Doppler assessment of maternal central venous hemodynamics during uncomplicated pregnancy : a comprehensive review.

W. Gyselaers*° MD PhD, T. Mesens* MD, K. Tomsin‡ BSc, L. Peeters# MD PhD

* Dept. Obstetrics & Gynaecology, Ziekenhuis Oost Limburg, Genk Belgium

° Dept. of Physiology, Hasselt University, Diepenbeek Belgium

‡ Institute of Biomedical Sciences, Hasselt University, Diepenbeek Belgium

Dept Obstetrics & Gynaecology, Maastricht University Medical Center, Maastricht The Netherlands

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Correspondence: Wilfried Gyselaers

Department of Obstetrics & Gynecology

Ziekenhuis Oost Limburg

Schiepse Bos 6

B-3600 Genk

Belgium

T: 0032 – 89 – 327524

F: 0032 – 89 – 327920

E: wilfried.gyselaers@zol.be

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Introduction

Doppler studies on hemodynamics of the cardiovascular system and intra-abdominal organ perfusion in non-pregnant individuals are usualy performed by cardiologists and radiologists. Specialists in Maternal-Fetal Medicine are also familiar with cardiovascular Doppler sonography, however they mostly focus on the fetal [1;2] or uteroplacental circulation [3-5]. Recently, several reports have been published on Doppler assessment of the maternal venous compartment, illustrating its feasibility and repeatability [6-11]. These studies have shown that the venous compartment is also subject to maternal cardiovascular adaptation during uncomplicated pregnancy [9;11]. In gestational diseases, such as preeclampsia, some of the observations show promising results with respect to the evaluation of maternal cardiovascular maladaptation [9;11] and prediction of subsequent disease [12]. Therefore, the maternal venous compartment is a new area to be explored in obstetric ultrasound imaging [13], in order to link Doppler observations to known features of gestational cardiovascular (patho)physiology [14-16] and to the information obtained from other parameters [17].

This paper offers a comprehensive review on Doppler assessment of the maternal venous compartment during uncomplicated pregnancy.

Literature sources

A literature search was conducted to identify all the published observational Doppler studies on maternal venous hemodynamics. Relevant citations in PubMed and Medline were searched using combinations of the keywords : Maternal physiology, Doppler, Hepatic veins, Renal interlobar veins, Pregnancy, Venous Hemodynamics, Venous Compartment, Central Veins, gestational cardiovascular adaptation, review. The reference lists of all known primary and review articles were examined for additional relevant citations. Relevant chapters from handbooks were searched in the Library of Hasselt University and in personal collections.

Definition and anatomy of the lower central venous compartment.

The venous system is responsible for the return of deoxygenated blood from the organs back to the heart. The central veins are the large single lumen veins, which are anatomically close to the heart. Basically they include the jugular veins, the upper and lower vena cava, the hepatic veins and the renal veins. The connection between the systemic venous system and the right atrium is open, as there is no interposition of an anatomical or functional valve mechanism. Therefore, intravascular measurements of venous pressures, flow-velocities and volumes in the central veins are a direct reflection of the function of the right heart [18;19]. In clinical practice, this principle is commonly used to estimate or measure the central venous pressure at the level of the jugular veins using both non-invasive and invasive methods [20].

There is an anatomical structure known as the valve of the inferior vena cava, which was first described by Eustachius [21]. Contrary to the semilunar valves of the arterial outflow tracts, this structure does not close the lumen of the vena cava intermittently, but it is merely a semilunar endocardial fold at the anterior site of the entrance of the inferior vena cave in the right atrium. It has an important function during foetal life to direct the oxygenated blood towards the open foramen ovale [21], but degenerates after birth.

The inferior Vena Cava (VCI) contains blood from the intra-abdominal and retroperitoneal organs, the gonads and the lower limbs. As illustrated in Figure 1a, the liver drains blood into the VCI through the hepatic venous tree, which consists of three main branches: the left, middle and right hepatic vein (HV). In many individuals, left and middle HV fuse before draining into the VCI and often an accessory inferior right HV is found [22]. Right and left HV respectively drain the largest and smallest liver volumes [22]. Hepatic veins are the sole exit of blood from the liver, and drain blood originating from both the portal vein and hepatic arteries [23;24]. The outflow of HV into the VCI is located at the cranio-posterior margin of the liver, underneath the diafragm, at a few centimeters distance from the right atrium.

Renal veins (RV) connect to the VCI at a distance of roughly 10 cm from the right atrium. This connection is usualy more caudal on the right than on the left side. As illustrated in Figure 1B, the right RV is half the length of the left RV, which is the one crossing the midline. Accessory renal veins are found more often on the right than on the left side [25]. On the right side, the proximal diameter of the RV is larger than on the left side [26]. The left RV is squeezed between the aorta and the Superior Mesenteric Artery, and sometimes this may provoke ortostatic hematuria [27]. This so-called Nutcracker phenomenon can aggravate during pregancy [28]. The left RV also drains blood from the left ovarian vein, which is another important interrenal morphological difference (Fig 1B).

There are many types of anatomical variants of the lower central venous system, not only due to a high frequency of accessory veins as explained above, but also due to abnormal embryogenesis. These congenital anomalies are found in all segments of the VCI: the hepatic, suprarenal, renal and infrarenal segment [29]. Congenital venous aberrations are usualy asymptomatic and are mostly found by accident. Their presence or absence have to be considered carefully in the pre-operative work-up of liver- of kidney transplantation [30;31]. Next to this, different types of congenital intrahepatic vascular shunts have been observed, such as arteriovenous connections, arterioportal shunts and portosystemic fistulas [32]. Both congenital aberrations and intrahepatic vascular shunts are responsible for a high variation of hepatic vein Doppler patterns in normal individuals without liver disease [33].

Physiology of venous hemodynamics

The venous compartment has an important role to play in human physiology. It is a large capacitance reservoir, containing 65-75% of the total blood volume. Of this, 75% is in the small veins and venules [34]. The splanchnic bed is the most important blood reservoir of the body, containing up to 25% of the total blood volume [34], of which the majority is in the liver bed [35;36]. The venous vascular walls contain collagen and elastin fibres, together with a circular layer of smooth muscle cells [37]. This histological structure serves physiologic properties as expansion, visco-elasticity and active contraction [34]. As such, the venous compartment contributes actively to the regulation of cardiac output [19;38]. Contrary to the arterial system, small changes of intravenous pressure have major impact on cardiac output [19]. In the control and regulation of cardiac output, the heart and veins cooperate as one functional unity [19]. Both anatomical and physiological properties allow the venous system to function as the main regulator of the circulating blood volume : in cases of hypovolemia (e.g. massive hemorrhage), reflex- induced venoconstriction mobilises stored blood from the venular bed into the circulation, and in cases of blood volume expansion (e.g. pregnancy), the majority of the excess volume is maintained in the venular bed.

The driving forces behind forward flow of blood in arteries and veins are different. In the arterial compartment, the contraction of the cardiac ventricles creates a positive pressure-gradient between the heart and the other parts of the human body, pushing the blood into the arterial system. In the venous compartment however, relaxation of the cardiac atria and ventricles create a negative pressure gradient between the heart and veins. This suction force is responsible for venous return [18;19].

Many physiologic variables are known to interfere with venous return and the shape of the venous pulse waves. Respiration movements are responsible for heaving of the venous pulse waves [39]. This may be counteracted by intraluminal obstruction, such as trombi, or by external

compression from intrapelvic masses [39]. An example of this is the gravid uterus, which is responsible for a rise of intravenous pressure of the femoral vein [16]. Ortostasis and gravidity reduce venous return, whereas this temporarily increases after changing to supine position until a new steady state is reached [19;38]. Veins, surrounded by skeletal muscular tissue, depend largely on contractions of these muscles to stimulate forward venous flow and to prevent stasis of blood. This is mainly true for the lower extremity, where this muscle pump activity is supported by mechanic compression from stockings for the prevention of deep vein thrombosis in cases of reduced mobility [40]. Several drugs and medications have been studied with respect to direct or indirect activity on venous wall muscular contractility [36].

Study of venous hemodynamics by Duplex Ultrasonography

Methods to study body venous tone have been reviewed by Pang [34]: they include mean circulatory filling pressure technique, constant CO reservoir technique, plethysmography, blood-pool scintigraphy, linear variable differential transformer technique and intravasular ultrasound. These techniques all have limitations and are difficult to perform in clinical setting, especially during pregnancy. Duplex Ultrasonography has been reported to be a simple, non-invasive and easily-accessible method to study venous hemodynamics, both in non-pregnant patients [41] as during pregnancy [6-8]. Because of high intra- and interobserver variation reported for Doppler- derived measurements [42;43], methodologic standardisation is needed, especially when interfering factors, as discussed above, are to be excluded.

A standardised Duplex Ultrasound examination has been reported, which allowed obtaining reproducible measurements of renal interlobar [9] and hepatic venous pulsewaves [11] by Duplex ultrasonography. Examinations were performed by a single ultrasonographer, using a 3,5-7 MHz probe (Hitachi EUB 6500). All women were examined in supine position at random occasion throughout the day, irrespective of food intake [44]. Both kidneys and liver were scanned in the transverse plane at the craniocaudal midportion of the organs (Fig 2a and 3a). The impact of breathing movements on the ultrasound image was demonstrated to every patient and the relevance of holding breath during Doppler measurements was explained and demonstrated. Once the patient was familiar with the instructions of the ultrasonographer, the examination was performed according to a standard protocol. (1) The direction of blood flow, as indicated by color Doppler, was used to differentiate right, left and middle branch of the hepatovenous (HV) tree from the portal branches and hepatic arteries (Fig 2A) and to distinguish renal interlobar veins (RIV) from arteries (Fig 3b). (2) The real time ultrasound image in combined B-D mode was frozen after visualisation of at least two to three similar venous Doppler flow patterns during interrupted breathing. (3) As the direction of the Doppler

beam was mostly parallel with the examined vessel, Doppler angle correction was rarely needed. If so, this was always within a maximum of +/-30°. (4) RIV maximum velocity (MxV) and minimum velocity (MnV) were plotted and printed. Similarly, velocities were measured of HV A-, X-, V- and Y-deflections. (5) Throughout the course of the ultrasound examination, interpretation of measured values by the ultrasonographer was avoided. (6) For every woman, three consecutive measurements were printed for each kidneys and the liver. (7) After the scan, RIV Delta Velocity (DeltaV) and Impedance Index (RIVI) were calculated as MxV-MnV and DeltaV / MxV respectively. (8) The mean of three measurements of RIV MxV, MnV and RIVI and of HV A-, X-, V- and Y-velocity was considered the organ-specific value, which was registered in the database. (9) Reproducibility of this methodolody was demonstrated in a set of 24 women by performing all measurements twice in the same individual and calculating the intra-class correlation coefficient using maximum likelihood estimation for the linear mixed model [45;46]. These intra-class coefficients were 0.88 for RIVI and 0.78, 0.88 and 0.62 for HV A-, V- and Y- velocity respectively [9;11].

Doppler studies of lower central hemodynamics in non-pregnant individuals.

As explained above, there are no anatomical valves at the level of the venous inflow tracts. Due to this open communication between the heart and central veins, the shape of the venous pulse and Doppler waves reflect the cardiac cycle of the right atrium [18;19]. This is well known for the pulse wave characteristics of the jugular veins [38], vena cava and hepatic veins [41]. The typical pulse wave characteristics of hepatic veins are illustrated in Figure 3a. As is shown, the A-deflection represents central venous backflow away from the heart during atrial contraction, the X-deflection represents forward cardiopetal flow following atrial relaxation which decelerates instants before opening of the tricuspid valve (V-deflection), the Y-deflection represents forward flow following ventricular relaxation. Sometimes, a C-deflection is also present instants after the A-deflection, and this represents the closure of the tricuspid valve. At increasing distance from the heart, the triphasic shape of the venous pulse wave, presented in Fig 2c, changes gradually towards a biphasic, monophasic and flat pattern. Biphasic venous pulse waves are usually observed in the liver during the second trimester of pregnancy (Fig 2d) and in renal interlobar veins of non-pregnant individuals (Fig 3c). Monophasic waveforms are a typical pattern at the level of RIV during third trimester pregnancy (Fig 3d). A flat pulse wave is the common pattern observed at the lower extremity [39] but is also frequently observed in the liver during the third trimester of pregnancy (Fig 2e) and in RIV during ureteral obstructive disease (Fig 3e) [47;48]. The same types of Doppler waveforms are also found in the venous circulation of the fetus: triphasic types are observed at the level of inferior vena cava and hepatic veins, biphasic waveforms s are present in the ductus venosus and flat patterns are found in the umbilical vein [49;50].

As explained above, anatomical variations and intrahepatic shunts are responsible for a large variation in the presentation of tri-, bi- and monophasic Doppler waves in the liver of healthy individuals [33]. Next to this, these patterns are also strongly influenced by cardiac and liver

diseases. Typical patterns of abnormal HV Doppler waveforms have been reported for restrictive and constrictive cardiopathy, tamponade, pulmonary hypertension and tricuspid regurgitation [51]. These patterns also show typical variations with respiration. Similarly, an association was reported between mono-and biphasic HV Doppler wave patterns and histology of liver steatosis [52;53], whereas the presence of triphasic waves virtually excludes fatty infiltration of the liver [52;54]. Monophasic patterns in HV have also been reported for impaired liver function due to cirrhosis [55], compression by intra-abdominal or intrahepatic masses [56] or HV thrombosis (Budd-Chiari Syndrome) [55;56].

In non-pregnant individuals, Doppler studies of renal interlobar veins are used in obstructive uropathy to distinguish physiological from pathological pyelocaliectasis [47;48], for non-invasive monitoring of transplant kidneys [57;58] and in the work up of renal vein occlusion [58;59].

Doppler studies of hepatic veins during pregnancy

As explained above, there is a high intra-and interindividual variation of HV Doppler waves, ranging between triphasic, biphasic and flat patterns [33;41]. Roobottom et al. reported that during the course of normal pregnancy, the HV waveforms changed from predominantly triphasic to predominantly monophasic patterns [8]. This is illustrated in Figure 2. Return from gestational patterns to normal during the course of postpartum has also been reported [60]. The Hepatic Vein A-deflection, known to represent central venous backflow during atrial contraction [13], was reported to convert to constant forward moving flow into the direction of the heart at around 22-24 weeks of gestation [11]. This gestational evolution resembles that of the known evolution of plasma volume expansion [16] and therefore, it was hypothesised that this phenomenon could result from dampening of cardiofugal flow by increasing intravascular filling [11]. Doppler derived estimations of hepatic flow during pregnancy have shown that hepatic perfusion increases significantly after 28 weeks compared to non-pregnant levels, and because the hepatic arterial blood flow remains unchanged, this effect is mainly due to the increase of the portal venous return [23;24].

Figure 4b shows the evolution of HV A-wave velocities, measured at 1-2 week intervals, between 9 weeks and term in an uncomplicated pregnancy. As is shown, the velocities change from positive velocities into the direction of the liver (triphasic waves) during early pregnancy, to negative velocities into the direction of the heart (bi- and monophasic waves) in the second trimester. In this particular case, the shift from tri- to biphasic and flat Doppler waves occurred at 25-27 weeks, but shortly returned to triphasic again at 32 weeks after which they became biphasic and flat again until term. This reversal illustrates the high intra-individual variation of HV waveforms during the third trimester of pregnancy. In a group of 13 unomplicated pregnancies, 3 different types of of evolution in HV Doppler waves during third trimesrter pregnancy were observed: (1) women presenting monophasic waveforms

only, (2) women having both mono- and biphasic waveforms, and (3) women presenting mono-, bi- and triphasic waveforms [11].

Doppler studies of renal interlobar veins during pregnancy

As is explained above, Doppler wave patterns in RIV of pregnant women gradually shift from biphasic to monophasic during the course of pregnancy (Fig 3 c+d) [9;10]. Retroperitoneal compression by the volume of the pregnant uterus is considered responsible for dilatation of the renal pyelon, especially on the right side [6;10], and this can be associated with the presence of flattened RIV Doppler waveforms (fig 3e).

Karabulut et al were the first to report lower RIVI values in pregnant women compared to non-pregnant individuals [6]. From the late second trimester onward, they observed that right kidney RIVI was 10-15 % lower than in the left one, and this was inversely related to pyelon diameter. This observation was considered to result from increased intrarenal interstitial pressure, due to retroperitoneal compression by the growing pregnant uterus. In a cross-sectional study [10] and in a prospective observational study [9], RIVI was observed to decrease gradually in both kidneys during first and second trimester of pregnancy, after which this decrease continued until 30 weeks at the right side only. Gestational evolutions of RIV Maximum and Minimum flow velocities were found to be similar to known gestational evolutions of Cardiac Stroke Volume and Renal Glomerular Filtration [9], which suggested an association with features of maternal gestational cardiovascular adapatation. Venous flow velocities in the right kidney were consistenly higher than in the left kidney, and this was linked to interrenal anatomical differences: as explained above, larger diameters and more accesory renal veins are present on the right side [25;26;61], which facilitate efflux of blood. Influx of ovarian blood and compression between Superior Mesenteric Artery and Aorta decelerate flow velocities in the left renal vein [27;28]. These anatomical differences also help to explain the lower RIVI values during the third trimester of pregnancy [9]. Fig 5 shows the normal pattern of variation of RIVI values in both kidneys, as measured at weekly intervals in a non-pregnant woman (Fig 4a) and in an uncomplicated third trimester pregnancy (Fig 5b).

As is depicted, the RIVI measurements of both kidneys in the non-pregnant individual show an undulation around 0.4, and the oscillation of this pattern is not the same in both kidneys. The RIVI values in third trimester pregnancy are lower on the right side than on the left one, and due to this the undulating curves of both kidneys are totally separated. Fig 4a illustrates the evolution of RIVI of both kidneys at 1-2 weeks intervals from 6 weeks before conception until delivery in a women with an uncomplicated pregnancy. As is shown, the undulating pattern is present both in the non-fertilized menstrual cycle as during pregnancy.

Towards a link between maternal venous Doppler parameters and known features of gestational cardiovascular physiology

Human pregnancy is subject to major adaptations of the maternal cardiovascular system [14;16]. These adaptations occur both at the arterial and venous sites of the circulation. Most Doppler studies on gestational hemodynamics focus the analysis of maternal uterine artery waveforms or the evaluation of fetal or uteroplacental circulation; the large number of publications on these topics have been reviewed extensively [2-5]. Doppler studies on maternal venous hemodynamics however are few.

As explained above, the tone of venous vascular walls and related venous compliance are crucial determinants of cardiac output through a direct impact on central venous pressure and preload of the right ventricle, which regulates stroke volume through the Frank-Starling mechanism [38]. Venous compliance, which is much larger than arterial compliance [62], depends on ageing, autonomic (dys)function, medication, systemic or vascular diseases [36] and parity [63;64]. During uncomplicated pregnancy, venous compliance and distensibility are increased [65] and this returns slowly to normal values within 3 months postpartum [66]. The functional ability of vessel walls to contract or relax and change vascular compliance can be studied by Duplex sonography : maximum (MxV) and minimum (MnV) flow velocities are measured to calculate venous impedance index, which is the venous equivalent of arterial resistivity index (RI), defined as (MxV-MnV)/MxV [48]. As explained in the previous chapters, Renal Interlobar Vein impedance index (RIVI) decreases during the course of pregancy, and this is consistent with an increase of venous compliance, as mentioned above [6;9;10]. As such, this evolution illustrates that Duplex sonography allows obtaining information on venous compliance or distensibility non-invasively, and that RIVI measurement can be considered a quantitative representation of venous tone or resistance. In this perspective, the undulating pattern of RIVI values in non-pregnant and pregnant women, as illustrated in figures 4 and 5,

is an interesting observation. This pattern suggests that the physiologic process of maintaining venous tone or compliance is a dynamic process with a slow variation in time, and that the activity of the vascular walls differs at various sites of the venous circulation.

The venous side of the splanchnic vascular bed plays a critical role in the homeostatic responses to changes of intravascular volume [63]. Up to 33% of the total blood volume is in the splanchnic venous bed, and 1/3 of this is in the liver [35;36]. Therefore, the splanchnic veins are called capacitance vessels [34;36]. Sympathetic nerve stimulation can mobilise up to 21% of the total blood volume into the circulation [36], hereby increasing cardiac output significantly [67]. Again, the contribution of the liver in this proces is important [36]. During pregnancy, alterations occur at the vascular walls of mesenteric veins, resulting in increased intravascular volumes at the expense of compliance [64]. Doppler derived estimations of hepatic flow during pregnancy have shown that hepatic perfusion increases significantly after 28 weeks compared to non-pregnant levels, and that this is mainly due to the contribution of the portal vein [23;24]. This evolution is associated with dampening of the HV A-wave, indicating that during the second trimester of pregnancy the normal physiologic backflow of blood from the right atrium into the hepatic venous system during atrial contraction reverses to constant forward moving flow into direction of the heart [11]. The gestational evolution of HV A-velocities was very similar to the known evolution of plasma volume expansion [11]. As such, the presence or absence of the HV A-wave as reported [11], together with the manifestation of triphasic, biphasic or flat HV Doppler wave patterns (Fig 2a-c), may be considered indirect Doppler representations of the status of hepatic venous intravascular filling. In this perspective, the large intra-individual variability in presenting different types of HV Doppler waves during the third trimester of pregnancy is another interesting observation [11]. This suggests that maintenance of intravascular filling may be another dynamic process, and that perhaps the

liver is actively involved in maintaining the circulating volume during the third trimester of pregnancy.

These observations are the basic elements of an interesting hypothesis, in which an active role is attributed to the maternal venous compartment for the regulation and maintenance of the pregnant woman’s circulating volume, which is known to be a crucial physiologic condition towards an uncomplicated course of pregnancy and normal outcome.

Conclusions

The review of publications presented in this paper illustrate that studies of the maternal venous compartment by Duplex ultrasonography are feasible. The reported results correlate well with known features of gestational cardiovascular physiology. Some of the observations open perspectives to investigate further into new hypotheses on the physiologic role for the venous compartment to play in the volume homeostatis during pregnancy, and as such Doppler studies of maternal venous hemodynamics may add to the current knowledge of gestational cardiovascular hemodynamics. Finally, the ressemblence between the maternal and fetal venous circulation suggests that improvement of our knowledge on dynamic events in the maternal venous circulation may help to understand better important aspects of venous hemodynamics of the fetus as well. Next to all this, ultrasonography is generelly accepted to be safe during pregnancy, and it is an examination easily accessible to all pregnant women undergoing obstetric scanning. These arguments are an open invitation for obstetric ultrasonographers to initate Doppler studies in the “forgotten field” of obstetrics: the maternal venous compartment.

Acknowledgements

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Figure 1

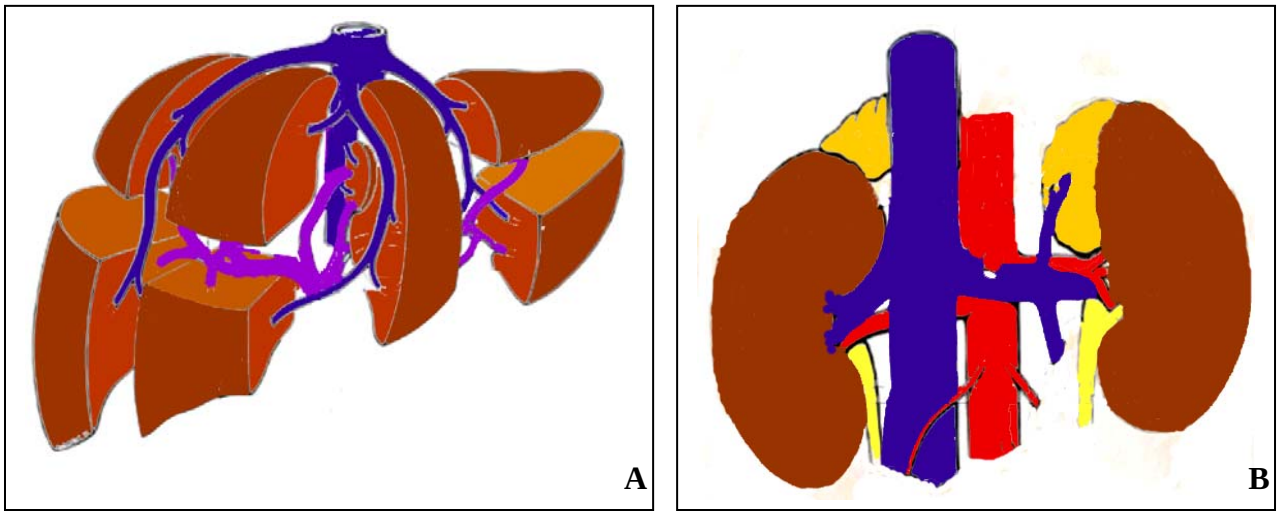


Figure 2

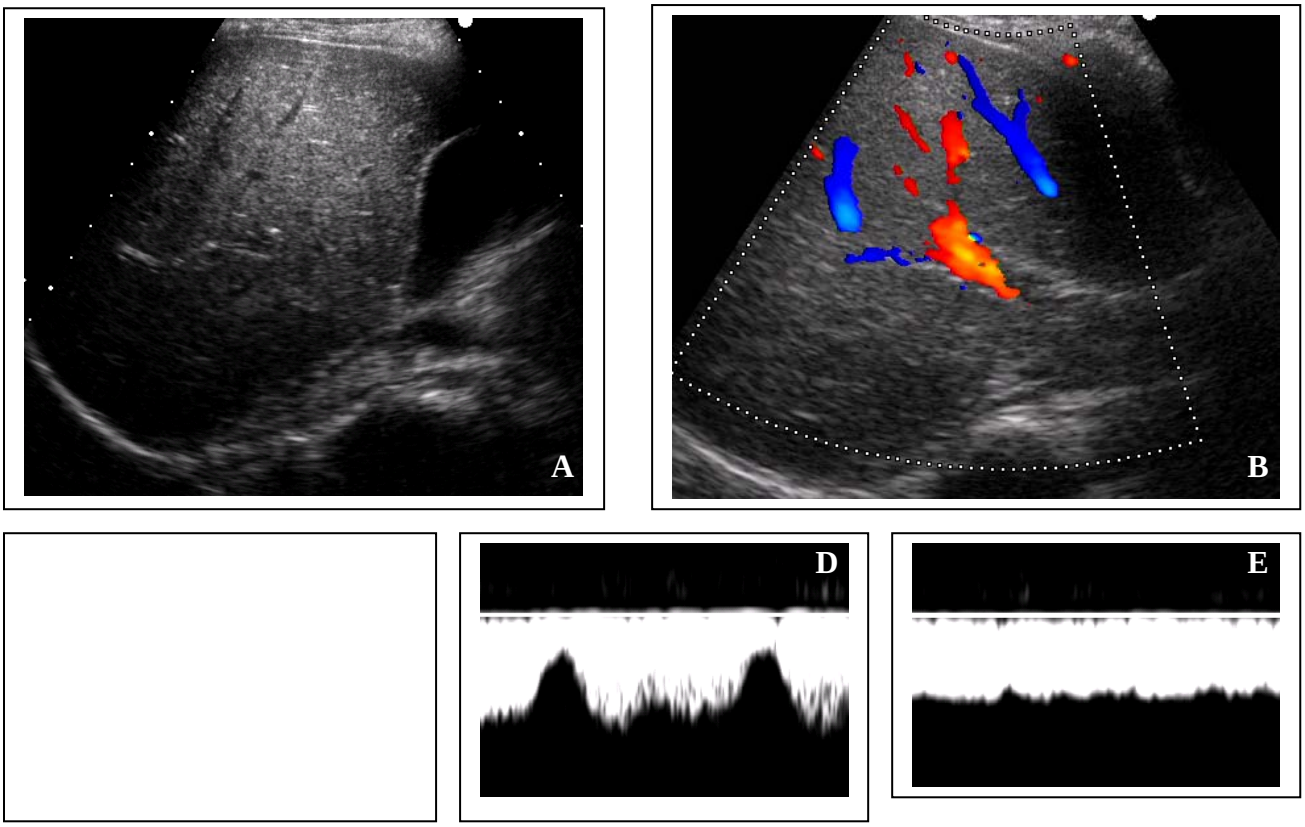


Fig 3

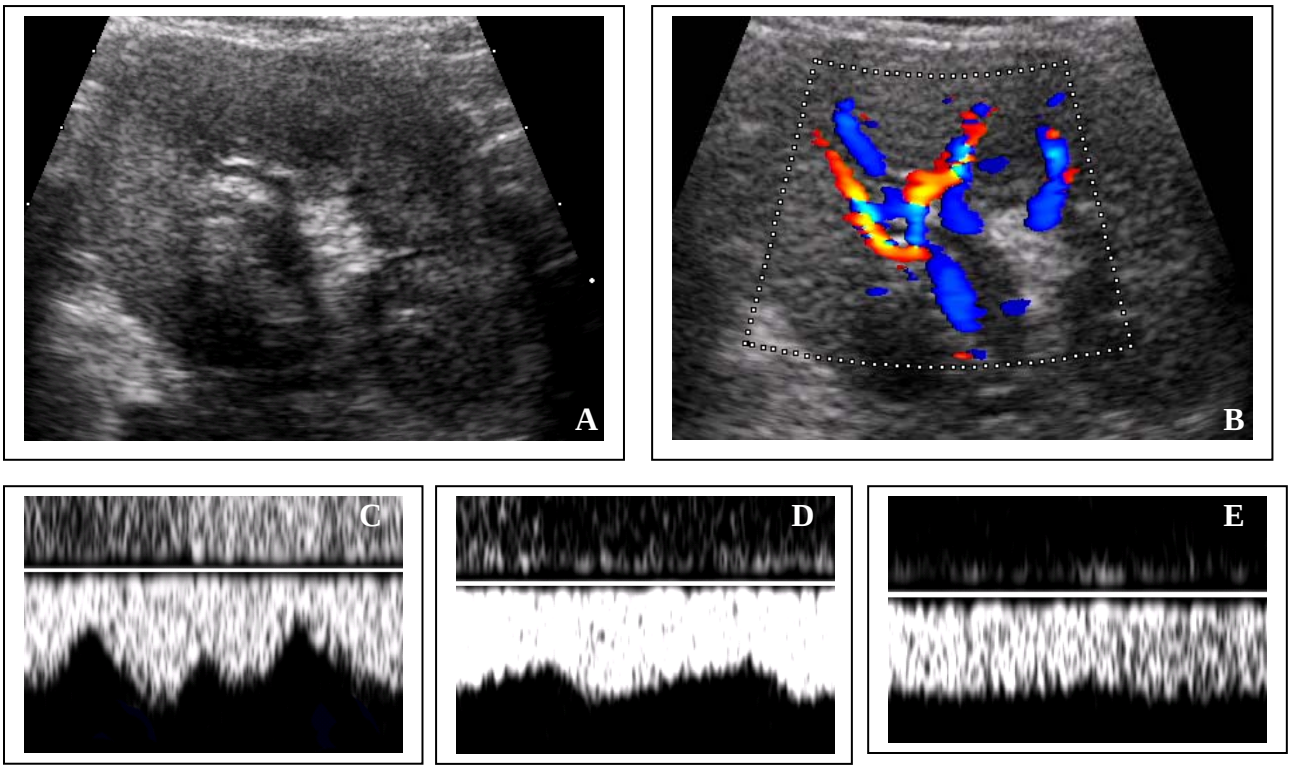
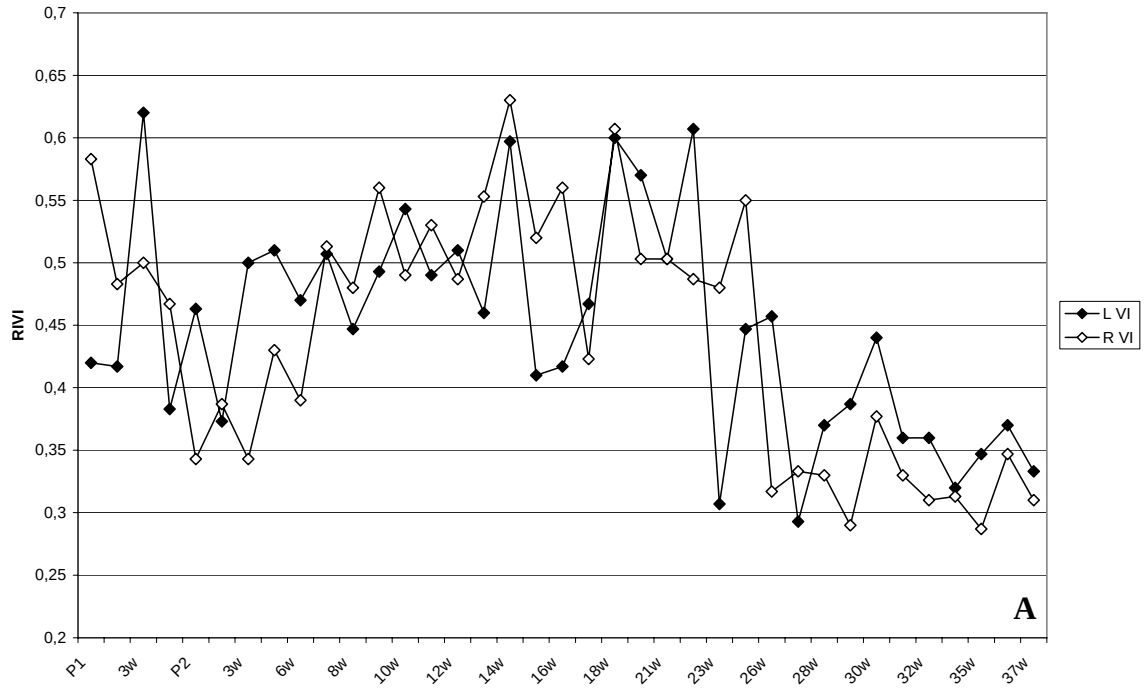


Fig 4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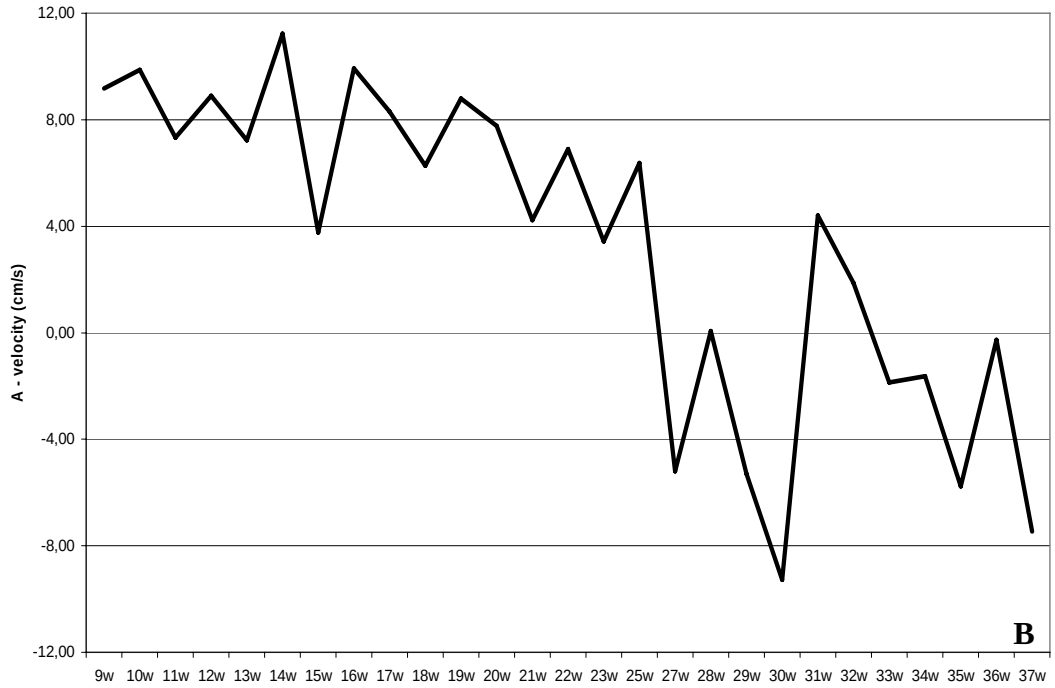
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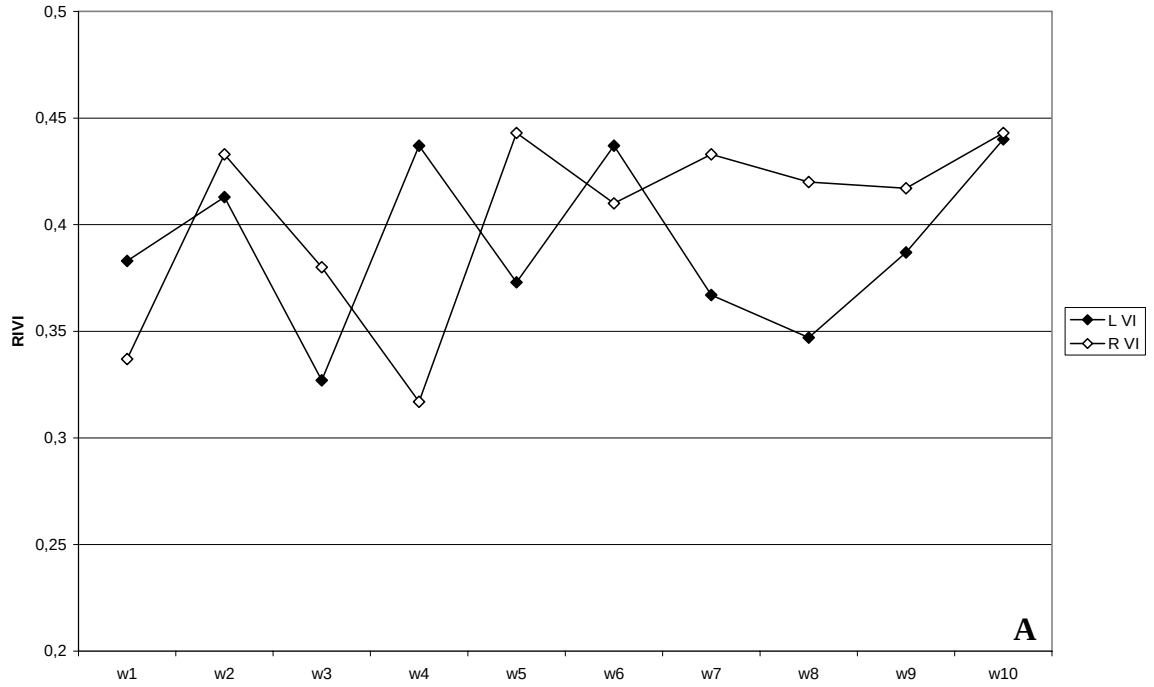
Fig 5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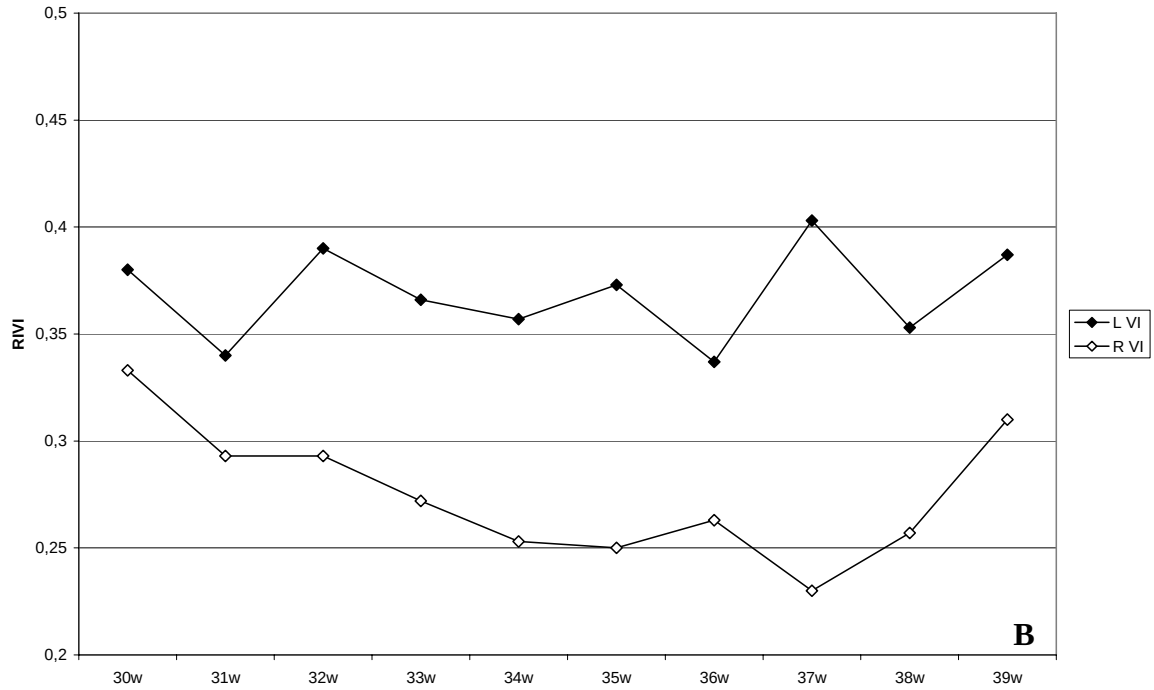
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Figure Caption List

Figure 1

Anatomy of the lower central venous compartment from liver to kidneys. As is shown in the left panel, there are 3 hepatic veins (HV): left, middle and right, which are often accompanied by additional braches. Usually, left and middle HV fuse before draining into the vena cava inferior (VCI) at a few centimeters caudal from the right cardiac atrium. The right panel shows that the right renal vein (RV) is shorter and inserts more caudally into VCI then the left RV. Next to this, the right RV has more accessory branches and a wider proximal diameter than the left RV. Also, the left LV is sometimes sandwiched between Aorta and Superior Mesenteric Artery (Nutcracker Syndrome) and drains blood from the left ovarian vein.

Figure 2

Illustrations of 2D- ultrasound and Doppler images of the intrahepatic vascular tree. Panel A shows the standard view of the liver, scanned intercostally at the craniocaudal midportion. Panel B shows the color Doppler image at this level, which enables distinguishing portal branches and hepatic arteries (red) from hepatic veins (blue). Panel C illustrates the typical triphasic HV Doppler wave pattern, in which the A-deflection represents backflow of blood from the right atrium into the hepatic venous circulation during atrial contraction. This pattern is mostly observed in non-pregnant individuals and during early pregnancy. Panel B illustrates a biphasic pattern, where the A-deflection is not reversed. This pattern is commonly observed during midgestation. Panel E illustrates the flat HV pattern, which is the most common pattern in term pregnancy.

Figure 3

Illustrations of intrarenal vascularity, as observed by 2D- ultrasound and Duplex sonography. Panel A shows the standard view of the kidney, scanned in transverse position at the level just above the renal hilus. The intrarenal pyelon can be identified easily. The interlobar vessels are located between the pyelon and the renal cortex. Color Doppler imaging, as illustrated in panel B, allows distinguishing interlobar arteries (red) from veins (blue). Panel C illustrates the typical biphasic pattern of renal interlobar veins, which is the most common pattern in non-pregnant individuals and during early and midgestation. Panel D shows the monophasic pattern, which is very common in term pregnancies. Panel E illustrates a flat pattern, which is frequently found during urological obstruction.

Figure 4

Graphical illustration of serial measruements of Renal Interlobar Vein Impedance Index (RIVI) (upper panel) and Hepatic Vein A (HVA) velocity (lower panel) at 2-weeks interval from preconception (RIVI) or early pregnancy (HVA) until term. As is shown, RIVI measurements of both kidneys have an undulating pattern where the highest values intermittently belong to the left or the right kidney. During the course of pregnancy, RIVI decreases and at term, right renal RIVI values are lower than those from the left kidney. Simultaneously, HVA-velocities shift from positive values reflcting triphasic HV Doppler wave patterns with blood flowing into the direction of the liver during atrial contraction, to negative values, representing biphasic or flat HV Doppler wave patterns with blood flowing into direction of the heart. In this woman, the conversion from cardiofugal to cardiopetal flow occurs around 26 weeks. She also presents a short reversal to positive HVA-values again at 32 weeks, after which HVA velocities turn negative again. The latter illustrates the intra-

individual variation of HV Doppler wave patterns during uncomplicated third trimester pregnancy.

Figure 5

Illustration of serial measurements of Renal Interlobar Vein (RIV) Impedance Index (RIVI) at weekly intervals in a non-pregnant individual (upper panel) and during uncomplicated third trimester pregnancy (lower panel). As is also illustated in figure 4, right and left RIVI values show an undulating pattern and no obvious relationship is observed between between the frequency of oscillation in both kidneys. During the third trimester of pregnancy, right RIVI values are consistently lower than those from the left kidney.

Reference List

(1) Malcus P. Antenatal fetal surveillance. Curr Opin Obstet Gynecol 2004; 16(2):123-128.

(2) Nicolaides K, Rizzo G, Hecher K. Placental and fetal Doppler. 1 ed. London UK: The Parthenon Publishing Group, 2000.

(3) Abramowicz JS, Sheiner E. Ultrasound of the placenta: a systematic approach. Part II: functional assessment (Doppler). Placenta 2008; 29(11):921-929.

(4) Papageorghiou AT, Leslie K. Uterine artery Doppler in the prediction of adverse pregnancy outcome. Curr Opin Obstet Gynecol 2007; 19(2):103-109.

(5) Cnossen JS, Morris RK, ter Riet G, Mol BW, van der Post JA, Coomarasamy A et al. Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis. CMAJ 2008; 178(6):701-711.

(6) Karabulut N, Baki YA, Karabulut A. Renal vein Doppler ultrasound of maternal kidneys in normal second and third trimester pregnancy. Br J Radiol 2003; 76(907):444-447.

(7) Bateman GA, Giles W, England SL. Renal venous Doppler sonography in preeclampsia. J Ultrasound Med 2004; 23(12):1607-1611.

(8) Roobottom CA, Hunter JD, Weston MJ, Dubbins PA. Hepatic venous Doppler waveforms: changes in pregnancy. J Clin Ultrasound 1995; 23(8):477-482.

(9) Gyselaers W, Molenberghs G, Van Mieghem W, Ombelet W. Doppler measurement of Renal Interlobar Vein Impedance Index in uncomplicated and pre-eclamptic pregnancies. Hypertens Pregnancy 2009; 28(1):23-33.

(10) Gyselaers W, Verswijvel G, Molenberghs G, Ombelet W. Interlobar Venous Flow Is Different between Left and Right Kidney in Uncomplicated Third Trimester Pregnancy. Gynecol Obstet Invest 2008; 65(1):6-11.

(11) Gyselaers W, Molenberghs G, Mesens T, Peeters L. Maternal Hepatic Vein Doppler Velocimetry During Uncomplicated Pregnancy and Pre-Eclampsia. Ultrasound Med Biol 2009.

(12) Gyselaers W, Mesens T. Renal interlobar vein impedance index: A potential new Doppler parameter in the prediction of preeclampsia? J Matern Fetal Neonatal Med 2009;1-3.

(13) Gyselaers W. Hemodynamics of the maternal venous compartment: a new area to explore in obstetric ultrasound imaging. Ultrasound Obstet Gynecol 2008; 32(5):716-717.

(14) Duvekot JJ, Peeters LL. Maternal cardiovascular hemodynamic adaptation to pregnancy. Obstet Gynecol Surv 1994; 49(12 Suppl):S1-14.

(15) Duvekot JJ, Peeters LL. Renal hemodynamics and volume homeostasis in pregnancy. Obstet Gynecol Surv 1994; 49(12):830-839.

(16) de Swiet M. The cardiovascular system. In: Chamberlain G, Pipkin F, editors. Clinical physiology in obstetrics. Oxford, UK: Blackwell Science Ltd, 1998: 33-70.

(17) Carty DM, Delles C, Dominiczak AF. Novel biomarkers for predicting preeclampsia. Trends Cardiovasc Med 2008; 18(5):186-194.

(18) Boulpaep EL. The heart as a pump. In: Boron WF, Boulpaep EL, editors. Medical physiology. Philadelphia: Elsevier Inc., 2005: 508-533.

(19) Berne R, Levy M. Control of cardiac output : coupling of heart and blood vessels. In: Berne R, Levy M, editors. Cardiovascular physiology. London: The C.V. Mosby Company, 2001: 199-226.

(20) Magder S. Central venous pressure: A useful but not so simple measurement. Crit Care Med 2006; 34(8):2224-2227.

(21) HICKIE JB. The valve of the inferior vena cava. Br Heart J 1956; 18(3):320-326.

(22) Neumann JO, Thorn M, Fischer L, Schobinger M, Heimann T, Radeleff B et al. Branching patterns and drainage territories of the middle hepatic vein in computer-simulated right living-donor hepatectomies. Am J Transplant 2006; 6(6):1407-1415.

(23) Grant EG, Schiller VL, Millener P, Tessler FN, Perrella RR, Ragavendra N et al. Color Doppler imaging of the hepatic vasculature. AJR Am J Roentgenol 1992; 159(5):943-950.

(24) Nakai A, Sekiya I, Oya A, Koshino T, Araki T. Assessment of the hepatic arterial and portal venous blood flows during pregnancy with Doppler ultrasonography. Arch Gynecol Obstet 2002; 266(1):25-29.

(25) Satyapal KS, Rambiritch V, Pillai G. Additional renal veins: incidence and morphometry. Clin Anat 1995; 8(1):51-55.

(26) Satyapal KS, Rambiritch V, Pillai G. Morphometric analysis of the renal veins. Anat Rec 1995; 241(2):268-272.

(27) Ahmed K, Sampath R, Khan MS. Current trends in the diagnosis and management of renal nutcracker syndrome: a review. Eur J Vasc Endovasc Surg 2006; 31(4):410-416.

(28) Itoh S, Yoshida K, Nakamura Y, Mitsuhashi N. Aggravation of the nutcracker syndrome during pregnancy. Obstet Gynecol 1997; 90(4 Pt 2):661-663.

(29) Fernandez-Cuadrado J, Alonso-Torres A, Baudraxler F, Sanchez-Almaraz C. Three-dimensional contrast-enhanced magnetic resonance angiography of congenital inferior vena cava anomalies. Semin Pediatr Surg 2005; 14(4):226-232.

(30) Mathews R, Smith PA, Fishman EK, Marshall FF. Anomalies of the inferior vena cava and renal veins: embryologic and surgical considerations. Urology 1999; 53(5):873-880.

(31) Pannu HK, Maley WR, Fishman EK. Liver transplantation: preoperative CT evaluation. Radiographics 2001; 21 Spec No:S133-S146.

(32) Gallego C, Miralles M, Marin C, Muyor P, Gonzalez G, Garcia-Hidalgo E. Congenital hepatic shunts. Radiographics 2004; 24(3):755-772.

(33) Pedersen JF, Dakhil AZ, Jensen DB, Sondergaard B, Bytzer P. Abnormal hepatic vein Doppler waveform in patients without liver disease. Br J Radiol 2005; 78(927):242-244.

(34) Pang CC. Measurement of body venous tone. J Pharmacol Toxicol Methods 2000; 44(2):341-360.

(35) Berne R, Levy M. Special circulations. In: Berne R, Levy M, editors. Cardiovascular Physiology. London: The C.V. Mosby Company, 2001: 241-270.

(36) Pang CC. Autonomic control of the venous system in health and disease: effects of drugs. Pharmacol Ther 2001; 90(2-3):179-230.

(37) Juncqueira L, Carneiro J. The circulatory system. In: Juncqueira L, Carneiro J, editors. Basic histology: text and atlas. New York: McGraw-Hill Professional, 2005: 205-222.

(38) Boulpaep EL. Regulation of arterial pressure and cardiac output. In: Boron WF, Boulpaep EL, editors. Medical physiology. Philadelphia: Elsevier Inc., 2005: 534-557.

(39) Lewis B. The peripheral veins. In: Rumack CM, Wilson SR, Charboneau JW, Johnson JM, editors. Diagnostic ultrasound. Philadelphia, USA: Elsevier Mosby, 2005: 1019-1035.

(40) Roderick P, Ferris G, Wilson K, Halls H, Jackson D, Collins R et al. Towards evidence-based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis. Health Technol Assess 2005; 9(49):iii-x, 1.

(41) Downey DB. The retroperitoneum and the great vessels. In: Rumack CM, Wilson RD, Charboneau JW, Johnson JM, editors. Diagnostic Ultrasound. Philadelphia, PA, USA: Mosby, Inc., 2005: 443-488.

(42) Lui EY, Steinman AH, Cobbold RS, Johnston KW. Human factors as a source of error in peak Doppler velocity measurement. J Vasc Surg 2005; 42(5):972-979.

(43) Nakai A, Oya A. Accuracy and reproducibility of ultrasound measurements in obstetric management. Gynecol Obstet Invest 2002; 54(1):31-36.

(44) Teichgraber UK, Gebel M, Benter T, Manns MP. Effect of respiration, exercise, and food intake on hepatic vein circulation. J Ultrasound Med 1997; 16(8):549-554.

(45) Verbeke G, Molenberghs G. Linear Mixed Models for Longitudinal Data. 2 ed. New York: Springer, 2001.

(46) Laenen A, Vangeneugden T, Geys H, Molenberghs G. Generalized reliability estimation using repeated measurements. Br J Math Stat Psychol 2006; 59(Pt 1):113-131.

(47) Oktar SO, Yucel C, Ozdemir H, Karaosmanoglu D. Doppler sonography of renal obstruction: value of venous impedance index measurements. J Ultrasound Med 2004; 23(7):929-936.

(48) Bateman GA, Cuganesan R. Renal vein Doppler sonography of obstructive uropathy. AJR Am J Roentgenol 2002; 178(4):921-925.

(49) Hecher K, Campbell S. Characteristics of fetal venous blood flow under normal circumstances and during fetal disease. Ultrasound Obstet Gynecol 1996; 7(1):68-83.

(50) Moll W. Venous return in the fetal-placental cardiovascular system. Eur J Obstet Gynecol Reprod Biol 1999; 84(2):133-137.

(51) Oh JK, Seward JB, Tajik AJ. Assessment of diastolic function and diastolic heart failure. In: Oh JK, Seward JB, Tajik AJ, editors. The echo manual. Philadelphia; USA: Lippincott Williams & Wilkins, 2007: 121-142.

(52) Schneider AR, Teuber G, Kriener S, Caspary WF. Noninvasive assessment of liver steatosis, fibrosis and inflammation in chronic hepatitis C virus infection. Liver Int 2005; 25(6):1150-1155.

(53) Colli A, Cocciolo M, Riva C, Martinez E, Prisco A, Pirola M et al. Abnormalities of Doppler waveform of the hepatic veins in patients with chronic liver disease: correlation with histologic findings. AJR Am J Roentgenol 1994; 162(4):833-837.

(54) Dietrich CF, Lee JH, Gottschalk R, Herrmann G, Sarrazin C, Caspary WF et al. Hepatic and portal vein flow pattern in correlation with intrahepatic fat deposition and liver histology in patients with chronic hepatitis C. AJR Am J Roentgenol 1998; 171(2):437-443.

(55) Bolondi L, Li BS, Gaiani S, Zironi G, Benzi G, Santi V et al. Liver cirrhosis: changes of Doppler waveform of hepatic veins. Radiology 1991; 178(2):513-516.

(56) Ohta M, Hashizume M, Tomikawa M, Ueno K, Tanoue K, Sugimachi K. Analysis of hepatic vein waveform by Doppler ultrasonography in 100 patients with portal hypertension. Am J Gastroenterol 1994; 89(2):170-175.

(57) Salgado O, Garcia R, Henriquez C, Rosales B, Sulbaran P. Severely elevated intrarenal arterial impedance and abnormal venous flow pattern in a normal functioning kidney graft. Transplant Proc 2003; 35(5):1772-1774.

(58) Zubarev AV. Ultrasound of renal vessels. Eur Radiol 2001; 11(10):1902-1915.

(59) Witz M, Kantarovsky A, Morag B, Shifrin EG. Renal vein occlusion: a review. J Urol 1996; 155(4):1173-1179.

(60) Pekindil G, Varol FG, Yuce MA, Yardim T. Evaluation of hepatic venous pulsatility and portal venous velocity with Doppler ultrasonography during the puerperium. Eur J Radiol 1999; 29(3):266-269.

(61) Satyapal KS. Classification of the drainage patterns of the renal veins. J Anat 1995; 186 (Pt 2):329-333.

(62) Wang JJ, Flewitt JA, Shrive NG, Parker KH, Tyberg JV. Systemic venous circulation. Waves propagating on a windkessel: relation of arterial and venous windkessels to systemic vascular resistance. Am J Physiol Heart Circ Physiol 2006; 290(1):H154-H162.

(63) Dhawan V, Brookes ZL, Kaufman S. Repeated pregnancies (multiparity) increases venous tone and reduces compliance. Am J Physiol Regul Integr Comp Physiol 2005; 289(1):R23-R28.

(64) Hohmann M, Zoltan D, Kunzel W. Age and reproductive status affect basal venous tone in the rat. Eur J Obstet Gynecol Reprod Biol 1996; 68(1-2):185-189.

(65) Sakai K, Imaizumi T, Maeda H, Nagata H, Tsukimori K, Takeshita A et al. Venous distensibility during pregnancy. Comparisons between normal pregnancy and preeclampsia. Hypertension 1994; 24(4):461-466.

(66) Skudder PA, Jr., Farrington DT, Weld E, Putman C. Venous dysfunction of late pregnancy persists after delivery. J Cardiovasc Surg (Torino) 1990; 31(6):748-752.

(67) Tyberg JV. How changes in venous capacitance modulate cardiac output. Pflugers Arch 2002; 445(1):10-17.