US DOPPLER IN THE EVALUATION OF LIVER TRANSPLANTATION

ECOGRAFÍA DOPPLER EN LA EVALUACIÓN DE TRASPLANTE DEL HÍGADO

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SUMMARY

Liver transplantation is an effective therapeutic method for treatment of multiple irreversible terminal liver disease, both acute and chronic. Advances in immunosuppressive therapy, surgical technique and post-surgical care have improved the prognosis of patients undergoing this procedure. The ultrasound with Doppler assessment is the image method which is most commonly used to assess these patients, both in the initial phase and during long-term follow-up. The advantages of ultrasound Doppler are the following: It is widely available, it can be portable, it does not cause side-effects, and it is not associated with ionizing radiation effects. In addition, it also allows an anatomical assessment of grey and functional scales, with flow evaluation of different vascular complications. The most common complications during liver transplantation, as well as the ones with the highest clinical importance are vascular complications: arterial thrombosis, venous thrombosis, stenosis, fistulas. In addition, one can find complications of biliary anastomosis, as well as collections, neoplasms and rejection. Normal and abnormal Doppler findings in patients undergoing liver transplantation are reviewed in this article.

RESUMEN

El trasplante de hígado es un método terapéutico efectivo para el tratamiento de múltiples enfermedades hepáticas terminales irreversibles, tanto agudas como crónicas. Los avances en la terapia inmunosupresora, la técnica quirúrgica y el cuidado perioperatorio han mejorado el pronóstico de los pacientes sometidos a este procedimiento. La ecografía con evaluación Doppler es el método de imagen más utilizado para valorar a estos pacientes, tanto en la etapa inicial como en el seguimiento a largo plazo. Tiene como ventajas estar ampliamente disponible, la posibilidad de volverse portátil, no generar efectos secundarios y no asociarse con efectos por radiación ionizante. Permite realizar una valoración anatómica en escala de grises y funcional con la evaluación del flujo de las diferentes anastomosis vasculares. Es el método diagnóstico ideal ante la sospecha de complicaciones vasculares. Las complicaciones más comunes y con más importancia clínica son las vasculares: trombosis arterial, trombosis venosa, estenosis, fístulas. También se encuentran complicaciones de la anastomosis biliar, las colecciones, las neoplasias y el rechazo. En este artículo se revisan los hallazgos normales y anormales en el Doppler de los pacientes sometidos a trasplante de hígado.

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Introduction

Liver transplantation is the treatment of choice in patients with terminal hepatic disease, whether it is acute or chronic. Advancements in surgical technique, in the preservation of organs, in immunosuppression therapy and in the early detection of post-surgical complications have increased survival after liver transplantation (1)

Early detection of post-surgical-complications is essential for the survival of the patients and the graft. The loss of a graft is a serious problem, due to the complexity of the surgical procedure and the low

availability of livers to perform transplantations. The clinical signs of complications are usually non-specific, and the diagnosis is frequently based on image methods (1).

The ultrasound with Doppler is the image method of choice (1). It is cost-effective, non-invasive, it does not have ionizing radiation, it is accessible and can be easily performed in the bed of the patient. It enables to evaluate hepatic anatomy and also the vascular structures with their anastomosis (2,3).

Several liver transplantations have been performed in our institution since 2004. Between February of 2004 and June of 2011, the Hospital Pablo Tobón Uribe has performed 279 cadaveric liver transplantations, and 279 adult and 28 children transplantations. All of the transplantations are cadaveric, and whole-liver transplantation or split-liver transplantation is performed mainly in pediatric patients.

Normal and abnormal Doppler findings are presented in this article, and they are documented with cases in our institution.

Surgical Technique

Knowledge of surgical technique is important when applying the transplanted liver Doppler. It is essential to review the surgical note, given that during surgery, events could occur that require modifying the technique, knowing if there was a need for vascular grafts.

Generally speaking, we will find biliary anastomosis and three vascular anastomosis. Liver transplantation is orthotopic, that is to say, the graft is placed in the anatomical area where the native liver was located.

Whole-liver transplantation

Biliary Anastomosis

Generally speaking, it is an end-to-end anastomosis of the biliary duct of the donor with the receptor (choledochal-choledoscotomy). This technique is ideal, since it prevents intestinal surgery, preserves the Oddi sphincter and reduces the risk of reflux of the intestinal content towards the biliary tree (1). However, this is not possible in all patients, since some of them present a short common hepatic duct, sickly or even not present. In these cases, a biliary enteric anastomosis (choledochal-jejunostomy). There is a greater risk of infection and bleeding with this technique (4).

In some centers, a T-tube is temporarily placed in the biliary anastomosis, which is later removed in an early post-operational period. This technique is not applied in our institution, and is being abandoned, since it is associated with a greater risk of biliary filtrations. Cholecystectomy is performed in all cases (5).

Anastomosis of the hepatic artery

It may have many variations. An end-to-end anastomosis between the common hepatic arteries of the receptor and the donor is attempted. If this anastomosis does not present an optimal flow, vascular grafts are inserted. The most common one is the use of the iliac artery of the donor, which is anastomosed with the anterior wall of the aorta (just below the exit level of the renal arteries), and with the hepatic artery of the receptor (6). The most utilized technique in our institution is "fish mouth" anastomosis, of the hepatic artery, in the origin of the gastroduodenal artery of the receptor.

Venous anastomosis

In our institution, venous anastomosis is performed with the piggyback technique. The supra-hepatic inferior vena cava of the implant is anastomosed to the venous confluence of the receptor, and the infra-hepatic inferior vena cava of the implant is bound. The main advantage of this technique is that it prevents clamping of the vena cava, and there is one less anastomosis to perform (infra-hepatic) (6).

Anastomosis of the portal vein

It is an end-to-end anastomosis. If the portal vein of the receptor has thrombosis, a bridge with a venous graft towards the superior mesenteric vein or towards the splenic vein can be created (1,6).

Split-liver transplantation

It is performed in pediatric patients when the donor is an adult. The liver is surgically removed in order to accommodate to the size of the receptor. Depending on the size of the donor and the receptor, the graft can be from the right lobe (segments V and VIII), from the left lobe (segments I and IV), or the left lateral segment (segments II and III).

Venous anastomosis is performed with the "piggyback" technique. The hepatic hilum will correspond to the bloody part of the liver, and its location is higher. Vascular anastomosis is technically harder (6).

When to perform an evaluation with ultrasound?

A routine ultrasound in a patient with a transplanted liver includes a greyscale evaluation of the hepatic parenchyma and the biliary path, and it requires a Doppler evaluation (7). An evaluation is performed on the first day, usually within the first six hours after the transplantation. Afterwards, another evaluation is performed 24 hours after the transplantation, and thereafter according to clinical evolution and laboratory parameters. Another evaluation is generally performed before releasing the patient from the hospital. In addition, ultrasounds with Doppler evaluations are performed in the latter follow-up, when there is a sign, biochemical or clinical alteration which could suggest a late compilation (6).

Protocol and technical considerations

The technique to perform the Doppler study of the transplanted liver could have many modifications, according to the circumstances of the performed study. An intra-operational evaluation could also be performed, where preferably, specially designed transducers may be used (8). If these transducers are not available, the evaluation can be performed with conventional transducers, and in these cases, high frequency lineal transducers are the best. Before the study is made, the utilized surgical technique must be read in the clinical history, since this helps us interpret the findings with greater ease.

Initially, transversal and longitudinal cuts of the liver and the abdomen are made in order to identify collections. The hepatic parenchyma is evaluated in order to identify infarct areas and the biliary system is examined in order to see dilatation or bilomas.

Subsequently, a greyscale evaluation of the vascular structures of the graft is performed, as well as a color Doppler evaluation of the structures. Lastly, a spectral record of the hepatic artery, hepatic veins, portal veins, superior mesenteric vein, portosplenic venous confluence,

splenic vein and inferior vena cava is obtained. If possible, an evaluation of vascular anastomosis is performed.

A greyscale, a Color Doppler and a spectral Doppler evaluation are then included. These are three levels of evaluation, and each one of them contributes information. The first level provides anatomic information, the Color Doppler shows the blood flow in the vessels and spectral Doppler represents the "wave shape" of the evaluated vessel (9,10).

In order to obtain the wave spectrum, a sample volume from 2 to 4 mm is generally used, located in the center of the vessel. The angle indicator line is placed parallel to the vessel and the angle then formed must be under 60o. If the angle is greater, an error while calculating velocity is generated.

Normal findings

Liver and perihepatic region

The hepatic parenchyma in the normal transplanted liver has a homogenous or slightly heterogeneous echogenicity. The biliary path must have a normal size. These patients do not have a biliary vesicle, given that in all cases of liver transplantation, a routine cholecystectomy is performed (5,7).

It is common to find little or a moderate quantity of free liquid in the abdominal cavity during the early post-operational period, especially in the perihepatic space, which is resolved seven to ten days after the transplant. It is also common to find scarce to moderate quantities of free liquid in the right pleural space (7).

Hepatic artery

Since it is a narrow structure, it is sometimes difficult to visualize it in greyscale, and is only identified with the Color Doppler evaluation. The normal hepatic artery has a wave which shows a rapid-ascension hepatic peak with a continuous diastolic flow. It has a low resistance. The acceleration time (which represents the time between the start of a systole until the first systolic peak) must be under 80 milliseconds, and the index of resistance (IR) must be between 0.5 and 0.7 (9,11,12) (figure 1).

It is important to evaluate it in the hepatic hilum, in the right lobe and the left lobe, since a wave or the normal hepatic artery which has been obtained in the hilum does not completely exclude an obstruction of the hepatic artery. If possible, the anastomosis site must also be evaluated (1,3).

After transplantation, the hepatic artery shows an increase in the index of resistance, as a result of the reperfusion edema inside of the graft. One must take into account that rejection, inflammation and administration of inotropic agents such as noradrenaline may produce a similar result. In the immediate post-operational period, an increase in the index of resistance does not predispose thrombosis or any other vascular complication (6) (figure 2).

Portal Vein

In greyscale, it is identified as an anechoic tubular structure. On occasions, it may have low-level echoes due to a slow flow, which must be carefully evaluated in order to differentiate them from thrombus.

The shape of the portal vein wave must show a continuous flow pattern towards the liver (hepatopetal), with variations in the velocity, caused by breathing (7) (figure 3).

Vena cava and hepatic veins

The hepatic veins are observed as anechoic tubular structures which coalesce in the inferior vena cava. The normal appearance of flow of the hepatic veins and the inferior vena cava is a multi-phasic flow pattern, which reflects the physiological changes of the blood during the cardiac cycle (7,9) (figure 4).

Complications of the liver transplantation and abnormal findings in Doppler ultrasound

Complications may be very varied and include complications of the biliary ducts, complications of the hepatic parenchyma, of the perihepatic space, of the abdominal cavity, vascular complications, and rejection. The complications of the biliary ducts, of the parenchyma, of the perihepatic space and the abdominal cavity are evaluated in greyscales and are not within the objective of this revision. The other complications, vascular, are the most feared and required a Doppler evaluation in order to be detected and characterized (11,13,14).

Vascular complications have an incidence of up to 9% in liver transplantations. These must be ruled out in all patients who present hepatic failure, biliary leakage, gastrointestinal bleeding, abdominal bleeding or sepsis (15-17). They occur more frequently in the early post-operational period. For this reason, the Doppler ultrasound is routinely performed (7).

Complications of the hepatic artery

The vascular complications that include the hepatic artery are the most serious ones. 75% of patients who present thrombosis of the hepatic artery will require a re-transplantation (15). Complications of the hepatic artery include thrombosis, stenosis, vasospasm, and pseudo-aneurysms. They must be diagnosed as soon as possible, in the early post-operational period, in order to perform an urgent re-vascularization of the graft. If this is not performed, the patient will require re-transplantation.

It is important to remember that the biliary ducts in the transplanted liver, unlike those in the native liver, depend solely on the irrigation of the hepatic artery, given that their complications lead to biliary ischemia, which could manifest itself as a fulminating hepatic failure, stenosis, filtration of the biliary path and bacteremias (18,19).

Dodd and collaborators found a sensitivity of 97% for complications of the hepatic artery, including thrombosis and stenosis, if one or more of the following Doppler criteria are proven: index of resistance under 0.5, systolic acceleration time over 80 milliseconds, not being able to find a flow in the hepatic artery or systolic velocity peak in the hepatic artery which is greater than 200 cm/s (7) (figure 5).

Thrombosis of the hepatic artery

Corresponds to 60% of all post-transplantation vascular complications. It is associated to a greater mortality rate, which can be between 20 and 60%, and is the second cause of graft failure during the early post-operational period (7). It is considered early when it occurs within

15 days after the transplantation. The risk factors for it to occur are: an increase in the time of cold ischemia, ABO incompatibility, receptor and donor vessels do not match in size, previous stenosis in the celiac trunk, infections due to cytomegalovirus and acute rejection (17). In addition, a latter thrombosis can be presented, which may occur even years after the transplantation has been performed, and is associated to chronic rejection or with sepsis (7). The incidence reports of this complication are varied and are found between 4 and 12% of adults. It is more frequent in children (1).

This has been the most frequent vascular complication in the hospital, with a rate of 6.1%. Most have been adults. In 17 out of 19 patients, it was presented as an early complication (under 11 days), and the diagnosis was performed with the study of the Doppler ultrasound, in 94% of the cases. Surgical management in 13 patients was performed. 8 of them required re-transplantation and four patients underwent endovascular management.

The early diagnosis of the thrombosis of the hepatic artery is extremely important, given that an early intervention such as thrombectomy, reconstruction of the hepatic artery or both could save the graft in some cases. However, most patients will require a re-transplantation. Even with the re-transplantation, mortality increases by 30% (1).

The diagnosis of thrombosis of the hepatic artery is performed when flow is not detected with the color Doppler ultrasound study or with the spectral Doppler ultrasound in the main hepatic artery, or in the intrahepatic branches. The Color Doppler leads to a correct diagnosis in 92% of cases (20) (figure 6).

One must take into account that false positives may occur, generally related to a reduction in the flow of the artery, in cases of severe hepatic edema, systemic hypotension or stenosis of the artery (2). False negatives have been described faced with the presence of periportal arterial collateral vessels, in cases of chronic thrombosis (1). Collateral vessels generally show a tardus parvus type wave, which suggests proximal stenosis (1).

Stenosis of the hepatic artery

The stenosis of the hepatic artery has been informed in 5-11% of transplanted livers. This complication usually occurs in the anastomosis site, within three months after the transplantation (1). If the stenosis is not subjected to treatment, it could lead to thrombosis of the hepatic artery, hepatic ischemia, biliary stenosis, sepsis and loss of the graft. Early detection is crucial in order to apply a treatment, whether with surgical reconstruction or with ball angioplasty, and to avoid re-transplantation. Stenosis is generally associated to lesion by clamping, or intimate trauma by catherers, which results in ischemia of the artery (7).

The Doppler ultrasound is the diagnostic method of choice, given that it has the potentiality of detecting the focal increase of the systolic velocity peak (over two to three times). Additionally, it can detect a turbulent flow distal to stenosis (1). In addition to this, a very frequent finding is the presence of intrahepatic tardus parvus flow, which is characterized by a systolic acceleration over 80 milliseconds and an index of resistance under 0.5 (21) (figures 5 and 7). This type of wave can also be seen in cases of chronic thrombosis of the hepatic artery, with collaterals and it is the differential diagnosis. If an intra-hepatic tardus parvus flow is identified, it is more probable that it is secondary to a stenosis than to a thrombosis with collaterals.

Low degree stenosis may be presented with a completely normal Doppler ultrasound. Therefore, when there is high clinical suspicion,
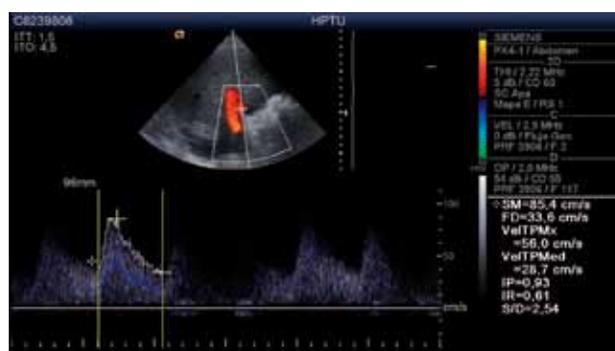

Figure 1. Normal hepatic artery. Its permeable color is seen with the color Doppler and low resistance can be seen in the spectrum (i.r.0,61).
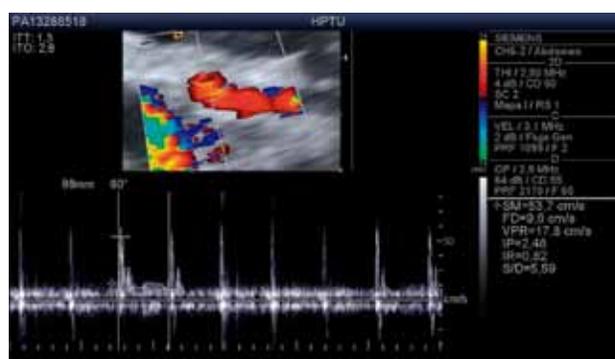

Figure 2: Early post-transplantation hepatic artery. Doppler in the first 24 hours of liver transplantation. An increase in the resistance index is demonstrated (i.r. 0,82).
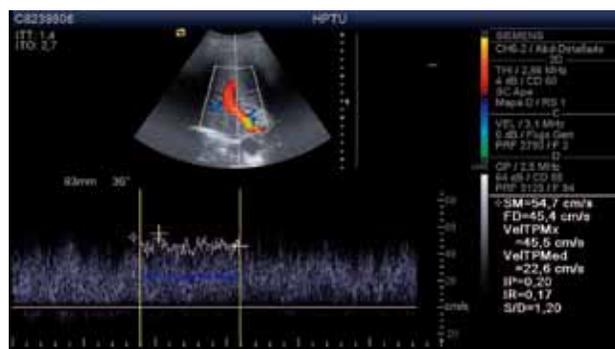

Figure 3. Normal portal vein. The oscillations in the flow velocities and flow with hepatic direction can be seen.
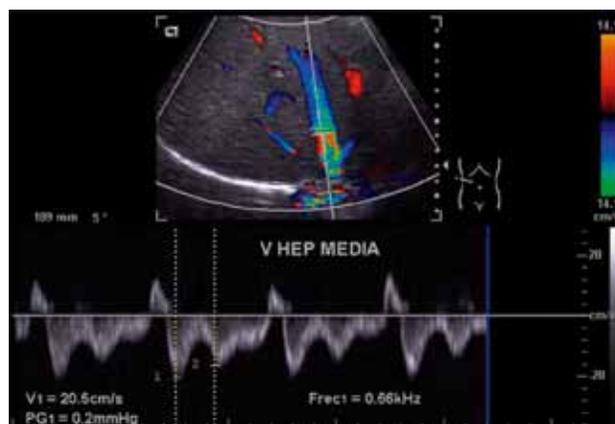

Figure 4. Normal hepatic vein. The normal three-phased pattern can be seen, which is a reflection of the cardiac cycle.

even if the ultrasound findings are negative, additional studies will be required, such as angiotomography, angioresonance and even arteriography (2).

Pseudo aneurysm

It is a complication which is not very frequent, and usually presents itself in the site of anastomosis, or can occur as a consequence of interventionist procedures. It could also originate in intrahepatic arterial branches after percutaneous biopsies or focal parenchymatous infections.

They are usually asymptomatic. In case of rupture, they can manifest themselves as an acute condition of hypovolemic shock. Additionally, a fistula can be formed between the pseudoaneurysm and the biliary path, or the gastrointestinal tract, resulting in hemobilia or hemorrhage of the superior digestive tract.

In the Doppler ultrasound, it can be seen as a rounded lesion in the trajectory of the hepatic artery which fills up with the Color Doppler and presents turbulent arterial flow with the pulsated Doppler.

Vasospasm

The arterial vasospasm with clinical impact has been observed in 1.3% of our patients. In two of them, it has been associated with infected perihepatic collections. Management consists of draining the collections when necessary, and management with intra-arterial vasodilators in other cases.

Complications of the portal vein

The complications of the portal vein post-transplantation are relatively rare, and include thrombosis and stenosis (1). Their incidence range from 1 to 13% (22). The stenosis of the portal vein the pediatric population is presented from 4 to 8%, and is more associated with reduced liver transplantation (23,24). These complications can cause symptoms similar to those of portal hypertension, which include bleeding by esophageal varicose veins, splenomegaly and ascites (22). The risk factors are: A defective surgical technique, an anomalous alignment, or an excessive alignment of the vessel, as well as states of hyper-coagulation due to previous surgeries.

Thrombosis of the portal vein

Thrombosis of the portal vein, post-transplantation, may occur in up to 3% of patients; it predominantly affects the extra-hepatic segment. This complication relates to a reduction in the flow of the portal vein, as well as the presence of portosystemic derivations before transplantation and previous splenectomy (23).

The thrombosis of the portal vein presents itself in 2.2% of patients who have received a transplantation in the Hospital. With the exception of two patients who died early, the other patients have received medical management with anti-coagulation. Two patients developed cavernomatous degeneration of the portal vein.

The thrombus in mode B is generally seen as an echogenic image inside of the vessel. This thrombus is presented with an irregular surface, located to the side of the vessel, producing a partial or total obstruction of the blood flow, which can be characterized by the color and spectral Doppler (figure 8). In children, the thrombus is frequently anechoic,

and it may go unnoticed in mode B; therefore, the use of color and spectral Doppler is absolutely necessary in order to prove their presence.

Partial thrombosis can mimic a stenosis. For this reason, a careful Doppler ultrasound examination must take in order to differentiate them. Occasionally, it is possible to find increased flow in the branches of the hepatic artery, as a secondary compensatory mechanism to portal thrombosis.

Portal vein stenosis

Portal vein stenosis has an incidence of 1% in the post-transplantation liver (22). The most frequent site is anastomosis, and it has a strong relation with the difference in size between the portal vein of the donor and the receptor. It may be asymptomatic or cause portal hypertension symptoms. One must be extremely careful when diagnosing stenosis, since this area can normally present a moderate change in size which shows an "aliasing" focus, and an increase in the velocity with color and spectral Doppler ultrasound.

Portal vein stenosis is present in 1.6% of cases. Out of all the vascular complications, it is the only one that has been more frequent in children than in adults. In all cases, it has been corrected with successful endovascular therapy.

Signs in mode B include a change in the size of the stenosis area, with a reduction of over 50%. This finding itself is not the diagnosis of stenosis. We must also look at a dilatation in the post-stenotic segment and an increase in the number of collaterals, or a change in the size of the portal vein, depending on the time of evolution. With the spectral Doppler, we will find a relation which is equal or greater than three, between the peak systolic velocity in the stenosis site, and the peak systolic velocity in the segment which is proximal to the stenosis. "Aliasing" can be seen with the Color Doppler. In addition, velocities between 100 and 300 cm/second can be seen in the immediate post-stenotic segment (23,24) (figure 9).

Complications of the hepatic veins and the venous exit tract

The complications of the hepatic veins have a low incidence, and reach up to 1% of all ransplanted livers. It is more frequent in children (5%) (22). Complications also include thrombosis and stenosis, as described in the other vascular alterations.

In the Hospital, the second most common vascular complication has been stenosis of the venous exit tract, with an incidence of 2.2%. The average time of appearance is 76 days, and all patients report signs of portal hypertension with ascites, splenomegaly and alteration of the hepatic function tests. Endovascular therapy has been performed in all patients, with angioplasty and placement of stent.

The stenosis of the hepatic veins occurs in the surgical sites and is closely related with the technique which was used at the moment of the transplantation. It is important to know that, although the mode B can show the echogenicity of the thrombus or the change in size of the stenosis, the use of a color and spectral Doppler is always necessary in order to observe the direction of the flow and their wave pattern. It is known that the normal three-phase pattern of the hepatic veins which is created by the right chambers of the heart may vary when an obstruction in the exit flow, whether by a thrombus or a stenosis. Because of this, it is important to perform not only a thorough examination, but also to monitor its evolution through time.
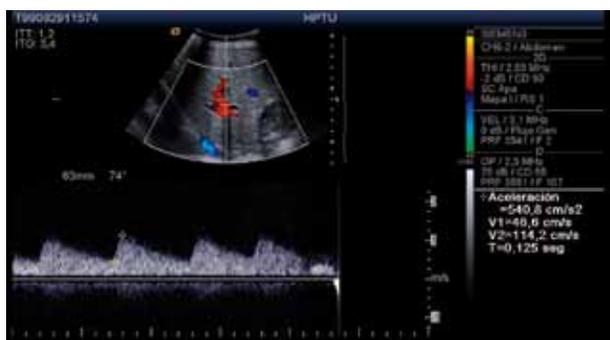
Figure 5. Stenosis of the hepatic artery. Tardus parvus wave in the intra-hepatic artery, with a time of acceleration of 125 milliseconds and an index of resistance of 0.45, which is caused by the stenosis in the anastomosis of the hepatic artery.

Figure 6. Thrombosis of the hepatic artery. The color Doppler ultrasound does not detect flow in the hepatic artery due to early thrombosis. Turbulent flow can be seen in the portal vein.

Figure 7. Stenosis of the hepatic artery. The study of the Doppler ultrasound shows a peak systolic velocity of 208 cm/second in the anastomosis, as well as an index of resistance of 0.84.

Figure 8. Thrombosis of the portal vein. A hypoechoic thrombus is observed inside of the light of the portal vein.
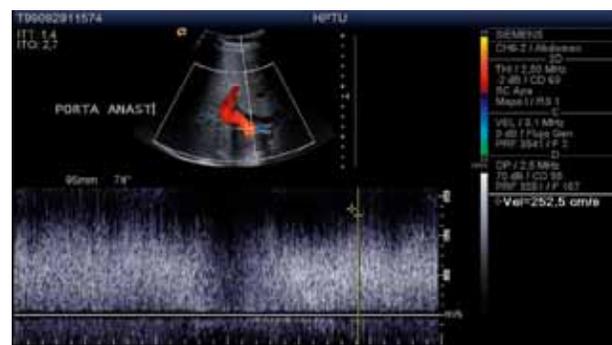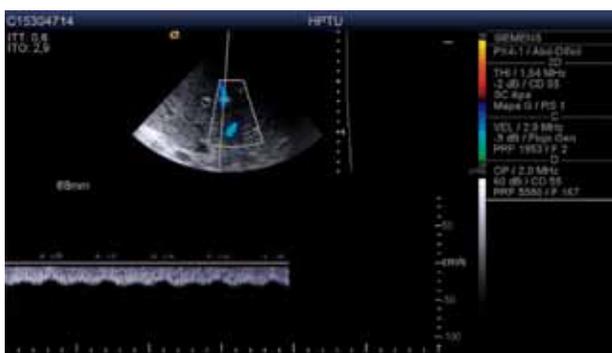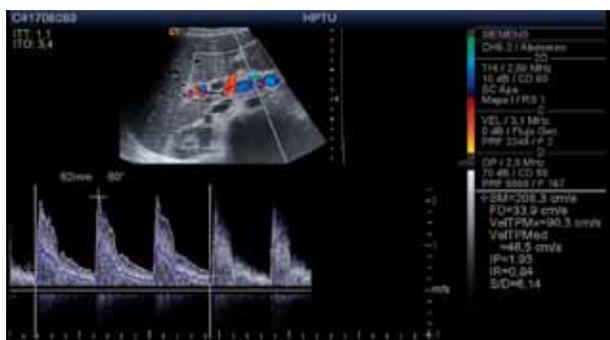

Figure 9. Stenosis of the portal vein. The peak systolic velocity in the site of anastomosis is increased and turbulent flow is detected with the color Doppler (aliasing) and with the spectral Doppler.
Note: The Doppler angle is not corrected in the image, which means that the registered velocity is not completely accurate.

Figure 10. Stenosis of hepatic veins. A single-phase pattern can be seen in this hepatic vein. It had a three-phase pattern in the previous study.

Figure 11. Thrombosis of the inferior vena cava. The Doppler ultrasound shows an image of the inferior vena cava, which shows a thrombus inside of the vein light.

The change of the pattern of the spectral waves (for example, passing from a three-phase to a two-phase and then to a single-phase wave) may be the only sign of stenosis of the hepatic veins (figure 10).

The direct ultrasound signs of stenosis of the hepatic veins are the visualization in mode B of the stenosis itself, and a turbulent post-stenotic flow with an increase in the velocities in the pulsated Doppler. The visualization of the single-phase flow in the hepatic veins is a sensitive indirect finding. However, it is unspecific for the diagnosis of significant stenosis. On the other hand, two-phase or three-phase flow identification enables to rule out significant stenosis in the hepatic veins.

Acute stenosis of the inferior vena cava can be caused by the discordance between the sizes of the anastomosed vessels or due to

rotations of the graft. Late stenosis tends to be secondary to fibrosis or intimal hyperplasia. Chronic stenosis of the inferior vena cava is most frequent in re-transplanted patients and in children.

Piggyback anastomosis, with preservation of the vena cava of the receptor and cava-cava anastomosis, is the preferred current technique for orthotopic liver transplantation. However, it is susceptible to suffering two types of complications: hemorrhage due to dehiscence of the suture of due to direct hepatic damage during surgery, and the Budd-Chiari syndrome. The treatment of choice for stenosis is percutaneous dilatation or the insertion of the Doppler ultrasound. Surgical treatment is preferred for cava thrombosis.

The thrombosis of the inferior vena cava and the hepatic veins is diagnosed when visualizing the intraluminal thrombus, accompanied by an absence of flow with color Doppler ultrasound and pulsated Doppler (figure 11).

Conclusion

The Doppler ultrasound is an essential tool for the evaluation of patients with liver transplants. The radiologist must know the manifestation of possible complications of this procedure, which currently is the treatment of multiple acute and chronic diseases of the liver.

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