPSS) Statistics version 21.0 and Stata. Binary logistic regression was performed to analyse the relationship between postoperative cardiopulmonary complications and clinical variables. To assess the relationship between OSA and length of hospital stay or requirement of step-up care, Mann-Whitney U-test was performed and quantile regression was employed to adjust for possible confounders in obtaining the adjusted odds ratio (OR).

RESULTS

There were 1400 patients of whom 1226 were deemed to be at high risk of moderate to severe OSA. In total, 332 used CPAP therapy (C-OSA) and 894 patients rejected CPAP therapy (R-OSA). One hundred seventy-four patients were deemed at L-OSA [Table 1]. The mean length of stay in hospital was 1.78 days amongst low-risk OSA patients, 2.70 days amongst R-OSA patients and 2.78 days amongst C-OSA patients, and was statistically significant (P < 0.001) [Table 1].
The mean length of stay in HD/SICU was 0.14 days amongst low-risk OSA patients, 0.35 days amongst R-OSA patients and 0.71 days amongst C-OSA patients, and was statistically significant (P < 0.001) [Table 1].

Multivariate linear regression showed that CPAP did not affect the length of stay in hospital (adjusted β =0.04, P = 0.856) [Table 2]. In terms of length of stay in HD/SICU, patients with the use of CPAP therapy had a 0.28 days (adjusted β =0.28, P < 0.0001) increase [Table 2].

There were four out of 1218 patients deemed at high risk of OSA who required unplanned step-up care, comprising two C-OSA and two R-OSA patients. Amongst 174 patients deemed at L-OSA, none required step-up care. Fisher’s exact test was performed which showed that there was no relation between the use of CPAP therapy (adjusted OR [aOR] 3.2, 95% CI 0.46, P = 0.237) and the requirement for step-up care.

There were 47 total complication events amongst all patients (3.4%). Overall, there were three complication events (1.7%) amongst patients with L-OSA, 29 complication events (3.2%) amongst patients with a high risk of OSA who declined CPAP therapy (R-OSA) and 15 complication events (4.5%) amongst patients with a high risk of OSA who used CPAP therapy (C-OSA) [Table 3]. There were no deaths.

A total of ten patients had cardiac complications (0.05%). One (0.6%) amongst the low-risk OSA group had cardiac complications, namely cardiogenic pulmonary oedema [Table 3].

Nine (0.4%) had cardiac complications amongst the high-risk of OSA group [R-OSA = 6 (0.6%), C-OSA = 3 (0.9%)] – one secondary to non-ST elevation myocardial infarction, four secondary to cardiogenic pulmonary oedema and four due to arrhythmias (three with atrial fibrillation, one with ventricular bigeminy) [Table 3]. Multivariate logistic regression showed that the association between CPAP use and postoperative cardiac complications was not statistically significant (aOR 2.3, 95% CI 0.75–7.1, P = 0.147). Increased age (aOR 1.06.
95% CI 1.01–1.11, \( P = 0.013 \) was statistically significant for increased cardiac complications [Table 4].

A total of 37 patients had respiratory complications (2.6%). Two patients (1.1%) amongst the low risk of the OSA group had respiratory complications while 29 events (3.2%) occurred amongst the high risk of the OSA group (R-OSA = 29 (3.2%), C-OSA = 15 (4.5%)) [Table 3].

Amongst the low-risk group, one patient was sent to SICU after prolonged surgery with no attempted extubation. One patient developed aspiration pneumonia secondary to difficult intubation requiring an unplanned SICU stay.

Twenty-seven patients with high risk of OSA developed postoperative desaturation. There were three unplanned SICU admissions – two patients in the R-OSA group developed aspiration pneumonia requiring postoperative prolonged mechanical ventilation, while one patient in the C-OSA group required reintubation secondary to obesity hypoventilation syndrome [Table 3].

Multivariate logistic regression suggested that age (aOR = 1.03, \( P = 0.036 \)) and Indian race had a higher adjusted odds risk of 3.4 (95% CI 1.05–11.1, \( P = 0.041 \)) for respiratory complications. There was no statistical significance between CPAP therapy use and respiratory complications (aOR = 1.6, \( P = 0.255 \)) [Table 3].

Preoperative compliance amongst patients was 13.6% (43/314), 18 patients were excluded as there was no available CPAP compliance data. Postoperative compliance was 10.2% (32/314), with exclusion of 18 patients who had day surgery and were discharged on postoperative day 0. Both pre- and postoperative compliance to CPAP therapy was 3.2% (9/296).

Univariate predictors for postoperative compliance were BMI \( \geq 32 \) kg/m\(^2\) (aOR 1.97, \( P = 0.023 \)), hypertension (aOR = 1.935, \( P = 0.008 \)), and symptoms of snoring from STOPBANG (aOR = 1.573, \( P = 0.069 \)). Stepwise regression with inclusion of univariate factors with \( P < 0.1 \) showed that hypertension was significant for postoperative compliance to CPAP therapy (aOR = 1.8, \( P = 0.038 \)) [Table 5].

There were nine patients who were compliant both pre- and postoperatively with CPAP therapy. They did not suffer any cardiorespiratory complications.

**DISCUSSION**

OSA has been associated with an increased risk of cardiac complications, especially atrial fibrillation, with the risk being higher in those with severe OSA.\(^{[9,10]}\) While CPAP therapy has been shown to mitigate cardiorespiratory complications in OSA patients, multivariate analysis using intention-to-treat suggested that CPAP therapy did not mitigate them. Poor adherence to CPAP therapy could explain...
ineffectiveness of CPAP therapy as it would have prevented cardiac remodelling and reduction of arrhythmogenicity. Similarly, poor adherence to CPAP therapy could likewise explain the results seen with pulmonary complications. By only starting CPAP therapy postoperatively, patients would find difficulty coordinating with the CPAP therapy machine, compounded by the effects of anaesthesia that would impede coordination further.\[^{11}\]

CPAP therapy intervention was not associated with a decreased length of stay in the current study. Possible reasons include CPAP therapy having affected other aspects of postoperative recovery – such as aerophagia from CPAP that may have slowed bowel recovery, and sleep disruption/fragmentation in patients unaccustomed to CPAP therapy that would have impaired postoperative recovery.\[^{12}\]

The current study found a nonadherence of 86.4% preoperatively and 89.8% postoperatively to CPAP therapy. Studies have found nonadherence to CPAP therapy for newly diagnosed untreated OSA ranging between 29 and 83%.\[^{1,11,13}\] Poor adherence to CPAP therapy has been mentioned in previous randomised controlled trials that have found no benefit of CPAP therapy in reducing postoperative complications.\[^{12}\] Hypertension was shown in the current study to be a factor predicting poor adherence to CPAP therapy. This was similar to a cohort study that postulated that patients with hypertension could be less motivated to undertake treatment as they may have already been
referred for CPAP therapy, largely due to the presence of hypertension rather than symptoms of OSA.\(^\text{[11]}\) Our patient population was picked up from the clinic and were largely asymptomatic; hence, there was a lack of perceived benefit in CPAP therapy,\(^\text{[13]}\) which could have contributed to poor adherence.

In contrast to the current guideline recommendations,\(^\text{[7]}\) our study did not find any difference between the mode of anaesthesia and incidence of postoperative complications. This result may reflect a Type II error as anaesthetists may have altered their techniques in offering opioid-sparing or multimodal analgesic techniques to minimise complications.\(^\text{[12]}\)

The strengths of this study include a large sample size with clear follow-up of postoperative complications. We were also able to account for the type of anaesthesia administered, unlike other large cohort studies. In addition, the study included patients who were started on CPAP therapy preoperatively, which avoided starting CPAP therapy postoperatively in CPAP-naïve patients and thus allowing for better tolerability to CPAP therapy. Finally, it was possible

| Race |
|--------------------|
| Malay |
| Indian |
| Others |
| BMI ≥37.5 |

Table 4: Factors that influence postoperative cardiac and respiratory complications

| Demographics | n | Age (Unadjusted OR (95% CI) P) | Gender (Adjusted OR (95% CI) P) | Race (Unadjusted OR (95% CI) P) | BMI (Unadjusted OR (95% CI) P) |
|--------------|---|---------------------------------|--------------------------------|--------------------------------|-----------------------------|

Table 5: Factors influencing compliance to postoperative CPAP therapy

| Demographics | Factors influencing compliance to CPAP therapy | Unadjusted OR (95% CI) P | Adjusted OR (95% CI) P |
|--------------|-----------------------------------------------|--------------------------|-----------------------|

*Statistically significant. OR – Odds ratio, CPAP – Continuous positive airway pressure, BMI – Body mass index

Referred for CPAP therapy, largely due to the presence of hypertension rather than symptoms of OSA.\(^\text{[11]}\) Our patient population was picked up from the clinic and were largely asymptomatic; hence, there was a lack of perceived benefit in CPAP therapy,\(^\text{[13]}\) which could have contributed to poor adherence.

In contrast to the current guideline recommendations,\(^\text{[7]}\) our study did not find any difference between the mode of anaesthesia and incidence of postoperative complications. This result may reflect a Type II error as anaesthetists may have altered their techniques in offering opioid-sparing or multimodal analgesic techniques to minimise complications.\(^\text{[12]}\)

The strengths of this study include a large sample size with clear follow-up of postoperative complications. We were also able to account for the type of anaesthesia administered, unlike other large cohort studies. In addition, the study included patients who were started on CPAP therapy preoperatively, which avoided starting CPAP therapy postoperatively in CPAP-naïve patients and thus allowing for better tolerability to CPAP therapy. Finally, it was possible
to account for the adherence to CPAP therapy and analyse postoperative complications per protocol to evaluate the true efficacy of CPAP therapy.

Limitations include the absence of PSG for confirmation of OSA, resulting in a lack of homogeneity in the population with regard to the severity of OSA. However, PSG is unlikely to be accessible to all patients at preoperative evaluation and the design of this study was based on this pragmatic understanding of studying patients with unrecognised OSA. In addition, the use of intraoperative opioids was not assessed and this could compound the incidence of respiratory complications. However, the use of opioids could be hard to analyse as a variety of surgical procedures were performed.

CONCLUSION

In conclusion, our findings suggest that when analysed per protocol, perioperative CPAP therapy was effective in preventing cardiorespiratory complications in patients who were compliant with the CPAP therapy. However, poor adherence to CPAP therapy was a barrier to effective treatment. Prospective studies could be performed to assess strategies to increase adherence to CPAP therapy.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Chung F, Memtsoudis SG, Ramachandran SK, Nagappa M, Opperman M, Cozowicz C, et al. Society of anesthesia and sleep medicine guidelines on preoperative screening and assessment of adult patients with obstructive sleep apnea. Anesth Analg 2016;123:452-73.
2. Ryan S, Taylor CT, McNicholas WT. Systemic inflammation: A key factor in the pathogenesis of cardiovascular complications in obstructive sleep apnea syndrome? Postgrad Med J 2009;85:693–8.
3. Wang CA, Palmer JR, Madden MO, Cohen-Levy W, Vakharia RM, Roche MW. Perioperative complications in patients with sleep apnea following primary total shoulder arthroplasty: An analysis of 33,366 patients. J Orthop 2019;16:382–5.
4. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157–63.
5. Tan A, Cheung YY, Yin J, Lim WY, Tan LW, Lee CH. Prevalence of sleep-disordered breathing in a multiethnic Asian population in Singapore: A community-based study: Sleep-disordered breathing in Singapore. Respirology 2016;21:943–50.
6. Lee RW, Vasudavan S, Hui DS, Prvan T, Petocz P, Darendeliler MA, et al. Differences in craniofacial structures and obesity in Caucasian and Chinese patients with obstructive sleep apnea. Sleep 2010;33:1075–80.
7. Perioperative Management of patients with obstructive sleep apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: An updated report by the American Society of Anaesthesiologists Task Force on perioperative management of patients with obstructive sleep apnea. Anaesthesiology 2014:120:268–86.
8. Solanki SL, Karan N, Parab SY. Obstructive sleep apnoea and its knowledge and attitude among Indian anaesthesiologists - A survey study. Indian J Anaesth 2019;63:648-52.
9. Chan MT, Wang CY, Seet E, Tam S, Lai HY, Chew EFF, et al. Association of unrecognized obstructive sleep apnea with postoperative cardiovascular events in patients undergoing major noncardiac surgery. JAMA 2019;321:1788–96.
10. Mathangi K, Mathews J, Mathangi CD. Assessment of perioperative difficult airway among undiagnosed obstructive sleep apnoea patients undergoing elective surgery: A prospective cohort study. Indian J Anaesth 2018;62:538-44.
11. Palm A, Midgren B, Theorell-Haglöw J, Ekström M, Ljunggren M, Janson C, et al. Factors influencing adherence to continuous positive airway pressure treatment in obstructive sleep apnea and mortality associated with treatment failure - A national registry-based cohort study. Sleep Med 2018;51:85-91.
12. Liao P, Yegneswaran B, Vairavanathan S, Zilberman P, Chung F. Postoperative complications in patients with obstructive sleep apnea: A retrospective matched cohort study. Can J Anaesth 2009;56:819–28.
13. Memtsoudis SG, Cozowicz C, Nagappa M, Wong J, Joshi GP, Wong DT, et al. Society of anesthesia and sleep medicine guideline on intraoperative management of adult patients with obstructive sleep apnea. Anesth Analg 2018;127:967–87.