Official Title: Pain Control in Colorectal Surgery: Liposomal Bupivacaine Block Versus Intravenous Lidociane
NCT04005859
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CAROLINAS HEALTHCARE SYSTEM
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Sponsor / Study Title:	**Carolinas HealthCare System-Department of Surgery / Pain Control in Colorectal Surgery: Liposomal Bupivacaine block versus Intravenous Lidocaine**
Protocol Number:	**(01-18-16)**
Principal Investigator: (Study Doctor)	**Kevin Kasten, MD**
Telephone:	[redacted] **(24 Hours)**
Address:	**Carolinas HealthCare System** **Carolinas HealthCare System-Center for Digestive Health** [redacted]

Please read this form carefully. Take time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign and date your name at the end of this form. You cannot take part in this research study until you sign and date this form.

INTRODUCTION

Dr. Kevin Kasten or Dr. Bradley Davis is asking you to participate in the above-named research study. This research study is being conducted to see if a different kind of anesthesia can improve the recovery of patients who must undergo a laparoscopic colectomy (removal of part or all of your colon) at Carolinas HealthCare System (CHS). You are one of 70 patients being asked to participate because you have been diagnosed with a colon problem that will require laparoscopic colectomy. The purpose of this study is to compare two forms of supplemental pain control used at the time of your surgery. Your pain control and recovery after surgery will be evaluated during your hospital stay and at scheduled intervals after you leave the hospital. Your participation in this study will last for 6 months after your surgery.

HOW THE STUDY WORKS

Currently, most colectomy patients at Carolinas Medical Center (CMC) receive intravenous (IV) lidocaine at the time of surgery, followed by IV medicine (for example, morphine, dilaudid) and oral

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opioid pain medication (for example, oxycodone, hydrocodone) after surgery. Opioid pain medications are very good at treating pain, but have some side effects such as nausea and constipation. Reducing the amount of opioid medication taken after surgery can reduce the chances of experiencing these side effects. IV lidocaine has been shown to reduce patients' pain and reduce the amount of opioid medications needed after surgery. IV lidocaine is what we currently use to help with pain control. Injections of liposomal bupivacaine (a long-acting relative of lidocaine) in the abdominal muscles (TAP block) before surgery have also been shown to reduce patients' pain and decrease opioid use. Because both treatments have been shown to reduce pain and the need for opioid medications after surgery, we plan to research which treatment is better.

If you agree to be in the study, you would be randomized to one of the two study treatment methods. Being randomized means that you are put in a group by a chance process, like flipping a coin. Your chance of receiving one of the study treatments is one in two (fifty-fifty chance). You won't know what group you are placed in. Although you will not know which study treatment you are receiving, this information can be determined in the event of an emergency.

There are two arms (study treatment groups) in this study. You will either receive intravenous lidocaine, or a TAP block of liposomal bupivacaine at the time of surgery. After surgery, you will receive standard pain medications, including intravenous and oral opioids, to treat your pain.

- Subject receiving IV lidocaine will receive IV lidocaine in the operating room, and for one hour after in the recovery room (PACU)
- Subjects receiving a TAP block with liposomal bupivacaine will receive the injections in the operating room, after they are unconscious (under anesthesia) and before the operation starts.

After the operation, all subjects will have band-aids on their abdomen so they cannot tell whether they had the TAP block, or the IV lidocaine.

We do not expect that either study treatment, IV lidocaine or TAP block, will completely control your pain. We expect you to need some opioids for pain control after surgery. You will still receive pain control as needed. We plan to compare how much additional medication you will need, to measure the effectiveness of each study treatment group.

After surgery, we will ask you about your pain at least every six hours for the first few days. We will record how much additional medication is required to treat your pain. We will also record signs that you are feeling better, such as moving around, eating, and passing gas (farting).

Once you leave the hospital we will ask to see you at two weeks and four weeks after surgery. We will ask you to bring your pain pills with you so we can see how much medication you needed. If you do not have an appointment near two or four weeks after surgery, we will call you and ask about your pain and remaining pills over the phone.

The study of IV lidocaine and liposomal bupivacaine TAP blocks is a subset of an Enhanced Recovery After Surgery (ERAS) program. ERAS is a program we have initiated to help people recover from surgery more quickly. It includes using many forms of non-opioid pain control, encouraging walking, and allowing patients to eat early after surgery. ERAS has been used with great success in colorectal surgery, allowing patients to feel better and go home sooner.

RISKS

The study poses minimal risk above and beyond the risks of the surgery itself. It involves comparison of two effective pain medications which are approved by the FDA. We expect that you will need additional medications to help control your pain after surgery. Regardless of your participation in this study we will regularly check and treat your pain after surgery until it is well controlled.

As with all medications, side effects may include allergic reaction. Allergic reactions may range from minor itching or rash to major reactions which can result in death.

Likely:

- Side effects of narcotic pain medication include itching, nausea, vomiting, constipation, drowsiness.
- One study treatment may be better than the other at treating pain. We will not know if one arm is superior to the other until after we perform this study.
- Subjects who receive the liposomal bupivacaine TAP block may feel additional soreness at the sites of injection. We believe that the pain relief from the medication will counter this.

Less likely:

- The most common adverse reactions following excessive administration of IV Lidocaine are:
    - Perioral (around the mouth) numbness
    - Nausea and vomiting

  It is rare to have side effects of serum lidocaine levels between 2-6 mcg/mL. We are careful not to exceed this amount.
- The same complications are rare but possible for overdosing of liposomal bupivacaine.
- Injection of liposomal bupivacaine into the abdominal muscles for a TAP block can cause bleeding or swelling in the abdominal wall.

Rare but serious

- Mild to moderate side effects of intravenous lidocaine (at serum levels 8-12 mcg/mL) include:
    - Nausea and vomiting
    - Severe dizziness

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  - Decreased hearing
  - Tremors
  - Changes in blood pressure and pulse.

  Nausea and vomiting without other lidocaine side effects in the postoperative setting is unlikely to be related to the lidocaine.

- Severe side effects intravenous lidocaine (at serum levels greater than 12 mcg/mL) includes:
  - Drowsiness
  - Confusion
  - Muscle twitching
  - Convulsions
  - Loss of consciousness
  - Cardiac arrhythmias (abnormal heart rhythms)
  - Cardiac arrest
- The same complications are rare but possible for overdosing of liposomal bupivacaine.

If you have problems that may be related to your study treatment, your study doctor may "break the code" to find out which group you are in. You would then no longer be in the study, and your postoperative care would continue as standard of care.

An additional risk to you is the release of information from your health records. The study doctors and the study site will protect your records so that your name, address, and phone number will be kept private. Nevertheless, there is still a small risk associated with this to your confidentiality.

The study poses minimal risk to subjects. Data collection from past medical records depends upon subject identifiers for data collection. HIPAA compliance in clinical and pathologic data handling will ensure protection of subjects' rights to privacy. Data access will be restricted to those involved in data collection or analysis.

INCLUSION/EXCLUSION CRITERIA

- Elective laparoscopic colectomy patients aged between 18 and 75 will be entered in the protocol.
- Exclusion: These patients will not be included in the study. If you have one or more of these problems, please notify your study doctor.
  - Allergy to lidocaine or similar medication
  - Chronic pain with daily opioid use before surgery

- Liver dysfunction
- Renal (kidney) insufficiency
- Epilepsy
- BMI greater than 40
- Sleep apnea
- Cardiac rhythm disorders
- Planned open procedures, or planned procedures other than colectomy

BENEFITS

This study may or may not improve your condition. The information gained from your case may benefit others with your condition. However, we believe the protocol may allow subjects to feel better faster, return to their daily activities faster, and return home from the hospital more quickly.

ALTERNATIVE PROCEDURE/TREATMENT

If you choose not to participate in this study, your colectomy will be performed to the current standards of care. You will not receive additional treatments that are not standard of care. You should talk with your study doctor about your options and their risks and benefits.

ADDITIONAL COST

Participating in this study should not increase your out of pocket expenses. There may be charges you are responsible for, such as a nutritional supplement and other liquids related to ERAS. Any additional charges will not be covered by Carolinas HealthCare System.

COMPENSATION

In the event that you are harmed as a result of your participation in this study, we will provide or arrange for treatment as necessary. This treatment, as well as other medical expenses, will be billed to you or your insurance company in the usual manner. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

If you become ill or are hurt while you are in the study, get the medical care that you need right away.

YOUR PAYMENT FOR BEING IN THE STUDY

You will not be paid for being in this study.

WITHDRAWAL

Your participation in this study is completely voluntary. You should feel under no pressure to be in the study. If you decide not to be in the study, which will not in any way harm your relations with your doctors or with Carolinas HealthCare System. You are free to stop being in the study if you

change your mind after entering it. This would not harm your relations with your doctors or Carolinas HealthCare System. Your decision will not result in any penalty or loss of benefits to which you are entitled.

- You may always say no. You do not have to take part in the study.
- If you start a study, you may stop at any time. You do not need to give a reason.
- If you do not want to be in a study or you stop the study at a later time, you will not be penalized or lose any benefits.
- If you stop, you should tell the study staff and follow the instructions they may give you.

Your part in the research may stop at any time for any reason, such as:

- The sponsor or the study doctor decides to stop the study.
- The sponsor or the study doctor decides to stop your part in the study for your safety.
- You need additional medicine.
- You do not follow the study rules.
- You have a new injury or illness.
- You decide to stop.

You may be asked to stop the study even if you do not want to stop.

Should the medical staff find parts of the protocol not appropriate for you then you will be excluded from parts of the study. This is to protect your individual medical needs. We will tell you about new medical findings that may affect your willingness to continue in the study.

CONFIDENTIALITY

The records of this study will be kept private. In any sort of report we might publish, we will not include any information that will make it possible to identify a patient. Your record for this study may, however, be reviewed and/or photocopied by Carolinas HealthCare System, or by representatives of the Food and Drug Administration or other government agencies. To that extent, confidentiality is not absolute.

To ensure that your information collected for this study will be kept private, your name will not be used whenever possible. A code will be used instead of your name. All of your study data will be kept in a secure location.

AUTHORIZATION

If you wish to take part in this clinical study, you will be asked to sign this consent form. It allows the study sponsor and the study investigator to collect and process any relevant personal health information collected from you during the study. These are activities routinely carried out during all clinical studies.

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You have been told that personal information about you (including sensitive personal health information, such as your medical history and your racial/ethnic origin if relevant to the study) will be reviewed, collected on a computer database, stored in electronic or manual files, audited, and/or otherwise processed by:

- The clinical study doctor and study staff
- Regulatory or other governmental authorities of the United States and other countries
- Carolinas HealthCare System employees
- Other persons or agencies as required by law or allowed by federal regulations

You have been told that your personal data are being collected and processed to:

- Check your suitability to take part in the study
- Compare and pool study treatment results with those of other subjects in clinical studies

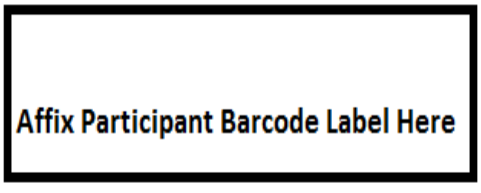
You have been told that your personal information may be processed within the U.S. or elsewhere in the world or transferred to or from the U.S. for review, processing and/or storage by an associated company or a carefully selected third-party organization. By signing this document, you explicitly consent to the transfer of your personal information, including sensitive personal information, collected during this clinical study, for review, processing and/or storage. Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, the groups are committed to keeping your personal health confidential.

You may refuse this authorization to transfer your personal information. If you choose not to agree to this authorization, you might be ineligible to participate in the study. If you decide not to sign this authorization, that will not harm your relations with your doctors or with Carolinas HealthCare System.

You have the right to inspect your medical record at any time. Your research record may be unavailable until the conclusion of the study. At that point, it will be available. Please speak with the study doctor if you desire to access your record.

You have been told whenever your personal information is processed; it will be kept confidential and secure, to the best of our ability. It will be used only for the purpose for which it was collected.

This Authorization does not have an expiration date. You have been told that according to the guidelines for good clinical practice, the study investigator and sponsor will keep your personal information for at least 6 years. If you do not withdraw this Authorization in writing, it will remain in effect indefinitely. If you wish to revoke authorization to use your personal information, you will notify the study doctor, Kevin Kasten, MD (1025 Morehead Medical Drive, Suite 300 Charlotte, NC), in writing. Some of the data obtained from your record prior to your revocation may still be used if considered necessary for the study.



WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  [redacted]
- or call **toll free**: [redacted]
- or by **email**: [redacted]

Please reference the following number when contacting the Study Subject Adviser: Pro00024189.

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STATEMENT OF CONSENT

I have read this form and its contents were explained to me. I agree to be in this research study for the purposes listed above. All of my questions were answered to my satisfaction. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing this form.

_____ ____/____/____ _____
Signature of Research Subject Date Time

_____
Printed Name of Research Subject

STATEMENT OF PERSON EXPLAINING CONSENT

I have carefully explained to the subject the nature and purpose of the above study. There has been an opportunity for the subject to ask questions about this research study. I have been available to answer any questions that the subject has about this study.

_____ ____/____/____ _____
Signature of Person Explaining Consent Date Time

_____
Printed Name of Person Explaining Consent

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