

Interobserver and interequipment variability of hepatic, splenic, and renal arterial Doppler resistance indices in normal subjects and patients with cirrhosis

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Background/Aims: Doppler arterial resistance indices are used to evaluate alterations in arterial hemodynamics in the liver, spleen, and kidney. The purpose of this study was to determine the interobserver and interequipment variability of hepatic, splenic, and renal arterial Doppler resistance indices, and the influence of a cooperative training program of the operators on the reproducibility of the results.

Methods: In the first part of the study, hepatic (PI-L, RI-L), splenic (PI-S, RI-S), and renal (PI-K, RI-K) pulsatility and resistive indices were measured by echo-color-Doppler in eight control subjects and ten patients with cirrhosis by three operators using three different machines. In the second part of the study, measurements were taken by the three operators in nine controls and nine patients with cirrhosis, after cooperative training, with a single machine.

Results: Significant interobserver variability was present for all parameters except RI-L. Significant interequipment variability was present for all parameters

except PI-S and RI-S. Only 0–3% of variance was equipment- or operator-related, while 58–72% was patient-related. Hepatic and renal coefficients of variation were similar in patients with cirrhosis and controls, while splenic coefficients of variation were higher in patients with cirrhosis than in controls. After training, differences among operators disappeared for all variables except RI-K, and the operator-related component of variance nearly disappeared for all parameters.

Conclusions: Hepatic, splenic, and renal arterial resistance indices show small but significant interobserver and interequipment variability. Interobserver variability can be decreased to non-significant levels by a common training program. Thus, these indices can be widely applied to the study of arterial circulation in these organs.

Key words: Cirrhosis; Doppler; Kidney; Liver; Resistance indices; Spleen.

DOPPLER ultrasonography allows the study of arterial blood supply of abdominal organs and of its modification in pathologic conditions. Because of the difficulty of obtaining reproducible measurements of flow, arterial resistance indices, which are independent of the diameter of the vessel and of the angle of insonation, have been introduced. In the kidney, resist-

ance indices have been demonstrated to correlate with renal blood flow and renovascular resistance (1) and glomerular filtration rate (2,3), and are used in the evaluation of disease states (4–9) and transplanted organs (10–12). Arterial resistance indices have been evaluated in a few studies on the liver and on the spleen (13–19). Their usefulness in the evaluation of portal hypertension has also been suggested (13,17,19).

Previous studies on echo-Doppler parameters of portal vein and superior mesenteric artery in patients with cirrhosis have shown an appreciable interobserver variability (20–23), which could be reduced to non-significant levels by a cooperative training program and

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the establishment of strict guidelines for measurements (22,23). Furthermore, significant interequipment differences, not only in portal vein velocity (22), but also in superior mesenteric artery resistance indices (23), have been demonstrated. No study on interobserver variability, with more than two observers from different laboratories, and on interequipment variability of resistance indices in the liver, spleen, and kidney, is available. This was the aim of our study.

Materials and Methods

Design of the study: Part 1

Interobserver and interequipment variability. To analyze the interobserver and interequipment variability, a study was designed with three expert operators (P.B., S.G., D.S.), from different centers in Italy, and three high-quality echo-Doppler machines: Toshiba (SSA270A), Aloka (2000), Esaote-Hitachi (590 AS).

Before the study, a general examination procedure was agreed on by the operators and they participated in a short training program to familiarize themselves with the use of the different machines.

On 3 consecutive days, 10 patients with cirrhosis (two males and eight females) and eight normal subjects (seven males and one female) were subjected to measurements. The patients were requested to fast for 12 h before the study and were examined after remaining supine for at least 15 min. The three different echo-Doppler machines were placed in separate rooms, thus permitting simultaneous study of three patients. Each operator consecutively examined each of the three patients using each of the three machines by rotating both operators and patients. Operators were unaware of one another's results. Therefore, each patient underwent 9 examinations; the total number of Doppler examinations for each organ was 162.

Informed consent was obtained from each subject and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Measurements and calculations

Hepatic indices. The transducer, with a 3.5–3.75 MHz convex electronic probe and Doppler crystal, was positioned below the costal margin. Color Doppler allowed identification of the left branch of the hepatic artery. The sample volume of the Doppler system was placed in this vessel and the blood flow velocity waveform was recorded. We chose this vessel because it is easier to visualize, and resistance indices do not differ from those measured in the right branch (17), and they correlate with those measured in the hepatic artery at the porta hepatis (24). Peak systolic, end diastolic and temporal mean flow velocity were then determined without

correction for the angle of insonation, and from them the pulsatility index (PI-L) and the resistive index (RI-L) were calculated according to the following formulae: $PI = (\text{Peak systolic velocity} - \text{end diastolic velocity} / \text{mean velocity})$; $RI = (\text{peak systolic velocity} - \text{end diastolic velocity} / \text{peak systolic velocity})$. Each result was the mean of three measurements. The right branch of the hepatic artery was not included in the results because it was poorly visualized in some subjects.

Splenic indices. The transducer, with a 3.5–3.75 MHz convex electronic probe and Doppler crystal, was positioned below the left costal margin or in the left costal spaces. Color Doppler allowed identification of the main branches of the splenic artery. The sample volume of the Doppler system was placed in these vessels and the blood flow velocity waveform was recorded. Peak systolic, end diastolic, and temporal mean flow velocity were then determined without correction for the angle of insonation, and from them the pulsatility index (PI-S) and the resistive index (RI-S) were calculated as previously reported. Each result was the mean of three measurements.

Renal indices. The transducer, with a 3.5–3.75 MHz convex electronic probe and Doppler crystal, was positioned below the right costal margin in the dorsolateral area of the right flank. Color Doppler allowed identification of the intrarenal arterial vascularization of the kidney. The sample volume of the Doppler system was placed in the interlobar arteries and the blood flow velocity waveform was recorded. Peak systolic, end diastolic and temporal mean flow velocity were then determined without correction for the angle of insonation, and from them the pulsatility index (PI-K) and the resistive index (RI-K) were calculated as previously reported. Each result was the mean of three measurements.

Design of the study. Part 2

Study of effect of cooperative training. Because systematic and nonsystematic variations were observed in the first part of the study, a second set of experiments was designed to minimize possible sources of variability in the measurement of echo-Doppler parameters. On the first day, six normal subjects were studied by the three operators, using a single machine. Working together under the guidance of an independent operator (M.Z.), the three operators tried to identify the possible sources of interobserver variability. At the end of the training program, a strict and uniform measurement protocol was defined (Table 1). On the following 3 days, nine normal subjects (four males and five fe-

TABLE 1

Guidelines for measurement of hepatic, splenic, and renal Doppler arterial resistance indices

General:

- 1) Measurement in suspended normal respiration
- 2) Sample volume: 3 mm
- 3) Visualization by color-Doppler
- 4) One cardiac cycle
- 5) Values result from the mean of three consistent measurements
- 6) Wallfilter=100 Hz
- 7) Manual tracing of the upper limit of the Doppler waveforms

Hepatic artery:

- 1) Left branch
- 2) Along the longitudinal tract of the left portal branch
- 3) PRF=4 kHz;

Splenic artery:

- 1) A main branch about 0.5–1 cm inside the organ
- 2) PRF=7 kHz

Renal artery:

- 1) Right kidney visualized longitudinally with an adequate angle to show interlobar arteries
- 2) Interlobar arteries along the border of medullary pyramids
- 3) PRF=3 kHz

males) and nine patients with cirrhosis (six males and three females) were studied according to the pre-defined protocol, using a single machine. The patients were examined on the basis of a pre-defined random sequence of operators. Operators were unaware of one another's results.

Measurements and calculations. Compared with the previous methodology, there were some adjustments. For the liver, it is important to visualize an adequate tract of the left arterial branch, avoiding placing the sample volume where the vessel bends. It is also important to study the branch in its most proximal tract. For the spleen, it is important to identify a major branch of the main artery just past the hilum, inside the spleen, avoiding more peripheral vessels, and to visualize a straight tract of the vessel. For the kidneys, it is important to make measurements in the interlobar arteries, after visualization of a sufficient tract of the vessel, which can be done if an adequate angle is obtained between the ultrasound beam and the kidney.

TABLE 2

Mean values of hepatic, splenic, and renal arterial resistance indices measured in control subjects and patients with cirrhosis by three operators using three machines

	Liver		Spleen		Kidney	
	PI	RI	PI	RI	PI	RI
Control subjects	1.22±0.23	0.67±0.05	0.77±0.06	0.53±0.03	0.99±0.12	0.60±0.04
Patients with cirrhosis	1.41±0.25	0.73±0.05	1.10±0.07	0.66±0.03	1.30±0.11	0.70±0.03

PI=pulsatility index; RI=resistive index.

Statistical analysis. To assess interobserver and inter-equipment variability, a mixed ANOVA test was used with a factorial design and three criteria sources, namely patients (random effects), operators, and machines (fixed effects). The ANOVA test permitted assessment of the significance of the operator and equipment effect by the F test, and division of the total variance into components related to patients, operators, and machines. Interaction terms and residual variance were cumulated in a term containing nonsystematic variance and measurement errors. Nonsystematic variance is the variance due to all other causes of variability that are not controlled in the present experimental setting. From variance components, SD among operators, machines, and operators and machines were calculated as square root of error variance + operator variance; error variance + equipment variance; and error variance + equipment variance + operator variance, respectively. Coefficient of variation (CV) was calculated as SD/mean value. A 95% confidence limit (CL) for a measure was estimated in absolute terms as $1.96 \times SD$. Because a single machine was used in the second part of the study, the data obtained were compared with those obtained with the same machine in the first part of the study. ANOVA was performed using a factorial design considering patients (random effect) and operators (fixed effect). Variance components, SD, CV, and 95% CLs were calculated accordingly. All statistical computations were performed using BioMedical Data Program statistical package (25).

Results

Part 1

Arterial resistance indices obtained in the liver, spleen, and kidney in patients with cirrhosis and normal subjects are shown in Table 2. Variability among the three consecutive measurements made by each operator with each machine showed the following CVs: for the liver: for RI: 4%; for PI: 11%; for the spleen: for RI: 5%, for PI: 9%, for the kidney: for RI: 4%; for PI: 8%.

TABLE 3

Mean values of hepatic, splenic, and renal arterial resistance indices according to different operators and machines, and F statistics of the ANOVA for interobserver and interequipment study, considering control subjects and patients with cirrhosis together

	Liver		Spleen		Kidney	
	PI	RI	PI	RI	PI	RI
Operator:						
N. 1	1.26±0.28	0.69±0.07	0.92±0.19	0.59±0.08	1.13±0.20	0.65±0.07
N. 2	1.32±0.28	0.70±0.07	0.99±0.21	0.61±0.08	1.16±0.20	0.65±0.07
N. 3	1.38±0.23	0.71±0.05	0.95±0.18	0.60±0.07	1.21±0.20	0.67±0.07
F	5.36	2.35	4.72	4.57	13.61	4.16
P	0.01	0.11	0.016	0.015	<0.0001	0.024
Equipment:						
N. 1	1.29±0.26	0.69±0.06	0.94±0.20	0.60±0.08	1.14±0.20	0.65±0.07
N. 2	1.29±0.23	0.70±0.06	0.95±0.20	0.60±0.08	1.16±0.20	0.66±0.07
N. 3	1.38±0.30	0.71±0.06	0.96±0.18	0.60±0.07	1.19±0.20	0.66±0.06
F	5.52	3.58	0.35	0.09	4.13	3.31
P	0.008	0.039	0.70	0.91	0.025	0.048

PI=pulsatility index; RI=resistive index.

TABLE 4

Standard deviations (SD), 95% confidence limits (CL), and coefficients of variation (CV) according to ANOVA in the interobserver and interequipment study, considering control subjects and patients with cirrhosis together

	Liver		Spleen		Kidney	
	PI	RI	PI	RI	PI	RI
SD among operators	0.21	0.05	0.14	0.05	0.12	0.04
SD among machines	0.21	0.05	0.14	0.05	0.11	0.04
SD among operators and machines	0.21	0.05	0.14	0.05	0.12	0.04
95% CL among operators	0.92-1.72	0.60-0.80	0.68-1.22	0.51-0.69	0.94-1.40	0.58-0.74
95% CL among machines	0.92-1.72	0.60-0.80	0.69-1.21	0.51-0.69	0.95-1.39	0.58-0.74
95% CL among operators and machines	0.91-1.73	0.60-0.80	0.68-1.22	0.51-0.69	0.93-1.41	0.58-0.74
CV among operators (%)	16	7	15	8	10	6
CV among machines (%)	16	7	14	8	10	6
CV among operators and machines (%)	16	7	15	8	10	6

PI=pulsatility index; RI=resistive index.

TABLE 5

Mean values of hepatic, splenic, and renal arterial resistance indices according to different operators before and after training using equipment N. 3, and F statistics of the ANOVA for interobserver study, considering control subjects and patients with cirrhosis together

	Liver		Spleen		Kidney	
	PI	RI	PI	RI	PI	RI
Before training:						
Operator N. 1	1.28±0.35	0.69±0.08	0.92±0.21	0.59±0.08	1.14±0.21	0.64±0.07
Operator N. 2	1.38±0.32	0.71±0.07	1.00±0.22	0.61±0.07	1.21±0.20	0.67±0.06
Operator N. 3	1.48±0.32	0.73±0.06	0.96±0.16	0.60±0.06	1.24±0.20	0.68±0.06
F	6.89	6.16	2.01	1.86	6.86	14.93
P	0.003	0.005	0.15	0.17	0.003	<0.0001
After training:						
Operator N. 1	1.18±0.33	0.66±0.08	0.97±0.34	0.59±0.10	1.15±0.37	0.64±0.10
Operator N. 2	1.22±0.38	0.66±0.09	0.90±0.25	0.57±0.08	1.20±0.32	0.66±0.07
Operator N. 3	1.17±0.39	0.65±0.09	0.92±0.27	0.58±0.10	1.11±0.28	0.62±0.07
F	0.38	0.59	2.53	2.62	2.01	3.89
P	0.68	0.56	0.09	0.09	0.15	0.03

PI=pulsatility index; RI=resistive index.

Interobserver and interequipment variability study. PI-L, PI-S, PI-K and RI-K, RI-S were significantly different between operators (Table 3); PI-L, PI-K, and RI-L, RI-K were significantly different between machines (Table 3). Considering patients with cirrhosis and normal subjects separately, differences between operators were not significant for PI-L, PI-S, RI-S in patients with cirrhosis, and for RI-K in controls.

When analyzing the variance of the hepatic, splenic, and renal resistance indices according to the ANOVA test, a small proportion of this variance was equipment-related (0–2%) or related to operators (0–3%). Patient variance represented 58–72% of the total variance, not far from an ideal situation, in which patient variance should approach 100%. SD, 95% CLs, and CV according to operators and machines were almost the same (Table 4). Hepatic and renal CVs were similar in patients with cirrhosis and in controls, while splenic CVs were lower in controls than in patients with cirrhosis (for PI: among operators: 9 vs 16%; among machines: 9 vs 16%; for RI: among operators: 6 vs 8%; among machines: 6 vs 8%).

Part 2

Study on the effect of cooperative training program. Because training was performed with a single machine, the data obtained after training were compared with those obtained with the same equipment before training. The mean values according to different operators are reported in Table 5. No significant differences among operators were observed after the training period for any of the variables considered, with the exception of RI-K. A similar pattern of changes was observed considering patients with cirrhosis and normal subjects separately.

When analyzing the components of variance according to ANOVA test (Fig. 1), operator variance nearly disappeared for all the parameters considered, allowing a situation closer to the ideal 100% variation due to patients. When considering patients with cirrhosis and controls separately, operator variance was relevant only for PI-K and RI-K in control subjects (26% and 32% respectively) compared to patients with cirrhosis (2.9% and 1.4%, respectively).

Discussion

The results of this study show an overall good reproducibility in the evaluation of arterial resistance indices in the liver, spleen, and kidney in both normal subjects and patients with cirrhosis. Nonetheless, a significant interobserver and interequipment difference was found, the former of which could be overcome by adequate training.

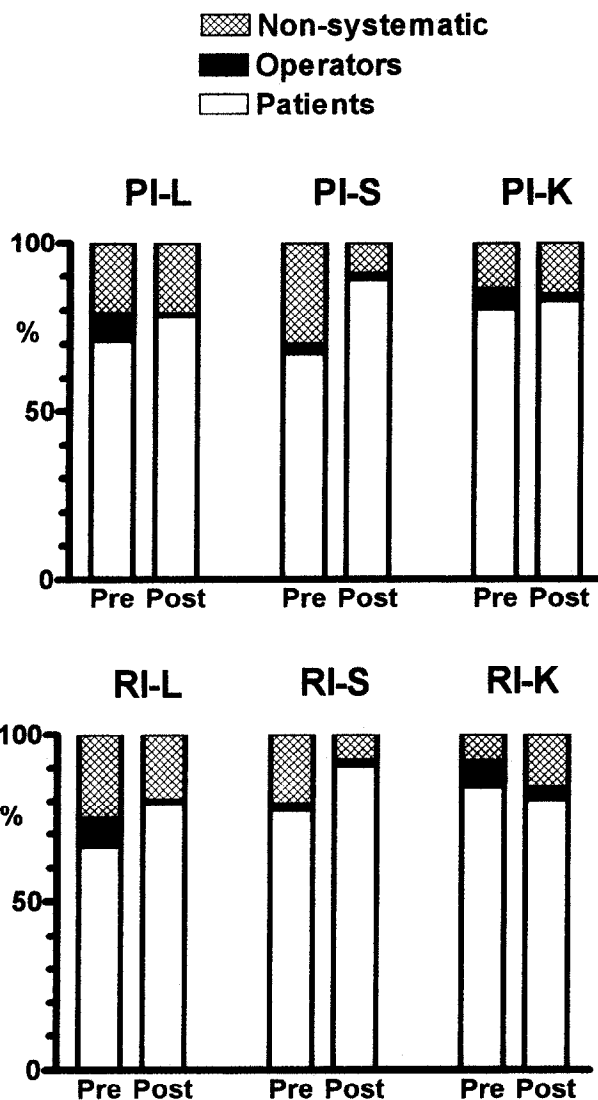


Fig. 1. Percent changes in variance components (due to patients, operators, or non-systematic) after cooperative training. PI=pulsatility index; RI=resistive index; L=liver; S=spleen; K=kidney; Pre=pre-training; Post=post-training.

Renal arterial resistance indices are widely used in the evaluation of different disease states like parenchymal and vascular nephropathies (4,7–9), transplantation (10–12), renal functional failure of cirrhosis (2,3,5,6). In this last condition, renal arterial resistance indices are correlated with creatinine clearance (2,3) and have been shown to have prognostic usefulness for development of hepato-renal syndrome (6) and outcome of liver transplantation (5). Alterations in hepatic and splenic Doppler arterial resistance indices have been recently shown in liver cirrhosis and in other pathologic splanchnic hemodynamic conditions (13–19). Intra- and inter-observer variability evaluated be-

tween two operators from the same laboratory have shown acceptable levels. No study is available on variability among more operators from different laboratories and among different machines.

In the first part of this study intraobserver variability for the three consecutive measurements was low, but a statistically significant difference was shown, both among operators and machines, although the variability could be considered of an acceptable level for all parameters. CVs approached 15% for PI-L and PI-S, 10% for PI-K, and was 6% to 8% for RI-L, RI-S, RI-K. Hepatic and renal CVs were similar in patients with cirrhosis and controls, while splenic CVs were much lower in control subjects than in patients with cirrhosis (for PI-S: 9% vs 16%; for RI-S 6% vs 8%). This observation can probably be explained by the fact that most patients with cirrhosis had splenomegaly, which increases splenic blood flow and alters the arterial vascularization of the organ, thus rendering the approach of the operator more variable. CVs for RI were smaller than those for PI in each organ. Such a good reproducibility is probably the consequence of the narrower range of this parameter compared to PI. Also measurement of mean velocity, used for calculation of PI, can be a source of variation. We studied variability of these indices only among machines and operators, so that we cannot draw any conclusion about their possibly different sensitivity in the evaluation of alterations in arterial circulation. Nonetheless, PI is usually considered better than RI for this purpose, but its calculation is not available on all machines.

The first part of the study demonstrated that, despite a general agreement on measurement rules, each operator naturally used a personal methodology of measurement. Nonetheless, variance due to operators was less than 3%. In the second part of the study, the common training program showed that variability due to operators can be further decreased to non-significant values, while non-systematic variance cannot be significantly reduced further.

Variability among different machines was very small, although it was statistically significant. Arterial resistance indices are calculated as the ratio between different flow velocities, and thus one would have expected these indices to be similar among different machines, as the difference in the evaluation of velocities by both hardware and software should equally affect the calculation of peak systolic, end diastolic and mean velocities. However, our previous study on the mesenteric artery (23) also showed a difference in resistance indices among machines. Although interequipment variability was very low, in order to obtain comparable

results from different ultrasonographic centers, it is recommended that manufacturers aim for uniform hardware and software elaboration of Doppler signals

On the basis of the differences between normal subjects and patients with cirrhosis observed in this study, interobserver variability does not seem to affect significantly the ability to recognize clinically relevant differences, and thus these indices can be widely used in the evaluation of arterial circulation.

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