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ORIGINAL ARTICLE

Respiratory Depression Following Ambulatory Urogynecologic Procedures: A Retrospective Analysis

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Abstract

Objective: To assess the rate of postanesthesia respiratory depression (RD) and test for potential associations with clinical characteristics of patients undergoing urogynecologic procedures at ambulatory surgical centers (ASCs). Postanesthesia RD is poorly characterized for patients undergoing urogynecologic procedures in ASCs.

Patients and Methods: Health records of adult patients undergoing urogynecologic procedures at an ASC from July 1, 2010, through December 31, 2015, were abstracted. Cases complicated by RD were identified, and analyses of risk factors were performed with generalized estimating equations (GEE).

Results: During the study time frame, 9105 patients underwent 9141 procedures, of which RD complicated 221 cases (mean [95% confidence interval (CI)] complication rate per 100 cases, 2.4 [2.1-2.8]). Risk increased with advancing age, male sex, obstructive sleep apnea (OSA), morbid obesity, and use of volatile anesthetics and airway secured. Patients with RD had longer anesthesia recovery (median [interquartile range], 135 [110-166] vs 105 [80-138] minutes; $P<.001$). Within 48 postprocedural hours, 290 ED visits or hospitalizations occurred, but this risk was not increased by RD (adjusted odds ratio [95% CI], 0.62 [0.30-1.26]; $P=.12$).

Conclusion: Postanesthesia RD after ambulatory urogynecologic procedures delay anesthesia recovery but are not associated with later complications. Patients with OSA or having other conditions related to OSA, or both, are at higher risk for RD.

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In the hospital setting, we have observed a strong association between episodes of postanesthesia respiratory depression (RD) and later development of postoperative pulmonary complications.[1-4] For example, patients who had episodes of RD in the postanesthesia care unit (PACU) had a 5-fold higher risk for receiving naloxone after PACU discharge to reverse opioid-induced RD or oversedation.[1,4] This association was even stronger for patients at risk for obstructive sleep apnea (OSA).[2,5]

Postoperative RD has not been well studied for the period after ambulatory surgery.[6] A systematic review of the potential effect of OSA on ambulatory surgical outcomes found 7 relevant studies and did not find an association between OSA and adverse anesthetic outcomes.[6] However, 2 of these studies reported that ambulatory surgical patients with, or at risk for, OSA had increased rates of transient oxyhemoglobin desaturations or supplemental oxygen requirements compared with patients who did not have OSA.[7,8] It is not clear whether these findings were due to postoperative RD *per se* or to other potential causes that may contribute to low oxyhemoglobin saturation after anesthesia and surgery. On the basis of that systematic review, a consensus statement by the Society of Anesthesia and Sleep Medicine asserted that "studies evaluating perioperative outcome in patients with OSA undergoing ambulatory surgery are sparse and of limited quality."[6]

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To our knowledge, no study has examined whether postoperative RD is a risk factor for adverse outcomes following ambulatory surgery.

Our institution has a distinctive practice in which patients in anesthesia recovery are assessed continuously for well-defined episodes of RD.[2,5] Importantly, the episodes are recorded in a systematic manner that facilitates accurate identification through use of electronic data abstraction software.[9] These techniques have allowed us to conduct studies of RD during anesthesia recovery in large cohorts of in-hospital surgical patients.[1,4,10,11]

In the current study, we evaluated RD following urogynecologic procedures at our institutional ambulatory surgical centers (ASCs). This cohort was selected because the procedures require general anesthesia or deep sedation[12] and thus potentially carry higher risk of RD than procedures that require less sedation (eg, cataract surgery) or are performed with regional anesthesia (eg, knee arthroscopy). The primary aims of this study were to determine the rate of RD during anesthesia recovery and to assess potential associations between this complication and patient and procedural characteristics. A secondary aim was to identify patients who required postoperative ED visits or hospitalizations following their procedures and to determine whether an association exists between these unplanned hospital visits and RD during anesthesia recovery.

METHODS AND MATERIALS

The Mayo Clinic Institutional Review Board approved this study (protocol number 16-004234; June 7, 2016). Consistent with Minnesota Statute 144.295, all patients in this study provided prior authorization for research use of their health records.

Study Setting

At our institution, 3 distinct ASCs collectively have 31 surgical and procedural suites. A supervising anesthesiologist is present at all times and evaluates all patients preoperatively. The anesthesiologist also is available to assist during perioperative and postoperative management. The ASC in-room anesthesia providers are certified RN anesthetists. After the procedure, patients are extubated in the procedure room and then undergo phase I and phase II anesthesia recovery under the care of an RN. During anesthesia recovery, nurses continuously monitor patients for signs of RD, defined as the occurrence of any of 4 types of respiratory-specific events: hypoventilation (3 episodes of <8 respirations per minute), apnea (episode of apnea ≥10 seconds), hypoxemia (3 episodes of oxyhemoglobin desaturations measured by pulse oximetry [oxygen saturation as measured by pulse oximetry {SpO_2} <90% with or without nasal cannula]), and pain/sedation mismatch. The last type is defined as a Richmond Agitation-Sedation Score[13] of −3 to −5 and a numeric pain score greater than 5 (scale, 0 to 10 [10, worst pain imaginable]).[2,5] Readiness for discharge is determined with widely used criteria.[14]

Study Design and Patient Selection

This retrospective study evaluated adult patients who underwent urogynecologic procedures under anesthesia care from July 1, 2010, through December 31, 2015, at our ASCs. Medical, surgical, and anesthesia records were electronically abstracted with use of previously described proprietary software.[9] PACU records were examined for the occurrence of RD, defined as a nursing-diagnosed respiratory-specific event.[2,5] In addition, a case was considered to be complicated by RD when a patient required unplanned reintubation or either an application of noninvasive positive pressure devices for RD or administration of naloxone or flumazenil, or both. Patient and procedural characteristics were assessed, along with their potential associations with RD, through a multivariable model. The determined outcomes included ED visit or hospitalization, or both, within 48 hours of the procedure and death within 30 days.

Data Abstraction

Presurgical variables included patient age; sex; morbid obesity (body mass index [BMI] ≥40 kg/m^2); history of OSA (preoperative screen was not performed consistently throughout the timeframe, thus results not included); past history of cardiovascular disease, pulmonary disease, or diabetes mellitus, or a combination; and home use of opioid analgesics or benzodiazepines, or both. Anesthetic and surgical records were reviewed for procedure type, categorized on anatomic location: cystoscopy, nonlaparoscopic

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uterine procedures (eg, dilatation and curettage, hysteroscopy procedures), prostate procedures, procedures on external genitalia, uterine laparoscopic procedures, neurostimulatory procedures, and extracorporeal shockwave lithotripsy) and duration; airway type (secured [endotracheal intubation or laryngeal mask airway] vs native airway); use of volatile anesthetics; dose of opioid medication (converted to intravenous morphine equivalents with use of the standard formula)[15,16]; and use of midazolam, ketamine, nondepolarizing neuromuscular drugs, and ketorolac. The PACU course was abstracted for duration of phase I recovery, episodes of respiratory depression, and the administered medications. Outcomes were determined, including an ED visit or hospitalization, or both, within 48 hours of the procedure and the 30-day mortality rate. All charts of patients who were identified as having had postoperative ED visits, hospitalization, or death underwent manual review of the event.

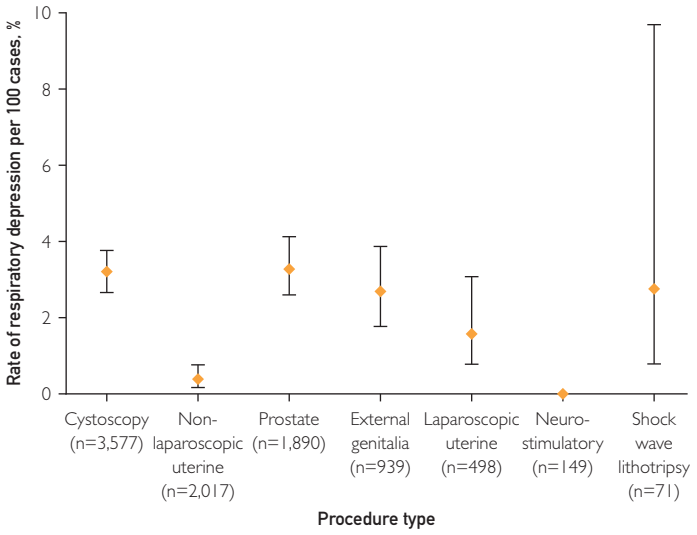

FIGURE. Incidence of respiratory depression following ambulatory urologic and gynecologic procedures under anesthesia. **Diamonds** indicate point estimates; **error bars** indicate the upper and lower bounds of the 95% confidence intervals.

Statistical Analysis

Data are presented as mean (standard deviation [SD]) or median (interquartile range [IQR]) for continuous variables and as number (percentage) for categorical variables. The primary end point was RD. In addition to univariate analyses, multivariable analysis was performed to assess potential associations between RD and patient and perioperative characteristics. Analyses were performed with generalized estimating equations (GEE) using a logit link function with robust variance estimates. Characteristics assessed as potential explanatory variables were determined by our previous investigations of postoperative RD.[10,11] All variables were included in a single multivariable model (ie, no statistical variable selection technique was used). To accommodate the possibility that the relationship between continuous variables and RD was nonlinear, we treated continuous variables categorically with categories defined to represent approximately quartiles or quintiles of the given variable.

To determine if rates of RD varied following different 7 procedure types, pairwise differences between groups were assessed using χ^2 tests with Bonferroni correction used to control for type 1 error from multiple comparisons.

We previously have found strong associations between RD during anesthesia recovery and adverse outcomes following in-hospital operations.[1,3,4] We performed secondary analyses to assess for a possible association between RD and postoperative ED visits or hospitalization.

Two-tailed P values less than .05 were considered statistically significant. Statistical analyses were performed with JMP Pro software version 13.0.0. (SAS Software Inc, Cary, NC).

RESULTS

In the study time frame, 9105 patients underwent a total of 9,141 urogynecologic procedures at our ASCs. The most commonly performed procedures were cystoscopy (n=3577 [39.1%]), nonlaparoscopic uterine procedures (n=2017 [22.1%]), prostate procedures (n=1890 [20.7%]), procedures on external genitalia (n=939 [10.3%]), uterine laparoscopic procedures (n=498 [5.4%]), neurostimulatory procedures (n=149 [1.6%]), and extracorporeal shockwave lithotripsy (n=71 [0.8%]).

Episodes of RD were recorded for 221 cases, yielding a mean (95% CI) complication rate of 2.4 (2.1-2.8) per 100 cases. These cases had the following types of episodes: 158 documented desaturations; 58 hypoventilation; 57

TABLE. Respiratory Depression During Anesthesia Recovery Following Ambulatory Urogynecologic Procedures

Patient Characteristics[a]	Respiratory depression (n=221)	No respiratory depression (n=8920)	*P* Value	Odds Ratio (95%CI)	*P* Value
Age, mean (SD), years	65.6 (12.1)	58.4 (16.7)	<.001		.001
<50				Reference	
50-59				2.48 (1.40-4.41)	
60-69				2.75 (1.57-4.81)	
≥70				2.98 (1.70-5.22)	
Male sex	191 (86.4)	4,713 (52.8)	<.001	3.73 (2.43-5.73)	<.001
Morbid obesity[b]	31 (14.0)	489 (5.5)	<.001	2.02 (1.25-3.25)	.014
Obstructive sleep apnea	100 (45.2)	1,074 (12.0)	<.001	3.68 (2.68-5.04)	<.001
Cardiovascular disease	42 (19.0)	758 (8.5)	<.001	1.26 (0.85-1.87)	.28
Diabetes mellitus	62 (28.7)	1,017 (11.8)	<.001	1.39 (0.98-1.96)	.08
Pulmonary disease	28 (12.7)	961 (10.7)	.51	0.82 (0.52-1.27)	.34
Home opioids	132 (59.7)	4,063 (45.6)	<.001	1.14 (0.85-1.53)	.38
Home benzodiazepine	18 (8.1)	811 (9.1)	.45	0.80 (0.47-1.36)	.37
Surgical duration, mean (range), min	40 (23-69)	25 (15-50)	<.001		.89
<15				Reference	
15-29				1.23 (0.76-2.00)	
30-44				1.29 (0.76-2.17)	
45-59				1.24 (0.70-2.19)	
≥60				1.24 (0.74-2.07)	
Anesthesia					
Airway management			<.001		
Native	18 (8.1)	2194 (24.6)		Reference	
Secured	203 (91.9)	6726 (75.4)		2.86 (1.68-4.86)	<.001
Use of volatile anesthetics	129 (58.4)	3,713 (41.6)	<.001	1.50 (1.12-2.03)	.006
Medications					
Opioids, mean (range), IVME mg[c]	11.7 (10.0-16.7)	10 (5.0-13.3)	<.001		<.001
<5				0.98 (0.38-2.55)	
5-9				Reference	
10-14				1.86 (1.24-2.80)	
≥15				2.47 (1.57-3.91)	
Midazolam	17 (7.7)	742 (8.3)	.74	1.48 (0.89-2.46)	.19
NDMR	17 (7.7)	679 (7.6)	.95	1.03 (0.59-1.78)	.92

[a]Values are presented as number and percentage of patients unless specified otherwise.
[b]Morbid obesity is defined as body mass index ≥40 kg/m^2.
[c]The most frequently used opioid in this cohort was fentanyl (n=8919; 97.6%).
IVME = intravenous morphine equivalents; NDMR = nondepolarizing muscle relaxant.

apnea; and 38 pain-sedation mismatch. Rates of RD by procedure type are presented in the Figure. Rates of RD were lower following nonlaparoscopic uterine procedures compared with cystoscopy, external genitalia, and prostate procedures ($P<0.001$ for all comparisons, Bonferroni threshold = 0.05/21=0.0024). The median Charlson Comorbidity Index scores were higher among those patients who had RD (5 [3, 7]) than those who did not (4 [2, 6]), $P<0.001$). The Table provides comparisons of clinical characteristics among patients with and without postoperative RD.

Anesthesia recovery was longer for cases complicated with RD (median [IQR], 135 [110-166] minutes vs 105 [80-138] minutes; $P<.001$). Four patients among these cases received naloxone in the PACU to reverse opioid-induced RD, but no unplanned tracheal reintubations or application of noninvasive positive pressure ventilation devices occurred. In 2 cases, naloxone was administered to

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facilitate return of respiration and tracheal extubation. The other 2 patients had been extubated but then became unresponsive—1 patient required bag-mask ventilation—but they recovered promptly after administration of naloxone.

Within the first 48 postprocedural hours, 290 ED visits (n=123) or hospitalizations (n=172) occurred (mean [95% CI] rate per 100 cases, 3.2 [2.8-3.6]). Ten visits or hospitalizations occurred for patients who had RD during anesthesia recovery. The reason was related to the surgical procedure for 8 patients: 1 patient was admitted because the patient had no responsible caretaker at home, and 1 patient was admitted overnight for observation following postoperative apnea. This latter patient was a frail (BMI, 15 kg/m^2) 80-year-old woman who underwent a cystoscopy and whose history included chronic obstructive lung disease, congestive heart failure, and OSA treated with a continuous positive airway pressure (CPAP) device. She did not bring her CPAP device to the ASC. No other ED visits or hospitalizations (n=280) were related to RD (Supplemental Table, available online at https://www.mcpiqojournal.org).

A secondary analysis was performed to assess whether RD during anesthesia was associated with postoperative ED visits or hospitalizations. No evidence was observed for a potential association (unadjusted odds ratio [OR] [95% CI], 1.31 [0.67-2.54]; *P*=.44; and adjusted [for clinical and procedural characteristics] OR [95% CI], 0.62 [0.30-1.25]; *P*=.12). Eleven patients died within 30 days. Of these cases, 9 deaths were related to cancer, 1 to pulmonary embolism at 2 weeks postprocedure, and 1 to an unknown cause at 3 weeks postprocedure. No deaths occurred among the patients who had postoperative RD.

DISCUSSION

Our main finding was that the rate of RD among outpatients at our ASCs was much lower for urogynecologic procedures than for inpatient laparoscopic procedures (153 per 1000 cases)[10] and elective joint arthroplasty (237 per 1000 cases).[11] We believe that the lower rates of RD in the current study are likely due to the less invasive nature of our ASC procedures and therefore the smaller requirement for opioids or other respiratory depressive medications.[10,11] Further, patients with higher disease burden (and thus higher risk) could be preferentially scheduled to undergo their procedures in hospital settings.

Comparison of our rate of RD with other studies after ambulatory surgery is difficult because of the different criteria, cohort characteristics *vis-à-vis* patient and procedural variables, and different definitions of ambulatory surgery. For example, Kurrek et al[7] reported that 29.8% of patients had transient oxyhemoglobin desaturations (SpO_2 ≤93%) after laparoscopic gastric banding. Their much higher rate is multifactorial in that all study participants were undergoing weight-loss procedures (average BMI, 43 kg/m^2), had increased rates of OSA (31%), and were undergoing more extensive surgical procedures. Finally, our definition of oxyhemoglobin desaturation was more stringent (SpO_2 of <90%). Similarly, in a series of patients undergoing orthopedic operations with regional anesthesia, Liu et al[17] reported a hypoxemia rate of 34%. However, all patients in that cohort had OSA (54% treated with CPAP) and were monitored overnight in the PACU, and hypoxemia was defined as a SpO_2 of <95%.

In the current study, we relied on nursing documentation to capture the cases complicated by respiratory depression.[2,5] We have used this definition in previous studies of patients undergoing in-hospital operations and have found clinically relevant associations with these episodes and later adverse outcomes.[1,2,4]

Our analysis of clinical factors associated with RD during anesthesia recovery found strong associations with male sex, OSA, morbid obesity, and increasing age, which may all be interrelated. We have observed that similar patient features carry increased risk of postoperative RD among hospital surgical patients.[1,3,4,10,11] As expected, anesthetic variables suggestive of more extensive procedures (ie, secured airway, greater opioid use, and use of volatile anesthetic agents) were associated with increased risk of RD. The different rates of RD among the different procedure types followed the observed association with RD and patient sex; prostate procedures had the highest rate (male-only procedures) and nonlaparoscopic uterine procedures (female-only procedures) had a lower rate (Figure).

At our institution, RD during anesthesia recovery in the hospital setting was strongly associated with further respiratory complications (eg, intensive care unit admission for new respiratory indications, pneumonia, need for noninvasive ventilatory support), including opioid-induced RD that required reversal with naloxone.[1,2,4] In the current cohort, the ASC patients who had RD had longer anesthesia recovery times. Also, 4 patients required naloxone, and 1 was admitted to the hospital because of recurrent apneic episodes. However, we observed no cases of severe RD following discharge from the ASCs. These findings are similar to the systematic review of outcomes of patients with OSA undergoing ambulatory procedures in which patients with OSA had higher likelihood of postoperatively transient desaturations or had greater supplemental oxygen requirements, or both, but were not at increased risk for serious morbidity or death.[6] A recent prospective observation trial of patients with and without OSA undergoing ambulatory surgery offered reassurance that sleep parameters did not change significantly in the postoperative period.[18]

In the current study, we reviewed all patients who had ED visits or hospitalizations within the first 48 postoperative hours. Less than 15% of the cases were related to unstable medical conditions (eg, chest pain) and not to the surgical procedure (Supplemental Table). Of the 8 unique ED visits or hospitalizations related to pulmonary causes, only 1 was due to RD. The involved patient was admitted directly from the ASC to the hospital. Of the 11 deaths, cause of death was known in 10 cases, none of which was from RD. Although the cause of the eleventh death is unknown, the death occurred 3 weeks following the procedure and therefore was not likely due to RD related to the anesthesia.

Limitations

This report has all the inherent limitations of a retrospective study design. The major limitation is that during the study time frame, the ASC screening process for OSA was not documented in a manner in which it could be retrieved through electronic data-abstraction techniques. This detail is important because OSA is often undiagnosed, and undiagnosed OSA is common among ambulatory surgical patients.[8] Unaccounted OSA could add bias to our results and could account in part for the association between sex and RD because OSA rates are higher among men than women.[19] In this cohort, patients were considered to have OSA if it was diagnosed at our institution or if they reported a history of this condition. Our definition of RD is specific to our institution, which could affect the generalizability of our results.

Another limitation is that our institution is somewhat distinctive because it is a major referral center located outside a major population center. Many patients travel several hours to our institution to undergo procedures and then return home later the same day. Thus, some patients may have required an ED visit or hospitalization outside our institution, and these adverse outcomes were not captured in our audit. Further, even though we did not encounter increased risk of adverse outcomes following RD, our study may not have been sufficiently powered to establish safety from rare adverse events. For example, we previously observed that the rate of dangerous RD after PACU discharge to standard surgical wards (defined as naloxone administration) to be approximately 1 per 1000 surgical procedures.[1,4] Thus, the current study, although representative of a relatively large cohort, would have inadequate size to establish safety meaningfully.

We urge caution in interpreting the lack of association RD and adverse outcomes and believe it prudent, when encountering a patient with postoperative RD at an ASC, to delay discharge from the facility until effects of residual sedation have dissipated or, if persistent, admit the patient to the hospital (as was done with our patient who had recalcitrant apnea).

CONCLUSIONS

RD during anesthesia recovery following urogynecologic procedures at our ASCs was less frequent than during anesthesia recovery from in-hospital procedures. Clinical features associated with OSA (ie, male sex, morbid obesity, and older age) and with OSA itself were associated with increased risk of RD, as were features associated with more extensive procedures. Unlike respiratory depressive episodes following in-hospital procedures, no association was observed between RD during anesthesia recovery and increased risk of postoperative complications. However, this

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observation must be interpreted cautiously, and we believe that it is prudent to delay the discharge of patients with RD until they are deemed able to be dismissed safely.

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SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at https://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for all data.

Abbreviations and Acronyms: **ASC** = ambulatory surgical center; **BMI** = body mass index; **CPAP** = continuous positive airway pressure; **IQR** = interquartile range; **OR** = odds ratio; **OSA** = obstructive sleep apnea; **PACU** = postanesthesia care unit; **RD** = respiratory depression; **SpO_2** = oxygen saturation as measured by pulse oximetry

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Potential Competing Interests: Dr Weingarten serves as a consultant to Medtronic in the role as chairman of the Clinical Endpoint Committee for the Prodigy Trial and has received research support from Respiratory Motion, Inc (study equipment) and unrestricted investigator-initiated grants from Merck & Co (active) and Baxter International (completed).

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