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Intra-Operative IV Fluid Management: Goal Directed Therapy with Esophageal Doppler Monitoring vs. Standard Weight Based Fluid Therapy

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WITH ESOPHAGEAL DOPPLER MONITORING VS. STANDARD

WEIGHT BASED FLUID THERAPY

A Major Paper Presented

by

Amanda K. Krueger

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Amanda Kay Krueger

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Abstract

Intravenous fluid management in the peri-operative period continues to be a debate in the anesthesia literature in terms of which fluid type is best along with how much fluid should be given. The majority of post-operative complications in colo-rectal surgery can be traced back to the amount of IV fluids patients receive. Most recently the term Goal-directed therapy (GDT) states that a more individualized approach to fluid management is not only safer but necessary. The Esophageal Doppler, a technology analyzing stroke volume and cardiac output intra-operative, may prove to be a safe way to provide GDT and decrease complications post-operatively. This systematic review examined the impact of the esophageal Doppler versus the traditional weight based fluid management technique on adult (>18 years of age) patient outcomes post-operatively after colo-rectal and abdominal surgery. The goal was to highlight best practices that will decrease adverse patient events and length of stay (LOS). Four out of the five randomized controlled trials analyzed for this review do report that ED use and GDT decrease complications and ICU admissions post-operatively versus utilizing a more standard approach to fluid management. Due to other social variables in discharging subjects, length of stay was not found to be decreased in GDT subject groups. In furthering anesthesia practice, standard fluid management techniques should be updated with a more individualized approach focusing on patient variables such as stroke volume and what the response is to fluid therapy intra-operatively.

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INTRA-OPERATIVE IV FLUID MANAGEMENT: GOAL DIRECTED THERAPY WITH ESOPHAGEAL DOPPLER MONITORING VS. STANDARD WEIGHT BASED FLUID THERAPY

Background/Statement of the Problem

One of the core responsibilities of a nurse anesthetist is the safe administration and management of intravenous (IV) fluid during the patient's peri-operative course. For the purposes of this proposal, the peri-operative period will be defined as the pre-operative, intra-operative & immediate post-operative time before transfer to a nursing unit or discharged home. Historically and presently, fluid requirements are estimated using a set of weight-based equations to determine the rate of a patient's maintenance IV therapy plus their oral deficit needing replacement due to fasting time prior to surgery. Further, estimated blood loss, third space losses and potential volume shifts from anesthetics and neuraxial (epidural and spinal) anesthesia must also be factored in to the equation (Gallagher & Vacchiano, 2015). Each patient also comes with unique diagnoses such as cardiac, pulmonary, liver or kidney dysfunction and extremes of age or any other circumstance that will lead the anesthetist to further change or alter the prescriptive fluids for that particular patient. In other words, the standard fluid management equations act as a general guideline but must be constantly adapted to each individual patient and to the events experienced during the actual surgery or intra-operative period.

For years the literature has been in constant debate on comparison of a liberal versus a more restricted IV fluid approach during the peri-operative period, with the answer most often being "not clearly defined" or "lack of evidence." However, clearly cited in the literature are the post-operative adverse effects of hypervolemia and

hypovolemia related to peri-operative fluid administration including end-organ failure leading to intensive care unit (ICU) admissions, longer lengths of hospital stay and increased health care costs (Gallagher & Vacchiano, 2015). Due to the continued evolvement of health care, nurse anesthetists must be well versed in current literature trends and focused on maintaining and providing safe, effective and individualized care for every patient that will pass through the operating room doors. New advances in technology and a recent growing trend in the literature is the utilization of goal-directed fluid therapy. Goal directed therapy utilizes non-invasive and/or invasive monitoring techniques to help the nurse anesthetist guide fluid administration in real time based on the patients stroke volume trends (Thompson, 2015). The most common method of monitoring stroke volume is use of the esophageal Doppler—a probe placed into the patient's esophagus after induction of anesthesia (Schober, Loer, & Schwarte, 2009). Comparison of the esophageal Doppler to standard weight-based modalities will enable the nurse anesthetist to make evidence based decisions on which method may have the most benefit to patients. The purpose of this study is to perform a systematic review that examines the impact of the esophageal Doppler versus the traditional weight based fluid management technique on adult (>18 years of age) patient outcomes post-operatively after colo-rectal and abdominal surgery. The goal is to highlight best practices that will decrease adverse patient events and length of stay (LOS).

Next, the review of the literature will be presented.

Literature Review

To construct a comprehensive review of the literature CINAHL, Pub Med and Medline were searched for a period of months from April 2015 through July 2015. Some of the keywords used to search included "esophageal doppler," "goal directed fluid management and therapy," "colo-rectal surgery," and "hemodynamic monitoring." A review of the articles found in the search are described below and further evaluated in tables in the appendices.

Intra-Operative Fluid Administration

For nurse anesthetists to properly and safely administer fluids to patients, an understanding of body fluid compartments and the types of fluids available is a crucial place to begin. Judy Thompson (2015) explained the basics of fluid management along with current fluid management practices. The human body is made up of a high percentage of water and consists of two different fluid compartments deemed intracellular (ICF) and extracellular (ECF). These two compartments are separated by semi-permeable and capillary membranes which are responsible for the movement of fluid within the body and therefore electrolyte balance (Thompson). Tissue trauma during surgery causes stress to the body and possible fluid overload if the patient's intravenous (IV) fluids are not managed appropriately. Hypervolemia causes the release of several inflammatory mediators as well as the destruction of the endothelial glycocalyx, an important structure in the vascular barrier that will cause adverse shifting of fluid (Thompson). A term referred to as third space losses or capillary leakage and interstitial edema, all of which can lead to poor tissue oxygenation (Thompson). In Table 1 on the next page is a list of the impact of hypervolemia and hypovolemia to the body.

Table 1

Clinical manifestations of hypervolemia and hypovolemia

Hypervolemia	Hypovolemia
Edema Ileus PONV (post operative nausea & vomiting) Pulmonary complications Increased cardiac demands Weight gain Impaired coagulation Venous congestion Heart failure Arrhythmia	Organ hypoperfusion—decreased oxygen transport SIRS Sepsis Multi-organ failure

Adapted from (Bungaard-Nielsen, Secher & Kehlet, 2009) & (Gallagher & Vacchiano, 2015)

These facts not only stress the importance of managing IV fluids appropriately but beg the question of what kinds of fluids are best to administer.

There are two different types of intravenous (IV) fluids given to treat different types of fluid and electrolyte imbalances, colloid and crystalloid (Thompson, 2015). Crystalloid fluids are the most commonly used and physiologically remain in the vascular space or the ECF when infused to hydrate the patient. Two commonly used crystalloids include normal saline (NS) and lactated ringers (LR). Colloids on the other hand expand the plasma volume and include fresh frozen plasma (FFP), albumin and others but may

come with infection, coagulopathy, and renal failure risk (Thompson). Colloids can be used to replace blood volume after trauma, surgery and burns. Morris & Rogerson (2011) conducted a literature review that included 10 studies to assess which type of fluids (colloids are crystalloids) are best when used with the esophageal Doppler (ED) peri-operatively. Their conclusions showed that the dosage of fluid therapy is more important than the kinds of fluids used in regards to improving patient outcomes and decreasing length of stay (Morris & Rogerson). They also reported that there are significant gaps in the literature and that more research is needed in the realm of fluid type optimization.

Methods of Managing Intra-Operative Fluids

Another frequently discussed question in the literature is which fluid prescription is best: restricted or liberal. A review article written by Bundgaard-Nielsen et al. (2009) that included seven randomized control trials concluded that the definition of liberal and restrictive fluid regimens varied throughout the literature. The authors also noted that the crystalloid vs. colloid discussion has yet to be resolved but did find that utilizing high amounts of crystalloid may induce hyperchloraemic acidosis (Bundgaard-Nielsen et al.). Their final recommendations supported a combined approach of using crystalloids to replace ECF losses while avoiding excess (hypervolemia) but also maximizing cardiac output (CO) with colloids individualized for each patient. The authors also introduced the phrase 'goal directed therapy' (GDT) in this review.

A study done by Brandstrup et al (2003) compared the effects of a restricted fluid management regimen to a standard fluid regimen on complications after colo-rectal resection. These authors note that IV fluid overload during surgery can decrease oxygen

tension and delay GI function recovery due to edema. A randomized, observer-blinded study was performed at 8 Danish hospitals on 172 adult patients admitted for elective colo-rectal resection. Cancer, diabetes mellitus, alcoholism, renal insufficiency and inflammatory bowel disease were all used as exclusion criteria. The restricted IV fluid regimen included no fluid preloading prior to an epidural, no replacement of third space losses, 500 mLs of 5% glucose in water less oral intake during fast, and HAES 6% for blood loss. The standard regimen included a 500mL epidural preload of HAES 6%, third space loss replacement with normal saline (NS) 0.9%, 500mLs of NS independent of oral intake and replaced 500mLs blood loss with 1000-1500mLs NS and blood loss of >500mLs was replaced with HAES 6%. Both groups started blood replacement therapy at losses >1500mLs dependent on hematocrit. The goal hematocrit was 25-35% and higher in patients with cardiac disease. With a p value of <0.0005, the restricted (R) group received significantly less fluids than the standard (S) group on post operative day one. After a median follow up time of 34 days, the authors found that the patients in the R group had an average of 1.2 complications and the patients in the S group had a 2.1 average of complications (p=0.032). Four patients died in the S group from pulmonary edema, pneumonia with sepsis, and pulmonary embolism while no patients died in the R group. The authors have concluded that IV fluid overload causes increased cardiopulmonary complications possibly from the effect of tissue healing issues that the S group experienced (Bandstrup et al.). The authors do acknowledge their small sample size and the unequal distribution of patients who smoke which may also affect results post-operatively.

In 1957, Holliday and Segar created an hourly fluid management protocol based on the patients' weight in kilograms (kg) entitled the '4-2-1 rule-,' it has been accepted and used widely ever since in the operating room (OR) (Thompson, 2015). The foundation of their work centered on the knowledge that a healthy adult must intake a sufficient amount of water to balance gastrointestinal, urinary and insensible losses throughout the day (Thompson). They then correlated their equation to the body's daily caloric expenditure along with daily fluid loss and developed the rule seen below in Table 2.

Table 2

Fluid Management: 4-2-1 Rule

Fluid Management 4-2-1 Rule	
Up to 10kg	**4**mL/kg/hr
11-20kg	Add **2**mL/kg/hr
>21kg	Add **1**mL/kg/hr

(Holliday & Segar, 1957).

This equation has been the basis of many other fluid calculations that have been developed and are relied on by many anesthesia practitioners to provide a baseline or initial fluid goal. Table 3 on the following page also further defines other conventional fluid management modalities used in anesthesia settings. Some methods will also be further explained in the following paragraphs.

Table 3

Description of conventional methods of fluid management

Hemodynamic Variable	Description of Standard Therapy
Maintenance therapy (4-2-1 method)	4mL/kg at 0-10kg of body weight; 2mL/kg at 10-20 kg; 1mL/kg at greater or equal to 20kg
NPO deficit	Maintenance x Fasting hours
Estimated blood loss (EBL)	1:1 Replacement with colloid solution; 3:1 replacement with crystalloid
ABL	Estimated blood volume (EBV)= Weight in kg x Average blood volume
Third space losses	0-2mL/kg for minimal tissue trauma; 2-4mL/kg for moderate tissue trauma; 4-8mL/kg for severe tissue trauma
Compensatory volume expansion	With neuraxial/regional anesthesia: 10mL/kg; without neuraxial/regional anesthesia 5-7mL/kg

(Adapted from Gallagher & Vacchiano, 2015)

Another methodology came about years later called the 'NPO deficit' which is still used today (Thompson, 2015). Risks for hypovolemia and dehydration increase the longer the patient has been NPO. If a patient has been NPO since midnight and their surgery doesn't begin until late afternoon, their hemodynamic status has a greater risk of becoming unstable. The basis for the NPO deficit is for the anesthesia provider to account for the time the patient has fasted and add them to their hourly fluid requirement to overcome this intravascular deficit and possibly adverse effects. The formula is as follows: Maintenance rate X Hours fasted = NPO deficit (Gallagher & Vacchiano, 2015).

Once the NPO deficit is calculated, it is then divided by half and that dose is given to the patient for the first hour and then subsequently quartered and that volume replaced for the following hours of the surgeries duration. Here is an example:

- Patient (pt) weighs 80kg, NPO for 10 hours:
  - Maintenance fluid therapy: 4mL/kg/hr for first 10kg= 40mLs, 2mL/kg/hr for the next 10kg=20mL and 1mL for each kg greater than 21 kg = 60mL = 40+20+60= 120mL/hr for maintenance OR 80kg + 40 = 120mL/hr (simplified way)
  - NPO deficit: 120mL/hr X 10 hours NPO = 1200mls
    - 1st hour: 1200/2 = 600mL/hr
    - 2nd hour: 600/2= 300mL/hr
    - 3rd hour: 300mL/hr

    (Thompson, 2015).

Over the years, problems such as inadequate fluid resuscitation, decreased perfusion to tissues and edema from excess fluid administration have arisen and placed this widely accepted practice into question (Thompson, 2015). Goal-directed therapy (GDT) is now the up and coming way researchers are advocating for patients to receive IV fluids during the peri-operative period. Goal-directed therapy is centered on a specific endpoint, such as cardiac output (CO), with the use of new technologies to predict fluid responsiveness and guide its management during surgery all while preventing tissue hypoxia and fluid overload (Thompson). A hot technology surrounding GDT is the use of the esophageal Doppler (ED).

Esophageal Doppler and Hemodynamic Measurements

To understand how the ED works, a discussion of hemodynamic monitoring is needed. Traditionally, anesthesia providers have utilized blood pressure (BP), heart rate (HR), urine output (UOP), central venous pressure (CVP), mean arterial pressure (MAP) blood lactate levels and correlation to patient status/changes to guide fluid replacement. An article by Johnson & Ahrens (2015) though cites the importance of reconsidering fluid replacement endpoints and focusing on stroke volume (SV). They remark that SV is more likely to alert practitioners to hypovolemia over the other mentioned monitoring parameters since SV is not influenced by most of the body's compensatory mechanisms. Esophageal Doppler allows measurement of SV directly by evaluating the three hemodynamic variables that affect SV: preload, contractility and afterload as related to the Frank Starling principle (Johnson & Ahrens). It also calculates an estimation of the patient's aortic diameter based on height and weight, further individualizing fluid treatment (Johnson & Ahrens). Their work in this article supports a growing body of evidence suggesting that the way anesthesia providers manage and track trends in fluid management may be outdated and in need of the exploration of monitoring SV trends.

The esophageal Doppler (ED) is a probe utilized for the measurement of stroke volume. The ED probe can be inserted either nasally or orally into the esophagus at approximately the 5th and 6th thoracic vertebra once the patient is asleep or anesthetized (Schober et al., 2009). At this point of insertion, the aorta and esophagus run parallel and proper placement allows for continuous measurement of aortic blood flow (per aortic wave forms and pulsatile sound patterns) by the nurse anesthetist on a monitor (Schober

et al.). This is advantageous because it allows for early response and recognition of hypovolemia while avoiding hypervolemia (Schober et al.).

Esophageal Doppler and Fluid Management: Overview

Gallagher and Vacchiano (2015) reported that Medicare and Medicaid systems support the use of esophageal Doppler monitoring (EDM) and provide a section in their article detailing its use and benefit. The authors reported that data analysis from three separate studies show that EDM guided fluid management resulted in earlier oral intake, decreased post operative nausea and vomiting, optimized stroke volume and shortened hospital stays (Gallagher & Vacchiano). Improved perfusion from better fluid guidance is the mechanism most believe is responsible for these positive findings. The EDM is inserted orally, after tracheal intubation and securing of airway, to the level of the mid-esophagus. Blood flow signals should then appear on the monitoring screen for calculation of left ventricular stroke volume and systolic flow time after heart rate correction (Gallagher & Vacchiano). Then, predetermined algorithms can then be utilized by the anesthesia provider to titrate fluids accordingly.

Algorithms have been developed to guide anesthesia practitioners in detecting trends and appropriately dosing IV fluids. Any new technology or equipment is not without risk and is not for every patient. Some risks of using the ED include minor trauma to buccal cavity, transient vagal response during insertion, epistaxis (nasal insertion), and tracheal or bronchial probe misplacement (Schober et al., 2009). Contraindications include patients with increased bleeding or injury risk, esophageal and/or oropharyngeal malformations strictures or tumors, patients on long term steroid

therapy and recent esophageal or upper airway surgery (Schober et al.). Each patient should be assessed preoperatively by the nurse anesthetist to first decide if they are a candidate for this modality. Another possible limitation of ED use on the health care side is the cost of this new technology as well as the training of providers on its use. Limitations of the ED itself include questionable and variable results in patients with aortic pathology, sepsis, sympathetic blockade from spinal anesthesia and aortic cross clamping during surgery (Schober et al.). Overall though, the authors concluded that the literature supports the ED's use due to the decrease in hospital length of stay from decreased post operative complications.

Hamzaoui, Monnet, and Teboul (2015) detailed the last decade's evolution of continuous and real-time monitoring techniques. Their discussion includes the ED as a current method of hemodynamic monitoring and its capabilities along with its limitations. The aim of using an ED is to continuously monitor patients' cardiac output (CO) status by blood flow measurements in the descending aorta derived from aortic blood velocity signals (Hamzaoui et al.). Left ventricular preload and the respiratory variability of aortic blood flow have been shown to be reliable markers of fluid responsiveness (Hamzaoui et al.). The patient's weight and age are also taken into account and plugged into the monitoring data. The authors note that the ED has been reported in numerous studies to decrease a patient's morbidity post surgery.

Monitoring technologies though are not without concerns and limitations and the authors discuss three limitations in the ED's use (Hamzaoui et al.). The first limitation is that changes in sympathetic tone may redistribute cardiac output in the arterial tree. Anesthetics are responsible for decreasing a patient's sympathetic tone and may skew

results and be of concern intra-operatively. The second limitation has to do with the machine or monitors estimation of the descending aorta diameter based on a patient's age and weight. If a patient is in shock or otherwise critically ill, the aorta may have variable compliance and wide changes in mean arterial pressure (MAP) cannot be correlated to cardiac output. Finally, if a patient is moving the esophageal probe can easily move out of proper positioning and the monitoring signal may be lost. In general anesthesia cases, patients are deeply anesthetized and/or paralyzed and movement is not necessarily a hindrance. The authors supported the use of the ED in operating rooms over critical care units (Hamzaui et al.).

Esophageal Doppler and Fluid Management: Research Studies

Non-Randomized Study. A prospective observational study was conducted over five months on 90 patients undergoing different types of surgery. Their aim was to evaluate if the respiratory variation of SV is a better predictor of fluid responsiveness than corrected flow time (FTc) with the ED (Guinot et al., 2012). With 53 patients out of 90 called "responders" to fluid interventions, they found that measuring respiratory variation in SV was a better predictor of hemodynamic status over FTc (Guinot et al.). Cardiovascular variables measured, which included heart rate (HR), blood pressure (BP), cardiac output (CO), flow time corrected (FTc), stroke volume (SV), mean arterial pressure (MAP), respiratory stroke volume variation (respSV) and respiratory peak velocity (respPV) were organized into a chart detailing the subjects baseline numbers and then the numbers after fluid administration. The data was then separated into responders and non-responders. The responder group had lower SV and CO at baseline and had higher respSV and respPV. The respSV and respPV in the responder group after IV fluid

administration was respectively 12 and 8 and in the non-responders respectively, 8 and 6. The authors found significant correlation between change in respSV and respPVwith a p<0.001. The ability of the respSV to predict fluid responsiveness in subjects was more accurate (p<0.0001) than the respPV ability to predict fluid responsiveness (p<0.01). In conclusion, the authors support the use of FTc as a multimodal approach in monitoring patients fluid status and recognized the limitations of their study as well as the need for further studies. This study was excluded from the systematic review evaluation of randomized clinical trials as this study is a prospective observational study and not all the subjects evaluated were undergoing abdominal surgeries.

Randomized control trials: Esophageal Doppler Use in Abdominal Surgeries.

The next and final section of the literature review will summarize randomized control trials concerning the use of the ED in abdominal surgeries. Five of these articles have been further summarized and analyzed in multiple tables in the appendices while the other two articles mentioned did not meet criteria for final analysis. However, the two articles not used for final analysis still provide pertinent information regarding ED use intra-operatively to better assess a patients IV fluid needs.

Randomized Clinical Trials Not Meeting Final Criteria for Systematic Review Analysis. Reisinger et al. (2015) conducted a randomized study at a single hospital to investigate if esophageal Doppler guided fluid management during colo-rectal surgery would increase intestinal perfusion and decrease intestinal injury. The authors used the intestinal fatty acid blood level test (I-FABP) to measure intestinal injury post-operative. Fifty-eight patients undergoing a colon resection over the age of 18 were

enrolled. Patients with contraindications to using the esophageal Doppler such as use of chronic steroids, esophageal varices or other esophageal pathology, and aortic valve disease were excluded. Patients in both the control and intervention group underwent a general anesthesia technique with the majority of patients having an epidural catheter placed for pain control and all patients having a radial arterial line inserted. The esophageal Doppler was inserted trans-nasally and measurements of stroke volume were recorded every fifteen minutes. Voluven and lactated ringers were the fluids of choice for intra-operative intravenous (IV) fluid management and titration. The 27 patients in the intervention group though had a fluid optimization protocol applied to their care and were given boluses of Voluven in 250mL increments as recommended by the algorithm (Reisinger et al.). The intervention group received a mean of 14.6mg/kg/hour of intravenous fluids while the control group received a mean of 16.2mg/kg/hr of IV fluids. One hour post-operative the I-FABP levels for the intervention and control group were respectively, 440.8mg/mL and 522.4mg/mL and median length of stay in days was 11 and 8, respectively. The authors concluded that since no major statistical differences existed between the two groups, they have no evidence that conventional methods of fluid management are outdated or of no value. Their findings do support though that global gastrointestinal perfusion was increased in the GDT fluid group (Reisinger et al.). This is based on the data collected that stroke volume optimization was higher in the intervention group than the control group. A limitation though is mentioned: that severe hypotension to warrant reduced GI perfusion may not be seen in these types of surgeries (Reisinger et al.) and suggestions for further exploration of this topic are presented. This

study did not examine the broad list of complications this systematic review has sought out to analyze and therefore was excluded from final analysis.

Feldheiser et al. (2015) conducted a prospective, blinded, parallel group, randomized trial at a single hospital with 41 patients being assigned to three different groups. The three different groups included a conventional fluid management group, an esophageal Doppler (ED) group and a pulse power wave analysis group. The first two groups are relevant for the purposes of this review. Patients were included if they were above the age of 18 and undergoing liver resection surgery. The study's aim was to compare the group's intra-operative hemodynamic trends and post-operative clinical course. A goal directed fluid algorithm was used for the ED group during surgery. During the statistical analysis of results, the ED group was found to have no decline in stroke volume in contrast to the conventional group. Both groups were administered crystalloids and colloids with the ED group receiving a mean amount of 3300mL of fluid and the conventional group receiving 3075mLs of IV fluid. Stroke volume variation for the ED group was reported as a mean of 8% and for the conventional group a mean of 12%. In regards to LOS, the mean LOS for the ED group was 9 days and 10 days mean stay for the conventional group. The authors cite three main findings. The ED group was more hemodynamically stable than the conventional group. The conventional group may have been more hypovolemic and had higher pain levels. The trending of hemodynamic status was overall poor between the two groups. Their overall conclusion was that no method of fluid management can be discounted and further prospective studies may be beneficial (Feldheiser et al.). This trial did not meet the entire inclusion criteria to be used for final analysis for this systematic review.

Randomized-Controlled Trials Meeting Systematic Review Inclusion Criteria for Final Review and Analysis. McKenny et al. (2013) evaluated 102 female patients undergoing major open gynecological surgery to assess post operative LOS after utilizing the ED monitor (EDM) intra-operatively. The purpose of this randomized prospective trial was to test the hypothesis that intra-operative EDM with SV optimization in major gynecologic surgery would decrease the post-operative LOS. The patients were placed into either a control group where conventional hemodynamic monitoring techniques were used or the ED group. Similarities between the two groups prior to any intervention were that the subjects were undergoing open surgery for malignancy excision of the uterus or adnexae, lymph node dissection or bowel resection. Each patient received a similar general anesthetic and a baseline SV assessed after induction of anesthesia. Post operatively, seven patients in the ED group experienced a total of eight complications while 11 of the control group patients experienced 15 total complications with a p value of 0.41. Complications included wound infection & dehiscence, pulmonary embolism, arrhythmia, and pelvic abscess. The ED group received more colloid and less crystalloid than the control group for a total of 2620mLs (ED) and 2881mLs (control) of IV fluid total. The authors cited multiple conclusions but overall could not conclude whether ED was better than traditional methods and vice versa. The study also lacked support for making conclusions based on what type of IV fluid provides better optimization for patients. The authors chose voluven, a starch based colloid, due to the evidence that it caused no adverse effects. They also hypothesized that postoperative analgesia may play a role in post operative complications and suggested that crystalloids may increase the risk of fluid overload over colloids. Limitations include the use of a single hospital and

lack of using flow-time correction measurement with stroke volume. Overall, the authors stated that not all patients will equally benefit from EDM of fluid status intra-operatively (McKenny et al.).

A study entitled *Esophageal Doppler Use in Bowel and Colo-rectal Surgery* (Conway, Mayall, Abdul-Latif, Gillian & Tackaberry, 2002) sought to examine the effect of utilizing the ED monitoring technique on colorectal resection patients on hemodynamic performance, hospital stay and post-operative complications. Fifty-seven patients were split randomly into a control group and an ED group, given a similar general anesthetic and FTc, SV, CO and cardiac index (CI) were recorded every 15 minutes. A fluid algorithm was utilized. The ED group received more colloid and more fluid overall than the control group which did not reach statistical significance and the CO in the control patients dropped while this did not happen in the ED group demonstrating a p value of 0.003 (Conway et al.). Five patients in the control group required critical care during their hospital stay and none in the ED group were transferred to higher acuity of care nor did they develop any signs of fluid overload or cardiac failure. This study provided support of ED in potentially improving a patient's hemodynamic status and decrease admission to the intensive care unit (ICU).

Wakeling et al. (2005) examined the outcomes of decreased LOS and time before return of gut function in patients undergoing major bowel surgery. The study was blinded and prospective consisting of 134 patients split into two groups: ED and CVP (conventional) group. These patients also underwent measurement of intestinal permeability and endotoxin via blood tests prior to surgery and on days 1 and day 5 post surgery. The ED group patients received increased amounts of colloid (p<0.01); both

received the same median amount of crystalloid and the ED group was found to have higher oxygen delivery at the end of surgery with a p value of <0.05. Morbidity was higher in the control group (p=0.013); complications included urinary retention, pulmonary complications, atrial fibrillation and new onset myocardial ischemia, which were split between the ED and control group. The intestinal permeability test did not differ between the two groups. This study did however show that the ED group had a decreased LOS (p<0.05) and recovered their gut function quicker than the control group. Wakeling et al. supported the use of ED with an SVO (stroke volume optimization) algorithm.

A study by Noblett, Snowden, Shenton, & Horgan (2006) evaluated patients with ED only. Their study aim was to use a protocol based fluid regimen in the operating room during elective colorectal resections to assess hemodynamic status on patient outcomes post-operative. Included in their double blind prospective randomized controlled trial was 108 patients all who had an ED placed to assess length of stay post op. Other clinical data assessed post operatively were return of GI function, morbidity, critical care stay and cytokine markers to assess for inflammation. The control group received fluid based on what the anesthetist felt was necessary and the control group received fluids based on the use of ED monitoring following an algorithm. The goal for both groups was to avoid hypoperfusion of tissues and organ failure while preventing fluid overload. Results included that the intervention group was able to tolerate diet earlier than the control group and had decreased adverse effects which were both significant findings with a p value of 0.029 and 0.043 respectively. More patients in the control group were admitted to ICU (p = 0.012) than the intervention group and received more vasoconstrictor support (p =

0.015). No statistical differences however existed in lower GI function between the two groups and no differences existed in volume of fluid administered. Bowel movements differed by one day between the two groups while time to flatus was the same. The fluid amount difference between the ED and control group was 131mls (colloid p value 0.397 and crystalloid p value of 0.077). No complications from the ED probe insertion and monitoring were reported. In regards to their cytokine marker evaluation, the intervention group had decreased levels of interleukin-6 (p =0.039) which the authors hypothesized may suggest a link between stable CO intra-operative reducing the systemic inflammatory response to surgical stress. As a final conclusion, Noblett et al. supported utilizing the ED with a protocol based fluid optimization algorithm to reduce gut hypoperfusion and benefit the patients post operatively.

Challand et al. (2012) placed 179 patients into two groups as either aerobically fit or unfit and then each group was randomized to receive either ED fluid care or a standard fluid regimen. The cardiopulmonary exercise test (CPET) was used to measure cardio-respiratory function in each of the patients pre-operatively. The authors hypothesis centered on questioning if using ED and GDT will reduce time to discharge and post op complications and if this would remain true even in the fit patient group. Both groups received similar amounts of IV fluid, with the ED group receiving an average of 1360mls of additional colloid administration. Four patients in the ED group suffered from intra-operative hemorrhage while two control patients experienced the same consequence. The GDT group at the end of surgery had a greater SV than the control group especially among the fit vs. the unfit population. Contradictory to the other studies discussed, this GDT group had increased ICU admissions and both group's time to discharge and LOS

were similar. The authors suggested that focusing on maximizing SV may decrease the risk of fluid overload but offered no clear answer that GDT is better than standard fluid monitoring (Challand et al.).

In conclusion, intravascular fluid balance is a basic physiologic need that must be optimized when the body is put through any kind of trauma including surgery. Anesthesia and surgical factors interrupt the body's fluid status and therefore may change a patient's hemodynamic status producing untoward outcomes. Throughout the years, multiple calculations and monitoring devices and techniques have evolved to continue offering patients the best and safest operative course with minimal post-operative side effects. Literature has documented for years the correlation between fluid volume status and adverse events in the post-operative period related to hypervolemia and hypovolemia. Therefore, an anesthesia provider must fully understand the body's fluid compartments, types of intravenous fluids available for replacement and the proper monitoring techniques in order to avoid hypovolemia as well as hypervolemia. As technology advances, the esophageal Doppler has emerged as a promising tool of real-time and continuous fluid status monitoring. It has a high safety profile and is easily inserted in patients with no contraindications. Multiple algorithms have been developed to further supplement its use by anesthesia providers along with understanding the relationship between stroke volume and cardiac output. The importance of individualization or goal-directed fluid management is being set forth into the mainstream as a new decade of fluid management evolves. Continued studies are needed to continue supporting the ED's efficacy and answer questions related to what types of intravenous fluids are best, but

overall the literature supports utilizing the ED as a form of goal directed fluid management intra-operatively.

Current Recommendations on Peri-Operative Fluid Management

      CHEERS-DREAM Mnemonic. In May 2015, the American Society of Enhanced Recovery held a meeting and began a campaign called CHEERS-DREAM with the aim to improve IV fluid management quality of care based on simple objectives. CHEERS-DREAM is a mnemonic that stands for carbohydrate loaded, hydrated, euvolemic, eunatremic, ready to start to drink eat and mobilize (Mythen & Grocott, 2016). The authors state that this simple mnemonic can be used daily by each anesthesia provider as a system to compare their fluid administration variables to. Cheers-Dream seeks to decrease harm to patients in regard to IV fluid administration in the peri-operative period.

      The Fluid Conundrum Continues in 2016. In the June 2016 issue of The Official Journal of the Anesthesia Patient Safety Foundation, Mythen and Grocott discussed the fact that perioperative IV fluid management, a basic and fundamental part of anesthesia care, continues to be highly variable from anesthesia provider to provider and still is lacking in favorable patient outcomes. The authors mentioned that goal directed fluid therapy does have some limitations including lack of availability of monitoring tools and provider lack of experience with instruments but do reaffirm that the literature continues to point to lower volumes of fluid administration being safer for patients. However, since fluid management continues to be highly complex the authors question if clarity will ever be found.

Enhanced Recovery After Surgery. Enhanced recovery after surgery (ERAS) programs or Fast Track surgery programs have been introduced into the peri-operative world as multi-modal guidelines to decrease complication rates and shorten hospital stay after colo-rectal surgery. In response to the changing landscape of healthcare, ERAS challenges traditional or standard surgical patient care against complex and detailed literature reviews recommending different and evidence based care. The ERAS was initiated by Professor Henrik Kehlet in the 1990's and was further developed in 2001 by a group of surgeons in London. Although several versions of ERAS have been published over the years, it continues to gain popularity in order to maximize patient care and decrease health care costs. A 2003 Consensus review paper and a guideline paper will be reviewed here in regards to the IV fluid management recommendations in colo-rectal surgery in the ERAS guidelines.

A Consensus review on ERAS by Lassen et al. and Enhanced Recovery after Surgery Group (2009) extracted data from an extensive review of meta-analyses, RCT's and systematic reviews to offer recommendations on optimal peri-operative care. The authors agreed with and accepted the principles that avoiding fluid overload and restricting fluid intra-operatively decreases post operative complications and hospital stay. They also stated that ED monitoring does help with fluid titration and is useful in high risk patients to improve ejection fraction and oxygenation and decrease complications. For patients experiencing hypotension with epidurals in place, ERAS recommends treating with vasopressors over fluid boluses. The authors do admit that high level evidence of fluid timing and type continue to be absent and further work is needed.

Gustafsson et al. (2012) created peri-operative guidelines in colonic surgery after a critical evidence appraisal on behalf of the ERAS society. They reported that the ERAS pathway has provided patients with a quicker recovery and therefore a short hospital stay. The authors agreed that IV peri-operative fluid management continues to be controversial yet of extreme importance as intravascular volume, a key component of CO, determines oxygen delivery to tissues. These guidelines support the use of minimally invasive monitors such as the ED to individualize fluids for each patient using SV measurements and recommend balanced crystalloids over NS to maintain electrolyte balance. ERAS also states to use vasopressors in patients experiencing hypotension due to epidurals or for other reasons and to use fluid boluses very conservatively.

As surgery and anesthesia continue to develop along with the changing landscape of healthcare today, we as providers must continually adapt and keep ourselves abreast of the newest recommendations and practice them for the good of the patients we serve. Patient care involves continuous simple tasks such as fluid management and the literature is clear that if we do not administer IV fluids appropriately and cautiously and tailored to individual patient needs we can cause our patients much harm and increase healthcare dollars by increasing length of stay.

In the next section, the framework used to guide this systematic review will be presented.

Theoretical Framework

Systematic reviews and meta-analyses remain the gold standard in healthcare for evaluating and disseminating current studies and their conclusions. They assist practitioners in making quality and safe evidence based decisions on patient care quickly and efficiently. Khan, Kunz, Kleijnen, & Antes (2003) stated that systematic reviews differ from other reviews and papers based on the exact step by step approach derived from a clearly constructed question, identification and appraisal of relevant studies, and precise methodology that allows for summarizing of the evidence properly. Their framework, which includes five steps to undertaking a systematic review, has been utilized for this project and each step is explained below.

The first step involves creating and framing a research question with these four components: the population, interventions, outcomes and study design (Khan et al., 2003). The question should guide the rest of the steps and only be changed if truly necessary. The second step stresses the importance of conducting a wide search of medical, nursing and scientific databases in order to capture and identify literature that will be of relevance to the review. This step leads directly into the third step which is determining the quality of the studies—a step of utmost importance though time consuming. When evaluating randomized trials it is prudent to assess the study designs as a marker of quality (Khan et al.). All studies also require an in-depth evaluation of biases, outcomes, data analysis procedures, variables and sample studied, to ensure continued quality and refinement. The two final steps Khan et al., discussed include summarizing and interpreting findings for guidance and use in clinical practice.

Next the methodology of the systematic review will be detailed and will point the reader to further developed charts in the Appendices used to organize the results gleaned from this systematic review.

Method

Purpose/Clinical Question/Outcomes to be Examined

The purpose of this study was to perform a systematic review that examined the impact of the esophageal Doppler versus the traditional weight based fluid management technique on adult (>18 years of age) patient outcomes post-operatively after colo-rectal and abdominal surgery. The goal was to highlight best practices that will decrease adverse patient events and length of stay (LOS). This clinical question asked was: What is the impact of using esophageal Doppler-guided IV fluid management (goal-directed therapy) intra-operatively versus weight based fluid management during colo-rectal and abdominal surgery on selected patient outcomes and length of stay? Specific outcomes examined include hypovolemia or hypervolemia, cardio-pulmonary status problems (arrhythmias, hypotension, heart failure, & pulmonary edema) along with acute renal failure, post-operative ileus, and abnormal electrolyte levels

Inclusion/Exclusion Criteria/Limits

Inclusion or eligibility criteria of the studies included: adult (>18 years of age); admitted for colo-rectal or abdominal surgery including gynecological and urological procedures; with concurrent evaluation of LOS, the measurement and comparison of fluid status using the traditional or esophageal Doppler technique as well as the monitoring of the patients post-operative course. Common clinical complications or outcomes that were assessed in each study were due to hypovolemia or hypervolemia and include cardio-pulmonary status problems (arrhythmias, hypotension, heart failure, & pulmonary edema) along with acute renal failure, post-operative ileus, and abnormal electrolyte levels. Studies or data were excluded if the esophageal Doppler was not utilized as a monitoring

technique, patients are younger than 18 years of age or patients have a pre-operative

diagnosis of chronic renal failure, atrial fibrillation, pulmonary edema, or arrhythmias.

Detailed Search Strategy and Any Limits

The search strategy is outlined in Table 4 below. Studies were immediately

passed over if the trials dealt with non-abdominal surgeries such as cardiac or

orthopedics. Limitations included randomized controlled trials and English only.

Table 4

Search Strategy

Keywords Used (AND/OR)	Electronic databases searched
Esophageal Doppler, Esophageal Doppler monitoring, Intraoperative fluid management, Perioperative fluid management, Traditional/Restrictive fluid management, Randomized controlled trials, Hemodynamic monitoring, Anesthesia fluid management, Goal directed fluid therapy, Colorectal surgery, Abdominal surgery, Elective and Non-elective surgery	Medline PubMed CINAHL

Data Collection for Each Study

Multiple data collection tables have been constructed and adapted and their

purpose is described in the next few paragraphs. First, a literature overview table shown

in Appendix A, adapted from Fineout-Overholt, Melnyk, Stilwell & Williamson (2010)

was used to extract pertinent data from each article. Key headings were selected that

would benefit and organize the data needed for this systematic review. The table provided

an evaluation of the articles' essential pieces of information and helped to appraise the

studies as well. The intent was to enable the analysis of evolving patterns, allow study

comparison, and the ability to confirm original findings throughout the systematic review

process (Fineout-Overholt et al.). Column headings for this Appendix are illustrated in

Table 5 below.

Table 5

Data Collection Column Headings, Appendix A

Study Number
Citation
Level of Evidence/Hypothesis
Design Method
Sample/Setting
Major Variables Studied
Measurement
Data Analysis
Findings

Two other tables created, shown in Appendix B and Appendix C, detail more

specific data extracted from each article related to anesthesia interventions and patient

outcomes. Both tables have allowed for cross referencing anesthesia methods with

outcomes for further comparison and assessment of findings. The data that was collected

in Appendix B entitled Anesthesia Interventions of Studies is illustrated on the next page.

Table 6

Data Collection Column Headings Specific to Anesthesia Course, Appendix B

Study number
Study Authors
Pre-op Interventions
Mean Values
Anesthesia Used
ED Information
Monitoring Type
Fluid Management (type/amount)
Post-op Analgesia
Outcomes

This table illustrates the anesthesia course from pre-operative to post-operative by detailing the type of anesthetic used, the exact fluid management techniques and the outcomes of the study. Appendix B also further sought to clarify information about placement of the esophageal Doppler (ED) and hemodynamic monitoring methods used.

Appendix C shows the pertinent complications reported in both the control group and the ED group along with the total and mean length of stay in the hospital. In addition to complications, it was also noted in the table if any of the subjects were transferred to the intensive care unit (ICU) or died. An illustration of the specific content is illustrated in Table 7 below.

Table 7

Data Collection Column Headings Specific to Complications, Appendix C

Study Number
Name of Study
Patient Complications reported (cardiac, pulmonary, renal, & electrolyte imbalances and deaths post surgery during hospital stay. ED vs. Control Group
Length of Stay (Day of surgery to discharge)

The post surgical patient complications evaluated are related to hypervolemia or hypovolemia and include cardio-pulmonary complications (arrhythmias, hypotension,

heart failure, & pulmonary edema), acute renal failure, post-operative ileus & abnormal electrolyte levels. The subject's total length of stay was also documented in this table.

Critical appraisal tool

Systematic reviews ensure high level quality based on the extensive appraisal of evidence utilized in the review. Fineout-Overholt et al. (2010) stated that the purpose of critical appraisal is to not simply find flaws but to determine if the study is credible in practice. Dartmouth College (2014) located in New Hampshire has created a Critical Appraisal Worksheet for systematic reviews which has been adapted and utilized in this review and can be seen in Appendix D. The table headings are listed in Table 8 on page 33.

Descriptive data synthesis

Two ways in which descriptive data synthesis can be achieved is by both the narrative and tabulation approach as a means to describe, not re-interpret the literature (Evans, 2002). The narrative discussion or literature review presented in the prior section is a critical portion of summarizing not only the studies individually but also across studies as themes begin to emerge. The multiple tables constructed (Appendix A, B, C & D) which were described above, have also served as a means of describing the data in the realm of tabulation and listing of the study characteristics. Both methods have allowed for a better understanding and interpretation of the literature. Evans stated that using both narrative and tabulation data synthesis allows a more comprehensive view of the literature by decreasing limitations of using just one method. Documentation of what the literature is reporting is an important goal of a systematic review in rendering accurate conclusions for clinical practice that may potentially benefit patient care. A final table

comparing across studies can be viewed in Appendix D which summarizes and compares

all the studies used for this systematic review and allows for a thorough discussion of

evidence translation into practice. The content of this table is shown below in Table 8.

Table 8

Comparison across Studies and Critical Appraisal

Study Number
Citation
Main question of systematic review
Comprehensive search strategy
Appropriate study design
Size of intervention or treatment effect
Results
Clinical importance? Can it be applied to my population?
Conflict of interest? Study flaws

Next, the results of the five clinical trials used for this systematic review will be detailed in terms of what the study procedures were, patient complications and length of stay.

Results

Five studies met the inclusion criteria for this systematic review. All five randomized control trials included complication data and hospitalization length of stay of a total of 574 subjects. Each study included a control group that was given IV fluids per standard algorithms based on anesthetist discretion and an EDM group where certain algorithms were followed based on SV data from the ED probe and fluid given accordingly. The tables found in Appendix A, B and C further detail information regarding the studies and the findings, methods and results.

In the trial conducted by Conway et al. (2002)[1] 57 subjects undergoing major bowel resections were studied (28 subjects were randomized to the control group and 29 subjects were randomized to the EDM group). These subjects were assessed with the Goldman Cardiac Risk Index along with standard ASA numbers. FTc, SV, CO, and CI were recorded in all subjects, but blinded to the anesthetist in the control group. The study overview table in Appendix A provides more information on the methodology, study findings and measurements used to analyze the data. The control group subjects were given a mean total of 55.2mL/kg (p=0.02) IV fluid and had a mean length of stay of 11 days. In Appendix B detailed information can be reviewed concerning subject pain management, details of the anesthetic used along with detailed placement of the ED and a fluid management outline for each group. Nine subjects experienced complications (Appendix C) and one subject died of surgical complications and cardiac failure. Three subjects in this group also spent three days in the ICU. The EDM group had no subjects admitted to the ICU, a total of five complications and a mean length of stay of 12 days. This group of subjects received a total IV fluid of 64.6mL/kg. Detailed complication

results and length of stay along with their p or significance levels as reported in the literature are provided in Appendix C.

Wakeling et al. (2005)[2] analyzed 128 subjects undergoing elective or semi-elective large bowel surgery. Besides duration of hospital stay the authors examined as a secondary outcome the time it took for subjects to tolerate a full diet in order to evaluate gut function. The study also included data from VBGs, CBCs, chemistry, albumin and CRP. Further detail on methodology and results can be found in Appendix A. All the subjects in this study were given two Fleet enemas the day before surgery along with 1-2L's Hartmanns solution overnight and the day of surgery each subject had a CVP line placed as well. Appendix B details information on ED placement, IV fluid management and type of anesthesia and pain management provided. The subjects were randomized and allocated into two groups: control or Doppler guided group. In the ED group the Doppler was measured continuously and fluid was guided by an SVO algorithm where these patients received an extra 250mLs of colloid if warranted. Therefore, the Doppler group received significantly more colloid than the standard group (p<0.01). The standard group of subjects was fluid managed with CVP readings targeting 12-15mmHg and the Doppler readings were blinded to the anesthetist. The ED groups hospitalization days were 10 compared to 11.5 days of the control group (p<0.05). Twenty four total complications were experienced by the ED group with zero deaths while the control group subjects experienced a total number of 38 complications and one subject participant death. Detailed complication information and length of stay along with p values can be found in Appendix C.

In a double blind RCT conducted by Noblett et al. (2006)[3] 103 subjects undergoing elective colo-resection were studied; 5 failed to complete the study. A succinct overview table of this study can be found in Appendix A. The groups started out with 54 subjects per group with a mean ASA score of 2. In addition to the outcomes of length of stay and GI function post operatively, the authors also evaluated cytokine markers of inflammation. All subjects received a standard general anesthetic and underwent Doppler monitoring. The ED groups were given colloid boluses based on a strict algorithm and in both groups crystalloid and blood were given based on intra-operative losses and standard hemodynamic monitoring. The intervention or ED group received 2298mLs of crystalloid and 1340mLs of colloid. Further information can be found in Appendix B detailing fluid management, type of anesthesia, ED placement and mean values. Eleven of those subjects required a blood transfusion and 16 required an inotrope. Fluid totals in the control group were 2625mLs of crystalloid and 1209mLs of colloid while 8 subjects received a blood transfusion and 26 received inotrope support. A P value of 0.015 stands for the inotrope therapy warranted for some subjects. Four subjects in the control group were sent to ICU post-operatively at some point during their course and one suffered death. Their total post op stay day was 9. The intervention group had zero ICU admissions and was ready for discharge in 7 days. Complication and length of stay information along with specific p values can be found in Appendix C.

A total of 179 subjects undergoing elective colo-rectal surgery in a double blind stratified RCT done by Challand et. al. (2011)[4] were evaluated by a GDT algorithm. Refer to Appendix A for a detailed overview of this study concerning methodology, outcomes, and sample information. Each subject also underwent cardiopulmonary testing

(CPET) in order to be classified as aerobically fit (123 subjects) or unfit (56 subjects).

Eighty-nine subjects were in the GDT group with ED fluid management guidance and 90

subjects in the standard or control group were administered fluid by standard therapy.

Some subjects received bowel prep pre-operatively and if so were admitted for 1-2L

Hartmann's solution overnight. The subjects in the GDT group received supplementary

colloid to maximize SV according to the algorithm used. Mean total fluids given in the

GDT group was crystalloid 3479mLs (p=0.51), colloids 358mLs (p=0.62) and 112mLs

PRBC's (p=0.31). The control group received 3593mLs of crystalloid (p=0.51), 335mLs

of colloid (p=0.62) and 81mLs of PRBC's (0.31). Detailed information on type of

anesthesia, pain management and ED placement can be found in Appendix B. The

authors found that SV in fit subjects in the GDT group was greater and in both groups,

unfit subjects were more likely to be admitted to the ICU versus the fit subject group.

Complications in the GDT were 10 serious post-op issues, 20 renal complications and 24

ICU admissions. One subject in this group died from pneumonia. The control group

subjects suffered 13 serious complications, 13 renal complications and 17 ICU

admissions. Within 30 days 2 subjects suffered death. Total GDT post op stay was 8.8

days while the control group was 6.7 days total post op stay. In this trial the GDT group

has increased length of stay and a significant amount of complications. Additionally, this

study was not powered to compare differences between the unfit and fit group. Appendix

C further organizes this information and provides p values for significance where

warranted.

McKenny et al. (2013)[5] studied ASA 1-3 subjects undergoing major laparotomies

for suspected gynecological malignancies in a tertiary hospital setting under general

anesthesia. One hundred and two subjects were split and randomly assigned to a control group (51 patients) and an EDM group (51 patients). Further details on study information can be found in an overview table in Appendix A. The subjects in the EDM group received a total of 2620mLs of IV fluid with SV measurement while the control group received a total of 2881mLs of IV fluid total based on the anesthesia providers' standard fluid management technique (p=0.22). More details on type of anesthesia, fluid totals and ED placement can be found in Appendix B. Total length of stay for the control group was seven days with no subject deaths and 11 subjects experiencing post-operative complications. The EDM group's length of stay was six days with seven subjects suffering complications but no subject deaths. P values for complications and length of stay are located in Appendix C.

Per the cross study assessment detailed in Appendix D, four out of the five articles collectively showed that the ED group had decreased complications, decreased to no difference in LOS and decreased ICU admissions. The subjects also showed an improvement in SV and CO improving oxygen delivery more so in the ED group than the control group. One study however, Challand (2011)[4] found that the ED group had an increased number of complications post-operatively. This may imply that this study GDT delivery was different from the other studies in the use of 6% starch solution. In Noblett (2006)[3] the exact fluids used was not made clear and in McKenny (2013)[5] and Wakeling (2005)[2] a gelatin based IV fluid was used. Conway (2002)[1] used a starch solution similar to the Challand (2011)[4] trial. As stated earlier, the exact type of fluids that are most beneficial still have yet to be determined. The fit subjects in the Challand (2011)[4] trial, the ones who performed well on CPET, may also have inappropriately received

additional fluids leading to possible fluid overload and increased complications. However, this study was not powered to evaluate the outcomes between the fit and unfit subject groups. The GDT group also had more subjects undergoing rectal resections. Patients or subjects who undergo rectal resections are usually kept on a liquid diet for 1-2 days prior to surgery and undergo extensive fluid shifts and losses intra-operatively. This may have contributed to the increased complications noted in this group.

Next, the summary and conclusions of this systematic review will be covered in detail along with the strengths and limitations of the literature available and any inconsistencies found.

Summary and Conclusions

A systematic review was performed to address the question: What is the impact of using esophageal Doppler-guided IV fluid management (goal-directed therapy) intra-operatively versus weight based fluid management during colo-rectal and abdominal surgery on selected patient outcomes and length of stay? The goal was to highlight best practices that will decrease adverse patient events and length of stay (LOS). An extensive literature search and review was performed in which the majority of the articles agreed that the age old issue of fluid management intra-operatively can still be improved for surgical patients. There was an abundance of literature relating to fluid issues intra-operatively.

Goal directed therapy utilizes non-invasive and/or invasive monitoring techniques to help the nurse anesthetist guide fluid administration in real time based on the patients stroke volume trends (Thompson, 2015). The most common method of monitoring stroke volume is use of the esophageal Doppler—a probe placed into the patient's esophagus after induction of anesthesia (Schober et al., 2009). Comparison of the esophageal Doppler to standard weight-based modalities will enable the nurse anesthetist to make evidence based decisions on which method may have the most benefit to patients. Colo-rectal and abdominal surgery was specifically analyzed due to the large bodily shifts in fluid status and the concurrent hemodynamic changes that follow. Limitations in the literature included multiple questions that still need to be answered including what types of fluids are best, which patients and surgeries will benefit from what kind of fluid prescription, and is a restrictive or a more liberal approach of fluid management safer.

The purpose of this study was to perform a systematic review that examined the impact of the esophageal Doppler versus the traditional weight based fluid management technique on adult (>18 years of age) patient outcomes post-operatively after colo-rectal and abdominal surgery.

Five articles out of an extensive literature search were chosen based on the identified inclusion and exclusion criteria. Four out of the five trials (Conway, 2002[1]; McKenny, 2013[5]; Noblett, 2006[3]; Wakeling, 2005[2];) showed consistently that use of an ED probe to monitor SV and CO status utilizing specific algorithms decreased complications and length of stay versus standard methods that have been in place for years. Limitations to the use of an ED probe are lack of anesthetist training and lack of finances to use this equipment and have it available. Complications with ED probe insertion were low across the studies. One study (Challand, 2011)[4] had inconsistent results compared to the other four trials. This study evaluated fit versus unfit patients after CPET testing but then wasn't powered to evaluate the outcomes between these patient groups. This trial found that the ED group actually had increased complications post-operatively possibly due to inappropriate use of the GDT algorithm and consequently overloading the subjects in the ED group. Another limitation in the Challand (2011)[4] study included the inability to determine if prolonged time to discharge was due to post-operative complications.

In regards to this systematic review, some limitations include the small number of five randomized controlled trials used for analysis along with the inconsistent results of one trial (Challand, 2011). Pain management and post-operative care was different for each subject in every study and not regulated closely. Pain causes a variety of pulmonary

and cardiac complications and may have contributed to the amount of complications post-operatively. In regards to the ED, no ED monitoring was done post-operatively which may allude to increasing information on fluid management and complication rate and length of stay. None of these trials utilized ERAS protocols either which has been shown to decrease complications after major colo-rectal surgery. Furthermore, while colo-rectal surgery was assessed, the difference between colon and rectal resections and the fluid shifts and possible dehydration prior to surgery is another variable that should be taken into consideration when deciding to use the information from this systematic review. All of the trials used were done in Europe and the BMI of the subjects assessed were not very comparable to the population seen here in the U.S. Increased BMI has been shown to have different effects on patients in regards to IV fluid and anesthesia management and changes the complication rate profile.

While much more research still needs to be done including larger trials, using GDT which includes the use of the ED has been shown to offer safer patient care in terms of fluid management. Increased use of colloids in the ED groups was shown to improve cardiac variables crucial to decreasing complications such as increased CO and SV which improve perfusion and oxygen delivery to tissues leading to decreased complications. The LOS was either decreased in the ED group or no change was found between the standard fluid groups and the ED groups. An important point to remember is that some discharges have also been related to social issues and the subject perception of readiness making it difficult to isolate post-operative complications as the only thing pertinent to time to discharge. Overall, the majority of the trials (four out of five) did support the use of GDT in colo-rectal surgeries to decrease complications and ICU admissions.

Next, recommendations and implications for anesthesia practice will be discussed.

Recommendations and Implications for Advanced Nursing Practice

Anesthesia providers need to employ continued vigilance in administering peri-operative fluids to patients while practicing the most current evidence based standards. Although fluid administration is a basic and daily part of care, if done improperly or carelessly, it can cause a variety of complications for patients. Patients presenting for anesthesia often come with significant challenges such as co-morbidities, dehydration, and acute illness which not only beg for an individualized IV fluid plan but also make IV fluid management more difficult and not as straight forward. Every single organ system and surgical factor must be taken into account when prescribing, administering and managing IV fluids in the peri-operative period.

Nurse anesthetists must continue to be involved in research and participate in yearly anesthesia conferences to ensure more continuing education as the data around fluid management continues to increase. Participating in anesthesia conference events allows dialogue with practitioners around the country and allows sharing of clinical information that can be utilized in each anesthesia provider's individualized practice. Nurse anesthetists can also play a large role in conducting more trials in regards to IV fluid management. More research needs to be done in regards to GDT in not only colo-rectal surgeries but other procedures as well. For hospitals and facilities that cannot afford esophageal Dopplers and the technology required, a question to be asked is what other methods can lead us to a more goal-directed approach to fluid management. Colloid versus crystalloid IV fluid use is another controversial topic that also requires further research and investigation in larger studies.

Anesthesia is given by way of standards of care and practice guidelines. No one policy exists stating the exact type and fluids each patient must receive. Every patient, in terms of their co-morbidities, and every surgical procedure, must be critically analyzed by the anesthetist and under their discretion a fluid plan prescribed. However, in relation to ED, algorithms do exist that help to guide fluid management. As research and trials continue to be conducted on IV fluid management, it is the hope of this author that care standards or practice guidelines can be developed. Nurse anesthetists can play a huge role in this process as they are at the head of the bed providing anesthesia care at the patient level daily.

It is the job of the nurse anesthetist to keep the patient safe and optimized during their procedure as well as dealing with any surgical complications that may arise. Knowledge of the body's physiology and the patho-physiology of illness along with the hemodynamic and physiologic changes of the surgery are crucial to making minute to minute decisions peri-operatively. Master's level and doctorate prepared nurse anesthetists are also in a position to precept and become educators in the profession. Updating the curriculum in GDT methods of fluid management along with increasing the knowledge of hemodynamic variables and their place in fluid management is crucial in progressing forward into the most evidence based care standards. A more restrictive and individualized approach to fluid management must be expressed to students as they prepare their daily care plans and participate in clinical situations. Without the ED equipment, pulse pressure variation and fluid bolus challenges are ways to gauge a patient's fluid status and need.

As standard fluid management plans such as the 4-2-1 method and CVP analysis become questioned in the literature and phased out in some facilities, new monitoring techniques, with the goal of individualizing care for each patient have now become a hot topic. One of the best ways identified in the literature is use of the ED technology in analyzing SV variation during surgery as it reveals explicitly the patient's volume status. Hypovolemia and hypervolemia have both been shown to be detrimental to patients, suggesting a more individualized and possibly restrictive approach to fluid management may be best in order to avoid fluid related complications post-operatively. As the ED, ERAS protocols and GDT continue to be utilized in more surgeries, increased research and information can be gleaned on its use and capabilities in promoting safer anesthesia care. At national anesthesia conferences per the American Association of Nurse Anesthestists (AANA), workshops on ERAS guidelines and IV fluid management continue to be a hot topic. Nurse anesthetists must continue to support the AANA and the lobbying in D.C. on Capitol Hill so that our profession can continue to grow and that we can fund further research on fluid management in the peri-operative period with the ultimate goal of providing the safest care possible to our patients. Until then, a more restrictive, individualized fluid management plan may be put in place and anesthesia providers should refresh their knowledge by the use of CEU's on hemodynamic variables and their relation to the body's fluid status. A daily and sometimes overlooked task should be revisited and altered in order to decrease the rate of complications, ICU admissions and possibly length of stay, which all decrease health care costs and allow for a healthier population.

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Appendix A

Overview of Studies included in the Systematic Review

Study #	Citation	Level of Evidence/ Hypothesis	Design Method	Sample/ Setting	Major variables studied	Measurement	Data Analysis	Findings
1	Conway, D. H., Mayall, R., Abdul-Latif, M. S., Gilligan, S., & Tackaberry, C. (2002). Randomised controlled trial investigating the influence of intravenous fluid titration using oesophageal Doppler monitoring during bowel surgery. *Anaesthesia*, 57,	II (RCT). The aim of this study was to examine the effect of EDM during colorectal resection on hemodynamic performance, hospital stay and post op complications.	Prospective, randomized controlled trial. Inclusion criteria: Pts undergoing major bowel resections. Exclusion criteria: pts having ER surgery, intrathoracic or esophageal surgery, known sensitivity to starch-based colloid or any history of esophageal disease. Prior to induction patients were randomized into Doppler or Control group.	57 pts, 29 Doppler group, 28 to control group. ASA & Goldman Cardiac Risk Indices were similar in pts. No information provided on hospital setting.	Hemodynamic parameters (CO, SV, FTc), peri-op morbidity (ASA & Goldman cardiac risk indices), hospital stay and time to tolerate oral diet. Complication pts had included: chest infection, delirium, PE, re-operation, cardiac failure, & arrhythmias.	Fluid algorithm, Pt characteristics, hemodynamic variables (FTc, SV, CO), Post op stay, Goldman Cardiac risk score.	Student T-test, Mann-Whitney U. Hemodynamic patterns analyzed by linear regression to calculate confidence intervals. Fisher's exact test.	CO increased significantly for the Doppler group while the control group CO remained unchanged. 5 control group pts required ICU admission post op. This study was unable to demonstrate an impact on LOS.

	845-849.							
2	Wakeling, H. G., McFall, M. R., Jenkins, C. S., Woods, W. G. A., Miles, W. F. A., . Fleming, S.C. (2005). Intraoperative oesophageal Doppler guided fluid management shortens postoperative hospital stay after major bowel surgery. *British Journal of Anesthesia*, 95(5),	II (RCT). Assessed whether using intraop ED guided fluid management to minimize hypovolemia would reduce post op hospital stay and minimize time before return of gut function after colo-rectal surgery.	Blinded, prospective controlled trial randomized. Inclusion criteria: undergoing elective or semi-elective bowel surgery. Exclusion criteria: <18y/o, hepatic pathology, perforated viscus, esophageal pathology, & coagulopathy. Randomized via sequentially numbered, sealed opaque envelope technique. Surgical team, nursing staff, & pts were all blinded.	Single centre used, 128 patients undergoing elective or semi-elective large bowel surgery to the ED group or the control group which used CVP and conventional methods.	Primary outcome: Duration of hospital stay— social factors delaying discharge were excluded. Secondary outcomes: time taken until pt could tolerate a full diet. VBG's, CBC, chemistry, albumin and CRP were also drawn and repeated.	SVO fluid algorithm, pt characteristic, hemodynamic & blood gas data, recovery & morbidity scores, & post op hospitalization days & recovery of gut function.	SPSS, Kolmogorov-Smirnoff test with Lilliefors significance correction and Levene's test of variance. ANOVA or Student t-test, Mann-Whitney U-test. ANCOVA. Pearsons correelation coefficient.	Pts in the Doppler fluid group were given a greater volume of colloid and had higher CO and SV than the control group at end of surgery. O2 delivery was also higher. ED use during large bowel surgery had reduced post op hospital stay. Supports the hypothesis.

	634-642.							
3	Noblett, S. E., Snowden, C. P., Shenton, B. K. & Horgan, A. F. (2006). Randomized clinical trial assessing the effect of	II. (RCT). Aim of study is to assess the effect of optimizing hemodynamic status, using a protocol driven intra-op fluid regimen, on the outcome following elective colo-rectal resection.	Pts recruited into a prospectively double blind RCT. Exclusion criteria: severe esophageal disease, recent esophageal or upper airway surgery, systemic steroids, moderate/severe aortic valve disease, bleeding diathesis, & pt choice. Blinding of both	108 pts undergoing elective colorectal resection. 5 failed to complete the study. 54 per group. Intervention group: fluid bolus administration based solely on Doppler assessed parameters (algorithm) Control group: received fluids based on the discretion of the	Primary outcome: LOS (discharge criteria: oral diet, lower GI function, adequate pain control orally, mobilization). Secondary outcomes: GI function, morbidity, critical care stay&	Fluid admin algorithm (FTc, SV)	Power analysis 0.8 with a significance level of 0.050. Kolmogorov-Smirnov tests, Student t test, Mann-Whitney U test. X2 and Fisher exact test. SPSS version 10	EDM group had decreased morbidity & reduced post op stay in pts undergoing elective bowel resection. No differences in overall volume of fluids. Intervention group: higher

	Doppler-optimized fluid management on outcome after elective colo-rectal resection. *British Journal of Surgery*, 93, 1069-1076.		surgical & anesthetic care teams to Doppler readings and to pt randomization.	anesthetist.	cytokine markers of inflammation.		Windows program. P<0.050 is statistically significant.	FTc, SV, CO & CI at end of the procedure—BP monitoring alone may not be enough to assess circulatory status accurately. Control group received more vasopressors, increasing inflammatory response.
4	Challand, C., Struthers, R., Sneyd, J. R., Erasmus, P.D., Mellor, N., . Minto, G. (2011). Randomized controlled trial of intraoperative goal-directed fluid therapy in	RCT. To validate the simplified GDT algorithm in pts undergoing elective colorectal surgery. Hypothesis: Intra-op GDT might reduce the time to Rfd & the complication rate in pts. The study asks would this also remain true in pts with good aerobic fitness?	Double blind stratified RCT. All patients undergoing major colorectal surgery underwent CPET on a stationary bicycle. Exclusion criteria: O2 consumption undetectable or measured <8.0 & pts where no CPET was done. Risk stratified as aerobically fit (AT>11) or unfit (AT 8.0-10.9).	179 patients. 89 to GDT, 90 to standard fluid management. 123 pts were fit & 56 patients deemed unfit and were randomized into either the intervention/GDT group or the control group.	Primary outcomes: oral diet tolerance, mobilization, oral analgesic pain control, return of lower GI function adequate stoma care. Secondary outcomes: LOS, ICU admission 30-90 day mortality 30 day readmission rate.	GDT algorithm. CPET.	Kolmogorov-Smirnox test. Student T-test. Mann-Whitney U test. X2 & Fishers exact test.	GDT group: Pts had increased intraop blood loss, UOP, CI, SV, & FTc vs. the control group. SVwas increased in the GDT group more so in fit pts than in unfit pts. GDT did not improve RfD or LOS. In fit pts, GDT had detrimental effects on the primary outcome measures. SV manipulation

	aerobically fit and unfit patients having major colorectal surgery. *British Journal of Anesthesia*, 108(1), 53-62.							solely by fluid treatment may be an overly simplistic approach to replenishing intra op tissue oxygen debt.
5	McKenny, M., Conroy, P., Wong, A., Farren, M., Gleeson, N., Walsh, C., . Dowd, N. (2013). A randomized prospective trial of intra-operative oesophageal Doppler-guided fluid administration in	II (RCT). To test the hypothesis that intra-operative fluid administration using EDM-guided SV optimization in pts. undergoing major GYN surgery reduces the post-op LOS.	Prospective, randomized, double blinded, controlled trial. Inclusion criteria: pts presenting for open surgery for excision of malignancy of uterus, lymph node dissection or bowel resection. Exclusion criteria: LVEF <30%, esophageal pathology or recent upper GI surgery, hypersensitivity to hydroxyl ethyl starch, significant renal or hepatic disease. Pts randomly assigned to two groups (ED &	102 pts (51 to ED group; 51 to control group). All pts underwent laparotomy for suspected malignancy. Acuity: ASA 1-3. Setting: Tertiary referral hospital. 19 pts in EDM group had ovarian CA, 17 had ovarian CA in control group.	Length of post operative stay, Fit for discharge time frame (tolerating oral diet, restored lower GI function, pain controlled with oral analgesics, capacity to mobilize and self care with minimal assistance), If any pts had: wound infection, renal dysfunction, pneumonia, unplanned ICU admissions.	Postop morbidity survey score (POMS), SV optimization algorithm.	Descriptive statistics, Student's t-test, Mann-Whitney U-test, chi squared test. To detect a difference in hospital stay for 2 days, for 80% power and at a significance level of 0.05, 50 pts were needed for each group.	No difference between the groups in POM and no difference in LOS. 7 pts in EDM group had post op complications and 11 in the control group experienced post op complications

major gynaecolo gical surgery. *Anaesthes ia*, 68, 1224-1231.		Control).					

Key: ASA= American Society of Anesthesiology Physical Class; BP= Blood pressure; CA= Cancer; CBC=Complete blood count; CI=Cardiac Index; CO=Cardiac Output; CPET=Cardiopulmonary exercise testing; CRP= C-reactive protein; CVP=Central venous pressure; ED=Esophageal Doppler; EDM=Esophageal Doppler monitoring; ER=Emergency; FTc= Flow time corrected; GDT= Goal directed therapy; GI=Gastrointestinal; ICU=Intensive Care Unit; Intra op: Intraoperative; LOS = Length of Stay; LVEF=Left ventricular ejection fraction; PE=Pulmonary Embolus; Post op=Post operative; POM= Post operative morbidity; POMS= Post operative morbidity score; Pt(s)= Patient(s);RCT=Randomized Control Trial; Rfd=Ready for discharge; SV= Stroke Volume; SVO=Stroke volume optimization; UOP=Urinary output; VBG=Venous blood gas.   Adapted from (Fineout-Overholt, Melnyk, Stillwell, & Williamson, 2010)

Appendix B

Anesthesia specific interventions of studies

Study #	Study Authors	Pre-op Interventions	Mean Values (Patient BMI, ASA classification and duration of surgery)	Anesthesia Used	ED information	Monitoring type	Fluid management (type/amount)	Post-op Analgesia	Outcomes
1	Conway, D. H., et al.	Routine use of bowel purgatives.	Means: Age Control 67.5, ED 66.5, ASA C 2, ED 1, surgery time C 2 hours, ED 2 hours.	IV induction, muscle relaxation, and ETT. Isoflurane in nitrous oxide and O2. Fentanyl for analgesia.	Following induction, 12g ED was passed orally into the mid-esophagus. Transducer mounted at 45 degrees to the tip of the probe.	Standard monitoring. CVP were utilized at the direction of the anesthetist. FTc, SV, CO & CI was recorded q15mins but the anesthetist was not aware of the results.	The Doppler group received additional fluid boluses of 3mL/kg according to an algorithm based on the ED readings. Group D: 28mL/kg colloid, Total: 64.6ml/kg. Control: 19.4mL/kg colloid, Total 55.2ml/kg.	Post op epidural used in some patients.	SV, FTc & CO increased significantly in ED group while remaining stable in the control group. Control group was relatively hypovolemic during surgery.

| 2 | Wakeling, H. G., et al. | All pts given a bowel prep using two Fleet doses on the afternoon before surgery. Pts could drink water until midnight. 1000-2000mLs of Hartmans solution was given to pts overnight to minimize dehydration during surgery. | Means: Age Control 69.6, SVO 69.1 BMI C 26, SVO 24.5, ASA 2 for both groups. | Induction: Propofol. Maintenance: Isoflurane in Nitrous oxide and O2 with vecuronium or rocuronium. Analgesia: Fentanyl and morphine. | ED probe inserted orally and positioned 35-40cm from teeth. Doppler measurement in control group was taken before surgery, after laparotomy, at the end of surgery and was measured continuously in the Doppler group. | Standard monitoring. Central line for CVP. Used CardioQ Doppler monitoring —velocity of blood flow in descending thoracic aorta was measured.

Control group: pts managed using routine CV monitoring and CVP measurements (target CVP 12-15mmHg) Anesthetist was blinded from ED measurements. | SVO fluid algorithm used.

Doppler group: In addition to routine fluid management also received 250mL boluses of colloid that was repeated if warranted. The fluid protocol was immediately started after probe placement. The ED group received more colloid. | Some patients received epidural analgesia post op. | Doppler group: Had a significant improvement in recovery and reduction in bed stay. CVP does not appear to improve outcomes—there was no correlation in blood volume and absolute CVP measurements. |

3	Noblett, S. E., et al.	None mentioned.	Means: Age Control 67.7, Intervention 62.3, BMI: C 26, I: 25, ASA C 2, I: 2, Duration of surgery C: 167 mins, I 149mins.	Standard volatile-based GA. Some pts received epidural analgesia that was continued 48 hours post op.	A medically qualified researcher with no involvement in post op care or decision making inserted ED and monitored hemodynamics.	Fluid administration algorithm. EKG, pulse oximeter, ETCO2, NIBP or IBP. All pts had continuous EDM. BP monitoring may not be sufficient to assess circulatory status accurately.	Colloid (colloid boluses followed a strict algorithm), crystalloid or blood given was based on intra-op losses and standard hemodynamics. Intervention group: (2298mLs crystalloid, 1340mLs colloid): Also received additional colloid boluses to maintain FTc of >0.35secs & further boluses given to optimize SV. 11 pts had a blood transfusion and 16 required an intrope. Control (2625mLs crystalloid, 1209mLs colloid) 8 pts had a blood	Epidural or PCA for 1st 48hrs post op then oral analgesics.	Primary outcome: LOS. Secondary: return of GI function, morbidity, ICU stay, cytokine markers. Bowel function, dietary intake and fluid administration were recorded on each post op day. Control: 1 post op death-MRSA pneumonia. 12 pts: n/v, ileus. 6 required ICU admission. 39% hypovolemia in OR. 26 pts received vasopressors. Intervention: Pts able to tolerate diet earlier and had reduced major complications. 3 pts n/v, ileus. 0 required ICU admission. Increased SV, FTc, CO & CI. Pulse & MAP similar for each group.

							transfusion, and 26 received an inotrope.\n\nNo differences in overall volume of fluid admin.		
4	Challand, C., et al.	Peri-operative care was conducted in line with enhanced recovery principles— bowel prep was discouraged.\n\nIf pts received bowel prep were admitted for 1-2L Hartmann's solution 12hrs prior to OR arrival.	Means overall: Age Control 65.9 GDT 66, ASA I 11 in both groups, II 52 control GDT 51 III/IV 27 both groups, Duration C 172mins, GDT 171 mins. Transfused in OR C 8, GDT 19, Blood loss C 250, GDT 500mLs.	General anesthetic.	Placed after induction and Doppler readings were recorder every 15 minutes.	Was not clear.	GDT: Pts received supplementary colloid aiming to maximize SV—per algorithm. 1360mLs mean of additional colloid per protocol, crystalloid 3479, colloid 358, PRBCs 112mLs.\n\nControl: 3500mLs, Crystalloid 3593, Colloid 335 mls. PRBC's 81mls.	Epidurals discontinued at 48-72 hours and oral analgesia at earliest opportunity.	GDT pts had more intra op blood loss and UOP than the control group and were more likely to receive a transfusion. Four GDT pts & 2 control pts had an intraop hemorrhage. GDT: CI increased more. At skin closure GDT pts had significantly greater SV, FTc, & CI. SV in GDT pts was greater in the fit vs. unfit patients. Unfit pts more likely to be admitted to the ICU than fit patients.

5	McKenny, M., et al.	None mentioned.	Both groups mean: age 58, BMI: 28, ASA: 2, surgery duration in EDM 150mins and in Control 149mins.	If indicated pt received an epidural catheter before induction. Induction: Fentanyl & Propofol, Rocuronium or Atracurium. Maintenance: Sevo in O2/Air, Remifentanil infusion.	EDM probe inserted after intubation orally or nasally to mid-esophagus.	EKG, SaO2, ETCO2, Arterial line. EDM group: baseline SV taken after induction.	EDM Group: (2620mLs total of fluid): 3ml/kg IV bolus of Voluven over 5 mins and then 5mins later SV measured. If the difference between the two measurements were >10%=repeat bolus until measurements <10%. Further SV measurements at 15min intervals & continuance of protocol. 1000mls crystalloid 1000mls Voluven administered and 8 pts were transfused. Received more colloid & less crystalloid intra-op during the first hour. No differences hourly.	Paracetamol, NSAIDS, morphine PCA, or epidural infusion of LA—was NOT standardized.	Primary outcome: LOS—no difference. Discharge criteria: no unresolved problems, oral diet tolerance, GI function (similar), pain control orally, capacity to mobilize & self care with minimal assistance. Secondary outcomes: time to oral diet, time first BM, POMS score (similar), wound infection, renal dysfunction, pneumonia. Other complications: unplanned admission to ICU. No difference between volume of blood loss, blood products used intra-op or number of patients requiring a transfusion.

						35pts had epidurals post op. Control group (2881mLs total fluid): Fluid managed by anesthetist discretion from conventional hemodynamics (UOP, SBP/CVP, replacing intra-op losses). SV & CI measured at beginning & end—monitor covered during procedure. 36 had post op epidurals for analgesia. Crystalloid 2000mls, Voluven 500mls given and 8 pts received blood products.		

Key: ASA=American Society of Anesthesiology Physical class; BM=Bowel movement; BMI=Body mass index; BP=Blood pressure; CI= Cardiac index; CO= Cardiac output; CV=Cardiovascular; CVP= Central venous pressure; EDM=Esophageal Doppler monitor; EKG= Electrocardiogram; ETCO2= End tidal carbon dioxide; ETT=Endotracheal tube; FTc= Flow time corrected; GA= General anesthesia; IBP=Invasive blood pressure; ICU=Intensive Care Unit; LA=Local anesthetic; LOS=Length of stay; MAP=Mean arterial pressure; MRSA=Methicillin resistant staphylococcus aureus; NIBP=Non-invasive blood pressure; NSAIDS=Non-steroidal analgesic; O2=Oxygen; OR=Operating room; PCA=Patient controlled analgesia; POMS= Post operative morbidity score; PRBC's= Packed red blood cells; Pts=Patients; SaO2= Oxygen saturation; SBP=Systolic blood pressure; SV=Stroke Volume; SVO=Stroke volume optimization; UOP=Urinary output

Appendix C

Post surgical patient complications related to hypervolemia or hypovolemia including cardio-pulmonary complications (arrhythmias, hypotension, heart failure, & pulmonary edema), acute renal failure, post-operative ileus & abnormal electrolyte levels as well as total patient length of stay in hospital.

Study #	Name of study	Patient complications reported (cardiac, pulmonary, renal, & electrolyte imbalances and deaths post surgery during hospital stay). **(ED vs. Control Group)**	Length of stay (day of surgery to day of discharge)
1	Conway, D. H., et al.	**Critical care days:** C 3 (p=0.02), Doppler 0. **At least 1 complication** (chest infection, delirium, pulmonary embolus, re-operation, cardiac failure, arrhythmias): Control group 9, Doppler group 5. No Doppler group patient had signs of fluid overload or cardiac failure.	**LOS:** Control 11 days, Doppler 12 days.

		1 control patient died in post op period (pt had significant cardiac cormorbidity) of surgical complications & cardiac failure.	
2	Wakeling, H. G., et al.	**SVO:** Pulmonary 8—1 patient had pulmonary edema, Renal 3, GI 9, CV 8. Total number of patients with complications: 24. No one died within 30 days. **Control:** Pulmonary 3, Renal 2 GI 29, CV 9. Total number of patients with complications: 38. 1 patient died within 60 days. Higher morbidity (p=0.013). **P values of complications:** Pulmonary p=0.121, Renal p=0.661, GI p<0.001, CV p=0.768.	**Post op hospitalization days:** Control 11.5 SVO: 10. Time until fit for discharge days: Control 11 SVO 9.5. P<0.05. Control group occupied hospital beds for a total of 840 days compared with 770 days for Doppler group.

		Labs: Control group pH 7.28, lactate 1.20, bicarbonate 23.05, Cl- 110, base excess -3.6. SVO: Base excess -5.10, Cl- 110, pH 7.26, lactate 1.25, bicarb 20.05	
3	Noblett, S. E., et al.	**Intervention:** 6 pts had a deviation from normal post operative course, 0 ICU admissions. **Control:** 7 deviation course, 4 ICU admission (p=0.012), 1 death (p=0.012). Complication rate P=0.043	**Ready for discharge days:** Control 9 Intervention: 6. P 0.003. **Total post op stay days:** Control 9, Intervention 7, P: 0.005.
4	Challand, C., et al.	**Control:** 60 deviations from post op course, 13 serious post op complications, 13 renal complications, 17 ICU admission. **GDT:** 63 deviations from	**LOS:** 2 days longer in GDT than in control group. **Ready for discharge days:** Control 4.9, GDT: 6.8 (p=0.09) **Total post op stay:**

		post-op course, 10 serious post op complications, 20 renal complications, 24 ICU admissions. Control group: Two 30 day mortalities. GDT: one patient died from pneumonia. Devation from normal post-op course: p=0.46, Serious complications: p=0.47, Renal complications: p=0.17, ICU admission: p=0.26, Mortality <30 days: p=1.0, <60 days: p=0.72.	Control 6.7 days, GDT 8.8 days. (p=0.09)
5	McKenny, M., et al.	**ED:** 7 pts experienced 8 p/o complications (arrhythmia 1, pulmonary edema 0, unplanned ICU admission 0) **Control:** 11 pts experienced 15 complications. (1 pt	LOS was not reduced in the EDM group. **LOS:** EDM 6 days. Control 7 days. P value: 0.5.

		admitted to ICU, arrhythmia 0, pulmonary edema 1). No one died. Complications p value 0.41, Pulmonary: pneumonia p=0.12, PE p=0.63, Pulmonary edema p=0.50, Cardiovascular: MI p=0.5, Arrythmia p=1.0. Unplanned ICU admission p =0.50.	

Key: CV=Cardiovascular; ED=Esophageal Doppler; EDM=Esophageal Doppler monitoring; GDT= Goal Directed Therapy; GI=Gastrointestinal; ICU=Intensive Care Unit; LOS=Length of stay; MI=Myocardial infarction; PE=pulmonary embolism; Pts=Patients; SVO=Stroke Volume Optimization;

Appendix D

Comparison across Studies and Critical Appraisal

Study #	Citation	Main question of Systematic Review (clear & focused?)	Comprehensive search strategy?	Appropriate study design?	Size of intervention or treatment effect?	Results?	Clinical importance? Can it be applied to my population?	Conflict of interest? Study flaws?
1	Conway, D. H., et al	Examine the effect of ED guided fluid administration during colorectal resection on hemodynamic performance, hospital stay & post-op complications.	No details on an evidence search.	Prospective RCT. Subjects undergoing major bowel resection.Pre-op assessment done on patients. Subjects received a standardized GA. 12Fr ED probe placed. Subjects randomized prior to induction (Doppler vs. Control). All subjects received fluids by anesthetist discretion.	57 subjects total. 29 to Doppler group (Group D), 28 to Control group (Group C). (Sample size calculation revealed that 26 subjects would be required to detect an increase in CO of 1L/min.) One subject in each group was withdrawn due to ED probe problems.	Group D received more colloid (p=0.02) and total fluid therapy—did not reach statistical significance Group D had increased SV, Ftc, & CO (confidence interval=0.31-1.43, p=0.003).	ED is comparable with other methods for estimating CO and SV. Improvements in cardiac performance and reduced complications & ICU stays using ED. No change in LOS was detected (study may have been underpowered). Mean age similar to our populations. Kg (weight) mean lower than our population	The algorithm used responds to trends/ changes in intravascular volume— reducing systematic errors. Monitors measuring aortic cross-sectional diameter may improve accuracy. Need a larger

				(Blinded)			along with ASA.	sample size. Benefits of improved peri-op intravascular volume may have been masked by post op care structure.

#	Author	Purpose		Design	Sample	Results	Findings	Comments
				(Blinded)			along with ASA.	sample size. Benefits of improved peri-op intravascular volume may have been masked by post op care structure.
2	Wakeling, H. G., et al.	Assessed whether intra-op ED guided fluid management to minimize hypovolemia would decrease hospital LOS and time before return of gut function in colo-rectal surgery.	No details given.	Elective or semi-elective large bowel surgery. Single center, blinded, prospective randomized controlled trial. Anesthetist & research nurse were unblinded and had no influence on post-op care. A common patient led post op care pathway was	134 were randomized (64 to ED group and 64 to control group—3 in each group did not receive the allocated intervention.)	No differences in age, BMI, ASA. ED group: 10 days, Control group 11.5 days (p<0.05). Significant correlation between increased post-op stay and advancing age. Subjects in ED group given significantly greater	13% reduction in hospital stay in the ED group—with a significant improvement in recovery. Absolute pressure based CVP target doesn't appear to improve outcome—no correlation between blood volume & absolute CVP measurements. Age is similar to our population;	State that it is unlikely that subject characteristics influenced the results significantly. The authors mention no conflict of interest. Increased study size than study 1.

				followed for all subjects. Subjects randomized by a sealed envelope and opened immediately before induction. ED measurements taken before operation, after laparotomay and at the end in the control group. ED group: ED measurements taken continuously and an SVO algorithm used. Anesthetist blinded to ED measurements in control group and used CVP and routine CV monitoring.		colloid (P<0.01) and achieved higher CO and SV and higher O2 delivery at end of surgery (p<0.05). See Appendix C for complications. No difference in blood transfusion requirements. No subjects died within 30 days of surgery; one pt in the control group died within 60 days of surgery. Control group occupied hospital beds for a total of 840 days; ED group 770 days. Oxygen delivery was	BMI is less and ASA score mean is comparable. Surgical procedures are similar to what's done in my population.	

						higher in the ED group at th e end of surgery.		
3	Noblett, S. E., et al.	To assess the effect of optimizing hemodynamic status—using an intra-op protocol fluid regimen—on outcome after elective colorectal resection.	No evidence search was mentioned.	Subjects undergoing elective colorectal resection were recruited prospectively into a double-blind randomized controlled trial. Complete blinding of both surgical and anesthetic teams to ED readings and subject randomization. Primary outcome measure: LOS. All subjects had continuous ED monitoring. Fluids were given by anesthetist based on intra-	108 subjects—54 per group. Five failed to complete the study.	No differences in subject demographics , risk indices, or duration/type of procedure. Subjects in ED group: reduced time to discharge (p=0.005) and a significant reduction in complications was observed (p=0.043).Mo re subjects in the control group required ICU admissions unplanned. Before induction, no significa nt difference in vital signs. CI	Protocol driven fluid administration by ED monitoring decreases morbidity and reduces post-op hospital stay. No complications were seen related to ED probe insertion or monitoring. Age, surgery and ASA similar to my population; BMI lower. No differences were found in overall volume of fluid given. ED group had higher FTc, SV, CO & CI—Blood pressure measuring alone may not be	Well powered study of a relatively homogeno us group and has a great extent of blinding. No conflict of interest mentioned.

					op losses and standard hemodynamic parameters. Subjects in intervention (ED) group received additional colloid boluses per algorithm. Post-op care was standard.		was increased in the ED group during surgery. Hypovolemia was present for 39% of OR time in control group.	sufficient to assess circulatory status. A greater number of control group subjects received vasoconstrictors.	
4	Challand, C., et al.	Aim was to validate the GDT algorithm in subjects undergoing elective colorectal surgery and hypothesized that the intra-op GDT might reduce the time to ready for discharge and complication rates. Further investigated if this would be true in subjects with good	No search strategy was mentioned.	Double blind stratified randomized controlled trial on pts undergoing major colorectal surgery. All subjects underwent CPET as part of their routine preop assessment and were risk stratified as unfit or fit and then allocated to ED or	179 subjects were randomized: 89 to ED group & 90 to control group. 123 were aerobically fit & 56 as unfit (were older). All randomized subjects completed the study.	Contrasting results from other studies. ED group subjects had more intra-op blood loss & UOP than control group. Four ED subjects experience hemorrhage. Fit subjects in the ED group had increased time to ready for discharge and had more unplanned	In the aerobically fit subjects the ED regimen was associated with detrimental effects. Age, ASA, and type of surgery comparable to my patient population. Increased use of epidurals in the study.	Imbalances between rectal and open procedures were in the ED group and had a greater use of epidurals. ED subjects received more pre-op IVF replaceme nt after bowel prep. Trial was not

		aerobic fitness.		control groups randomly. Subjects to ED group received supplementary colloid per algorithm by investigator. Group allocation, ED readings and algorithm guided administration were concealed from other staff in OR. Post op care was standard and pre-op care used enhanced recovery principles. Primary outcomes were ready for discharge and secondary outcome was LOS.		ICU admissions. Two control group subjects died and one subject died in the ED group within 30 days of surgery. Unfit subjects were more likely to be admitted to the ICU and time to ready for discharge and LOS were similar between ED and control group unfit subjects.		powered to compare outcomes between fit & unfit subjects. Periop care and IV fluid therapy varied widely between anesthetists. Subjective elements of when a surgeon feels a subject can cope at home vary and blur the outcome measures. Grading system for complications used failed to convey duration of adverse

								events and couldn't determine if a prolonged time to discharge readiness was due to persistent complicatio ns.
5	McKenny, M., et al.	Aim was to test the hypothesis that intra-op SV optimization in subjects undergoing major gyne surgery reduces the post-op LOS. Incidence of adverse post-op outcomes was also examined.	No search strategy was mentioned.	Prospective, randomized, double blinded controlled trial on subjects with an ASA of 1-3 undergoing major elective gyne surgery (excision of a malignancy) at a tertiary hospital. Subjects were randomly assigned via sealed envelope. ED subjects were given IV boluses of	102 were enrolled in this study; 51 to ED group and 50 to Control (one in control had their surgery cancelled)	No difference in LOS or total number of post-op bed days. Fewer complications in the ED group. ED group received more colloid and less crystalloid.	At home hospital do not do a lot of gyne surgery. Age and ASA similar to my patient population but BMI is lower.	Subjects did not undergo enhanced principles like coloresecti on subjects do and did not receive pre-op IV fluids. Study did not have standardize d post-op analgesia. Applicabilit y may be reduced because of

				Voluven.Primary outcome measured was LOS.				the single hospital design and this study only used SV, no FTc.

Key: ASA=American Society of Anesthesiologist; CI=Cardiac index; CO=Cardiac output; CPET=Cardiopulmonary Exercise Testing; CV=Cardiovascular; CVP=Central venous pressure; ED=Esophageal Doppler; Ftc=Flow time corrected; Gyne=Gynecological; ICU=Intensive Care Unit; IVF=Intravenous fluids; Kg=kilogram; LOS=Length of stay; O2=Oxygen; OR=Operating room; Pts=Patients; RCT=Randomized control trial; SV=Stroke volume.