

Summer 8-19-2018

Implementation and Compliance with a Goal-Directed Fluid Therapy (GDFT) Protocol for Hip Arthroplasties: A Two-Year Review

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Implementation and Compliance with a Goal-Directed Fluid Therapy (GDFT) Protocol for Hip
Arthroplasties: A Two-Year Review

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Abstract

Background: Historically, goal-directed fluid therapy (GDFT) has been shown to improve patient outcomes when used in the perioperative setting for specific cases (colorectal, etc). When anesthesia providers use GDFT protocols, intraoperative fluid therapy is” patient specific” via the use of dynamic patient-specific physiologic parameters.

Objectives: The aim of the study is to assess whether GDFT improved patient-specific fluid administration. A secondary aim was to assess adherence to the instated GDFT protocol.

Method: A retrospective chart review was conducted on 201 patients undergoing total hip arthroplasty (THA) procedures following implementation of a GDFT protocol at the University of Illinois at Chicago Hospital.

Results: The compliant group consisted of older, heavier, sicker (higher ASA score) patients whom had more EBL during surgery. The compliant group showed a moderate-strong positive correlation between fluid output and fluid administration ($r=0.664$), while the group that did not utilize the EV-1000™ monitor and GDFT protocol had a weaker linear relationship ($r=0.373$).

When the protocol was used, practitioners were compliant in over 50 percent of cases for over 70 percent of the surgical time.

Conclusion: Trends suggest improved patient-specific precision of fluid administration when a GDFT protocol is used. Further evaluations of a GDFT for THA procedures should be conducted for increased protocol validity.

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Background

Anesthesia providers administer intravenous fluid replacement during the perioperative period. Fluid replacement can include crystalloid, colloid, or blood products for patient maintenance, dehydration, and intraoperative fluid loss. Literature suggests that both inadequate and excessive fluid administration can have negative impacts on patient outcomes (Peng, Li, Cheng, & Ji, 2014, Horosz, Nawrocka, & Malec-Milewska, 2016). Too much fluid can result in tissue edema and organ dysfunction, while not enough fluid can result in poor organ perfusion and organ injury. Other negative outcomes include: increased length of hospital stay, post-operative ileus, metabolic derangements, organ dysfunction, and cardiovascular compromise. Horosz, Nawrocka, and Malec-Milewska (2016) state that excessive crystalloid administration can result in tissue edema, hindering intestinal anastomoses and delaying return of intestinal motor functions (possibly leading to prolonged paralytic ileus). By eliminating preoperative bowel preparations the patient's preoperative fluid and electrolyte status is assumed to be normal, thus decreasing the need for high-volume intraoperative fluid replacement.

Traditionally, fluid management approaches have utilized formulas and fixed-volume methods to maintain euvolemia in the intraoperative period. These methods include weight-based calculations assessing basal requirements as well as preoperative fluid deficits. Intraoperatively, anesthesia providers analyze static and dynamic indicators such as mean arterial pressure, heart rate, central venous pressure, urine output, actual/estimated blood loss, and arterial blood gases to guide fluid replacement administration (Trinooson & Gold, 2013). The previously described decision-making process for fluid administration has led to wide spread differences in intraoperative fluid therapy from provider-to-provider. Recent goals for

intraoperative fluid administration are aimed at goal-directed fluid therapy. The target of goal-directed therapy is optimization of cardiac output and end organ tissue oxygen delivery while preventing both fluid overload and under resuscitation (Warnakulasuriya, Davies, Wilson, & Yates, 2016).

Newer innovations for measurement of patient fluid status have helped provide quantitative indicators for fluid administration. For example, volume status indicators such as stroke volume variation and cardiac index or cardiac output used to only be available via invasive monitors such as pulmonary artery catheters. These invasive monitors' benefits often did not outweigh the risk of placement and thus, were not routinely used. As new technology has become available it is possible to monitor such values with non-invasive monitors for routine surgical procedures. Non-invasive monitors include esophageal doppler and plethysmographic variability index (measured via pulse-oxymetry).

In 1995, Danish surgeon, Henrik Kehlet published controversial thoughts surrounding perioperative care that encompass unbalanced fluid administration. Those thoughts served as a stepping stone for the enhanced recovery after surgery (ERAS) protocols that are seen in practice today (Horosz, Nawrocka, & Malec-Milewska, 2016).

ERAS recommendations include the following:

Preoperative preparation and counseling, curtailed fasting, avoidance of preoperative bowel preparation, preoperative supply of carbohydrate-rich drinks, the avoidance of pharmacological premedication, thromboembolism prophylaxis, antibiotic prophylaxis, epidural anaesthesia, intraoperative use of short-acting anaesthetics and opioids, restricted parenteral supply of sodium and fluids, prevention of hypothermia, prevention of postoperative nausea and vomiting (PONV), pain management based on non-opioid

drugs, early enteral nutrition, stimulation of GI motor activity, limited use of naso-gastric tubes, preferences for laparoscopy (with short transverse incisions), avoidance of post-operative drains when possible, early mobilization, early removal of urinary catheters, and evaluations of the implemented protocol and treatment outcomes (Horosz, Nawrocka, & Malec-Milewska, 2016, p. 49-50).

ERAS protocols call for physiologically-guided intraoperative fluid replacement due to the multitude of complications associated with under- or over-hydration. The current research study aims to evaluate the compliance and utility of a GDFT protocol at UIC hospital. Evaluation of the GDFT protocol includes compliance with the protocol as well as measuring variability in fluid administration.

Problem Statement

The wide variation of fluid administration among providers, as well as the potential for detrimental patient outcomes necessitates an inquiry into fluid administration protocols. Recent implementation of GDFT protocol for use in a selected patient population e.g. total hip arthroplasties at University of Illinois at Chicago hospital will be analyzed for clinical compliance and impact on fluid administration.

Purpose Statement

The purpose of this study is to examine the implementation of a GDFT protocol in the intraoperative period for total hip arthroplasties utilizing retrospective analysis of electronic medical records.

Clinical Questions

In the 24 months following the implementation of a goal directed therapy protocol,

1. Does use of a GDFT protocol result in less fluid administration?

2. Does use of a GDFT protocol reduce variability in net fluid administration (i.e. Improve precision)?
3. What is the percentage of time that providers are compliant with the GDFT protocol when the EV-1000™ monitor is used?

Conceptual Framework

This study is guided by two conceptual frameworks. The first, Quality Assurance Model Using Research (QAMUR), is a continuation of the conceptual framework utilized during the conception of University of Illinois' GDFT protocol (Watson, Bulechek, & McCloskey, 1987). Following identification of a problem and review of the literature, this model is then used for either research utilization or research conduction. Original research was utilized to create a GDFT protocol and this follow-up study will conduct new research to examine the effect of protocol implementation.

The second conceptual framework used is the Consolidated Framework for Implementation Research (CFIR) (Breimaier, Heckermann, Halfens, & Lohrmann, 2015). The CFIR uses five domains (intervention characteristics, outer setting, inner setting, characteristics of individuals, and process) to explain why an implementation may or may not succeed (Breimaier, Heckermann, Halfens, & Lohrmann, 2015). This second theory is useful for exploration of anesthesiologists' actions that did not seem to be driven by patient-specific data or protocol doctrine.

Literature Review

Search Method

A computerized databases search was conducted for this literature review using the various combinations of key terms: “fluid administration”, “goal directed therapy”, “enhanced

recovery after surgery”, “intraoperative fluid”, and “orthopedic surgery”. Academic Search Complete, PubMed and CINAHL databases search yields were reviewed and the most recent research articles were selected for review. Fourteen articles were found to be highly relevant to the proposed study and are included in this literature review.

Current Views on Goal-Directed Fluid Therapy

Goal-directed fluid therapy (GDFT) is an individualized approach to perioperative fluid administration using a variety of monitoring devices and dynamic variables including the corrected flow time (FTc) and stroke volume (SV), which are objectively provided by a cardiac output monitoring device (Miller, Roche, & Mythen, 2015). In the past decade, multiple studies have examined GDFT versus traditional intraoperative fluid administration. Recent published studies have also described various dynamic fluid status markers such as stroke volume variation (SVV), pulse pressure variation (PPV) and systolic pressure variation (SPV) as reliable indicators of “fluid responsive physiology” and therefore triggers for intraoperative fluid administration (Gallagher & Vacchiano, 2014; Miller, Roche, & Mythen, 2015). GDFT uses the principle of SV optimization through the use of SVV data. SVV and SV data are objective parameters available to anesthesia providers when using a cardiac output monitor; used to tailor fluid therapy to individual patients (Miller, Roche, & Mythen, 2015). Response to SVV is based on the principle that cardiac output operates under the Frank-Starling law (Miller, Roche & Mythen, 2015). Frank-Starling and colleagues demonstrated that an increase in ventricular filling results in an increased pressure, and thus an increased force of cardiac output, or stroke volume (SV) (Solaro, 2007). SVV is a dynamic indicator that indirectly gives information about the filling pressure of the heart. An increase in SVV is indicative of low filling pressures, thus GDFT protocols call for administration of fluid.

SVV is considered a “dynamic” indicator of fluid status since data is acquired constantly, as opposed to “static” traditional indicators such as heart rate (HR), mean arterial pressure (MAP), and central venous pressure (CVP) that are collected only at discrete time points. These indicators do not necessarily reflect an individual’s fluid status. HR, MAP, and CVP can be increased or decreased due to a variety of reasons such as pain or patient positioning (Miller, Roche, & Mythen, 2015). The goal of using SVV to direct fluid administration is to reduce confounding factors such as pain or patient positioning.

Another commonly used indicator guiding intraoperative fluid therapy is urine output (UO). As urine output declines, providers often increase the rate and volume of infusing fluids. Norberg et al. (2005) conducted an animal study that demonstrated a lack of correlation between urine output and fluid administration. In this study, sheep were divided into three groups: 1) infusion of crystalloid solution only 2) hemorrhage only, and 3) hemorrhage plus infusion. Results demonstrated that in the sheep that were hemorrhaged and received an infusion, there was pronounced oliguria regardless of fluid infusion (Norberg et al., 2005). Increased administration of fluid in the presence of oliguria resulted in fluid retention and expansion of the tissue compartment (Norberg et al., 2005). The results of this study translate into the intraoperative environment, as many anesthesia providers continue to bolus fluids based on decreased urine output. Norberg et al.’s study highlights the lack of correlation between urine output and volume status post fluid administration. Fluid administration based on urine output has the potential for over resuscitation.

GDFT Protocol in Orthopedic Surgeries

A randomized control group trial by Peng, Li, Cheng, and Ji (2014) compared goal-directed fluid therapy to a control group of subjects undergoing orthopedic surgery. The GDFT

group received fluid based on individualized SVV as opposed to the control group (no GDFT protocol) that received fluid administration based on traditional indicators such as HR, MAP, and CVP. SVV is a reflection of a patient's individual cardiac performance. Indicators such as MAP, and CVP are numbers that may be ideal for one patient, but at the same value, may provide inadequate organ perfusion in another patient. Researchers collected data regarding the variables mentioned above, as well as time to passage of flatus post-operatively, and volume of fluid administered (Peng et al., 2014). The results of the study revealed that the GDT group had fewer hypotensive episodes, shorter postoperative time to flatus, and received lower volumes of intraoperative fluid (1,850ml compared to 2,225ml) (Peng et al., 2014).

Benes et al. (2015) also compared a GDFT group to a control group (no GDFT protocol) in patients who underwent total knee arthroplasty or total hip arthroplasty. The GDFT protocol in this study was based off of pulse pressure variation (PPV). PPV is a measure that is then used to calculate SVV. Fluid was administered to keep the PPV lower than thirteen percent. Benes et al. (2015) found that subjects in the control group received significantly higher amounts of fluid and had a higher incidence of postoperative complications such as ileus, respiratory compromise and postoperative infection. Subjects in the control group also had a longer length of hospital stay compared to the GDFT group.

GDFT Protocol in High-Risk Surgeries

Increased intraoperative fluid administration is implicated in several postoperative complications, such as delayed wound healing and wound infections. A randomized controlled trial by Scheeren, Wiesnack, Gerlach, and Marx (2013) demonstrated that postoperative wound infection was significantly lower in a GDFT group versus the control group when undergoing high-risk surgeries (defined based on patient specific criteria such as comorbidities and urgency

of surgery). This study does include potential confounding factors, such as increased transfusion of blood products in the control group. This may induce immunosuppression and predispose the subjects to poor wound healing, however the rate of wound infections in the GDFT group compared to the control was significant, with zero rate in GDFT group versus seven wound infections in the control group (Scheeren, et al., 2013).

Negative Patient Outcomes Averted by GDFT Protocols

Miller, Roche, and Mythen (2015) have identified key patient outcomes for GDFT protocols, which include reduced length of hospital stay, reduced incidence of postoperative complications such as wound infections, and reduced mortality 180 days post-surgery. Horosz, Nawrocka, and Malec-Milewska (2016) reiterate the fact that intra-operative over-hydration is detrimental to the patient. Patients who received less than 2,000 milliliters (mls) in the intraoperative period had a decreased length of hospital stay by an average of three days. The authors also cited that treatment of hypotension with vasopressors as opposed to a fluid bolus reduced the number of postoperative complications by 22% in the Enhanced Recovery After Surgery (ERAS) protocol group (Horosz, Nawrocka, & Malec-Milewska, 2016). This is important to note because intraoperative hypotension is often treated with a fluid challenge first, administering 100-500mls of crystalloid over a short period of time. If the patient is hypotensive due to hypovolemia, the hypotension will resolve with fluid administration. These fluid challenges can drastically increase the total amount of intraoperative fluid the patient receives.

Miller, Roche, and Mythen (2014) state that even a modestly positive postoperative fluid balance can be detrimental. A weight gain of 3kg (6.6 lbs) after elective colonic resection has been shown to be associated with delayed recovery of gastrointestinal function, increased complication rate, and extended length of hospital stay. The authors introduce the term “zero

balance therapy” and propose that be the terminology used in this patient population. Miller, Roche, & Mythen (2014) also discuss the implementation of goal-directed therapy in ERAS patients that resulted in an increase in fluid administration when compared to zero balance therapy. This is probably attributed to the lack of preoperative hypovolemia traditionally experienced due to bowel preps and long NPO times. Finally, the authors also touched upon the fact that traditional markers used to guide fluid therapy intraoperatively (such as heart rate and mean arterial blood pressure) are not always reliable indicators of blood volume (Miller, Roche, & Mythen, 2014).

Not all studies reported decreased intraoperative fluid administration due to GDFT protocols. Phan, An, D’Souza, Rattray, Johnston, and Cowie (2014) conducted a randomized, prospective blind study to compare patient outcomes between GDFT ERAS protocol group versus traditional fluid restriction group. Pahn et al. (2014) study resulted in the GDFT protocol group receiving more boluses and an overall higher volume of intraoperative colloid administration compared to the fluid restriction group. However, no differences in patient outcomes in terms of length of hospital stay and post-surgical complications were seen (Phan et al., 2014).

Trinooson and Gold (2013) performed a literature review of studies that compared GDFT protocols with control groups in high risk surgical procedures where fluid administration was at the discretion of the anesthesia provider. Conclusions from that literature review included an overall increase in fluid administration as opposed to decreased fluid administration. However, a decrease in the number of postoperative complications (7 studies out of 12), and decreased length of hospital time (7 studies out of 12) in the GDFT group were reported (Trinooson & Gold, 2013).

In summary, a few studies found no significant difference between GDFT protocols and GDFT protocol groups in key patient outcomes, but the majority of studies that utilized GDFT protocols resulted in improved postoperative key patient outcomes, as seen in Table 1. In studies that used GDFT protocols, it is important to evaluate the data based on compliance with the GDFT protocol as a low compliance rate could skew outcomes against GDFT when, in fact, in the compliant group outcome may be better.

Table 1. Evidence-Based Table on Goal-directed Fluid Therapy							
Author and Year	Study Objectives	Methods (Design, Sample Size, Setting, Human Subjects Issues)	Study Variables or Constructs Measured or Variables Controlled for by Researchers	Instrument/s Used to Measure the Construct/s	Statistics Used for Data Analysis	Study Findings	Conclusion
Phan, An, D'Souza, Rattray, Johnston, and Cowie, 2014	Comparison of fluid restriction vs. oesophageal Doppler-guided goal-directed therapy (GDT) in elective major colorectal surgery (ERAS program)	Prospective blinded study, n=100, multi-centre setting in Fitzroy, Victoria, Australia, study had institutional ethics approval, patients consented to participate	Fluid volume, type of fluid (fluid restriction protocol versus goal-directed protocol), primary outcome: length of stay (LOS), secondary outcomes: complication rate, change in hemodynamic variables and fluid volumes	Variables mentioned in previous column were obtained via patient's chart	Primary outcomes= power analysis, secondary outcomes: continuous data= t-test, non-parametric data= Mann-Whitney U test, hemodynamic parameters= paired t-test, dichotomous data= chi-square statistics	-GDT group had higher volume of intraoperative colloid (P=0.012). -Primary outcome of LOS was similar between groups: restrictive median=6 & GDT median=6.5 (P=0.421). -There was no statistical significance between groups in regards to secondary outcome of complications. -There were more MAJOR complications in the restrictive group than GDT group (nine vs. one, P=0.007).	-GDT group received more boluses and an overall larger volume of fluid in the peri-operative period than the restrictive group. -GDT did not confer any significant clinical advantage within an ERAS pathway. -There was no difference in LOS, or minor or major complications between the two groups.

<p>Pavlovic, Diaper, Ellenberger, Frei, Bendjelid, Bonhomme, and Licker, 2016</p>	<p>Outcomes following emergency surgery between two different goal-directed therapy (GDT) groups . 1. Control group going off of standard fluid status indicators 2. Optimized group using data from PiCCOplus monitor (CI, GEDVL, EVLWL)</p>	<p>Prospective randomized trial, n=43, conducted in a single academic centre in Helsinki, ethics approval, consent by patient and/or family</p>	<p>Fluid volume and type administered, administration of inotropes, variables driving fluid administration/inotrope use: control group= PPV and conventional targets (MAP, HR, UO, Hb, lactate) intervention group= CI, GEDVI, EVLWI. Primary outcomes= intraoperative change in arterial blood lactate and short-term organ dysfunction. Secondary outcomes= Hospital and ICU LOS, and composite morbidity index ranking.</p>	<p>Data points gathered retrospectively from patient chart.</p>	<p>Mann-Whitney or student t tests were used for continuous data and Fisher's exact tests for categorical data.</p>	<p>-There was no difference in intraoperative fluids administered between the two groups. -Dobutamine was used in 9 out of 20 patients in optimized group, while none in the control group received dobutamine. -Blood lactate levels changed little in the two groups (-0.2+/- 1.2mm/l in control group and -1.2 +/- 1.4mm/l in optimized group, p=0.078). -ICU and hospital LOS did not differ significantly between groups. -Mortality= 13% in control group and 25% in optimized group was actually much less than predicted by morbidity index ranking (60+/- 20 in control and 62+/- in</p>	<p>-In high risk emergency patients, GDT utilizing PiCCO-derived parameters led to increased use of intraoperative inotropes that were associated with less favorable outcomes -The trial was interrupted due to interim analysis on efficacy and safety.</p>
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						<p>optimized group). -Optimized group had more major complications (95%) versus the control group (40%), P<0.001.</p>	
<p>Scheeren, Wiesenack, Gerlach, and Marx, 2013</p>	<p>Randomized trial of high-risk surgical patients assigned to control group or goal-directed therapy (GDT) group. GDT was based on continuously monitored stroke volume variation (SVV) and stroke volume (SV). Control group had no practice changes.</p>	<p>Prospective randomized multicentre study, n=64, ethical approval from ethics committee of University Hospitals, Rostock, Germany. Patients gave informed consent prior to participation.</p>	<p>Hemodynamic parameters that were collected: heart rate (HR), mean arterial pressure (MAP), arterial oxygen saturation by pulse oximetry (SpO2), central venous pressure (CVP), stroke volume variation (SVV), and stroke volume (SV). Data from the flotracs system (SVV and SV) were made available to the GDT group but was hidden from the control group. A protocol for fluid therapy based on SVV and SV was then followed in the GDT group. Primary outcomes= number of complications (infectious, cardiac, respiratory, renal, hematologic and abdominal), SOFA score (organ dysfunction)</p>	<p>Data was gathered via chart review and entered into statistical software.</p>	<p>Number of complications developed post surgery, maximum SOFA score, comparison performed either by using t-test or Mann-Whitney test (if data deviated from normal distribution.</p>	<p>-During surgery, both groups received similar amounts of fluids (P=0.86). - HR, MAP, CVP, SV and SVV were comparable between groups. -SVV decreased in the GDT group (from 9.1 to 8.0%, P=0.048) but not in the control group (8.9 to 8.8%). -Time that SVV <10% was greater in the GDT group versus the control (P=0.41). -Post-operative wound infections was significantly lower in the GDT group (0 vs. 7, P=0.01). -The number of post-operative</p>	<p>-Fluid management based on SVV and SV optimization decreases post-operative wound infections. -Larger follow-up studies are needed but findings suggest that goal-directed strategy might decrease post-operative organ dysfunction. -Higher volume of blood transfusions in the control group and resulting immunosuppression may contribute to decreased wound healing.</p>

						<p>complications per patient and maximum SOFA score was all lower in the GDT group, although not statistically significant.</p> <p>-The control group tended to receive more red blood cells than the GDT (685 vs. 319 ml, P=0.063).</p>	
Fischer, et al., 2016	<p>Comparison of post-operative colorectal surgical patients using photoplethysmography and perioperative hemodynamic optimization algorithm versus a control group (data from EV1000 monitor unavailable). Outcomes being examined are post-operative complications.</p>	<p>Randomized, controlled, two-arm trial, n=160, randomized via scratch card that is generated using permuted blocks, IRB approval obtained from University Hospital of Caen in France, consent obtained from participants</p>	<p>Control group variable= mean arterial pressure (MAP), photoplethysmography group variable= stroke volume (SV) and MAP. Primary outcome=incidence of postoperative complication during 30 days following surgery. Secondary outcomes= total number of postoperative complications, length of hospital stays, and postoperative mortality.</p>	<p>Data collected by blinded third party.</p>	<p>Primary outcome comparison performed by Fisher exact or Pearson chi-square test.</p>	<p>Study is taking place from December 2014 tentatively until December 2016.</p>	<p>Limitations of study include: population being limited to colorectal surgery patients, study population is of intermediate risk (not high-risk).</p>
Norberg, et al., 2005	<p>Assessing fluid shifts in three groups of sheep: A. Infusion only B. Hemorrhage only and C. Hemorrhage plus infusion.</p>	<p>Randomized trial using animal subjects, n=12 (4 per group), approval obtained from</p>	<p>Variables include: cardiac output (CO), mean arterial pressure (MAP), transcapillary flow, plasma volume, and urine output.</p>	<p>Data was gathered in real time during the experiment.</p>	<p>Comparison of transcapillary flow amongst the three groups was done using the Wilcoxon</p>	<p>- No significant difference in CO was noted between the three groups.</p> <p>-MAP was transiently</p>	<p>-Hemorrhage caused an inhibition of renal output.</p> <p>-There was a marked impairment of diuresis after hemorrhage that caused an</p>

		the Institutional Animal Care and Use Committee of the University of Texan Medical Branch, Galveston, TX.			signed ranks test. Interventions were assessed at the 0.05 level of significance.	decreased in group B and increased in group A, group C had higher MAP than hemorrhage alone (B). -Cumulative urinary output was 924+/-371 (group A), 255+/- 135ml (group B), and 537 +/- 233ml (group C).	accumulation of infused crystalloids outside the vascular space. This supports the theory that difficulty of determining optimal blood volume substitution during surgery and hemorrhage and supports the suggestion that overhydration might be a common feature, especially if urinary output is used as a monitor of hydration.
Benes, Zatloukal, Simanova, Chytra, and Kasal, 2014	Evaluation of cost-effectiveness of goal-directed therapy (GDT) implementation.	Direct comparison between study groups and control groups originally in a randomized study, n=120 (60 per group), approval from ethics committee at Charles University in Czech Republic was received and informed consent from participants was obtained.	Variables assessed included: postoperative complications (further divided into subcategories), hospitalization costs, patient care costs, clinical examinations/procedure costs, biochemistry, antimicrobials, radiology diagnostics, and other.	Data was retrospectively collected from patients whom participated in a previous GDT study.	Mann-Whitney and Kruskal-Wallis tests were used to assess the difference between study groups.	-The occurrence of any complication, regardless of allocation, increased the costs of postoperative care by 2295+/- 3611 Euros. -The overall costs of care tended to be lower for GDT versus control (p=0.596), although not statistically significant. -GDT intervention reduced the number of complications (34 vs. 78; p=0.007).	-The mean cost per patient in the GDT group was lower than the control -Overall, the incidence of postoperative complications was lower for the GDT group compared to the control.

<p>Benes, et al, 2015.</p>	<p>Assessment of postoperative morbidity when using goal-directed therapy (GDT) versus control group in two patient surgical categories: total knee arthroplasty and total hip arthroplasty.</p>	<p>Randomized, two-stage study, n=120 (40 per group: control, GDT, and restrictive), IRB approval received from Charles University Hospital in Czech Republic, all patients gave informed consent.</p>	<p>Primary outcome= number of patients with any postoperative organ or infectious complication. Secondary outcomes= hospital length of stay and all-cause mortality.</p>	<p>Blinded investigators evaluated patient data.</p>	<p>For intergroup comparison: one-way ANOVA. For time-dependent variables: repeated measures ANOVA. Categorical variables tested using chi-square test. Tested at significance level of p=0.005.</p>	<p>-Rate of complications was higher in control group when compared to GDT group (88% vs. 55%, p=0.02). -Length of hospital stay was increased in control group, likely attributed to the higher incidence of complications</p>	<p>-Control group patients received significantly higher amounts of fluid compared to both protocol groups. -Overall, GDT has decreased level of postoperative complications.</p>
<p>Trinooson and Gold, 2013</p>	<p>Literature review of RCTs measuring the impact of perioperative goal-directed therapy (GDT) on outcomes among patients undergoing high-risk surgical procedures</p>	<p>12 randomized controlled human trials were included; results further narrowed by only including patients inside the perioperative arena, all studies represented level 2 evidence.</p>	<p>Variables included volume (pulse variation, stroke volume, stroke volume variation), flow (cardiac output, cardiac index, SV), oxygen delivery (mixed venous saturation), postoperative complications and morbidity</p>	<p>Literature review conducted by authors</p>	<p>Varied among studies</p>	<p>Common themes noted throughout studies: -Decrease in hospital stay among GDT group (100%)</p>	<p>-More research needs to be done, i.e. Large multi-site trials of various GDT protocols are needed to further evaluate the effects of GDT modalities.</p>
<p>Warnakulasuriya, Davies, Wilson, and Yates, 2016</p>	<p>Examining a difference in fluid administration when using Pleth Variability Index (PVI) compared to esophageal Doppler in low risk patients undergoing major colorectal surgery.</p>	<p>Randomized controlled trial, n=34, ethics approval granted by NRES Committee-Yorkshire and The Humber-Leeds West,</p>	<p>Primary outcome= total volume of fluid administered in the intraoperative period. Secondary outcomes= differences in 24 hour fluid balance, biochemical markers of tissue perfusion, morbidity at days 1,3,5, and 7, the</p>	<p>Data points collected during trial.</p>	<p>Statistical significance level= p<0.05. Analysis of data achieved using independent samples t-test, analysis of variance, Mann-Whitney U test</p>	<p>-There was no significant difference in volume of fluid administered using PVI or Doppler. -Biomarkers did not significantly vary among groups</p>	<p>-In low-risk patients undergoing major colorectal surgery there was no significant difference in fluid administration, postoperative morbidity, or hospital length of stay.</p>

		conducted at the York Hospital, written informed consent was obtained.	presence of complications, and length of hospital stay.		and Fisher exact test.	-Post-operative complication rate was higher in the Doppler group; however they did not reach statistical significance. -Median hospital length of stay was 7 for both groups (p=0.735);	
Miller, Roche, and Mythen, 2014	Literature review of components of ERAS protocols and management of perioperative fluids	Varied	Pre-intra- and post-operative fluid management, Fluid challenge, goal-directed therapy, complications	Info gathered via lit. review	Multiple	-One study (Noblett, et a.) had a statistically significant reduction in complications and hospital length of stay in the GDT group (P=0.04, and P=0.005 ,respectively)	-GDT has been shown to decreased hospital LOS and complications after major surgery. -In the absence of other concerns, perioperative oliguria should be tolerated. -Intraoperative oliguria was not associated with renal failure, fluid overload results in tissue edema which may directly impact an encapsulated organ such as the kidney and participate in the formation of acute kidney injury.
Peng, Li, Cheng, and Ji, 2015	Evaluation of the influence of stroke volume variation (SVV)-based goal-directed therapy (GDT) on splanchnic organ functions and postoperative complications in patients undergoing orthopedic surgery.	Randomized controlled trial, n=80 (40 in intervention, 40 in control group), approval from Institutional Research Ethics Committee,	Variables: stroke volume variation (SVV), heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), urine output (UO), time to passing first flatus. Intraoperative organ perfusion (via arterial and gastric intramucosal pH, and PCO2 of gastric intramucosa.	Chart Review	Normally distributed data analyzed via paired or unpaired t-tests. Nonnormally distributed data tested via Mann-Whitney U test and Wilcoxon rank-	The mean HR in the GDT group was lower than the control (p=0.028), there were fewer hypotensive episodes in GDT group (p=0.021), Volume of intraoperative	Main findings: SVV based GDT reduced required volume of intraoperative fluids, maintained hemodynamic stability, and improved perioperative gastrointestinal function.

		informed consent obtained from subjects.	Hemodynamic data, hospitalization, postoperative complications, and mortality also recorded.		sum test. Categorical data analyzed via Fisher's exact test. $P < 0.05$ considered statistically significant for each test.	fluid administration was lower in GDT group ($p = 0.036$). Time to first flatus was shorter in GDT group ($p = 0.042$).	There was no difference in urine output, hospitalization, complications, or mortality.
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Methods

Research Design

This study utilized a quantitative, retrospective study design. Utilizing a retrospective chart review of the specific patient population (hip arthroplasties at University of Illinois at Chicago Hospital), key concepts were used as data points. The data was analyzed for statistical significance and correlation between fluid therapy administration versus patient output (including urine output and estimated blood loss). Patient indicators and total fluid administration volume were also analyzed for variance between patient ASA score or the use of EV-1000™ monitoring.

Sample and Setting

This review was approved by the Institutional Review Board (IRB) at UIC and an IRB Authorization Agreement was made between UIC and DePaul University's IRB. Subjects of this study included patients undergoing total hip arthroplasty (THA) at University of Illinois at Chicago (UIC) Hospital. Case information was obtained from UIC's electronic charting system, Cerner SA-Anesthesia.

The sample size was 201 patients over a 23-month period, starting from implementation of GDFT protocol in January 2016. Inclusion criteria included: male and female patients aged 28-88 years, ASA status I, II, III, surgery duration greater than 60 minutes (so as to analyze intravenous fluid administration in milliliters per kilogram per hour). Exclusion criteria include: ASA IV, emergency surgery, surgery duration less than 60 minutes, and vulnerable populations (pregnant women, children).

Definitions of Key Concepts

Key concepts of this study include:

Fluid administration. The concept of fluid administration is important, both conceptually and operationally. Conceptually, one must understand that fluid administration entails replacement of vascular volume and effects patient status and outcomes. Operationally, this study looks at fluid administration in terms of quantity and quality. Fluid quantity is measured in milliliters. Quality of fluid is documented as type of fluid: crystalloid (lactated ringers or normal saline) or colloid (albumin).

Length of surgery. The length of surgery puts fluid administration into context. Generally, the longer the surgery, the more blood loss is involved and/or the need for more fluid replacement increases.

Patient indicators. Patient indicators serve as clues as to why a type or quantity of fluid was given, but also as an indicator for patient's response to fluid administration. Indicators included in this study were: estimated blood loss (mls), stroke volume variation (SVV), and urine output (mls).

ASA status: The American Society of Anesthesiologists physical class status places patients into classes I-VI. Classification is based on physical health with class I being a young, healthy patient and class VI as a brain dead patient. Classes I-III include: healthy, mild, and moderate systemic disease, respectively. Only ASA I-III were included in this study to minimize physiologic fluid shifts, deficits, and responses to fluid administration and blood loss that may be more profound when a patient is unhealthy.

Human Subjects Protection

Subjects of this study are protected in the following ways. Access to study data is limited to the primary investigator, Michelle Pavlik, BSN, RN, and committee members, Randal Dull, Ph.D, MD, and Karen Kapanke, DNP, CRNA, whom have all completed Collaborative

Institutional Training Initiative (CITI) training. Strict adherence to Health Insurance Portability and Accountability Act (HIPAA) is maintained. All patient information was collected and stored using a password protected medical record database. The data analyst had access to datasets with patient data in order to ensure validity and accuracy. A de-identified dataset was provided for analysis using arbitrary numbers attached to each patient. Finally, this study was approved by institutional review boards at both UIC and DePaul University.

Data Collection

Data collection was completed with assistance from UIC Data Analyst Yash Patel. Data was pulled from Cerner SA-Anesthesia by using their Business Objects query system. Data was separated into the following four datasets: *Descriptive*, *ClinicalEvents*, *Actions*, and *MonitoredValues* (see Appendix A). There was one record in the Descriptive dataset that corresponds to each patient case. Clinical events included any drug or fluid administered. The Actions dataset captured monitoring instruments (i.e EV-1000™). The monitored values dataset contained blood pressure, stroke volume variation, stroke volume index, and other values captured by the EV-1000™ and monitoring equipment.

Cases were grouped into two categories: compliant and non-compliant. The compliant group consisted of cases utilizing the EV-1000™ monitor (and thus utilizing the GDFT protocol) while the non-compliant group did not. Use of the EV-1000™ device was inferred from the appearance of SVV values in the case record.

Objective #1: Evaluate IVF administration amongst groups. Did the EV-1000™ group receive less fluid when compared to the non-EV-1000™ group?

Objective #2: Is there less variability i.e. more precision in net fluid administration when the EV-1000™ is used?

Objective #3: What is the percentage of compliance with the GDFT protocol when the EV-1000™ was used?

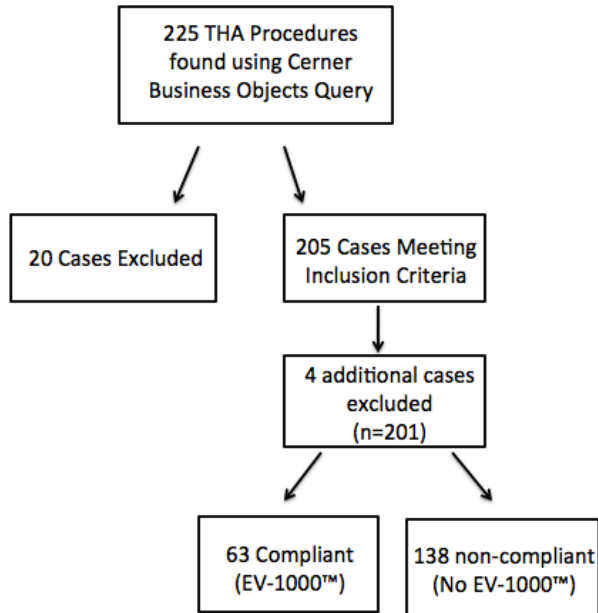
Data Analysis

Intraoperative data was analyzed using the programming language R. Frequencies, means, and standard deviations were calculated for descriptive statistics. Means and standard deviations were used for analysis of net fluid administration, ASA category, primary vs. re-do THA, as well as body weight comparison amongst the EV-1000™ compliant and non-compliant groups. A two-tailed t-test was used to analyze estimated blood loss between EV-1000™ and non-EV-1000™ groups. A 95% confidence interval was reported with a *p* value of ≤ 0.05 considered statistically significant.

Histograms were used to display intraoperative SVV distribution and stacked bar plots were used to analyze fluid administration per each patient (n=201). Finally, scatter plots were used to display fluid output vs. input for compliant and non-compliant cases.

Results

A total of 225 adult total hip arthroplasty cases were obtained via Cerner Powerchart for analysis. Thirteen cases were duplicates and seven had body weights of zero kilograms recorded and were thus excluded from the study. Four cases were additionally excluded from the study due to incomplete or missing data. The sample size was then split into two categories, compliant and non-compliant based on the use or non-use of the EV-1000™ monitor.



The study sample included 102 males and 103 females ranging in age from 28-88 years. Ranges of additional sample descriptives are provided in Appendix A, Figure 2. There were a total of sixty-three cases that used the EV-1000™ monitor and 138 that did not.

Use of the EV-1000™ monitor was demonstrated by evidence of monitor-specific parameters (SVV, SVI, etc.) on the electronic anesthesia record. From cases that used the EV-1000™ monitor, a time weighted mean SVV was calculated using a midpoint Riemann Sum (Figure 3a) and a compound logical function was used to calculate percent time compliant (Figure 3b). Percent time compliant is defined as the percentage of time that the SVV value fell within the identified goal value of less than twelve percent, per GDT Protocol (Figure 8). Percent SVV and percent time compliant values are represented as histograms in Figures 3a and 3b. The mean percent SVV is left skewed, meaning the mean SVV for majority of compliant cases did fall within the goal percentage of less than twelve percent. Figure 3b shows the histogram for

percent time compliant which was right skewed. Over fifty percent of cases using the EV-1000™ monitor were compliant for seventy percent or greater of the total surgical time.

Cumulative fluid values were calculated using the formula (Lactated Ringers + Normal Saline 0.9% + Albumin), which was then compared to cumulative EBL and urine (EBL + Urine) on the same graph (Figures 4a, 4b, & 4c). Cumulative fluid administration varied from 500-9,500mL as seen in Figure 4a. Figures 4b and 4c show cumulative fluid values for compliant and non-compliant groups with the mean being 2,508mL and 2,410 respectively.

Net fluid administration was calculated with the formula (Cumulative Fluids – Cumulative Output (EBL + Urine) / Patient Weight/Procedure Duration) with the resultant units in milliliters per kilogram per minute (ml/kg/min). Net fluid administration did not vary amongst groups with the mean = 0.11mL/kg/min (SD= 0.08) in the compliant group and 0.12mL/kg/min (SD= 0.09) in the noncompliant group. In addition, net fluid administration values were colored by ASA value (Figures 5b and 5c). As Figure 5b shows, patients in the compliant group consisted of almost fifty percent ASA classification threes and ASA twos (SD= 0.50), while the non-compliant group had significantly more ASA twos (SD= 0.46) (Figure 5c). The mean ASA classification for the compliant group was 2.49 and 2.27 in the non-compliant group.

Mean values, standard deviations (SD), and p-values were analyzed for both the compliant and non-compliant groups at a 95% confidence interval (CI) using a two-tailed t-test, in the following categories: EBL, Fluids (cumulative), Net Fluid administration, ASA category, Patient Weight and Patient Age (Figure 6). No significant correlations were found, however trend is that the compliant group consisted of older, heavier, sicker (higher ASA score) patients whom had more EBL during surgery (compliant EBL mean=728.65, non-compliant EBL mean=536.34).

Cumulative output was plotted against fluid administration for total THA cases as well as compliant and non-compliant groups (Figures 7a, 7b, and 7c). The reference line in these graphs represents a predicted 1:1 relationship between fluid loss and replacement, utilizing the formula $([3 \times \text{EBL}] + \text{Urine})$. The calculated correlation coefficient for fluid output versus input for all THA cases was moderately positive ($r=0.515$). Figure 7b shows a moderate-strong positive correlation between fluid output and fluid administration in the compliant group ($r=0.664$), while the group that did not utilize the EV-1000™ monitor and GDFT protocol (Figure 7c) had a weaker linear relationship ($r=0.373$). The data points for cases on figures 7a, 7b, and 7c are also color coded according to a formula calculating patient weight multiplied by surgical duration (kg x min). Data points plotted in blue have a lower *weight x duration* score and the data points progress in color to an orange color as the *weight x duration* score increases.

Discussion

This single-center study evaluated the implementation and compliance with a goal-directed fluid therapy protocol for THA procedures during a two-year period. Overall, there was low implementation of the GDFT protocol, with 69 percent of THA cases being non-compliant with use of the EV-1000™ monitor. Such low overall protocol implementation may be attributed to the fact that the facility only owns a couple of EV-1000™ monitors which may have already been in use when some THA procedures started. When the monitor was used, providers followed the protocol correctly as evidenced by the high percentage of time compliant.

The results of this retrospective chart review showed a higher amount of fluid administration when the GDFT protocol was used; the opposite of researchers' hypothesis of less overall fluid administration in the GDFT group. However, a higher EBL and higher ASA score was noted in the GDFT protocol-compliant group. Follow-up studies should include randomized

groups to avoid this issue. It can be hypothesized that anesthesia providers were more likely to use the EV-1000™ monitor for older, heavier, sicker patients or when a greater amount of EBL was expected.

Net fluid administration did not significantly vary amongst groups, with a mean of 0.11mL/kg/min administered in the EV-1000™ compliant group and 0.12mL/kg/min in the non-compliant group. While the overall net amount of fluid administration was not decreased when the GDFT protocol was used, there was a stronger correlation between fluid loss and administration in the GDFT compliant group ($r=0.664$). The coloring of case's *weight x duration* was significant. A case with a lower *weight x duration* score would be predicted to receive less fluid based on traditional replacement formulas and the more orange the data point gets the more fluid replacement (i.e. more blue data points in quadrant III and more orange data points in quadrant I). This predicted pattern is observed in the non- EV-1000™ group where traditional IVF replacement calculations are used (Figure 7c) but there is no obvious pattern of distribution in the compliant group (Figure 7b). This leads researchers to believe that fluid administration precision did in fact improve, meaning the right patient got the right amount of fluid. While this trend would be more heavily emphasized with a larger compliant group, these results are positive. These results demonstrate the goal of a truly patient-specific GDFT intervention during this study when the EV-1000™ monitor was used.

Limitations

Although this two-year review on implementation of a GDFT protocol showed promising trends there were limitations. The most significant limitation being the small sample size of cases that utilized the EV-1000™ monitor and protocol. As noted above, there may have been provider-dependent discretions when deciding to use the monitor and protocol.

Patient factors could not be controlled, specifically in relation to practitioner interventions (ie. fluid bolus). Intravenous fluid administration is often guided by patient vital signs and controlling those variables could have provided a more accurate assessment of patient-directed fluid administration precision.

Recommendations

There are two recommendations based on this study's findings. First, effort should be made to increase GDFT protocol use amongst anesthesia providers during THAs at UIC. Trends found in this study look promising and a more robust sample size would benefit further evaluations. Re-energizing the implementation of this protocol can be achieved by anesthetist education/reminders as well as ease of access to the protocol (i.e. placing protocol on each anesthesia cart or in rooms where THA procedures are performed). While more costly, it may be beneficial to increase the amount of EV-1000™ monitors available for use at the facility. Second, further evaluation of this GDFT protocol is needed to draw strong conclusions, especially if controlled factors can be increased in subsequent studies. With more promising trends in relation to GDFT protocols, one can infer that it may be beneficial to expand the protocol to other surgical specialties in the future.

Conclusion

While the volume of fluid administration did not vary significantly between the two groups that were compared, there was a stronger correlation between patient-specific output and input when a GDFT protocol was used. Small sample size may have contributed to decreased study strength but the trends looked promising. Further research needs to be done to evaluate the effect of a GDFT protocol, ideally after increased provider utilization of protocol. Follow-up studies may look at patient outcomes such as length of hospital stay or complications amongst

EV-1000™ and non- EV-1000™ groups. Continued studies may also look at other factors in conjunction with GDFT protocol such as use of tranexamic acid to decrease EBL as well as vasopressor use in relation to fluid administration. This retrospective chart review revealed promising trends and serves to be a good guide for further protocol evaluations.

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Appendix

Figure 1

##	Descriptive	ClinicalEvents	Actions	MonitoredValues
##	205	1056939	17722	695921

Columns pulled by Table:

```
## $Descriptive
## [1] "Case Number"           "Person Name- Full"
## [3] "Financial Number"      "Sex"
## [5] "Patient Weight"       "Actual Anesthesia Type"
## [7] "Actual Procedure"     "Actual Surgery Duration"
## [9] "Age- Years (Visit)"   "Anesthesia Duration"
## [11] "ASA Class"            "Procedure Duration"
## [13] "Actual Start Date and Time" "Procedure Start Date and Time"
## [15] "Procedure End Date and Time" "Surgical Case Specialty"
##
## $ClinicalEvents
## [1] "Case Number"           "Person Name- Full"
## [3] "Financial Number"      "Clinical Event"
## [5] "Clinical Event Result" "Clinical Event Result Units"
## [7] "Clinical Event End Date & Time"
##
## $Actions
## [1] "Case Number"           "Person Name- Full"
## [3] "Financial Number"      "Action Performed Date & Time"
## [5] "Action Name"           "Action Detail Description"
##
## $MonitoredValues
## [1] "Case Number"           "Person Name- Full"
## [3] "Financial Number"      "Monitor Category Name"
## [5] "Monitor Unit of Measure" "Monitor Name"
## [7] "Monitored Value Date & Time" "Monitor Charted Value"
```

Figure 2

```

SummaryDescriptiveStats[["SummaryTables"]]

## $Sex
##
## FEMALE    MALE
##    102    103
##
## $`Actual Anesthesia Type`
##
##    Block Epidural    General    Spinal
##         2         15         175         13
##
## $`Actual Procedure`
##
##                Total Hip Arthroplasty Total Hip Arthroplasty Revision
##                                176                                29
##
## $`ASA Class`
##
##    1    2    3
##    1 135  69
##
## $`Surgical Case Specialty`
##
## Orthopedics SN
##                205

SummaryDescriptiveStats[["SummaryRanges"]] %>% lapply(paste, collapse = " to ")

## $`Patient Weight`
## [1] "36.8 to 146.2"
##
## $`Actual Surgery Duration`
## [1] "65 to 850"
##
## $`Age- Years (Visit)`
## [1] "28 to 88"
##
## $`Anesthesia Duration`
## [1] "138 to 1109"
##
## $`Procedure Duration`
## [1] "36 to 850"
##
## $`Actual Start Date and Time`
## [1] "2016-01-05 07:12:00 to 2017-12-26 09:18:00"

```

Figure 3a

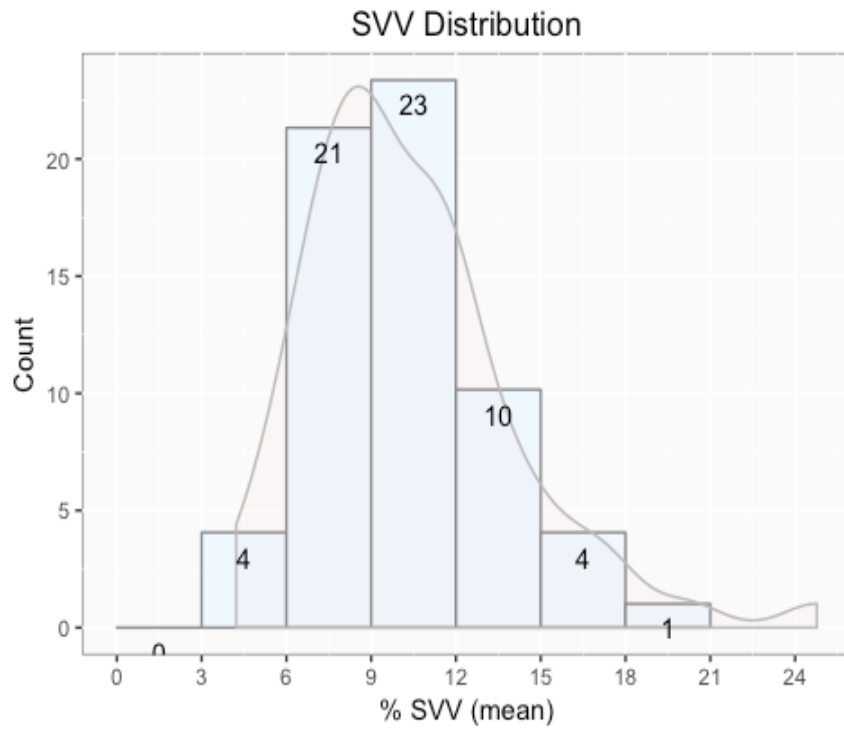


Figure 3b

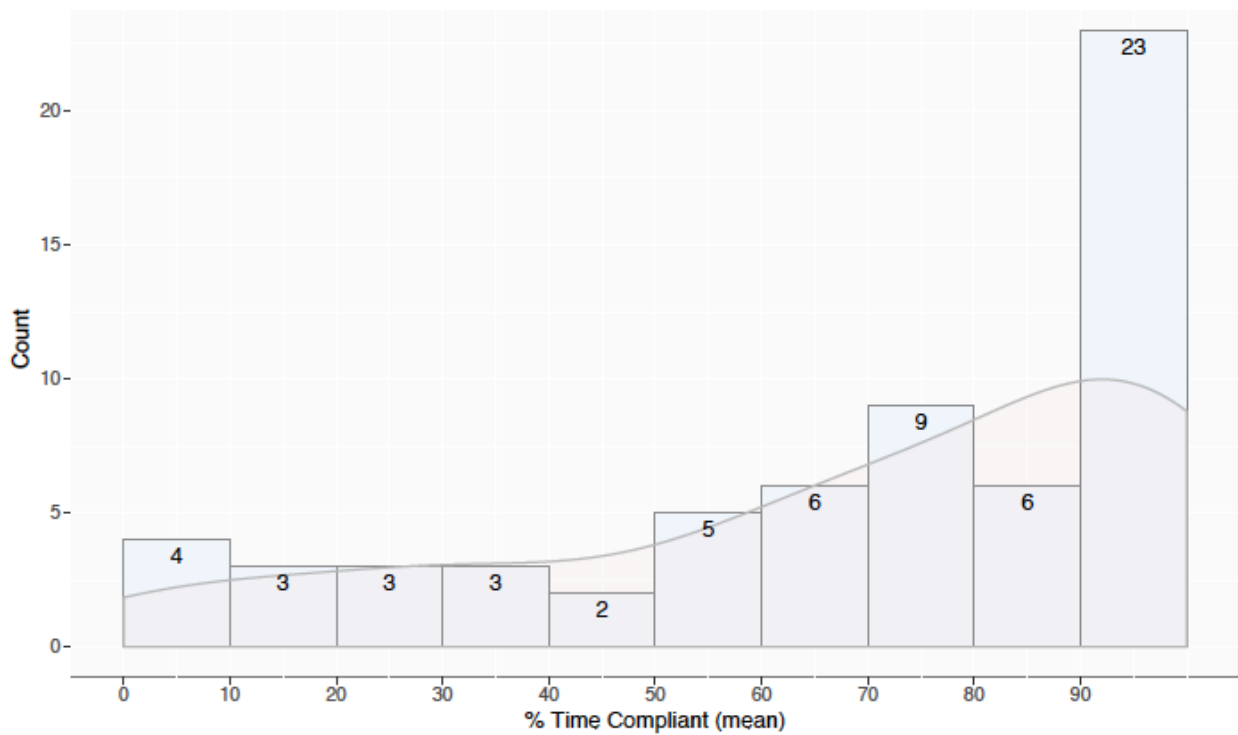


Figure 4a

Cumulative EBL & Urine vs Fluids-In: All Hip Cases

Fluid Stdev: 1279; EBL_Urine Stdev: 709

EBL (mL) Fluids (mL) Urine (mL)

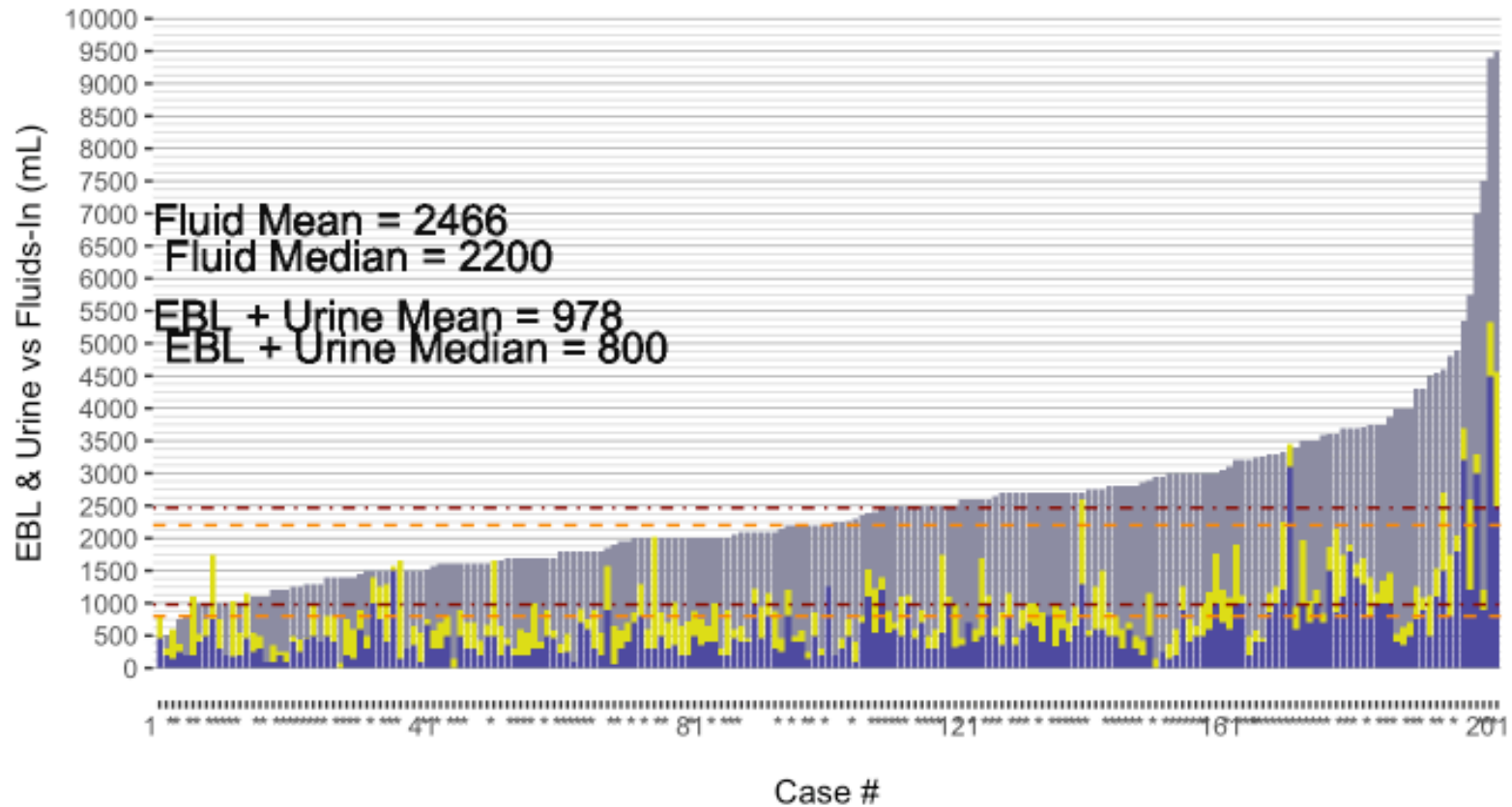


Figure 4b

Cumulative EBL & Urine vs Fluids-In: EV1000 Cases

Fluid Stdev: 1592; EBL_Urine Stdev: 956

EBL (mL) Fluids (mL) Urine (mL)

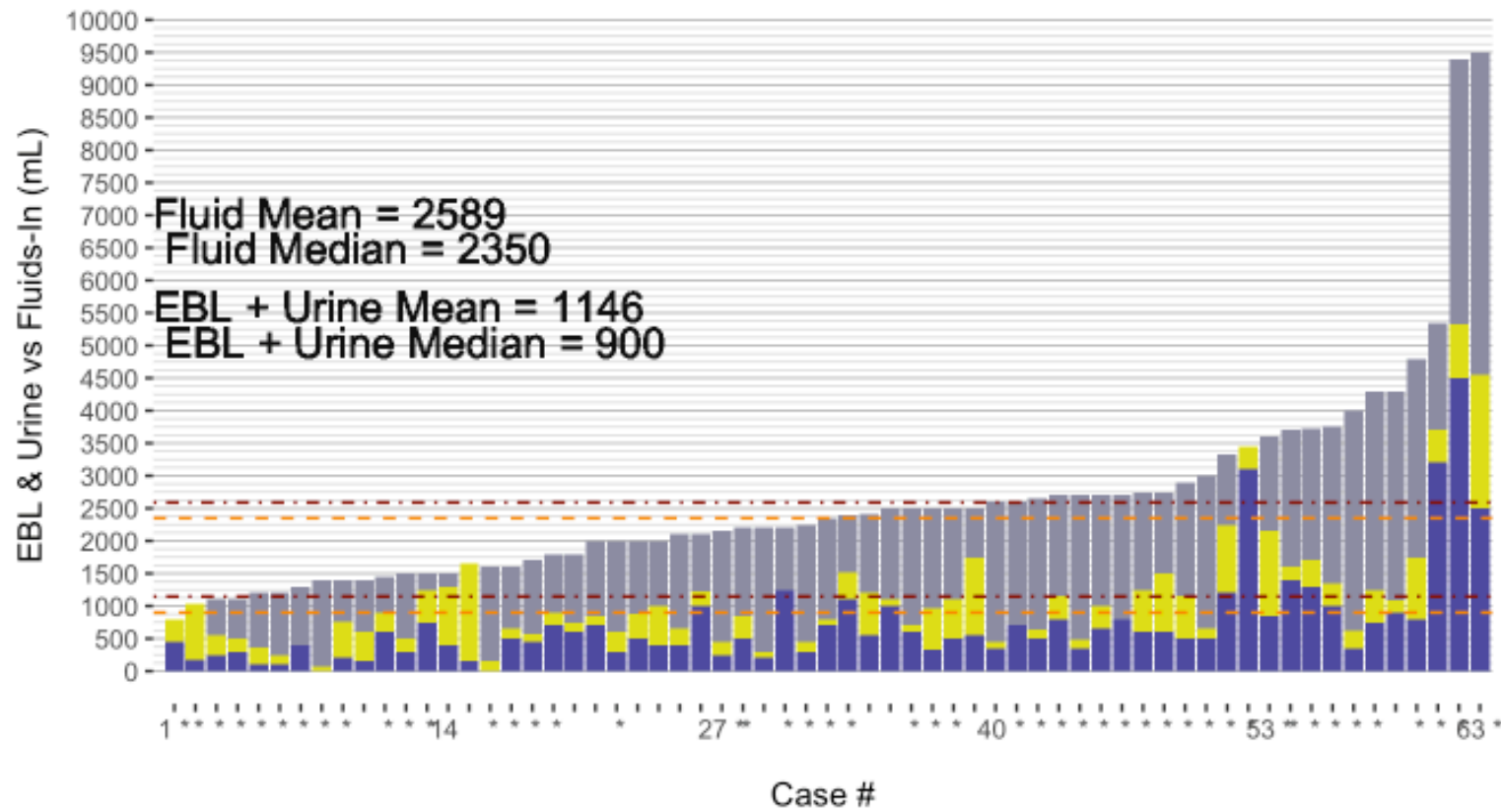


Figure 4c

Cumulative EBL & Urine vs Fluids-In: Non-EV1000 Cas

Fluid Stdev: 1110; EBL_Urine Stdev: 549

EBL (mL) Fluids (mL) Urine (mL)

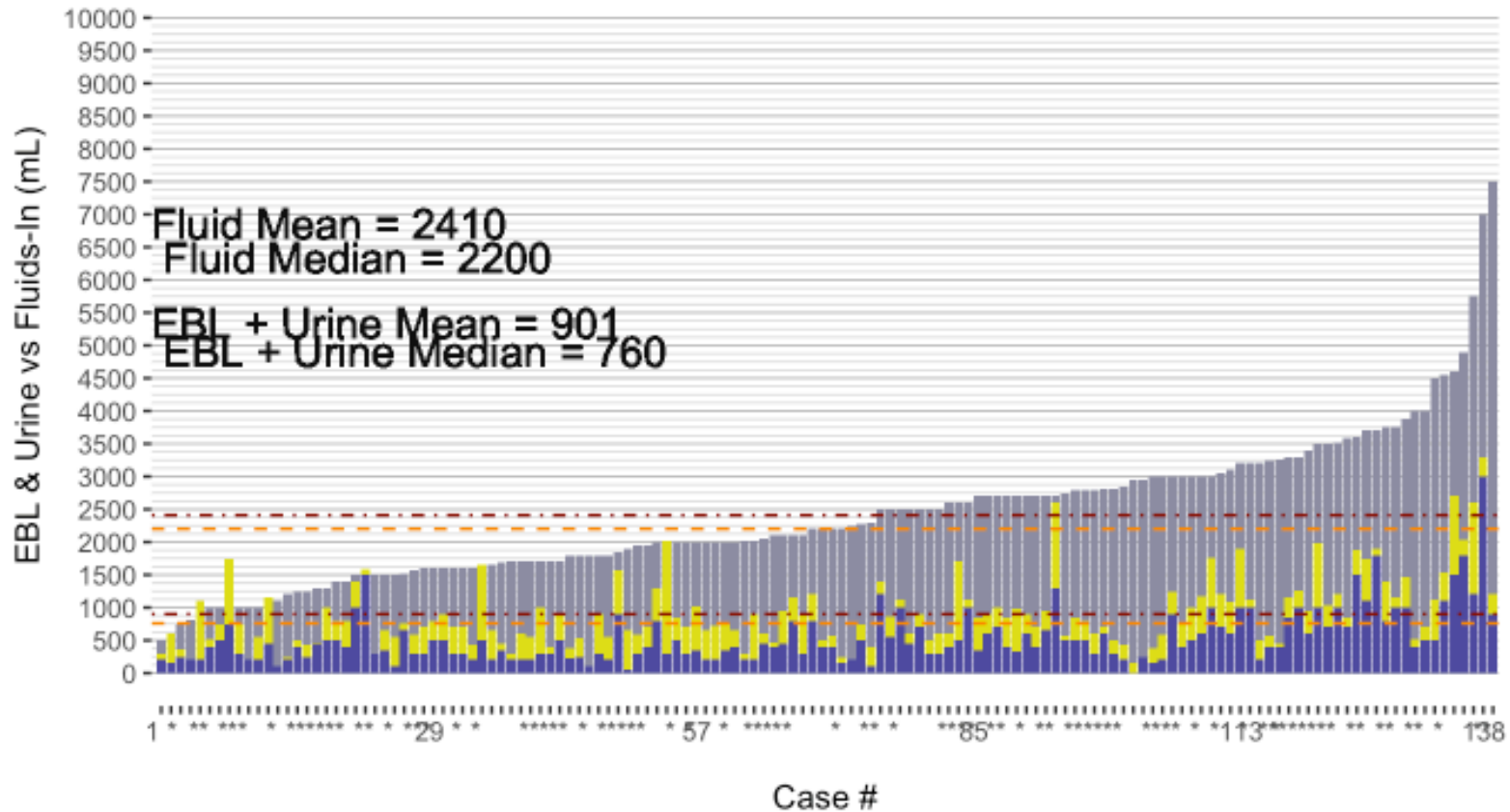


Figure 5a

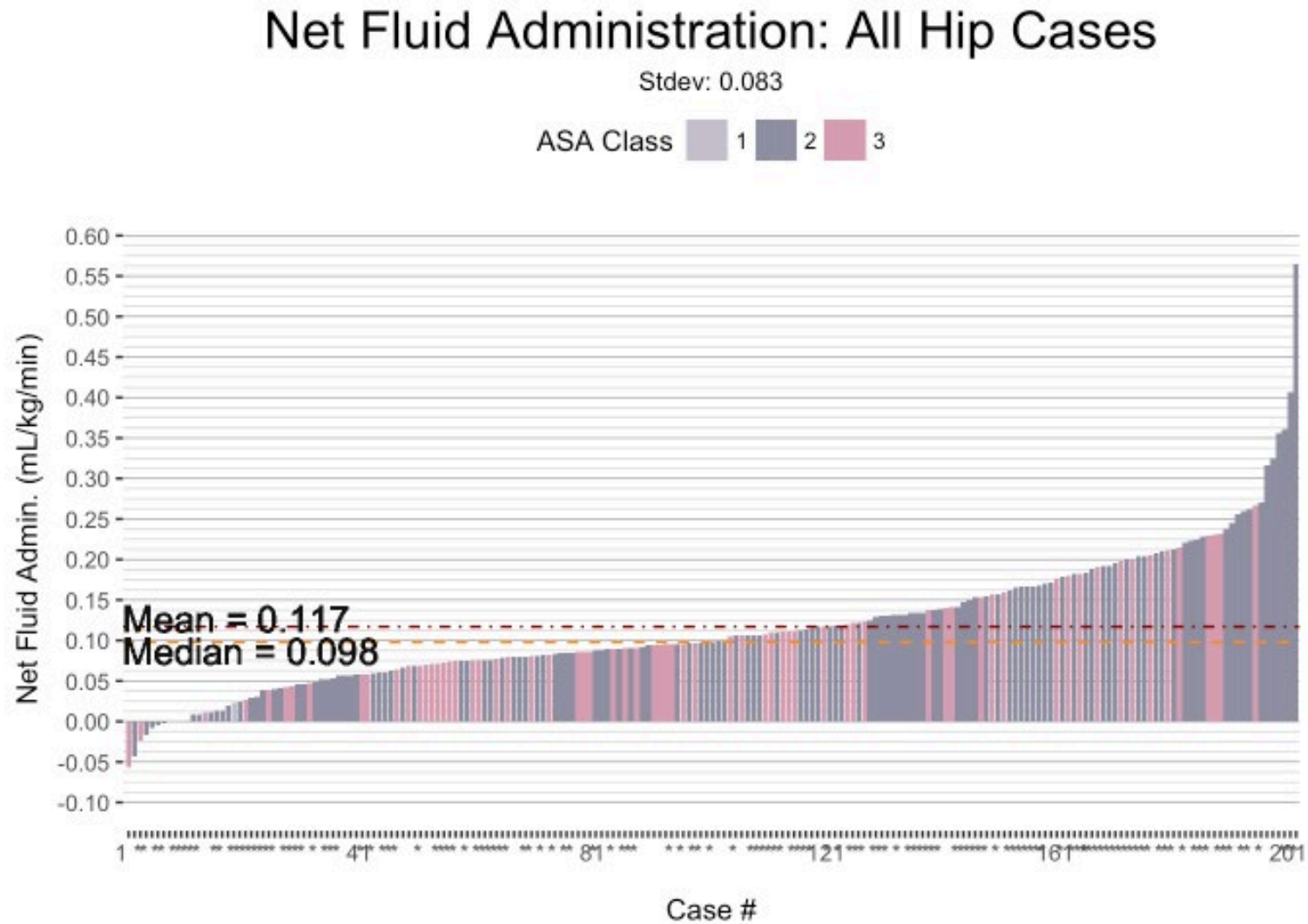


Figure 5b

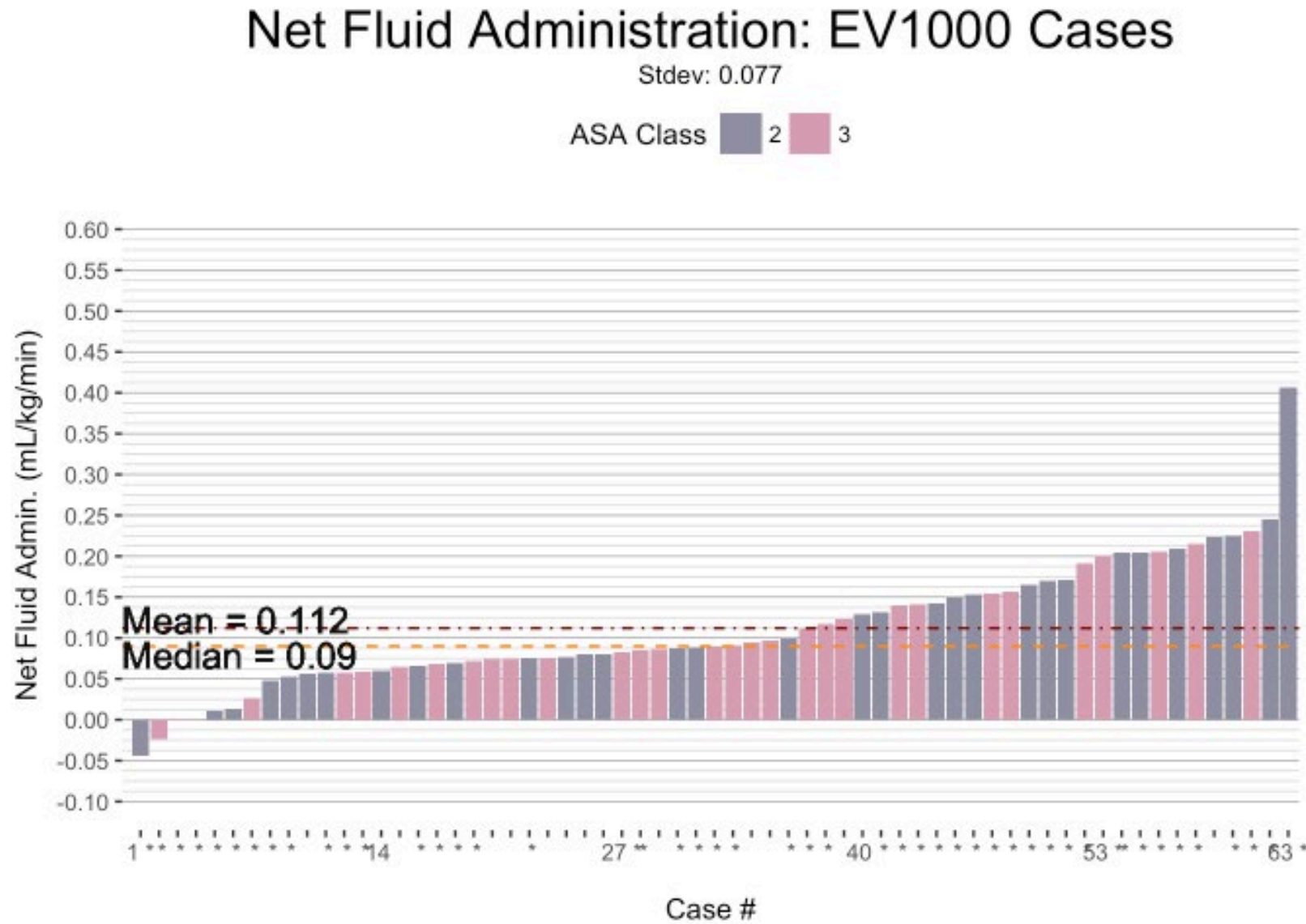


Figure 5c

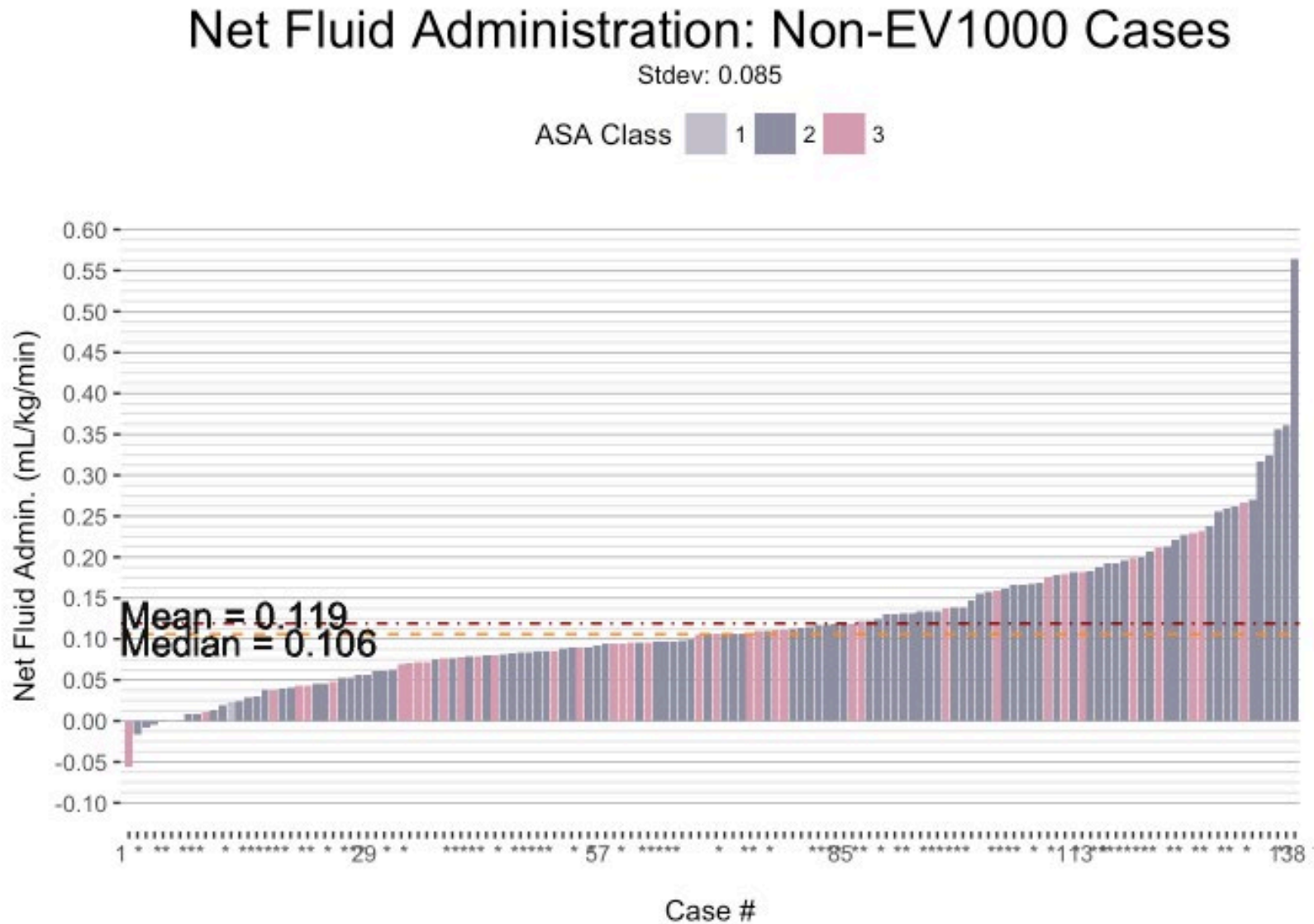


Figure 6

	Parameter	Mean	SD	MeanSD_Interval	p
1	EBL EV	728.65	773.13	-44.479733215104 to 1501.78132051669	0.07
2	EBL NonEV	536.34	413.66	122.679014589507 to 950.002144830783	0.07
3	Fluids EV	2588.99	1591.78	997.206304517326 to 4180.7720192922	0.42
4	Fluids NonEV	2409.62	1109.89	1299.72883951903 to 3519.50431265488	0.42
5	Net Fluid Admin EV	0.11	0.08	0.0354101676061502 to 0.188868012586802	0.58
6	Net Fluid Admin NonEV	0.12	0.09	0.0336124082495262 to 0.204250503712204	0.58
7	ASA EV	2.49	0.50	1.98811086138452 to 2.99601612274246	0.00
8	ASA NonEV	2.27	0.46	1.80739839516087 to 2.7288334888971	0.00
9	Weight EV	90.64	20.15	70.4917037728396 to 110.786074004938	0.30
10	Weight NonEV	87.49	19.48	68.0024683913754 to 106.968546101378	0.30
11	Age EV	60.30	9.47	50.8289868808919 to 69.7741877222827	0.09
12	Age NonEV	57.67	11.12	46.5520512005269 to 68.7957748864296	0.09

Figure 7a

Output vs Input Fluid: All Hip Cases

135, 65, and 17 cases above, below, and near the slope = 1 line
 StdevEBLUrine:1776; StdevFluids:1279

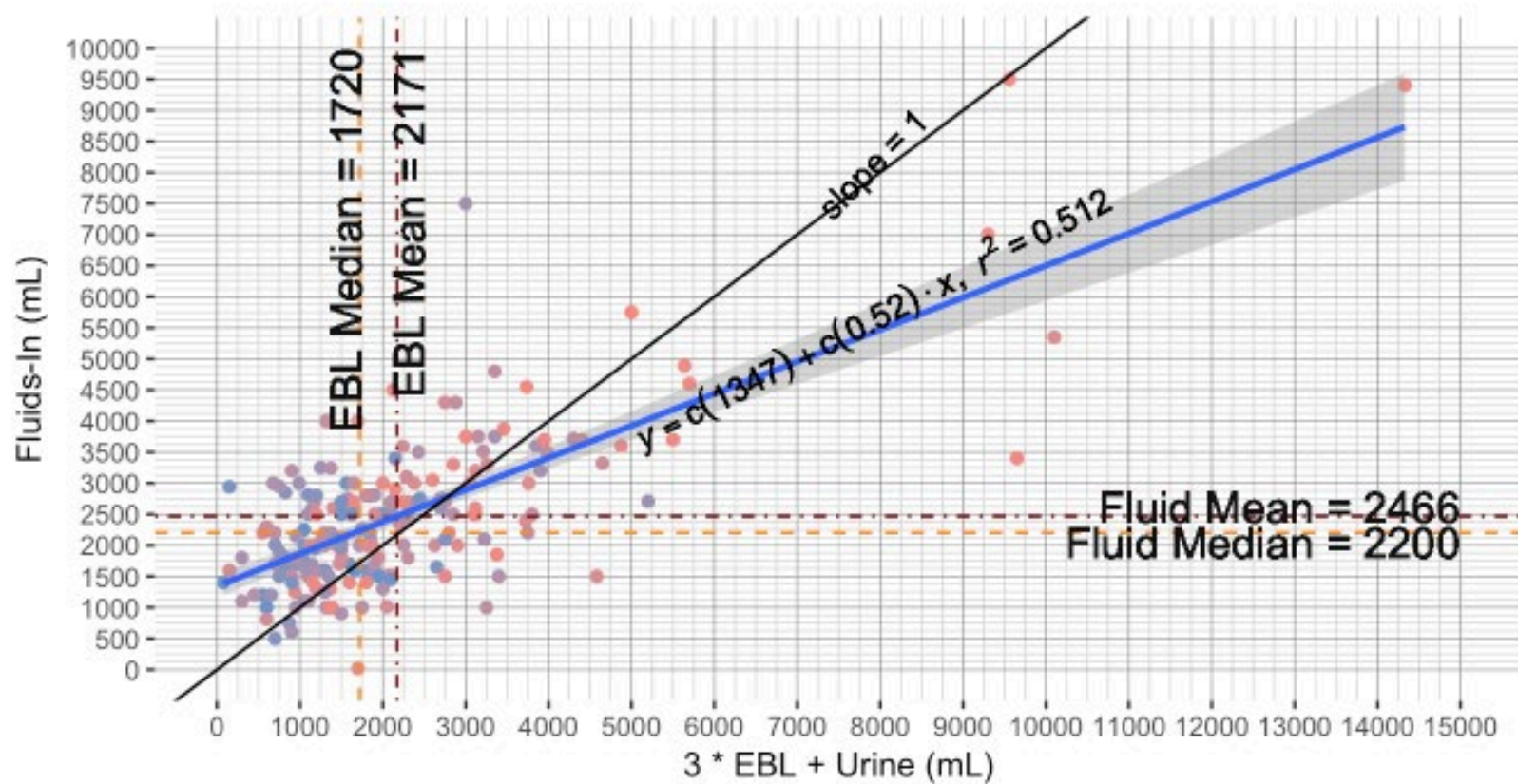


Figure 7b

Output vs Input Fluid: EV1000 Cases

38, 24, and 8 cases above, below, and near the slope = 1 line
 StdevEBLUrine:2453; StdevFluids:1592

Weight * Duration 

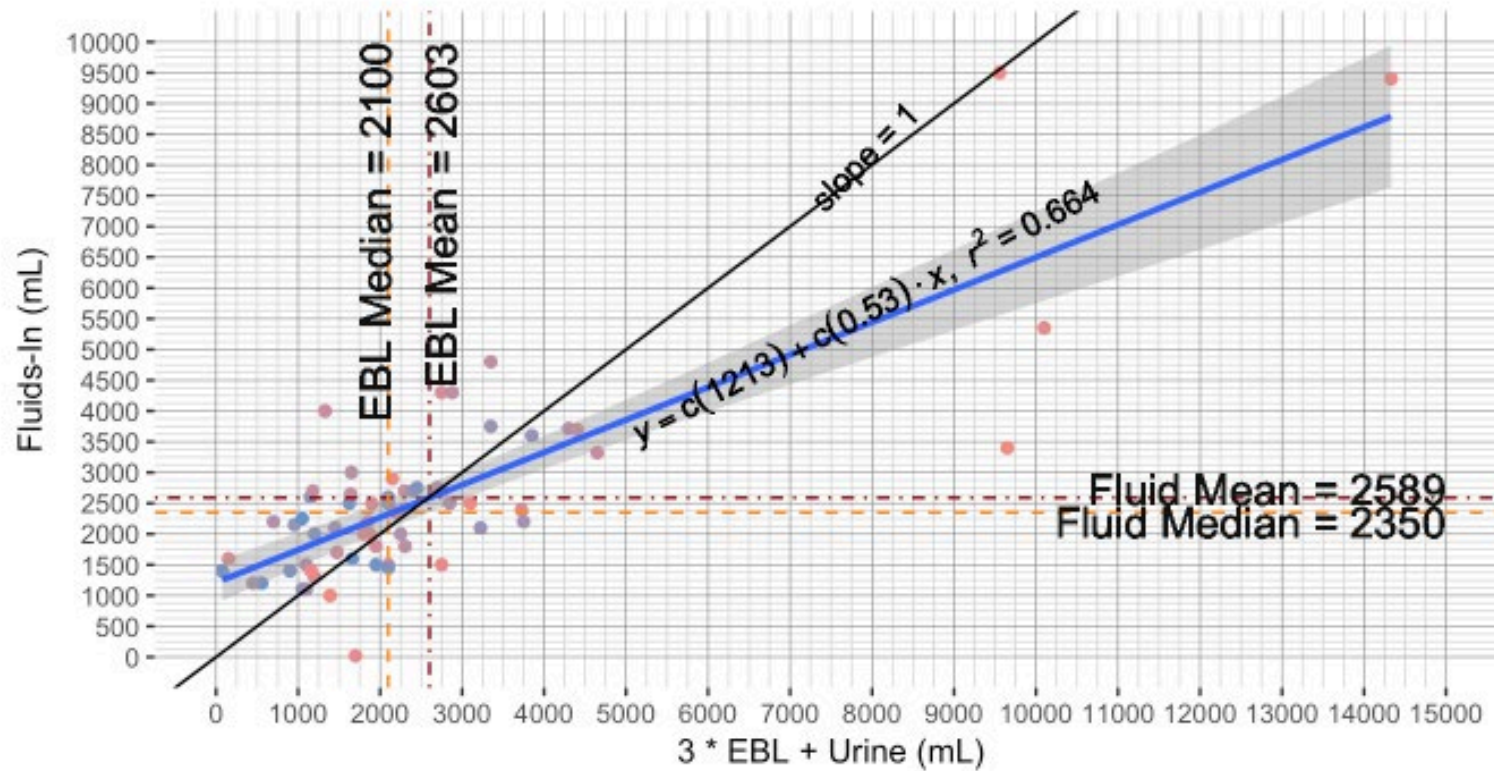


Figure 7c

Output vs Input Fluid: Non-EV1000 Cases

97, 41, and 9 cases above, below, and near the slope = 1 line
 StdevEBLUrine:1325; StdevFluids:1110

Weight * Duration 
 25 50 75 100

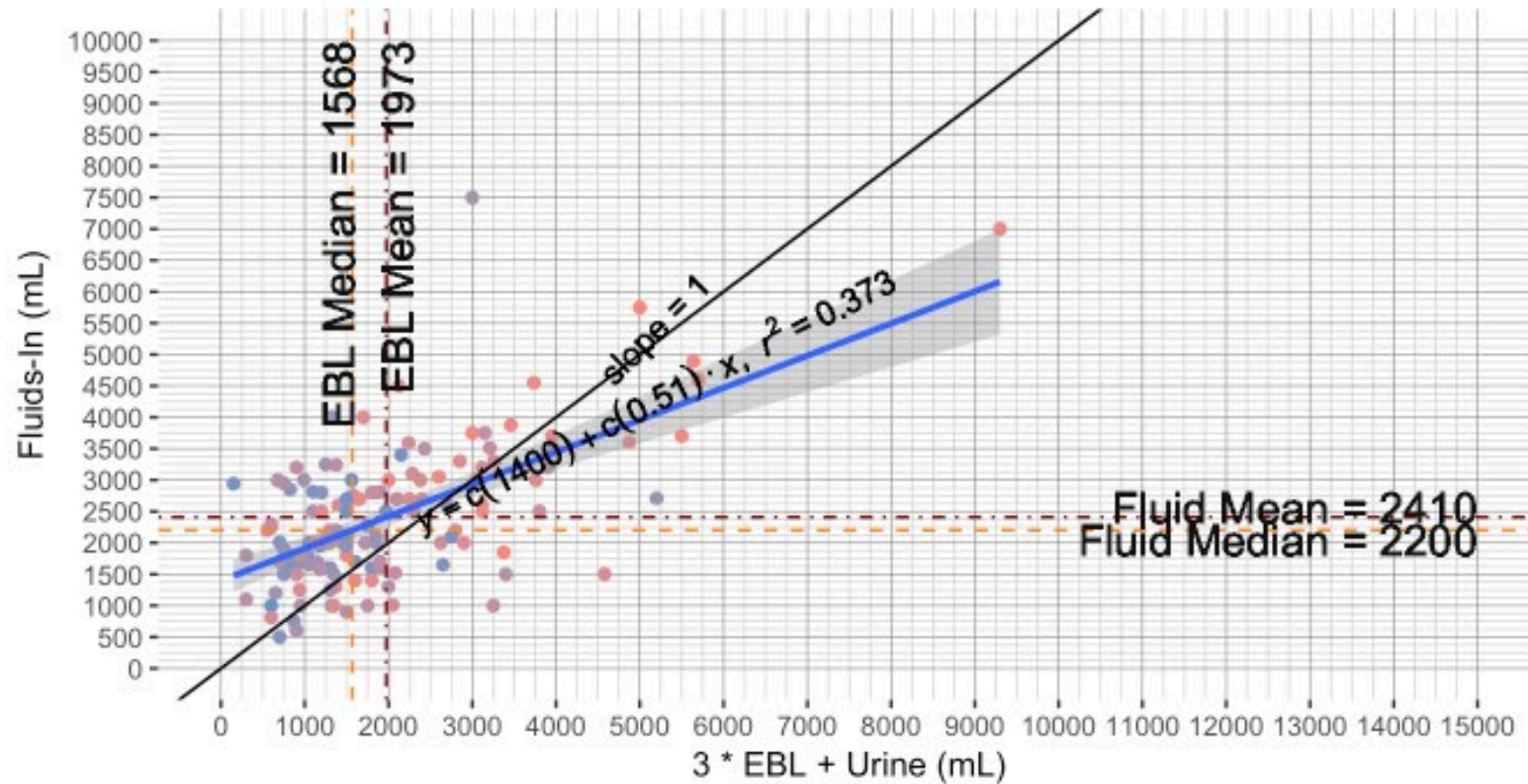


Figure 8

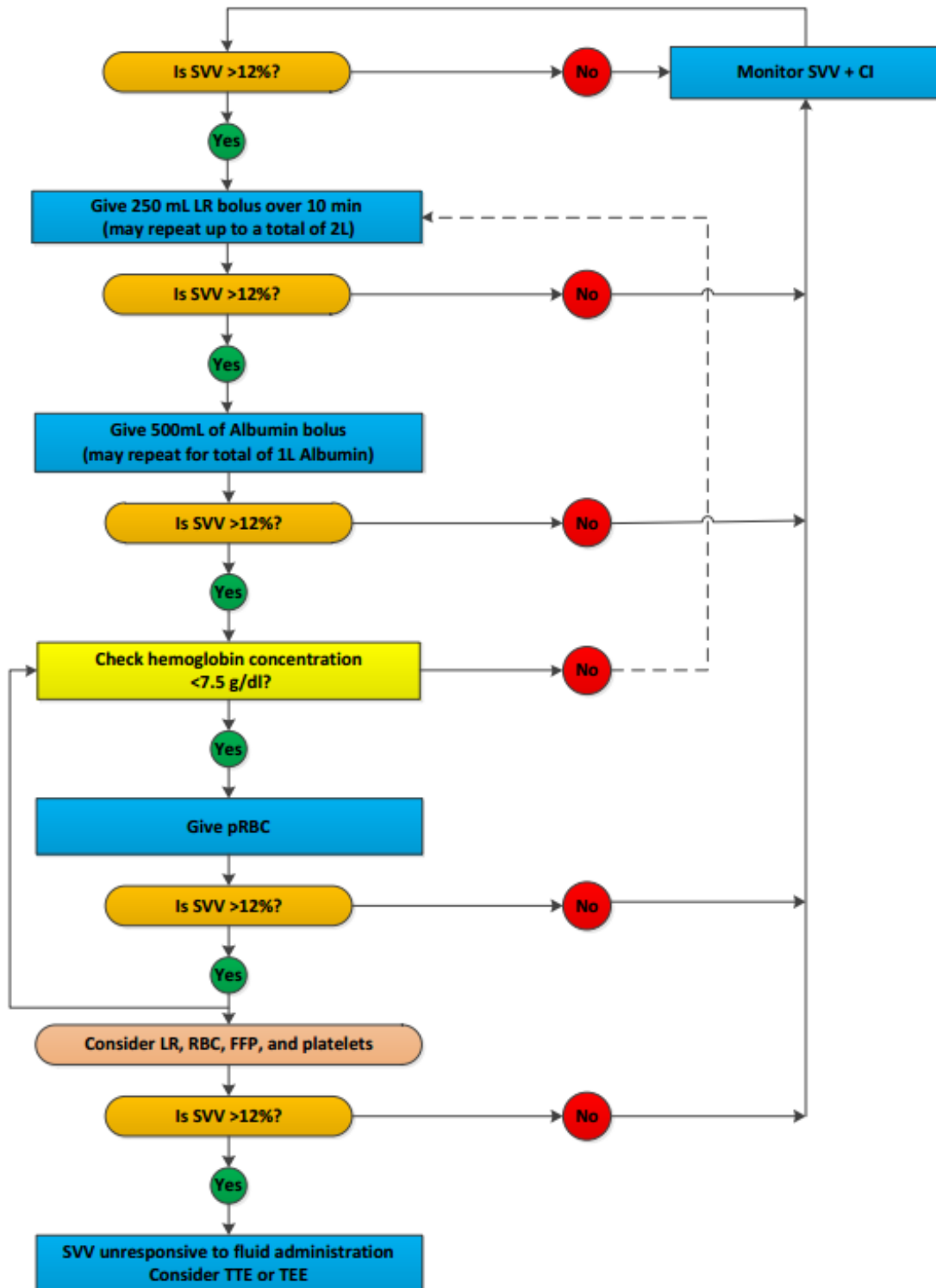


Figure 9



Approval Notice
Amendment to Research Protocol and/or Consent Document – Expedited Review
UIC Amendment # 4

April 13, 2018

Randal O. Dull, MD, PhD
 Anesthesiology
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 Suite 3200 West, M/C 515
 Chicago, IL 60612
 Phone: (312) 996-1522 / Fax: (312) 996-4019

RE: Protocol # 2015-0880
"Evaluation of Perioperative Intravenous Fluid Administration and Development of a Goal-directed Therapy Protocol in Adult Total Hip Arthroplasty Procedures"

Dear Dr. Dull:

Members of Institutional Review Board (IRB) #3 have reviewed this amendment to your research and/or consent form under expedited procedures for minor changes to previously approved research allowed by Federal regulations [45 CFR 46.110(b)(2)]. The amendment to your research was determined to be acceptable and may now be implemented.

Please note the following information about your approved amendment:

Amendment Approval Date: April 13, 2018

Amendment:

Summary: UIC Amendment #4 received April 12, 2018, is an Investigator-Initiated amendment adding Michelle Pavlik and Karen ~~Kapanko~~ from DePaul University. In addition, Bernadette Roche and Susan ~~Krawczyk~~ were removed from the Appendix P.

Please note the Review History of this submission:

Receipt Date	Submission Type	Review Process	Review Date	Review Action
04/12/2018	Amendment	Expedited	04/13/2018	Approved

Please be sure to:

→ Use your research protocol number (2015-0880) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements on the guidance,
"UIC Investigator Responsibilities, Protection of Human Research Subjects"
 (<http://trigger.uic.edu/depts/ncsr/research/protocolreview/irb/policies/0924.pdf>)

Please note that the UIC IRB #3 has the right to ask further questions, seek additional



information, or monitor the conduct of your research and the consent process.

Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.

We wish you the best as you conduct your research. If you have any questions or need further help, please contact the OPRS at (312) 996-1711 or me at (312) 413-1835. Please send any correspondence about this protocol to OPRS via OPRS Live.

Sincerely,

Kerry A. Day, BA
IRB Coordinator, IRB # 3
Office for the Protection of Research Subjects

cc: David Eric Schwartz, Anesthesiology, M/C 515

Figure 10

Appendix L1 – Institutional Review Board (IRB)/Independent Ethics Committee (IEC) Authorization Agreement Version 1.0 8/09/07	Office for the Protection of Research Subjects (OPRS) Institutional Review Board (IRB) 1737 West Polk Street (MC 672) 203 Administrative Office Building Chicago, IL 60612 Phone: 312.996.1711 Fax: 312.413.2929 www.research.uic.edu

Name of Research Project: Evaluation of perioperative intravenous fluid administration and development of a goal-directed therapy protocol in adult total hip arthroplasty procedures

Name of Principal Investigator: Randal Dull (UIC), Michelle Pavlik (DePaul)

Sponsor or Funding Agency: N/A

Award Number, if any: N/A

Other support, describe: N/A

Name of Institution Providing IRB Review (Institution A):

OHRP Federalwide Assurance (FWA) Number:

IRB Registration #: (choose):

University of Illinois at Chicago (UIC)

FWA00000083

IRB00000115 UIC IRB #1

IRB00000116 UIC IRB #2

IRB00000117 UIC IRB #3

Name of Institution Relying Upon UIC IRB Review (Institution B): DePaul University

OHRP Federalwide Assurance (FWA) Number: 00000099

The Officials signing below agree that Institution B may rely on the UIC IRB for review, approval, and continuing oversight provided by the University of Illinois at Chicago under its Assurance for the project identified above.

This agreement is applicable only to the project named above and to no other research in which Institution B may be engaged in presently or in the future.

The review, approval, and continuing oversight performed by the relied-upon UIC IRB will meet the requirements of the HHS regulations for the human subject protection at 45 CFR 46, as well as the requirements of UIC's OHRP-approved Assurance. The UIC IRB will follow its written procedures for reporting its findings and actions to appropriate officials at Institution B. Relevant minutes of IRB meetings will be made available to Institution B upon request.

Institution B remains responsible for ensuring compliance with the IRB's determinations and with the terms of its OHRP-approved FWA, or other applicable laws or regulations.


This document must be kept on file at both institutions and must be provided to OHRP upon request.

Signatures:

Authorized Official at the University of Illinois at Chicago (Institution A):

 Date: _____
 Mitra Dutta, PhD
 Vice Chancellor for Research

Authorized Official at Institution B:


 Date: 6-7-18
 Print Full Name: Lawrence Hamer, PhD