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DOES ROTEM-GUIDED THERAPY INFLUENCE POSTOPERATIVE CHEST TUBE OUTPUT IN ON-PUMP CABG?

A research project submitted to
the Graduate College of Business
Marshall University

Final defense submitted in partial fulfillment of requirements for
the
Doctorate of Management Practice in Nurse Anesthesia
(DMPNA) degree
conferred by Marshall University (MU) in partnership with the
Charleston Area Medical Center (CAMC) based on a
Collaborative agreement between the
MU College of nosiness and the CAMC School of Nurse Anesthesia

By
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November 15, 2017

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TABLE OF CONTENTS

	PAGE
COVER PAGE……...	i
SIGNATURE PAGE……...	ii
TABLE OF CONTENTS……...	iii
EXECUTIVE SUMMARY…….	iv
INTRODUCTION	
• Background and Significance……..	1
• Literature Review……	2
• Significance of the Problem and Research Purpose……	5
METHODOLOGY	
• Research Hypothesis……	6
• Research Design and Setting……...	6
• Sample Population and Description of Sample……...	7
• Procedure/Protocol……..	8
• Data Collection and Instruments…….	8
• Statistical Design and Analysis……...	8
RESULTS	
• Presentation, Analysis and Interpretation of Data……...	9
DISCUSSION	
• Discussion of Study Results…….....	13
• Study Limitations…….....	15
CONCLUSIONS…….	16
IMPLICATIONS AND RECOMMENDATIONS…….....	16
REFERENCES……	18
APPENDICES	
• Appendix A: ASA Classification……	23
• Appendix B: ICD 10-CM codes……..	24
• Appendix C: Data Collection Tool……..	27
• Appendix D: IRB Approval Form……...	28

EXECUTIVE SUMMARY

Abstract: The purpose of this study was to identify the association between ROTEM-guided therapy and chest tube output in patients who have undergone elective on-pump CABG.
Introduction: In open heart surgery, there are a variety of ways that coagulation disturbances occur, such as hemodilution of coagulation factors and platelets, a reduction in coagulation factors due to the use of cardiopulmonary bypass the administration of the anticoagulant heparin, and altered temperature. Severe bleeding is frequently associated with open-heart surgery, especially on-pump coronary artery bypass grafting (CABG). Thromboelastometry using rotational thromboelastometry (ROTEM) is a point-of-care testing that can show specific defects in the coagulation process and help guide the way the deficiencies are replaced. ROTEM uses a sample of patients' blood and forms a clot, creating a graphic and numerical representation of the clotting process.
Methodology: This study used a retrospective, quantitative, case-control design at Charleston Area Medical Center in West Virginia. A chart review was conducted on adult patients who underwent elective on-pump CABG from January 1, 2012 to June 1, 2016. A review of medical records was conducted on 200 patients at CAMC Memorial Hospital. The sample was grouped a ROTEM-guided therapy group (n=100) and non-ROTEM-guided therapy group (n=100). Patient characteristics of age, gender, race, and Body Mass Index (BMI) kg/m^2 were collected. Clinical characteristics of cardiopulmonary bypass time (CPB) in minutes, number of bypasses, and chest tube output at 1 hour, 2 hours, 4 hours, and 8 hours measured in milliliters (ml) were collected. Means were compared using the Independent t-test for age, BMI, CPB, number of bypasses, chest tube output at 1 hour, at 2 hours, at 4 hours, and at 8 hours. Chi-square test was used to compare gender and race. A multiple step-wise linear regression was used to determine a relationship between chest tube output at 1, at 2, at 4, and at 8 hours with age, gender, race, BMI, CPB, and ROTEM-guided therapy (RGT).
Results: There was no statistical significance found between the ROTEM-guided therapy and chest tube output at 1, 2, 4, or 8 hours. The mean age for the total sample was 58.5 years, mean number of bypasses 3.67, and mean BMI was 29.4. Of the 200 patients, 154 (76%) were male, 46 (23%) were female. Statistical significance was found in the RGT group and number of bypasses ($p=0.027$); and RGT and CPB ($p<0.001$). A statistically significant association was also found between BMI and chest tube output 1 hour ($p=0.001$), at 2 hours ($p=0.001$), at 4 hours ($p<0.001$), and 8 hours ($p<0.001$).
Discussion: This study found that as BMI increases with patients undergoing on-pump CABG was associated with decreased chest tube output. Though there was longer CPB time and slightly more bypasses conducted on patients who received ROTEM-guided therapy, the amount of chest tube output was not significant different than patients who did not receive ROTEM-guided therapy. The association between the independent variables age, gender, cardiopulmonary bypass time, and number of bypasses with chest tube output at each hour measured was not significant. The literature is conflicting on the efficacy of ROTEM with decreasing chest tube output but supports the findings of increased BMI with decreased chest tube output. Several limitations were identified and discussed.
Conclusion: This study revealed there was no difference in chest tube output between the patients who received ROTEM-guided therapy and those who did not receive ROTEM-guided therapy. However, the study did reveal that increasing of BMI may lead to lower intraoperative blood loss.

Implications/Recommendations: Improvements should continue to be made on point-of-care coagulation testing. Anesthesia practitioners may benefit from algorithms regarding ROTEM and continual assessment of practice and protocol may prove beneficial.

Key Words: ROTEM, CABG, chest tube output, BMI

INTRODUCTION

Background and Significance

In open heart surgery, abnormalities of the coagulation system can be problematic. There are a variety of ways that coagulation disturbances occur, such as hemodilution of coagulation factors and platelets, a reduction in coagulation factors due to the use of cardiopulmonary bypass (CPB), the administration of the anticoagulant heparin, and altered temperature. Severe bleeding is frequently associated with open-heart surgery, especially on-pump coronary artery bypass grafting (CABG). Surgery patients undergoing cardiovascular revascularization have some of the highest rates of blood product administration. Risk is associated with the administration of blood products. There is an inverse association between the amount of product transfused and patient outcomes.

Thromboelastometry using rotational thromboelastometry (ROTEM) is a point-of-care testing that can show specific defects in the coagulation process and help guide the way the deficiencies are replaced. ROTEM uses a sample of patients' blood and forms a clot, creating a graphic and numerical representation of the clotting process (Kroll, 2010). When ROTEM-guided therapy is used, studies show there is a significant reduction in blood product administration in CABG patients (Ak et al., 2009; Deppe et al., 2016; Weber et al., 2012). While ROTEM is not a new technology, it is not widely utilized among anesthesia providers.

Blood loss is a useful guide to coagulation status. In cardiovascular surgery, especially CABG, chest tubes are inserted to allow blood to drain into a collection device. The current literature has conflicting understanding of the role of ROTEM associated with cardiac surgery. The efficacy of the ROTEM testing and the therapy to follow being effective in some studies and not as effective in others. The current case-control study investigates the relationship between ROTEM-guided therapy and chest tube output in on-pump CABG patients.

Literature Review

Blood product administration is not without risk. Most notably are complications regarding immune suppression and infection resulting in approximately $17 billion in annual cost (Murphy et al., 2007; Shander, Hofmann, Gombotz, Theusinger, & Spahn, 2007).
In the United States, cardiovascular surgery accounts for 24% of transfused packed red blood cells (PRBC), 20% transfusion of platelets, and 34% transfusion of plasma (Cobain, Vamvakas, Wells, & Titlestad, 2007). To compare populations of surgeries relating to the abdomen are 17% PRBC, 19% platelets, and 26% plasma. Transfusion of PRBC, fresh frozen plasma (FFP), and platelets can lead to serious adverse outcomes such as associated with acute lung, renal failure, hypervolemia, neurologic events, and cardiac complications (Khan et al., 2007; Koch et al., 2006; Spiess et al., 2004). Transfusion of PRBC has a strong association with infection; the more PRBCs transfused the higher the incidence of infection (Murphy et al., 2007).

Bleeding in excess after cardiac surgery is often treated with administration of blood products, which increases the risk of re-exploration, resulting in morbidity and mortality (Koch et al., 2006; Murphy et al., 2007). Identifying the characteristics of patients with a high risk for coagulopathies is critical, especially in cardiac surgery. From just one unit, a measurement of the amount of blood product in a container, of PRBC transfused the risk of mortality increases by 77% and when the PRBC transfusions exceed 5 units, risk of death increased dramatically (Koch et al., 2006). The development of strategies to reduce the need for transfusion has been an ongoing concern and struggle for health care providers, especially in open-heart surgeries.

In open-heart surgery, factors that effect a patient's bleeding are heparin, cardiopulmonary bypass (CPB), hypothermia, type of open heart surgery, and other factors specific to the patient. High levels of the drug heparin are usually needed for CPB and are

monitored using an activated clotting time (ACT) test during the case (Mittermayr et al., 2005). Anticoagulation must be used during cardiac surgery to limit the chance of clot formation in the extracorporeal circuit of the CPB (Makar et al., 2010). As blood passes through cardiopulmonary bypass circuit it travels through plastic, non-endothelial surfaces, activating the clotting mechanism and thus the need for anticoagulant medications like heparin (Despotis et al., 1996). Heparin is used because it is effective and reversible with protamine (Ferraris et al., 2007). A lengthy time on CPB has been shown to increase the volume of chest tube drainage and to increase the likelihood of re-exploration (Despotis et al., 1996; Moulton, Creswell, Mackey, Cox, & Rosenbloom, 1996). While on CPB, excessive dilution of blood and coagulation factors can occur, diminishing oxygen carrying capacity, creating tissue acidosis, and extravascular fluid shifts (Daniel, 1996). Hypothermia, or lower temperatures of the patient, have also been associated with increasing chest tube drainage (Despotis et al., 1996). Valve surgeries also account for a larger amount of blood loss (Hardy et al., 1991; Moulton et al., 1996).

Focusing on the patient factors associated with coagulopathies has been instrumental in the prediction of bleeding in cardiac surgery. In cardiac surgery, patients who had a high risk of coagulopathies were: age greater than 70 years, a low preoperative red blood cell count, preoperative antithrombotic or antiplatelet drugs, complex or re-exploration surgeries, emergency surgeries, and patient comorbidities such as bleeding disorders, diabetes, renal failure, and disease of the liver (Ferraris et al., 2007; Moulton et al., 1996). Patients in a higher risk group have a higher incidence for cardiac tamponade and re-exploration, resulting in a longer length of stay and an increase in morbidly and mortality (Čanádyová, Zmeko, & Mokráček, 2012). Another study found that surgical re-exploration doubles the incidence of mortality (Ranucci et al., 2008). The more risk factors a patient has, the higher mortality after re-

exploration (Kristensen, Rauer, Mortensen, & Kjeldsen, 2012). Thromboelastography has been shown to decrease the number of re-explorations, length of stay, and blood product administration (Spalding et al., 2007; Spiess, Gillies, Chandler, & Verrier, 1995).

Thromboelastography (TEG) has been available since 1948 where Hartert used the fibrin polymerization process and charted it as visualized graphical data (Hartert, 1948). TEG is classically known for having a sample of blood with a small cuvette slowly rotated to imitate venous flow and activate coagulation (Kroll, 2010). The process of using thrombelastography has advanced over the years, resulting in today's technology of the thromboelastometry. Thromboelastometry is referred to more commonly by a brand name, ROTEM. ROTEM is slightly different as the cuvette is stationary and as the wire probe oscillates, a clot forms and impedes movements of the probe and measures several variables from the clot formation and lysis (Kroll, 2010). ROTEM minimizes susceptibility to mechanical variables, like shocks and vibrations to the equipment. This point-of-care testing can provide graphic and numerical representation of the coagulation proteases and inhibitors, the fibrinolytic system, and the sum of platelet function at bedside within 30 minutes (Luddington, 2005).

Standard coagulation essays, plasma thromboplastic (PT) and partial thromboplastin (PTT), platelet count and fibrinogen concentrations are at times insufficient for monitoring coagulation when multiple factors affecting coagulation exist (Mallett & Cox, 1992). ROTEM has been proven to be a faster method in which to detect coagulopathies in cardiac patients in numerous studies.

Clot evaluations with ROTEM measures these parameters as a 1) guide for transfusion of fresh frozen plasma (FFP), 2) the clot strength to assess platelet function, and 3) heparinase to assess protamine dosage requirement (Luddington, 2005). ROTEM assessments examine

coagulation either with an intrinsically activated test (INTEM) or an extrinsically activated test (EXTEM) (Lang et al., 2005). The fibrin-specific clot formation (FIBTEM) shows the assessment of fibrin levels without the interaction of platelets by the inhibition of the platelets using cytochalasin D (Ogawa et al., 2012). Under INTEM heparinase neutralization is tested (HEPTEM) to detect heparin and the effect heparin has on coagulation (Mittermayr et al., 2005).

The predictive function of ROTEM analysis and blood loss as been studied well, as ROTEM is used in a variety of surgeries including cardiac, liver-transplantation, trauma and obstetrics (Kroll, 2010). Transfusion and ROTEM algorithms that specify certain characteristics of the assessment and administration of blood products are usually research-based but vary from hospital to hospital. These algorithms have been shown to decrease the amount of blood products transfused (Ak et al., 2009; Deppe et al., 2016; Weber et al., 2012).

ROTEM-guided therapy has been associated with saving half the cost of conventional management of coagulopathies (Weber et al., 2012). Due to the increase of morbidity associated with transfusion, which is dose dependent, ICU and postoperative hospital stays can increase, thereby increasing costs (Murphy et al., 2007). It was predicted in their study avoiding transfusions of PRBC could have a cost saving of 50%. In another study, implementation of ROTEM-guided therapy decreased the administration of PRBC by 25% and platelets administration by 50%, while also noting that overall after implementation of ROTEM-guided therapy there was a cost saving of over 40% (Spalding et al., 2007).

Significance of the problem and Research Purpose

Blood loss is a useful guide to coagulation status. In cardiovascular surgery, especially CABG, chest tubes are inserted to allow blood to drain into a collection device. This study

investigated the relationship between ROTEM-guided therapy and chest tube output in on-pump CABG patients. Specific aims included:

1. Expand upon the relationship between ROTEM-guided therapy and chest tube output.
2. Identify the efficacy of ROTEM-guided therapy at CAMC.
3. Compare the amount of blood loss, measured in chest tube output, in CABG surgery with ROTEM-guided therapy, measured in milliliters of chest tube drainage.

METHODOLOGY

Research Hypothesis

The hypothesis of this study was that in adult patients aged 18-70 years with ASA physical classification status of III-IV who underwent elective CABG using ROTEM-guided therapy there would be less blood loss, measured in chest tube output, than patients who did not receive ROTEM-guided therapy.

Research Design and Setting

The design of this study is a retrospective case-control conducted at Charleston Area Medical Center (CAMC), Charleston, West Virginia. The case-control type of study was chosen due to the time constraint, ability to look at multiple risk factors, and control for confounding variables.

Sample Population and Description of Sample

The sample population included patients, who underwent elective on-pump CABG surgery at CAMC from January 1, 2012 to June 1, 2016. A review of medical records was conducted on 200 patients at CAMC Memorial Hospital. Two groups of 100 patients each were

established for comparison; a ROTEM-guided therapy group and non-ROTEM-guided therapy group.

The subjects were identified by The International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) codes 36.1 (Bypass anastomosis for heart revascularization), 36.2 (heart revascularization by arterial implant), 39.61 (cardiopulmonary bypass).

The ICD-10-CM codes included coronary artery bypass for one, two, three, and four or more bypasses (Appendix A).

Inclusion criteria:

1. Male and female adult patients 18 to 70 years of age
2. ASA physical status classification III-IV
3. Underwent elective CABG and admitted to the CAMC Memorial Hospital cardiac ICU.

Exclusion criteria:

1. Emergent CABG surgery
2. Valve surgeries
3. Patients who underwent redo-CABG
4. Patients who took direct oral anticoagulants (glycoprotein IIb.IIIa antagonist or clopidogrel) within 5 days of surgery and low-molecular weight heparin until the day of surgery
5. Patients with diabetes mellitus, impaired renal function (creatinine greater than 2 mg/dL), and liver disease with elevated liver function tests (ALT greater than 56, AST greater than 40)

Procedures and Protocol

A retrospective study was performed using patient information gathered from the CAMC EMR system for patients who underwent elective CABG using simple randomization of 2000 charts. The sample consisted of 200 patients, 100 patients met the ROTEM-guided therapy guidelines, while the other 100 had no ROTEM assessment completed. Data was collected from the patients' preoperative, intraoperative anesthesia record, perfusion records, and post anesthesia records. Data collected from the anesthesia records included: gender, race, age, height, weight, Body Mass Index (BMI), ASA physical status classification (Appendix B), length of CPB, and number of bypasses. Gender was classified as male or female. Age was measured in years. BMI is a calculation, measured in kg/m2, using height in meters and weight in kilograms to determine a person's level of obesity. Length of CPB was measured in minutes. Measured chest tube output was recorded at 1, 2, 4, and 8 hours' post admission to the cardiac ICU. Chest tube output was measured in milliliters.

Placement in the ROTEM-guided therapy group (RGT) was determined if the patient had a ROTEM testing complete and reviewed by an anesthetist.

Data Collection and Instrumentation

Microsoft excel was used by the researchers to organize data collection. Each patient was given a number in the order in which the data was collected. The number was in no way linked the data collected to the patient it belongs to (Appendix C).

Statistical Design and Analysis

The purpose of this study was to determine if there was less blood loss, measured in chest tube output in milliliters, between the elective on-pump CABG patient who received ROTEM-guided therapy and those who did not (yes=1, no=0). The independent variable was ROTEM-guided therapy and the dependent variables were chest tube output at 1, 2, 4, and 8 hours.

Control variables included in the regression are, BMI kg/m^2, ASA physical status classification, race (white and non-white), gender (male=0, female =1), length of CPB (minutes), and number of bypasses. Stepwise regression was performed to estimate if there was an association between the amount of blood surgical loss and ROTEM-guided therapy. A t-test was conducted to determine any differences between the two groups in terms of age, body mass index, number of bypass, and length of cardiopulmonary bypass. Chi-squared test was employed to compare gender, race, and ASA. A p-value of <0.5 was considered statistically significant.

Ethical Considerations

This study was approved by the CAMC and West Virginia University-Charleston Division Institutional Review Board on June 30, 2017 (Appendix D).

RESULTS

Presentation, Analysis and Interpretation of Data

Patients were categorized into a non-ROTEM guided therapy group (NRGT – control group (n=100)) and were compared to patients in ROTEM-guided therapy group (RGT – case group (n=100)) (Table1). All patients were ASA physical status classification IV. There were 154 male patients and 46 female patients. Male patients comprised of 75 in the NRGT and 79 in the RGT. Female patients comprise of 25 in the NRGT and 21 in the RGT. Of the sample 195 patients identified as white and 5 patients identified as non-white. The NRGT had 97 patients identifying as white and 3 patients identified as non-white, while the RGT had 98 patients identifying as white and 2 non-white. The Chi-Square difference test was used to compare the distribution of gender and race between NRGT and RGT. Results revealed no significant difference in gender (p=0.502). Results revealed no significant difference in race (p=0.651). There is an equal split of gender and race between NRGT and RGT.

Table 1 also presents the results of the independent t-test analysis, displaying no significant difference in the mean age between the NRGT and the RGT (NRGT of 57.81 years versus RGT of 59.19 years; p= 0.163). There was also no difference in BMI between the NRGT and the RGT (NRGT of 29.047 kg/m^2 versus RGT of 29.804 kg/m^2; p= 0.344). However, with a p-value of less than 0.05 being significant, the number of bypasses was slightly greater in the ROTEM-guided therapy group than the non-ROTEM guided therapy group (NRGT of 3.51 bypasses versus RGT of 3.83 bypasses; p= 0.027). CPB time was significantly different between non-ROTEM-guided therapy and the ROTEM-guided therapy group with the ROTEM-guided therapy group having a significantly longer time on bypass (NRGT 89.46 minutes versus RGT 114.22 minutes p<0.001).

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Table 1: Demographic and Clinical Characteristics (n=200)

	Total Sample (n=200)	**NRGT (n=100)**	**RGT (n=100)**	**P-value**
Gender (%)				0.502
Male	154 (76)	75 (37.5)	79 (39.5)	
Female	46 (23)	25 (12.5)	21 (10.5)	
Race (%)				0.651
White	195 (97.5)	97 (48.5)	98 (49)	
Non-White	5 (2.5)	3 (1.5)	2 (1)	
Age (mean, SD)	58.5 ± 6.98	57.81 ± 7.035	59.19 ± 6.899	0.163
BMI kg/m^2 (mean, SD)	29.43 ± 5.64	29.047 ± 6.085	29.80 ± 5.159	0.344
Number of Bypasses (mean, SD)	3.67 ± 1.03	3.51 ± 0.959	3.83 ± 1.074	0.027
CPB time (minutes) (mean, SD)	101.84 ± 40.69	89.46 ± 36.244	114.22 ± 41.288	<0.001

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Table 2 shows the results of the independent t-test analysis displaying the mean chest tube output for the NRGT and RGT at 1, 2, 4, and 8 hours. The chest tube output was measured

in cumulative amounts not isolated hours. So, the first hour would have an effect upon the second and so on. The mean chest tube output at 1 hour with NRGT having 162.3 ml versus RGT having 150.9 ml (p=0.446). The mean chest tube output at 2 hours with NRGT having 240.5 ml versus RGT having 226.7 ml (p=0.491). The mean chest tube output at 4 hours with NRGT having 366.2 ml versus RGT having 339.8 ml (p=0.381). The mean chest tube output at 8 hours with NRGT having 531.6 ml versus RGT having 527.3 ml (p=0.925). There was no significant difference in the mean chest tube output between the NRGT and RGT at 1, 2, 4, and 8 hours. However, in the RGT there was less each hour, just not statistically significant.

Table 2: Independent T-test on chest tube output at 1 hour, 2 hours, 4 hours, and 8 hours (n=200)

	Group	Mean	Std. Deviation	Std. Error Mean	P-value
Chest tube output (ml) at 1 hour	NRGT (n=100)	162.3	105.3	10.5	0.446
	RGT (n=100)	150.9	109.7	10.9	
Chest tube output (ml) at 2 hour	NRGT (n=100)	240.5	141.7	14.2	0.491
	RGT (n=100)	226.7	141.9	14.2	
Chest tube output (ml) at 4 hour	NRGT (n=100)	366.2	225.9	22.6	0.381
	RGT (n=100)	339.8	198.6	19.9	
Chest tube output (ml) at 8 hour	NRGT (n=100)	531.6	337.5	33.8	0.925
	RGT (n=100)	527.2	320.7	32.1	

Multiple step-wise linear regression was performed to estimate the association between the RGT status and the dependent variable, chest tube output at 1, 2, 4, and 8 hours while controlling for covariates (Table 3). This test revealed no statistical significance between the RGT status and the chest tube output variable but there was a significant association between BMI and each hour of measurement. Interestingly, for every increase in the BMI by 1 point, chest tube output decreased, and at increasing amounts at each measured hour. Chest tube output at hour 1 showed that for every 1 point BMI increased, chest tube output decreased by 4.28ml

(p=0.001). At the "Chest tube output at 2 hour" measurement, it was shown that for every 1 point of increased BMI, chest tube output decreased by 5.79ml (p=0.001). At the 4th hour of chest tube output measurement, for every increase of BMI, a decrease of 10.03ml of chest tube output was seen (p<0.001). And finally, at the 8th hour of measurement, every BMI increase of 1 point showed a decrease of 16.91ml of chest tube output (p<0.001).

Table 3: Results of Stepwise Linear Regression on Chest Tube Output

Dependent Variable	Model 1	Unstandardized coefficients		Standard Coefficients		
		B	Std Error	Beta	t	P-value
Chest tube output (ml) at 1 hour	Constant	282.529	39.499		7.153	<0.001
	BMI	-4.283	1.318	-0.225	-3.24	0.001
Chest tube output (ml) at 2 hour	Constant	404.121	52.021		7.768	<0.001
	BMI	-5.795	1.736	-0.231	-3.337	0.001
Chest tube output (ml) at 4 hour	Constant	648.089	77.346		8.379	<0.001
	BMI	-10.029	2.582	-0.0266	-3.884	<0.001
Chest tube output (ml) at 8 hour	Constant	1027.083	118.616		8.659	<0.001
	BMI	-16.913	3.959	-0.290	-4.272	<0.001

DISCUSSION

Discussion of Study Results

This current study found no significantly decreased chest tube output in elective CABG patients between patients who did or did not received ROTEM-guided therapy. The RGT group did not have a statistically different chest tube output compared to the NRGT group. However, as shown in table 3, the RGT group did have slightly more bypasses than the NRGT group and significantly longer CPB time. This can be interpreted in two ways: (1) Even though with more bypasses and longer CPB, the RGT maintained the same amount of chest tube output as the group with less bypasses; or (2) the RGT does not alter blood loss because the chest tube output

is approximately the same. With each bypass comes the risk of bleeding so maintaining close to same amount of chest tube output comparatively may be a sign of success of control of excessive blood loss.

This study finding that while at each interval, the RGT group had less blood loss than the NRGT, the amount of chest tube output was not significantly different between the two groups, is not line with prior studies. A prospective study of elective cardiac surgeries identifying the use of a simple ROTEM based algorithm compared to a control non-algorithm showed a significant decrease in postoperative blood loss at 4 hours, 12 hours, and 24 hours (Nuttall et al., 2001). In another prospective study by Weber, et al., there was a significant decrease in chest tube output at 6, 12, and 24 hours between a conventional group and ROTEM group. However, it must be noted that these studies included aortic, CABG, redo, and valve surgeries, which each surgery may have different amounts of bleeding typically seen. In another study of only aortic surgeries with high-risk cardiac patients, chest tube output was notably similar between the ROTEM and control group at 12 and 24 hours (Girdauskas et al., 2010). The study control variables may play a role in governing the relationship between variable as they are different from these other studies. There continues to be a differing of opinion on usage of ROTEM and the efficacy of thromboelastography as a point of care assessment of coagulation.

CPB has been shown to have a great influence on postoperative hemorrhage in the literature, with the increase of CPB time increasing the chance of hemorrhage in most studies (Christensen, Krapf, Kempel, & von Heymann, 2009). However, CPB in the present study was not associated with an increase in bleeding. In regards to the longer time on bypass, this factor may indicate that the patient had a higher chance of bleeding and trigger the anesthetist to obtain

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a ROTEM and correct the deficiencies. This could also account for the chest tube output similarities as well.

There was a greater frequency of male subjects (76%) to female subjects (23%) in the sample with 97.5% of the sample being white. However, this is similar to a meta-analysis which had 93.4% male subjects white, and 91% of female subjects white; 70.3% of the subjects were male and 29.7% were female (Vaccarino, Abramson, Veledar, & Weintraub, 2002). The smaller percentage of female gender may be due to the association with increased morbidity and mortality to CABG than the male gender and with better outcomes being noted with off-pump CABG in the female gender. (Brown et al., 2002). With off-pump CABG being utilized this would account for the decrease in female gender in the sample in this study. In this study gender and race did not have an association with chest tube output.

This study finding that an association was found between chest tube output and the independent variable of BMI is consistent with previous studies, indicating that an increase in patient weight has an effect on blood loss. Patients with a smaller BMI, less than 25 kg/m^2, have a higher risk for bleeding and are at risk for re-exploration due to the bleeding (Karthik, Grayson, McCarron, Pullan, & Desmond, 2004). A recent study shows that for every increase in kilogram of weight there is a decreased risk of transfusion. (Mazlan, Ayob, Hussein, Namasiwayam, & Wan Mohammad, 2017). The increase of a BMI with decrease of a chest tube output aids in support of this predictable model.

Study Limitations

There are multiple limitations to acknowledge in this study. First, the study design was retrospective, so selection bias cannot be ruled out. The sample size may not have been adequate due to the design, and no use of a power analysis. Increasing the sample size may have an impact

on the study. In addition, the present study has no ability to estimate causality between variables. A longitudinal study design would correctly investigate casual relationship.

The present study used convenient sampling technique thereby the study findings are limited to CAMC patients, not representing WV or the national level.

This study compares the non-ROTEM-guided therapy to the use of ROTEM-guided therapy in on pump, elective CABG. This sample of data essentially compared one particular portion of the practice of two different anesthesiologists. Comparing the results between a ROTEM-guided and non-ROTEM-guided group taking into consideration the practice of all cardiovascular anesthesiologists at CAMC may prove more beneficial.

Another potential caveat is documentation error by various clinicians. An error in documentation could lead to inappropriate inclusion or exclusion of subjects. There may be inconsistencies in measuring, such as rounding and transcription error. Using a retrospective design, the data could be misinterpreted, misread, or there could be improper documentation.

Several factors outside of the assessment of thromboelastography can contribute to postoperative chest tube output, including but not limited to; medications, hypothermia, acidosis, and surgery-related causes.

CONCLUSIONS

This study revealed there was no difference in chest tube output between the patients who received ROTEM-guided therapy and those who did not receive ROTEM-guided therapy. With a significantly longer time on cardiopulmonary bypass and slightly more bypasses in the ROTEM-guided therapy group, ROTEM should be considered as an effective and beneficial intervention. However, the study did reveal that increasing of BMI may lead to lower intraoperative blood

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loss. This may seem unreasonable to manipulate clinically and may not be a clinically significant amount; however, it is still worth noting.

IMPLICATIONS AND RECOMMENDATIONS

Assessment of bleeding and implementation of the transfusion of blood products are integral components to the success of CABG patients. Therefore, it is imperative to improve methods on the conversation of blood loss. This study does not provide statistically significant clinical evidence of a relationship between RGT and decreasing chest tube output in elective on-pump CABG patients. RGT was only measured by each anesthetist's application and parameters of practice. A guideline is available for the anesthetist in the facility; however, following the guideline was upon the anesthetist's purview. Having an algorithm for assessment and transfusion may provide benefit for the anesthetist with less experience using RGT. Algorithms have been shown useful in previous studies with success, and routinely updating the algorithms would also be beneficial. To improve upon this study, measuring the amount and type of blood products administered to each group might also be advantageous rather than chest tube output alone.

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APPENDICES

Appendix A

One Coronary Bypass: 0210093 (Bypass Coronary Artery, One Artery from Coronary Artery with Autologous Venous Tissue, Open Approach), 0210098 (Bypass Coronary Artery, One Artery from Right Internal Mammary with Autologous Venous Tissue, Open Approach), 0210099 (Bypass Coronary Artery, One Artery from Left Internal Mammary with Autologous Venous Tissue, Open Approach), 021009C (Bypass Coronary Artery, One Artery from Thoracic Artery with Autologous Venous Tissue, Open Approach), 021009W (Bypass Coronary Artery, One Artery from Aorta with Autologous Venous Tissue, Open Approach), 02100A3 (Bypass Coronary Artery, One Artery from Coronary Artery with Autologous Arterial Tissue, Open Approach), 02100A8 (Bypass Coronary Artery, One Artery from Right Internal Mammary with Autologous Arterial Tissue, Open Approach), 02100A9 (Bypass Coronary Artery, One Artery from Left Internal Mammary with Autologous Arterial Tissue, Open Approach), 02100AC (Bypass Coronary Artery, One Artery from Thoracic Artery with Autologous Arterial Tissue, Open Approach), 02100AF (Bypass Coronary Artery, One Artery from Abdominal Artery with Autologous Arterial Tissue, Open Approach), 02100AW (Bypass Coronary Artery, One Artery from Aorta with Autologous Arterial Tissue, Open Approach),

Two Coronary Bypass: 0211093 (Bypass Coronary Artery, Two Arteries from Coronary Artery with Autologous Venous Tissue, Open Approach), 0211098 (Bypass Coronary Artery, Two Arteries from Right Internal Mammary with Autologous Venous Tissue, Open Approach), 0211099 (Bypass Coronary Artery, Two Arteries from Left Internal Mammary with Autologous Venous Tissue, Open Approach), 021109C (Bypass Coronary Artery, Two Arteries from Thoracic Artery with Autologous Venous Tissue, Open Approach), 021109W (Bypass Coronary

Artery, Two Arteries from Aorta with Autologous Venous Tissue, Open Approach), 02110A3 (Bypass Coronary Artery, Two Arteries from Coronary Artery with Autologous Arterial Tissue, Open Approach), 02110A8 (Bypass Coronary Artery, Two Arteries from Right Internal Mammary with Autologous Arterial Tissue, Open Approach), 02110A9 (Bypass Coronary Artery, Two Arteries from Left Internal Mammary with Autologous Arterial Tissue, Open Approach), 02110AC (Bypass Coronary Artery, Two Arteries from Thoracic Artery with Autologous Arterial Tissue, Open Approach), 02110AF (Bypass Coronary Artery, Two Arteries from Abdominal Artery with Autologous Arterial Tissue, Open Approach), 02110AW (Bypass Coronary Artery, Two Arteries from Aorta with Autologous Arterial Tissue, Open Approach)

Three Coronary Bypass: 0212093 (Bypass Coronary Artery, Three Arteries from Coronary Artery with Autologous Venous Tissue, Open Approach), 0212098 (Bypass Coronary Artery, Three Arteries from Right Internal Mammary with Autologous Venous Tissue, Open Approach), 0212099 (Bypass Coronary Artery, Three Arteries from Left Internal Mammary with Autologous Venous Tissue, Open Approach), 021209C (Bypass Coronary Artery, Three Arteries from Thoracic Artery with Autologous Venous Tissue, Open Approach), 021209F (Bypass Coronary Artery, 021209W (Bypass Coronary Artery, Three Arteries from Aorta with Autologous Venous Tissue, Open Approach), 02120A3 (Bypass Coronary Artery, Three Arteries from Coronary Artery with Autologous Arterial Tissue, Open Approach), 02120A8 (Bypass Coronary Artery, Three Arteries from Right Internal Mammary with Autologous Arterial Tissue, Open Approach), 02120A9 (Bypass Coronary Artery, Three Arteries from Left Internal Mammary with Autologous Arterial Tissue, Open Approach), 02120AC (Bypass Coronary Artery, Three Arteries from Thoracic Artery with Autologous Arterial Tissue, Open Approach), 02120AF (Bypass Coronary Artery, Three Arteries from Abdominal Artery with Autologous

Arterial Tissue, Open Approach), 02120AW (Bypass Coronary Artery, Three Arteries from Aorta with Autologous Arterial Tissue, Open Approach)

Four or more Coronary Bypass: 0213093 (Bypass Coronary Artery, Four or More Arteries from Coronary Artery with Autologous Venous Tissue, Open Approach), 0213098 (Bypass Coronary Artery, Four or More Arteries from Right Internal Mammary with Autologous Venous Tissue, Open Approach), 0213099 (Bypass Coronary Artery, Four or More Arteries from Left Internal Mammary with Autologous Venous Tissue, Open Approach), 021309C (Bypass Coronary Artery, Four or More Arteries from Thoracic Artery with Autologous Venous Tissue, Open Approach), 021309F (Bypass Coronary Artery, Four or More Arteries from Abdominal Artery with Autologous Venous Tissue, Open Approach), 021309W (Bypass Coronary Artery, Four or More Arteries from Aorta with Autologous Venous Tissue, Open Approach), 02130A3 Bypass Coronary Artery, Four or More Arteries from Coronary Artery with Autologous Arterial Tissue, Open Approach), 02130A8 (Bypass Coronary Artery, Four or More Arteries from Right Internal Mammary with Autologous Arterial Tissue, Open Approach), 02130A9 (Bypass Coronary Artery, Four or More Arteries from Left Internal Mammary with Autologous Arterial Tissue, Open Approach), 02130AC (Bypass Coronary Artery, Four or More Arteries from Thoracic Artery with Autologous Arterial Tissue, Open Approach), 02130AW (Bypass Coronary Artery, Four or More Arteries from Aorta with Autologous Arterial Tissue, Open Approach)

Appendix B

The ASA classification is a numeric scale developed by the American Society of Anesthesiologists to determine the general health of the patient. The classifications are:

I. A normal patient who is health.

II. A patient with mild systemic disease.

III. A patient with severe systemic disease.

IV. A patient with a severe systemic disease that is a constant threat to life.

V. A moribund patient who is not expected to survive without surgery.

VI. A brain-dead patient whose organ are being removed for transplant donation.

(Anesthesiologists, 2017)

Appendix C

Study Number	Age (years)	BMI (kg/m^2)	ASA	Race	Gender (Male=0, female=1)	ROTEM-guided therapy (0=no, 1=yes)	Cardiopulmonary bypass time (minutes)	Number of Bypass	Chest tube at 1 hour (ml)	Chest tube at 2 hour (ml)	Chest tube at 4 hour (ml)	Chest tube at 8 hour (ml)
1												
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Appendix D

IRB Approval Form

New study by expedited review: Approved

CAMC INSTITUTE
RESEARCH AND GRANTS
ADMINISTRATION

June 30, 2017

RE: Initial Review Submission Packet 06/30/2017 07:16:42 AM EDT regarding study number 17-350 Does ROTEM-guided therapy influence postoperative chest tube output in on-pump CABG?

Dear Mike Frame:

Your request for expedited approval of the new study listed above has been reviewed. This type of study qualifies for expedited review under FDA and DHHS (OHRP) regulations.

This is to confirm that your application is approved. The following items are approved:

Submission Components			
Form Name	Version	Outcome	
Study Document			
Title	Version #	Version Date	Outcome
IRB Protocol submission Woodburn v3	Version 1.0	06/29/2017	Approved

The accrual goal is 200. You must submit a request to the IRB to increase enrollment beyond the approved accrual goal.

You are granted permission to conduct your study as described effective immediately. The study is subject to continuing review on or before **06/29/2018**, unless closed before that date.

Please note that any changes to the study as approved must be promptly reported and approved prior to implementation. Some changes may be approved by expedited review; others require full board review.

Also, serious and/or unanticipated adverse events must also be reported as required by law and in accordance with CAMC/WVU Charleston Division IRB policies. Contact CAMC / WVU Charleston Division IRB at (304) 388-9970 or email april.white@camc.org if you have any questions or require further information.

Sincerely,

Chris Terpening, PhD, PharmD
Chair, CAMC/WVU IRB

3110 MacCorkle Ave. SE, Room 3283 Charleston, WV 25304 (304) 388-9970 Fax (304) 388-9976