Reducing Perioperative Blood Transfusions: An Evidence-based Approach Using Process Improvement Methodologies

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Table of Contents

Introduction **5**
Literature Review **7**
Current Transfusion Guidelines 8
Patient Blood Management Interventions 9
Erythropoiesis-stimulating agents and iron supplementation 10
Intraoperative blood salvage 11
Antifibrinolytics 12
Programs to reduce blood transfusions 13
Lean Six Sigma 15
Methodology **17**
Setting 17
Study Design 17
Conceptual Model 18
Define 18
Measure 19
Analyze 19
Improve/Implementation 20
Control 22
Results **23**
Blood Transfusion Rates 25
Number of Units Transfused 25
Tranexamic Acid 26
Over-transfusions 27
Complications 28
Discussion **28**
Limitations 31
Dissemination 31
Conclusion **32**
Appendices A-E **34**
References **39**

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Abstract

Background: Institutional data from the Mayo Clinic in Rochester Minnesota shows that the blood transfusion rate is twice the national average, and is implemented in a non-standardized fashion. Blood transfusions pose many risks to critically ill patients. The aim of this quality improvement project was to answer the research question: What are the effects of utilizing Lean Six Sigma (LSS) methodology and evidence-based interventions to standardize the blood transfusion practices, and decrease blood transfusion rates, for women undergoing cytoreduction surgery for ovarian and endometrial cancer at a large academic hospital?

Methods: The Define, Measure, Analyze, Improve, and Control framework, adopted from LSS quality improvement methods, was applied in this study. A root cause analysis conducted in the study setting, identified reasons why patients were over-transfused. A literature review was conducted to identify evidence-based interventions. Education was provided to the department of gynecology oncology surgery, anesthesia and nursing staff in the study setting. The multidisciplinary team implemented the following interventions; follow updated institution wide transfusion guidelines, communicate between the anesthesia provider and surgeon every 500 mL of fluid in the suction canister, utilize the hemostasis checklist, and administer a Tranexamic acid (TA) 15mg/kg one time dose in the operating room (OR), prior to incision for patients who met criteria.

Results: A total of 184 cases in the pre-implementation group identified in a retrospective chart audit, and 89 cases in the post-implementation group that met the study criteria, were investigated. Overall, the blood transfusion rate in the post-implementation group was decreased by 56.4% ($p<0.001$), and the number of packed red blood cells (pRBCs) transfused, decreased from 169 units to 39 units ($p<0.0023$). The number of intraoperative pRBCs significantly decreased from 148 units in the pre-implementation group, to 33 units post-implementation ($p<0.001$). 60.7% of women received TA. The rate of over-transfusion remained at 43% in both cohorts. There was a significant decrease in readmission rates ($p<0.002$) for the post-implementation group.

Conclusions: Lean Six Sigma, multidisciplinary teamwork, and evidence based interventions can significantly decrease blood transfusion rates, and the number of packed RBCs transfused, without increasing negative outcomes for patients. This quality improvement project demonstrated that Tranexamic Acid can be administered for gynecologic oncology surgeries without causing adverse effects, in women with ovarian or endometrial cancer. Results of this project suggest that efforts to decrease the over-transfusion rate should focus on transfusing pRBCs in single units, and limiting transfusions for hemoglobin >7g/dl.

Data Sources: PubMed, Embase, and CINAHL were utilized for the literature review.

Keywords: blood transfusion guidelines, Tranexamic acid, cytoreduction surgery, ovarian carcinoma, blood transfusions, process improvement, Lean Six Sigma

Introduction

A blood transfusion is not a benign intervention. Clinicians must weigh the risks and benefits for every patient. Blood therapy is given in order to increase blood volume, increase blood flow or improve oxygen transportation.[1] However, blood transfusions carry risks for negative side effects, are a limited and costly resource, and not everyone is willing to receive blood.

Blood transfusions have the potential to cause numerous adverse effects. Complications can include acute lung injury, transfusion-transmitted infection, venous thromboembolism, immunomodulation, circulatory overload, and mortality.[2-4] Blood transfusions present specific risks for patients with cancer. Individuals with cancer are at a greater risk for developing infections and cancer recurrence, secondary to transfusion-related immunomodulation.[5,6]

According to the National Blood Collection and Utilization Report,[2] the gap between the supply and demand for blood is increasing. Supply of packed red blood cells (PRBCs) through autologous donations is declining significantly. Compared to 17.3 million units collected in 2008, whole blood and red blood cell collection decreased 9.1% to 15.7 million units in 2011.[2] Approximately 13.1 million units of packed red blood cells (PRBC) are transfused every year.[2,7]

Hospital expenses for blood and associated handling costs are increasing while reimbursement rates are falling. On average, a hospital pays $225.42 for one unit of leukocyte reduced red blood cells.[2,8] This cost is a slight increase from the 2008 National Blood Collection and Utilization survey and does not include laboratory or supply costs.[2] The American Association of Blood Banks (AABB) projects a decline in reimbursement by 55% for a majority of the laboratory and supply costs associated with processing, handling, and storing a unit of packed red blood cells.[9]

In 2013, the Centers for Medicare and Medicaid Services (CMS) initiated hospital value-based purchasing in an effort to improve the quality of healthcare.[10] The initiative allows CMS to pay hospitals based on the quality of care provided. As of 2011, CMS reimbursed approximately 86.4% of the cost of a unit of packed red blood cells (PRBCs).[2] Reimbursement rates from CMS can fluctuate according to set quality metrics such as blood transfusions and related outcomes. Blood transfusions can lead to increased cost for hospitals and patients, poor outcomes and less reimbursement from CMS.

Lean Six Sigma (LSS) has been a long-standing quality improvement methodology. Most people relate to Lean with Toyota's great success in the 1980's.[11] Lean is a holistic approach to continuous improvement. Lean eliminates waste, engages personnel, advocates for patient and staff satisfaction, and promotes a high quality of care.[11] Hospital case studies have been presented to show that LSS is successfully utilized in healthcare. Mayo Clinic, ThedaCare and New York City Health and Hospitals Corporation, are among several hospitals that have implemented and sustained LSS for several years.[11-13] LSS methodology has helped hospitals decrease infection rates,[14] increase operating room (OR) efficiency,[13] and increase safety outcomes.[15]

Mayo Clinic Rochester has a higher incidence of blood transfusions compared to the national average in procedures for gynecological malignancies. Institutional data shows the blood transfusion rate from 2004-2010 was 57.3%. The transfusion process is approached in a non-standardized fashion, and could potentially increase the risk of mortality and cancer recurrence in patients with ovarian cancer.[16] The high transfusion rate could negatively impact reimbursement with the adoption of value-based purchasing and carries the potential for negative patient outcomes.

The purpose of this project is to examine the relationship between standardizing a blood transfusion practice utilizing LSS and evidence-based interventions, and the effect this has on the blood transfusion rates in women undergoing open procedures for ovarian or endometrial cancer. This will be accomplished by answering the research question: What are the effects of utilizing Lean Six Sigma methodology and evidence-based interventions to standardize blood transfusion practices, and decrease blood transfusion rates, for women undergoing cytoreduction surgery for ovarian and endometrial cancer, at a large academic hospital?

Literature Review

Increasing economic demands, along with the desire to utilize best practice to optimize patient outcomes, require hospitals to investigate strategies to reduce unnecessary blood transfusions. Patient blood management (PBM) has become a highlighted topic, brought forth by the United States Department of Health and Humans 2011 National Blood Collection and Utilization Survey.[2] Patient blood management incorporates all aspects of patient evaluation and decision-making processes in regard to transfusions with the intent of reaching the best possible outcomes for every individual.[2]

Hospitals that run a PBM program provide education to staff and implement interventions to optimize a patient's hemoglobin level and minimize blood loss. Interventions such as enteral and parenteral iron replacement, Erythropoietin injection, intraoperative blood salvage, Tranexamic Acid administration, and Lean Six Sigma have been examined and have been shown to be beneficial in specific situations.[3] A literature review was performed for the years 2011-2016 to examine strategies that could be implemented in the perioperative period to potentially reduce blood transfusions in women undergoing open procedures for gynecological malignancies.

Current Transfusion Guidelines

Several transfusion guidelines exist in the medical literature. The Society of Thoracic Surgeons (STS) formulates evidence-based patient blood management recommendations for the cardiothoracic patient population.[16] The American Society of Anesthesiologists (ASA) write recommendations based on scientific evidence to provide guidelines for perioperative patients.[17] The Society of Critical Care Medicine (SCCM) offers transfusion recommendations for critically ill and trauma patients.[18] The American Association of Blood Banks (AABB) publishes general transfusion guidelines for all clinical practitioners.[19]

There are some commonalities found amongst the pre-existing guidelines. All organizations recommend not transfusing solely based on a trigger hemoglobin level. Instead, transfuse a patient based on the entire hemodynamic picture.[16-19] Clinicians should evaluate and consider patient-related factors such as age, comorbidities, amount of blood loss, and risk for ischemia in the decision-making process.[1, 16-19] All of the existing guidelines recommend a blood transfusion at a hemoglobin level less than 6g/dl, rarely transfuse at hemoglobin greater than 10g/dl, and leave ambiguity for hemoglobin levels between 6-10 g/dl.[16-19]

Restrictive blood transfusion practice

Blood products are a life-saving but limited resource. Blood transfusions have been identified as, "one of the top five most frequently overused therapeutic procedures in the United States".[20(pg.2753)] Blood transfusions have the potential to increase morbidity and mortality in critically ill and surgical patients.[1,4,21,22] One unit of pRBCs significantly increases the risk of 30-day mortality, morbidity, pneumonia, and sepsis.[22] Transfusing two units of pRBCs significantly increases these risks as well as surgical site infection.[22] Therefore, pRBCs should be transfused one unit at a time.

In 1990, the transfusion requirements in critical care (TRICC) trial demonstrated that a restrictive blood transfusion practice significantly decreased mortality in patients without cardiac disease.[23] Following the TRICC trial, Carless et al. confirmed that a restrictive blood transfusion practice does not increase the rates of cardiac events, pneumonia, thromboembolism, and mortality.[24] The current evidence recommends a transfusion trigger hemoglobin of 7 g/dl in a patient without cardiac disease.[18-20,23-25] Restrictive blood transfusion policies are safe for critically ill patients and should be considered for women undergoing surgery for ovarian cancer.

<u>Patient Blood Management Interventions</u>

Anemia is a significant problem for individuals with ovarian or endometrial cancer. Low hemoglobin levels are associated with decreased functional capacity, poor quality of life, cancer recurrence, and death.[26,27] Anemia is a leading risk factor for a blood transfusion.[28] The rate of anemia has been found to be as high as 95% in women with ovarian cancer who have also received neoadjuvant chemotherapy.[26] Women undergoing surgery for advanced stage ovarian cancer are at risk for severe bleeding related to the length of procedure, tumor biology, neoadjuvant chemotherapy or radiation, and complexity of the procedure.[29] The high incidence of pre-operative anemia, along with the risks associated with surgery, emphasize the importance of addressing interventions to potentially decrease a high blood transfusion rate.

Erythropoiesis-stimulating agents and iron supplementation

Erythropoiesis-stimulating agents (ESAs) are an effective pharmacologic intervention to increase hemoglobin levels for patients with chronic kidney disease, those undergoing high blood loss surgeries, and those receiving myelosuppressive chemotherapy.[28] Erythropoietin has been shown to be highly effective in increasing hemoglobin levels and has been known to produce the equivalent of 1 unit of blood per week of treatment.[30] Erythropoietin is especially effective in cancer patients when it is administered with iron therapy.[28] As with every intervention, providers should weigh the risks and the benefits for every individual.

Cancer patients are susceptible to complications from ESAs. The most common complications are increased mortality rate and increased risk of thromboembolic events.[31-34] Erythropoietin has been shown to increase mortality by 10%.[32] ESAs significantly increase the risk of cancer recurrence and death in patients with ovarian cancer.[31] Currently, Erythropoietin has a black box warning to alert providers of the serious risks associated with the use of ESAs in patients with cancer.[35]

Not only is the administration of ESAs potentially hazardous, but also time-consuming to reach a therapeutic effect. Erythropoietin and iron therapy require weeks to achieve the best results.[35] Gynecology-oncology surgeons, at the Mayo Clinic in Rochester, offer women with ovarian cancer next day surgery. This is an enormous satisfier for patients. Next day surgery does not allow for the time that is required of iron supplementation and Epoetin.

There are only two current studies in the literature that address benefits and risks of ESAs in cancer patients.[31,33] Neither of the studies discuss perioperative use and outcomes of Erythropoietin in ovarian cancer patients. The documented negative outcomes, along with limited research available, prevent the use of Erythropoietin in practice in an attempt to improve perioperative blood transfusion rates for women undergoing open surgical procedures for malignant gynecological tumors.

Intraoperative blood salvage

Intraoperative blood salvage (IBS) involves the collection, filtration, washing, and administration of shed blood during surgery.[36] A variety of surgical specialties, especially orthopedic and cardiac surgery, utilize IBS as a cost-effective and safe method to reduce the rate of allogenic blood transfusions.[37] IBS has been shown to decrease the requirement for allogenic blood transfusions by 38%.[38] The use of IBS in patients with cancer has been a controversial topic for decades. The hesitancy to use IBS with cancer patients stems from one case study published in 1975.[39] As a result of this case report, providers conclude that administration of salvaged blood during surgery in a patient with cancer would lead to diffuse metastases of cancer.

Numerous studies have since been performed on the topic of IBS and its role in cancer surgery. There are two interventions that can make IBS safer for the patient with cancer. The type of filter used in the blood salvage machine can impact how well cancer cells are removed. Evidence advocates for the use of leukocyte depletion filters.[37,40-42] Leukocyte depletion filters are effective in the removal of tumor cells and do not increase the risk of cancer recurrence.[40-42] Another recommended intervention is the practice of irradiating salvaged blood prior to administrating the blood to the patient.[43]

Cell saver has been studied in patients with prostate adenocarcinoma, hepatocellular carcinoma, cervical, and spine cancer. All of the studies suggest that IBS is safe to use on patients with cancer.[36,40,44-50] None of the studies show that IBS causes metastatic disease. [36,40,44-50] Research in the surgical specialty of gynecology oncology surgery is limited to cervical cancer. Studies on the use of IBS in high blood loss procedures for ovarian cancer are nonexistent. Also, the research done on liver, spine, cervical, and prostate cancer are retrospective chart reviews or prospective cohort studies. [30,34,38-44] There is no strong evidence to support the use of IBS in ovarian cancer surgery.

Antifibrinolytics

Tranexamic acid (TA) is a synthetic amino acid that inhibits plasminogen activation. Tranexamic acid was introduced into practice more than 40 years ago, and has been used in a variety of surgical settings to reduce the amount of blood loss, and blood transfusions administered to patients.[51] Tranexamic acid is the antifibrinolytic of choice in the perioperative period.[28] Several, recent studies support the efficacy of TA in an array of surgical settings including cardiac,[52] orthopedic,[53,54] trauma, [55,56], and plastics.[57] No serious adverse events have been reported as a result of TA administration.[55,56,58]

Venous thromboembolism

In comparison to other patient populations, patients with cancer are at risk for venous thromboembolic (VTE) events. Most recent data suggests a VTE rate of 16% in women diagnosed and treated for ovarian cancer.[59] A venous thromboembolic event can be a dangerous complication. VTE is the leading cause of death in patients receiving chemotherapy.[60,61] Intra-operative interventions such as low molecular weight Heparin and intermittent sequential compression devices can be applied to provide prophylactic prevention of a VTE. Despite documented interventions, VTE rates remain high in patients with cancer receiving chemotherapy.[59,61]

Three randomized control trials (RCTs) have examined the effects of Tranexamic acid administration in cancer patients; breast, prostate and ovarian.[51,62,63] A randomized double-blind, placebo-controlled study showed that TA can be effective in significantly reducing blood loss and blood transfusions in this population.[51] The dose of TA was 15mg/kg administered one-time prior to incision.[51] The VTE rate was 7% with a majority of them occurring in the placebo group.[51] Tranexamic acid has been shown to be safe, free from adverse effects while decreasing blood loss and intraoperative blood transfusions in a multitude of surgical specialties, including procedures for advanced ovarian cancer.[51,58]

Programs to reduce blood transfusions

The pressure to conserve blood, improve quality of care, and increase hospital revenue has required hospitals to examine their blood transfusion practices. In 2007, the University of Alabama at Birmingham implemented a restrictive blood transfusion policy for patients undergoing surgery for gynecologic malignancies.[64] The transfusion initiative consisted of two guidelines: no pRBC transfusion until the hemoglobin drops below 7g/dl, and transfusions were to be administered one unit at a time.[64] Clinicians were required to document the indication for transfusion. Gynecologic oncologists tended to transfuse two units of pRBCs at a time despite the guidelines. The overall compliance rate was 81.1%, but only 64.7% of the transfusions were administered one unit at a time.[64] There was no significant difference in infection rates, thrombotic events, and mortality between the compliant and noncompliant transfusions.[64] The results of this retrospective chart review suggest that a restrictive blood transfusion practice is safe in patients undergoing surgery for ovarian cancer.

A prospective study looked at the appropriateness of perioperative blood transfusions in undergoing cancer surgery. Over-transfusion was defined as a postoperative hemoglobin exceeding 10g/dl.[65] Based on this criterion, more than half of patients were over-transfused. The rate of over-transfusion was highest in patients who received two units of pRBCs.[65]

New York Methodist Hospital (NYMH) implemented a monitoring program to ensure the appropriateness of blood transfusions based on current evidence. The program was a multidisciplinary effort. The protocol allowed for one unit of pRBCs to be made available for patients with a hemoglobin greater than 7g/dl, and two units of pRBCs if hemoglobin was less than 6g/dl.[5] Physicians were required to document and justify the need for blood. If the blood bank technologist discovered that the requests did not meet the protocol criteria, the request was sent to a departmental reviewer. This process emphasized patient safety.[5] The program was monitored for two years following implementation. The blood transfusion rate decreased 33.2% in the first year and 38.1% in the second year.[5] The decrease in transfusion rates reduced the complication rates and cost of blood products.[5]

Several hospitals have had success in implementing different interventions to reduce the rates and increase the appropriateness of blood transfusions.[5,64,65] Restrictive transfusion policies, monitoring programs, and transfusion of one unit of pRBCs at a time have resulted in decreased complications, increased appropriateness of transfusions, and costs savings to the hospital. Women undergoing debulking surgery could benefit from similar interventions in a large academic hospital.

Lean Six Sigma

Lean and Six Sigma are quality improvement methodologies that have been around since the late 1980’s. Lean is a patient-centered process which emphasizes supporting the mission of the organization, utilizing the capabilities of individuals, adding value, and correcting existing system problems.[11] Six Sigma is designed to identify and correct the causes of errors.[15] A higher level of sigma is equivalent to a higher level of quality.[66] Six Sigma encompasses a five-stage process: Define, Measure, Analyze, Improve and Control (DMAIC).[15] Six Sigma provides the statistical rigor while Lean results in the reduction of waste in a process. Together, LSS can improve the quality of care, increase customer satisfaction, decrease costs, and increase revenue.[15]

Lean and Six Sigma principles complement each other. They have been used simultaneously in healthcare since 1998.[15] Implementation of quality improvement (QI) methodologies has aided healthcare professionals in the quest to provide exceptional patient care. Significant improvements have been made across outpatient, inpatient, and operating room settings. LSS has been successfully utilized in healthcare to improve operating room efficiency, optimize the patient experience, decrease operation complications, decrease patient infection rates, and decrease mortality.[15] Specifically, in the perioperative setting, LSS has shown significant improvement in patient care through increasing operating room efficiency and decreasing mortality.[13,67,68]

There are no randomized control trials related to the use of LSS in the operating room environment. However, specific studies have shown that LSS can contribute to significant improvements in patient care and the function of an organization. The noteworthy successes of

LSS suggest there is a place for the use of LSS in improving the patient experience, decreasing cost, and decreasing negative patient outcomes.

Patient blood management is a topic undergoing intense scrutiny. Researchers are advocating for the conservation of a valuable resource with the goal of optimizing patient outcomes and increasing hospital revenue. Surgical patients with advanced ovarian or endometrial cancer present with unique risks. They are often anemic from neoadjuvant chemotherapy, undergoing procedures that could result in a large amount of blood loss, and are susceptible to cancer recurrence along with thromboembolic events.

Current guidelines support the use of a restrictive blood transfusion policy and the transfusion of one unit at a time for stable patients undergoing open procedures for ovarian, therefore, should not be implemented in this quality improvement project. Tranexamic Acid has been shown to be a safe and effective intervention in gynecologic oncology procedures. Lean Six Sigma methodology has shown success when utilized in the health care setting. There are no studies in which LSS was utilized to decrease a blood transfusion rate in gynecology-oncology surgery.

This study attempts to answer the following question: What are the effects of utilizing Lean Six Sigma methodology and evidence-based interventions to standardize blood transfusion practices, and decrease blood transfusion rates, for women undergoing cytoreduction surgery for ovarian and endometrial cancer, at a large academic hospital?

Methodology

Doctors Bradley Narr (Chair of the Department of Anesthesia and Perioperative Medicine), Bobbie Gostout (Chair of the Department of Gynecology Surgery), and Ann Sullivan (CRNA supervisor), supported the investigation of the research question at Mayo Clinic, Rochester, Minnesota. This quality improvement project was a multi-disciplinary effort. The steering team consisted of Sumer Wallace, MD, Christopher Jankowski, MD, Sean Dowdy, MD, Jamie Bakkum-Gamez, MD and Jessica Halverson, CRNA. The team attended the Academy of Excellence in Healthcare at The Ohio State University Fisher College of Business, where they underwent extensive training in LSS principles and applied knowledge gained to this project. This continuous improvement project offered high-payback in the form of cost savings, patient outcomes, and encouraging multidisciplinary collaboration.

Setting

The Mayo Clinic Rochester (MCR) is a 2,000 bed, academic medical center located in the upper Midwest. Mayo Clinic Rochester is comprised of two hospitals, along with an outpatient surgery center. There are approximately 87 operating rooms between the two campuses: Rochester Methodist Hospital (RMH) and Saint Marys Hospital. The gynecology-oncology operating rooms are located on the RMH campus. Mayo Clinic, Rochester, Minnesota IRB and the University of Michigan, Flint IRB approved this project as exempt because it is a quality improvement study.

Study Design

The quality improvement project was approached using LSS strategies. The framework for the study was define, measure, analyze, improve, and control (DMAIC). DMAIC is a five step data-driven process improvement tool utilized in continuous improvement.[69] The conceptual model for this quality improvement initiative can be seen in Figure 1.

Conceptual Model

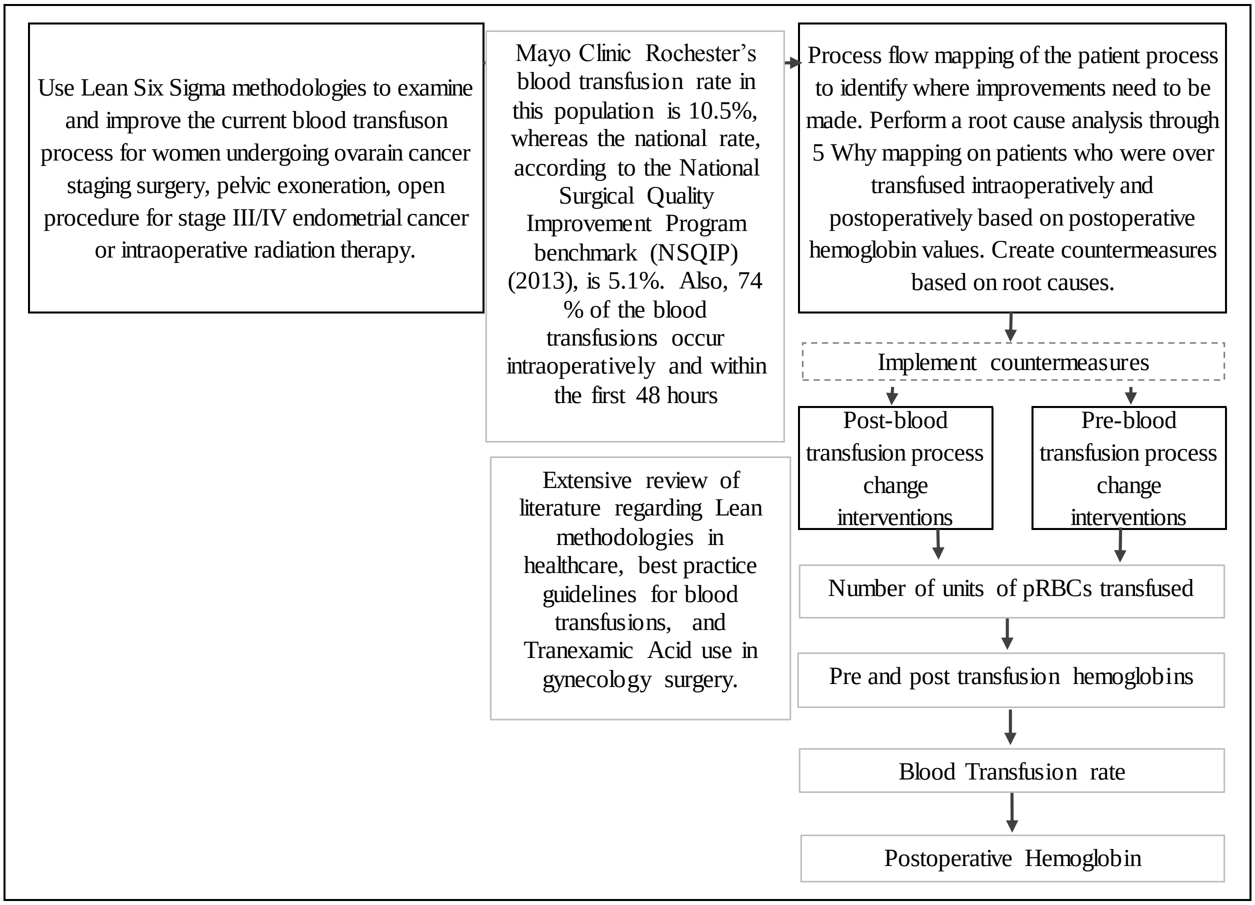


Figure 1 Conceptual model for gynecologic oncology perioperative blood transfusion process improvement project

Define

The define phase involves identifying the problem, setting a goal, and establishing the project timeline. The steering team identified the problem and the current status of Mayo Clinic's transfusion rate in gynecology-oncology surgery. The team proposed a goal of 30% reduction in blood transfusion rates in women undergoing malignant abdominal surgical procedures. The project timeline is embedded in the A3 as shown in Appendix A.

The steering team established that an intraoperative transfusion would be any transfusion administered intraoperatively through the post-anesthesia care unit (PACU) stay. A postoperative transfusion is one that occurs from the time the patient leaves the PACU through 48 hours postoperative. The post-transfusion hemoglobin goal for this population is 8.5-9.5g/dl.

Measure

The purpose of the measure phase is to establish baseline data. Institutional data shows the blood transfusion rate from 2013-2014 was 56%. Further investigation of data showed investigators that open malignant abdominal procedures account for 57% of blood transfusions in the gynecology surgery department. Data pulled from 2010-2014 disclosed that the majority of blood transfusions in gynecologic oncology surgery occurred during the intraoperative and immediate forty-eight hours postoperative phases. The data obtained allowed researchers to determine where to focus efforts in order to make the largest impact on high blood transfusion rates.

Analyze

The current blood transfusion process was analyzed by developing a flow map, otherwise known as a swim lane map. Appendix B depicts the standard flow of the perioperative transfusion process. The process map allowed the team to identify areas of opportunity for improvement.

The process map highlighted ambiguity surrounding the blood transfusion process, specifically during the intraoperative and postoperative period (Appendix B). Following this discovery, the team performed a “5 Why” root cause analysis. The analysis was performed by mapping the process on individual patients who were over-transfused intraoperatively, postoperatively, or both based on postoperative hemoglobin of 9.5 g/dl. The root cause maps allowed researchers to follow the flow of patient management intraoperatively and postoperatively. Appendix C illustrates an example of an intraoperative “5 Why” cause map. Appendix D depicts an example of a postoperative “5 Why” cause map. The cause maps provided clarity and revealed that patients were over-transfused for the following reasons:

- large academic center with many learners along with no standardized guidelines
- pRBCs were administered two units at a time
- trigger hemoglobin was higher than evidence suggests it should be
- debulking and malignant abdominal surgeries are complex, long cases resulting in a large amount of blood loss and fluid volume shifts

Improve/Implementation

In response to the root cause analysis, the team created countermeasures with the intent to improve the process, to decrease blood transfusion rates, and to improve patient care. The first countermeasure was created with the goal of decreasing blood loss: administration of TA. Tranexamic acid has been studied vigorously and is being utilized in many other surgical specialties.[51-57] A study performed by Lundin et al. supports the safety and efficacy of the use of TA in gynecology-oncology surgical patients.[51] The gynecology-oncology providers assessed the patient for exclusion criteria in the prescreening clinic. The exclusion criteria can be seen in Table 1. When a patient was a candidate for TA, the surgical team ordered the infusion the evening before surgery. Tranexamic Acid is administered in the operating room prior to incision in a one-time dose of 15ml/kg. To assure patient safety, the incidence of VTE was monitored continuously by the gynecology-oncology surgical team.

Table 1. Exclusion Criteria for Tranexamic Acid

1. Treatment with anticoagulation in the last month 2. Allergy to TA 3. History of present lab signs of bleeding disorder, coagulopathy, or thromboembolic state 4. History of MI in the last year 5. Present unstable angina or severe CAD 6. Reduced renal function (creatinine >2.5) 7. Acquired defective color vision

A group of countermeasures was created to address communication in the operating room (OR). All providers in the operating room stopped at critical junctures during the operation to discuss current blood loss and status of the surgery. This communication occurred when there was at least five hundred milliliters of fluid (blood, ascites, etc.) in the suction canister. During this hard stop, the multidisciplinary team discussed the phase of the surgery and hemostasis of the surgical field.

The gynecology-oncology surgeons created a hemostasis checklist to improve communication, and identify a checkpoint at which the surgeon examined the abdomen for any sign of active bleeding. The hemostasis list was a hard stop prior to closing the surgical wound. The circulating registered nurse (R.N.) called out each site, and the surgeon examined said site and affirmed hemostasis.

Concurrently with this project, Dr. Kor developed an institution-wide transfusion guideline supported by best practice.[1,17,64] The blood transfusion guideline made the following recommendations:

- RBC transfusion should be considered if Hb <7 g/dL,

- RBC transfusion may be beneficial in patients with acute coronary syndrome with Hb ≤ 8 g/dL,
- Hemoglobin concentration ≤8 g/dL with symptoms thought to be related to anemia, including:
  - Hypotension unresponsive to fluid resuscitation
  - Unexplained tachycardia unresponsive to fluid resuscitation
  - Cardiac chest pain
  - Congestive heart failure

Following development of countermeasures, the steering team educated staff and learners throughout the department of anesthesia, the department of gynecology surgery, and the department of nursing. The education was in the form of presentations at several staff, quality improvement, and department meetings. The entire process for this quality improvement project was compiled into an A3 (Appendix A). Project implementation occurred on September 28, 2015.

Control

Following International Review Board (IRB) approval at Mayo Clinic, Rochester Minnesota, and University of Michigan, Flint, a quantitative, retrospective chart review of gynecologic-oncology patients was performed. A quantitative study was selected because the study was carefully designed prior to the data collection. A data collection tool was utilized to collect hard data in the form of numbers and statistics. Subsequently, adult women scheduled to undergo a laparotomy procedure for ovarian or endometrial cancer were included in the pre-implementation group for this study.

Permission to review the patient's electronic medical record (EMR) was obtained on all patients entering the Mayo Clinic health system and documented electronically. Charts were reviewed for all gynecology-oncology patients who met inclusion criteria. The pre-implementation cohort included patents who had a laparotomy procedure for ovarian or endometrial cancer between September 1, 2014 and September 25, 2015. The post-implementation cohort included patients having a laparotomy procedure for ovarian or endometrial cancer after September 27, 2015 through March 30, 2016.

Abstracted data included patient demographics, cancer type and stage, surgical procedure, pre-operative hemoglobin, postoperative hemoglobin, number of packed red blood cells (pRBC) units transfused, where the transfusion occurred (intraoperative, postoperative), estimated intraoperative blood loss, if TA was administered, if the transfusion was appropriate based on new guidelines, length of surgery, postoperative complications, and 30 day mortality. The data was collected and placed in an excel spreadsheet (Appendix E). The data collection tool was saved on a private computer drive in the Mayo Clinic server.

Results

A total of 184 women were included in the pre-implementation group, and 89 women in the post-implementation group in this project. Demographic and surgical variables are outlined in Table 2. The mean age for the pre-implementation cohort was 62.4 years and 64.0 years for the post-implementation cohort. Ovarian cancer (82.6% and 83.1%) was the most common diagnosis in both groups. A majority (83%) of patients in both cohorts had advanced stage or recurrent cancer. A majority (98%) of women in both cohorts were ASA II or III. Within the surgical variables, there was a decrease in operative time from 279.3 to 241.7 minutes (p=0.01) and a reduction in estimated blood loss from 500 mL to 300 mL (p=0.009).

Table 2. Demographic, Surgical, and Postoperative Variables in Pre and Post Intervention Groups

Characteristics	Pre-intervention (N=184)	Post-intervention (N=89)	p-value✦
Age, Mean(SD)	62.4 (12.4)	64 (11.6)	0.32
BMI (kg/m^2), Mean (SD)	28.7 (7.7)	29.2 (7.9)	0.62
ASA score			
I	3 (1.6%)	2 (2.2%)	
II	107 (58.3%)	41 (46.1%)	
III	74 (40.2%)	46 (51.7%)	
Prior history of VTE	19 (10.3%)	7 (7.9%)	0.52
Current tobacco use	13 (7.1%)	12 (13.5)	0.08
Cardiovascular disease	59 (32.1%)	38 (42.7%)	0.08
EBL (mL), Median (IQR)	500 (250,800)	300 (200, 600)	0.009
Operative time (min), Mean (SD)	279.3 (118.6)	241.7 (105.6)	0.01
Diagnosis			0.91
Ovarian cancer	152 (82.6%)	74 (83.1%)	
Endometrial cancer	32 (17.4%)	15 (16.9%)	
Stage			0.50
I-II	31 (16.8%)	15 (16.9%)	
III-IV	107 (58.2%)	46 (51.7%)	
Recurrent	46 (25.0%)	28 (31.5%)	
Presence of ascites	49 (26.6%)	21 923.6%)	0.59
Volume of ascites (mL), Median (IQR)	1100 (300,2500)	1100 (600, 2000)	0.62
Length of stay (days), Median (IQR)	4 (3, 6)	4 (3, 6)	0.87

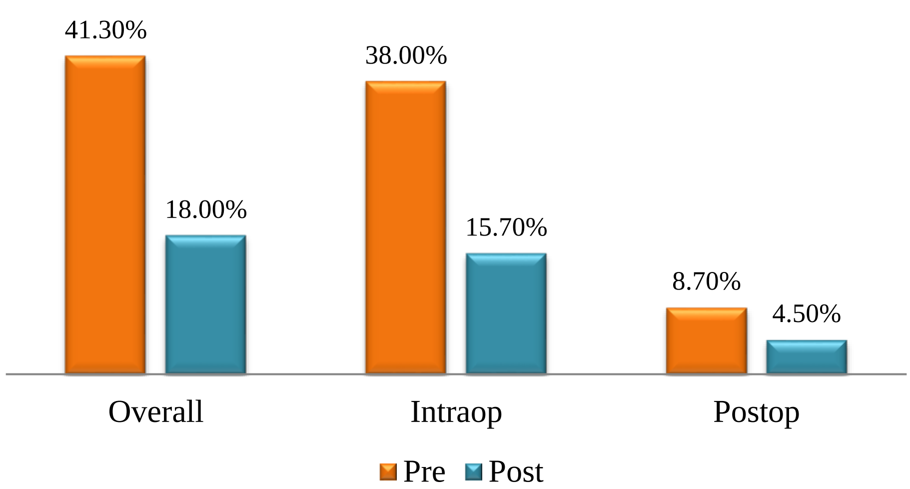
Abbreviations: IQR, interquartile range; SD, standard deviation

✦Comparisons between cohorts were evaluated using the two-sample t-test for age and BMI, the Wilcoxin rank sum test for ASA score, EBL, volume of ascites and length of stay, and the chi-square or Fisher's exact test for categorical variables.

Blood Transfusion Rates

Institutional data from the study setting showed the transfusion rate was twice the national average, 5.1%, from 2004-2010. The transfusion rate for the year prior to the implementation of guideline-based interventions was 41.3%, at the Mayo Clinic. The overall blood transfusion rate following the implementation of quality improvement methods and evidence-based interventions, was significantly decreased to 18.0% ($p<0.001$). Intraoperatively, the blood transfusion rate significantly decreased from 37.5% to 15.7% ($p<0.001$). There was a reduction in the postoperative transfusion rate from 8.7% to 4.5% ($p=0.21$). Figure 2 depicts the significant reduction in blood transfusion rates overall, in the intra-operative phase, and in the post-operative phase of patient care.

Figure 2. Transfusion Rates



Number of Units Transfused

Another variable measured in this quality improvement project was the number of packed red blood cells transfused. Overall, the number of pRBCs transfused decreased from 169 units to 39 units ($p<0.0023$). The number of intraoperative pRBCs significantly decreased from 148 units in the pre-implementation group, to 33 units post-implementation (p<0.001). Details of the number of units transfused in the perioperative phase and 48 hours postoperative can be seen in Table 3.

Table 3. Number of Packed Red Blood Cell Units Transfused

Number of Units	Pre-intervention (N=184)	Post-intervention (N=89)
Intraoperative Units		
0	115 (62.5%)	75 (84.3%)
1	26 (14.1%)	4 (4.5%)
2	21 (11.4%)	6 96.7%)
3	10 (5.4%)	3 (3.4%)
4	10 (5.4%)	0 (0.0%)
5	2 (1.1%)	0 (0.0%)
8	0 (0.0%)	1 (1.1%)
Postoperative Units		
0	168 (91.3%)	85 (95.5%)
1	11 (6.0%)	2 (2.2%)
2	5 (2.7%)	2 (2.2%)
Intra- or Postoperative Units		
0	108 (58.7%)	73 (82.0%)
1	25 (13.6%)	5 (5.6%)
2	27 (14.6%)	6 (6.7%)
3	12 (6.5%)	3 (3.4%)
4	7 (3.8%)	0 (0.0%)
5	4 (2.2%)	1 (1.1%)
6	1 (0.5%)	0 (0.0%)
8	0 (0.0%)	1 (1.1%)

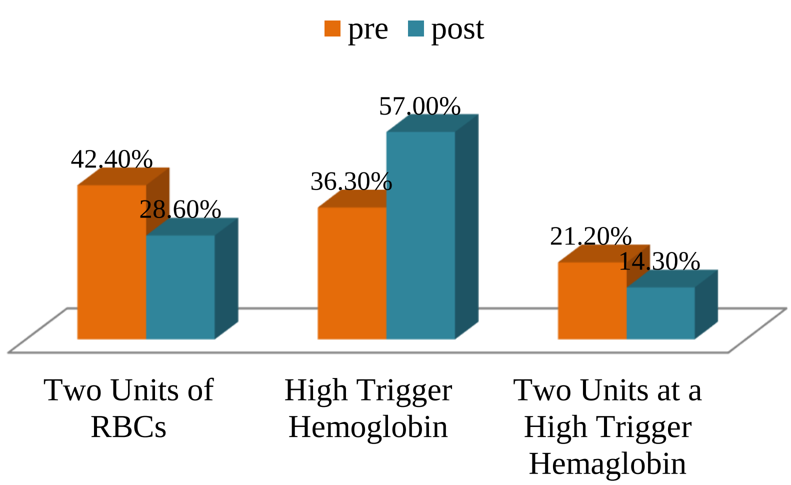
Tranexamic Acid

Prior to project implementation, the department of gynecology-oncology did not use Tranexamic acid. However, post-implementation, 60.7% of patients received TA based on the current evidence-based guidelines. Of the 54 women who received TA, 20.4% also received a blood transfusion. There were 35 patients who did not receive TA secondary to meeting exclusion criteria for TA administration as listed in Table 1, surgeon preference, or provider unfamiliarity with the protocol. Five patients (14%) who did not receive TA also received a blood transfusion.

<u>Over-transfusions</u>

Over-transfusions were measured according to best practice transfusion guidelines, the department goal of post-operative hemoglobin between 8.5-9.5g/dl, and the number of pRBC units transfused at a time. There were three primary reasons for an over-transfusion; a transfusion was administered at a higher than recommended trigger hemoglobin, two units were transfused at a time, or a patient received two units for a higher than recommended hemoglobin. The rate of over-transfused patients remained at 43% for both groups. There was significantly more blood loss in patients who were considered over-transfused ($p<0.001$) in both cohorts. Figure 3 displays the root causes that contributed to over-transfused patients in each cohort.

Figure 3. Root Causes of Overtransfusions



Complications

Table 4 illustrates the various complication variables between the pre and post implementation groups. The rate of readmission was significantly higher in the pre-implementation group at 12.5% (p=0.002). There were no other significant differences in complications. The VTE rate was monitored throughout the study to ensure safety of TA administration. There was no incidence of VTE in patients who received TA.

Table 4. Comparison of Complications

Postoperative Complications w/in 30 days	**Pre-implementation (N=184)**	**Post-implementation (N=89)**
Readmission	23 (12.5%)	1 (1.1%)
Reoperation	8 (4.3%)	0 (0.0%)
Infection- Pulmonary	6 (3.3%)	2 (2.2%)
Infection- Sepsis	8 (4.3%)	0 (0.0%)
Infection- Wound	10 (5.4%)	4 (4.5%)
Infection- pelvic Abscess	1 90.5%)	0 (0.0%)
Unplanned ICU admit post-op	6 (3.3%)	0 (0.0%)
Post-op anastomosis leak	1 (0.5%)	0 (0.0%)
Post-op perforation, non-anastomosis leak	1 (0.5%)	0 (0.0%)
Small bowel obstruction	1 (0.5%)	0 (0.0%)
DVT/PE	3 (1.6%)	1 (1.1%)

Discussion

This quality improvement project was a complex process that emphasized multidisciplinary teamwork, Lean Six Sigma methodologies, and evidence-based interventions. This study shows that multidisciplinary teamwork along with evidence-based guidelines can successfully improve patient care. The Department of Gynecologic Oncology Surgery, along with the Department of Anesthesia and Perioperative Medicine, at the Mayo Clinic, significantly reduced the blood transfusion rate by 56.4%, and significantly decreased the units of pRBCs transfused.

Blood is an expensive, scarce resource that when administered to patients, can potentially result in negative outcomes such as VTE, longer hospitalization, and mortality.[2-4] Cancer patients are vulnerable to cancer recurrence and infection as a result of blood transfusions.[6] The negative effects, expense, and scarcity of blood requires hospitals to examine transfusion practices in the best interest of patient outcomes and economics.

Lean Six Sigma provided a framework to define, measure, analyze, improve and control the blood transfusion process, for women undergoing open procedures for ovarian or endometrial cancer. Lean Six Sigma has been used successfully in healthcare and perioperative care to improve the quality of care, increase customer satisfaction, decrease costs, and increase revenue.[15] Mapping sessions and root cause analysis implemented during this project, allowed the team to identify gaps in standardization, and to determine causes for over-transfusion in gynecology-oncology surgery.

Based on the knowledge gained from the measurement and analytic stages of this project, the steering team created countermeasures to improve the transfusion process. The team recommended staff communications in the operating room following the occurrence of 500mL of fluid in the suction canister, and a hemostasis checklist was implemented to be utilized at the end of the case. The team provided education amongst several departments regarding the measures to standardize the blood transfusion process.

A literature review provided evidence-based interventions that potentially decrease blood transfusion rates. Several studies support the safety and efficacy of restrictive blood transfusion practices in critically ill patients.[18-20, 23-25] Current evidence suggests providers can safely transfuse for a hemoglobin less than 7g/dl in healthy patients, and 8g/dl in a patient with coronary artery disease.[18-20, 23-25] The updated, institution-wide, transfusion guidelines contributed to the success of this project.

Another evidence-based countermeasure was the implementation of TA. Prior to this study, TA was not utilized in the gynecologic oncology surgery. Lundin et al. showed that TA 15mg/kg administered once immediately before incision reduces blood loss and transfusion rates, in women undergoing surgery for advanced stage ovarian cancer.[51] This study demonstrated that TA can be utilized in the gynecologic oncology population, without causing adverse effects.[51] The current project reiterates the findings from Lundin et al. in that Tranexamic acid was administered at the same dose within thirty minutes prior to incision. Blood transfusion rates were significantly decreased to 18% ($p<0.001$), and blood loss was decreased by 200ml ($p=0.009$). Study findings indicated that there were no negative outcomes related to TA.

Few studies are published on efforts made to improve blood transfusion processes. New York Methodist Hospital established a monitoring program to ensure compliance with institutional transfusion guidelines.[5] This monitoring program achieved great success in decreasing the rate of unnecessary blood transfusions and hospital expense. Another study examined the compliance of a restrictive transfusion policy in gynecology-oncology surgery. This study showed that a restrictive transfusion recommendation can be implemented in gynecologic oncology patients.[64] However, it also revealed that improvement could be made to administer more blood in single unit increments, and limit transfusions for hemoglobin greater than 7g/dl.[64]

Limitations

The over-transfusion rate remained high for the institution described in this study, before and after implementation of several interventions. A weakness of this study is the inability to capture all the factors contributing to the perceived need for a transfusion. Despite the existing quality assurance documentation surrounding a blood transfusion at this hospital, other variables remain unknown. The rate of over-transfusions may be related to an individual patient's status such as low urine output, position changes, or physiologic responses to the procedure. Clinicians in this study were not asked to chart details surrounding their transfusion decision process. Examining health care providers' documentation practices may afford greater insight in the management of blood loss. Efforts can be made to address over-transfusion with the intent to further reduce the number of units transfused.

Dissemination

The author presented this quality improvement project at the Mayo Clinic Institutional Process Improvement meeting on January 22, 2016. The steering team will present this project for one continuing education credit at a staff conference open to 300 Certified Registered Nurse Anesthetists (CRNAs) on June 5, 2017. On October 3, 2017, the steering team will be attending the 43rd Annual Mayo Clinic Seminar for Nurse Anesthetists. The team will be presenting a tale titled: "Beyond Enhanced Recovery: Using ERAS Pathways as a Platform for Continuous Improvement"

Conclusion

Despite education and evidence-based countermeasures surrounding current blood transfusion recommendations, the rates of over-transfusions remained unchanged at 43% between the two cohorts. The rate of blood transfusions that occurred at a higher than recommended trigger hemoglobin, increased from 36.3% to 57.0%. There are variables which could contribute to the unchanged over-transfusion rate; however, this study did not implement a monitoring system or documentation requirement to capture real-time factors that were involved in the decision to transfusion at a higher hemoglobin or to transfuse two units of blood at a time. This is an area of research that has the potential to further improve the blood transfusion process.

Control for long-term sustainment of this work requires monitoring the blood transfusion rates, number of pRBCs transfused, and over-transfusion rates. Currently, there is no monitoring in place for the variables in this study. The Department of Anesthesiology and Perioperative Medicine, along with the Department of Gynecology Surgery, is working on long term monitoring of all enhanced recovery pathways and quality improvement interventions.

While this project achieved several good outcomes, there is still much that can be learned and studied to possibly further improve the blood transfusion process. Define, measure, analyze, improve and control (DMAIC) could be applied to the high rate of over-transfusion. This type of project would require departmental support again and training in the use of quality improvement methodologies.

There were several benefits as a result of this project. The design of this study raised awareness that, in a large academic center, multidisciplinary efforts can achieve great outcomes for our patients. Providers willing to embrace change and advocate for a lean culture made significant improvements in patient care. The education provided prior to implementation raised awareness of how to apply quality improvement methodologies to address a clinically relevant problem. The process also illustrated the importance of implementing best practice when faced with the decision to administer a blood transfusion to a woman with ovarian or endometrial cancer.

Patient blood management is an important topic in today's healthcare market. Strategies such as incorporating a restrictive blood transfusion protocol, addressing problems in the current system as identified in a root cause analysis, formulating acceptable countermeasures, and establishing sustainability can benefit both the hospital and patient. These strategies significantly reduced the overall blood transfusion rate by 56.4% and the intraoperative blood transfusion rate by 58.1%. The countermeasures in this project resulted in a significant decrease in the number of pRBCs transfused intraoperatively. This project proves that a multidisciplinary approach, when combined with evidence based guidelines and Lean Six Sigma principles, can lead to a successful process change in healthcare and ultimately assure clinicians are giving the best patient care possible.

Appendices A-E

Appendix A: A3

Reducing Perioperative Blood Transfusion in Gyn/Oncology Patients A3 Form

Date: 7/1/2015

Background:

Mayo Clinic aims to deliver the highest quality and most affordable care. Blood transfusion can lead to increased cost, patient dissatisfaction, and poor outcomes.

Current Condition:

Malignant abdominal hysterectomy has the highest rate of transfusion in our department at 57%.

Problem Statement:

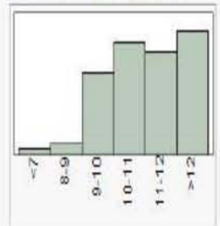
Our transfusion rate is higher than the national benchmark(NSQIP)(10.7% vs. 5.1%) and is approached in a non-standardized fashion.

Problem Analysis/Root Cause:

Non standardized approach to blood transfusions
Large academic center with many providers and learners
Transfuse 2 units at a time
Trigger Hemoglobin is higher than evidence suggests it should be
High blood loss procedure
No standardized education

Ovarian Cancer Procedures Requiring Transfusion 2013-2014

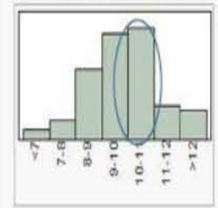
Preoperative Hemoglobin:



Frequencies

Level	Count	Prob
<7	1	0.01235
8-9	2	0.02469
9-10	15	0.18519
10-11	21	0.25926
11-12	19	0.23457
>12	23	0.28395
Total	81	1.00000

Postoperative Hemoglobin:



Frequencies

Level	Count	Prob
<7	2	0.02469
7-8	4	0.04938
8-9	15	0.18519
9-10	23	0.28395
10-11	24	0.29630
11-12	7	0.08642
>12	6	0.07407
Total	81	1.00000

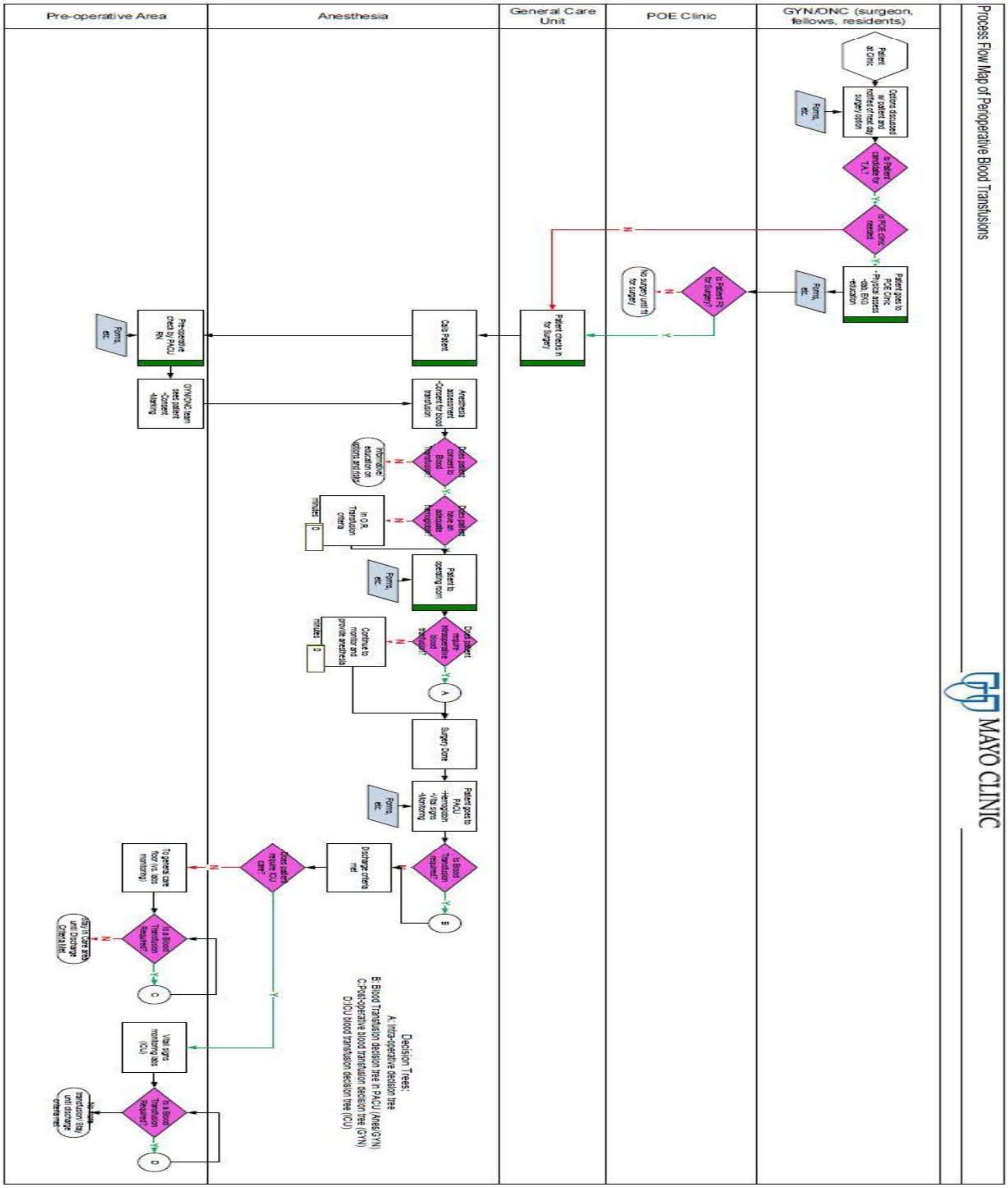
Countermeasures:

1	Tranexamic Acid
2	Institution-wide transfusion gudielines
3	Increase communication intraoperatively
4	Hemostatsis checklist
5	Postoperative bleeding order set
6	Trainee and staff education
7	Timing and amount of blood draws

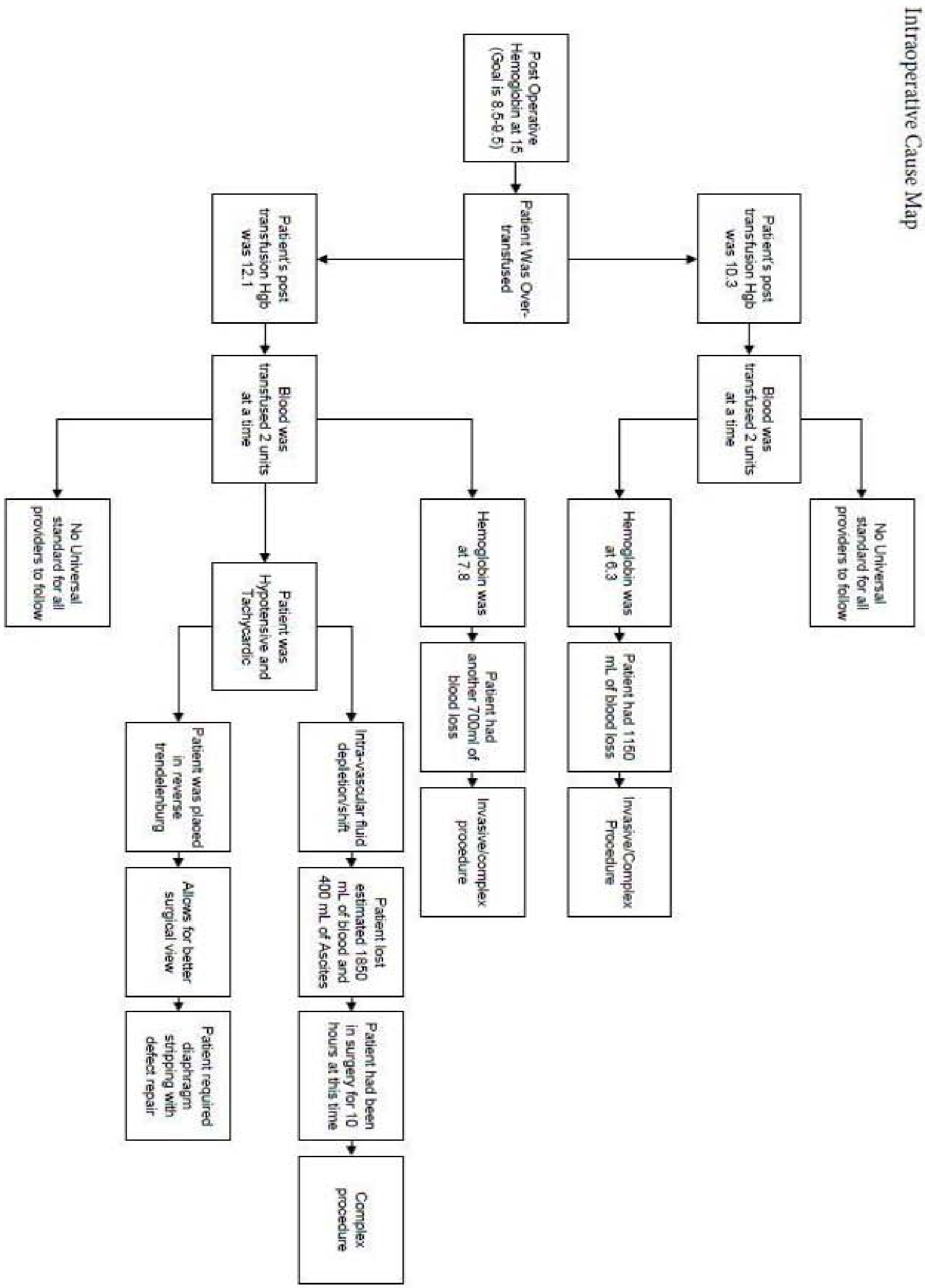
Action Plan:

	What	Who	When	Status
1	Project Charter	Steering Team	06/29/15	Complete
2	Process mapping	Steering Team	07/01/15	Complete
3	5 Why Analysis	Steering Team	07/24/15	Complete
4	Cause Maps	Steering Team	07/26/15	Complete
5	Project status checkpoint (transfusion module)	Steering Team	9/14/2015	Complete
6	Stakeholder Analysis	Steering Team	09/15/15	Complete
7	Fellow/PA education	Steering Team	09/16/15	Complete
8	Resident education	Steering Team	09/21/15	Complete
9	Anesthesia dept. education	Steering Team	09/23/15	Complete
10	GYN division meeting	Steering Team	09/23/15	Complete
11	Project Implementation	Steering Team	09/28/15	Complete
12	Develop a Control Plan	Steering Team	11/15/15	
14	Data Collection	Steering Team	12/15/15	
15				

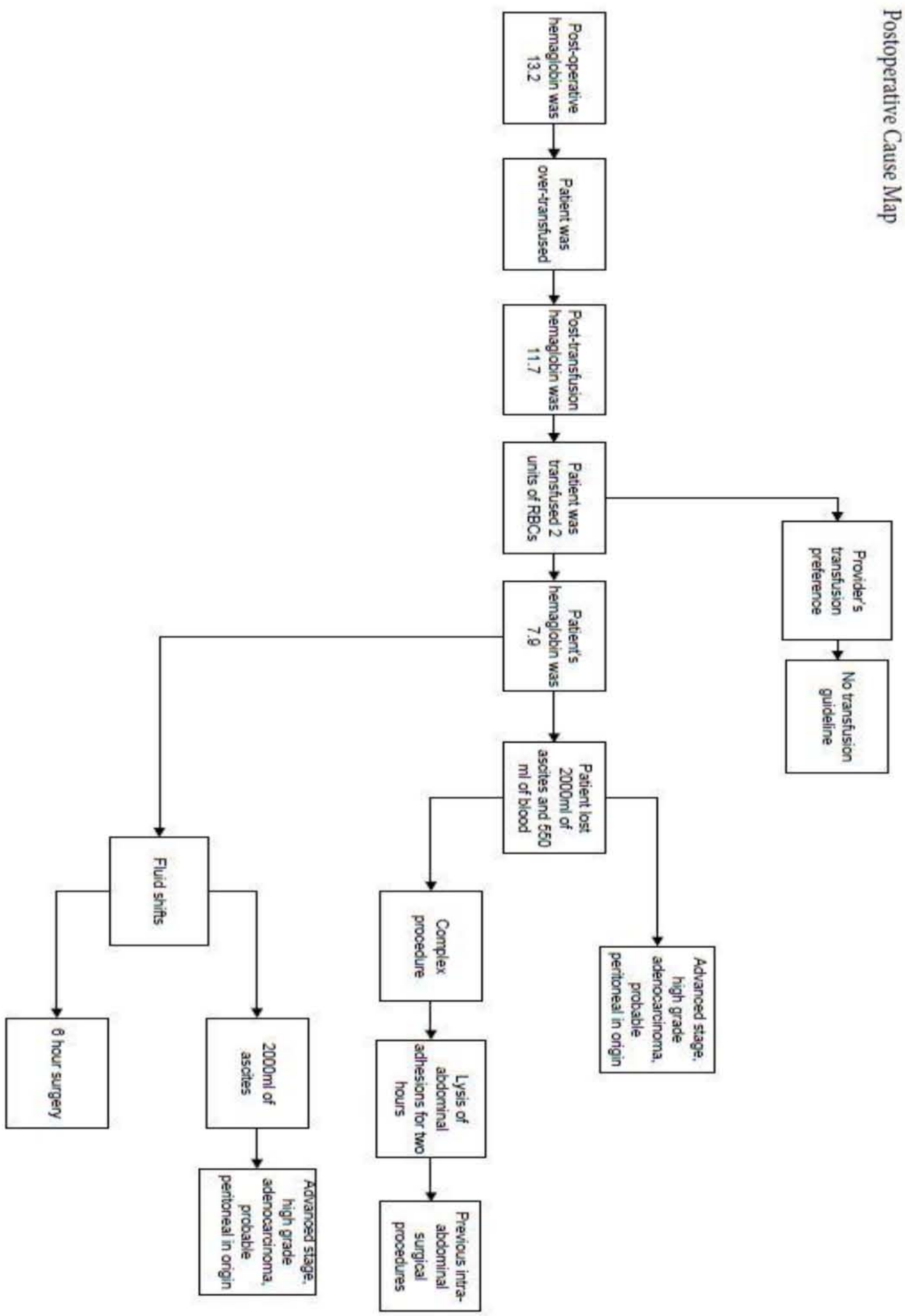
Appendix B: Process Flow Map of Perioperative Blood Transfusions



Appendix C: Intraoperative Cause Map



Appendix D: Postoperative Cause Map



Appendix E: Data Collection Tool

Pt. Study #	Clinic #	DOS	Age(yrs)	BMI	ASA	LOS	Cancer/Stage	Ascites	EBL (ml)	Type of surgery	Preop Hgb (g/dl)	Postop Hgb (g/dl)	Blood Tx	Pre Tx Hgb	Post-TX Hgb	When did blood tx occur	Appropriate Tx	# of units tx	Neoadjuvant therapy	Tranexamic Acid	Comorbidities	Postoperative Complications	30 Day mortality
1																							
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