Official Title: Impact of Transjugular Intrahepatic Portosystemic Shunts on Liver Stiffness

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University of Pennsylvania Research Subject Informed Consent and Health Insurance Portability and Accountability Act (HIPAA) Authorization Form

Protocol Title:	**Impact of Transjugular Intrahepatic Portosystemic Shunts on Liver Stiffness**
Investigators:	Kimberly Forde, MD Department of Gastroenterology, Hepatology Hospital of the University of Pennsylvania 2 Dulles, 3400 Spruce St., Philadelphia, PA 19104 Daytime Phone Number: 215.349.8222 Marina Serper, MD Department of Gastroenterology, Hepatology Hospital of the University of Pennsylvania 2 Dulles, 3400 Spruce St., Philadelphia, PA 19104 Daytime Phone Number: 215.349.8222 David Kaplan, MD Department of Gastroenterology, Hepatology Hospital of the University of Pennsylvania 2 Dulles, 3400 Spruce St., Philadelphia, PA 19104 Daytime Phone Number: 215.349.8222 Rebecca Wells, MD 421 Curie Boulevard 905 Biomedical Research Building II/III Philadelphia, PA 19104 Daytime Phone Number: 215 573-1860 Anil Chauhan, MD Department of Radiology, Abdominal Imaging Hospital of the University of Pennsylvania 1 Silverstein, 3400 Spruce Street, Philadelphia, PA 19104 Gregory Nadolski, MD Department of Radiology, Vascular and Interventional Radiology Hospital of the University of Pennsylvania 1 Silverstein, 3400 Spruce Street, Philadelphia, PA 19104 Daytime Phone Number: 267.251.9926
Sponsor:	National Cancer Institute
24-Hour Emergency Contact	Interventional Radiology Fellow On Call 215.662.2222 (ask to be connected to Interventional Radiology Fellow on Call)

Why am I being asked to volunteer?

You are being invited to participate in a research study, because you have been diagnosed with symptomatic portal hypertension secondary to cirrhosis requiring transjugular intrahepatic portosystemic shunt creation.

Cirrhosis is a disease involving the liver in which the liver becomes replaced with scar, or fibrosis. Sometimes cirrhosis is referred to as hardening or scarring of the liver. Cirrhosis can result in elevated blood pressure in the portal vein, the blood vessel that brings blood from the intestine to the liver to process absorbed nutrients and remove toxins from the blood. Elevation in the blood pressure in the portal vein is termed portal hypertension. Portal hypertension can cause symptoms of fluid accumulation in the abdomen called ascites or chest called hepatohydrothorax, or bleeding from dilated veins along the esophagus or stomach called varices.

When either fluid accumulation or bleeding varices occurs from portal hypertension, a transjugular intrahepatic portosystemic shunt, or TIPS, may be placed to relieve the symptoms. A TIPS is a type of stent graft, a tube of metal and fabric, inserted between the portal vein and the vein that drains the liver to divert blood through the liver, lower portal vein blood pressure, and relieve symptoms of portal hypertension. A TIPS is created by an interventional radiologist under imaging guidance with ultrasound and X-rays. The TIPS is created by entering the blood stream at a vein in the neck and then traveling to the veins that carry blood away from the liver, the hepatic veins. Next a needle is passed between the hepatic vein and the portal vein. A wire is then placed through the needle before it is removed. The stent graft is then advanced over the wire until it is properly positioned between the two veins.

Your participation is voluntary which means you can choose whether or not you want to be part of the study. If you choose to participate, you will be asked to undergo a specific type of ultrasound before and after the TIPS creation. This special ultrasound measurement will be done at the same time you normally would be undergoing ultrasound of the liver before and after the TIPS creation if you were not participating in the study.

Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of participating in the study, and what you will be asked to do if you choose to participate. The research team is going to talk to you about the study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, other doctors, or whoever helps you make medical decisions. You may find some of the medical language difficult to understand. Please ask the research team and/or the study doctor any questions you have regarding this form or the research study. If you decide to participate, you will be asked to sign this consent form.

What is the purpose of this research study?

The creation of aTIPS lowers the pressure within the portal vein and relieves symptoms of portal hypertension (bleeding varices or fluid accumulation in the abdomen or chest). However, how this change in blood pressure impacts liver stiffness, a measure of severity of cirrhosis, is unknown.

The purpose of this study is to examine whether liver stiffness changes before and after TIPS creation.

Some preliminary studies suggest liver stiffness may be an independent mechanism by which cancer develops in the liver. Additionally, if liver stiffness can be decreased by TIPS creation, in the future TIPS may be used to slow or reverse cirrhosis before it is symptomatic. The present study would provide preliminary evidence that TIPS not only lower portal hypertension but also decrease stiffness in the liver.

How many people will be in this research study?

A total of 20 patients will be recruited at the Hospital of the University of Pennsylvania.

What am I being asked to do?

Prior to TIPS placement, patients routinely undergo ultrasounds to examine the hepatic and portal vein blood flow. Additionally, 1-2 weeks after TIPS creation, patients have a repeat ultrasound to evaluate the blood flow in the TIPS. An ultrasound is an imaging system that sends sound waves into the body and measures the reflection of these sound waves off our your body to create an image. Ultrasound is painless and non-invasive.

If you participate in this study, you are being asked to allow the study team to measure the stiffness of your liver using ultrasound elastography, also called acoustic radiation force impulse (ARFI). This would be performed at the same time as your ultrasounds before and after TIPS creation. Elastography is not normally performed as part of the ultrasound before and after TIPS creation. Elastography is a special type of ultrasound which sends a sound wave of a specific frequency and intensity into the liver tissue. When the ultrasound machine receives the reflection of the sound wave back, the change in sound wave characteristics can be used to measure liver stiffness. Elastography is also painless. The addition of elastrography will add an additional 5 to 10 minutes to the ultrasound test.

Additionally, at the time of TIPS creation, a sample of your blood (about 1 tablespoon) will be drawn through the device inserted into the blood stream to create TIPS. This blood sample will be used for research purposes only. The blood will be used to analyze proteins or other factors in the blood stream that may correlate or cause liver stiffness.

After TIPS creation, no additional therapies or interventions beyond those performed for routine clinical care will be performed if you participate. The study team will also obtain information regarding your medical history related to cirrhosis and portal hypertension, medications to lower portal hypertension and other health conditions from your medical records. No additional clinic visits are required if you participate in this study. However, your medical records will be reviewed up to 12 months after TIPS creation to obtain information about relief of symptoms of portal hypertension.

Women who are able to become pregnant will be tested for pregnancy by urine pregnancy test (UPT). The results of this test must be negative to join the study. For subjects who are able to become pregnant, a repeat UPT will be performed on the day of TIPS procedure prior to the intervention.

What are the possible risks?

The direct risks of participating in the study are minimal beyond the risk of the TIPS procedure itself. The additional imaging with elastography (ARFI) obtained on ultrasound before and after TIPS creation is painless. However, obtaining these images will require an extra 5-10 minutes of imaging time. The volume of blood drawn for research purposes is small. Thus, it is unlikely to cause side effects such as weakness, fatigue, or lightheadedness. Since the blood will be drawn while you are under sedation for TIPS, it will be painless.

Your participation in this study would permit the investigators to collect personal health information and data about you. Personal health information and data from your clinical visits and future imaging studies regarding function of the TIPS will be recorded in a password protected electronic database, which is only accessible by members of the study team. The results of the data will be reported in aggregate and anonymously. This means your information will not be reported by itself or with any personal identifiers, such as name or date of birth. However, risk of loss of confidentiality is still possible. Finally, as with all investigations, the research may involve risks that are currently unforeseeable.

What are the possible benefits?

There may be no direct benefit to you. Future patients may benefit from the better understanding of the changes in liver stiffness after TIPS creation.

What other choices do I have if I do not participate?

You do not have to participate in this study. If you choose not to participate in this study, you could choose to undergo liver ultrasound and TIPS creation as part of routine clinical care, to participate in another research study, or to receive no care at all.

Will I have to pay for anything if I participate?

You will incur no additional charges for participating in the study.

Will I be paid for being in this study?

No, there will be no financial compensation for participation in this study.

What happens if I am injured from being in this study?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in this consent form.

How long will I be in this research study if I participate? Can I leave the study before it ends?

Patients who participate in this study will be followed for 1 month (30 days) after TIPS creation. Additionally, your clinical records may be reviewed to determine outcomes of the TIPS relative for up to 12 months following TIPS creation. Your participation in this study is completely voluntary and you may withdraw at any time without affecting your present or future care. You may be withdrawn from the study if your physician finds it necessary or in your best interest.

What information about me may be collected, used, or shared with others?

Your name, age, medical record numbers, telephone number and dates and results from examinations, tests, procedures, and imaging related to the treatment of liver disease and management and outcomes of your TIPS.

Why is my information being collected?

Your information will be used by the investigators to perform the research, to oversee the research, and to contact you if necessary. Your personal information will not be used in reporting the outcomes of this study. This information is collected to ensure the data from the investigation is recorded correctly.

Who may use and share information about me?

The investigators for the study and the study team may use or share your information for this research study. Additionally, information may be shared with regulatory oversight organizations such as the Institutional Review Board at the

University of Pennsylvania and the FDA. All information shared between study team members will be through a password protected electronic database system to protect privacy and confidentiality. However, there is still potential risk to confidentiality and privacy. If your personal health information is shared outside of the University of Pennsylvania, you data may no longer be covered by federal privacy protections once disclosed outside of the covered entity.

How long may the investigators use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire. Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study, unless you have given written authorization, the University of Pennsylvania's Institutional Review Board grants permission, or as permitted by law.

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to participate in this research study.

Who can see or use my information? How will my personal information be protected?

Every attempt will be made by the investigators to keep all information collected in the study strictly confidential, except as may be required by a court order or by law. If necessary, authorized representatives at the University of Pennsylvania's Institutional Review Board (IRB), a committee charged with protecting the rights and welfare of research subjects, or the FDA (Food and Drug Administration) may be provided access to our research records. If any publication or presentation results from this research, study participants' data will be reported only in aggregate form without any individually identifiable information. Additionally, a description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. 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.

What if new information becomes available about this study?

You will be provided with a copy of this document for your records. If new information about this study is discovered, you will be informed.

Electronic Medical Records and Research Results

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record. If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient), and are participating in a research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within either of these systems and are participating in a research study that uses services at University of Pennsylvania, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate University of Pennsylvania workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by University of Pennsylvania to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

Who can I call with questions, complaints, or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

Conclusion:

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, you have been given the opportunity to ask questions, your questions have been answered to your satisfaction, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study. Upon signing below, you will receive a copy of this consent form.

Name of Subject (Please Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Please Print)	Signature	Date