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**Comparison of balloon versus straight catheter for  
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16 Alexander Zipprich, Matthias Winkler, Thomas Seufferlein, Matthias M. Dollinger  
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21 Department of Internal Medicine I, Martin-Luther-University Halle-Wittenberg  
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28 Corresponding author:  
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30 Alexander Zipprich, MD  
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32 First Department of Internal Medicine  
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34 Martin-Luther-University Halle-Wittenberg  
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36 Ernst-Grube-Str. 40  
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38 06120 Halle/Saale  
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40 email: [alexander.zipprich@medizin.uni-halle.de](mailto:alexander.zipprich@medizin.uni-halle.de)  
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## Abstract

Background & Aims: The hepatic venous pressure gradient (HVPG) is used as an estimation of portal pressure (PP) in the management of patients with cirrhosis. Two methods are available using either a straight (SC) or a balloon catheter (BC), but have never been compared head-to-head. The aim of the study was to compare the two methods regarding reproducibility and reliability.

Methods: In 47 patients with liver cirrhosis, HVPG was assessed using both catheters in sequence. In another 29 patients, the wedged hepatic venous pressure (WHVP) determined either with SC or BC was correlated with a direct measurement of PP. Variation coefficient and intraclass correlation coefficient were calculated.

Results: Variation coefficients for BC were 0.07 (HVPG), 0.02 (WHVP) and 0.06 (free hepatic venous pressure (FHVP)). Variation coefficients for SC were 0.17 (HVPG), 0.06 (WHVP) and 0.07 (FHVP), demonstrating a significantly wider variation of the HVPG and WHVP measurements ( $p < 0.001$ ). Comparison of WHVP with PP revealed a correlation coefficient of 0.72 ( $p = 0.004$ ) using BC and 0.58 ( $p = 0.011$ ) using SC.

Conclusions: Measurements with the balloon catheter currently represent the most reliable and reproducible method to assess HVPG. The results are of particular clinical relevance, if repeated measurements are required for therapeutic adjustments.

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### Introduction

In patients with cirrhosis increased intrahepatic resistance and vasodilatation of the splanchnic circulation will eventually lead to a rise in portal pressure (1). Portal hypertension, however, directly correlates with the development of cirrhotic complications and the mortality thereof. To assess portal pressure quantitatively, a catheter has to be introduced into the hepatic vein to determine free (FHVP) and wedge (WHVP) hepatic venous pressure. The difference between the two measurements, i.e. the hepatic venous pressure gradient (HVPG), is then commonly used as an estimation of the portal pressure (2).

Traditionally regarded as a tool for research, HVPG has first been suggested to be of clinical value in the early 1950s (3,4). Since then, its clinical potential has been repeatedly re-evaluated when studies demonstrated that the degree of portal hypertension quantified by HVPG may predict decompensation of liver disease, outcome after variceal bleeding or surgery for hepatocellular carcinoma, and ultimately long-term survival of patients with cirrhosis (3-11). A 20% reduction of HVPG is usually considered a good hemodynamic response associated with a lower risk to develop complications related to portal hypertension, mainly variceal bleeding (12). However, reproducibility and reliability of HVPG measurements are crucial before a method to determine HVPG can be implemented in everyday clinical practice used by a multitude of different investigators.

Several authors investigated the reliability of HVPG measurements as a surrogate marker for portal pressure. In one study, correlation between a single measurement of HVPG and portal pressure was high with a correlation coefficient of at least 0.93

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2 independently of the etiology of the cirrhosis (13). In contrast, measurements in three  
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4 different hepatic veins varied by as much as 60% in another study, questioning  
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6 reproducibility and hence the clinical validity of the procedure (14). The contrasting  
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8 results, however, were obtained by two different methods of measurement using a  
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10 balloon catheter (15) or a straight catheter to wedge the hepatic venous flow.  
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12 Although the balloon catheter is considered to be more reproducible and reliable, a  
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14 direct comparison of both methods has not been performed so far (2,15).  
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21 The aim of this study was to compare the two available methods to measure HVPG -  
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23 balloon and straight catheter - head-to-head and to assess reproducibility and  
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25 reliability of both.  
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## Methods

HVPG was assessed in 76 patients with histologically proven cirrhosis prior to treating portal hypertension by medication or TIPS implantation. In 47 of the patients, a straight and a balloon catheter were used in sequence to measure HVPG during the same procedure. In another 29 patients, the WHVP was measured using either the straight or the balloon catheter followed by direct intraportal assessment of the pressure. All patients gave written informed consent to the above described procedures; the study was carried out in agreement with the declaration of Helsinki.

### Measurement of the hepatic venous pressure gradient using two different methods

All measurements were performed in fasting patients in a supine position after stopping any portal pressure reducing agents or anti-hypertensive medication for a minimum of 24 hours. The hemodynamic assessment included right heart catheterization and measurement of the HVPG. Right heart catheterization was conducted using a quadruple-lumen thermodilution catheter (Abbott Lab., USA) inserted into the internal jugular vein under local anaesthesia with continuous assessment of mean arterial pressure (MAP) and heart rate using automated non-invasive monitoring (Sirecust, Siemens AG, Germany). Standard measurements included central venous pressure (CVP), cardiac output (CO), and systemic vascular resistance (SVR).

Each FHVP and WHVP measurement was repeated three times using a 7 French straight catheter (MP A1, Cordis Corporation, USA) and a 7 French balloon catheter (Standard Occlusion Balloon Catheter, Boston Scientific, USA) in sequence. The FHVP was assessed 2 to 3 cm proximal to the confluence of the hepatic veins with

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the position of the each catheter controlled radiologically. To measure the WHVP, the straight catheter was advanced into the hepatic vein until a wedged position was achieved. Alternatively, the balloon catheter was inflated achieving likewise a wedge position of the catheter. In both measurements, the appropriate wedge position was documented radiologically and by the characteristic pattern of the wedged curve (figure 1) as suggested by Groszmann et al. (2). Before the recording of the tracings, both free and wedge hepatic venous pressure were allowed to stabilize for 45s to 60s. The HVPG was calculated as the difference of the two measurements (HVPG = WHVP – FHVP).

#### Measurement of the WHVP and portal pressure

The direct intravascular portal pressure was assessed together with the WHVP during the procedure of implanting a transjugular intrahepatic portosystemic shunt. The WHVP was measured either with a straight or a balloon catheter as described above. Thereafter, the portal vein was punctured using a transjugular biopsy needle. A guide wire was introduced into the portal vein and advanced to the confluence of the vessel followed by a 7 French catheter for measuring the portal pressure. The guide wire was removed and the right position of the catheter in the portal vein documented radiologically. Before the measurements the portal pressure tracings were allowed to stabilize for 45s to 60s.

#### Statistical examination

Data were expressed as the means  $\pm$  standard deviation (SD). The variation coefficient for each catheter was calculated by the standard deviation divided by the means. T-test for paired samples was used to compare data of repeated



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measurements. To compare the two different catheters to each other, the mean of the three single measurements were calculated. The intraclass correlation coefficient was calculated to compare data of different measurements. Bland-Altman plots were constructed to compare the different measurements.

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## Results

### Patients description

Mean age of patients was  $55 \pm 12$  years, the mean Child-Pugh score  $9.2 \pm 2.4$  (Child-Pugh class: A: n=9; B: n=30; C: n=37). The etiology of cirrhosis was in the majority alcoholic liver disease (n=62). Remaining patients suffered from cryptogenic cirrhosis (n=4), NASH (n=3), hepatitis C (n=2), hemochromatosis (n=2), PSC (n=1), PBC (n=1) or autoimmune hepatitis (n=1). Refractory ascites was the indication for TIPS implantation in the respectively treated 29 patients.

### Measurements with balloon and straight catheter in comparison

47 patients were assessed hemodynamically using straight and balloon catheter in sequence. Hepatic pressures determined with the balloon catheter (figure 1) were  $14.7 \pm 7.2$  mmHg (HVPG),  $13.0 \pm 4.4$  mmHg (FHVP) and  $27.9 \pm 8.6$  mmHg (WHVP), respectively. Calculation of the variation coefficients for the triplicate measurements revealed only minor variations of the absolute values with a coefficient of 0.07 for the HVPG, 0.02 for the WHVP and 0.06 for the FVHP (figure 2).

Hepatic pressures determined using the straight catheter (figure 1) were  $13.1 \pm 6.5$  mm Hg (HVPG),  $12.8 \pm 4.6$  mm Hg (FHVP) and  $26.1 \pm 8.4$  mm Hg (WHVP). Compared with the values obtained using the balloon catheter, variation coefficients for the triplicate measurements using the straight catheter demonstrated a significantly wider variation with a coefficient of 0.17 for the HVPG ( $p < 0.001$ ; figure 3) and 0.06 for the WHVP ( $p < 0.001$ ), respectively. Only the measurements of the FHVP showed the same consistency with the straight as compared with the balloon catheter with no statistically significant difference between the two coefficients ( $p = 0.57$ ). Thus, the

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balloon catheter was more precise in determining the HVPG than the straight catheter, a result of the smaller variation of the WHVP when using the balloon to assess the wedged pressure.

In addition to the variation coefficient of each method, the intraclass correlation coefficient was calculated to assess the concordance between measurements obtained with both catheters. With high intraclass correlation coefficients between all three hepatic pressures, i.e. HVPG 0.87 (95%CI 0.74-0.93,  $p < 0.001$ ), FHVP 0.88 (95%CI 0.80-0.93,  $p < 0.001$ ) and WHVP 0.92 (95%CI 0.79-0.96,  $p < 0.001$ ), both methods showed good agreement on absolute values.

#### Comparison of WHVP and portal pressure

In 29 patients, the WHVP obtained by either balloon ( $n=13$ ) or straight ( $n=16$ ) catheter was correlated with a direct intravascular assessment of the portal pressure. Using the balloon catheter, the WHVP was  $26.8 \pm 5.4$  mmHg (HVPG  $24.3 \pm 5.4$  mmHg) compared with a pressure of  $26.8 \pm 4.6$  mmHg as determined directly within the portal vein. The median of the difference between the two measurements was 0.5 mmHg (interquartile range: -3.25 – 2.5; figure 4) with an intraclass correlation coefficient of 0.72 ( $p=0.004$ ).

Using the straight catheter, the WHVP was  $32.8 \pm 8.8$  mmHg (HVPG  $24.1 \pm 5.6$  mmHg) compared with a direct intravascular portal pressure of  $33.4 \pm 7.4$  mmHg. The median difference between the two measurements was 1 mmHg (interquartile range: -9.00 – 3.00; figure 4) and the intraclass correlation coefficient only 0.58 ( $p=0.011$ ). Thus, measurements obtained with the balloon catheter showed a higher correlation with

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the directly determined intraportal pressure than measurements obtained with the straight catheter.

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### Discussion

Within recent years, assessment of the HVPG has become a clinical tool with prognostic relevance recommended by an increasing number of experts in the management of patients with liver cirrhosis (2, 16). Although qualitative evaluation of portal hypertension is possible by indirect means such as endoscopy or ultrasound, only the quantitative HVPG offers the potential for rapid and subtle therapeutic adjustments in affected patients (9, 17-19). The hemodynamic response to treatment with beta-blockers, for instance, has long been advocated to prevent variceal bleeding (9, 20). A good response can be determined by an absolute value or by a relative decrease in HVPG. Traditionally, a 20% drop in HVPG is the threshold value considered an adequate response. However, recent studies have suggested that a 10% reduction may have a protective effect, too (17, 21, 22). Reproducibility and reliability of HVPG measurements are therefore crucial taking into account that even minor changes in HVPG have been proven relevant and may be used to support clinical decisions.

In response to conflicting reports on the accuracy of available methods, a recent systematic review attempted to evaluate HVPG measurements as an estimation of portal pressure (14, 23). The two techniques - balloon and straight catheter - correlated well with direct portal pressure measurements, however, a comparison between the two methods failed on account of the available data. Our study is the first to compare balloon and straight catheter head-to-head, with the balloon catheter producing the more consistent and reliable results. Assessment of the WHVP, in particular, appears to be the weakness of the straight catheter, affecting the calculation of the HVPG as a consequence. One possible explanation could be

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hemodynamic differences between hepatic veins as a result of heterogenic liver damage proven in a number of studies assessing the sampling variability of liver biopsies (24). The peripheral positioning of the straight catheter, too, might cause an underestimation of the portal pressure in case of small intrahepatic shunts, present in up to 50% of patients (25). In fact, the only study evaluating HVPG measurements (straight catheter) in different hepatic veins describes considerable hemodynamic heterogeneity, in part due to the presence of intrahepatic shunts (14).

The technical properties of the balloon catheter appear to eliminate such hemodynamic variations by covering a greater territory. Its clinical application has even been suggested to complement liver biopsy (26-28). In our study too, the balloon catheter produced more consistent wedged pressure measurements which also correlated better with the direct intravascular portal pressure. The correlation between WHVP determined by the straight catheter and the direct portal pressure, in contrast, remained poor supporting the concept of heterogeneous hemodynamics within different hepatic veins.

One limitation of our study is the comparably low correlation between WHVP and portal pressure. Previous reports demonstrated more conform results for the two pressures, although with the lowest intraclass correlation coefficient in alcoholic cirrhosis (13). In patients with sinusoidal portal hypertension, WHVP equals portal pressure. However, a number of studies suggest a pre-sinusoidal component to the portal hypertension in non-alcoholic cirrhosis such as primary biliary cirrhosis or viral hepatitis (29,30). In our study with nearly 16% non-alcoholic liver disease, pre-sinusoidal changes might well be more prevalent than previously reported.

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In conclusion, the balloon catheter currently represents the most reliable and reproducible method to assess HVPG. The consistency of the results obtained with the balloon catheter is particularly important, if repeated measurements are required for therapeutic adjustments in the management of cirrhotic patients.

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Figure 1

Representative radiological image of the wedge hepatic venous pressure (WHVP) measurement using the straight catheter (left figure) and the balloon catheter (right figure).

Figure 2

Bland-Altman plot of the hepatic venous pressure gradient (HVPG) measured using the balloon catheter. Points are representing the difference from the mean of three single measurements of the HVPG. Lines represent the 1.96 standard deviation of the mean as a threshold for good agreement. Please note the smaller standard deviation and therefore lower variability of the measurement compared to figure 3.

Figure 3

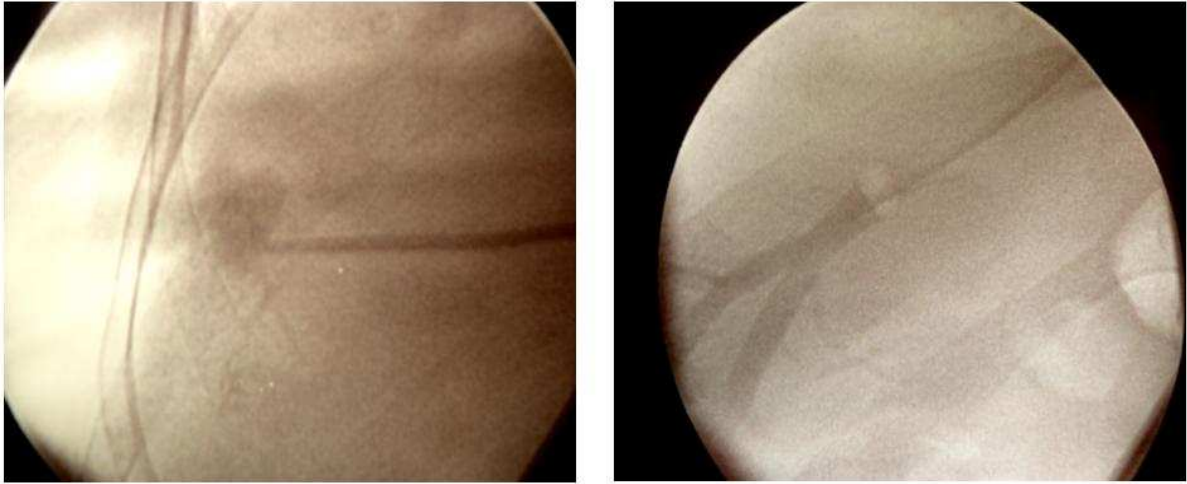
Bland-Altman plot of the hepatic venous pressure gradient (HVPG) measured using the straight catheter. Points are representing the difference from the mean of three single measurements of the HVPG. Lines represent the 1.96 standard deviation of the mean as threshold for good agreement. Please note the greater standard deviation and therefore higher variability of the measurement compared to figure 2.

Figure 4

Bland-Altman plot of the wedge hepatic venous pressure (WHVP) compared to the directly measured portal pressure. Squares represent measurements using the balloon catheter, triangles represent measurements using the straight catheter. Symbols are showing the difference of the WHVP from the portal pressure.

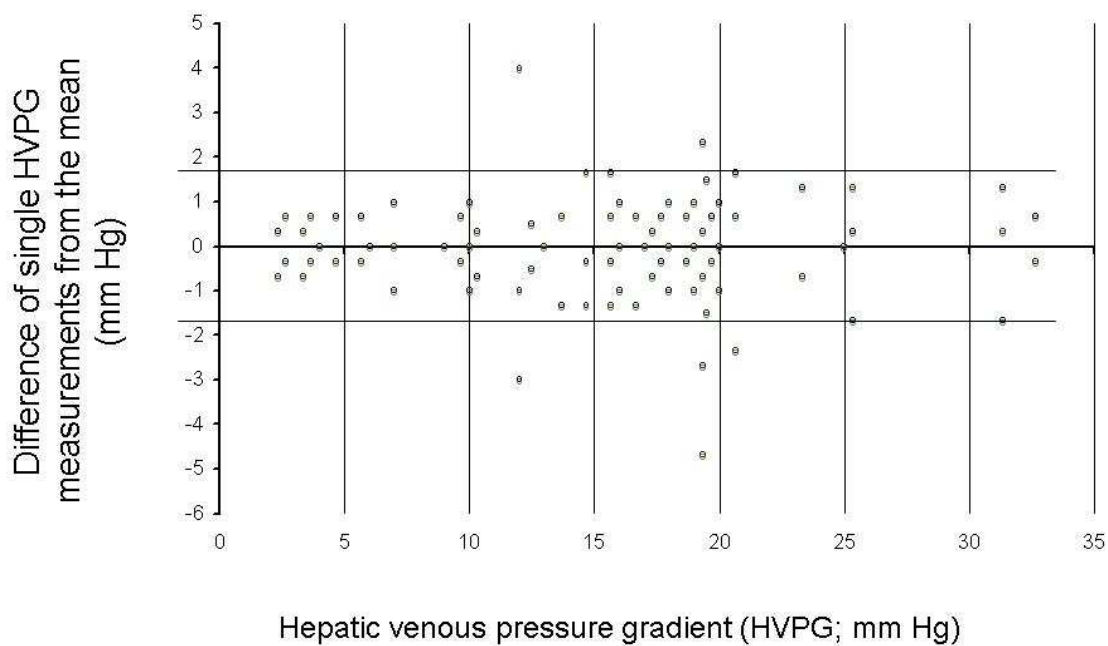
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Figure 1



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Figure 2

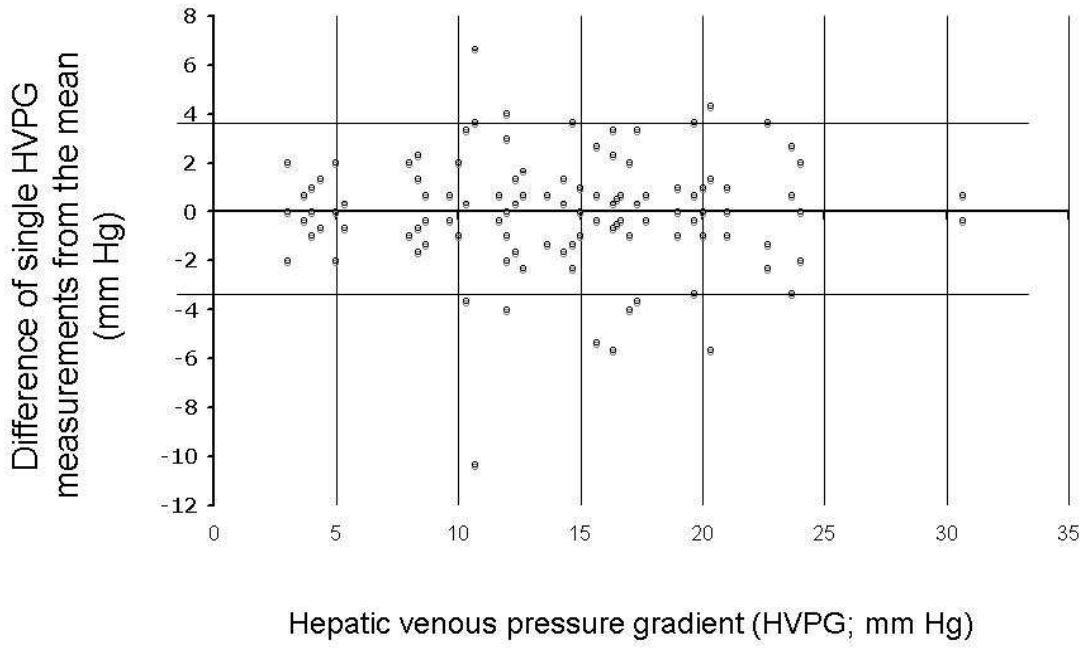


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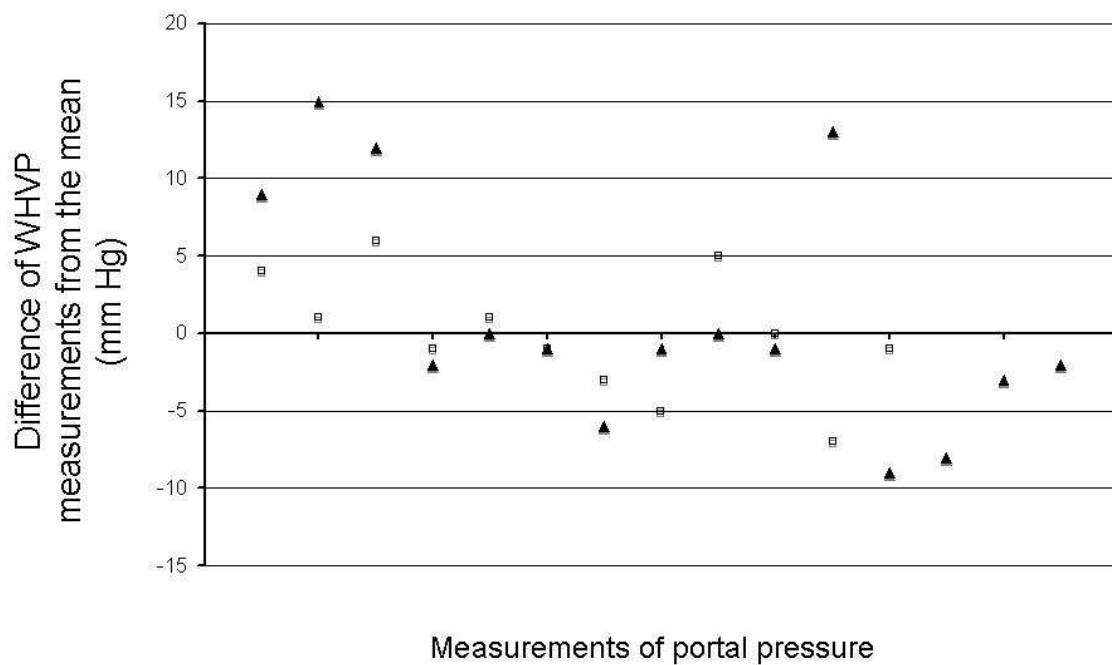
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Figure 3



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Figure 4



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**STARD checklist for reporting of studies of diagnostic accuracy**  
(version January 2003)

Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	1
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	3
METHODS			
<i>Participants</i>	3	The study population: The inclusion and exclusion criteria, setting and locations where data were collected.	5
	4	Participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	5
	5	Participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in item 3 and 4? If not, specify how participants were further selected.	Yes
	6	Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	5
<i>Test methods</i>	7	The reference standard and its rationale.	N/A
	8	Technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	5
	9	Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	5
	10	The number, training and expertise of the persons executing and reading the index tests and the reference standard.	N/A
	11	Whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	N/A
<i>Statistical methods</i>	12	Methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	6
	13	Methods for calculating test reproducibility, if done.	6
RESULTS			
<i>Participants</i>	14	When study was performed, including beginning and end dates of recruitment.	
	15	Clinical and demographic characteristics of the study population (at least information on age, gender, spectrum of presenting symptoms).	8
	16	The number of participants satisfying the criteria for inclusion who did or did not undergo the index tests and/or the reference standard; describe why participants failed to undergo either test (a flow diagram is strongly recommended).	N/A
<i>Test results</i>	17	Time-interval between the index tests and the reference standard, and any treatment administered in between.	5
	18	Distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	5
	19	A cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	
	20	Any adverse events from performing the index tests or the reference standard.	
<i>Estimates</i>	21	Estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	8
	22	How indeterminate results, missing data and outliers of the index tests were handled.	
	23	Estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	
	24	Estimates of test reproducibility, if done.	
DISCUSSION	25	Discuss the clinical applicability of the study findings.	11