PARTICIPANT INFORMED CONSENT FORM

Title of Study: The PRICE Trial: Phlebotomy resulting in controlled hypovolemia to prevent blood loss in major hepatic resections

Principal Investigator (PI): Dr. Guillaume Martel, (613) 737-8899 x76979

Sponsor: Ottawa Hospital Research Institute (OHRI)

Funding: Canadian Surgical Research Fund

Participation in this study is voluntary. Please read this Participant Informed Consent Form carefully before you decide if you would like to participate. Ask the study doctor and study team as many questions as you like. We encourage you to discuss your options with family, friends and/or your healthcare team.

Why am I being given this form?

You are being asked to participate in this research study because you are a patient who will be having a portion of the liver removed surgically (liver resection), here at The Ottawa Hospital. We want to help reduce bleeding during and after this operation. The information we learn from this study will also help us plan a bigger national study in the future.

Why is this study being done?

Major liver surgery, the procedure that you will be having, can sometimes lead to significant blood loss or hemorrhage. Blood loss in liver surgery is a key reason for worse outcomes and complications after surgery. Sometimes, blood loss may require you to have a blood transfusion. Research studies in North American hospitals suggest that up to one quarter of patients require a blood transfusion at the time of surgery or shortly after. Blood transfusions are usually very safe, but they can lead to allergic reactions or to the transmission of infectious diseases in extremely rare cases.

Surgeons and anesthesiologists utilize many techniques to decrease the risk of bleeding and hemorrhage during liver surgery. Many of these techniques will be used during your surgery, as they are part of the standard of care.

The goal of this research is to determine if whole blood phlebotomy will reduce bleeding and blood transfusion in patients having a liver operation.

Phlebotomy is a simple technique for which the anesthesiologist removes one or two pints of blood from you into a special collection bag. This is done in a similar fashion as if you were donating blood at a blood donation clinic. The exact amount of blood is decided upon based on your body weight (7-10 mL/kg). This will be done while you are asleep and the surgery is underway. You will be carefully monitored by the anesthesiologist. Your blood will never leave the sterile collection bag, specifically designed for that purpose. Once the liver surgery is completed, but before you wake up, your blood will be given back to you.

This technique is thought to decrease the pressure within the large veins of the liver (known as the hepatic veins). As a result, we expect less bleeding while the liver is being cut. As mentioned, once the piece of liver is removed from you, your blood will be given back to you.

We estimate that 62 participants will be enrolled in the study from The Ottawa Hospital.

How is the study designed?

Whether you get the surgery by the usual method or the usual method plus phlebotomy will be decided randomly. Randomization means that you are put into a group by chance, similar to flipping a coin.

This study will be double-blinded, which means that you will not be told in advance if you will have the phlebotomy during surgery or not. Your surgeon will also not know what you are receiving; only the anesthesiologist will be aware of the intervention and only after surgery is underway. Blinding helps to remove any bias or pre-conceived notions from affecting the outcome of the study. You will be told 30 days after surgery.

What is expected of me?

If you decide to participate in this study, you will undergo a major liver resection, as explained by your surgeon. There is nothing required of you as part of this study.

Your stay in hospital and the care you receive will not be affected by this study. After you are discharged from hospital, you will have appointments scheduled to visit your surgeon on a regular basis. This will happen whether you participate in the study or not. If you choose to participate, all data will be collected while you remain admitted in hospital, as well as at the postoperative clinic visits. You will not have anything extra to do. You may be called once by the study coordinator one month after surgery.

How long will I be involved in the study?

Phlebotomy is a short-term intervention. It will only last for the duration of your liver surgery, while you are asleep under anesthesia. All relevant data to be collected after surgery will be available within 30 days of the operation. Your participation in the study will last during the time of surgery and the one telephone call one month after surgery.

Your participation in the study may be stopped for any of the following reasons:

- The study doctor feels it is in your best interest.
- You need treatment that would interfere with the study.
- You do not follow the study staff's instructions.

What are the potential risks I may experience?

It is unlikely that phlebotomy will result in more risk than the standard of care. Previous research using this technique has not shown any special additional risk associated with receiving a phlebotomy. In fact, previous research suggests that patients receiving phlebotomy bleed less during surgery and have the same risk of complications as other liver surgery patients.

Phlebotomy could theoretically lead to any physiologic effect associated with blood loss. These effects could have implications for any major organ system, due to decreased blood flow. These could include but are not limited to myocardial ischemia (heart attack), cerebrovascular accident (stroke), acute renal failure (kidney failure) possibly requiring dialysis, coagulopathy (blood clotting abnormalities), or hepatic insufficiency (liver failure). That being said, these risks already exist with any liver surgery, simply on the basis of potentially significant blood loss. In order to be considered for liver surgery, you have already been seen by your surgeon and considered fit enough. Patients who are fit enough for liver surgery can also generally tolerate phlebotomy. You were asked to participate in the study because you met special study criteria based on your medical history, and this makes you eligible to participate in our study.

In addition, there is always a small chance of risks that we do not know about. The potential extremely rare additional risks we know about are listed below:

- Potential risk for clerical error with the blood (<1%)
- Theoretical risk of bacterial contamination of the collection bag, tubing, and as a consequence, whole blood (<1%)

Risks of Insurability:

We will take all reasonable steps to keep your research information confidential. Should someone not involved in the research find out that you took part in this research study, or if you choose to share your results (if they are provided to you), there is a possibility that this could affect your insurability under certain policies of insurance, depending on the exclusions in such policies.

Can I expect to benefit from participating in this research study?

You may not receive any direct benefit from your participation in this study. Your participation may allow the researchers to provide better treatments in the future for participants who need the same operation.

This study will select by chance which treatment you will receive. Participants in one arm of this study may do better or worse than participants in the other arm.

Do I have to participate? What alternatives do I have?

You can choose not to participate in this study. If you choose not to participate, you will still receive the usual operation that is done for your liver resection. Your study doctor will discuss this option with you.

Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now, and then change your mind later without affecting the medical care, education, or other services to which you are entitled or are presently receiving at this institution.

If I agree now, can I change my mind and withdraw later?

You may withdraw from the study at any time without any impact on your current or future care at this institution.

- If you decide to stop your study participation, you need to tell your surgeon or your nurse before you have your operation.
- You may also choose to discontinue your participation in the study.
- If you withdraw your consent, the study team will no longer collect your personal health information for research purposes, unless it is needed for review of safety.

What compensation will I receive if I am injured or become ill in this study?

In the event of a study-related injury or illness, you will be provided with appropriate medical treatment and care. Financial compensation for lost wages, disability or discomfort due to an injury or illness is not generally available. You are not waiving any of your legal rights by agreeing to participate in this study. The study doctor and The Ottawa Hospital Research Institute still have their legal and professional responsibilities.

Will I be paid for my participation or will there be any additional costs to me?

The phlebotomy procedure will be provided to you free of charge as long as you are participating in the study. However, you will not receive any payment or have to pay for anything if you participate in this study.

How is my personal information being protected?

- If you decide to participate in this study, the investigator(s) and study staff will look at your personal health information and collect only the information they need for this study. “Personal health information” is health information about you that could identify you because it includes information such as your name, address, telephone number, date of birth, new and existing medical records, or the types, dates and results of various tests and procedures.
- Information that identifies you will be released only if it is required by law.
- All information collected during your participation in this study will be identified with a unique study number (for example participant # AB01), and will not contain information that identifies you.
- Documents or samples leaving the Ottawa Hospital will only contain the coded study number.
- A Master List provides the link between your identifying information and the coded study number. This list will only be available to Dr. G. Martel and his staff and will not leave this site.
- The Master List and coded study records will be stored securely.
- You will not be identified in any publications or presentations resulting from this study.
- For audit purposes only, your original study records may be reviewed under the supervision of Guillaume Martel’s staff by representatives from:
    - the Ottawa Health Science Network Research Ethics Board (OHSN-REB),
    - The Ottawa Hospital Research Institute.
- Research records will be kept for 10 years, after this time they will be destroyed.
- Research records will be kept for 10 years, as required by the OHSN-REB.

A description of this clinical trial is available on http://www.ClinicalTrials.gov (NCT02548910). This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Do the investigators have any conflicts of interest?

There are no conflicts of interest to declare related to this study.

What are my responsibilities as a study participant?

It is important to remember the following things during this study:

- Ask your study doctor or the study coordinator if you have any questions or concerns.
- Call the study doctor if you experience any side effects, even if you are unsure whether it has anything to do with this study.

Will I be informed about any new information that might affect my decision to continue participating?

You will be told in a timely fashion of any new findings during the study that could affect your willingness to continue in the study. You may be asked to sign a new consent form.

Who do I contact if I have any further questions?

If you have any questions about this study, or if you feel that you have experienced a study-related injury or illness, please contact Dr. Guillaume Martel at 613-737-8899 x76979 or the study staff at 613-737-8899 x 71484.

The Ottawa Health Science Network Research Ethics Board (OHSN-REB) has reviewed this protocol. The Board considers the ethical aspects of all research studies involving human participants at the Ottawa Hospital Research Institute. If you have any questions about your rights as a study participant, you may contact the Chairperson at 613-798-5555, extension 16719.

Consent to Participate in Research

- I understand that I am being asked to participate in a research study on reduction in blood loss during major liver resection via the phlebotomy procedure.
- This study was explained to me by _____.
- I have read, or have had it read to me, each page of this Participant Informed Consent Form.
- All of my questions have been answered to my satisfaction.
- If I decide later that I would like to withdraw my participation and/or consent from the study, I can do so at any time.
- I voluntarily agree to participate in this study.
- I will be given a copy of this signed Participant Informed Consent Form.

_____	_____	_____
Participant's Printed Name	Participant's Signature	Date

Investigator or Delegate Statement

I have carefully explained the study to the study participant. To the best of my knowledge, the participant understands the nature, demands, risks and benefits involved in taking part in this study.

_____	_____	_____
Investigator/Delegate's Printed	Investigator/Delegate's Signature	Date

Assistance Declaration

Was the participant assisted during the consent process? ❑ Yes ❑ No

❑ The consent form was read to the participant/substitute decision-maker, and the person signing below attests that the study was accurately explained to, and apparently understood by, and consent was freely given by the participant/substitute decision-maker.

❑ The person signing below acted as a translator for the participant/substitute decision-maker during the consent process. He/she attests that they have accurately translated the information for the participant/substitute decision-maker, and believe that the participant/substitute decision-maker has understood the information translated.

_____	_____	_____
Name of Person Assisting (Print)	Signature	Date