In Vivo Flow-Independent T2 Measurements of Superior Mesenteric Vein Blood in Diagnosis of Chronic Mesenteric Ischemia: A Preliminary Evaluation[1]

King C. P. Li, MD, FRCPC, Ronald L. Dalman, MD, Graham A. Wright, PhD

Rationale and Objectives. The authors attempted to determine whether the T2 relaxation time of superior mesenteric vein (SMV) blood would decrease in patients with chronic mesenteric ischemia after a meal.

Materials and Methods. Thirty-two patients without chronic mesenteric ischemia and eight patients with symptomatic chronic mesenteric ischemia underwent magnetic resonance (MR) imaging. All examinations were performed with a 1.5-T unit, a modified Carr-Purcell-Meiboom-Gill sequence, final section-selective pulse of 180°, and spiral readout gradients. Measurements of SMV blood T2 were obtained after at least 6 hours of fasting and 15 and 35 minutes after ingestion of 240 mL of a liquid nutritional supplement. Maximal change of the SMV blood T2 was expressed as a percentage of the fasting T2 in all patients.

Results. In control patients, SMV blood T2 increased postprandially by 9.4% ± 1.3 (95% confidence level; range, 6.8%–11.9%) (data range, –7.3% to 25.6%) compared with fasting T2. In symptomatic patients, SMV blood T2 decreased postprandially by 15.8% ± 2.2 (95% confidence level; range, –20.1% to –10.7%) (data range, –7.9% to –25.3%). The difference between the two groups was statistically significant ($P < .0001$ by Student unpaired t test).

Conclusion. Measurement of SMV blood T2 is a promising test for chronic mesenteric ischemia diagnosis. Therefore, conversion of T2 measurements to estimate oxygen saturation may not be necessary for all cases of this clinical indication.

Key Words. Magnetic resonance (MR), vascular studies; mesentery, ischemia.

Chronic mesenteric ischemia is a disease characterized primarily by atherosclerosis of the mesenteric arteries (1–3). Although most patients with chronic mesenteric ischemia present with a classic triad of clinical symptoms that consists of postprandial abdominal pain, food aversion, and weight loss, many other disease processes, including peptic ulcer disease and pancreatic neoplasms, have very similar clinical manifestations. Currently, mesenteric angiography is the most commonly used method to confirm the diagnosis of chronic mesenteric ischemia. Stenosis or occlusion of at least two of the three main mesenteric arteries is considered supportive of this diagnosis (4,5). However, owing to the rich collateral supply in the mesenteric circulation, stenosis or even occlusion of all three mesenteric arteries has been observed in asymptomatic patients (4,5). As a result, it has been suggested that anatomic information alone is insufficient to confirm the diagnosis of chronic mesenteric ischemia (1–3).

Because abdominal pain occurs in patients with chronic mesenteric ischemia only after ingestion of food, it is assumed that the abdominal pain results from increased metabolic demand, which outstrips the ability of the mesenteric vasculature to increase blood flow to the bowel. This hypothesis is supported by data from isolated intestinal loop experiments (6–12). It has been demonstrated that

Acad Radiol 1999; 6:530–534

[1] From the Departments of Radiology (K.C.P.L.) and Surgery (R.L.D.), Stanford University School of Medicine, Stanford, Calif, and Sunnybrook Medical Center, Toronto, Ontario, Canada (G.A.W.). Received February 8, 1999; revision requested March 4; revision received March 18; accepted March 19. Supported in part by National Institutes of Health grants DK 46901 and HL47448 and by the Society of Gastrointestinal Radiologists Research Award. R.L.D. supported by American Heart Association California Affiliate Grant-in-aid Award. **Address reprint requests to** K.C.P.L., Department of Radiology, Room H-1307, Stanford University Medical Center, 300 Pasteur Dr, Stanford, CA 94305.

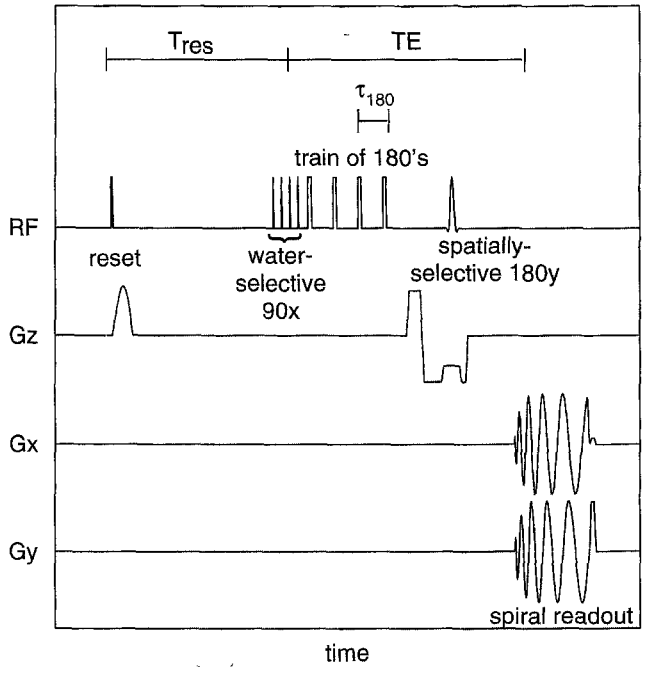

Figure 1. Pulse sequence for in vivo estimation of blood T2. T_{res} = time from reset to excitation; *RF* = envelope of the radiofrequency signal applied to the object; G_x, G_y and G_z = field gradients applied along the corresponding spatial axes. As shown, the sequence images an axial section.

intestinal oxygen extraction increases as blood flow decreases, so that the level of oxygen uptake remains normal over a wide range of blood flow. However, when blood flow decreases below a threshold level, oxygen extraction cannot increase any further, which leads to a decrease in oxygen uptake in the intestine and eventually to mesenteric ischemia and infarction (6–12). As oxygen extraction in the small bowel increases, the oxygen saturation of blood from the superior mesenteric vein (SMV) should decrease. Therefore, we should be able to diagnose mesenteric ischemia by measuring the oxygen saturation of SMV blood in vivo.

Paramagnetic substances that are homogeneously distributed enhance the relaxation of protons by a process called proton-electron dipolar–dipolar proton-relaxation enhancement. This process shortens T1 and T2 in parallel. However, paramagnetic substances that are not homogeneously distributed produce selective T2 shortening (13). Because deoxyhemoglobin in red blood cells is paramagnetic and inhomogeneously distributed, whereas oxyhemoglobin is not paramagnetic, an increase in the percentage of hemoglobin that is deoxygenated leads to a decrease in blood T2. Therefore, if we can accurately measure the T2 of flowing blood in vivo, we should be able to estimate the percentage of hemoglobin that is oxygenated. We have previously demonstrated that we could accurately estimate oxygen saturation in a canine model by using a modified Carr-Purcell-Meiboom-Gill sequence for flow-independent T2 measurements (14) and by using in vitro experiments to establish a calibration curve to convert T2 measurements to oxygen saturation (15). We subsequently studied 10 patients with atherosclerotic disease (control patients) and six patients with symptomatic chronic mesenteric ischemia by using this method. In the 10 control patients, oxygen saturation of the SMV increased by 4.6% ± 0.6 after a meal challenge, whereas in the patients with chronic mesenteric ischemia, oxygen saturation of the SMV decreased by 8.8% ± 0.7 postprandially (16).

These preliminary results demonstrated the potential of using in vivo magnetic resonance (MR) oximetry to diagnose and monitor chronic mesenteric ischemia. However, in vitro calibration of blood T2 and oxygen saturation can take up valuable imaging time on the MR unit and requires considerable expertise. Elimination of the in vitro calibration step would help the dissemination of this method to other institutions and decrease the clinical time required to carry out the test.

The purpose of this experiment, therefore, was to determine whether the T2 of SMV blood would decrease in patients with chronic mesenteric ischemia after a meal. If this hypothesis proved to be true, T2 measurements of SMV blood could be used to diagnose this condition without conversion to oxygen saturation.

MATERIALS AND METHODS

Flow-Independent T2 Measurements

We modified the basic Carr-Purcell-Meiboom-Gill sequence used in spectrometer studies of blood to address the challenges of the in vivo environment. The resulting sequence has been fully described previously (Fig 1) (15,16). Briefly, the pulse sequence uses a series of rapid, regular non–section-selective 180° pulses to refocus the spins and minimize the loss of coherence due to flow or other motions. A final section-selective 180° pulse, followed by a rapid spiral readout, is used to minimize dephasing during the readout. Because the pulse sequence is designed to minimize the dephasing due to any motion, respiratory compensation or gating techniques were not used. For measurements of SMV blood T2, the sequence was used with the body coil and the following parameters: repetition time of 2,000 msec, refocusing interval (t_{180}) of 12 msec; echo times of 30, 78, 126, and 222 msec on consecutive interleaves of the sequence; 20 spiral acquisitions

per image; and two excitations, yielding total imaging time of 5 minutes 20 seconds. Section thickness in this single-section technique was 7 mm, and in-plane resolution was 1.8 mm. For the T2 measurements, a region of interest was selected to cover the SMV to a margin roughly corresponding to a threshold of 50% of the maximum intensity in the vessel (Fig 2). This ROI selection was done to minimize the effect of volume averaging at the edges of the vessels. Typically, each region of interest covered 10–15 voxels measuring $2 \times 2 \times 7$ mm each.

Experiments

All procedures involving human subjects in this study were approved by the Stanford University Administrative Panel on Human Subjects in Medical Research. The study included 32 patients with abdominal pain who were referred for abdominal MR imaging but who later proved not to have chronic mesenteric ischemia and eight patients who had symptomatic chronic mesenteric ischemia. The control patients included 14 men and 18 women with a mean age of 59.7 years ± 17.7 (range, 22–83 years). These patients were recruited for the MR studies, and informed consent was obtained from every patient. One control patient underwent the MR study twice, once before stent-graft placement for treatment of aortic dissection and once after stent-graft placement. Therefore, a total of 33 MR control studies were obtained.

The patients with symptomatic chronic mesenteric ischemia included five men and three women with a mean age of 62.9 years ± 13.1 (range, 37–82 years). These patients were scheduled for mesenteric revascularization surgery for treatment of chronic mesenteric ischemia. All of the patients studied had the classic clinical triad of postprandial abdominal pain, weight loss, and food aversion and had significant stenoses or occlusions of at least two of the three mesenteric vessels. MR findings were not used to influence the decision on performance of the surgery. For each subject, MR measurements of SMV blood T2 were obtained after 6 hours or more of fasting and 15 and 35 minutes after ingestion of 240 mL of a liquid nutritional supplement (Ensure; Ross Laboratories, Columbus, Ohio). The maximum change in postprandial SMV blood T2 was calculated in each subject. All symptomatic patients underwent revascularization surgery after the MR studies. Postoperative resolution of the symptoms occurred in all patients, confirming that the symptoms were indeed caused by chronic mesenteric ischemia. Two symptomatic patients underwent MR examinations postoperatively after complete resolution of their of symptoms. The postoperative MR study protocol was exactly the same as that of the preoperative studies.

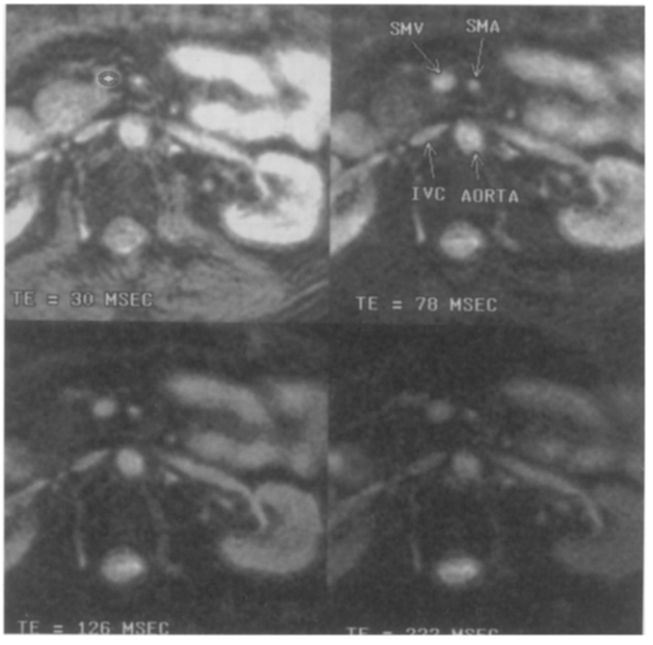

Figure 2. Images obtained during in vivo measurement of SMV blood T2 in an asymptomatic patient after a meal challenge. The image with echo time of 30 msec shows a typical region of interest used to obtain the T2 measurement. *SMA* = superior mesenteric artery, *IVC* = inferior vena cava.

Statistical Analysis

Maximum postprandial changes in SMV blood T2 for the control and symptomatic patients were compared with a two-tailed Student unpaired *t* test.

RESULTS

Figure 3 shows a scatterplot of the maximum postprandial changes in SMV blood T2 in the asymptomatic and symptomatic patients. In the 33 control studies, SMV blood T2 increased postprandially by 9.4% ± 1.3 (95% confidence level; range, 6.8%–11.9%) (data range, –7.3% to 25.6%). In the symptomatic patients, SMV blood T2 decreased postprandially by 15.8% ± 2.2 (95% confidence level; range, –20.1% to –10.7%) (data range, –7.9% to –25.3%). The difference between the maximum postprandial change in SMV blood T2 in the asymptomatic and symptomatic patients is statistically significant according to a two-tailed Student unpaired *t* test ($P < .0001$). When –7.5% is used as the threshold for a positive test, no overlap existed between the two groups of patients. In the two symptomatic patients who underwent both preoperative

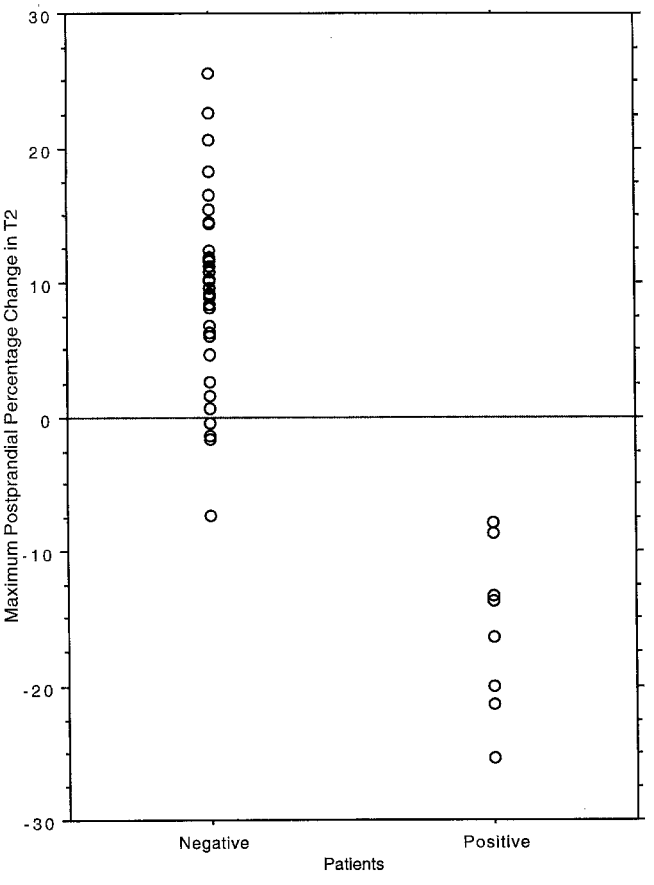

Figure 3. Scatterplot comparing maximum postprandial changes in SMV blood T2 of 32 asymptomatic patients (33 examinations) and of eight patients with chronic mesenteric ischemia. Notice that the postprandial SMV blood T2 changes in asymptomatic patients were all above –7.5%, whereas these changes in patients with chronic mesenteric ischemia were all below –7.5%.

and postoperative MR studies, the MR results were abnormal preoperatively and normal postoperatively. The maximum postprandial preoperative changes in SMV blood T2 in these two patients were –20.0% and –12.0%, while the corresponding postoperative values were 0.4% and 27.7%, respectively.

DISCUSSION

Many investigators have started to explore the use of functional data to diagnose chronic mesenteric ischemia (17–22). Duplex ultrasonography (US) has received much attention in this area. The physiologic postprandial increase in mesenteric blood flow has been demonstrated with duplex US (20). However, duplex US is operator dependent, and in patients with excessive adipose tissue or overlying bowel gas, mesenteric blood flow studies may be difficult or impossible to perform. Accurate volume flow rate is also difficult to obtain with duplex US because the cross-sectional areas of the vessels are difficult to measure accurately. Results of our previous studies suggest that measurements of SMV oxygen saturation during fasting and at 15 and 35 minutes after a meal are sufficient to establish or exclude the diagnosis of chronic mesenteric ischemia. The results of our current investigation demonstrate further that postprandial changes in SMV blood T2, without conversion to oxygen saturation, may be adequate for the diagnosis in a large number of patients. This finding has important implications on the clinical applicability of this diagnostic test. Because it takes only about 15 minutes of total imaging time to obtain SMV blood T2 measurements, these measurements can be integrated easily into any routine abdominal MR imaging examination.

We have previously reported that certain physical factors affect the relationship between blood T2 and oxygen saturation (23). These factors include temperature, hematocrit, and pH of blood in vivo. However, we found that as long as the temperature was within 37°C ± 5, hematocrit was within 45% ± 5, and pH was within 7.4 ± 0.1, the accuracy of the estimated oxygen saturation was within ±3% of the oximeter measurements. Similarly, the relationship between blood T2 and oxygen saturation was also affected by the changes in red blood cell membrane permeability (24). We are in the process of determining the extent to which population variability in the calibration can be attributed to red blood cell membrane permeability. Obviously, at this stage, for patients known to have potential confounding processes that could affect the reliability of uncalibrated data, such as anemia and polycythemia, in vitro conversion of blood T2 to oxygen saturation should still be performed.

In patients with postprandial abdominal pain, food aversion, and weight loss, MR imaging examinations can be tailored to detect abdominal neoplastic and inflammatory processes, as well as chronic mesenteric ischemia. This comprehensive MR examination should obviate multiple diagnostic tests and invasive procedures, such as abdominal angiography, in the majority of patients. With the advent of contrast-enhanced MR angiography, integration of anatomic and functional information is also possible during the MR imaging examination. Although the sequence we used for obtaining T2 measurements in SMV blood is not commercially available, other investigators have used a cardiac-triggered, flow-compensated, gradient-echo imaging sequence for the same purpose and have achieved promising results (25). If the clinical demand is sufficient, it is highly probable that this type of sequence

will be commercially available in the future. We have also been experimenting with a faster pulse sequence for obtaining in vivo blood T2 measurements. Our hope is that in the future the total imaging time will be less than 5 minutes.

In conclusion, our results demonstrate that in vivo flow-independent T2 measurement of SMV blood is a promising test for diagnosis of mesenteric ischemia. Therefore, in vitro blood calibration for conversion of T2 measurements to estimates of oxygen saturation may not be necessary in all patients for this clinical indication.

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