Automated Closed-Loop Propofol Anesthesia versus Desflurane Inhalation Anesthesia in Obese Patients Undergoing Bariatric Surgery: A Comparative Randomized Analysis of Recovery Profile

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Abstract

Purpose

Precision general anesthesia (GA) techniques that minimizes presence of residual anesthetic and facilitate recovery, are desirable in patients with morbid obesity. Automated administration of propofol TIVA, which facilitates precision propofol delivery by factoring-in continuous patient input variable (BIS) to establish a closed feedback loop system; may help mitigate concerns related to propofol's lipid solubility and adverse accumulation kinetics in patients with morbid obesity. This randomized study evaluated recovery from patients with morbid obesity undergoing bariatric surgery under propofol TIVA automated by a closed-loop anesthesia delivery system (CLADS) versus desflurane GA.

Methods

Forty patients, randomly allocated to receive propofol TIVA (CLADS group) or desflurane GA (desflurane group), were evaluated for postoperative recovery (early and intermediate) (*primary objective*); intraoperative hemodynamics, anesthesia depth consistency, anesthesia delivery performance characteristics, patient satisfaction, and incidence of adverse events (sedation, pain, postoperative nausea and vomiting) (*secondary objectives*).

Results

No difference was found for the time-to-eye-opening (CLADS group: 4.7[3,6.7] minutes versus desflurane group: 5.6[4,6.9] minutes, *P*= 0.576), time-to-extubation (CLADS group: 6.7[4.7,9.3] minutes versus desflurane group: 7[5.8,9.2] minutes, *P*= 0.528), ability-to-shift score from OR table to the transport bed (CLADS group: 3[3,3.5] versus desflurane group: 3[3,4], *P*= 0.703), and time taken to achieve a modified Aldrete score 9/10 (CLADS group: 15[15,37.5] minutes versus desflurane group: 15[15,43.7] minutes, *P*= 0.867).

Conclusion

Automated propofol TIVA as administered by CLADS, which matched desflurane GA in respect to depth of anesthesia consistency and post-anesthesia recovery profile; can be explored further as an alternative anesthesia technique in patients with morbid obesity.

Clinical trial registration number: Clinicaltrials.gov protocol and results registration system ID: NCT03099616. Date of registration: 28/03/2017

Introduction

Morbidly obese patients are vulnerable to post-surgery adverse respiratory outcomes (upper airway obstruction, hypoventilation) due to their abnormal bodily constitution, including, lower upper airway smooth muscle tone, excessive oropharyngeal soft tissue, among others [1, 2]. Since the tailing effect of

general anesthesia (GA) [3–5] can accentuate the above and result in life-threatening hypoxemia and/or ventilation abnormalities following bariatric surgery; a precision GA technique that minimizes presence of residual anesthetic, is highly desirable. While inhalation GA with desflurane vapor (low blood: gas/oil: gas partition co-efficient, faster elimination profile) remains the technique-of-choice for severely obese individuals undergoing surgery [3]; total intravenous anesthesia (TIVA) with propofol, an otherwise effective and popular alternative to desflurane GA in non-obese patients, is limited by its potential to delay recovery from anesthesia owing to its adverse accumulation kinetics (high lipid solubility, slow elimination) [6]. From a technical standpoint also, propofol TIVA is a sub optimal option because the conventional manual control administration may be imprecise [7, 8] and the automated target-controlled infusions (TCI) of propofol delivery fare inconsistently in the morbidly obese having hyper-variable clinical-metabolic profile [9, 10].

The closed-loop anesthesia delivery system (CLADS), a patented automated infusion technology, is a computer-controlled system that administer propofol TIVA with far greater precision than manual methods. CLADS, which uses applied controlled algorithm by factoring-in patient's EEG input variable (Bispectral index [BIS]) to close the feedback loop; individualizes propofol TIVA for each patient with high-end real-time regulation of infusion rate to a pre-determined anesthesia depth target (BIS = 50) [11, 12]. A multi-centric evaluation demonstrated CLADS-driven propofol TIVA to establish more robust GA state and early recovery than manual-infusion counterpart [13]. Contextually, though TCI-controlled propofol TIVA has been evaluated versus desflurane GA for patients with severe obesity [6, 14], the information on automated propofol TIVA remains limited [15].

This randomized study evaluated the hypothesis that CLADS-controlled automated propofol TIVA will also offer an effective anesthesia depth and rapid recovery from anesthesia as compared to desflurane GA in patients undergoing bariatric surgery with respect to: early and intermediate recovery profile (*primary objective*); intraoperative hemodynamics, anesthesia depth consistency, anesthesia delivery system performance characteristics, patient satisfaction; and incidence of postoperative adverse events (sedation, pain, postoperative nausea and vomiting) (*secondary objectives*).

Methods

After Institutional Ethics Committee approval (approval no. EC/01/17/1105, name of Ethics Committee: Institutional Ethics Committee; date of approval: 25/03/2017) and written informed consent, forty-participants aged 18–65 years, ASA physical status II/III, BMI $\geq$ 35 kg/m^2, of either sex, and undergoing elective laparoscopic bariatric surgery were included in this single centre prospective, double-blinded (patients and outcome assessors), two-arm, randomized controlled study.

Patients with uncompensated cardiovascular disease, pulmonary dysfunction, hepato-renal or endocrinology disorders, allergy/hypersensitivity to drugs, history of substance abuse, and those with anticipated requirement of postoperative ventilation; were excluded from the study. The study was

registered at clinicaltrials.gov protocol and results registration system (ID: NCT03099616; Date of registration: 28/03/2017).

The enrolled patients were randomly allocated (1:1 ratio) to one of the two groups based on a computer-generated random number table:

CLADS Group (n = 20): propofol TIVA (induction, maintenance) administered by automated CLADS.

Desflurane Group (n = 20): GA induced with CLADS propofol and maintained with desflurane inhalation.

Randomization sequence concealment included opaque-sealed envelopes with alphabetic codes. The patients were enrolled by the author MG. Author PC generated the random allocation sequence and assigned patients to intervention. Authors NS and AD conducted the cases. The authors BCP and JS, the blinded outcome-assessors; followed up the patients.

In the OR, standard (ECG, NIBP, pulse oximeter) and processed EEG (BIS monitor) monitoring was applied. Following preoxygenation, anesthesia was induced with fentanyl citrate 2-μg/kg and propofol delivered by CLADS (dosing based on lean body weight [LBW]) [16] to a target end-point BIS value of 50. Tracheal intubation was facilitated by atracurium besylate (0.5-mg/kg) bolus.

For anesthesia maintenance, in the 'CLADS group', CLADS-controlled propofol infusion with infusion rate based on adjusted body weight (ABW) [17] to a depth of anesthesia target of BIS-50 was used. Whereas, in the 'desflurane group', the vaporizer dial concentration was titrated to maintain a target BIS-50 throughout the duration of surgery.

Oxygen-air mixture (FiO_2 0.50) was employed for ventilation in both the groups.

Intraoperative analgesia and skeletal muscle relaxation was maintained by fentanyl infusion (1.0-μg/kg/h) and intermittent atracurium boluses (guided by train-of-four [TOF] peripheral neuromuscular monitoring).

All the patients received paracetamol 1-gm 30-min before the end of surgery. GA was discontinued at the completion of skin closure. Residual neuromuscular blockade was reversed based on ¾ TOF score. Tracheal extubation was undertaken once the patients were wide awake and obeying commands.

Intraoperative heart rate and non-invasive blood pressure (@5 min interval) and the use of 'on-demand' drugs to counter hemodynamic events (vasopressors, vasodilators) were recorded. Adequacy of anesthesia depth was determined by 'the percentage of the time BIS remained ± 10 of the target of BIS-50'. CLADS' performance metrics was analyzed with Varvel criteria [18] including, median performance error (MDPE), median absolute performance error (MDAPE), wobble, and the global score.

After discontinuation of anaesthesia delivery (0-time point), early recovery from anaesthesia was assessed by time-to-eye-opening and time-to-extubation.

Early recovery from anesthesia was assessed by patient's ability to shift themselves from the operating room (OR) table to the transport bed as graded along a 5-point scale [6]: 0-cannot move, needs help; 1-moves only head, needs help; 2- moves head and one leg, needs help; 3- moves head and both legs, needs help; 4-able to move alone without help.

Intermediate recovery was assessed the time to achieve 9–10 point on a10-point modified Aldrete score [19]. Observer's assessment of alertness/sedation scale (OASS) (score-1: deeply sedated to score-5: wide awake) was employed to assess incidence of postoperative sedation [20]. Postoperative pain relief and nausea and vomiting (PONV) was assessed using a 10-cm visual analogue scale (0: no pain; 10: severe pain) and a 3-point Likert scale (0: no nausea/vomiting, 1: nausea, 2: vomiting), respectively.

'Rescue' analgesia included fentanyl bolus (0.5 μg /kg) for VAS score ≥ 5. Ondansetron 4-mg was given for PONV (score ≥ 1). At 24-hr time point, patient satisfaction was assessed using a 10-point numeric rating scale (1: not satisfied; 10: fully satisfied) [21].

Statistical Analysis

Statistical analysis was performed by the SPSS program for Windows, version 17.0 (SPSS, Chicago, Illinois) and included comparison of baseline, primary, and secondary outcome variables. Continuous variables are presented as mean ± SD or median [1st, 3rd quartile] and categorical variables as absolute numbers and percentage. Data were checked for normality using Shapiro-Wilk test before statistical analysis. *Baseline variables* (demographic parameters, time profile, type, and nature of surgery) were analyzed using standardized difference [22]. Normally distributed continuous variables such as intraoperative hemodynamics were compared using the student's-t test, whereas the Mann-Whitney U test, was used for those variables which were not normally distributed such as early recovery: time-to-eye-opening, time-to-extubation, and the ability of the patients to shift them from the OR table to the transport bed and intermediate recovery: time to achieve a modified Aldrete score of 9 or 10, postoperative adverse events (sedation and pain). Categorical variables such as frequency of use of drugs for maintaining hemodynamics and PONV were analyzed using either the chi-square test or Fisher exact test.

In a previous study [6], the time-to-eye opening with *desflurane* and *propofol* were 4.2 ± 1.3 minutes and 10.7 ± 6.9 minutes, respectively. Based on above, to posit a significant difference in time-to-eye opening, a samples size of 15 patients/group was required to provide 90% power with a bilateral α-risk value of 0.05. We recruited 40-patients to cover up for unanticipated post-recruitment losses.

Results

Of the total 40 patients enrolled for the study, thirty-three completed the study endpoints. The study was conducted from 4th April 2017 to 2nd December 2019. Data from seven patients (CLADS group-3; desflurane group-4) was not analysed (Fig. 1).

No difference was found in demographic (age, gender, body weight, height, BMI), anaesthesia (duration of anaesthesia, fentanyl consumption) and surgical (duration of surgery and type of surgery) parameters between the two groups (Table 1).

Table 1
Patient Characteristics

	CLADS Group (n = 17)	**Desflurane Group (n = 16)**	**Standardized Difference**
Age (yrs.)	44.1 ± 11.8	44.4 ± 13.7	0.023
Sex (male: female)	6:11	6:10	
TBW (kg)	123.8 ± 9.9	120.7 ± 29.5	0.123
ABW (kg)	84.3 ± 12.3	84.1 ± 17.5	0.013
Height (cm)	160.7 ± 17.1	163.3 ± 10.6	0.183
BMI (kg/m^2)	45.2 ± 7.4	44.9 ± 8.6	0.037
Surgery time (min)	166.1 ± 39.2	141.8 ± 32.2	0.677
Anesthesia time (min)	204.7 ± 44.2	179.5 ± 34.5	0.636
Type of surgery:	12 (70.6%)	13 (76.5%)	
Laparoscopic Sleeve Gastrectomy	2 (11.8%)	1 (6.2%)	
Laparoscopic Gastric Bypass	3 (17.6%)	2 (12.5%)	
Robotic Sleeve Gastrectomy			
Fentanyl consumption (µg)	353.9 ± 85.1	314.4 ± 39.3	0.596
TBW: total body weight; ABW: absolute body weight			
Values expressed as mean (SD) & frequency (%)			
Standardized difference defined by Austin method $1.96\times\sqrt{[(n1+n2)/(n1\times n2)]}$			

No difference was found between the two groups for time-to-eye-opening (CLADS group: 4.7 [3, 6.7] minutes versus desflurane group: 5.6 [4, 6.9] minutes, $P = 0.576$) and time-to-extubation (CLADS group: 6.7 [4.7, 9.3] minutes versus desflurane group: 7 [5.8, 9.2] minutes, $P = 0.528$). The median ability to shift from OR table to the transport bed (CLADS group: 3 [3, 3.5] versus desflurane group: 3 [3, 4], $P = 0.703$) was not significantly different for the two groups.

There was no difference in the two groups in terms of time to achieve a modified Aldrete score 9 or 10 (CLADS group: 15 [15, 37.5] minutes versus desflurane group: 15 [15, 43.7] minutes, $P = 0.867$) and

median patient satisfaction score (CLADS group: 10 [9.5, 10] versus desflurane group: 10 [9, 10], *P* = 0.329) (Table 2).

Table 2
Postoperative recovery profile

	CLADS Group (n = 17)	Desflurane Group (n = 16)	P - value
Time to eye opening (sec)	4.7 [3, 6.7]	5.6 [4, 6.9]	0.576*
Time to extubation (sec)	6.7 [4.7, 9.3]	7 [5.8, 9.2]	0.528*
Ability to shift from OR table to transport bed	3 [3, 3.5]	3 [3, 4]	0.703*
Time to achieve modified Aldrete score 9 or 10	15 [15, 37.5]	15 [15, 43.7]	0.867*
Patient satisfaction score	10 [9.5, 10]	10 [9, 10]	0.329*
OR: operating room			
Values expressed as median [1st, 3rd quartile]			
P< 0.05 significant			
* Mann Whitney U test			

No difference was noted in the intraoperative heart rate (Table 3) and non-invasive mean arterial pressure (NIMAP) (Table 4), and in the percentage of time intraoperative heart rate (CLADS group: 86 [33, 92.5] versus manual group: 76 [61.5, 98]; *P* = 0.564) and NIMAP (CLADS group: 79 [64, 89.5] versus manual group: 76 [60, 91.5]; *P* = 0.928) remained within 20-percent of respective baseline values; between the two groups.

Table 3
Perioperative heart rate (beats per minute)

	CLADS Group (n = 17)	Desflurane Group (n = 16)	P - value
Baseline	75.5 ± 11.4	80.8 ± 13.4	0.226†
Post induction	74.9 ± 14.3	76.5 ± 13.7	0.753†
Post intubation	87.3 ± 13.2	87.7 ± 14.4	0.925†
Post incision	72.6 ± 13.7	71.4 ± 19.2	0.829†
Post PNP	75.2 ± 14.8	81.4 ± 19.7	0.313†
15- mins post PNP	77.1 ± 14.6	75.6 ± 13.6	0.754†
30- mins post PNP	78.1 ± 16.9	79.9 ± 17.8	0.765†
45- mins post PNP	80.8 ± 16.6	81.6 ± 13.1	0.888†
60- mins post PNP	73.6 ± 22.3	81.2 ± 12.7	0.243†
75- mins post PNP	81.0 ± 17.6	81.6 ± 14.9	0.913†
90- mins post PNP	80.6 ± 17.9	82.1 ± 12.1	0.787†
105- mins post PNP	79.2 ± 16.4	81.2 ± 13.8	0.760†
120- mins post PNP	76.0 ± 16.2	85.0 ± 12.1	0.334†
135- mins post PNP	79.3 ± 14.6	95.5 ± 2.1	0.188†
150- mins post PNP	80.0 ± 22.6	96.5 ± 0.7	0.387†
Post deflation	80.0 ± 18.3	76.6 ± 13.1	0.539†
Post extubation	88.4 ± 14.7	100.6 ± 16.5	0.032†

PNP: pneumoperitoneum

Values expressed as mean ± S. D.

P< 0.05 significant

† Student-t test

Table 4
Perioperative non-invasive mean arterial pressure (mmHg)

	CLADS Group (n = 17)	Desflurane Group (n = 16)	P - value
Baseline	103.2 ± 12.6	110.1 ± 14.9	0.162†
Post induction	87.1 ± 15.1	95.8 ± 17.1	0.129†
Post intubation	111.9 ± 10.9	112.7 ± 22.3	0.905†
Post incision	91.9 ± 16.5	90.9 ± 18.9	0.872†
Post PNP	111.1 ± 14.6	114.6 ± 19.4	0.561†
15- mins post PNP	102.4 ± 19.9	106.1 ± 18.3	0.575†
30- mins post PNP	104.1 ± 14.6	97.3 ± 16.2	0.215†
45- mins post PNP	103.5 ± 13.6	105.1 ± 17.1	0.777†
60- mins post PNP	100.2 ± 15.6	105.4 ± 15.8	0.350†
75- mins post PNP	108.5 ± 11.2	106.6 ± 18.1	0.725†
90- mins post PNP	108.7 ± 13.0	108.4 ± 16.3	0.953†
105- mins post PNP	105.9 ± 14.9	109.4 ± 15.8	0.584†
120- mins post PNP	105.8 ± 14.8	110.0 ± 11.1	0.619†
135- mins post PNP	112.0 ± 12.8	115.0 ± 7.1	0.770†
150- mins post PNP	115.0 ± 11.9	115.5 ± 3.5	0.959†
Post deflation	102.5 ± 7.2	99.2 ± 12.0	0.337†
Post extubation	106.6 ± 10.2	108.9 ± 16.0	0.636†

PNP: pneumoperitoneum

Values expressed as mean ± S. D.

P< 0.05 significant

† Student-t test

The heart rate following the extubation of trachea was significantly greater in the desflurane group (CLADS group: 88.4 ± 14.7 beats per min versus desflurane group: 100.6 ± 16.5 beats per min, *P* = 0.032). Intragroup repeated measure analysis of heart rate and non-invasive blood pressure showed no variation in the values at different time points from the baseline values.

Anaesthesia depth consistency (% of time BIS within ± 10 of target BIS) (CLADS group: 78% [71.5%, 84.5%] versus desflurane group: 80.5% [69%, 85.2%], P = 0.787) was comparable for the two groups.

After creation of pneumoperitoneum, the BIS values were significantly lower in the desflurane group than the CLADS group at 15-minutes (CLADS group: 55 [52, 58] versus desflurane group: 47.5 [40.7, 56.7], P = 0.036), 30-minutes (CLADS group: 58 [51, 61.5]versus desflurane group: 50.5 [41.2, 55.7], P = 0.015), and 45-minutes (CLADS group: 54 [49.5, 58.5] versus desflurane group: 50 [44.7, 52.7], P = 0.036) post-pneumoperitoneum. The BIS values at tracheal extubation were not significantly different (CLADS group: 94 [91.5, 95] versus desflurane group: 92 [90.5, 96.7], P = 1.000) between the two groups.

The performance characteristic of CLADS was assessed as per the Varvel criteria parameters. While the median performance error (CLADS group: 8 [6, 12] versus desflurane group: 2 [-8, 7.5], P = 0.004) was found to be significantly lower in the desflurane group. No difference was noted for the median absolute performance error (CLADS group: 12 [10, 14] versus desflurane group: 12 [10, 13.5], P = 0.851), wobble (CLADS group: 9 [8, 11] versus desflurane group: 10 [8, 11.5], P = 0.693), and global score (CLADS group: 28.2 [22.8, 33] versus desflurane group: 25.7 [22.9, 37.7], P = 0.857).

In the ‘CLADS’ group, the propofol requirements for maintenance of TIVA was 5.5 ± 1.3 mg/ kg/ h (Fig. 2).

In the first 24-hour post-surgery, no difference was found in the postoperative sedation scores, VAS scores for pain, and in the incidence of PONV between the two groups (*Table 5*).

Table.5

Postoperative adverse events: sedation, pain and PONV

	CLADS Group (n=17)	Desflurane Group (n=16)	P - value
Sedation (OASS)			
0-6 hrs.	5 [4.5, 5]	5 [4, 5]	0.390*
6-12 hrs.	5 [5, 5]	5 [5, 5]	0.139*
12-24 hrs.	5 [5, 5]	5 [5, 5]	0.303*
Pain (VAS score)			
0-6 hrs.	5 [3, 8]	4.5 [3, 8]	0.756*
6-12 hrs.	4 [2, 6]	3 [3, 4]	0.522*
12-24 hrs.	3 [1, 4]	3 [2, 4]	0.869*
PONV (Likert scale)			
0-6 hrs.			
score 0	10 (58.8%)	8 (50%)	
score 1	6 (35.3%)	6 (37.5%)	0.769#
score 2	1 (5.9%)	2 (12.5%)	
6-12 hrs.			
score 0	9 (52.9%)	10 (62.5%)	
score 1	8 (47.1%)	5 (31.2%)	0.424#
score 2	0 (0%)	1 (6.2%)	
12-24 hrs.			
score 0	15 (88.2%)	10 (62.5%)	
score 1	2 (11.8%)	6 (37.5%)	0.118#
score 2	0 (0%)	0 (12.5%)	

OASS: Observer assessment of alertness and sedation scale; VAS: visual analogue scale; PONV: post-operative nausea and vomiting

Values expressed as median [1st, 3rd quartile], frequency (%)

P< 0.05 Significant

* Mann Whitney U test

Discussion

Early and adequate recovery from GA remains an important goal in morbidly obese patients. Contextually, the choice of hypnotic agents, presence of residual neuromuscular blockade, and opioid analgesics; all influence recovery from anesthesia, more so in the obese who have altered body constitution and upper airway dynamics. Importantly, since presence of residual anesthetic may delay recovery from GA, in the larger scheme of preventing adverse postoperative respiratory outcomes in the morbidly obese, targeting rapid recovery by employing an efficient and precision GA technique, merit exploration [1]. The present study which evaluated automated CLADS-controlled administration of propofol TIVA versus inhaled desflurane-based GA in patients who underwent laparoscopic bariatric surgery; found no difference in the 'early' (time-to-eye opening, time-to-extubation) and 'intermediate' (time to achieve a 9/10 modified Aldrete score) post-anesthesia recovery profile.

Desflurane is preferred over isoflurane/sevoflurane GA in the morbidly obese patients for its rapid elimination profile and negligible residual presence after discontinuation of anesthesia [3]. Though propofol TIVA has been an attractive alternative for its associated advantages, e.g., lower incidence of PONV [23] and lower greenhouse effect [24]; the inconsistency in dosing scalars and administration techniques has limited its role in bariatric surgery [6]. Other pressing issues which hamper recovery from anesthesia with propofol TIVA are risk of accumulation and/or the hemodynamic depression, especially when administered based on total body weight (TBW) [9]. Technically also, the TCI-based propofol TIVA is relatively unsuitable for bariatric surgery because, while the TCI pumps based on 'Marsh' model has a pre-potential for over-dosing [9]; those running on 'Schneider' model tends to overestimate propofol clearance in adults (females-BMI > 37 kg/m^2; males-BMI > 42 kg/m^2) with a possibility of paradoxical increase the propofol infusion rate [10].

Recently, the introduction of computer-controlled automated infusion systems, which are designed to deliver high-precision robust propofol TIVA while preserving hemodynamic stability, have reinvigorated much interest [25, 26]. There is plethora of high-end evidence to support safety and efficacy of these automated systems in adults undergoing cardiac/non-cardiac surgical procedures [11]. The particular interest in employing CLADS-controlled propofol TIVA for patients undergoing bariatric surgery has a basis in that it factors-in patient's EEG response and individualizes propofol infusion rate by continuous real-time titration.

In a study involving 36 morbidly obese patients who underwent laparoscopic gastroplasty, the mean time-to-eye-opening was significantly lower in patients receiving desflurane GA versus those who received propofol by TCI infusion pump titrated to maintain BIS between 45 and 55 [6]. In a study involving 36 morbidly obese patients who underwent laparoscopic gastroplasty, the mean time-to-eye-opening (desflurane group: 4.2 ± 1.3 minutes versus propofol group: 10.7 ± 6.9 minutes, $P < 0.05$) and time-to-extubation (desflurane group: 5.6 ± 1.4 minutes versus propofol group: 13.2 ± 7.6 minutes, $P < 0.05$) was

significantly lower in patients administered desflurane inhalation GA as compared to those who received propofol by TCI pump titrated manually to maintain BIS between 45 and 55. [6] In contrast, in the current study where propofol TIVA was administered and maintained by automated CLADS; no difference was found for the same set of recovery parameters, viz. time-to-eye-opening and time-to-extubation versus desflurane GA. Juxtaposing post-anesthesia recovery parameters of the above with the present study; indicates indirectly towards the possible superiority of CLADS over TCI system and that CLADS-controlled propofol TIVA could be a valid alternative to desflurane GA in patients with severe obesity.

In terms of the recovery parameter, i.e. patient's ability-to-shift themselves from OR table to the transport bed, while the patients belonging to both the group (CLADS or desflurane) the present study demonstrated a median 'ability-to-shift' score of 3 (able to move head and both legs, needed little help to shift themselves); in the Juvin et al study [6], the score was significantly different between the desflurane(score-3) versus TCI propofol TIVA(score-1).

Also, the PACU discharge readiness time as per the eligibility processed by assessment of modified Aldrete score in the propofol CLADS and desflurane groups was found to be much lower than what is previously reported by Juvin et al [6] (propofol group: 198 ± 109 minutes versus desflurane group: 126 ± 56 minutes, $P > 0.05$) and Elbakry et al [14] (TIVA [propofol + dexmedetomidine] group: 43.3 ± 10.4 minutes versus Desflurane group: 52.1 ± 9.7 minutes, $P = 0.01$).

Still, the caveat (dissimilar study methodology) which preclude comparing the present study with historical evidence [6, 14], especially in the absence of evidence on difference in recovery profile between TCI versus CLADS propofol TIVA; the contextual superior recovery profile of our study can only suggest that techniques to administer propofol TIVA may have an important role in post-anesthesia recovery of morbidly obese patients, and that it requires further exploration.

To the best of our knowledge, there has been no study yet that has compared best of inhaled GA (desflurane) versus the most precise way to administer propofol TIVA. At an applied level, the present study felt the need to undertake evaluation of automated propofol TIVA versus desflurane GA in the morbidly obese patients where it is most relevant and would matter the most in curbing post-surgery recovery issues.

This study highlighted two important aspects of automated propofol TIVA in morbidly obese patients; *first*, it fared well in establishing a robust GA state, and *second*, though having altogether different delivery mechanisms; CLADS propofol-TIVA, with the exception of MDPE, matched desflurane GA in respect to performance parameters (MDAPE, wobble, and global score).

The limitations of the present study which hampers generalizability includes, issues with methodological construct (per-protocol versus gold-standard intention-to-treat analysis), limited staff participation (2-anaesthesiologists conducted all the study cases), and that all secondary endpoints were not controlled by adjustment for multiple testing (high type-1 error).

In view of the study results and the above stated limitations, automated (CLADS) administered propofol TIVA can be explored further in terms of:

i) Adequately powered non-inferiority trial to evaluate automated propofol TIVA versus desflurane GA.

ii) Moving further from the 'first step' of exploration, i.e., assessing early and intermediate surrogate recovery parameters (as in the present study), to study late recovery and postoperative respiratory outcomes (incidence of respiratory impairment, OSA, hypoxemia)
iii) Incorporating a third group involving BIS-guided effect-site controlled target-controlled infusion TCI-system (e.g., Eleveld model) [27] and study how the pharmacokinetic optimization along with pharmacodynamic control (continuous BIS control variable)

In conclusion, automated CLADS controlled propofol TIVA, by virtue of comparable depth of anesthesia, early recovery profile, and near-similar system performance to inhaled desflurane GA; can be explored further in the morbidly obese patients.

Declarations

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Competing interests

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Author contributions

1. Amitabh Dutta: This author conceptualized the study, supported project preparation, conducted the cases, and supported manuscript preparation.
2. Nitin Sethi: This author helped in study conceptualization and methodological construct, conducted the cases, and led manuscript preparation.
3. Goverdhan D Puri: This author helped the study investigators with technical inputs on a continuous basis, analyzed consistency of the generated data, and reviewed the manuscript for scientific representation.
4. Jayashree Sood: This author helped to follow-up the patients, did data management, and analyzed the final manuscript.
5. Prabhat K Choudhary: This author helped in data collection and analysis, took overall clinical responsibility of the study patients, and supported manuscript development.

6. Anil K Jain: This author helped in assessing eligibility for recruitment, enrolled patients into study, and structured the manuscript.
7. Bhuwan C Panday: This author helped to follow-up the patients, provided logistic support, took responsibility of overall trial supervision, and critical manuscript evaluation.
8. Manish Gupta: This author helped in controlling random sequence allocation, assigned the eligible enrolled patients into different groups, and critically reviewed the final manuscript in terms of readability and expression consistency.

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Figures

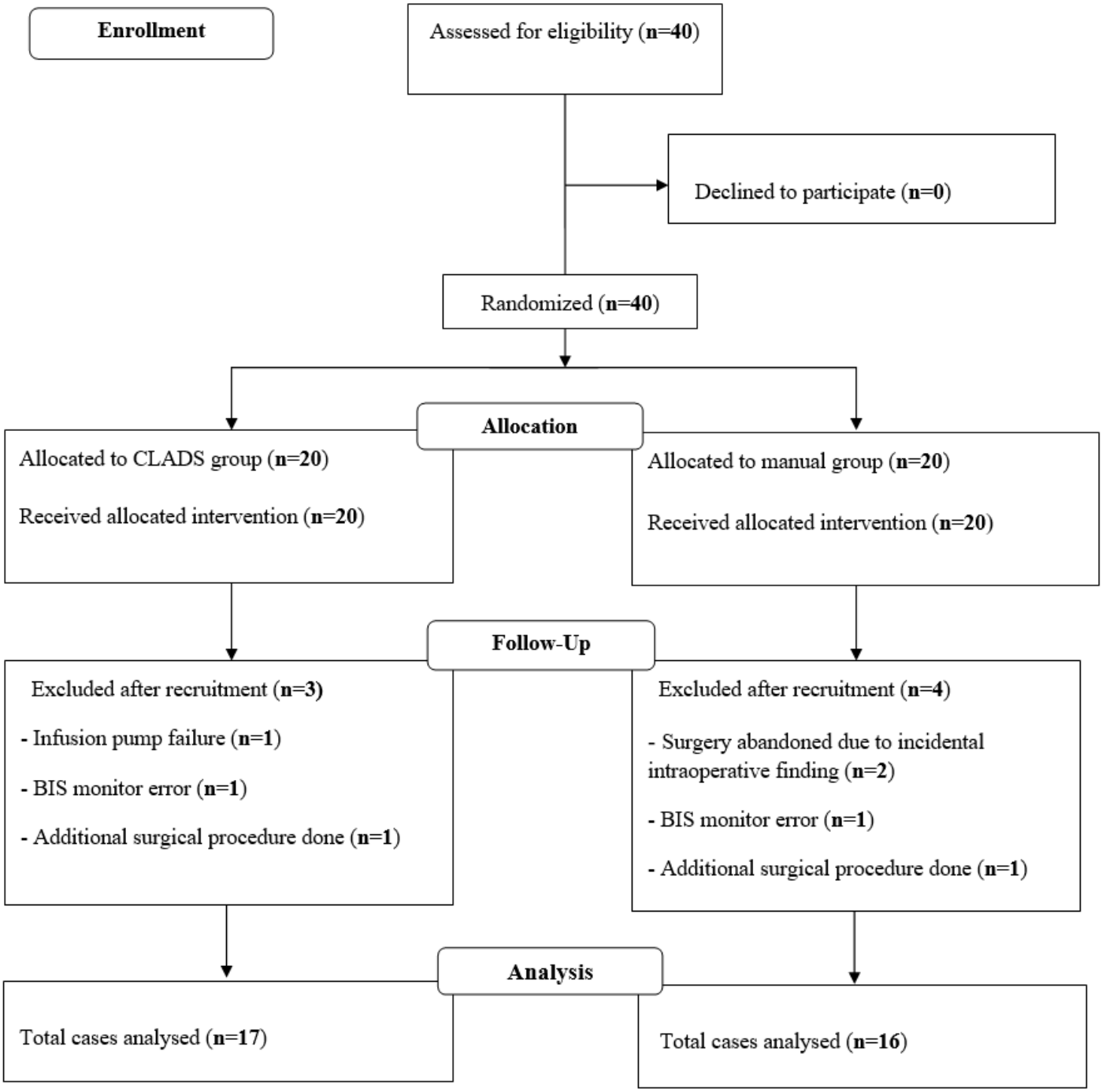

Figure 1

Consort Flow Diagram

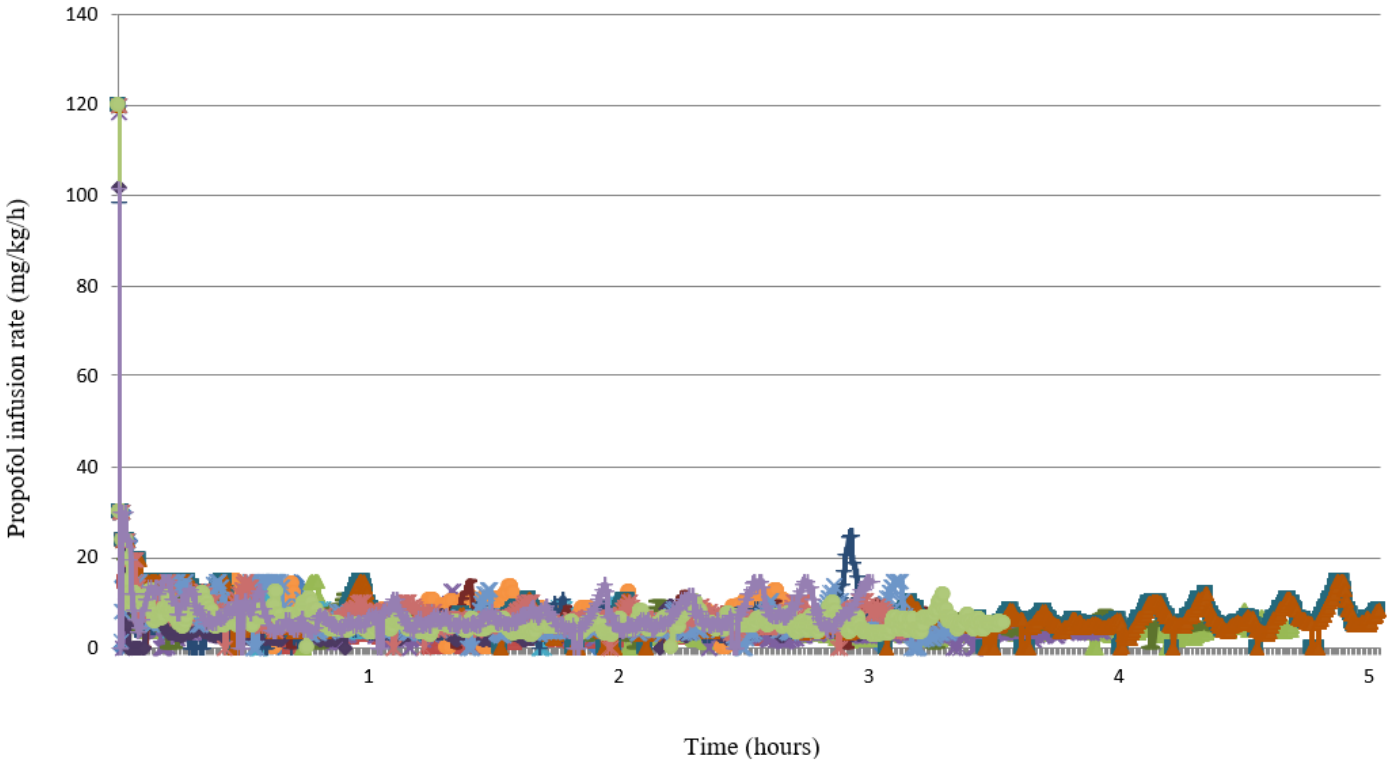

Figure 2

Propofol infusion rate versus time