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An Integrative Review of Fluid Management in Cardiac Surgery

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AN INTEGRATIVE REVIEW OF FLUID MANAGEMENT IN CARDIAC SURGERY

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Abstract

Adequate fluid administration during and after cardiac surgery is essential to ensure adequate oxygen delivery to the tissues, while simultaneously avoiding the dangers of hypervolemia and fluid overload. In both cardiac and non-cardiac surgery there has been debate on what the best approach to fluid management is, what hemodynamic parameters should be used to assess fluid requirements, and what type of fluids should be used. There are several studies in non-cardiac surgery that examine these issues, while they are fewer in the field of cardiac surgery. An integrative review design was used to examine the current evidence on fluid management practices in cardiac surgery. Thirteen studies were included in this review. They included four studies of surveys on fluid management practices, eight studies that utilized goal directed therapy (GDT), and one observational study on fluid administration practices in cardiac surgical patients. The results showed that arterial blood pressure (ABP), central venous pressure (CVP), and echocardiography were used most often to monitor volume status. Crystalloids were used most frequently for volume replacement. In the studies utilizing GDT, fluid administration was often based on stroke volume variation (SVV) and cardiac index (CI) goals. A slight trend towards increased fluid administration was seen in the GDT groups. Fluid bolus volumes ranged from 100 to 500 ml. The GDT groups had a slight trend toward decreased length of both hospital and ICU stay. An important limitation of the review was that none of the studies were conducted in the United States of America.

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An Integrative Review of Fluid Management in Cardiac Surgery

Background/Statement of the Problem

Fluid management in cardiac surgery is a crucial component of care. Fluid shifts and hypovolemia are common in the intraoperative and immediate postoperative period and may be caused by various factors that induce physiological alterations. Some of these factors include anesthetic agents, cardiopulmonary bypass (CPB), and/or blood loss (Norris, 1993). Adequate fluid resuscitation during and after cardiac surgery is essential to ensure adequate oxygen delivery to the tissues. It is important to provide enough fluid to maintain perfusion; at the same time, hypervolemia and fluid overload should be avoided. In both cardiac and non-cardiac surgeries there is debate on what hemodynamic parameters should be used to assess fluid requirements and responsiveness, what type of fluids should be used, and whether a restrictive or liberal approach improves outcomes (Bignami, Guarnieri & Gemma, 2017; Della Roca et al., 2014; Marik, Monnet, & Teboul, 2011). Some specialties such as thoracic surgery involving the lungs, generally use a restrictive approach to fluid management. This approach is based on studies that showed an increased incidence of pulmonary edema and acute lung injury in patients having surgery for lung cancer and post pneumonectomy, who received excessive intraoperative fluid infusion (Licker et al., 2003; Parquin, Mehiri, Herv & Lescot, 1996). Multiple studies have also been conducted in non-cardiac surgeries comparing a restricted vs. liberal perioperative fluid administration approach. Some of these included pancreatectomy, abdominal vascular surgery, colonic surgery, lung resection, pancreaticoduodenectomy, and major abdominal surgery (González-Fajardo, Mengibar, Brizuela, Castrodeza, & Vaquero-Puerta, 2009; Grant et al., 2016; Holte et al., 2007; Matot et al.,2013; van Samkar et al., 2015; Vermeulen, Hofland, Legemate, & Ubbink,

2009). The results have been mixed, with some studies showing favorable outcomes with fluid restriction, some showing no significant difference and some having shown this approach to be harmful. While there are ample studies that compare a restricted vs. liberal approach in non-cardiac surgery, they are fewer in cardiac surgery (Mariscalco & Musumeci, 2014). Currently there are only two trials, both by Vretzakis and colleagues (2009; 2010), that assessed blood transfusion requirements when using a restricted vs. liberal perioperative intravenous fluid (IVF) approach in cardiac surgery patients.

Goal directed therapy (GDT) is an approach that has been gaining support for several years and has been studied in both non-cardiac and cardiac surgeries. Goal directed therapy utilizes fluid management strategies that use patient-specific hemodynamic outcomes to optimize physiologic stability, cardiovascular volume, tissue oxygenation, nutrient delivery, microvascular flow, and end organ perfusion while minimizing complications associated with perioperative fluid volume depletion or overload (Trinooson & Gold, 2013). Some hemodynamic measurements commonly utilized in GDT include cardiac output (CO) and stroke volume (SV), left ventricular end-diastolic area that is measured by transesophageal echocardiography (TEE), SVV and pulse pressure variation (PPV) (Gutierrez, Moore, & Liu, 2013). There are several studies that have evaluated perioperative GDT therapy in both non-cardiac and cardiac patients. Some of these include GDT in off-pump coronary artery bypass graft (CABG), high risk CABG, abdominal surgery, high risk surgery and high risk cardiac surgery, (Kapoor, Magoon, Rawat, & Mehta, 2016; Osawa et al., 2016; Ramsingh, Sanghvi, Gamboa, Cannesson, & Applegate, 2013; Scheeren, Wiesenack, Gerlach, & Marx, 2013; Walker & Young, 2015). These studies compared a GDT approach to “usual or standard

care"; however, what constituted usual or standard care itself was variable. The hemodynamic parameters used, as well as the devices used to predict fluid needs in the GDT approach, also varied between studies.

The advanced practice registered nurse (APRN) is often involved in the care of the patient undergoing cardiac surgery. The nurse anesthetist mostly cares for the patient in the preoperative and intraoperative phases of surgery, while the acute care nurse practitioner (NP), or the acute care clinical nurse specialist (CNS) predominantly manage postoperative care. Because fluid management is such a critical piece, it is essential for all APRNs to have a comprehensive understanding of this subject.

An integrative review of literature was conducted in order to gain a better understanding of fluid management practices involved in cardiac surgery. The purpose of this review was to explore and analyze the current evidence in published literature on fluid management in cardiac surgery patients.

Next, the review of literature will be presented.

Literature Review

The literature databases searched included CINAHL, Medline and PubMed. Key search terms included combinations of fluid management, hypovolemia, fluid overload, hemodynamics, hemodynamic monitoring, surgery or operation or surgical procedure or surgical treatment, cardiac surgery, or heart surgery, or cardiovascular or coronary artery bypass or cardiopulmonary bypass and goal directed therapy. Searches were limited to the English language and the adult age group 19 years and older. No time limits were used for the literature review.

Using EBSCO host with CINAHL and Medline databases, fluid management and surgery or operation or surgical procedure or surgical treatment yielded 267 articles from 1975 to 2017. Fluid management and cardiac surgery, or heart surgery, or cardiovascular or coronary artery bypass or cardiopulmonary bypass yielded 93 articles from 1985 to 2017. Goal directed therapy and cardiovascular or coronary artery bypass or cardiopulmonary bypass yielded 56 articles from 2004 to 2017. PubMed was also searched using similar terminologies. In addition, articles cited within those that were initially examined were also located and evaluated.

Articles pertaining to fluid balance concepts, hemodynamic monitoring and parameters that guide fluid resuscitation, general fluid management approaches in adult cardiac and non-cardiac surgeries and different types of fluids used in perioperative fluid management were selected and used to build the literature review. Articles that studied fluid management in conjunction with very specific conditions, for example brain surgery, scoliosis, renal failure, heart failure, or those that also assessed drug effects such as those from the use of diuretics, were not included. Studies that did not have a direct

bearing on fluid management, for example those that studied cost or quality initiatives associated with fluid administration, were also excluded.

Fluid Balance and Imbalance

Many factors can alter the body's fluid balance resulting in either hypovolemia or fluid overload. Hypovolemia is a clinical state in which significant loss of blood or plasma volume results in inadequate tissue perfusion. A reduction in blood volume and a fall in systolic pressure, triggers a sympathetic response that leads to peripheral vasoconstriction and tachycardia. Tachycardia and increased cardiac contractility can increase myocardial oxygen requirement. Blood flow to the skin and peripheral tissues is reduced to preserve perfusion of vital organs such as the brain, heart, liver, and kidneys. If tissue perfusion remains inadequate, a state of acidosis results from anaerobic metabolism, which leads to impaired performance of vital organs (Baskett, 1990). Up to 10% of the total blood volume can be lost without affecting either CO or arterial pressure. Greater than 10% loss diminishes CO due to decreased preload. Arterial pressure also declines with more than 20% loss of total blood volume (Kreimeier, 2000). Hypovolemia can be caused by various factors such as blood loss from trauma or surgery, dehydration from inadequate fluid intake, diarrhea, vomiting, fever, burns, diuretic therapy, adrenal insufficiency, and hyperglycemia (Grossman & Porth, 2014).

Fluid overload contributes to the pathogenesis of several clinically important complications including hypoxemia, myocardial edema and organ edema (Bellomo, Raman, & Ronco, 2001). Excessive fluid volume or fluid overload can be caused by disorders of renal function, heart failure, liver failure, corticosteroid excess, and excessive IVF and blood administration (Grossman & Porth, 2014).

Intravenous fluid administration is one of the most frequently used therapies provided in hospitals and is indicated in the management of hypovolemia, sepsis, perioperative correction of volume losses, hemodynamic alterations, or oliguria, that are believed to be volume responsive. When administered appropriately, IVF improve outcomes; however, inappropriate use can result in increased morbidity, length of hospital stay, and even mortality. Inappropriate IVF management can take the form of inadequate resuscitation, which can result in tissue hypoperfusion, or in over-resuscitation, which can lead to tissue edema and electrolyte imbalance (Hoste et. al., 2014). Appropriate intravenous fluid management requires appropriate hemodynamic monitoring to guide therapy and to avoid the risk for under as well as over resuscitation. Hemodynamic monitoring parameters and how they relate to fluid administration will be discussed in the next section.

Hemodynamic Parameters to Guide Fluid Therapy

The first step in hemodynamic management is to determine the adequacy of tissue and organ perfusion. Clinical indices of inadequate tissue perfusion may include low mean arterial pressure (MAP) and urine output, altered mentation, decreased capillary refill, skin mottling, cold extremities, increased blood lactate, altered arterial pH, decreased base excess, and bicarbonate values, and decreased mixed venous oxygen saturation (Schulman, 2002). Heart rate, blood pressure (BP), and urine output are the traditional clinical parameters used to determine decreased perfusion, however they may still be within normal range in early stages. As shock progresses and the body is unable to sustain a compensatory response, tachycardia, hypotension and oliguria may ensue. It is also important to note that the heart rate may not be appropriately elevated in the elderly,

or in those who take certain cardiac medications, while it may be elevated for reasons other than decreased perfusion, such as hyperthermia, pain or anxiety (Shulman). Vasoconstriction resulting from hypothermia, vasopressors, and catecholamine response due to stress or pain can increase the systemic vascular resistance (SVR) and therefore BP, regardless of actual intravascular volume. This is because the BP is a function of CO and SVR rather than tissue perfusion itself. Urine output can be an unreliable guide in the elderly, those with renal dysfunction, or hypothermic patients, as they may be unable to adequately concentrate urine, and consequently have an output that falsely appears to be adequate (Schulman).

Fluid management is often the first intervention performed to improve tissue perfusion. However, it is important to remember that the goal of administering fluid is to improve the SV, which then improves tissue perfusion. Two concepts that are relevant to this discussion include fluid challenge and fluid or volume responsiveness.

Fluid challenge. A fluid challenge is a method of identifying those patients who are likely to benefit from an increased intravenous volume in order to guide further volume resuscitation. If the fluid challenge results in an increase of SV and the CO by at least 10–15% the patient is considered as being fluid responsive. The choice of fluid for a challenge may be a colloid, crystalloid, or blood, as indicated by clinical need. A volume of around 200 ml or 3 ml/kg given over about five minutes is generally considered standard (Cecconi, Parsons & Rhodes, 2011).

Fluid responsiveness. Fluid responsiveness is the likelihood that a fluid challenge will result in increased SV (Marik, Monnet & Teboul, 2011). The only reason to fluid load a patient is to increase SV which then improves tissue perfusion. If the fluid

challenge does not increase SV, volume loading serves the patient no useful benefit and actually may be harmful, with excessive fluid resuscitation having been shown to be associated with increased complications, increased length of ICU and hospital stay, and increased mortality (Marik & Cavallazi, 2013; Marik, Monnet & Teboul, 2011).

Practitioners have used different static and dynamic parameters to guide and predict fluid responsiveness over the years. Static measurements of pressure were the first indices developed to assist with predicting fluid responsiveness. These measurements are obtained at a given condition or time point and are presumed to reflect preload. They include CVP and pulmonary artery occlusion pressures, as well as surrogates obtained through echocardiography including the inferior vena cava diameter and the end-diastolic volume (Mackenzie & Noble, 2014).

Dynamic parameters are predictors of fluid responsiveness based on the heart-lung interactions and are determined by the changes in preload indices induced by intrathoracic pressure changes during mechanical ventilation. They include pulse pressure variation (PPV), stroke volume variation (SVV), and plethysmographic variability index (Mackenzie & Noble, 2014). A few of these measurements will be discussed below.

Central venous pressure. CVP is very commonly used to assess fluid responsiveness and guide therapy, even though studies have shown that this measure has low predictive value for fluid responsiveness (Eskesen, Wetterslev & Perner, 2016; Marik, Baram, & Vahid, 2008; Marik & Cavallazi, 2013;). In the study by Eskesen et al. (2016), the investigators analyzed 1148 data sets of CVP and fluid responsiveness predictability. They grouped CVP ranges as low (< 8 mmHg), intermediate (8–12 mmHg), and high (>12 mmHg), and assessed fluid responsiveness in relation to this

classification. The review included 51 studies, most of which were done in the ICU and the operating room setting. The individual patient data set, showed that 47 % of the CVP values were in the lower CVP subgroup, 30 % in the intermediate, and 23 % in the higher subgroups. When analyzing positive predictive value, the area under the receiver operating characteristic curve was 0.57 for the lower, 0.54 for the intermediate, and 0.56 for the higher CVP subgroup (95 % CI [0.52, 0.62]). Thus, the results showed that the overall predictive value of CVP for fluid responsiveness was low.

Pulse pressure variation. Ventilation-induced variation of pulse pressure and SV, which are dynamic parameters, are often used to predict fluid responsiveness. The increase in intrathoracic pressure during positive pressure inspiration causes a reduction of the preload, and therefore the SV. In patients who are hypovolemic, there is greater SVV and PPV. These methods do have limitations and cannot be used in patients with spontaneous respiration, low tidal volumes, arrhythmias, or in conditions where there is decreased lung compliance (Monnet, Marik, & Teboul, 2016).

Sá Malbouisson et al. (2017) studied the effect of PPV-guided intraoperative fluid loading in high-risk surgical patients on postoperative outcomes compared to the standard fluid resuscitation practice. This was a multicenter study that was conducted in three hospitals in São Paulo, Brazil. The patients were 60 years of age or older, with comorbidities, who were undergoing major surgery. The intervention group patients were managed with fluid loading based on PPV, while those in the control group were managed using CVP and MAP. There were 84 subjects in each group. The PPV-guided intraoperative fluid therapy was associated with a decrease in postoperative complications (*OR*: 0.59; 95% CI [0.35,0.99]). There was a significant reduction in the

postoperative and the hospital length of stay: eight days in the intervention group vs. 11 days in the control group. The hazard ratio for the postoperative length of hospital stay was 0.6 (95% CI [0.42 - 0.88]). After 24 hours of ICU stay, significantly (p=0.027) fewer patients in the study group required continued mechanical ventilation compared to the control group. The volume of crystalloids infused was significantly (p=0.001) lower in the PPV group (median[IQR] 4500 ml [3200-6500]) compared to the control group (5000 ml [3750-8862]). Significantly (p=0.01) fewer blood units were transfused during surgery in the PPV group (1.7 U [0.9-2.0 U]) compared to the study group (2.0 U [1.7-2.6 U]

These findings suggested that the use of PPV can improve fluid management practices and improve patient outcomes; however as mentioned earlier, it cannot be used in patients with spontaneous respiration, low tidal volumes, arrhythmias, or in conditions where there is decreased lung compliance.

Approaches to Fluid Replacement in the Surgical Patient

Perioperative fluid management practices are highly variable and much discussion has been ongoing for years. There has been debate on what type of fluid; colloid or crystalloid, is most optimal; and whether a liberal or a restricted approach improves outcomes (Della Roca et al., 2014). Meta-analyses on the types of fluids have had varying conclusions, and there is no clarity in this regard. A liberal fluid administration approach was most commonly used in the past, because fluid depletion from fasting and insensible losses tended to be overestimated, and liberal fluid infusion was not considered as harmful (Myles et al., 2017). However, the perils of excessive fluid administration and overload are being increasingly recognized, and a restrictive approach is gaining favor (Myles et al.). Goal directed therapy is another fluid management approach that is

increasingly being studied and used in surgery. Many studies have been conducted in various types of surgeries, comparing liberal, standard, and restrictive fluid approaches, and those using goal directed approaches. Some of these approaches and their evidence in literature, are described briefly below.

Liberal or standard versus restricted approach. There are no standardized definitions for 'standard', 'restricted', or 'liberal' fluid regimens. Studies that compare these approaches have varying definitions Thus, some studies define as liberal, what other studies define as standard, and what some call standard, others refer to as restrictive. The results of studies comparing these approaches have been mixed, and it is difficult to determine if a liberal approach is safer than a restrictive approach, or whether neither of these is beneficial. A few studies comparing these approaches are described below.

A liberal approach was tested by Maharaj and colleagues (2005). They randomized 80 patients between the ages of 18 and 50 years, who were scheduled for laparoscopic gynecologic surgery to the study group, which was the large volume infusion group and to the control group. The control group received one preoperative fluid bolus of 3 ml/kg compound sodium lactate, whereas the large volume infusion group received a volume of 2 ml/kg/hour of fasting time. The overall incidence of postoperative nausea and vomiting in the first 72 postoperative hours was significantly reduced ($p < 0.05$, Fisher's exact test) in the large volume group compared to the control. The large volume infusion group also had significantly decreased postoperative pain scores and required significantly less supplemental analgesia ($p < 0.05$, Fisher's exact test). One of the limitations of this study is the fact that these patients had relatively long

fasting times, (12–13 hours), which occurred despite instructions to fast for six to eight hours from solids, and for four hours from fluids. This could account for the significant effect that the larger volume had on these outcomes.

Varadhan and Lobo (2010) conducted a meta-analysis of IVF therapy in nine randomized controlled trials with 801 patients undergoing major elective open abdominal surgery. When restricted fluid regimens were compared with standard or liberal fluid regimens, there was no difference in post-operative complication rates or length of hospital stay. However, the researchers then reclassified and defined the fluid regimens. Restricted fluid therapy was fluid amount of less than 1.75 L/day; liberal fluid therapy or fluid overload was greater than 2.75 L/day; and both of these were considered to be a state of fluid imbalance. An amount between 1.75L to 2.75 L/day was considered balanced. With this reclassification, they found that the more balanced group had significantly fewer complications (risk ratio 0.59; 95% CI [0.44, 0.81]), p=0.0008) and shorter length of hospital stay (weighted mean difference -3.44 days; 95% CI [-6.33, -0.54]), p=0.02) than those who received less than or more than the balanced amount. One drawback of this meta-analysis was that the complications are not detailed or specified.

Schol, Terink, Lancé, and Scheepers (2016) conducted a systematic review and meta-analysis that compared liberal vs. restrictive fluid approach in elective general surgery patients. A total of 12 RCTs were included in the systematic review and 1397 patients were analyzed with 693 in the restrictive protocol and 704 in the liberal protocol groups. Overall, the liberal group received more fluids than the restrictive group (M= 4048 ml vs. M=2019 ml).

The total number of patients with a complication was significantly higher with the liberal fluid group (relative risk [RR] 0.65; 95% CI [0.55,0.78]). Percentages of bleeding, sepsis, and peritonitis did not differ between the two groups; however, pneumonia, cystitis, and wound infections were more common in the liberal group (RR 0.62; 95% CI [0.48,0.79]). More transfusions were needed in the liberal fluid group (RR 0.81;95% CI [0.66-0.99]), although the postoperative re-bleeding did not differ between groups (RR 0.76; 95% CI [0.28,2.06]). One of the limitations of this systematic review and meta-analysis was the heterogeneity of the included studies. There was a broad variety of participants with respect to age and comorbidities, as well as the type of surgery which could have had an influence on the results (Schol et al.).

Jia and colleagues (2017) conducted a meta-analysis of studies that compared perioperative restrictive fluid therapy to liberal or conventional fluid therapy in patients undergoing major abdominal surgery. Specifically, they investigated the rate of post-operative morbidity or complication rates, time to flatus, and the length of hospital stay. They included 13 RCTs, with 1052 patients, of whom 525 received restricted fluid regimens, and 527 patients received the standard or liberal or conventional fluid regimens. The types of surgery performed were heterogeneous across the studies and included hepato-gastroenterological and abdominal vascular procedures.

The overall analysis revealed that the patients in the restricted group had a lower rate of complications in comparison with the patients in the control group; however, this did not reach statistical significance. Subgroup analysis showed that there was no significant difference in complication rates, time to flatus, or the length of stay in hepato-gastroenterological surgeries. However, abdominal vascular surgery patients in the

restricted group had fewer overall complications; (pooled *OR*: 0.12; 95 % CI [0.03,0.47], $p = 0.002$) and a lower risk of cardiopulmonary complications (pooled *OR*: 0.09; 95 % CI [0.02, 0.43], $p = 0.002$). The vascular restricted fluid group also had shorter time to first flatus than the patients in the control group (pooled difference in the mean: −1.74; 95 % CI −2.12 to −1.35, $p < 0.001$), and a shorter length of hospital stay; (pooled difference in the mean: −4.31; 95 % CI [−6.64, −1.97], $p < 0.001$).

Limitations in this study included significant heterogeneity with respect to the definitions of 'restrictive' and 'standard' fluid therapies. The total amount of perioperative fluid given ranged from 1.41 to 5.97 liters in the restrictive group, and from 1.56 to 6.6 liters in the standard or liberal group. There was also heterogeneity in the types of surgery that were performed in the studies (Jia et al.).

Huang, Chua, Gill, and Samra (2017) conducted a systematic review and meta-analysis on studies that compared different fluid regimens in patients undergoing pancreaticoduodenectomy. The aim of the study was to examine the impact of perioperative fluid administration on perioperative outcomes after this procedure. Eleven studies; seven retrospective trials, and four RCTs comprising 2842 patients, were initially included in the review. Nine of these studies compared complications rates of high vs. low fluid volume regimen. Of these nine, two studies compared restrictive vs. standard regimens. Of the original 11 studies, seven studies were included in the meta-analysis and four were not included because of heterogeneity in reporting outcomes. There were no differences in length of hospital stay, or complications specific to the pancreas, pulmonary, cardiovascular, gastrointestinal, hepatobiliary, urogenital, wound, reoperation rate, and overall morbidity. There was also no difference in the 30 and 90-day mortality

rates in low or high fluid groups. As in other meta-analyses, a limitation was the lack of uniformity in the categorization of what constituted restricted, standard, or liberal fluid regimens.

Goal directed fluid therapy. Trinooson and Gold (2013) described GDT as an approach that utilizes fluid management strategies that use patient-specific hemodynamic outcomes, such as a target SV or CO to optimize physiologic stability, cardiovascular volume, tissue oxygenation, nutrient delivery, microvascular flow, and end organ perfusion, while minimizing complications associated with perioperative fluid volume depletion or overload. The concept of GDT has been around for more than thirty years; however, there is still no consensus as to what the most effective goals should be, or how best to assess and monitor fluid needs. After studying this topic for three years, Navarro and colleagues (2015), who were part of the International Fluid Optimization Group, concluded that GDT should at least have two steps. The first step is determining whether the patient requires hemodynamic support or augmentation of cardiovascular function. The second step is considering fluid bolus therapy if the patient is fluid responsive. Ripollés-Melchor and colleagues (2016) included the use of vasopressors and inotropes to the concept of GDT, and referred to the approach as goal-directed hemodynamic therapy (GDHT). They defined it as a method for determining the optimal dose of fluid therapy, inotropes, and vasopressors through a clinical algorithm to optimize cardiac output and delivery to the tissues in order to prevent situations of hypoperfusion and fluid overload. Over the years several studies as well as reviews have been performed of GDT in surgery. A few of these are discussed below.

Studies of GDT in surgical patients. A stratified meta-analysis of perioperative fluid management strategies in major surgery was conducted by Corcoran, Rhodes, Clarke, Myles, and Ho (2012). They hypothesized that while GDT tends to use greater amounts of fluid, similar to the liberal fluid administration approach, perioperative fluid therapy without hemodynamic goals is not equivalent to GDT. To test this hypothesis, they conducted a stratified meta-analysis to assess whether these two approaches to managing perioperative fluid therapy would have different effects on the outcomes of patients undergoing major surgery. They included RCTs that evaluated a liberal vs. restrictive (LVR) fluid approach as compared to those that used GDT in patients undergoing major surgery. A therapy was considered GDT if it targeted a measurable hemodynamic variable, such as CO or PPV, rather than conventional measures such as arterial BP, urine output, or CVP. Trials that exclusively studied cardiac, neurosurgical, obstetric, trauma, burns, or critically ill patients were excluded. The primary outcome was postoperative mortality. Secondary outcomes were organ-specific complications, recovery of bowel function, and length of hospital stay.

Corcoran et al. (2012) grouped studies into two strata, the GDT stratum, and the LVR stratum. The GDT stratum included 24 studies with 3861 patients from 10 countries. The LVR stratum had 12 studies on LVR fluid therapy involving 1160 patients. When the LVR stratum was analyzed, results showed that patients in the liberal group of the LVR stratum received larger amount of fluid (mean difference 1570 mL; 95% CI [986 , 2154]), had a higher risk of pneumonia (RR 2.2; 95% CI [1.0 to 4.5], $p = 0.04$), pulmonary edema (RR 3.8; 95% CI [1.1,13], $p = 0.03$), and a longer hospital stay (mean difference 2

days; 95% CI [0.5,3.4]) than those in the restrictive group. Bowel recovery also took longer in the liberal fluid group.

Comparison and analysis of GDT therapy to non-GDT in the second stratum showed the GDT group also received greater amounts of fluid as compared to the non-GDT group (mean difference 467 mL; 95% CI [331, 603]), had shorter hospital length of stay (mean difference 2 days; 95% CI [1, 3]), lower rates of pneumonia (RR 0.7;95% CI [0.6, 0.9]) and renal complications (RR 0.7; 95% CI [0.5, 0.9]), and faster recovery of bowel function.

Finally, the GDT group was compared with the liberal fluid group. Both the liberal approach and the GDT approach used greater amounts of fluid than the comparison groups in each stratum. When the GDT group was compared to the liberal fluid therapy group, however, the liberal fluid approach was associated with an increased length of hospital stay (mean difference 4 days; 95% CI [3.4, 4.4]), increased time to first bowel movement (mean difference 2 days; 95% CI [1.3, 2.3]), and an increased risk of pneumonia (RR 3; 95% CI [1.8, 4.8]). Mortality, wound infection, and renal failure were not significantly different between liberal approach and GDT. The study did not make any cross comparisons between the GDT group and the restricted fluid arm of the LVR stratum, so it is uncertain if GDT would have been considered superior or inferior to the restricted fluid approach. An important limitation of the study were the differences between the surgical case types, trial designs, and type of fluids used, which possibly resulted in heterogeneity of outcome results (Corcoran et al., 2012).

Ripollés-Melchor et al., (2016), conducted a meta-analysis to assess the benefits of perioperative GDHT in terms of mortality and complications in adult patients

undergoing elective or emergency noncardiac surgery. They selected for analysis RCTs in which GDHT was compared with conventional fluid therapy that used standard monitoring parameters. A total of 10 RCTs comprising1527 patients were included.

The primary result that was analyzed was mortality. The analysis of all 10 RCTs, showed that the use of perioperative GDHT compared with conventional fluid therapy significantly reduced mortality (RR, 0.63; 95% CI [0.42,0.94] p = .02). The secondary result was the number of patients with complications; only nine RCTs reported this number. There were no differences in the number of patients with complications between the GDHT and control groups (RR, 0.76; 95% CI [0.50,1.17] p = .21) Sub-analyses showed that the effects of GDHT on mortality were attributed to the GDHT trials that used supra-physiological goals, rather than physiological, and those that used perioperative GDHT rather than those than only used postoperative GDHT (Ripollés-Melchor et al.).

Some of the limitations included the fact that when the sensitivity analysis was performed including only the articles of higher methodological quality, it did not confirm the results that were previously obtained. One of the studies used other interventions forming part of the enhanced recovery after surgery protocol, in addition to the GDHT. Many of the trials were single-center trials, and sample sizes were small, with only one trial having more than 100 patients per group (Ripollés-Melchor et al.).

More recently, Sun, Chai, Pan, Romeiser, and Gan (2017) conducted a systematic review and meta-analysis to evaluate the effect of perioperative GDHT in comparison to conventional fluid therapy on postoperative recovery in adults undergoing major abdominal surgery. They included patients older than 16 years of age, who were

undergoing major abdominal surgery. Subjects either received perioperative fluids based on explicit measured goals for parameters such as cardiac output or index, SVV, PPV, mixed venous oxygen saturation, and lactate or were managed using conventional fluid administration strategies. In this case, standard parameters such as BP, heart rate, urine output, and CVP were used to guide fluid therapy. The GDHT group was the study group, while the conventional fluid group was the control group. The authors included 45 RCTs, which yielded 6344 patients, of whom 3406 received perioperative GDHT. The sample sizes of the RCTs ranged from 27 to 1994.

The results showed that there was a significant reduction in short term mortality in the GDHT group (5.2) compared to the control group (7.0 %) RR 0.75: 95% CI [0.61,0.91] p=0.004. The GDHT group also had an overall reduction in the rate of complications (RR 0.76; 95% CI [0.68,0.85] p<0.0001). Gastrointestinal function recovery was also significantly faster in the GDHT group. This was evidenced by shortened time to first flatus by 0.4 days (95% CI [−0.72, −0. 08], p=0.01) and the time to toleration of oral diet by 0.74 days (95% CI [−1.44 to −0.03] p<0.0001). Limitations of the meta-analysis included the fact that the GDHT strategy varied between trials, including fluid management, monitoring methods, therapeutic goals, and perioperative care environment. About half of the included studies had small sample sizes that were less than 100 and possibly lacked statistical power. Another limitation was that when the authors restricted the sensitivity analysis to studies with higher methodological quality, and those with larger sample size, the results were not confirmed (Sun et al.).

Cardiac Surgery and Fluid Balance

Cardiac surgeries such as CABG, valve replacements, and aortic surgery are major procedures that are performed under general anesthesia. Cardiovascular operations and procedures totaled about 7.6 million in 2010 (American Heart Association, 2016). Morbidity and mortality in cardiac surgery is influenced by many factors such as whether the surgery was elective or emergent, with the latter increasing the risk for adverse outcome, the use of CPB vs. off-pump surgery, patient comorbidity, and various other factors. Patient management and fluid therapy indications may also differ greatly from the OR to the ICU (Bignami, Guarnieri, & Gemma 2017). To maintain hemodynamic stability and adequate perfusion, patients often require treatment with fluids and vasopressors. Often, patients receive large amounts of fluids in the form of crystalloids, colloids and blood products intraoperatively as well as postoperatively. While patients require enough fluid to maintain adequate perfusion, excessive administration of fluid, as well as fluid shifts into the interstitial spaces, can lead to fluid overload in the postoperative phase.

Fluid overload in cardiac surgery. Morin et al. (2011) conducted a prospective trial comparing the frequency of post-operative complications to fluid status in patients undergoing CABG surgery. A group of 109 adult patients undergoing CABG surgery in a Canadian hospital were recruited for the trial. The surgeries for all the patients were performed while on CPB. The researchers measured post-operative fluid overload by weight gain. The maximum weight gain over eight days was the value used for fluid overload. The investigators divided the weight gain into three categories: less than 1 kg; 1 to 5 kg; and more than 5 kg. These categories were chosen arbitrarily by the investigators, and were not based on any definition in the literature. The complications were divided

into major and minor. Major complications included death, myocardial infarction, cardiac arrest, low cardiac output syndrome, cardiac tamponade, mediastinal exploration for bleeding, cerebral vascular accident, respiratory failure requiring prolonged intubation, renal failure, and deep sternal wound infection. Minor complications included atrial fibrillation, supra-ventricular tachycardia, new heart block, transient ischemic attack, delirium, pneumonia, leg wound infection, arm wound infection, and superficial sternal wound infection.

There was no death in either group. Among the 20 patients who presented with a post-operative weight gain less than 1 kg, the counts of major, minor and no complications were respectively 1, 7, and 12. Out of 62 patients with a weight gain of 1 to 5 kg, the counts of major, minor and no complications were 7, 21, and 34. In the group of 27 patients with a weight gain more than 5 kg., the counts of major, minor and no complications were 13, 8 and 6. A significant association was found between type of complication and fluid overload ($p = 0.001$), when the group that had weight gain more than 5 kg was compared with the other two groups. Between the groups that had less than 1 kg and 1 to 5 kg weight gain, there was no significant difference. It is important to note that for patients with major complications, 43.36% were in NYHA class III or IV compared to 0% in NYHA class I or II. The median left ventricular ejection fraction was better (55%) in patients without complications, than patients who presented with minor or major complications (50%). It is possible that these variables may have had a confounding effect on the results. The researchers suggested that the likely causes of fluid overload in cardiac surgery patients would include excessive perioperative fluid replacement and the systemic inflammatory reaction caused by CPB, which ultimately

results in increased capillary permeability and leakage of fluid in the extra-vascular space. They also endorsed a goal of administering minimal amount of fluids, that are adequate to maintain CO. The study itself however, while presenting the average amount of fluids used in the intraoperative and postoperative periods, did not seek to look for associations between volume administered and the fluid overload or complications.

Fluid Management in the Cardiac Patient

Background. Patient responses to surgery and bypass can vary greatly based on multiple factors such as age, genetics, and comorbidities. The goal of postoperative hemodynamic management is the maintenance of adequate end-organ perfusion without overloading the heart. The first steps in this process are assessment and optimization of intravascular volume, which in the immediate postoperative period can be decreased by persistent third spacing, warming, diuresis, vasodilation, and bleeding. Patients with ventricular hypertrophy or diastolic dysfunction usually require greater filling pressures. Persistently low filling pressures despite aggressive fluid administration may be caused by bleeding or vasodilation. In such cases calculation of CO and SVR can help determine the cause (Khalpey, Schmitto, & Rawn, 2012).

Fluid management in cardiac surgery involves decisions on when to administer fluid, how much to administer, as well as what type of fluid will be most beneficial. The timing and quantity of fluid to be administered is usually based on hemodynamic goals or indices such as the MAP, CVP or CO. However, the use of GDT with other indices such as the SVV are also being studied in cardiac surgery. With regard to the type of fluid, there is debate on the role of colloids vs. crystalloids, with numerous studies having been

conducted on their effects on outcomes. These areas will be discussed briefly in the following sections.

Restrictive versus liberal approach. Vretzakis and colleagues (2009) assessed blood transfusion requirements when using a restricted vs. liberal perioperative IVF approach in cardiac surgery patients. Their hypothesis was that because hemodilution contributes to increased transfusion requirements, restriction of parenteral fluids in comparison to a liberal fluid administration policy would lead to less use of packed red cells (PRCs). They randomized 130 elective cardiac surgery patients to either a restricted or a liberal group. The authors found that intraoperatively transfused units were significantly ($p < 0.0001$) lower in the study group (0.32 +/- 0.77 units/patient) vs. the control group (1.26 +/- 1.05 units/ patient) The number of patients who were transfused was also significantly ($p < 0.0001$) lower in the study group (11 out of 65) vs. the control group (44 out of 65). The study was considered to be under-powered, so the same investigators did a second study on 192 elective cardiac surgery patients in 2010. They found similar results with this study as well. Significantly ($p < 0.04$) fewer study group patients required transfusion in the study group (62 out of 100), compared to the control group (75 out of 92). They study group also received significantly ($p < 0.0001$) fewer PRC units (113) than the control group (176) (Vretzakis et. al., 2010).

Goal directed therapy in cardiac surgery. Aya, Cecconi, Hamilton, and Rhodes (2013) conducted a meta-analysis to investigate whether a goal-directed hemodynamic approach to therapy in the perioperative period was associated with improved postoperative outcomes in cardiac surgical patients. The primary outcome was hospital mortality. The secondary outcome measures were postoperative morbidity and hospital

length of stay. They defined GDT as perioperative monitoring and manipulation of hemodynamic parameters to reach either normal or supra-normal pre-determined values. A total of five RCTs with 699 cardiac surgical patients were included in the meta-analysis.

There were 15 deaths in three studies, while two studies had no deaths. Analysis when combining all the groups showed that GDT did not reduce the mortality in the intervention group (pooled *OR*: 0.69; 95% CI [0.19, 2.56] *p*=0.58). When analyzing morbidity, there were 21 complications in the GDT group and 51 in the control group. In the pooled analysis, there was a significant reduction in the overall complication rate (OR:0.33; 95% CI [0.15,0.73] *p*=0.006). Hospital length of stay was significantly reduced in the GDT group, (MD: 22.21; 95% CI [23.84, 20.57] *p*=0.008). There were several study limitations including a small number of studies, inclusion of only single-center studies with small sample sizes, and heterogeneity in the therapeutic goals and hemodynamic parameters used (Aya et al.).

Walker and Young (2015) designed a study to assess the effect of a postoperative GDT, or as they also called it, a "standardized hemodynamic protocol" (SHP), on the administration of fluid and vasoactive drugs after high-risk cardiac surgery. This study was conducted in a hospital in New Zealand. It was a single-center, interventional pilot study. It compared a prospective cohort of 40 high-risk cardiac surgical patients from 2010 to 2011, with a retrospective cohort of 40 consecutive patients in 2009. The prospective cohort received SHP, while the retrospective cohort received usual care. A pulmonary artery catheter was inserted in all the study patients to guide therapy. The protocol guided administration of fluids, vasopressors, inotropes, and vasodilators to

target a cardiac index (CI) greater than 2 L/min/m2, a mixed venous oxygen saturation greater than 60%, and a MAP of 65 to 75 mmHg, for the first 12 hours of surgery.

There was no significant difference in the duration of vasopressor infusion between the two groups. The SHP cohort received significantly (p <0.001) more fluid (4687±2284) in the first 12 hours postoperatively than the usual care cohort (1189±1344 ml). The SHP cohort also had a significantly (p=0.049) higher rate of reintubation (4 in 37 [10.8%]) vs. the usual care group (0 in 40 [0%]). There was one death from the SHP group, which was not deemed to be related to fluid overload. Some of the limitations of the study included the use of historical controls, which can inherently increase bias, the time span between the groups which could lead to change in staff or patterns of care, the small sample size, and the fact that this was a single center study (Walker & Young).

Osawa and colleagues (2016) conducted a trial on 126 high risk patients undergoing coronary artery bypass surgery or valve repair. Subjects were randomized to the GDT arm which was guided by CO measurement, or to the group that was guided by conventional parameters. In the GDT group, a CI of greater than 3 L/min/m was targeted with IVF, inotropes, and blood transfusion starting from CPB and ending eight hours after arrival to the ICU. Goal directed therapy using fluids, inotropes, and blood transfusion reduced 30-day major complications; lower rate of infection ([12.9% vs 29.7%] p = 0.002) and low cardiac output syndrome ([6.5% vs 26.6%] p = 0.002). The GDT group also had lower cumulative dosage of inotrope ([12 vs 19 mg/kg] p = 0.003) and a shorter ICU ([3 vs 5 days] p < 0.001) and hospital length of stay ([9 vs 12 days] p = 0.049). There were however, no differences in 30-day mortality (Osawa et al.).

Kapoor and colleagues (2017) studied the effect of GDT on patients undergoing off-pump CABG surgery. There were 66 patients in the GDT group and 76 patients in control group. The GDT arm utilized CI, SVR index, oxygen delivery index, SVV, continuous central venous oxygen saturation, global end-diastolic volume, and extravascular lung water measurements to guide therapy, in addition to standard hemodynamic management that the control arm used. Goal directed therapy was continued for 48 hours postoperatively in the ICU. The GDT arm had a significantly ($p < 0.001$) shorter length of hospital stay (7.42 ± 1.48) compared to the conventional arm (5.61 ± 1.11 days). The GDT group also had a significantly ($p < 0.001$) shorter length of ICU stay (4.2 ± 0.82) compared to the conventional arm (2.53 ± 0.56 days), and significantly ($p = 0.005$) lower duration of inotrope usage (3.24 ± 0.73) compared to the conventional arm (2.89 ± 0.68 h). The two groups did not differ in duration of ventilated hours, mortality, and other complications.

As shown here, there are studies in the literature that have found benefits when using GDT. However, it is difficult to make definite conclusions, as there is considerable variation between studies of the goals of therapy and the hemodynamic parameters and the monitoring devices that were utilized. One study had a goal of CI >3 while another was >2.5. Hemodynamic parameters that were considered GDT in one study were considered part of the control group in another. Devices used to measure hemodynamic parameters also differed between studies.

Fluid types. The type of fluid that is used also has a significant impact on the hemodynamic outcomes in cardiac surgery patients. Colloids and crystalloids are the two main types of resuscitation fluids.

Crystalloids. Crystalloids include electrolyte containing fluids. Normal saline, which is widely used, is increasingly being considered as 'unbalanced' because of the lack of other essential extracellular ions including potassium, bicarbonate, calcium, magnesium, and phosphorous as well as its' chloride rich content. This is thought to induce renal artery vasoconstriction, acute kidney injury and hyperchloremic metabolic acidosis (Frazee & Kashani, 2016). Balanced solutions such as lactated Ringers or Plasma-Lyte are considered to be superior choices. However, in the SPLIT trial by Young et al. (2015), where they compared the effect of balanced crystalloids to normal saline on ICU patients, it was found that the use of balanced crystalloids did not reduce the risk for developing acute kidney injury. Reddy et al. (2017) conducted a post hoc subgroup analysis on cardiac surgery patients in the ICU who were part of the saline vs. balanced crystalloid/Plasma-Lyte SPLIT trial. The subgroup study included 954 patients, of which 475 patients received Plasma-Lyte, and 479 received saline. One hundred and twenty eight of 475 patients (26.9%) in the Plasma-Lyte group received blood or a blood product compared to 94 of 479 patients (19.6%) in the saline group (OR: 1.51; 95% CI [1.11,2.05]; $p = 0.008$). This was an unexpected finding, as the researchers had expected to find that balanced solutions would reduce blood transfusion requirements as compared to saline.

Colloids. Colloids are high-molecular-weight compounds that provide plasma expansion by remaining in the intravascular space and increasing the oncotic pressure. They include albumin, starches, dextrans, and gelatins, and are often used as an alternative to crystalloid solutions in fluid management (Mitra & Khandelwal, 2009). Finfer and colleagues (2010) studied the type of resuscitation fluids used in 391 ICUs

across 25 countries. Geographic and regional practices influenced fluid choice rather than patient characteristics, but overall colloids were used more often as a resuscitation fluid than crystalloids. The data showed 48% of resuscitation episodes being treated with colloids as compared to 33% with crystalloids, with the remaining treated with blood products.

Several studies have been conducted in septic, non-cardiac and cardiac surgery patients to evaluate the effect of colloids and the results seem to indicate that colloids may have fewer benefit, and higher risk. A few of the studies are discussed briefly.

Navickis, Haynes, and Wilkes (2012) conducted a meta-analysis of RCTs that compared the impact of hydroxyethyl starch (HES) to albumin on bleeding after surgery using CPB. They included 18 RCTs with 970 patients who received colloids perioperatively for volume expansion (nine trials), pump priming (five trials), or both (four trials). Compared with albumin, HES significantly ($p < .001$) increased postoperative bleeding by 33.3% of a pooled SD, more than doubled the risk for reoperation due to bleeding (RR; 2.24; [$p = .020$]), and significantly increased the transfusion of red blood cells by 28.4% of a pooled SD ($p < .001$), of fresh frozen plasma by 30.6% ($p = .008$), and of platelets by 29.8% ($p = .027$). Albumin was found to improve hemodynamics in this meta-analysis. However, there were no differences in fluid balance, ventilator time, intensive care unit stay, or mortality (Navickis et al.)

In a cohort study by Bayer et. al. (2013), of 6478 patients who underwent cardiac surgery with CPB, treatment with synthetic colloids including both starch and gelatin was associated with a higher risk of renal failure and greater use of renal replacement therapy. Gelatin was associated with a higher risk of hospital death (*OR*: 1.72; 95% CI [1.15,

2.58], $p = 0.008$), than treatment with crystalloid or starch. There was no difference in the time to achieve hemodynamic goals or vasopressor cessation among groups. While the crystalloid group required more fluid volume initially, by the second day, it was similar to the colloid group. These investigators concluded that the use of starches and gelatins had less benefit than harm and their use was not advisable unless there was further evidence of their safety.

Frenette et. al. (2014) conducted a retrospective cohort study of patients undergoing on-pump cardiac surgery to examine the risk of acute kidney injury (AKI) associated with the use colloids. Acute kidney injury was defined by the RIFLE (risk, injury, failure, loss and end-stage kidney disease) risk and Acute Kidney Injury Network (AKIN) stage 1 serum creatinine criterion within 96 hours after surgery. The cohort included 984 patients who either underwent CABG and/or valve replacement surgery. Persons with known kidney disease were excluded from the study.

With respect to colloid administration, 82%, 43% and 16% of individuals received HES 6%, pentastarch 10% or albumin, respectively. In the patients who developed AKI, and who also received colloids, the greatest risk for AKI was associated with the use of albumin (*OR*: 3.9; 95% CI [2.1,6.8]; $p < 0.001$). Risk was marginal with the use of pentastarch 10% (*OR*: 1.7; 95% CI [1.0 ,3.0]; $p = 0.06$) and absent with the use of HES 6%. To address any indication bias, the researchers matched 141 cases who received albumin to 141 controls with a similar risk profile, who did not receive albumin and developed a propensity score. In this analysis, albumin was associated with an increased AKI risk (RIFLE risk: 12% vs. 5%, $p = 0.03$; AKIN stage 1: 28% vs. 13%, $p = 0.002$). They repeated propensity matching in 50 cases and 50 controls without postoperative

hemodynamic instability and still identified a significant association between the use of albumin and AKI; AKIN stage 1 AKI (30% vs. 8%, $p = 0.005$). Consideration should be given to the fact that this is a single-center study with limitations inherent to its retrospective design (Frennete et al.).

Summary: Challenges in Fluid Management and Cardiac Surgery

Fluid management in surgical patients has been a challenging subject, because of the difficulty to define or accurately measure volume deficit, predict fluid responsiveness and replenish just enough, but not too much fluid. Inadequate replenishment can lead to obvious dangers such as shock and organ damage, but also affect recovery by increasing issues such as nausea and vomiting, poor wound healing and infection. Fluid overload on the other hand can lead to complications related to increased tissue edema, such as of the lungs or the abdomen. Getting the balance right is of utmost importance, but difficult to achieve. While restricted fluid regimens are increasingly finding favor, the absolute amount of fluid that is defined as liberal in one study might be defined as standard in a different study, while a standard amount of fluid may be a restrictive amount in another. The same problem exists with GDT. The studies are varied and use different devices to predict fluid requirements and have different target parameters. The results have also not been consistent. On top of these issues, is the one of fluid type: crystalloid vs. colloid; colloid vs. colloid (starch, gelatin or albumin); and crystalloid vs. crystalloid (normal saline or lactated Ringers solution) debate.

Cardiac surgeries are different from other surgeries in many ways. They are major surgeries, often involving the use of CPB and cardioplegia. Patients may experience prolonged hypothermia, more than in other surgeries. Often CPB results in a systemic

inflammatory response which causes capillary leak and causes fluid to leave the intravascular space into the interstitial space. These, among other factors, increases the risk for hemodynamic alterations. Because of these differences, it is important to study the issues of fluid and hemodynamics specific to this specialty. There are several studies on various aspects of fluid management in cardiac surgery; however, there is still much debate on how best to administer fluids, what hemodynamic indices are the most reliable guides, and what type of fluid provides the most benefit and least risk. Fluid management in cardiac surgery is a difficult and challenging subject and requires continued exploration and examination.

Next, the theoretical framework that guided this review will be presented.

Theoretical Framework

The integrative review method is an approach that utilizes research built on diverse methodologies to study a problem. Unlike a systematic review that may only use RCTs, an integrative review allows the use of experimental, nonexperimental, quantitative or qualitative studies to find evidence. Whittemore and Knafl published an article in 2005 where they presented an updated and modified integrative review framework. This framework purposes to enhance rigor when combining various methodologies. It consists of five stages. These stages included; problem identification, literature search, data evaluation, data analysis, and presentation. All the stages of this framework, except for data evaluation were used. Polit and Beck's (2016) approach for critiquing studies, was the method used for data evaluation. The four stages by Whittemore and Knafl (2005), and how they were used for this review are briefly described below.

Problem Identification

The authors describe the first stage of the integrative review as the clear identification of the problem and the purpose of the review. This is followed by a determination of the variables of interest which include the concepts, target population and health care problem. Likewise, in this review, the problem was identified and articulated clearly. The variables of interest that would be researched were determined. Some of these variables included standard fluid management practices, different approaches and hemodynamic parameters used in cardiac surgery.

Literature Search

The second stage of the review involves the formulation of a well-defined literature search strategy, and includes all relevant literature on the problem. The

literature search process should be clearly documented and include the search terms, the databases used, additional search strategies, and the inclusion and exclusion criteria for selection of sources. This review utilized these guidelines to formulate a well-defined strategy to identify and utilize relevant literature. It clearly documented the search strategies in the method section. In keeping with the scope of the integrative review method, studies that utilized diverse methodologies were incorporated. They included RCTs, observational studies, retrospective and prospective studies and surveys.

Data Analysis

In this stage the data from primary sources is organized, categorized and summarized. The evidence is interpreted and synthesized in a thorough and unbiased manner. The stages of data analysis included data reduction, data display, data comparison and drawing of conclusions and verification. Using these as a guide, the data obtained from the selected articles in this review was thoroughly examined, organized and cross analyzed. This allowed for conclusions to be made which are presented at the end of the paper.

Presentation

The conclusions are reported in a diagrammatic or tabular format. Clear and detailed evidence from primary sources are provided to support conclusions. Implications for practice are emphasized as well as those for research and policy initiatives. All methodological limitations of the review are explicitly stated. Using this as a guide this review summarized the evidence obtained and presented conclusions. It also explicitly stated the limitations of the review and finally presented recommendations for practice and implications for future research.

Data Evaluation

The data evaluation method by Polit and Beck (2016), was used to critically appraise all literature evaluated in this integrative review. This method involves the careful evaluation of every aspect of a study article. In keeping with their guidelines, every area and section of the research paper was critiqued. Some of these include the title, the abstract, the problem statement, and the research methodology. This method is further elaborated in the next section of this review.

Next, the method will be presented.

Method

Purpose of the Project

The purpose of this review was to explore and analyze the current evidence in published literature on fluid management in cardiac surgery patients.

Design

The design was an integrative literature review.

Inclusion Criteria

Quantitative studies on fluid management in adult cardiac surgery patients were included. In keeping with the integrative review design, there was no restriction on level of evidence. Observational studies, cohort studies, and surveys were included, as well as RCTs. On pump and off pump procedures were included. Only English language studies were included. Relevant data that has been generated within the last 5 years; from 2012 to October 2017 were included.

Exclusion Criteria

The articles that were excluded from this review included those which involved

- Studies on the pediatric population;
- Non-cardiac surgeries or procedures such as aortic arch replacement which may be more of a vascular surgery;
- Studies that seek to show relationship between two hemodynamic indices rather than those that study fluid management on outcomes;
- Studies that seek to evaluate certain predictors of fluid responsiveness;
- Qualitative studies;
- Fluid management that is primarily related to the priming solution used for CPB;

- Studies that primarily focus on a population with a specific disease or condition, such as renal failure or heart failure;
- Studies that provided no data on the fluid volumes that were utilized.

Data Collected

A variety of data were collected from the articles that were included in this review. While most of the studies yielded information regarding parameters that guided fluid management, data on fluid types was obtained from studies on surveys. Patient outcome data was obtained from the studies comparing GDT to standard care. The data that were collected include the following;

- Comparison between studies of what was considered as standard or usual care and what was the GDT;
- Hemodynamic parameters that guided fluid management;
- Outcomes of the therapy on postoperative recovery, such as time to extubation, duration of inotrope or vasopressor usage;
- Complications if available;
- Length of stay, including ICU and hospital stay;
- Mortality;
- Duration of ventilation;
- Use of inotropes and vasopressors;
- Review of fluid administration will include the type of fluid and their volumes.

Assessment Criteria

Polit and Beck's (2016) critical appraisal guidelines were used to assess the quality of the study articles. Their quantitative research critique guide was used for this

review. Every area and section of the research paper was critiqued. These included the title, the abstract, the problem statement, the research question, the literature review and the conceptual framework. Critique of the methodology included the research design, the population and sample, and the data collection and measurement instruments. Data analysis of the findings and a discussion of the interpretation of the results was conducted. Finally, the critique reviewed protection of human rights and appropriate study participant safeguards, including institutional board review by an external organization. General issues such as the presentation of the paper, use of appropriate flow charts and clarity of the writing were also considered (Polit &Beck, 2016).

Next, the results section will be presented.

Results

After duplicates were removed, 695 articles were found to be suitable for further review based on database searching. Of these, 50 abstracts were reviewed after excluding articles based on inclusion/exclusion criteria. Further examination led to a full text review of 21 articles, of which 13 study articles met inclusion criteria and were included in this review (Figure 1).

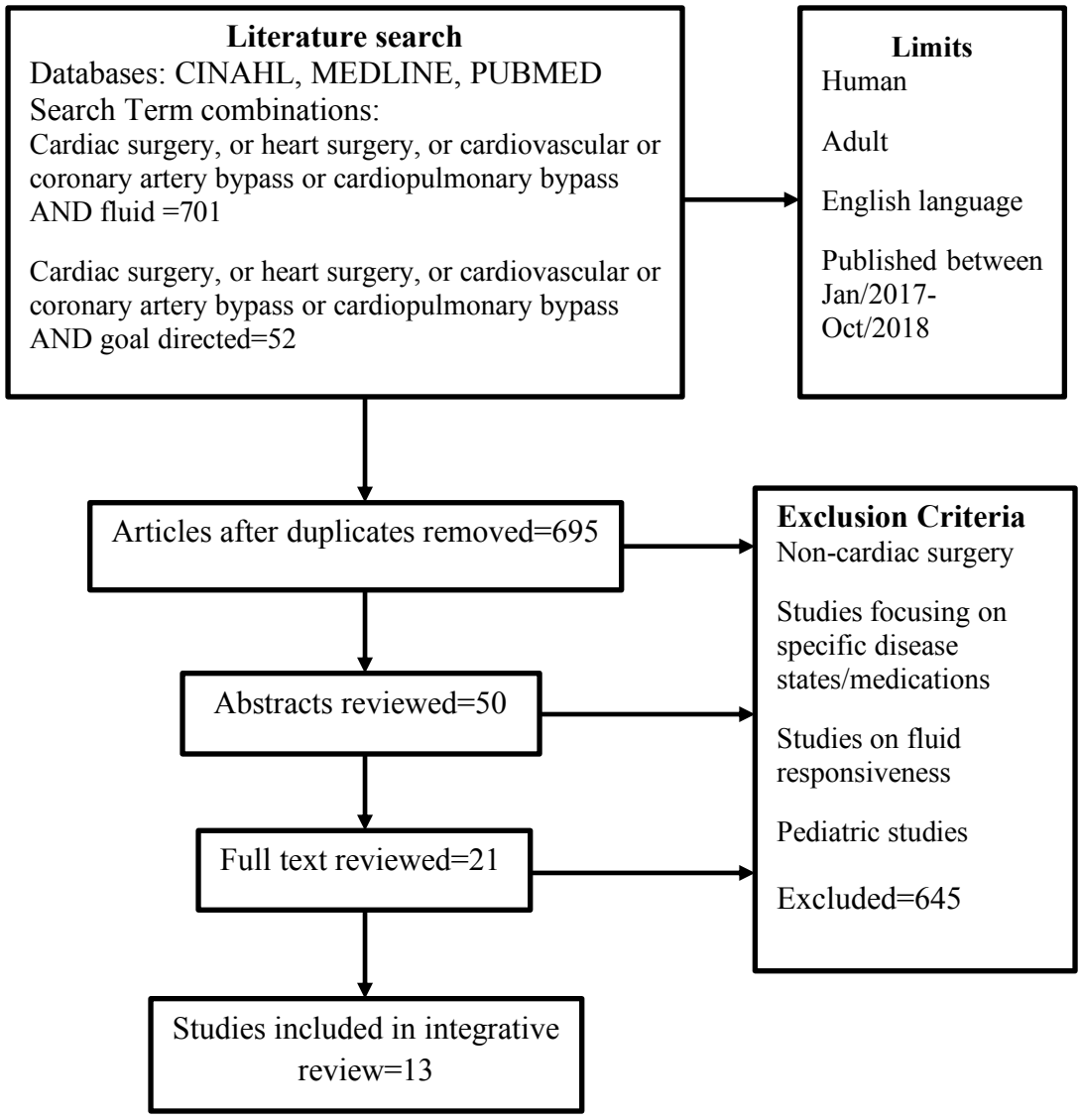

Figure 1. Flow chart depicting search method and results.

Of the 13 studies identified, four were surveys that sought to examine practices related to cardiac surgery including fluid management. All of these were conducted in European countries. There was one observational study that was conducted in order to study fluid management practices in ICUs in Australia and New Zealand. Finally, there were eight studies that examined the effects of GDT in cardiac surgery patients. The results of these studies will be discussed in the next few pages. First, the surveys will be briefly discussed. These will be followed by a discussion of the observational study, and finally by a discussion of the studies on GDT.

Studies on Postal and Online Surveys

Kastrup et al. (2013) conducted a survey of German ICU physicians regarding management practices in cardiac surgery (Appendix A, Table A-1). One aspect of this survey included questions related to volume monitoring and replacement strategies. The authors compared the results of this 2012 survey to a similar survey done in 2005. The investigators found that for monitoring of fluid therapy, there was a significantly (p=0.006) increased use of the systolic pressure variation in 2012 (32.6%), compared to 2005 (14.6%). There was significantly (p=0.027) increased use of the left ventricular end diastolic area index with the TEE ; 13.6% in 2012 compared to 8.3% in 2005. There was also significantly (p=0.025) increased utilization of extravascular lung water measurement with transpulmonary thermodilution; 14.1% in 2012 compared to 8.1% in 2005. For volume therapy, there was a significant (p=0.007) reduction in the use of HES with 38.7% in 2012 compared to 63.4% in 2005, with a corresponding significant (p=0.042) increase in the use of crystalloids 41.9% in 2012 compared to 22.4% in 2005 (Kastrup et al.).

Sponholz, Schelenz, Reinhart, Schirmer, and Stehr, (2014) surveyed German anesthesia departments involved in cardiac surgery regarding hemodynamic monitoring, catecholamine and fluid therapy practices (Appendix A, Table A-2). The investigators found that fluid administration was most often based on CVP, TEE and arterial blood pressure curve. All these methods had a median value of 2 on a Likert Scale of 1 to 5, where 1 is common and 5 is rare. With regard to fluid choices, crystalloids were the fluids of first choice during and after surgery (median; 2).

Bignami et al. (2015) surveyed cardiothoracic ICU's to determine current management practices in cardiac surgery, and included questions on fluid administration (Appendix A, Table A-3). The results showed that for monitoring volume status, CVP was used most frequently (26.7 %), followed by arterial BP (19.7 %) and echocardiography (5.6 %). The first choice for volume replacement were crystalloid solutions in 86.8 %, followed by artificial colloids in 11.8 % of the centers.

Protsyk et al. (2017) surveyed ICUs in 18 European countries to determine current perioperative fluid management practices in cardiac surgery patients (Appendix A, Table A-4). The investigators found that balanced crystalloids alone were most frequently used for intraoperative management (74%). Crystalloids along with synthetic colloids were used 15% of the time and other fluids; alone, or in combination were used 11% of the time. The results of this survey were limited by a small survey response rate of only 28 %.

Observational Study on Fluid Administration Practices in Cardiac Surgery

Parke, McGuiness, Gilder, and McCarthy (2014), conducted an observational, multi-center, prospective study in four ICUs in New Zealand and Australia to obtain data

on fluid administration practices in cardiac surgery (Appendix B). The study included 235 patients. The number of fluid boluses given were 1226, with an average volume of 504 ml per bolus. The median total IV fluid intake was 4493 ml/patient (interquartile range [IQR], 2842–5498 ml), of which the median fluid given for volume expansion in the first 24 hours was 2250 ml (IQR, 1250–3500 ml). The decision to administer a fluid bolus was made 45% of the time by an ICU resident, 40% by nursing staff, and 12% by an ICU specialist. The most common primary indication for fluid administration was hypotension (65%), while the most common secondary indication was low CVP (42.9%). Nurses were more likely than doctors to administer crystalloid (83.6% v 52.7% of boluses) and more likely to cite hypotension (69.9% v 61.3%) or low CVP (16.4% v 7%) as the primary indication. Crystalloid fluid was used for 65% of the boluses (Parke et al., 2014).

Studies on Goal Directed Therapy in Cardiac Surgery

Goepfert et al. (2013) conducted a prospective RCT involving CABG and/or aortic valve replacement to compare outcomes of a GDT to usual care (Appendix C, Table C-1). They randomized 50 patients to the study or GDT group and 50 to the usual care group. Fluid administration in the usual care group was based on CVP. If the CVP was less than 8 mm Hg, fluid boluses were administered. If the CVP was greater than 8 mm Hg, but the MAP remained less than 65 mm Hg, catecholamines were initiated. In the GDT group, fluid was administered to the patients until the stroke SVV was less than or equal to 10%. If the SVV was less than 10 %, but the CI remained less than 2.0 l/min m-2, vasopressors were initiated.

The results showed that there was no significant (p=0.221) difference in fluid intake between the two groups (mean 11,701 ± SD 2,175 ml in the study group vs. 12,313 ± 3,281 ml in the control group. While there was no difference in the amount of crystalloids utilized, significantly ($p < 0.001$) more colloid was administered in the study group both intraoperatively (mean 1293 ml in the control group vs. 880 ml in the study group), as well as in the postoperative ICU period; (mean 1774 ml in the study group vs. 1237 ml in the control group) (p =0.008).

In terms of outcomes of the GDT, there was significantly (p = 0.002) reduced intraoperative norepinephrine use in the study group mean 9.0 ± SD 7.6 µg/kg vs. 14.9 ± 11.1 µg/kg in the control group, significantly (p = 0.004) fewer post-operative complications (40 in the study group vs. 63 in the control group), and significantly (p = 0.001) shorter time to reach ICU discharge criteria, (15 ± 6 h in the study group vs. 24 ± 29 h in the control group) and significantly (p = 0.018) shorter length of ICU stay (42 ± 19 h in the study group vs. 62 ± 58 h in the control group) (Goepfert et al.).

Thomson, Meeran, Valencia, and Al-Subaie (2014) conducted a prospective observational study to assess the effect of a nurse driven GDT that maximized stroke volume for 8 hours postoperatively in cardiac surgery patients (Appendix C, Table C-2). This was a single center study conducted in an ICU in the UK. There were 123 patients in the GDT group and 141 in the standard therapy group.

Fluid administration in the standard therapy group was based on perceived clinical need, MAP, CVP, lactate level, urine output, and base deficit. The GDT utilized CO and SV measurements along with CVP. The intervention started with recording of baseline SV, CO, and CVP, followed by the administration of 250 ml of fluid bolus. If

this resulted in the SV increasing by 10 % or more, the fluid bolus was repeated until the SV no longer increased with fluid boluses by 10 %. If the CVP increased by six points at any time, the fluid boluses were stopped.

The results showed that there was no significant ($p = 0.09$) difference in the volume of intravenous fluid administered in both groups during the first eight hours in the ICU (2704 [1393] mL in the usual care group vs. 2905 [1367] mL in the GDT group). The incidence of acute kidney was significantly ($p = 0.002$) decreased in the GDT group: 6.5% in the GDT group vs. 19.9% in the usual care group. The median duration of hospital stay was significantly ($p = 0.004$) lower in the GDT group, six days compared to the usual care group (seven days). There was significantly *(p*=0.04) reduced incidence of ICU readmissions in the GDT group 4(3.3%) compared to the usual care group 13(9.2%) (Thomson et al., 2014)

Fellahi and colleagues (2015) conducted a prospective RCT that compared the impact of a GDT on patients undergoing CABG to standard care during the intraoperative period (Appendix C, Table C-3). The GDT utilized CO which was measured using a special type of endotracheal tube called the endotracheal cardiac output monitor (ECOM). There were 44 patients in the control group and 48 in the study group. In the control group, the fluid was administered based on the usual hemodynamic parameters including BP, CVP, urine output, skin mottling, and arterial pulse pressure variation. In the ECOM group a fluid bolus of 100 ml was administered when the SVV was greater than 11%, and repeated until correction of SVV to less than 11%. If the CI remained less than 2.4 l/min m-2, despite corrected SVV, then dobutamine would be initiated.

Significantly (p= 0.042) more patients in the ECOM group received fluid loading (n=41) compared to the control group (n=30). However, the total intraoperative amount of fluid was significantly (p= 0.035) decreased in the ECOM group (mean 400 ml) when compared with the control group (mean 500). The only significant difference in outcome between the two groups was the time to extubation which was significantly (p= 0.005) decreased by 60 minutes on average in the ECOM group when compared with the control group (Fellahi et al.).

Parke, McGuiness, Gilder, McCarthy, and Cowdrey (2015) conducted a prospectively randomized interventional feasibility study to trial using a conservative post-operative fluid administration protocol in cardiac surgery (Appendix C, Table C-4). They randomized 74 patients to the usual care group and 70 to the intervention group. In the intervention group a fluid bolus consisting of 250 to 500 ml was administered if the CI was less than 2.5 l/min m-2 and the SVV was greater than 13 %. If these parameters were at goal and the patient remained hypotensive with MAP less than 65 mmHg, vasoconstrictor medications were initiated. Fluid administration in the usual care group was based on the nurses' discretion up to a limit of two liters, when they deemed it was necessary. MAP and CVP were most commonly used to determine fluid requirement in this group.

The results showed that the intervention group received significantly (p<0.001) less fluid bolus (median [IQR] 1620ml [500–3410]) compared to the usual care group (median 2520 ml [1440–5250ml]) as well as significantly (p=0.001) lower overall IVF volume (median 2050ml [910–4280 ml]) compared with the usual care group (median 2980ml [2070–6580 ml]) from ICU admission until extubation. The total amount of

fluids administered from admission to 24 hours were also significantly (p=0.02) less in the intervention group (median 4350 ml [2790–6160 ml]) than in the usual care group (median 5080 ml [3930–7320 ml]). There was no significant difference in any outcomes between the two groups. (Parke et al.).

Walker and Young (2015) studied the effect of a postoperative GDT in high-risk cardiac surgery (Appendix C, Table C-5). This study was a single-center, interventional pilot study conducted in a hospital in New Zealand. It compared a prospective cohort of 40 high-risk cardiac surgical patients with a retrospective cohort of 40 patients. The prospective cohort received the intervention, while the retrospective cohort had received usual care. The intervention involved the administration of fluids, and vasoactive medications to target a CI greater than 2 l/min/m2, a mixed venous oxygen saturation greater than 60%, and a MAP of 65 to 75 mmHg, for the first 12 hours of surgery.

The results showed that there was no significant difference in the duration of vasopressor infusion between the two groups. The intervention group received significantly (p <0.001) more fluid (4687±2284) in the first 12 hours postoperatively than the usual care cohort (1189±1344 ml). The intervention group also had a significantly (p=0.049) higher rate of reintubation (4 in 37 [10.8%]) vs. the usual care group (0 in 40 [0%]) (Walker & Young).

Shreshta, Pradhan, and Koirala (2015) conducted a prospective RCT on a small sample of cardiac surgery patients in Nepal to study the impact of early GDT on postoperative outcomes (Appendix C, Table C-6). They randomized 20 CABG and valve repair/replacement patients to the study/GDT group and 15 to the control group. Hemodynamic parameters for both groups included CVP (6 -10 mmHg), MAP (60 -90

mm Hg), and urine output greater than 1 ml/kg/hr. Additional monitoring parameters for the GDT group included CI, SVV, stroke volume index (SVI), SVR, ScVO2 and blood lactate level. The intervention involved the administration of 100 ml fluid boluses for CI less than 2.2 l/min/m2, and if the CVP less than 6 mmHg or the SVV was greater than 10%. The duration of the intervention was from the opening of sternum until eight hours post-surgery.

The results showed that the study group received more total fluid than the control group, although the difference did not reach statistical significance (1199.04 ± 638.701 in the GDT group vs. 938.32 ± 736.151 in the control group). There was a significant (p=0.041) reduction in ventilator time in the study group ([M] 10.48 ± [S.D] 7.640 hours) compared to the control group (16.429 ± 11.801hours). The duration of inotrope usage was also significantly (p=0.032) lower in the study group (23.2 ± 17.870 hours) than the control group (39.12 ± 18.615 hours). There was no difference in mortality, rate of complications or length of stay between the two groups (Shreshta et al.).

Osawa and colleagues (2016) conducted an RCT to study the effect of GDT on outcomes in high risk cardiac surgery (Appendix C, Table C-7). They randomized 62 high risk patients undergoing CABG or aortic valve repair to a GDT group and 64 to the usual care group. Usual care interventions were guided by heart rate, ScVo2 >70 %, lactate level<3, urine output > 0.5 ml/kg/hr and MAP >/ 65. In the GDT group, CI of greater than 3 L/min/m was targeted with IVF, inotropes, and blood transfusion starting from CPB and ending eight hours after arrival to the ICU.

In first eight hours following ICU admission, the median volume of fluid bolus administered differed significantly ($p < 0.001$) between groups (1,000 mL [IQR, 625–

1500] in the GDT group vs. 500 mL [IQR, 500–1000] in the usual care group. The total amount of fluid administered was greater in the GDT group (median [IQR] 1056 ml (257–1568 ml) than in the control group (894ml (229–1595 ml) but this did not reach significance (p=0.85). In terms of outcomes, the GDT group had significantly (p=0.002) lower rate of infection (12.9%) compared to the usual care group (29.7%), and significantly (p=0.003) reduced incidence of low cardiac output syndrome (6.5% in the GDT group vs. 26.6% in the usual care group). The GDT group also had significantly (p = 0.003) lower cumulative dosage of inotrope (12 in GDT group vs. 19 mg/kg in the usual care group), and a significantly (p = 0.049) shorter ICU (3 days in the GDT group vs. 5 days in the usual care group) and hospital length of stay ([9 days in the GDT group vs. 12 days in the usual care group] p = 0.049). There were however, no differences in 30-day mortality (Osawa et al.).

Kapoor et al. (2016) studied the effect of GDT on patients undergoing off-pump CABG (Appendix C, Table C-8). They randomized 66 patients to the GDT group and 76 patients to the control group. In the control group, therapy was guided by CVP, MAP, end tidal CO2 (EtCO2), temperature, arterial blood gas analysis, hematocrit and urine output. In the GDT group, in addition to these measures, CI, SVV, continuous central venous oxygen saturation and ELVI measurements were utilized. The intervention consisted of the administration of 100 ml fluid bolus if the CI was less than 2.2 l/min/m2, the CVP was less than 6 mmHg or the SVV was greater than 10%. This was repeated until these goals were achieved. Goal directed therapy was continued for 48 hours post-operatively in the ICU.

The results showed that the extra fluid administered was significantly (p=0.003) more in the GDT group (376.33 ± 55.23 ml) than the control group (343.33 ± 62.02 ml). In terms of outcomes, the GDT arm had a significantly ($p < 0.001$) shorter length of hospital stay (7.42 ± 1.48 days) compared to the conventional arm (5.61 ± 1.11 days). The GDT group also had a significantly ($p < 0.001$) shorter length of ICU stay (4.2 ± 0.82) compared to the conventional arm (2.53 ± 0.56 days), and significantly ($p = 0.005$) lower duration of inotrope usage (3.24 ± 0.73 hours) compared to the conventional arm (2.89 ± 0.68 hours). The two groups did not differ in duration of ventilated hours, mortality, and other complications (Kapoor et al.).

Cross Analysis of Studies

In this section, the cross analysis findings of the four surveys on practices in cardiac surgery and the eight studies on GDT in cardiac surgery will be presented. One study by Parke et al. (2014) is not categorized under either of these headings and has already been discussed in the previous section. The cross analysis of the surveys will be presented first followed by that of the GDT studies.

Postal and online surveys. The postal and online surveys that are included in this review (Bignami et al., 2015; Kastrup et al., 2013; Protsyk et al., 2017; Sponholz et al., 2014) were all conducted in European countries between 2012 and 2017 (Appendix D, Table D-1). All surveys except for the study conducted by Protsyk and colleagues (2017) sought to obtain knowledge about basic and advanced hemodynamic monitoring techniques, volume replacement strategies, and the use of vasopressor or inotropic drugs utilized in cardiac surgery. Protsyk and colleagues' survey design addressed only the fluid types used in cardiac surgery.

The survey research done by Sponholz et al. and Bignami et al. found that CVP and ABP were most often used often to monitor volume status along with echocardiography. Additionally, Kastrup et al. discovered that there was increased use of TEE, systolic pressure variation and extravascular lung water monitoring in the centers surveyed (Appendix D, Table D-2). All the survey results (Bignami et al., 2015; Kastrup et al., 2013; Protsyk et al., 2017; Sponholz et al., 2014) found that crystalloids were the fluid of first choice for volume replacement (Appendix D, Table D-2). While the survey by Kastrup and colleagues (2013) found that there was a reduction in the use of HES compared to a previous survey in 2005 (Appendix D, Table D-2), HES was still popular and was the fluid of second choice for volume replacement (Bignami et al., 2015; Kastrup et al., 2013; Sponholz et al. 2014)The latest survey by Protsyk and colleagues (2017), however, found that when colloids were used, gelatin was more popular than HES or albumin (Appendix D, Table D-2).

Goal directed therapy in cardiac surgery. Eight studies based on GDT in cardiac surgery have been included in this review (Appendix E, Table E-1). All eight studies sought to determine the most appropriate manner of fluid administration by targeting preset goals. One of them by Parke and colleagues (2015), had the specific aim to reduce IV fluid administration.

Five of the studies were RCTs, one was a prospective observational study (Thomson et al., 2014) one was a prospective randomized feasibility study (Parke et al., 2015), and one was a prospective study in which the intervention group was compared to a retrospective cohort (Walker & Young, 2015). All the studies except the one by Kapoor

et al. (2016) were conducted in single centers. Kapoor and colleagues conducted their study in two centers.

Two of the studies evaluated GDT during the intra-operative period; (Fellahi et al., 2015; Goepfert et al., 2013), three evaluated GDT during the postoperative period (Parke et al., 2015; Thomson et.al, 2014; Walker & Young, 2015), and the last three evaluated the effects of GDT in the intraoperative as well as postoperative phase of surgery (Kapoor et al., 2016; Osawa et al., 2016; Shreshta et al., 2015) The studies were all conducted with CABG or/and valve surgery patients, with three studies specifically conducted with high risk patients (Kapoor et al., 2016; Osawa et al., 2016; Walker & Young, 2015).

All the studies provided data on the hemodynamic goals for fluid therapy and administration of vasoactive medications in the GDT group (Appendix E, Table E-2). All authors except Walker & Young (2016), also provided data about the standard monitoring methods or interventions in the usual care group. The usual care group in most of the studies included treatment based on CVP, MAP or ABP and urine output. In the study by Goepfert et al. (2013), fluid boluses were administered in the usual care group if the CVP was less than 8 mm Hg. However, if the CVP was greater than 8 mm Hg, and the MAP remained less than 65 mm Hg, catecholamines were initiated. In the study by Parke et al. (2015), nurses were allowed to administer up to two liters of crystalloid fluid based on their own clinical judgment of hemodynamic inadequacy, MAP, and CVP measurements. In the study conducted by Thomson and colleagues (2014), the patients in the usual care received IV fluids based on the perception of clinical need, which was guided by arterial and venous pressures, serum lactate concentrations, urine output, and base deficit.

The GDT interventions included algorithms that involved fluid administration based on SVV and CI. Many studies had a goal for SVV less than or equal to 10 % and fluid was administered until this goal was achieved (Goepert et al., 2013; Kapoor et al., 2016; Shrestha et al., 2015; Thomson et al., 2014); however, two of the studies had a higher limit to treat the SVV (Fellahi et al., 2015 [SVV 11 %]; Parke, et al., 2015 [SVV 13 %]). Target goal for CI in most studies were between 2.0 and 2.5 l/min/m2. The study by Osawa and colleagues (2016) had a higher target of CI 3.0 l/min/m2. and fluid or vasopressor/inotropes were administered to achieve these targets. In addition to CI and SVV, MAP goals were provided by many of the studies and had targets of 65 mm Hg or greater (Parke et al., 2015; Kapoor et al., 2016; Walker & Young, 2015). Fluid bolus volumes ranged from 100 ml to 500 ml, given repeatedly until targets were achieved. The studies by Shrestha et al. (2015) and Kapoor et al. (2016) also utilized CVP measurements in the GDT arm of their studies and fluid was administered for CVP less than 6 mm Hg.

Data on the amount of fluids used was reported in all the studies (Appendix E, Table E-3); however, comparison of fluid amounts administered was somewhat difficult because the data provided by different studies varied with regard to the timing of administration. Despite this, a slight trend toward more fluid being administered in the GDT groups compared to the usual care groups is discernible. The exception was the study by Parke et al. (2015), where the investigators were studying a conservative fluid approach and administered less fluid. Walker & Young's (2016) study was remarkable in that the GDT group received almost four times more fluid and had poorer outcomes when compared to the control group. In the study by Goepfert et al. (2013), the GDT group

received more colloid than the control group. In the study by Fellahi et al., even though more fluid boluses were administered, the total intraoperative fluid amount was actually less than the control group.

In terms of outcomes, the length of hospital stay or time to discharge was reported in all the studies except for the one by Walker and Young. A trend toward a decreased length of hospital stay in studies using GDT is discernible from the cross analysis table (Appendix F, Table F-1). The length of ICU stay has been reported in all the studies (Appendix F, Table F-2). Four of the eight studies (Goepfert et al., 2013; Kapoor et al.,2016; Osawa et al.,2016; Thomson et al., 2014.) reported a significant decrease in length of ICU stay in the GDT groups.

Mortality data has been reported in six of the eight studies (Appendix F, Table F-3). Parke et al. reported one death in the control group, while Goepfert et al. did not report any deaths or mortality data. The data in the cross analysis table indicates that there is no discernible effect of GDT on mortality.

Complications have been reported in all studies except the one by Kapoor (Appendix F, Table F-4). Significantly fewer complications were reported in the studies done by Goepfert et al., Osawa et al., and Thomson et al. The study by Thomson et al. looked only at renal complications. Osawa et al. found a significant decrease in infections and low cardiac output syndrome. Walker & Young's (2015) study findings, on the other hand, showed a significant increase in reintubations in the GDT group. Overall there is no discernable trend towards a decrease in complications from the use of GDT.

Time to extubation has been reported in all the studies (Appendix F, Table F-5), except in the one by Thomson et al. Three studies had significantly decreased time to

extubation in the GDT group (Fellahi et al., 2015; Kapoor et al., 2016; Shrestha et al., 2015) while Walker & Young's study had increased time to extubation in the GDT group. Observation of the cross analysis table does not clearly indicate a trend towards decreased time to extubation.

All the studies in this review except for those by Thomson et al. (2014) and Parke et al.(2015) reported the use of vasopressors and/or inotropes (Appendix F, Table F-6). Two studies reported significantly less dose and duration of vasopressors and inotropes (Goepfert et al., 2013; Osawa et al., 2016), while two studies reported decreased duration of inotrope use (Kapoor et al., 2016; Shrestha et al., 2015). The studies by Fellahi et al. and Walker & Young, reported increased use of inotropes and vasopressors in the GDT group. Overall, no trend can be discerned from observation of the data.

Next, the summary and conclusions will be presented.

Summary and Conclusions

Fluid management is an essential element in cardiac surgery. It is critical that fluids are administered appropriately in order to avoid the dangers of hypovolemia as well as fluid overload. Fluid management in surgery is a complex field with varying evidence regarding best approaches to administration, types of fluids to use, and the most appropriate parameters in assessment. While there is a considerable amount of literature on this subject in non-cardiac surgery, evidence on best practices pertaining to cardiac surgery is not as well defined or established. The purpose of this integrative review was to research the current evidence that is available regarding fluid management in cardiac surgery.

The updated and modified integrative review framework by Whittemore and Knafl (2005) was used to guide this review. An extensive review of literature which incorporated fluid balance concepts, hemodynamic monitoring and parameters that guide fluid resuscitation, fluid management approaches in adult cardiac and non-cardiac surgeries, and different types of fluids used in perioperative fluid management was included in the review. This was done in order to help the reader understand the current issues and practices in the field of fluid management.

This was followed by a search for studies that demonstrated what the usual or standard practices related to fluid management in the cardiac surgery population were, as well as any studies that sought to compare different approaches to fluid administration. Only two studies, both by Parke et al. (2014 & 2015), were found that exclusively studied fluid administration in cardiac surgery. Four surveys on practices in cardiac surgery, all of them conducted in Europe, were identified, and the fluid management aspects of the

surveys were used for this review. Additional information regarding fluid management in cardiac surgery was obtained by examining studies on GDT in cardiac surgery. While the focus of these studies was not exclusively fluid management, fluid administration was an important part of the therapies administered.

The critical analysis method by Polit and Beck (2016) was utilized to critically appraise the quality of the studies. The quality of all the studies was found to be adequate and allowed them to be included in this review. The studies were carefully reviewed and then cross-analyzed.

Cross-study analysis of the results found that in cardiac surgery, CVP and ABP were most often used often to monitor volume status along with echocardiography. It is important to note that CVP has not been shown to be a good predictor of fluid status. Other measures used included the urine output, serum lactate concentrations, urine output, and base deficit. The study by Kastrup et al. (2013) showed that in terms of volume monitoring there was increased used of TEE, systolic pressure variation, and extravascular lung water monitoring in the centers surveyed.

In terms of fluid choice, the European studies found that crystalloids were the first fluid of choice for volume replacement. In addition, while HES was still commonly used, in general, its' used had decreased. The most recent survey by Protsyk et al. (2017) showed that when colloids were used, gelatin was more often used than HES.

The studies that used GDT in cardiac surgery most often used algorithms that involved fluid administration based on SVV and CI. Several of the studies had a goal for SVV less than or equal to 10 % and fluid was administered until this goal was achieved. Cardiac index targets for most studies were between 2.0 and 2.5 l/min/m2. When fluid

boluses were administered, the volumes often ranged from 100 ml to 500 ml, given repeatedly, until targets were achieved.

With regard to fluid volumes used, there was a slight trend toward an increased amount of fluid administered in the GDT groups as compared to the usual care groups. The exception was the study by Parke et al. (2015), where the investigators trialed a conservative fluid approach and found that administering smaller volumes of fluid based on targeted goals did not result in negative outcomes. This was highlighted by research such as that conducted by Walker and Young (2015). They found that when almost four times more fluid was administered in a GDT group, it resulted in increased incidence of reintubation. Overall, however, it is difficult to make any definite conclusion about fluid amounts because the fluid data reported in the studies varied in terms of timing of administration.

This review showed that there is evidence supporting a slight trend toward decreased length of stay in the hospital as well as a discernible decrease in ICU in the GDT groups. There was no decrease in mortality between the GDT and the usual care groups in any of the studies. With regard to the use of inotropes and vasopressors, three studies showed a decrease in the duration/dose of inotropes and vasopressors, but it is difficult to make any conclusion because the data reported varied with regard to the agent used, timing of administration and question asked. In respect to number/incidence of complications, three of the eight studies resulted in a decrease in number of complications in the GDT group compared to the usual care group, but an overall trend toward decreased incidence of complications could not be concluded. Likewise, while three studies resulted in decreased time to extubation, a trend toward reduced duration of

mechanical ventilation could not be concluded. In the study by Walker and Young, (2015), the GDT group had significantly higher incidence of reintubation. This was attributed by the authors to the protocol design which lead to the delivery of almost four times more fluid in the GDT group than the usual care group. The protocol involved repeatedly administering fluid as long as there was a rise of CI >10% in response to a fluid bolus. This was also the only study which compared a prospective cohort to a matched retrospective cohort. While discussing limitations of the study, the investigators suggested that the time separation between the two groups could have allowed for changes in staffing and changes in practice that arose with the passage of time.

There are several limitations to this review. The studies are a mix of RCTs, surveys, and observational studies. Articles used in this study were not all peer reviewed. These include the surveys by Protsyk et al. (2017) and Sponholz et al. (2014), as well as the two studies by Parke et al. (2014 & 2015) and the study by Shreshta et al. (2016). However, these publications were used in this review to maximize the amount of evidence that could be obtained. There were no studies found that were conducted in North America, which is noteworthy because this review is being conducted in the United States of America, and it is important to obtain data on practices in this country. Without a good understanding of what the current practices are, it is difficult to apply any findings or make recommendations. Other limitations included the fact that the GDT interventions varied in terms of timing, methods, type of devices, and risk profile of patients, which may have had an impact on the outcomes. The cross-analysis of the studies was based on observation, without the use of any statistical method to analyze the results. There were a limited number of articles that dealt purely with the question of fluid administration, and

the two articles that studied it were both by the same investigator (Parke et al., 2014 & 2015).

In conclusion, fluid management in cardiac surgery is an important and challenging aspect of cardiac surgical practice. It is essential to administer fluid that is adequate to prevent hypovolemia and hypoperfusion but it is also important to temper this with caution and be vigilant to avoid over administration of fluid. Much more study is required to ascertain best practices for volume monitoring and fluid administration. Research in North America on what parameters practitioners use to administer fluid, what type of fluids are most often used, what devices or methods are used to monitor fluid status and their effects on outcomes, may help to increase our understanding of this complex area of practice.

Next, the recommendations and implications for advanced nursing practice will be presented.

Recommendations and Implications for Advanced Nursing Practice

Nurses have a major role in the care of the patient undergoing cardiac surgery. The ICU staff nurse receiving the patient out of the OR must be skilled in assessing and managing the patient in the immediate postoperative phase when there is high risk for complications and deterioration. The nurse juggles multiple tasks that include but are not limited to receiving a thorough hand off report from the anesthesia provider, assessment and management of hemodynamic values, hypothermia, laboratory results, mechanical ventilation, titration of vasopressors or inotropes, and alerting the provider about complications. An important skill that is part of this gamut of tasks is fluid management.

The APRN in the role of the nurse anesthetist, who is managing the intraoperative care of the patient, is often the one who makes decisions on whether to use advanced monitoring devices such as a PAC to measure CI/CO or devices that measure indices such as SVV. Often these decisions are made based on the risk profile of the patient and specific comorbidities. These advanced devices can help to monitor and manage fluid management with more precision. It is therefore recommended that a goal-directed approach be used, especially when managing high risk patients.

The APRN in the role of the NP is often the one who manages the pre- and post-operative care of the patient. This involves placing orders for fluids which may include crystalloids and/or colloids. Alternately, they may have to place a hold on fluids in favor of vasoactive and inotropic medication or blood products. A thorough understanding of fluid management concepts, perils of fluid under and over resuscitation, and best fluid choices is necessary to optimize care, prevent complications, and improve outcomes.

Based on this review, the APRN can make some practice recommendations to guide fluid management practices in cardiac surgery. Some of these recommendations

may include orders to administer fluid as small boluses when there is suspicion of hypovolemia. Suspicion of hypovolemia might be based on MAP, or if advanced monitoring is available, on the CO/CI, or SVV. A bolus of 250 ml to 500 ml of fluid should be administered. If the patient responds to the bolus with improvement of MAP and CO/CI or with a decrease in SVV, they are fluid responders and these boluses may be repeated until they stop responding to the bolus. The recommendations could also include advice to avoid administering large fluid boluses as liter bags without stopping to see if the patient is responding to the fluid. This is important not only because of the danger of fluid overload, but also because hypotension or decreased CO can often be caused by factors other than hypovolemia. These factors include decreased cardiac contractility or vasodilatation in the immediate postoperative period. These conditions may require inotropes or vasopressors instead of fluid and it is important to use these agents appropriately in the correct context. If there is any doubt as to how best to manage the patient's hemodynamic values, the staff nurse should seek clarification from the surgeon or the APRN managing care of the patient.

Advanced practice nurses in all roles, including in the role of the CNS, are in a pivotal position to provide education and mentoring of staff nurses regarding the issues of fluid management. Examples of educational topics may include the perils of hypervolemia/fluid overload or administration of fluid based on fluid responsiveness. If a GDT protocol is instituted in the APRN's work site, the APRN should educate, train and evaluate the knowledge of the nurses who will implement it.

The APRN, in collaboration with the surgeons, staff nurses, and anesthetists can lead efforts to create fluid administration policies or protocols. An example of this could

be a policy that prevents the staff nurse from administering more than two liters of fluid without first alerting the provider in the immediate postoperative period. The APRN can also lead quality and safety initiatives related to fluid management practices. This could take the form of chart audits to review fluid administration data, patient outcomes such as the duration of ventilation, complications, and length of stay. It could also involve the development of educational initiatives for staff and other providers and assessing the results of these of initiatives on fluid practices and patient outcomes.

Fluid management in cardiac surgery is a difficult and challenging subject and requires continued exploration and examination. There is much debate on how best to administer fluids, what hemodynamic indices are the most reliable guides, and what type of fluid provides the most benefit and least risk. The APRN can further this body of knowledge by initiating or participating in research initiatives. Some ideas for research could include an investigation of the current postoperative fluid management practices in cardiac surgery in the APRN's work area,

exploration of clinical decision making in prescribing and administering fluids, retrospective chart review of fluid balance and postoperative outcomes, comparing a new GDT protocol to usual care, and comparing the outcomes of crystalloid bolus infusions to colloid bolus infusions.

In all these ways, the APRN in the role of the nurse anesthetist, CNS, and the NP can make valuable contributions to the field of fluid management in cardiac surgery and improve patient outcomes.

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Appendices

Appendix A: **Critical Appraisal of Studies Featuring Postal surveys**

Table A-1: Kastrup et al., 2012. Clinical impact of the publication of S3 guidelines for intensive care in cardiac surgery patients in Germany: results from a postal survey.

Table A-2: Sponholz et al., 2014. Catecholamine and volume therapy for cardiac surgery in Germany--results from a postal survey.

Table A-3: Bignami et al., 2015. Clinical practice in perioperative monitoring in adult cardiac surgery: is there a standard of care? Results from an national survey.

Table A-4: Protsyk et al., 2017. Fluid Management in Cardiac Surgery: Results of a Survey in European Cardiac Anesthesia Departments.

Appendix B: **Observational Study On Fluid Use in Cardiac Surgery**

Appendix C: Studies on Goal Directed Therapy in Cardiac Surgery

Table C-1: Goepfert et al., 2013. Individually optimized hemodynamic therapy reduces complications and length of stay in the intensive care unit: a prospective, randomized controlled trial.

Table C-2: Thomson et al., 2014 Goal-directed therapy after cardiac surgery and the incidence of acute kidney injury.

Table C-3: Fellahi et al., 2015. Early goal-directed therapy based on endotracheal bioimpedance cardiography: a prospective, randomized controlled study in coronary surgery.

Table C-4: Parke et al., 2015. A Randomised feasibility study to assess a novel strategy to rationalise fluid in patients after cardiac surgery.

Table F-4: Complications

Table F-5: Time to Extubation / Duration of Mechanical Ventilation

Table F-6: Use of Inotropes/Vasopressors

Appendix A

Critical Appraisal of Studies Featuring Postal surveys

Table A-1

Kastrup et al., 2013. Clinical impact of the publication of S3 guidelines for intensive care in cardiac surgery patients in Germany: results from a postal survey.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title conveyed the content and premise of the study and the population, which involved a postal survey conducted to assess clinical practice in cardiac surgery patients.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract did not clearly articulate the intent of the study. Other components including the method, results and conclusion were clear and concise.
Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Did the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used?	The researchers stated the problem clearly and provided a good reason to conduct a new study. They used a quantitative approach to conduct the research, which was appropriate for the nature of the study.
Hypotheses or research questions	• Was the research hypotheses explicitly stated? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population?	The study described the results of a postal survey conducted to evaluate current clinical practices surrounding cardiac surgery. There was no hypothesis or research question.
Literature review	• Was the literature review up-to-date and based mainly on primary sources?	The study had a brief literature review that introduced available evidence, and used mainly primary sources.

	• Did the review provide a state-of-the-art synthesis of evidence on the problem?	
Conceptual/theoretical framework	• Were key concepts adequately defined? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified?	The study did not identify a conceptual framework.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? Was the study externally reviewed by an IRB/ethics review board?	There was no documentation of ethics review or participant safeguards. This may not be applicable, owing to the nature of the study.
Research design	• Was the most rigorous design used, given the study purpose? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	A survey was sent to ICU physicians from an address database by two German medical societies of cardiothoracic surgery and anesthesiology, collected by them, and then returned to the authors of the study.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the sample size based on a power analysis?	The survey targeted ICU physicians who provided care for cardiac surgery patients. No details on type of surgery or patient characteristics were provided.
Data collection and measurement	• Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described	A survey comprising 37 questions covering four major areas that included the different basic and advanced hemodynamic monitoring techniques, volume replacement strategies, and use of vasopressor or inotropic drugs in different clinical situations was sent out to ICU physicians, which were filled and returned anonymously.

Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity?	The questionnaire itself was provided in the appendix. Of the surveys sent out, 77.5% were returned completed.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used? • Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed?	Appropriate statistical methods were used to analyze the data. Tests used included Mann–Whitney U-test and the chi-square tests.
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates meta-analysis with sufficient information needed for EBP?	P value less than 0.05 was considered significant. Findings were presented with information about statistical significance. Results showed that compared to previous survey in 2005, there was increased use of systolic pressure variation (32.6% [2012] compared to 14.6% [2005]{p=0.006}), TEE (13.6% [2012] compared to 8.3% [2005]{p=0.027}), and extravascular lung water (14.1% [2012] compared to 8.1% [2005]{p=0.007}) for volume monitoring. There was increased use of crystalloids (41.9% [2012] compared to 22.4% [2005]{p=0.007}) and decreased use of HES (38.7% [2012] compared to 63.4% [2005]{p=0.006}).

		Results were presented with good use of graphs and tables.
Interpretation of the findings	• Were findings interpreted and discussed within the context of prior research? • Were the issue of clinical significance discussed? • Did the report address generalizability of the findings?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of the study in clinical practice, as well as for further research.
Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in an academic journal, and has been peer reviewed.
Summary assessment	• Despite any limitations, do the study findings appear to be valid	The study findings do appear to be valid.

Note. TEE= transesophageal echocardiography; HES=hydroxyethyl starch.

Table A-2

Sponholz et al., 2014. Catecholamine and volume therapy for cardiac surgery in Germany--results from a postal survey.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title conveyed the content and premise of the study and the population. It was a study of a postal survey on volume and catecholamine therapy in cardiac surgery.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract clearly and concisely outlined the main features of the study.
Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Did the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used?	The researchers stated the problem clearly and provided a good reason to conduct a new study. They used a quantitative approach to conduct the research, which was appropriate for the nature of the study.
Hypotheses or research questions	• Was the research hypotheses explicitly stated? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population?	No hypothesis was stated. The aim of the study was to present the results of a postal survey evaluating current intraoperative hemodynamic monitoring, catecholamine and volume therapy practices at German cardiothoracic centers.
Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem?	Literature review was limited. The problem was introduced using mainly primary sources.
Conceptual/theoretical framework	• Were key concepts adequately defined?	The study did not identify a conceptual framework.

	• Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified?	
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? Was the study externally reviewed by an IRB/ethics review board?	Ethics Committee approval was obtained. Informed consent requirement was waived because of the anonymous nature of the study.
Research design	• Was the most rigorous design used, given the study purpose? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	The research design was a postal survey. This was an appropriate design for the purpose of the study.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the sample size based on a power analysis?	The survey was sent to department heads of 81 centers performing cardiac surgery. The study provided adequate detail such as the number and type of surgery.
Data collection and measurement	• Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described	The method was described adequately. The 23 item survey that was mailed included areas pertaining to hemodynamic monitoring practices and volume replacement strategies, as well as other areas such as catecholamine usage in cardiac surgery.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity?	The survey itself was provided in the appendix. Of the questionnaires that were returned, and after excluding those from centers that also included pediatric surgery, 50 questionnaires were included in the study.

Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used? • Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed?	Categorical data depicted by frequencies and values were graded on Likert scales. Analysis included percentages with median, mean, minimum and maximum values with 95% CI.
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates meta-analysis with sufficient information needed for EBP?	Results showed that on a 1 to 5 categorical Likert scale with 1 being the most common and 5 being rare, volume monitoring most commonly utilized undulating arterial pressure curve (median 2), CVP (median 2) and TEE (median 2). Crystalloids were the fluids of first choice during and after surgery (median 2). The data was presented and summarized well with good use of graphs and tables.
Interpretation of the findings	• Were findings interpreted and discussed within the context of prior research? • Were the issue of clinical significance discussed? • Did the report address generalizability of the findings?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of the study in clinical practice, as well as for further research.
Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used.

Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in an academic journal, but has not been peer reviewed.
Summary assessment	• Despite any limitations, do the study findings appear to be valid	The study findings do appear to be valid.

Note. TEE= transesophageal echocardiography; CVP=central venous pressure; CI=confidence interval

Table A-3

Bignami et al., 2015. Clinical practice in perioperative monitoring in adult cardiac surgery: is there a standard of care? Results from an national survey.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title conveyed the content and premise of the study and the population. It was a survey of the standards of care and clinical practice in cardiac surgery.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract clearly and concisely outlined the main features of the study.
Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Did the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used?	The researchers stated the problem clearly and provided a good reason to conduct a new study. They used a quantitative approach to conduct the research, which was appropriate for the nature of the study.
Hypotheses or research questions	• Was the research hypotheses explicitly stated? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population?	No hypothesis was stated. The aim of the survey was to investigate current clinical practice, hemodynamic monitoring and the use of inotropic drugs after cardiac surgery in Italy.
Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem?	The authors conducted a brief review of literature that introduces the problem and the evidence that is available, using mainly primary sources.
Conceptual/theoretical framework	• Were key concepts adequately defined? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified?	The authors did not identify a conceptual framework.

Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? Was the study externally reviewed by an IRB/ethics review board?	The authors stated that no data regarding individual patients was collected and that research was carried out in compliance with the Helsinki Declaration. There was no mention of an IRB or ethics board review.
Research design	• Was the most rigorous design used, given the study purpose? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	The research design was a postal survey. This was an appropriate design for the purpose of the study.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the sample size based on a power analysis?	The survey was sent to 92 Centers performing adult cardiac surgery. The researchers provided details about the numbers and type of cardiac surgery.
Data collection and measurement	• Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described	The method was described adequately. A survey comprising 33 questions covering both intra- and postoperative issues were emailed to anesthesiologists in cardiothoracic ICUs, which after completion was emailed or faxed back to the researchers.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity?	The survey itself was provided in the appendix. The researchers were able to include 77.2% of the returned surveys in their analyses after excluding those that involved pediatric patients.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used?	Results were presented as percentages, which was appropriate for the nature of the study.

	• Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed?	
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates meta-analysis with sufficient information needed for EBP?	The data was presented in a narrative with percentages, as well as with graphs in the form of bar charts which are summarized well. The results showed that for monitoring volume status, CVP was used most frequently (26.7 %), followed by ABP (19.7 %) and echocardiography (5.6 %). The first choice for volume replacement were crystalloid solutions in 86.8 %, followed by artificial colloids in 11.8 % of the centers
Interpretation of the findings	• Were findings interpreted and discussed within the context of prior research? • Were the issue of clinical significance discussed? • Did the report address generalizability of the findings?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of the study in clinical practice, as well as for further research.
Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used.

Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	This study was published in an academic journal, and has been peer reviewed.
Summary assessment	• Despite any limitations, do the study findings appear to be valid	The study findings appear to be valid.

Note. CVP=central venous pressure; ABP=arterial blood pressure.

Table A-4

Protsyk et al., 2017. Fluid Management in Cardiac Surgery: Results of a Survey in European Cardiac Anesthesia Departments.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title conveyed the content and premise of the study and the population. It was a postal survey of fluid management in cardiac surgery in European cardiac anesthesia departments.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract clearly and concisely outlined the main features of the study.
Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Did the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used?	The researchers stated the problem clearly and provided a good reason to conduct a new study. They used a quantitative approach to conduct the research, which was appropriate for the nature of the study.
Hypotheses or research questions	• Was the research hypotheses explicitly stated? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population?	No hypothesis was stated. The aim of the study was to evaluate current fluid management practices in cardiac surgery in Europe.
Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem?	Literature review was limited. The problem was introduced using mainly primary sources.
Conceptual/theoretical framework	• Were key concepts adequately defined? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified?	The study did not identify a conceptual framework.

Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? Was the study externally reviewed by an IRB/ethics review board?	Ethics Committee approval was obtained.
Research design	• Was the most rigorous design used, given the study purpose? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	The research design was an online survey. This was an appropriate design for the purpose of the study.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the sample size based on a power analysis?	The survey questionnaire was sent to 379 cardiac surgery anesthesiologists in 18 European countries. The study provided adequate detail such as the number and type of surgery.
Data collection and measurement	• Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described	The method was described adequately. The 26 item online questionnaire included areas related to perioperative fluid therapy practices in cardiac surgery patients. Most of the questions evaluated the type of fluid used and reasons for selecting them.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity?	The questionnaire itself was provided in the appendix. The response rate was only 28%, with 106 returned questionnaires, of which 5 were incomplete.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used? • Were type I and Type II errors avoided or minimized?	Results given as amounts and percentages.

	• In intervention studies, was an intention-to-treat analysis performed?	
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates meta-analysis with sufficient information needed for EBP?	The investigators found that balanced crystalloids alone were most frequently used for intraoperative management (74%). Crystalloids along with synthetic colloids were used 15% of the time and other fluids; alone, or in combination were used 11% of the time. The data was presented and summarized well with good use of graphs and tables.
Interpretation of the findings	• Were findings interpreted and discussed within the context of prior research? • Were the issue of clinical significance discussed? • Did the report address generalizability of the findings?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of the study in clinical practice, but not for future research.
Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in an academic journal, but has not been peer reviewed.
Summary assessment	• Despite any limitations, do the study findings appear to be valid	The response rate for the online survey was very low, therefore the results may not be generalizable.

Appendix B

Study On Fluid Use in Cardiac Surgery

Parke, 2014. Intravenous fluid use after cardiac surgery: a multicenter, prospective, observational study.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title identified the intent of the study and the population.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract outlined all the components of the study clearly and concisely
Introduction Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Is the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used –that is, was a quantitative approach appropriate?	The researchers stated the problem clearly and provided a good reason to conduct this study. They used a quantitative method to study this problem, which is appropriate for the nature of the study.
Hypotheses or research questions	• Were research questions and/or hypotheses explicitly stated? If not, was their absence justified? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population? • Were the questions/hypotheses consistent with existing knowledge?	No hypothesis was stated. The aim of the study was to evaluate the current practice of fluid administration to patients after cardiac surgery.
Literature review	• Was the literature review up-to-date and based mainly on primary sources?	There was a brief literature review based on current and primary sources that was used to introduce the problem.

	• Did the review provide a state-of-the-art synthesis of evidence on the problem? • Did the literature review provide a strong basis for the new study?	
Conceptual/theoretical framework	• Were key concepts adequately defined conceptually? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified? • Were the questions/hypotheses consistent with the framework?	The study did not identify a conceptual framework.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? • Was the study externally reviewed by an IRB/ethics review board? • Was the study designed to minimize risks and maximize benefits to participants?	The researchers mentioned that the requirement for informed consent was waived by the ethics committees in the four countries where the study was conducted.
Research design	• Was the most rigorous design used, given the study purpose? • Were appropriate comparisons made to enhance interpretability of the findings? • Was the number of data collection points appropriate? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	This was a prospective observational study and was an appropriate design for the intent of the study.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the best possible sampling design used to enhance the sample's representativeness? Were sampling biases minimized?	The population was identified as adult patients admitted to the ICU after cardiac surgery. Details of type of surgery and basic demographic characteristics were provided.

	• Was the sample size based on a power analysis?	Two hundred and thirty five patients participated in the study.
Data collection and measurement	• Were the operational and conceptual definitions congruent? • Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described and were they good choices, given the study population and the variables being studied? • Did the report provide evidence that the data collection methods yielded data that were reliable, valid and responsive?	Demographic data was collected by trained research staff at each site using a standardized data collection form. A data dictionary with definitions and descriptions for all data points was provided to each site. The data was collected prospectively by the person administering the fluid.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity? • Were data collected in a manner that minimized bias? Were the staff who collected data appropriately trained?	Observational study. No intervention was administered.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used, given the level of measurement of the variables, number of groups being compared, and assumptions of the texts? • Was a powerful analytic method used? (e.g., did the analysis help to control for confounding variables)? • Were type I and Type II errors avoided or minimized?	Data was presented as means with SDs and medians with interquartile ranges. Kruskal–Wallis test was used to test differences between sites.

	• In intervention studies, was an intention-to-treat analysis performed? • Were problems of missing values evaluated and adequately addressed? •	
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates a meta-analysis, and with sufficient information needed for EBP?	The researchers found that postoperatively, cardiac surgical patients receive 4–5L of fluid input in the first 24 hours, of which almost 50% is from fluid boluses prescribed by nursing or junior medical staff for the indication of hypotension. The findings were summarized well and tables and figures were added.
Discussion Interpretation of the findings	• Were all major findings interpreted and discussed within the context of prior research and/or the study's conceptual framework? • Were casual inferences, if any, justified? • Was the issue of clinical significance discussed? • Were interpretations well-founded and consistent with the study's limitations? • Did the report address the issue of the generalizability of the findings?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed. The issue of generalizability was discussed. The researchers stated that because the study only observed a convenience sample in a small number of sites, the results may not be universally applicable.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of the study in clinical practice, as well as for further research. They stated their intention to conduct an RCT to assess the efficacy of a goal-directed strategy aimed at reducing fluid administration in patients after cardiac surgery.

General Issues Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study? • Was the report written in a manner that makes the findings accessible to practicing nurses?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in an academic journal, but has not been peer reviewed. The researchers are ICU specialists and nurses with research training.
Summary assessment	• Despite any limitations, do the study findings appear to be valid—do you have confidence in the *truth* value of the results? • Does the study contribute any meaningful evidence that can be used in nursing practice or that is useful to the nursing discipline?	The study findings appear to be valid despite its limitations.

Note. SD=standard deviation, RCT=randomized controlled trial.

Appendix C

Studies on Goal Directed Therapy in Cardiac Surgery

Table C-1

Goepfert et al., 2013. Individually optimized hemodynamic therapy reduces complications and length of stay in the intensive care unit: a prospective, randomized controlled trial.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title clearly identified the key variables but did not identify the population.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract outlined all the components of the study clearly and concisely.
Introduction Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Is the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used –that is, was a quantitative approach appropriate?	The researchers stated the problem clearly and provided a good reason to conduct a new study. They used a quantitative method to study this problem, which was appropriate for the nature of the study.
Hypotheses or research questions	• Were research questions and/or hypotheses explicitly stated? If not, was their absence justified? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population? • Were the questions/hypotheses consistent with existing knowledge?	The hypothesis was clearly stated and appropriately worded. It asked the question; “Does a goal-directed hemodynamic therapy, based on the combination of functional and volumetric hemodynamic parameters, improve outcomes in patients with cardiac surgery”.

Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem? • Did the literature review provide a strong basis for the new study?	The study had a brief literature review based on current and primary sources that was used to introduce the problem.
Conceptual/theoretical framework	• Were key concepts adequately defined conceptually? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified? • Were the questions/hypotheses consistent with the framework?	No conceptual framework was articulated.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? • Was the study externally reviewed by an IRB/ethics review board? • Was the study designed to minimize risks and maximize benefits to participants?	Approval was obtained from the government ethics committee prior to the study. Informed consent was obtained from all patients.
Research design	• Was the most rigorous design used, given the study purpose? • Were appropriate comparisons made to enhance interpretability of the findings? • Was the number of data collection points appropriate? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	Yes. This was a single-site, prospective, controlled, randomized, parallel-arm, open label trial. While blinding of the caregiving physicians was impossible, outcomes were assessed by independent researchers in order to reduce potential bias.
Population and sample	• Was the population identified? Was the sample described in sufficient detail?	The population was described in sufficient detail and consisted of patients undergoing CABG, AVR, or combined CABG and

	• Was the best possible sampling design used to enhance the sample's representativeness? Were sampling biases minimized? • Was the sample size based on a power analysis?	AVR surgeries under CPB. There were 50 patients in the study/GDT group and 50 in the control group. The sample size was determined by power analysis.
Data collection and measurement	• Were the operational and conceptual definitions congruent? • Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described and were they good choices, given the study population and the variables being studied? • Did the report provide evidence that the data collection methods yielded data that were reliable, valid and responsive?	The study did not provide detail on how the data was collected or measured. It was presumed that this was done through monitoring devices, medical records, and via direct observation. The primary outcome was fitness to be discharged from the ICU. Secondary outcomes included post-operative complications and the need for vasopressor support.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity? • Were data collected in a manner that minimized bias? Were the staff who collected data appropriately trained?	The intervention was described well and seemed well designed. The intervention included administering fluid until SVV< /10% or optimal global end diastolic volume index was reached unless ELWI>12 in which case fluid was stopped. If SVV<10, but CI > 2.0, then vasopressors, atropine, red blood cells or pacing was administered as appropriate.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used, given the level of measurement of the variables, number of groups being compared, and assumptions of the texts?	Detailed analysis of outcome variables was conducted. Appropriate statistical methods were used. Data was presented as mean, SD and median. Tests used: t-test, Mann Whitney rank sum test, Fisher exact test, Poisson Regression.

	• Was a powerful analytic method used? (e.g., did the analysis help to control for confounding variables)? • Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed? • Were problems of missing values evaluated and adequately addressed?	Measures to minimize type I and II errors were taken. P value less than 0.025 was considered significant. Intention-to-treat analysis was performed.
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates a meta-analysis, and with sufficient information needed for EBP?	Findings were presented with information about statistical significance. The authors found that in the GDT group there was significantly reduced intraoperative norepinephrine use (9.0 ± SD 7.6 µg/kg vs. 14.9 ± 11.1 µg/kg in the control group [p = 0.002]), incidence of complications(40 in the study group vs. 63 in the control group[*p*=0.004]), time to reach ICU discharge criteria (15 ± 6 h in the study group vs. 24 ± 29 h in the control group [*p*=0.001]) and length of ICU stay (42 ± 19 h in the study group vs. 62 ± 58 h in the control group [*p*=0.018]). There was no difference in the amount of fluid intake between the group, however more colloids were administered in the study group. The findings were summarized well and tables and figures were added. The findings were presented in a manner that facilitates future meta-analysis.

Discussion Interpretation of the findings	• Were all major findings interpreted and discussed within the context of prior research and/or the study's conceptual framework? • Were casual inferences, if any, justified? • Was the issue of clinical significance discussed? • Were interpretations well-founded and consistent with the study's limitations? • Did the report address the issue of generalizability ?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed. The researchers suggested that early implementation of therapy with appropriate goals improves outcomes. The report did not mention the issue of generalizability of findings.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	Implications for clinical practice and further research were discussed. The researchers stated that large multicenter trials are required to further prove the utility of these methods in daily clinical practice.
General Issues Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in an academic journal, and has been peer reviewed. The researchers include professors, and senior anesthesiology ICU physicians.
Summary assessment	• Despite any limitations, do the study findings appear to be valid—do you have confidence in the *truth* value of the results? • Does the study contribute any meaningful evidence that can be used in nursing practice or that is useful to the nursing discipline?	The study findings do appear to be valid despite its limitations.

Note. CABG= coronary artery bypass graft; AVR= aortic valve replacement; CPB= cardiopulmonary bypass; GDT= goal directed therapy; SVV=stroke volume variation; ELWI=extravascular lung water index; CI=cardiac index; SD=standard deviation

Table C-2
Thomson et al., 2014 Goal-directed therapy after cardiac surgery and the incidence of acute kidney injury.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title clearly identified the key variables and the population.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract outlined all the components of the study clearly and concisely
Introduction Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Is the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used –that is, was a quantitative approach appropriate?	The researchers stated the problem clearly. They stated that a significant number of patients develop AKI with subsequent increased mortality after cardiac surgery. GDT to maximize CI has improved outcomes in noncardiac surgery. The researchers intended to study the safety and outcomes of a GDT in cardiac surgery patients in their facility.
Hypotheses or research questions	• Were research questions and/or hypotheses explicitly stated? If not, was their absence justified? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population? • Were the questions/hypotheses consistent with existing knowledge?	They researchers stated their aim, which was to evaluate assess the safety of a recently introduced GDT in patients after cardiac surgery and its impact on renal dysfunction. They implied that GDT can improve outcomes in their discussion. However, they did not state a hypothesis.
Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem?	The article had a brief literature review and mainly used primary sources in the introduction of the problem.

	• Did the literature review provide a strong basis for the new study?	
Conceptual/theoretical framework	• Were key concepts adequately defined conceptually? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified? • Were the questions/hypotheses consistent with the framework?	No conceptual framework was articulated.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? • Was the study externally reviewed by an IRB/ethics review board? • Was the study designed to minimize risks and maximize benefits to participants?	This work was part of a clinical evaluation of GDT in the cardiac surgery setting with the aim to improve fluid administration on the ICU. Therefore, formal ethical approval and informed consent were not required in accordance with the UK National Health Service research authority
Research design	• Was the most rigorous design used, given the study purpose? • Were appropriate comparisons made to enhance interpretability of the findings? • Was the number of data collection points appropriate? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	This was a prospective, single-center, observational study, and was suitable for the purpose of clinical evaluation, however by virtue of its design it lacked rigor, and had limited validity.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the best possible sampling design used to enhance the sample's representativeness? Were sampling biases minimized? • Was the sample size based on a power analysis?	Adult patients undergoing on- and off-pump CABG, AVR, or combined CABG and AVR admitted to the ICU after surgery were included. Additional patient characteristics were presented in a table and provided sufficient detail. No power analysis was

		done. Patients who received the GDT were considered to be the study group. Other patients who did not receive the GDT because of the lack of persons trained to administer it, were considered to be the usual care/control group.
Data collection and measurement	• Were the operational and conceptual definitions congruent? • Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described and were they good choices, given the study population and the variables being studied? • Did the report provide evidence that the data collection methods yielded data that were reliable, valid and responsive?	The primary outcome measure was AKI, and the secondary outcomes were total fluids administered in the first 8 postoperative hours, need for renal replacement therapy, duration of hospital and ICU stay, and ICU readmission No detail about data collection was provided, other than it was collected prospectively. Data was presumed to have been obtained from specific monitoring devices that were used and from the medical records.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity? • Were data collected in a manner that minimized bias? Were the staff who collected data appropriately trained?	The intervention was described in detail and adequately in the study. There were 123 patients in the study group, of which, 20 patients were excluded from the analysis due to interruption of, or incomplete GDT. The intervention involved recording baseline SV, CO, CVP, then administering 250 ml fluid bolus. If SV increased by >/10 % the bolus would be repeated.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis?	Appropriate statistical methods were used to analyze variables. Continuous data were presented as mean, SD or median IQR. Categorical data were

	• Were appropriate statistical methods used, given the level of measurement of the variables, number of groups being compared, and assumptions of the texts? • Was a powerful analytic method used? (e.g., did the analysis help to control for confounding variables)? • Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed? • Were problems of missing values evaluated and adequately addressed? •	presented as ratios and percentages. Statistical significance was determined by using 2-tailed Student t test, Mann-Whitney U and Fisher exact tests. P value less than 0.05 was considered significant. Measures to minimize type I and II errors were not addressed. Intention-to-treat analysis was not performed.
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates a meta-analysis, and with sufficient information needed for EBP?	Findings were presented with information about statistical significance. The results showed that there was no significant difference in the volume of intravenous fluid administered in both groups during the first 8 hours in the ICU The incidence of acute kidney was significantly decreased in the GDT group (6.5% in the GDT group vs. 19.9% in the usual care group [p=0.02]). The median duration of hospital stay was lower in the GDT group (6 days in the GDT group vs. 7 days in the usual care group [p=0.02]). There was significantly reduced incidence of ICU readmissions in the GDT group compared to the usual care group (4[3.3%] in the GDT group vs. 13[9.2%] in the control group {p=0.04}).

		There was good use of tables. Data may not be useful for future meta-analyses as this was an observational study.
Discussion Interpretation of the findings	• Were all major findings interpreted and discussed within the context of prior research and/or the study's conceptual framework? • Were casual inferences, if any, justified? • Was the issue of clinical significance discussed? • Were interpretations well-founded and consistent with the study's limitations? • Did the report address the issue of the generalizability of the findings?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed. The report did not address the issue of generalizability of the findings.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers suggested that a nurse delivered GDT which maximized stroke volume in the first 8 hours after cardiac surgery improved outcomes. They suggested that these findings could be a basis for conducting an RCT in this group of patients.
General Issues Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study? • Was the report written in a manner that makes the findings accessible to practicing nurses?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in an academic journal, and has been peer reviewed. The researchers are MDs who work in cardiothoracic ICUs.

Summary assessment	• Despite any limitations, do the study findings appear to be valid—do you have confidence in the *truth* value of the results? • Does the study contribute any meaningful evidence that can be used in nursing practice or that is useful to the nursing discipline?	The study findings do appear to be valid despite its limitations.

Note. CABG= coronary artery bypass graft; AVR= aortic valve replacement; CPB= cardiopulmonary bypass; GDT= goal directed therapy; AKI=acute kidney injury; CVP=central venous pressure; SV=stroke volume; CO= cardiac output; SD=standard deviation; IQR=interquartile range

Table C-3
Fellahi et al., 2015. Early goal-directed therapy based on endotracheal bioimpedance cardiography: a prospective, randomized controlled study in coronary surgery.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title identified some variables and the population.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract outlined all the components of the study clearly and concisely
Introduction Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Is the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used –that is, was a quantitative approach appropriate?	The researchers stated the problem clearly and provided a good reason to conduct a new study. They used a quantitative method to study this problem, which was appropriate for the nature of the study.
Hypotheses or research questions	• Were research questions and/or hypotheses explicitly stated? If not, was their absence justified? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population? • Were the questions/hypotheses consistent with existing knowledge?	The hypothesis was clearly stated and appropriately worded and suggested that GDT using an endotracheal cardiac output monitor (ECOM) would improve intraoperative hemodynamics, result in less postoperative complications and earlier hospital discharge in patients undergoing CABG.
Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem?	The article had a brief literature review that was used to introduce the problem and was based on mainly primary sources.

	• Did the literature review provide a strong basis for the new study?	
Conceptual/theoretical framework	• Were key concepts adequately defined conceptually? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified? • Were the questions/hypotheses consistent with the framework?	The study did not identify a conceptual framework.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? • Was the study externally reviewed by an IRB/ethics review board? • Was the study designed to minimize risks and maximize benefits to participants?	Institutional approval was obtained from the Ethical committee prior to the study. Informed consent was obtained from all participants.
Research design	• Was the most rigorous design used, given the study purpose? • Were appropriate comparisons made to enhance interpretability of the findings? • Was the number of data collection points appropriate? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	This was a single-site, prospective, controlled, randomized, parallel-arm trial. While it was not possible to blind the investigators to patient assignment because of the use of the ECOM device, an independent investigator blinded to the patient group assignment assessed the predefined postoperative complications and endpoints for all patients.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the best possible sampling design used to enhance the sample's representativeness? Were sampling biases minimized? • Was the sample size based on a power analysis?	The population was described in sufficient detail and consisted of patients undergoing CABG, with CPB. One hundred consecutive patients were randomly allocated to the GDT/ECOM group or the control group. The sample size was based on power analysis.

Data collection and measurement	• Were the operational and conceptual definitions congruent? • Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described and were they good choices, given the study population and the variables being studied? • Did the report provide evidence that the data collection methods yielded data that were reliable, valid and responsive?	The study did not provide detail on how the data was collected or measured. It was presumed that this was done through monitoring devices, medical records, and via direct observation. The primary outcome was fitness to be discharged from the ICU. Secondary outcomes were true hospital discharge, the time to reach extubation, the length of stay in ICU, the number of major adverse cardiac events, and in-hospital mortality.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity? • Were data collected in a manner that minimized bias? Were the staff who collected data appropriately trained?	The intervention was described well and seemed well designed. It consisted of the administration of 100 ml fluid bolus for SVV> 11. After correcting SVV to <11, if the CI remained <2.4 dobutamine was initiated. Two patients in the study group had a change in surgical procedure and were excluded from analysis and 5 of the 48 ECOM group patients did not receive the intervention because of unavailability of the device. They were kept in the ECOM group for intention-to- treat analysis, but switched to the control group for analysis.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis?	Detailed analysis of outcome variables was conducted. Appropriate statistical methods were used. Mean ± SD or median used for non-normally distributed variables. Between

	• Were appropriate statistical methods used, given the level of measurement of the variables, number of groups being compared, and assumptions of the texts? • Was a powerful analytic method used? (e.g., did the analysis help to control for confounding variables)? • Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed? • Were problems of missing values evaluated and adequately addressed?	group comparisons were done using t test, Mann–Whitney test, Fisher's exact test or Chi squared test as appropriate. Intention-to-treat analysis was performed.
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates a meta-analysis, and with sufficient information needed for EBP?	P value less than <0.05 was considered significant. Hazard ratios were given with their 95 % CI. Findings were presented with information about statistical significance. The results showed that more patients in the study group received fluid loading (41) than in the control group (30), however the total intraoperative fluid amount was lower in the study group (400 ml in the study group vs. 500 ml in the control group [p=0.042]). The results also showed that there was decreased time to extubation in the GDT group by an average of 60 minutes (p=0.005). The findings were summarized well and tables and figures were added. The findings were presented in a manner that may facilitate future meta-analysis.

Discussion Interpretation of the findings	• Were all major findings interpreted and discussed within the context of prior research and/or the study's conceptual framework? • Were casual inferences, if any, justified? • Was the issue of clinical significance discussed? • Were interpretations well-founded and consistent with the study's limitations? • Did the report address the issue of the generalizability of the findings?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of the study in clinical practice, as well as for further research. They recommended large scale studies using ECOM in high-risk patients undergoing cardiac and noncardiac surgery to further determine its utility in improving outcomes.
General Issues Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study? • Was the report written in a manner that makes the findings accessible to practicing nurses?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was used.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in an academic journal, and has been peer reviewed. The researchers are MDs in anesthesia, critical care and cardiothoracic departments.
Summary assessment	• Despite any limitations, do the study findings appear to be valid—do you have confidence in the *truth* value of the results?	The study findings appear to be valid despite its limitations.

	• Does the study contribute any meaningful evidence that can be used in nursing practice or that is useful to the nursing discipline?	

Note. CABG= coronary artery bypass graft; CPB= cardiopulmonary bypass; GDT= goal directed therapy; SVV=stroke volume variation; CI= cardiac index; SD=standard deviation.

Table C-4
Parke et al., 2015. A Randomised feasibility study to assess a novel strategy to rationalise fluid in patients after cardiac surgery.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title did not clearly indicate the key variables or intervention, but included the study population.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract outlined all the components of the study clearly and concisely.
Introduction Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Is the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used –that is, was a quantitative approach appropriate?	The problem was stated clearly and provided a good argument for a new study. A quantitative approach was used which is appropriate for the nature of the study.
Hypotheses or research questions	• Were research questions and/or hypotheses explicitly stated? If not, was their absence justified? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population? • Were the questions/hypotheses consistent with existing knowledge?	The hypothesis was clearly stated and specified the key variables involved in the study. It questioned whether a stroke volume variation-based algorithm could reduce the amount of IVF fluid administered to patients, after cardiac surgery, and if a reduced fluid strategy was safe and practical?
Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem?	The literature review was a brief introduction to the problem, and used mainly primary sources. It did not provide a state-of-the-art synthesis of evidence of the problem.

	• Did the literature review provide a strong basis for the new study?	
Conceptual/theoretical framework	• Were key concepts adequately defined conceptually? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified? • Were the questions/hypotheses consistent with the framework?	No conceptual framework was articulated.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? • Was the study externally reviewed by an IRB/ethics review board? • Was the study designed to minimize risks and maximize benefits to participants?	The study was approved by the Regional Ethics Committee. Written informed consent was obtained by research staff from all study participants, before enrolment.
Research design	• Was the most rigorous design used, given the study purpose? • Were appropriate comparisons made to enhance interpretability of the findings? • Was the number of data collection points appropriate? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	A prospectively randomized study design was used. Blinding was not feasible. It was a single center study, using specific hemodynamic instruments, therefore, generalizability was limited.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the best possible sampling design used to enhance the sample's representativeness? Were sampling biases minimized? • Was the sample size based on a power analysis?	Population was identified and described in detail. It consisted of patients 16 years or older undergoing cardiac surgery, with CPB, where 74 were allocated to usual care and 70 to intervention group. The sample size was calculated based on power analysis.

Data collection and measurement	• Were the operational and conceptual definitions congruent? • Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described and were they good choices, given the study population and the variables being studied? • Did the report provide evidence that the data collection methods yielded data that were reliable, valid and responsive?	The variables were measured by ICU and research nurses at the bedside, as well as downloaded from hemodynamic monitors. Data collection method was adequately described. The main outcome was a comparison of the amount of fluid used between the two groups. The secondary outcome was the incidence of AKI.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity? • Were data collected in a manner that minimized bias? Were the staff who collected data appropriately trained?	The intervention was described adequately. It consisted of fluid bolus (250- 500 ml) administered for CI < 2.5 and SVV>13. All patients who were randomized to the study group received the intervention, and none were lost to follow up. Research nurses were involved in data collection.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used, given the level of measurement of the variables, number of groups being compared, and assumptions of the texts? • Was a powerful analytic method used? (e.g., did the analysis help to control for confounding variables)? • Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed?	All the aspects determined by the hypothesis were tested. Continuous data was tested for normality using histograms. Between-group comparisons for continuous data was performed by means of Student's t test or the Mann-Whitney U test and categorical data with the use of the $\chi 2$ test. P value <0.05 was considered statistically significance. Data were analyzed according to the intention-to-treat principle.

Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates a meta-analysis, and with sufficient information needed for EBP?	Data was presented with information about statistical significance, however there was no data on effect size or precision estimates. The results showed that the GDT group received significantly less fluid bolus (median [IQR] 1620ml [500–3410]) compared to the usual care group (2520 ml [1440–5250ml] {p<0.001}) as well as significantly lower overall IVF volume (2050ml [910–4280 ml]) compared to the usual care group (2980ml [2070–6580 ml] {*p*=0.001}) from ICU admission until extubation. The total amount of fluids administered from admission to 24 hours were also significantly less in the GDT group (4350 ml [2790–6160 ml]) than in the usual care group (median 5080 ml [3930–7320 ml] {*p*=0.02}). There was no significant difference in any outcomes between the two groups. Findings were summarized and presented well with the use of tables. Findings may facilitate future meta-analysis.
Discussion Interpretation of the findings	• Were all major findings interpreted and discussed within the context of prior research and/or the study's conceptual framework? • Were casual inferences, if any, justified? • Was the issue of clinical significance discussed? • Were interpretations well-founded and consistent with the study's limitations?	The findings were discussed within context of previous research. Clinical significance and generalizability were discussed. The researchers suggested that by using advanced hemodynamic monitoring strategies, fluid administration volumes can

	• Did the report address the issue of the generalizability of the findings?	be individualized to patient need, and overall volumes of fluid can be reduced. The researchers suggested that the results are generalizable as all patients presenting for cardiac surgery were invited for enrollment, with small percentage of declines, and no loss to follow up.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of this feasibility study in clinical practice and for further research. They recommended large, appropriately powered studies that utilize a conservative fluid management strategy in cardiac surgery patients.
General Issues Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was used.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	The study has been published in a peer reviewed journal. The researchers have background in research and in cardiothoracic intensive care.
Summary assessment	• Despite any limitations, do the study findings appear to be valid • Does the study contribute any meaningful evidence that can be used in nursing practice or that is useful to the nursing discipline?	The study findings do appear to be valid despite its limitations.

Note. CPB= cardiopulmonary bypass; GDT= goal directed therapy; SVV=stroke volume variation; CI= cardiac index; IVF=intravenous fluid.

Table C-5
Walker & Young, 2015. Fluid administration, vasopressor use and patient outcomes in a group of high-risk cardiac surgical patients receiving postoperative goal-directed haemodynamic therapy: a pilot study.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title clearly identified the key variables, the intervention, and the study population.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract outlined all the components of the study.
Introduction Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Is the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used –that is, was a quantitative approach appropriate?	The problem was stated clearly and it argued the necessity for further study. A quantitative approach was the most appropriate method to study this problem
Hypotheses or research questions	• Were research questions and/or hypotheses explicitly stated? If not, was their absence justified? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population? • Were the questions/hypotheses consistent with existing knowledge?	The hypothesis as well as the key variables were stated clearly. The researchers hypothesized that a GDT protocol could reduce vasopressor duration, and optimize fluid administration in high risk cardiac surgery patients.
Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem? • Did the literature review provide a strong basis for the new study?	The literature review was limited, but was based mainly on primary sources.

Conceptual/theoretical framework	• Were key concepts adequately defined conceptually? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified? • Were the questions/hypotheses consistent with the framework?	No conceptual framework was articulated.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? • Was the study externally reviewed by an IRB/ethics review board? • Was the study designed to minimize risks and maximize benefits to participants?	The research was approved by the Health and Disability Ethics Committee of New Zealand. Written informed consent was obtained from eligible patients.
Research design	• Was the most rigorous design used, given the study purpose? • Were appropriate comparisons made to enhance interpretability of the findings? • Was the number of data collection points appropriate? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	This was an interventional pilot study, that was a sub-study of a larger research project. It compared a prospective cohort with a similar retrospective cohort, and therefore is not as rigorous as an RCT would have been. It was a single-center trial therefore results have limited external validity. In addition, the prospective/retrospective comparison design allowed for possible staffing and practice differences between the two groups.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the best possible sampling design used to enhance the sample's representativeness? Were sampling biases minimized? • Was the sample size based on a power analysis?	The population and sample were identified and described in detail. The population comprised high risk cardiac surgery patients older than 18 years of age. The study group included 40 patients in the prospective cohort who received the intervention. It was compared to a matched group that had

		surgery a year earlier and which received "usual care". This group was considered to be the control group. A power analysis was not performed.
Data collection and measurement	• Were the operational and conceptual definitions congruent? • Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described and were they good choices, given the study population and the variables being studied? • Did the report provide evidence that the data collection methods yielded data that were reliable, valid and responsive?	The primary outcome was duration of post-operative noradrenaline infusion. The secondary outcomes included 12 hour amount of IVF, duration of mechanical ventilation, rate of reintubation, 24 hour dose of noradrenaline, peak S. creatinine and the duration of ICU stay. Data from the prospective cohort was collected by a research nurse from the OR and the ICU. Data from the retrospective cohort were recorded by the research physician from historical patient notes. These methods were appropriate for this research design.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity? • Were data collected in a manner that minimized bias? Were the staff who collected data appropriately trained?	The intervention was described adequately. It consisted of administration of fluid bolus of 5 ml/kg if CI <2.0, SVo2<60 %, MAP <65. If volume unresponsive, vasopressors, inotropes or blood transfusion would be considered. All the patients in the intervention group received the intervention. However the data recorded for some variables were incomplete in the records, and therefore the cohort size for those variables was decreased.

Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used, given the level of measurement of the variables, number of groups being compared, and assumptions of the texts? • Was a powerful analytic method used? (e.g., did the analysis help to control for confounding variables)? • Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed? • Were problems of missing values evaluated and adequately addressed? •	Analyses was undertaken to address each research question. Appropriate statistical methods were used. Nonparametric Mann–Whitney U test was used to compare sample medians. Normally distributed data were compared by analysis of variance. Categorical data were compared using the chi-squared test. Small-sample categorical data were compared with Fisher's exact test. A two-sided p value less than 0.05 was considered statistically significant. There was no discussion of methods to minimize type I and II errors. Intention-to-treat analysis was not performed.
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates a meta-analysis, and with sufficient information needed for EBP?	Findings were presented with information about statistical significance, however there was no data on effect size. The results showed that the GDT group received significantly (p <0.001) more fluid (4687±2284) in the first 12 hours postoperatively than the usual care cohort (1189±1344 ml). It also had a significantly (p=0.049) higher rate of reintubation (4 in 37 [10.8%]) vs. the usual care group (0 in 40 [0%]) There was good use of tables. Data may not be useful for meta-analyses because of the retrospective research design.

Discussion Interpretation of the findings	• Were all major findings interpreted and discussed within the context of prior research and/or the study's conceptual framework? • Were casual inferences, if any, justified? • Was the issue of clinical significance discussed? • Were interpretations well-founded and consistent with the study's limitations? • Did the report address the issue of the generalizability of the findings?	The findings were discussed within context of previous research. Clinical significance and generalizability were discussed. The researchers suggested that the results may not be generalizable to all cardiac surgical patients because of the small study size, use of a specific protocol, and the high-risk population that was targeted.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The study findings implied that the intervention increased complications, and therefore it resulted in cessation of the intervention. No further research implications were discussed.
General Issues Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in a peer reviewed academic journal. Both the researchers are ICU intensivists.
Summary assessment	• Despite any limitations, do the study findings appear to be valid—do you have confidence in the *truth* value of the results? • Does the study contribute any meaningful evidence that can be used in nursing practice or that is useful to the nursing discipline?	The study findings do appear to be valid despite its limitations.

Note. RCT= randomized controlled trial; GDT= goal directed therapy; CI= cardiac index; IVF=intravenous fluid; MAP=mean arterial pressure; Svo2= mixed venous oxygen saturation

Table C-6

Shrestha et al., 2015. A prospective randomized study of goal oriented hemodynamic therapy in cardiac surgical patients.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title clearly identified the intervention and the study population, but not the dependent variables/outcomes.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract outlined all the components of the study clearly and concisely
Introduction Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Is the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used –that is, was a quantitative approach appropriate?	The researchers did not made a case for why a new study was required. They briefly discussed the research in this area and then stated the aim of the study, which was to evaluate early post- operative outcomes in cardiac surgery patients after the adoption of an early goal directed hemodynamic therapy. In studying this area, a quantitative approach was the most appropriate method.
Hypotheses or research questions	• Were research questions and/or hypotheses explicitly stated? If not, was their absence justified? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population? • Were the questions/hypotheses consistent with existing knowledge?	The researchers did not state a hypothesis. The aim of the study was to evaluate early post- operative outcomes in cardiac surgery patients after the adoption of an early goal directed hemodynamic therapy.
Literature review	• Was the literature review up-to-date and based mainly on primary sources?	The study had a brief literature review, and mainly used primary sources. It provided a

	• Did the review provide a state-of-the-art synthesis of evidence on the problem? • Did the literature review provide a strong basis for the new study?	good summary of the current evidence that has emerged in this area of science.
Conceptual/theoretical framework	• Were key concepts adequately defined conceptually? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified? • Were the questions/hypotheses consistent with the framework?	No conceptual framework was articulated.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? • Was the study externally reviewed by an IRB/ethics review board? • Was the study designed to minimize risks and maximize benefits to participants?	The study was approved by IRB/ethics board. Informed consent was obtained prior to the study.
Research design	• Was the most rigorous design used, given the study purpose? • Were appropriate comparisons made to enhance interpretability of the findings? • Was the number of data collection points appropriate? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	The study design was a prospective RCT. Blinding was not possible because the intervention being used required specific devices. External validity was limited because it was a single center study.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the best possible sampling design used to enhance the sample's representativeness? Were sampling biases minimized?	The population was identified details are provided. It consisted of patients between the ages of 15 and 75 years, undergoing open cardiac surgery, including CABG and valve surgeries. There were 100 patients

	• Was the sample size based on a power analysis?	enrolled in the study with 50 in the experimental group and 50 in the control group. The sample size was based on power analysis.
Data collection and measurement	• Were the operational and conceptual definitions congruent? • Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described and were they good choices, given the study population and the variables being studied? • Did the report provide evidence that the data collection methods yielded data that were reliable, valid and responsive?	Details about data collection were not provided. Data was presumed to have been obtained from specific monitoring devices that were used and from medical records. Outcome indicators included mortality, length of ICU and hospital stay, use of ventilator, use of inotropes, organ dysfunctions, need for hemodialysis and wound complication.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity? • Were data collected in a manner that minimized bias? Were the staff who collected data appropriately trained?	Intervention was described in detail and adequately in the study. It consisted of fluid bolus 100 ml administered if CI < 2.2 l/min/m2, CVP < 6 mmHg or SVV >10%. The study did not explicitly state if the study group participants all received the interventions.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used, given the level of measurement of the variables, number of groups being compared, and assumptions of the texts? • Was a powerful analytic method used? (e.g., did the analysis help to control for confounding variables)?	Appropriate statistical methods were used to analyze data. Student unpaired t test, Chi square test, and one way ANOVA were used as appropriate. P value less than 0.05 were considered significant.

	• Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed? • Were problems of missing values evaluated and adequately addressed?	There was no discussion of methods to minimize type I and II errors. Intention-to-treat analysis was not performed.
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates a meta-analysis, and with sufficient information needed for EBP?	Findings were presented with information about statistical significance and precision of estimates with CI of 95 %. There was a significant (p=0.041) reduction in ventilator time in the study group ([M] 10.48 ± [S.D] 7.640 hours) compared to the control group (16.429 ± 11.801hours). The duration of inotrope usage was also significantly (p=0.032) lower in the study group (23.2 ± 17.870 hours) than in the control group (39.12 ± 18.615 hours). There was good use of tables and the data may be useful for future meta-analyses.
Discussion Interpretation of the findings	• Were all major findings interpreted and discussed within the context of prior research and/or the study's conceptual framework? • Were casual inferences, if any, justified? • Was the issue of clinical significance discussed? • Were interpretations well-founded and consistent with the study's limitations? • Did the report address the issue of the generalizability of the findings?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed. The study was limited because it was single centered, and blinding was not possible. It also did not stratify the patients who were at higher risk, and included different types of cardiac surgeries, all of which could reduce validity and generalizability.

Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of the study in clinical practice, but not those for further research. They suggested the implementation of perioperative goal-directed strategies as part of quality improvement programs.
General Issues Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study? • Was the report written in a manner that makes the findings accessible to practicing nurses?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in an academic journal, however this article has not been peer reviewed. The researchers are cardiothoracic and vascular surgery physicians.
Summary assessment	• Despite any limitations, do the study findings appear to be valid—do you have confidence in the *truth* value of the results? • Does the study contribute any meaningful evidence that can be used in nursing practice or that is useful to the nursing discipline?	The study findings do appear to be valid despite its limitations.

Note. RCT= randomized controlled trial; CABG= coronary artery bypass graft; CI= cardiac index; CVP=central venous pressure; SVV=stroke volume variation; SD=standard deviation.

Table C-7

Osawa et al., 2016. Effect of Perioperative Goal-Directed Hemodynamic Resuscitation Therapy on Outcomes Following Cardiac Surgery: A Randomized Clinical Trial and Systematic Review.

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title clearly identified the intervention and the study population.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract outlined all the components of the study clearly and concisely.
Introduction Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Is the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used –that is, was a quantitative approach appropriate?	The researchers briefly but clearly states the problem and the need for the new study. They used a quantitative method to study this problem, which was appropriate for the nature of the study.
Hypotheses or research questions	• Were research questions and/or hypotheses explicitly stated? If not, was their absence justified? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population? • Were the questions/hypotheses consistent with existing knowledge?	The researchers did not state a hypothesis. They stated that the aim of the study was to investigate whether a GDT protocol was superior to standard care in high-risk patients undergoing cardiac surgery.
Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem?	The study had a brief review of literature that was used to introduce the problem and the intervention. It was based mainly on primary sources. It did not provide an up-to-date synthesis of evidence on the problem.

	• Did the literature review provide a strong basis for the new study?	
Conceptual/theoretical framework	• Were key concepts adequately defined conceptually? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified? • Were the questions/hypotheses consistent with the framework?	No conceptual framework was articulated.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? • Was the study externally reviewed by an IRB/ethics review board? • Was the study designed to minimize risks and maximize benefits to participants?	Study protocol was approved by the Heart Institute Ethics Committee in accordance with the Helsinki Declaration of the World Medical Association and informed consent was obtained prior to study enrollment.
Research design	• Was the most rigorous design used, given the study purpose? • Were appropriate comparisons made to enhance interpretability of the findings? • Was the number of data collection points appropriate? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	A prospective RCT design was used. Eligible patients were randomly assigned to receive either GDT or usual care. While blinding not feasible for those administering the intervention, outcome assessors were blinded to study-group assignments. This was a single-center trial conducted in a cardiology reference hospital, therefore the results had limited external validity.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the best possible sampling design used to enhance the sample's representativeness? Were sampling biases minimized? • Was the sample size based on a power analysis?	The population sample was identified and described in detail. The study had 126 high risk patients undergoing CABG and/or valvular surgery, over the age of 18, with 62 assigned to the GDT group and 64 to the

		usual care group. Sample size was based on power analysis.
Data collection and measurement	• Were the operational and conceptual definitions congruent? • Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described and were they good choices, given the study population and the variables being studied? • Did the report provide evidence that the data collection methods yielded data that were reliable, valid and responsive?	Independent variables were measured using appropriate hemodynamic measurement instruments. Dependent variables were presumed to have been obtained from medical records. The primary outcome was the 30-day mortality and major post-op complications. The secondary outcomes included 30-day incidence of delirium, venous thromboembolism, seizure, and AKI.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity? • Were data collected in a manner that minimized bias? Were the staff who collected data appropriately trained?	Intervention was described in detail and adequately in the study. It involved administration of 250 ml fluid bolus for CI <3.0 and SVI < 35 mL/m2. If CI remained <3.0, but the SVI was >35 mL/m2 then dobutamine infusion was administered. Most of the participants allotted to the study group received the intervention, with only 1 out of the 62 being managed according to standard care because of an equipment issue. Data was collected by three blinded assessors who were experienced in the cardiac surgery ICU.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis?	Primary and the secondary outcomes were all analyzed. Appropriate statistical methods were used. Continuous variables were reported as mean SD or medians with IQR

	• Were appropriate statistical methods used, given the level of measurement of the variables, number of groups being compared, and assumptions of the texts? • Was a powerful analytic method used? (e.g., did the analysis help to control for confounding variables)? • Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed? • Were problems of missing values evaluated and adequately addressed? •	and categorical variables as proportions. Continuous variables were compared using Student t test or Mann-Whitney U test. Categorical variables used Pearson chi-square or Fisher exact test. A two-sided p value less than 0.05 was considered statistically significant. All analyses were conducted according to the intention-to-treat principle without assumptions being made for missing or unavailable data.
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates a meta-analysis, and with sufficient information needed for EBP?	The results showed that the GDT group had significantly (p=0.002) lower rate of infection (12.9%) compared to the usual care group (29.7%), and significantly (p=0.003) reduced incidence of low cardiac output syndrome (6.5% in the GDT group vs 26.6% in the usual care group). The GDT group also had significantly (p = 0.003) lower cumulative dosage of inotrope 12 in GDT group vs 19 mg/kg in the usual care group), and a significantly (p = 0.049) shorter ICU (3 days in the GDT group vs. 5 days in the usual care group) and hospital length of stay ([9 days in the GDT group vs 12 days in the usual care group] p = 0.049). The findings were presented with information about statistical significance,

		however there was no data on effect size. There was good use of tables. The data will allow for future meta-analyses.
Discussion Interpretation of the findings	• Were all major findings interpreted and discussed within the context of prior research and/or the study's conceptual framework? • Were casual inferences, if any, justified? • Was the issue of clinical significance discussed? • Were interpretations well-founded and consistent with the study's limitations? • Did the report address the issue of the generalizability of the findings?	Findings were discussed within context of previous research. Clinical significance and generalizability were discussed. The researchers suggested that a GDT started early in the OR and continued into the immediate postoperative period may reduce complications in high risk cardiac surgery. They acknowledged that the results may have limited external validity by virtue of being a single-center trial, conducted in a cardiology reference hospital.
Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of the study for further research. They recommended future studies that use GDT beyond the first few immediate post-operative hours. This trial only continued GDT up to 8 hours post-operatively. They also recommended multimodal monitoring techniques that can detect early organ dysfunction in these future trials.
General Issues Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was used.

	• Was the report written in a manner that makes the findings accessible to practicing nurses?	
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	Study was published in a peer reviewed academic journal. Many of the researchers have advanced medical degrees and PhDs and are affiliated with research university hospitals in Brazil, UK, Germany and Italy.
Summary assessment	• Despite any limitations, do the study findings appear to be valid—do you have confidence in the *truth* value of the results? • Does the study contribute any meaningful evidence that can be used in nursing practice or that is useful to the nursing discipline?	The study findings do appear to be valid despite its limitations.

Note. RCT= randomized controlled trial; CABG= coronary artery bypass graft; GDT= goal directed therapy; AKI=acute kidney injury; IQR=interquartile range; SD=standard deviation.

Table C-8

Kapoor et al., 2016. Perioperative utility of goal-directed therapy in high-risk cardiac patients undergoing coronary artery bypass grafting:"A clinical outcome and biomarker-based study".

Aspect of the Report	Critiquing Questions	Detailed Critiquing Guidelines
Title	• Is the title a good one, succinctly suggesting key variables and the study population?	The title clearly identified the intervention and the study population.
Abstract	• Did the abstract clearly and concisely summarize the main features of the report (problem, methods, results, conclusions)?	The abstract outlined all the components of the study clearly and concisely.
Introduction Statement of the problem	• Was the problem stated unambiguously, and was it easy to identify? • Is the problem statement build a persuasive argument for the new study? • Was there a good match between the research problem and the methods used –that is, was a quantitative approach appropriate?	The researchers briefly described the problem and built a reasonable argument for the new study. They used a quantitative method to study this problem, which was appropriate for the nature of the study.
Hypotheses or research questions	• Were research questions and/or hypotheses explicitly stated? If not, was their absence justified? • Were questions and hypotheses appropriately worded, with clear specification of key variables and the study population? • Were the questions/hypotheses consistent with existing knowledge?	No hypothesis was stated. The aim of the study was to evaluate the utility of a GDT in high risk cardiac surgery patients.
Literature review	• Was the literature review up-to-date and based mainly on primary sources? • Did the review provide a state-of-the-art synthesis of evidence on the problem? • Did the literature review provide a strong basis for the new study?	The study had a brief review of literature that was used to introduce the problem and the intervention. It did not provide an up-to-date synthesis of evidence on the problem.

Conceptual/theoretical framework	• Were key concepts adequately defined conceptually? • Was a conceptual/theoretical framework articulated—and, if so, was it appropriate? If not, is the absence of a framework justified? • Were the questions/hypotheses consistent with the framework?	No conceptual framework was articulated.
Method Protection of human rights	• Were appropriate procedures used to safe-guard the rights of study participants? • Was the study externally reviewed by an IRB/ethics review board? • Was the study designed to minimize risks and maximize benefits to participants?	Ethical clearance form IRB and informed consent from the patients was obtained prior to the study.
Research design	• Was the most rigorous design used, given the study purpose? • Were appropriate comparisons made to enhance interpretability of the findings? • Was the number of data collection points appropriate? • Did the design minimize biases and threats to the internal, construct, and external validity of the study (e.g., was blinding used, was attrition minimized)?	The study used a prospective RCT design. Blinding was not possible because of the nature of the intervention. The researchers did not state any specific precautions taken to reduce bias or threats to validity.
Population and sample	• Was the population identified? Was the sample described in sufficient detail? • Was the best possible sampling design used to enhance the sample's representativeness? Were sampling biases minimized? • Was the sample size based on a power analysis?	The population and sample were identified and basic characteristics were provided in a table. The sample consisted of 130 high risk patients undergoing CABG on CPB.
Data collection and measurement	• Were the operational and conceptual definitions congruent?	The study did not provide information regarding how the data was collected or measured. The study mentioned that some

	• Were key variables measured using an appropriate method (e.g., interviews, observations, and so on)? • Were specific instruments adequately described and were they good choices, given the study population and the variables being studied? • Did the report provide evidence that the data collection methods yielded data that were reliable, valid and responsive?	data was collected from medical records and by contacting patients via telephone after discharge. Presumably much of the data was obtained through monitoring devices, and possibly via direct observation. The primary outcome was fitness to be discharged from the ICU. Secondary outcomes included post-operative complications and the need for vasopressor support.
Procedures	• If there was an intervention, was it adequately described, and was it rigorously developed and implemented? Did most participants allocated to the intervention group actually receive it? Was there evidence of intervention fidelity? • Were data collected in a manner that minimized bias? Were the staff who collected data appropriately trained?	The intervention was described well and appears well designed. It involved administering a fluid bolus of 100 ml if CI < 2.2 l/min/m2, CVP < 6 mmHg or SVV >10%. Five patients in the study group were excluded from the study because of certain complications that they developed.
Data Analysis	• Were analyses undertaken to address each research question or test each hypothesis? • Were appropriate statistical methods used, given the level of measurement of the variables, number of groups being compared, and assumptions of the texts? • Was a powerful analytic method used? (e.g., did the analysis help to control for confounding variables)? • Were type I and Type II errors avoided or minimized? • In intervention studies, was an intention-to-treat analysis performed?	Detailed analysis of outcome variables was conducted. Appropriate statistical methods were used. Data was presented as number, percentage, mean, SD, median, IQR. Tests used included t test, Mann Whitney U test, Wilcoxon signed-rank test, Pearson's Chi- square test and Fisher's exact test. P value less than 0.05 was considered significant.

	• Were problems of missing values evaluated and adequately addressed?	There was no discussion on measures to minimize type I and II errors. Intention-to-treat analysis was not performed.
Findings	• Was information about statistical significance presented? Was information about effect size and precision of estimates (confidence intervals) presented? • Were the findings adequately summarized, with good use of tables and figures? • Were findings reported in a manner that facilitates a meta-analysis, and with sufficient information needed for EBP?	Findings were presented with information about statistical significance. The results showed that the GDT arm had a significantly ($p < 0.001$) shorter length of hospital stay (7.42 ± 1.48 days) compared to the conventional arm (5.61 ± 1.11 days). The GDT group also had a significantly ($p < 0.001$) shorter length of ICU stay (4.2 ± 0.82) compared to the conventional arm (2.53 ± 0.56 days), and significantly ($p = 0.005$) lower duration of inotrope usage (3.24 ± 0.73 hours) compared to the conventional arm (2.89 ± 0.68 hours). There was good use of tables. The findings were presented in a manner that may facilitate future meta-analysis.
Discussion Interpretation of the findings	• Were all major findings interpreted and discussed within the context of prior research and/or the study's conceptual framework? • Were casual inferences, if any, justified? • Was the issue of clinical significance discussed? • Were interpretations well-founded and consistent with the study's limitations? • Did the report address the issue of the generalizability of the findings?	The findings were discussed within context of previous research, and the clinical significance of the study was discussed. The researchers suggested that perioperative GDT can shorten the duration of ventilator dependency, ICU and hospital stay in high-risk cardiac surgical patients. The report did not address the issue of generalizability of the findings.

Implications/ recommendations	• Did the researchers discuss the implications of the study for clinical practice or further research—and were those implications reasonable and complete?	The researchers discussed the implications of the study in clinical practice, as well as for further research. They recommended future studies that include the use of volume status markers such as extravascular lung volume.
General Issues Presentation	• Was the report well-written, organized, and sufficiently detailed for critical analysis? • In intervention studies, was a CONSORT flowchart provided to show the flow of participants in the study? • Was the report written in a manner that makes the findings accessible to practicing nurses?	The report was written and organized well and allowed for critical analysis. CONSORT flow chart was not used, however the study had a flow chart that combined patient allocation with the intervention and the usual care details.
Researcher credibility	• Do the researchers' clinical, substantive, or methodologic qualifications and experience enhance confidence in the findings and their interpretation?	The study was published in an academic journal, and has been peer reviewed. The researchers are physicians in cardiac anesthesia and critical care areas.
Summary assessment	• Despite any limitations, do the study findings appear to be valid—do you have confidence in the *truth* value of the results? • Does the study contribute any meaningful evidence that can be used in nursing practice or that is useful to the nursing discipline?	The study findings do appear to be valid despite its limitations.

Note. RCT= randomized controlled trial; CABG= coronary artery bypass graft; CPB= cardiopulmonary bypass; GDT= goal directed therapy; SVV=stroke volume variation; CI=cardiac index; IQR=interquartile range; SD=standard deviation.

Appendix D

Cross Analysis of Studies that Surveyed Practices in Cardiac Surgery

Table D-1
Basic Information and Goals of the Surveys

First author	Year	Country	Design	Goal	Number of questionnaires or participants
Kastrup	2012	Germany	Postal Survey	Evaluate hemodynamic monitoring, volume replacement, vasopressor and inotropic usage in clinical practice.	62
Sponholz	2014	Germany	Postal survey	Evaluate hemodynamic monitoring, fluid monitoring and volume therapy.	50
Bignami	2015	Italy	Fax and email	Evaluate hemodynamic monitoring, fluid monitoring and volume therapy.	81
Protsyk	2017	18 European countries	Online survey	Evaluate fluid therapy choices.	106

Table D-2.
Survey Results on Volume Monitoring Methods Used and Fluids Used for Volume Replacement

First author	Volume monitoring methods used	Fluid types
Kastrup	Increased use of Systolic pressure variation, TEE, and extravascular lung water in 2012 compared to 2005.	Reduction in the use of HES with 38.7% in 2012 compared to 63.4% in 2005, and a corresponding significant increase in the use of crystalloids ; 41.9% in 2012 compared to 22.4% in 2005.
Sponholz	Undulating arterial pressure curve, CVP and TEE used most.	Crystalloids were the fluids of first choice during and after surgery (median 2), followed by HES (median 3).
Bignami	BP, CVP, echocardiography used most.	The first choice for volume replacement were crystalloid solutions in 86.8 %, followed by artificial colloids in 11.8 % of the centers. The second choice was artificial colloids in 66.7 % of centers, HES being the most frequently used.
Protsyk	Not obtained.	Balanced crystalloids most frequently used for intraoperative management than were other solutions (74%) followed by a combination of crystalloids and synthetic colloids (15%). When colloids were used, gelatin was preferred to HES or albumin (60% vs. 24 % vs. 16%) respectively.

Note. CVP=central venous pressure; TEE= transesophageal echocardiography; HES= hydroxyethyl starch; BP=blood pressure.

Appendix E

Goal Directed Therapy in Cardiac Surgery

Table E-1
Goal directed therapy: Basic information

First Author, Year	Country	Study Type	Type of surgery	Number of participants	Timing
Goepfert, 2013	Germany	Prospective RCT	CABG and/or valve surgery	Control group 50 Study group 50	Intraoperative
Fellahi, 2015	France	Prospective RCT	Elective CABG with CPB	Control group-44 Study group-48	Intraoperative
Thomson, 2014	United Kingdom	Prospective observational study	CABG and/or aortic valve surgery; both on and off pump.	Standard therapy- 141 GDT-123	Postoperative
Parke, 2015	Australia/ New Zealand	Prospective randomized feasibility study	Elective cardiac surgery with CPB	Usual Care -74 Study group-70	Postoperative
Walker, 2015	New Zealand	Prospective interventional study compared with retrospective cohort	High risk cardiac surgery	Usual Care- 40 Study group-40	Postoperative
Shrestha, 2015	Nepal	Prospective RCT	Cardiac surgery	Usual Care-15 Study group-20	Intraoperative and Postoperative
Osawa, 2016	Brazil	Prospective RCT	High risk cardiac surgery	Usual care-64 Study group-62	Intraoperative and postoperative
Kapoor, 2017	India	Prospective RCT	CABG on CPB	Control 60 GDT 60	Intraoperative and postoperative

Note. RCT= randomized controlled trial; CABG= coronary artery bypass graft; CPB= cardiopulmonary bypass; GDT= goal directed therapy.

Table E-2
Hemodynamic monitoring and therapy goals

First author	Goals for therapy and intervention in GDT group	Usual Care
Goepfert	Administer fluid until SVV< /10% is reached unless ELWI >12 in which case fluid is stopped. If SVV<10, but CI > 2.0, then administer vasopressors, atropine, RBC, or pace as appropriate.	Administer fluid for CVP< 8. If CVP> 8 and MAP< 65, initiate catecholamines.
Fellahi	Administer 100 ml fluid bolus for SVV> 11. After correcting SVV to <11, measure CI. If CI<2.4 start dobutamine.	Fluid administration based on BP, CVP, urine output, skin mottling, and arterial pulse pressure variation.
Thomson	Record baseline SV, CO, CVP, then administer 250 ml of fluid bolus. If SV increases by >/10 % repeat bolus.	Fluid administration based on perceived clinical need, MAP, CVP, lactate level, urine output, base deficit.
Parke	Administer fluid bolus (250- 500 ml) for CI < 2.5 and SVV>13. If not, and MAP<65, consider starting vasoconstrictor.	Fluid administration up to 2 liters by nurses based on clinical judgment, MAP or CVP.
Walker	Administer fluid bolus of 5 ml/kg if CI <2.0, SVo2<60 %, MAP <65. If volume unresponsive consider vasopressors, inotropes or blood transfusion.	No data
Shrestha	Fluid bolus 100 ml administered if CI < 2.2 l/min/m2, CVP < 6 mmHg or SVV >10%.	CVP, MAP, ABG analysis, hematocrit, urine output
Osawa	Fluid bolus 250 ml administered if CI <3.0 and SVI < 35 mL/m2. If CI remains <3.0, but the SVI is >35 mL/m2 then start dobutamine infusion.	HR 70-100 ScVo2 >70 % Lactate level<3 Urine output > 0.5 ml/kg/hr MAP >/ 65
Kapoor	Fluid bolus 100 ml administered if CI < 2.2 l/min/m2, CVP < 6 mmHg or SVV >10%. Until goals achieved.	CVP, MAP, EtCO2, temp, ABG analysis, hematocrit, urine output.

Note. GDT=goal directed therapy; SVV= stroke volume variation; SVI= stroke volume index; SV=stroke volume; CO= cardiac output; SvO2=mixed venous oxygen saturation; EVLWI= extravascular lung water index; CI= cardiac index; MAP= mean arterial pressure; RBC= red blood cells; CVP= central venous pressure; ABP= arterial blood gas; EtCO2= end tidal.

Table E-3
Fluid Data

First author	Timing/hours	Fluid	GDT/ Study group.	Usual care/Control group.	P value
Goepfert	From induction until ICU discharge	Total fluids	Mean ± SD, [Median] (11,701 ± 2,175 [11,325] ml	12,313 ± 3,281 [11,746] ml	0.227
		Total Crystalloids	3,698 ± 1,121 [3,700]	4,451 ± 2,608 [4,000]	0.34
		Total colloids	3,067 ± 1,165 [3,000]	2,117 ± 1,062 [2,000] ml	<0.001
		Crystalloids	2,168 ± 554 [2,000] ml	2,028 ± 535 [2,000] ml	0.36
	Intraoperative alone	Colloids	1,293 ± 501 [1,500] ml	880 ± 397 [1,000] ml	<0.001
	ICU fluid therapy	Crystalloids	1,529 ± 947 [1,500] ml	2,423 ± 2,470 [2,000] ml	0.16
		Colloids	1,774 ± 996 [1,500] ml	1,237 ± 988 [1,000] ml	0.008
Fellahi	Intraoperative period	Total fluid loading	mean ± SD 400 [200–1,000]	500 [100–1,100	0.035
		Patients (fluid loading)	41 (85)	30 (68)	0.042
Thomson	Postoperative 8 hours	Total fluids	2704 (1393) mL	2905 (1367) mL	0.09
Parke	Post-op until extubation.	Bolus fluid	median (IQR) 1620 ml (500–3410 ml)	2520 ml (1440–5250)	<0.001
		Total fluid	2050 (910–4280	2980 (2070–6580	0.001
	Post op until 24 hours.	Bolus fluid	2760 ml (1690–4500),	3750 ml (2250–5550,	0.02

		Total fluid	4350 (2790–6160	5080 (3930–7320)	0.002
Walker	First 12 hours	Total fluid	Mean SD 4687 ± 2284	1189 ± 1344	<0.001
Shrestha	From opening of sternum until 8 hours post-op	Additional fluid given	Mean ± SD 1199.04 ± 638.701	938.32 ± 736.151	0.062
Osawa	First 8 hours following ICU admission.	Fluid bolus	Median (IQR) 1,000 mL IQR, 625–1,500	500 mL, (IQR) 500–1,000	<0.001
Kapoor	Induction to 8 hours post-op	Extra fluid administered	Mean ± SD 376.33 ± 55.23 ml	343.33 ± 62.02 ml	P = 0.003

Note. GDT= Goal directed therapy; ICU=intensive care unit; IQR= interquartile range; SD= standard deviation.

Appendix F

Cross Analysis of Outcomes of GDT Studies

Table F-1
Length of hospital stay/time to discharge

First Author	GDT/Study group	Usual care/Control group	P value
Goepfert	Time to reach discharge criteria: 5.3 ± 3.5 (5.0) days	6.4 ± 3.3 (6.0)	<0.001
Fellahi	Days (extremes) 8(6-58)	8(7-22)	0.727
Thomson	Median(IQR) 6(4) days	7(8)	0.004
Parke	Median(IQR) 6.2 (5–8) days	6.5 (6–8)	0.64
Walker	Not measured		
Shrestha	Mean ± SD 7.64 ± 3.001days	9.10 ± 5.389	0.097
Osawa	Median (IQR) 9(8-16) days	12(9-22)	0.049
Kapoor	7.17 ± 1.93 days	7.94 ± 1.64	0.025

Note. GDT= Goal directed therapy; IQR= interquartile range.

Table F-2
Length of ICU stay

First Author	GDT/Study group	Usual care/Control group	P value
Goepfert	42.0 ± 18.7 (39.0) h	62.9 ± 58.2 [44.0]	0.018
Fellahi	96 (38–425) hours	95 (41–480)	0.606
Thomson	Median 20 hours	24 hours	0.001
Parke	Median (IQR) 22.7 (20–46) hours	25.9 (21–48)	0.23
Walker	Median (IQR) 24.7 (22.1–46.85) hours	22.5 (14.5–29.25)	0.06
Shrestha	Mean ± SD 53.82 ± 29.727 hours	76.3 ± 37.768	0.089
Osawa	Median (IQR) 3(3-5) days	5(4-7)	<0.001
Kapoor	3.41 ± 0.75 days	3.74 ± 0.59	0.012

Note. GDT= Goal directed therapy

Table F-3
Mortality

First Author	GDT/Study group	Usual care/Control group	P value
Goepfert	None reported	None reported	
Fellahi	1	2	0.605
Thomson	2 (1.6%).	2(1.4%)	0.89
Parke	None reported	1	Not reported
Walker	1	0	0.51
Shrestha	2	3	0.653
Osawa	3 (4.8)	6 (9.4)	0.49
Kapoor	2	6	0.272

Note. GDT= Goal directed therapy

Table F-4
Complications

First Author	GDT/Study group	Usual care/Control group	P value
Goepfert	Total number of complications. 43	75	0.004
Fellahi	Total number of complications. 22	19	0.836
Thomson	Incidence of AKI 8(6.5%). Patients requiring dialysis 4(3.3%). Readmission to ICU 4(3.3%)	28(19.9%) 15(10.6%) 13(9.2%)	0.002 0.021 0.04
Parke	New onset atrial fibrillation AKI		No significant difference No significant difference
Walker	Reintubation 4/37 (10.8)	0/0	0.049
Shrestha	Wound complication 4 Dialysis 3 Re-operation 4 Organ Dysfunction 0.44 (0- 4; total 15)	8 6 6 0.66 (0- 4; total 21)	0.457 0.468 0.638 0.592
Osawa	Infections 8 (12.9) Low cardiac output syndrome 4 (6.5)	19 (29.7) 17 (26.6)	0.022 0.002
Kapoor	Not reported		

Note. GDT= Goal directed therapy; AKI= Acute kidney injury.

Table F-5
Time to extubation / duration of mechanical ventilation

First Author	GDT/Study group	Usual care/Control group	P value
Goepfert	Mean±SD (median) 10.8 ± 4.7 (10.0) hours	12.5 ± 6.0 (11.0)	0.12
Fellahi	510 (360–1,110) minutes	570 (320–1,520)	0.005
Thomson	Not reported		
Parke	10.8 (9–15) hours	12.4 (9.1–23)	0.14
Walker	14.5 (6.4–21.5)	11.5 (7–17)	0.27
Shrestha	10.48 ± 7.640 hours	16.429 ± 11.801	0.041
Osawa	Median (IQR) 7.25 (5.5–9) hours	8.2 (6.6–11.5)	0.09
Kapoor	18.05 ± 4.53 hours	19.89 ± 3.96	0.025

Note. GDT= Goal directed therapy; SD= standard deviation; IQR= interquartile range.

Table F-6
Use of inotropes/vasopressors

First Author	GDT/Study group	Usual care/Control Group	P value
Goepfert	Intra-op duration of norepinephrine use: 214 ± 110 (213) min Intra-op cumulative norepinephrine dosage 9.0 ± 7.6 (7.7) µg/kg	278 ± 113 (283) min 14.9 ± 11.1 (13.2)	0.008 0.002
Fellahi	No of patients receiving dobutamine: Number (%) 21 (44) No of patients receiving vasopressors: 16 (33)	7 (16). 13(30)	0.003 0.660
Thomson	Not reported		
Parke	Use of vasoactive drugs		No significant difference
Walker	Use of vasopressin 4 (10) Use of norepinephrine 8 (1.8–24.4)	1 (2.5) 5.6 (2.13–13.48)	0.06 0.28
Shrestha	Duration of use of inotropes: 23.2 ± 17.870 hrs	39.12 ± 18.615	0.032
Osawa	Cumulative ICU dobutamine dosage (mg/kg) 12 (6–22) Duration of dobutamine use (hrs) 54 (49–80) Cumulative ICU norepinephrine dosage (µg/kg) 0 (0–231) Duration of norepinephrine use (hrs) 0 (0–65)	19 (11–31) 76 (56–111) 369 (0–1,051) 78 (0–112)	0.003 0.001 <0.001 0.001
Kapoor	Duration of inotrope use (SD) 2.81±(0.94) days Number of times inotropes adjusted (SD) 3.12± (0.80)	3.09± (0.59) 2.77±(0.91)	0.063 0.029

Note. GDT= Goal directed therapy; SD= standard deviation; IQR= interquartile range; Min=minutes; Hrs=hours.