Operative Gynecological Laparoscopy Under Conscious Sedation

Maurizio Rosati, MD, Silvia Bramante, MD, PhD, Fiorella Conti, MD, Antonella Frattari, MD, Maria Rizzi, MD, Robert A. Roman, MD

ABSTRACT

Background and Objectives: Operative laparoscopy is generally performed under general anesthesia. Local anesthesia and conscious sedation may be useful in select short procedures. In the present study, we evaluated safety and efficacy of operative laparoscopy under conscious sedation.

Methods: Retrospective observational study evaluating patients undergoing gynecologic laparoscopy. Laparoscopy under conscious sedation was performed for each patient with umbilical direct insertion of a 12-mm port, followed by 2 ancillary ports at 1 cm medially to the anterior superior iliac spine. Conversion to conventional laparoscopy or laparotomy was recorded. Conscious sedation was obtained using Remifentanil and Propofol, administered by an infusion system based on pharmacokinetic and pharmacodynamic models. Local anesthesia was administered at port insertion sites and for paracervical block. Pain intensity was evaluated with the Visual Analog Scale (VAS). Adverse events and drug concentrations throughout the procedure were retrieved.

Results: Our study population included 166 patients. They underwent laparoscopic unilateral versus bilateral salpingo-oophorectomy, ovarian cystectomy, bilateral salpingo-oophorectomy and omentectomy for a borderline ovarian tumor, myomectomy; or underwent surgery for unexplained infertility evaluation, pelvic pain, staging of ovarian cancer. Mean duration of pneumoperitoneum was 22.3 ± 7.2 min. Rate of conversion to laparoscopy under general anesthesia was 17/166 (10.2%) and there were only 3 cases of patients with low tolerability to the procedure. No severe adverse events occurred. Hospital discharge occurred in all unconverted cases after 6 to 18 h.

Conclusions: Operative laparoscopy under conscious sedation and local anesthesia appears to be a feasible technique in gynecologic surgery with no adverse patient outcomes.

Keywords: Conscious sedation, Laparoscopy, Minimally invasive surgery.

Unit of Obstetrics and Gynecology, Santo Spirito Hospital, Pescara, Italy (Drs Rosati, Bramante, and Conti).

Unit of Anaesthesia and Intensive Care, Santo Spirito Hospital, Pescara, Italy (Drs Frattari and Rizzi).

Camran Nezhat Institute, Palo Alto, CA, USA (Dr Roman).

Address correspondence to: Maurizio Rosati, MD, Santo Spirito Hospital, Via Fonte Romana 8, Pescara, Italy, 65124, Telephone: +39854252302, Fax: +39854252428, E-mail: maxmach@hotmail.com

INTRODUCTION

In gynecologic surgery, operative laparoscopy is commonly performed under general anesthesia to ensure adequate abdominal muscle relaxation for induction of pneumoperitoneum (PNP), allow safe placement of laparoscopic ports, and assist with bowel mobilization during Trendelenburg position.[1] Endotracheal intubation is beneficial to avoid aspiration and respiratory complications secondary to the induction of general anesthesia and PNP.[1] However, laparoscopy has been performed on awake patients with administration of local anesthesia at the surgical sites for postoperative pain management.[2–6] With only local anesthesia, the abdominal cavity is not anesthetized, and patients can experience a vagal response and discomfort. To compensate, the surgeon needs to minimize peritoneal insufflation with reduced

intraperitoneal pressure and time of PNP to avoid patient discomfort.[2–6]

The development of videolaparoscopy by Dr. Camran Nezhat, using optics and instruments smaller than 5 mm in diameter, has facilitated conscious procedures with improved visualization and decreased surgical trauma.[4–7] However, other limiting factors such as patient anxiety and pain tolerance with port insertion and PNP can affect a patient's ability to undergo a conscious procedure.[3] Therefore, conscious sedation is administered as an adjunct with intravenous agents such as opioids or hypnotics to decrease patient pain and anxiety.[8]

It is important for providers to familiarize themselves with the indications, risks, and route of administration of sedatives. From a pharmacokinetic standpoint, it is important that anesthetic drugs have a rapid onset of action, are easy to titrate, provide adequate analgesia, have minimal effects on the cardiovascular and respiratory systems, allow for quick recovery, and cause minimal postoperative nausea and vomiting (PONV).[9–133] At present, no single agent has all of the aforementioned qualities and a combination of different medications are needed to achieve these desired goals.[14–17] Moreover, available infusion systems, based on pharmacokinetic and pharmacodynamic models, may help to maintain and adjust depth of sedation through accurate monitoring and prediction of drug concentrations at the effect site and to minimize adverse events.[18–24]

Surgical technique must also be adjusted during laparoscopy with conscious sedation; surgeons must consider that, in absence of general anesthesia, there is no suppression of bowel peristalsis, and a higher hypothetical risk of bowel injury.[25]

Rosati et al. recently published a case series with 5 patients undergoing bilateral salpingo-oophorectomy under conscious sedation.[26] In that report, we labeled the sedation procedure Operative Laparoscopy in Conscious Sedation (OLICS). This retrospective observational study is focused on the feasibility and safety profile in a larger cohort of selected patients undergoing operative laparoscopy under conscious sedation with administration of local anesthesia.

METHODS

Data Collection

Patient data was retrospectively collected on 166 patients undergoing operative laparoscopy using local anesthesia and conscious sedation between July 2015 and July 2019. Patient demographics, indication for surgery, duration of PNP, and duration of surgery were collected. We recorded the proportion of patients with adverse intraoperative events (including hypotension and hypoxemia), rate of conversion from conscious sedation to general anesthesia, and postoperative complications. Propofol and Remifentanil concentrations at specific operative time points (injection of local anesthesia, port insertion, PNP induction, and central surgical time) were collected if available. Patient satisfaction scores also were collected.

Conversion to standard laparoscopy under general anesthesia or laparotomy was recorded.

Final approval of retrospective data collection was obtained from the local ethics committee on April 28, 2016. All patients signed an informed consent to undergo anesthesia at our unit, including permission to start the procedure under local anesthesia and conscious sedation with the option to switch to general anesthesia in the event of poor patient tolerance or surgical indication. A full explanation of the procedure and events surrounding surgery was provided at time of consent.

Sedation Procedures

All subjects underwent appropriate preoperative fasting. On arrival in the operating room (OR), an intravenous catheter was placed and normal saline was given at the rate of 4 ml/kg/h. One to 2 mg of Midazolam was administered intravenously unless contraindicated. The Dräger anesthesia systems (Zeus) and monitoring systems (Infinity C700) were used in combination with B. Braun pumps connected to the 2 dimensional and time trends display, Smart Pilot® View (Drager, Lubeck, Germany) (**Figure 1**). Propofol and Remifentanil concentrations were manually set. The Smart Pilot® View displays prospectively calculated concentrations at the effect site using advanced mathematical modelling algorithms based on pharmacokinetic and pharmacodynamic models, Schneider for Propofol[27–28] and Minto for Remifentanil,[29–30] and depicts the interactions between the two drugs.[31–32] It also displays the stage of sedation the patient is currently at and will be.[2,31] Beyond the parameters measured (electrocardiography, heart rate, blood pressure, oxygen saturation, capnography) and depth of sedation by Bispectral Index (BIS),[33–34] an instant numerical calculation (0–100) of the synergistic effects of hypnotics and analgesics, called the Noxious Stimulus Response Index (NSRI), was reported.[35–37]

Infusions were set according to the patient's age and body weight. The rate of Propofol infusion ranged between 2 to
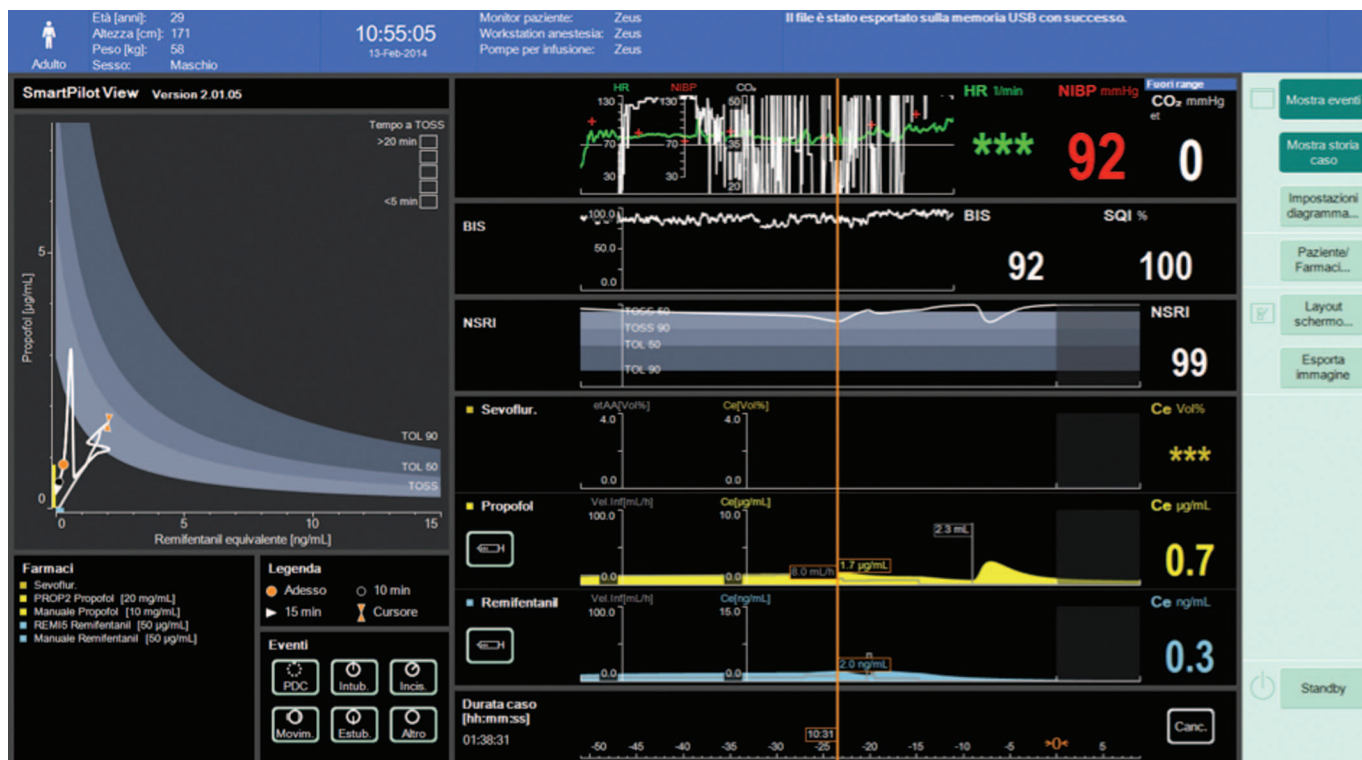
Figure 1. The Smart Pilot® View displays prospective calculated concentrations at the effect site.

4 mg/kg/h, while the rate of Remifentanil infusion ranged between 0.05 to 0.1µg/kg/min. Local anesthesia was administered both at the cervix and port insertion sites, generally after 5 min of infusion. The infusions of Propofol and Remifentanil were stepwise titrated to achieve the desired level of sedation and analgesia. Importantly, the depth of sedation was increased at certain stages of surgery, such as port insertions and peritoneum distension, by varying the infusion rates of each drug. Supplemental oxygen via a face mask was provided at deeper levels of sedation as needed. Effect site concentration of Propofol and Remifentanil, BIS, NSRI, heart rate, systolic blood pressure, and oxygen saturation were collected at baseline, during administration of local anesthesia, during port insertion, during PNP induction, at the start of the procedure, and mid-surgery.

Pain was quantified using a VAS from awake patients at the time of local anesthesia administration, during port insertions and induction of PNP, at the end of the procedure, and 30 min postoperatively. Other parameters (BIS and NSRI) were collected to monitor the patient during deep sedation. Patients who met the Post-Anesthetic Discharge Scoring System (PADSS) discharge criteria were transferred directly from the OR to a ward.[38] Our routine

postoperative analgesia consisted of Paracetamol 1000 mg IV, Ketorolac 30 mg IV, and Tramadol 50 to 100 mg IV. Patients also received Ondansetron 4 mg and Ranitidine 50 mg with all doses titrated according to age.

Surgical Procedures

All surgical procedures were performed by two gynecologic surgeons, M.R. and S.B. Patients were placed in the low lithotomy position with the arms along the body, using warm blankets on the upper body. The abdomen and vagina were gently prepared with warmed betadine solution, and a Foley catheter 14G coated with 1% lidocaine gel was placed in the bladder. One percent Mepivacaine (10 ml) was injected at the 3, 9, and 12 o'clock positions of the cervix, after the surgeon gently pulled the plunger of the syringe to ascertain that the needle was not in a blood vessel. The umbilical area was radially injected with approximately 5 ml of 1% Mepivacaine and 5 ml of 0.5% Levobupivacaine. Ten ml of 1% Mepivacaine and 10 ml of 0.5% Levobupivacaine were later injected at the lateral port sites 1 cm medial to the anterior superior iliac spine bilaterally. Once we achieved adequate regional anesthesia, a 12 mm skin infraumbilical incision was made and a 12 mm cannula was placed using the direct access

technique while gently lifting the anterior abdominal wall.[39–40] The abdomen was insufflated with CO_2 gas at a maximum pressure of 8 mm Hg. A 12 mm laparoscope with an operative channel (Karl Storz GmbH, Tuttlingen, Germany) was used. The patient was placed in a gentle Trendelemburg position (max 15°). In order to obtain one more operative channel, a 90° angle laparoscope was used. One or two ancillary ports were placed, under direct laparoscopic visualization, through 5 mm skin incisions 1 cm medially to the anterior superior iliac spine. Insufflation pressure was 8 mm Hg, for up to 30 min. A grasper was inserted through the right ancillary cannula for manipulation of bowel or adnexa, the suction-irrigator was introduced through the left ancillary cannula and the bipolar forceps were introduced through the operative channel of the laparoscope. Multifunctional instruments, such as the ENSEAL® 45 cm device (Ethicon Endo-Surgery Inc, Cincinnati, OH, USA) or the LigaSure® 44 cm device (Covidien, Dublin, Ireland), inserted through the operative channel of the laparoscope were used as an alternative to standard bipolar forceps in order to optimize timing of the procedures.

Laparoscopies were performed for multiple indications including Breast Cancer (BRCA) 1–2 gene mutation, ovarian cyst, chronic pelvic pain, infertility, borderline ovarian tumor, ovarian cancer, and subserosal myomas. Diagnostic laparoscopy was performed on all patients to evaluate the presence of adhesions, endometriosis, ovarian cysts, and peritoneal carcinomatosis in advanced stage ovarian cancer. Moreover, in all patients with infertility, a chromoperturbation was also performed to evaluate tubal patency, and all patients with chronic pelvic pain underwent laparoscopic pain mapping, during which the patient was able to speak with the surgeon and the anesthesiologist to identify painful trigger points.[41–42] In five patients with pelvic pain, a Laser Uterosacral Nerve Ablation (LUNA) procedure was performed by using a CO_2 laser (Smart Clinic 50w, DEKA, Florence, Italy) attached to the operative laparoscope.

Adhesions and endometriosis were diagnosed in 33 patients with chronic pelvic pain and infertility, and they were ablated by using a CO_2 laser (Smart Clinic 50w, DEKA, Florence, Italy).[43–44] Fifteen infertile patients with polycystic ovarian syndrome underwent ovarian drilling. Salpingo-oophorectomy was performed by using multifunctional instruments, such as the ENSEAL® 45 cm device (Ethicon Endo-Surgery Inc, Cincinnati, OH, USA) or the LigaSure® 44 cm device (Covidien, Dublin, Ireland), inserted through the operative channel of the laparoscope. When necessary, surgical specimens were extracted using a 10 cm endobag inserted through the 12 mm umbilical port while a 5 mm optic was inserted into the 5 mm left cannula.

In case of a borderline ovarian tumor, omentectomy was also performed together with bilateral salpingo-oophorectomy by using the Ligasure® 44 cm device (Covidien, Dublin, Ireland).

Enucleation of ovarian cysts were performed successfully without spillage by using the CO_2 laser (Smart Clinic 50w, DEKA, Florence, Italy). The atraumatic development of the plane between the cyst wall and the ovarian tissue was an important first step. The ovarian cortex was incised by CO_2 laser, using a Kelly forceps as backstop after it was introduced between the capsule and the ovarian cortex. Traction was gently applied to the cyst wall with countertraction on the ovarian cortex. Finally, the unbroken cyst was placed in a 10 cm endobag, as above described, and then extracted. If the specimen was too large to remove through the existing incisions, cyst fluid was aspirated inside the endobag prior to removal.

Laparoscopic myomectomy was performed for subserosal myomas. Vascular pedicles of the myomas were coagulated and cut by using multifunctional devices, while the coagulation of the uterine wall was performed with bipolar forceps. A 10 cm endobag was inserted through the 12 mm umbilical port. The edges of the bag were extracted, removing the cannula through the umbilical incision and extending the diameter of the incision to 2 to 2.5 cm. Surgical specimens were safely morcellated in the endobag using a knife and two Kocher clamps with no spread of surgical specimens into the abdominal cavity.

Finally, laparoscopy was performed to evaluate the ability to resect advanced ovarian cancer according to the Fagotti score or to perform a peritoneal/ovarian biopsy.[45]

Statistical Analysis

Continuous variables were reported as a mean and standard deviation (SD). Categorical variables were reported in frequency and percentage (%). All statistical calculations were performed using the Stata 10.1 Software package (Stata Corp., College Station, TX, USA, 2007).

RESULTS

Between July 2015 and July 2019, 166 patients undergoing laparoscopy under conscious sedation were included in the study. Patient characteristics are summarized in **Table 1**. Mean age was 44.4 ± 12.2 years old (range 27 to 79

Table 1.
Patient Characteristics Included in Our Study

Variable	Mean ± SD or N (%)
Age (yr), mean ± SD	44.4 ± 12.2
Preoperative BMI, mean ± SD	22.8 ± 3.0
ASA class	
1	117
2	47
3	2
Comorbidities	26
Hypertension	16
Diabetes	6
Ascites	4

BMI, body mass index; ASA, American Society of Anesthesiology; PNP, pneumoperitoneum.

years old). American Society of Anesthesiologists (ASA) score was 1 to 3 (70.5% ASA 1, 28.3% ASA 2, 1.2% ASA 3) and mean BMI was 22.8 ± 3.0 (range 18 to 35). The most frequent surgical procedure was laparoscopic bilateral salpingo-oophorectomy (due to presence of BRCA-1 gene mutation, ovarian cysts, ovarian teratoma, or ovarian borderline cancer with omentectomy), followed by laser ablation of endometriosis for infertility or pelvic pain (**Table 2**). Duration of PNP was 22.3 ± 7.2 min, with duration of surgery ranging from 20 to 58 min, which is equivalent to the operative times reported in the literature for the same procedures in conventional laparoscopy.

No surgical postoperative complications occurred in our study, defined as either early (within 30 d) or late (over 30 d) according to the Memorial Sloan Kettering Cancer Center complication scale. Estimated blood loss (EBL) was

Table 2.
Procedures Performed Under Conscious Sedation

Salpingo-oophorectomy (unilateral or bilateral)	74
Salpingo-oophorectomy and omentectomy	1
Enucleation of ovarian cyst	4
Laparoscopic myomectomy	7
Ovarian cancer triage- peritoneal or ovarian biopsies	27
Ovarian drilling	15
Laser ablation of endometriosis	33
L.U.N.A. procedure	5

<100 ml in all cases. No clinically significant hypotensive episodes occurred intraoperatively or postoperatively.

Concentrations of Propofol and Remifentanil and percentages of patients maintaining spontaneous breathing and verbal contact at baseline (T0), port insertions (T1), PNP induction (T2) and central surgical time (T3) are shown in **Figure 2**. Inadequate spontaneous ventilation was related to higher concentrations of drugs infused to manage port insertion and PNP induction and was successfully managed with brief bag-valve-mask ventilation and/or reduction of drug concentrations. All patients were able to speak with the surgeon and/or the anesthetist shortly after lowering the concentration of Propofol and Remifentanil, whenever necessary during the procedure.

Rate of conversion to conventional laparoscopy was 17 out of 166 (10.2%); only 3 conversions were due to low tolerance with the procedure; the other 14 were due to intraoperative findings (**Table 3**). Optimal pain control was reported in all cases, with VAS score <4 when reported. No episodes of PONV occurred. No patients required additional analgesic drugs before discharge. All women reported high to very high satisfaction. PADSS at discharge were all >9. Patients were discharged within 18 h of the procedure in all cases not converted to general anesthesia (mean discharge time 11.5 ± 3.8 h).

DISCUSSION

In the last two decades, the number of gynecologic pathologies that can be surgically treated with laparoscopy under conscious sedation and local anesthesia has greatly increased.[2,3,4,8,46–48] Conscious sedation offers the advantage of the patient being mostly awake or quickly arousable, and breathing spontaneously (**Table 4**); furthermore, fast-track recovery may decrease hospitalization costs.[3,49]

Our group recently published a case series of 5 patients undergoing bilateral salpingo-oophorectomy under conscious sedation [26]. In that report, we labelled the sedation procedure with the acronym OLICS (Operative Laparoscopy In Conscious Sedation), as all 5 patients included were able to follow their surgical procedures on the monitor. Patients could speak with the surgeon and the anesthetist whenever needed such as during pain mapping performed to identify the trigger points of chronic pelvic pain.[26] In the present study, we report a larger patient cohort obtained using the same procedure on patients with different surgical indications. In the current study, a higher level of sedation was required for port
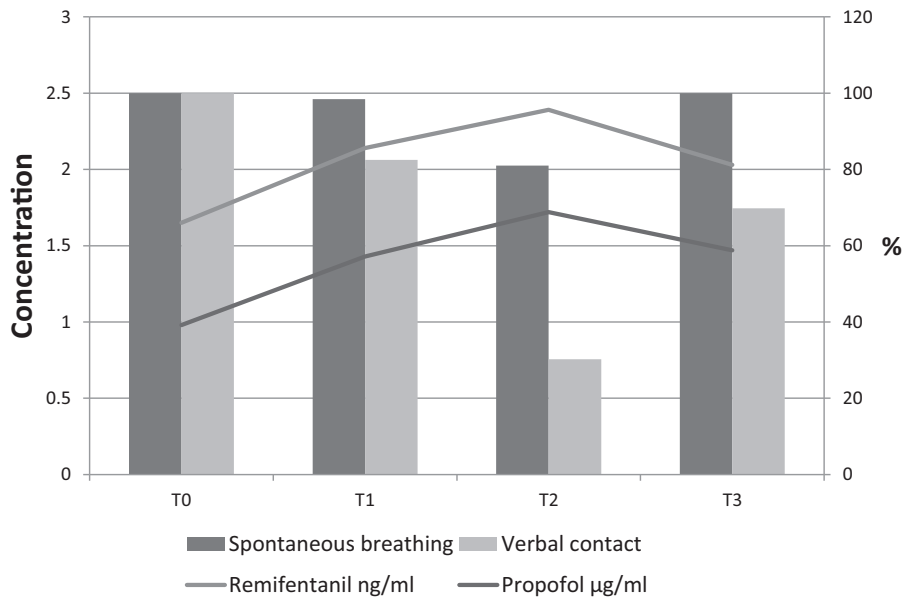
Figure 2. Propofol and Remifentanil effect site concentrations and corresponding percentages of spontaneous breathing and verbal contact.

Table 3.
Indications for Conversion to General Anesthesia

Low tolerance to the procedure	3
Pelvic adhesions	7
Endometriosis treatment	3
Intramural uterine myoma treatment	1
Poor surgeon work space	3
Total	17

insertions and PNP induction. This was carried out, however, without reducing the safety profile of the procedure; therefore, the patients could transition from a conscious sedation to a deeper sedation whenever needed, in accordance with ASA definitions for continuum of depth of sedation.[50–51]

Successful operative laparoscopy under conscious sedation in our series was related to several factors. Most of the patients who underwent OLICS had an ASA 1 to 2, a BMI >25, no history of pelvic surgery, were well-motivated to avoid general anesthesia, and were well-informed about the procedure. To decrease patient anxiety, a full explanation of the procedure and preoperative and postoperative expectations were reviewed with the patient.[52–53] Quality of sedation was important to complete the procedure under conscious sedation. The combination of Propofol as a hypnotic agent and Remifentanil as an an-

algesic agent represented an appealing combination for tailored sedation.[9,13,54–54] Advantages of our procedure include rapid induction, maintenance of anesthesia, rapid emergence, adequate pain control, and adequate sedation that can allow patients to be readily arousable. It lacks unwanted side effects such as nausea, vomiting, and shivering. Combined with low dose Propofol, Remifentanil provides synergistic analgesia with local anesthesia, thereby enhancing patient comfort during the surgical procedure without compromising hemodynamic stability.[55–56] Optimal pain control was obtained in all cases, as documented by the adequate VAS scores obtained at all evaluated time points.

Furthermore, the choice of infusion technique may have been clinically significant and affected patient tolerability of the procedure. In clinical practice, manual infusion of boluses leads to multiple peaks and troughs of drug concentrations, possibly inducing more episodes of cardiovascular and respiratory depression.[19,55] In contrast, infusions based on a Pharmacokinetic/Pharmacodynamic model system provided steady-state drug concentrations that avoided drug overshooting.[21–24,31] In addition to the measured parameters, such as heart rate and blood pressure, the software displays the chronological sequence of the applied pharmaceuticals and their effects in a two-dimensional representation. This means that the anesthesiologist may be aware – like a pilot – at which calculated stage of sedation the patient is and what is the prediction

Table 4.
Continuum of Depth of Sedation. Definition of General Anesthesia and Level of Sedation/Analgesia.

	Minimal Sedation Anxiolysis	Moderate Sedation/Analgesia ("Conscious Sedation")	Deep Sedation/Analgesia	General Anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulation	Purposeful response following repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous Ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular Function	Unaffected	Usually maintained	Usually maintained	May be impaired

for the immediate future.[31,57] Additionally, this device displays the optimal drug concentration ratio for a given effect in the average patient.[57] As a consequence, it appears to be an ideal tool for a safe approach to managing sedation in operative laparoscopy, allowing fast changes of sedation level and analgesia (**Table 4**), to accommodate painful surgical stimuli and specific patient requirements.

However, to make the procedure feasible, expert and fast execution of the surgical technique was key. To minimize stress during the procedure, the ancillary ports were limited to only two (omitting the 10-mm suprapubic cannula typically used in our unit in this type of operation). With the same purpose, the multifunctional devices were helpful instruments, allowing for simultaneous cutting and sealing.[26] Low pressure of PNP (8 mm Hg) and gentle Trendelenburg position (15 degrees) were other key issues for maintenance of spontaneous breathing and minimizing heart complications and patient discomfort. Low pressure PNP may help decrease post-operative abdominal pain, shoulder pain, and PONV.[26,58–60]

On the other hand, careful patient selection criteria is required because of the time constraint associated with conscious sedation (<30 min PNP), which precludes its utilization in cases with longer operational times and surgical complexity. Secondly, in our experience it may be offered only to patients with no prior history of pelvic surgery, BMI <30, and with minimal comorbidities. There is no augmentation in perceived pain levels during bowel, uterine, or tubal manipulation, allowing the surgeon to freely perform surgery. There was no evidence of direct correlation between the operating steps and patient discomfort, whereas it seems to depend more on the depth of sedation. Peristalsis and patient awareness represented a limitation to the surgical procedure in only few cases (**Table 3**), while the majority of conversions to standard laparoscopy were linked to pelvic adhesions, endometriosis treatment, or myomectomy for intramural myoma which prolonged the surgical time.

Our present study highlights that operative laparoscopy with conscious sedation and local anesthesia may be a feasible and safe alternative for patients undergoing low complexity and short-duration gynecological surgery, with improved patient recovery and decreasing hospitalization stay. Future studies should examine the safety and efficacy of operative laparoscopy with conscious sedation and local anesthesia, ideally with as a multicenter trial encompassing several gynecologists, to corroborate our findings.

References:

1. Nezhat CR, Nezhat F, Luciano A, Siegler A, Metzger D, Nezhat CH. Operative Gynecologic Laparoscopy. Principles and Techniques. Anesthetic considerations specific to laparoscopy. Published by McGrow-Hill Inc. 1995:71–73.

2. Palter SF, Olive DL. Office microlaparoscopy under local anesthesia for chronic pelvic pain. *J Am Assoc Gynecol Laparosc.* 1996;3(3):359–364.

3. Gupta L, Sinha S, Pande M, Vajifdar H. Ambulatory laparoscopic tubal ligation: a comparison of general anesthesia with local anesthesia and sedation. *J Anaesth Clin Pharmacol.* 2011; 27(1):97–100.

4. Nezhat C, Nezhat F, Nezhat C, Seidman DS. Operative laparoscopy: redefining the limits. *JSLS.* 1997;1(3):213–216.

5. Demco LA. Patient-assisted laparoscopy. *J Am Assoc Gynecol Laparosc.* 1996;3(Supplement 4):S8.

6. Demco L. Effect of heating and humidifying gas on patients undergoing awake laparoscopy. *J Am Assoc Gynecol Laparosc.* 2001;8(2):247–251.

7. Zullo F, Pellicano M, Zupi E, Guida M, Mastrantonio P and Nappi C. Minilaparoscopic ovarian drilling under local anesthe-

sia in patients with polycystic ovary syndrome. *Fertil Steril.* 2000;74(2): 376–379.

8. Pellicano M, Zullo F, Fiorentino A, Tommaselli GA, Palomba S, Nappi C. Conscious sedation versus general anesthesia for minilaparoscopic gamete intra-fallopian transfer: a prospective randomized study. *Hum Reprod.* 2001;16(11):2295–2297.

9. Urman RD, Kay AD. Moderate and deep sedation in clinical practice. Cambridge, UK: Cambridge University Press; 2012.

10. Servin FS, Billard V. Remifentanil and other opioids. *Handb Exp Pharmacol.* 2008;182:283–311.

11. Hoḧener D, Blumenthal S and Borgeat A. Sedation and regional anesthesia in the adult patient. *British Journal of Anesthesia.* 2008;100(1):8–16.

12. Tobias JD, Leder M. Procedural sedation: a review of sedative agents, monitoring, and management of complications. *Saudi Journal of Anesthesia.* 2011;5(4):395–410.

13. Wang D, Chen C, Chen J, et al. The use of Propofol as a sedative agent in gastrointestinal endoscopy: a meta-analysis. *PLoS One.* 2013;8(1):e53311.

14. Rosow C. Anesthetic drug interaction: an overview. *J Clin Anesth.* 1997;9:S27–S32.

15. Hendricks JFA, Eger EI, Sonner JM, Shafer SL. Is synergy the rule? a review of anesthetic interactions producing hypnosis and immobility. *Anesth Analg.* 2008;107:494–506.

16. Bouillon TW. Hypnotic and opioid anesthetic drug interactions on the CNS, focus on response surface modeling. *Handb Exp Pharmacol.* 2008;182:471–487.

17. Bouillon TW, Bruhn J, Radulescu L, et al. Pharmacodynamic interaction between Propofol and Remifentanil regarding hypnosis, tolerance of laryngoscopy, bispectral index, and electroencephalographic approximate entropy. *Anesthesiology.* 2004; 100(6):1353–1372.

18. Newson C, Joshi GP, Victory R, White PF. Comparison of Propofol administration techniques for sedation during monitored anesthesia care. *Anesth Analg.* 1995;81(3):486–491.

19. Masui K, Upton R, Doufas AG, et al. The performance of compartmental and physiologically based recirculatory pharmacokinetic models for propofol: a comparison using bolus, continuous, and target-controlled infusion data. *Anesth Analg.* 2010; 111(2):368–379.

20. Leslie K, Clavisi O, Hargrove J. Target-controlled infusion versus manually-controlled infusion of propofol for general anesthesia or sedation in adults. *Cochrane Database Syst Rev* 2008; CD006059.

21. Ihmsen H, Schraag S, Kreuer S, Bruhn J, Albrecht S. Target-controlled infusion. Clinical relevance and special features when using pharmacokinetic models. *Anaesthesist.* 2009;58:708–715.

22. Moerman AT, Herregods LL, De Vos MM, Mortier EP, Struys MM. Manual versus target-controlled infusion remifentanil administration in spontaneously breathing patients. *Anesth Analg.* 2009;108:828–834.

23. Struys MM, Sahinovic M, Lichtenbelt BJ, Vereecke HE, Absalom AR. Optimizing intravenous drug administration by applying pharmacokinetic/pharmacodynamics concepts. *Br J Anaesth.* 2011;107(1):38–47.

24. Minto CF, Schnider TW. Contributions of PK/PD modeling to intravenous anesthesia. *Clin Pharmacol Ther.* 2008;84(1):27–38.

25. Demco L. Complications of microlaparoscopy and awake laparoscopy. *JSLS.* 2003;7(2):141–145.

26. Rosati M, Bramante S, Conti F, Rizzi M, Frattari A, Spina T. Laparoscopic salpingo-oophorectomy in conscious sedation. *JSLS.* 2015;19(3). pii:e2015.00031. DOI: 10.4293/JSLS.2015.00031.

27. Schnider TW, Minto CF, Gambus PL, et al. The influence of method of administration and covariates on the pharmacokinetics of propofol in adult volunteers. *Anesthesiology.* 1998;88(5): 1170–1182.

28. Absalom AR, Mani V, De Smet T, Struys MM. Pharmacokinetic models for Propofol defining and illuminating the devil in the detail. *Br J Anaesth.* 2009;103:26–37.

29. Minto CF, Schnider TW, Egan TD, et al. Influence of age and gender on the pharmacokinetics and pharmacodynamics of remifentanil. I. Model development. *Anesthesiology.* 1997;86(1): 10–23.

30. Minto CF, Schnider TW, Shafer SL. Pharmacokinetics and pharmacodynamics of remifentanil. II. Model application. *Anesthesiology.* 1997;86(1):24–33.

31. Cirillo V, Zito Marinosci G, De Robertis E, et al. Navigator and SmartPilot View are helpful in guiding anesthesia and reducing anaesthetic drug dosing. *Minerva Anestesiol.* 2015;Jan 19.

32. Schumacher PM, Bouillon TW, Leibundgut D, Sartori V, Zbinden AM. Anaesthesia advisory display (AAD): real time guidance through the pharmacokinetic and interaction pharmacodynamic relationship during simultaneous administration of multiple drugs. *Anesthesiology.* 2004;101:A504.

33. Bruhn J, Myles SP, Sneyd R, Struys FRM. Depth of anesthesia monitoring: what's available, what's validated and what's next? *Br J Anaesth.* 2006;97:85–94.

34. Sahinovic MM, Absalom AR, Struys MM. Administration and monitoring of intravenous anesthetics. Current Opinion in *Anesthesiology.* 2010;23:734–774.

35. Schumacher PM, Bouillon TW, Leibundgut D, Hartwich V, Luginbuehl M. Time-based online display of a noxious stimulus response index based on pharmacological data. *Anesthesiology.* 2007;107:A17.

36. Luginbuehl M, Schumacher PM, Vereecke H, Heyse B, Struys M. Noxious stimulation response index (NSRI): validation of a novel anesthetic depth index. *Anesthesiology.* 2009;A1602.

37. Luginbühl M, Schumacher PM, Struys M. Noxious stimulation response index: a novel anesthetic state index based on hypnotic-opioid interaction. *Anesthesiology.* 2010:112(4):872–880.

38. Phillips NM, Haesler E, Street M, Kent B. Post-anaesthetic discharge scoring criteria: a systematic review. *JBI Library of Systematic Reviews.* 2011;9(41):1679–1713.

39. Jacobson MT, Osias J, Bizhang R, et al. The direct trocar technique: an alternative approach to abdominal entry for laparoscopy. *JSLS.* 2002;6(2):169–174.

40. Tinelli A, Malvasi A, Mynbaev OA, et al. Bladeless direct optical trocar insertion in laparoscopic procedures on the obese patient. *JSLS.* 2013;17(4):521–528.

41. Demco L. Pain mapping of adhesions. *J Am Assoc Gynecol Laparosc,* 2004;11(2):181–183.

42. Demco LA. Pain referral patterns in the pelvis. *J Am Assoc Gynecol Laparosc.* 2000;7(2):181–183.

43. Demco L. Patient-assisted laparoscopy in the diagnosis and management of endometriosis. *J Am Assoc Gynecol Laparosc.* 1996;3(4 supplement):S8–9.

44. Demco L. Review of pain associated with minimal endometriosis. *JSLS.* 2000;4(1):5–9.

45. Fagotti A, Ferrandina G, Fanfani F, et al. A laparoscopy-based score to predict surgical outcome in patients with advanced ovarian carcinoma: a pilot study. *Ann Surg Oncol.* 2006; 13(8):1156–1161.

46. Demco LA. Effect on negative laparoscopy rate in chronic pelvic pain patients using patient-assisted laparoscopy. *JSLS.* 1997;1(4):319–21.

47. Demco L. Mapping the source and character of pain due to endometriosis by patient-assisted laparoscopy. *J Am Assoc Gynecol Laparosc.* 1998;5(3):241–245.

48. Demco L. Patient-assisted laparoscopy in the diagnosis and management of endometriosis. *J Am Assoc Gynecol Laparosc.* 1996;3(4 supplement): S8–9.

49. Kehlet H, Slim K. The future of fast-track surgery. *Br J Surg.* 2012;99:1025–1026.

50. American Society of Anesthesiologists. Continuum of depth of sedation definition of general anesthesia and levels of sedation/analgesia. October 13, 1999, amended on October 21, 2009. Available at http://www.asahq.org.

51. Continuum of depth of sedation: definition of general anesthesia and levels of sedation/analgesia. American Society of Anesthesiologists www.asahq.org.

52. Yunker A, Steege J. Practical guide to laparoscopic pain mapping. *J Minim Invasive Gynecol.* 2010;17(1):8–11.

53. Demco L. Complications of microlaparoscopy and awake laparoscopy. *JSLS.* 2003;7:141–145.

54. Li M, Mei W, Wang P, et al. Propofol reduces early postoperative pain after gynecological laparoscopy. *Acta Anaesthesiol Scand.* 2012;56(3):368–375.

55. Chan WH, Chang SL, Lin CS, Chen MJ, Fan SZ. Target-controlled infusion of propofol versus intermittent bolus of a sedative cocktail regimen in deep sedation for gastrointestinal endoscopy: comparison of cardiovascular andrespiratory parameters. *J Dig Dis.* 2014;15(1):18–26.

56. Coskun D, Gunaydin B, Tas A, Inan G, Celebi H, Kaya K. A comparison of three different target-controlled remifentanil infusion rates during target-controlled propofol infusion for oocyte retrieval. *Clinics (Sao Paulo).* 2011;66(5):811–815.

57. Brochure SmartPilot?View Dräger. Accessed at www.draeger.com/smartpilotview as of 15th May.

58. Gurusamy KS, Samraj K, Davidson BR. Low pressure versus standard pressure pneumoperitoneum in laparoscopic cholecystectomy. *Cochrane Database of Systematic Reviews.* 2009;15(2): CD006930.

59. Topçu HO, Cavkaytar S, Kokanal K, Guzel AI, Islimye M, Doganay M. A prospective randomized trial of postoperative pain following different insufflation pressures during gynecologic laparoscopy. *Eur J Obstet Gynaecol Reprod Biol.* 2014;182: 81–85.

60. Fletcher SJ. Hemodynamic consequences of high- and low-pressure pneumoperitoneum during laparoscopic cholecystectomy. *Surg Endosc.* 2000;14:596–597.