Goal Directed Fluid Optimization Using Plethysmography Variability Index in Laparoscopic Bariatric Obese Patients. Is It The Answer?

Abstract:

Objective: To compare effect of goal-directed fluid replacement using Plethysmography Variability Index (PVI) guidance versus liberal fluid regimen in elective laparoscopic bariatric surgery on pulmonary oxygenation and gastrointestinal, cerebral and renal function.

Materials and Methods: This randomized controlled trial included 60 consecutive patients; 20-40 years old with body mass index (BMI) > 40 scheduled for elective laparoscopic bariatric surgery between June 2010 and December 2011. Patients were randomized to 'liberal' (**LF**) or 'goal directed' (**GD**) fluid infusion group. All patients received 500 ml lactated Ringer's solution then 1-2 ml/kg/hour in GD group or 6-8 ml/kg/hour in LF group. A 5-min bolus infusion of 200 ml of 6% hydroxyl ethyl starch (HES) was administered if PVI goes > 14, urine output < 0.5 ml/kg/h, heart rate > 100/min or decreased systolic blood pressure > 20% of baseline value. This colloid bolus was repeated till 20 ml/kg is reached then LR solution is used for further boluses. Primary outcome measures were length of hospital stay, postoperative hypoxemia assessed by PO_2/FiO_2 ratio and serum Lactate level.

Results: Intra-operatively, lactate level and volumes of infused Ringer's lactate and HES were significantly lower in GD group ($p < 0.001$). PVI was significantly higher in GD group ($p < 0.001$). Intra-operatively, lactate level and urine output were significantly lower in GD group ($p < 0.001$). Postoperatively, the GD group showed significantly lower urine output ($p < 0.001$), and shorter time to recovery ($p < 0.001$) to first bowel movement ($p < 0.001$) and to resume normal diet ($p < 0.001$). Hypoxemia, diuresis and fatigue were significantly more frequent in LF group. No significant difference in other postoperative complications.

Conclusion: Goal-directed, PVI-guided intraoperative fluid replacement significantly improved clinical outcome compared to liberal fluid intake. PVI guidance provides a sensitive and accurate determinant of fluid responsiveness and allowed for lower fluid intake. We recommend GD intraoperative fluid replacement with PVI and ABG guidance in morbidly obese patients undergoing laparoscopic bariatric surgery.

Key words: *Bariatric- goal directed-lactate-PVI-liberal*

Introduction

Perioperative fluid administration is an integral part for almost any surgical procedure and consequently is an everyday issue for most anesthesiologists. In recent years, several studies have shown renewed interest in perioperative fluid therapy demonstrating that different fluid therapy regimens can influence the postoperative outcome. In morbidly obese patients, perioperative fluid therapy has double-edged implications. In normal weight individuals, it has been shown that during minor or medium sized procedures liberal intraoperative fluid administration improves perioperative physiologic organ function and patient recovery and reduces hospital stay.[1] Nevertheless, in obese patients this may lead to hypertension, pulmonary edema and increased requirement for ventilatory support. On the other side, fluid restriction may result in acute tubular necrosis and organ dysfunction.[2]

To avoid deleterious effects of volume expansion, preload dependence assessment is crucial to guide fluid therapy. Thus the principle goal is optimizing cardiac preload. Measuring volume responsiveness, occasionally referred to as *'goal-directed'* approach, seems to be an interesting alternative to direct fluid replacement protocols.[3]

As static parameters of measuring cardiac preload as central venous pressure (CVP) and pulmonary artery wedge pressure (PAWP) [4] have been shown to be of little help in decisions regarding fluid replacement, dynamic parameters relying on respiratory variations in stroke volume, have been recently shown to be better indictors of fluid responsiveness.[5]

Plethysmography Variability Index (PVI) is an algorithm that measures the respiratory variability of the pulse amplitude in fingertip transmission plethysmography and thus has the ability to predict fluid responsiveness and guide fluid management.[6] PVI has been incorporated in our study to guide goal directed fluid regimen hoping to improve postoperative outcome.

The purpose of this randomized controlled trial was to compare goal-directed - using PVI guidance - versus liberal fluid replacement regimens in bariatric patients undergoing elective laparoscopic surgery regarding their effects on pulmonary oxygenation, resuming bowel movement, cerebral function recovery and diuresis.

Materials and Methods

After local hospital Ethical Committee approval and obtaining written informed consent from the patients, 60 consecutive patients ASA II and III with age range 20-40 years and body mass index (BMI) > 40 scheduled for elective laparoscopic bariatric surgery in the period from June 2010 to December 2011 were enrolled in this randomized controlled trial.

Exclusion criteria were history of uncompensated cardiac disease (including arrhythmias), respiratory disease, renal dysfunction (creatinine > 50% of upper limit of normal value) or significant liver dysfunction (liver enzymes > 50% of upper limit of normal value).

Preoperative fluid status was standardized in all patients by ensuring that all patients were fasting since midnight before the operation and drank 200 ml of water at 6:00 am on the morning of surgery and that all surgeries were done in the morning.

All patients were premedicated with oral ranitidine and oral midazolam 3 mg, 2 hours preoperatively. Upon arrival to the operating room, patients were randomized by the sealed envelope procedure to either 'liberal' (**LF**) or 'goal directed' (**GD**) fluid infusion group. The randomization code was not known to the investigators until the end of the study.

Egg crate padding was placed under the knees and below the heels of the patients so as to create a degree of flexion. Pneumatic compression device consisting of a compressor

and an inflatable cuff covering the entire leg was applied to help preventing deep venous thrombosis formation.

Following preoxygenation, anesthesia was induced with propofol 200-350 mg intravenously (2-4 mg/kg), fentanyl 2 µg/kg and was maintained with isoflurane. Rocuronium 0.4-0.6 mg/kg was used to facilitate endotracheal intubation and increments were used to maintain neuromuscular block throughout surgery. Ventilation was adjusted to an end tidal CO_2 ($ETCO_2$) of 35-40 mm Hg, with a tidal volume of 13-15 ml/kg ideal body weight. Heart rate, non-invasive and invasive arterial blood pressure using 22 gauge arterial radial cannula, oxygen saturation, capnography, inhaled gas concentration and temperature were continuously measured in all patients using (Drager infinity vista XL). Normothermia throughout the operation was maintained with a Bair-Hugger (Augustine Medical, Eden Praire, MN, USA). Masimo Rainbow SET Pulse CO-Oximetry (Masimo (NASDAQ: MASI) readouts from an additional fingertip sensor measured every 2.5 min.

The fluids were administered and controlled by an anesthetist not involved in patient assessment. Patients assigned to Goal-directed fluid group received 500 ml crystalloid lactated Ringer's solution then 1-2 ml/kg/hour, while Liberal fluid group received 500 ml crystalloid then 6-8 ml/kg/hour. An additional 5-min bolus infusion of 200 ml colloid 6% hydroxyl ethyl starch (HES) was administered if one or more of the following criteria occur: PVI rising above 14, urine output < 0.5 ml/kg/h, heart rate > 100/min or decreased systolic blood pressure more than 20% of baseline values. This colloid bolus was repeated till 20 ml/kg is reached then LR solution is used for further boluses. At the end of surgery, arterial blood samples were taken, the lactate concentration was measured using an ABL 620 analyzer (Radiometer, Copenhagen, Denmark), and venous blood sample was taken to measure serum creatinine concentrations.

At the end of surgery, all patients received 8 mg ondansterone and 30 mg ketorolac. In the post anesthesia care unit (PACU) (the surgical ward personnel were unaware of group assignment and were not part of investigator team) the Aldrete score was measured (Table 1). This score is designed to assess the patients' transition from phase I recovery to phase II recovery, from discontinuation of anesthesia until return of protective reflexes and motor function; time to recovery. The total score is 10. Patients scoring ≥ 8 and/or are returned to similar preoperative status are considered fit for transition to phase II recovery; hence time to recovery is recorded. The postoperative morbidity were recorded ; overnight pulse oximetry is used to establish patient's night time arterial oxygen saturation, occurrence of fatigue was measured on10 point fatigue scale 1 = no fatigue and 10 = worst fatigue imaginable after surgery , urine output, time to first bowel movement and time to resume normal diet.

Table 1: Aldrete score

Score	**2**	**1**	**0**
Respiration	Able to take deep breath and cough	Dyspnea/shallow breathing	Apnea
O_2 Saturation	Maintains >92% on room air	Needs O_2 inhalation to maintain O_2 saturation >90%	Saturation < 90% even with supplemental O_2
Consciousness	Fully awake	Arousable on calling	Not responding
Circulation	BP± 20 mm Hg preop	BP± 20-50 mm Hg preop	BP± 50 mm Hg preop
Activity	Able to move 4 extremities	Able to move 2 extremities	Able to move 0 extremities

Primary outcome measures were postoperative hypoxemia and serum lactate level. Postoperative hypoxemia was assessed by the arterial oxygen tension/fractional inspired oxygen ratio (PO_2/FiO_2); a widely used oxygenation index. A ratio above 300 is indicative of adequate ventilation, below which patients usually require ventilatory assistance in the form of CPAP. **Secondary outcome** measures were hemodynamics (heart rate, invasive blood pressure) gastrointestinal signs (nausea, vomiting, time to regain intestinal movement), postoperative ileus), cerebral function recovery (drowsiness), serum creatinine, diuresis and rhabdomyolsis.

Statistical methods: Data were analyzed using IBM SPSS Advanced Statistics version 20.0 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation. Qualitative data were expressed as frequency and percentage. Chi-square test (Fisher's exact test) was used to examine the relation between qualitative variables. For quantitative data, comparison between two groups was done using independent sample t-test. A p-value < 0.05 was considered significant.

Results:

The two studied groups were comparable in age and BMI. There were no significant differences between the two groups regarding duration of anesthesia and surgery and initial baseline systolic blood pressure. There was statistically significant difference between the two groups regarding heart rate (p = 0.005), however, the values were within the clinically accepted range. There was no significant difference between the two groups regarding frequency of associated morbidity (Table 2).

Intra-operatively (Table 3), lactate level was significantly lower in GD group (p < 0.001). Liberal group received significantly higher volumes of lactates and HES (p < 0.001). PVI was significantly higher in GD group (p < 0.001). There was no significant difference between the groups in peak airway pressure (p = 0.133). Urine output was significantly lower in GD group (p < 0.001).

Postoperatively, the GD group showed significantly lower urine output (p < 0.001), and shorter time to recovery (p < 0.001) first bowel movement (p < 0.001) and time to resume normal diet (p < 0.001). Hypoxemia ($PO_2/FiO_2 > 300$) was significantly more frequent in LF group (p = 0.007), so as fatigue (p = 0.020). Diuresis was more frequent in LF group (p = 0.009). There was no significant difference in other postoperative complications (Table 4).

Table 2: Demographic and baseline clinical and laboratory data of the two studied groups

	LF group (n=30)	GD group (n=30)	P value
Age (yrs)	38.1±5.5	36.4±6.2	0.265
Gender (M/F)	16/14	12/18	0.301
BMI (kg/m^2)	40.6±4.9	39.5±5.4	0.414
Duration of anesthesia (min.)	147.8±12.1	141.5±19.2	0.134
Duration of surgery (min.)	127.4±18.7	119.8±22.2	0.157
Systolic blood pressure (mmHg)	135.0±18.0	132.6±17.8	0.615
Heart rate (beats/min.)	91.0±10.3	99.4±12.1	0.005
SPO_2 (%)	96.5±2.0	96.2±2.1	0.617
PO_2/FiO_2 ratio	391±68	386±73	0.785
Hypertension, No.(%)	9 (30.0%)	11 (36.7%)	0.584
Preoperative DM, No.(%)	10 (33.3%)	8 (26.7%)	0.573

Table 3: Intraoperative criteria of the two studied groups

	LF group (n=30)	GD group (n=30)	P value
Lactate level (mmol/L)	1.41±0.40	0.86±0.15	< 0.001
Intraoperative Ringer's lactate (ml)	2236±221	1407±27	< 0.001
Intraoperative hestril (ml)	464±89	250±0	< 0.001
Plethysmography variability index (PVI)	13.3±0.8	15.5±1.4	< 0.001
Peak airway pressure (cmH_2O)	37.1±2.8	36.1±2.3	0.133
Urine Output (ml)	210±32	165±25	< 0.001

Data as mean±SD

Table 4: Postoperative criteria of the two studied groups

	LF group (n=30)	GD group (n=30)	p value
Urine Output (ml, mean±SD)	2110±106	1930±95	< 0.001
Time to first bowel movement (hrs, mean±SD)	22.0±1.5	11.5±2.3	< 0.001
Time to resume normal diet (hrs, mean±SD)	31.4±4.6	20.6±6.5	< 0.001
Time to recovery (minutes, mean±SD)	95±32	45±8	< 0.001
Systolic Blood Pressure (Hg, mean±SD)	142±15	120±21	< 0.001
Pulse (beats/min, mean±SD)	91±11	93±6	0.386
PO_2/FiO_2 ratio	294±23	332±25	< 0.001
PO_2/FiO_2 ratio < 300, No.(%)	12 (40%)	3 (10%)	0.007
Fatigue, No.(%)	19 (63.3%)	10 (33.3%)	0.020
Drowsiness, No.(%)	7 (23.3%)	5 (16.7%)	0.519
Postoperative Morbidity, No.(%)			
Nocturnal hypoxemia	7 (23.3%)	2 (6.7%)	0.071
Hypotension	14 (46.7%)	8 (26.7%)	0.108
Diuresis	18 (60.0%)	8 (26.7%)	0.009
GIT Complications, No.(%)			
Nausea & vomiting	7 (23.3%)	12 (40.0%)	0.165
PO ileus	8 (26.7%)	4 (13.3%)	0.197
Length of hospital stay	3 (1-3)	2 (1-3)	0.687

* No p value because number of cases in the two groups is small
Time to recovery = Aldrete score 8-10

Discussion

We found an improved outcome in recovery parameters in goal directed group in comparison to liberal fluid intake group. These parameters included cerebral recovery as presented by the significantly shorter time in the postoperative recovery room, significantly less time to first flatus passage, as well as diminished intraoperative lactate levels in the former group. Postoperative hypoxemia and diuresis were less frequent in goal directed group.

With lack of standardization, available data cannot allow general evidence based recommendations in procedure-specific perioperative management of fluids.[7]This is particularly true in morbid obesity. These patients are more liable to complications with

inadequate or over infusion. On one hand, fluid restriction in obese patients may lead to acute tubular necrosis and organ dysfunction.[5] Liberal fluid intake, on the other hand, poses a risk in the postoperative recovery and healing especially in obese patient.[1] Furthermore, in a systematic review of over 80 randomized clinical trials,[7] recommended avoiding fluid overload in major surgical operations. Nisanevich et al. [8] presented higher infection rates and longer hospitalization periods in patients receiving liberal fluid intake.[9]

There is a general concept advocating liberal fluid intake. It states that preoperatively patients are dehydrated, with an increased insensible perspiration with surgical incisions, and renal excretion can dispense with fluid overload.[10] This cannot be applied to obese individuals as a rule. Hence, fluid optimization via goal directed fluid administration in an attempt to reach the best target for such patients seems an attractive and promising alternative.

We found a statistically significant postoperative decline in PO_2/FiO_2 ratio in both groups. However, it reached below 300 in 40% of the liberal fluid group compared to 10% of the goal directed group ($p = 0.007$). PO_2/FiO_2 is a very important tool to assess proper tissue oxygenation. It overrides the use of oximetry as was performed by other studies.[11]

Liberal fluid administration studies have detected a propensity towards pulmonary congestion, leading to hypoxia.[1] Also, invasive monitoring and postoperative ventilation correlated with the amounts of infused fluids in such patients as well as the postoperative weight gain.[12] This poses a higher need for postoperative oxygen therapy and ventilatory support. Adequate tissue perfusion and oxygenation is important for wound healing. In fact, risk of surgical wound infection is inversely proportional to tissue oxygenation.[13]

We found less total need of intake of crystalloids, and lower lactate levels in the goal directed, PVI guided approach when compared to the liberal group. Serum lactate levels are an indirect and sensitive detector of intravascular fluid volume adequacy, and tissue hypoxia. Furthermore, aggressive crystalloid infusion showed impeded oxygen consumption.[14] Similarly, Forget et al.[6] showed lower lactate levels and improved fluid management, in major abdominal surgery patients performing PVI guided fluid replacement. Functional parameters as pulse pressure variation, PVI, and stoke volume variation SVV, proved more sensitive and specific than cardiac filling pressures CVP and PAWP in fluid administration assessment. Cannesson et al.[15] showed that PVI significantly affected fluid responsiveness, with a cut off more than 14% to detect responders from no responders. Recently, Hood et al. [16] showed a significant predictive value of fluid responsiveness of PVI when compared to the costly, more tedious, yet accurate endoscopic Doppler assessment method for stroke volume. Hence PVI can provide a good noninvasive alternative detector of preload adequacy, and proper intraoperative fluid management.

We found a statistically significant lower intraoperative urine output volume in the goal-directed group. Nevertheless, this did not have any clinical significance in the total patient outcome or recovery parameters. Recently**,** Matot et al.[17] challenged the popular concept that urinary output is of a high significance intraoperatively. They showed urine output to be low despite the use of high volume fluid therapy. Hence, urinary output should not have a significant impact on decisions in intraoperative fluid administration.

Conclusion and recommendations: Intraoperative fluid replacement in a goal-directed, PVI-guided manner significantly improved clinical outcome compared to liberal fluid intake. The former group showed lower lactate levels, better oxygenation and tissue perfusion, as well as improved cerebral and bowel recovery. PVI guided technique, provided a sensitive and accurate determinant of fluid responsiveness and allowed for

lower fluid intake. Urine output, despite varying in volume, did not carry clinical significance in the outcome in either group. Hence, we recommend GD intraoperative fluid replacement with PVI and ABG guidance in morbidly obese patients undergoing laparoscopic bariatric surgery.

References:

1. Chappell D, Jacob M, Hofmann-Kiefer K, Conzen P, Rehm M. A rational approach to perioperative fluid management. Anesthesiology. 2008 Oct;109(4):723-40.
2. Leykin Y, Pellis T, Del Mestro E, Fanti G, Marzano B. Perioperative management of 195 consecutive bariatric patients. Eur J Anaesthesiol. 2008 Feb;25(2):168-70.
3. Zimmermann M, Feibicke T, Keyl C, Prasser C, Moritz S, Graf BM, Wiesenack C. Accuracy of stroke volume variation compared with pleth variability index to predict fluid responsiveness in mechanically ventilated patients undergoing major surgery. Eur J Anaesthesiol. 2010 Jun;27(6):555-61.
4. Hofer CK, Müller SM, Furrer L, Klaghofer R, Genoni M, Zollinger A. Stroke volume and pulse pressure variation for prediction of fluid responsiveness in patients undergoing off-pump coronary artery bypass grafting. Chest. 2005 Aug;128(2):848-54.
5. Kumar A, Anel R, Bunnell E, Habet K, Zanotti S, Marshall S, Neumann A, Ali A, Cheang M, Kavinsky C, Parrillo JE. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. Crit Care Med. 2004 Mar;32(3):691-9.
6. Forget P, Lois F, De Kock M. Does PVI Improve Fluid Management During Major Abdominal Surgery. Critical Care. 2009; 13(Suppl. 1):P204
7. Holte K, Kehlet H: Fluid therapy and surgical outcomes in elective surgery: A need for reassessment in fast-track surgery. J Am Coll Surg 2006; 202:971-89

8. Nisanevich V, Felsenstein I, Almogy G, Weissman C, Einav S, Matot I: Effect of intraoperative fluid management on outcome after intraabdominal surgery. Anesthesiology 2005; 103:25-32
9. Prowle JR, Echeverri JE, Ligabo EV, Ronco C, Bellomo R. Fluid balance and acute kidney injury. Nat Rev Nephrol. 2010 Feb;6(2):107-15.
10. Holte K, Kehlet H: Compensatory fluid administration for preoperative dehydration: Does it improve outcome? Acta Anaesthesiol Scand 2002; 46:1089-93
11. Karbing DS, Kjaergaard S, Smith BW, Espersen K, Allerød C, Andreassen S, Rees SE. Variation in the PaO_2/FiO_2 ratio with FiO_2: mathematical and experimental description, and clinical relevance. Crit Care. 2007;11(6):R118.
12. Lowell JA, Schifferdecker C, Driscoll DF, Benotti PN, Bistrian BR: Postoperative fluid overload: Not a benign problem. Crit Care Med 1990; 18:728-33
13. Gottrup F, Firmin R, Rabkin J, Halliday BJ, Hunt TK: Directly measured tissue oxygen tension and arterial oxygen tension assess tissue perfusion. Crit Care Med 1987; 15:1030-6
14. Valenza F, Aletti G, Fossali T, Chevallard G, Sacconi F, Irace M, Gattinoni L. Lactate as a marker of energy failure in critically ill patients: hypothesis. Crit Care 2005;9(6): 588–93
15. Cannesson M, Desebbe O, Rosamel P, Delannoy B, Robin J, Bastien O, Lehot JJ. Pleth variability index to monitor the respiratory variations in the pulse oximeter plethysmographic waveform amplitude and predict fluid responsiveness in the operating theatre. Br J Anaesth 2008;101(2): 200–6
16. Hood JA, Wilson RJ. Pleth variability index to predict fluid responsiveness in colorectal surgery. Anesth Analg. 2011 Nov;113(5):1058-63.
17. Matot I, Paskaleva R, Eid L, Cohen K, Khalaileh A, Elazary R, Keidar A. Effect of the volume of fluids administered on intraoperative oliguria in laparoscopic bariatric surgery: a randomized controlled trial. Arch Surg. 2012 Mar;147(3):228-34.