Irish Journal of Medical Science (1971 -) (2019) 188:173–177
https://doi.org/10.1007/s11845-018-1844-8

ORIGINAL ARTICLE

Three-dimensional indices of renal perfusion in normal pregnancy and pre-eclampsia

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Received: 6 April 2017 / Accepted: 8 June 2018 / Published online: 18 June 2018

Abstract

Introduction We compared renal perfusion in normal pregnant women and women with pre-eclampsia using three-dimensional (3D) ultrasound. We measured the flow index (FI), vascular index (VI) and vascularisation flow index (VFI) which are believed to reflect vascularity and flow intensity.

Methods Fourteen patients with normal pregnancy and 16 patients with pre-eclampsia were recruited. Imaging was conducted using a Voluson E8 machine and a 6-MHz trans-abdominal probe. The inferior border of the maternal left kidney was scanned. Volumes were acquired using 3D power Doppler angiography (3D-PDA). The FI, VI and VFI were generated using 'histogram' facility.

Results Maternal characteristics between normal pregnant women and women with pre-eclampsia were not different in terms of maternal age, gestation or body mass index. Depth of insonnation was not different between groups. The FI, VI and the VFI were not different between groups. The mean (SD) for FI was 27.9 (7.4) vs. 27.1 (6.5) between women with normal pregnancy vs. women with pre-eclampsia. For VI, mean (SD) was 72.3(31.6) vs. 79.4 (28.7) respectively. For VFI, mean (SD) was 20.8 (10.8) vs. 20.8 (8.1) respectively. Using the Mann-Whitney *U* test, no statistical differences between groups were apparent. There was no correlation between FI measurements and maternal creatinine (Pearson's R square = 0.04; $p = 0.45$) or with maternal urea levels (Pearson's R square = 0.20; $p = 0.10$).

Conclusion Using 3D ultrasound, we failed to demonstrate a difference in maternal renal perfusion in normal pregnancy compared to pre-eclampsia. The lack of observed difference may be a reflection of the high variability in 3D measurements (i.e. poor investigative tool) rather than a true lack of difference in renal perfusion.

Keywords 3D ultrasound · Pre-eclampsia · Renal perfusion

Introduction

Pre-eclampsia is characterised by systemic endothelial dysfunction [1] and an impaired balance between vasodilative and vasoconstrictive factors [2, 3]. All maternal organs can be affected. The pathology seen in the maternal kidney is that of endotheliosis. These renal changes are believed to lead to decreased renal perfusion [1, 4]. Although intuitively likely, direct evidence of reduced renal perfusion is poor. Using Doppler ultrasound, Bahser and colleagues found that the resistance index and the pulsatility index of the intrarenal vessels were elevated compared to normal pregnancy [4]. Other investigators did not find evidence of increased intrarenal resistance index but did find a change in waveform in women with pre-eclampsia [5]. Lafayette and colleagues found a reduction on glomerular filtration rate in women with pre-eclampsia but their experimental data suggested that this was not related to haemodynamic changes [6]. In contrast, Moran and colleagues demonstrated that reduced glomerular filtration rate was in part related to reduced renal plasma flow [7].

Recently, with the advent of three-dimensional (3D) ultrasound, physicians have been able to obtain in vivo indices of perfusion. These indices are flow index (FI), vascular index (VI) and vascularisation flow index (VFI) which are believed to reflect vascularity and flow intensity [8, 9]. Recent work

Synopsis
Three-dimensional indices of renal perfusion are not different in pre-eclampsia compared to normal pregnancy.

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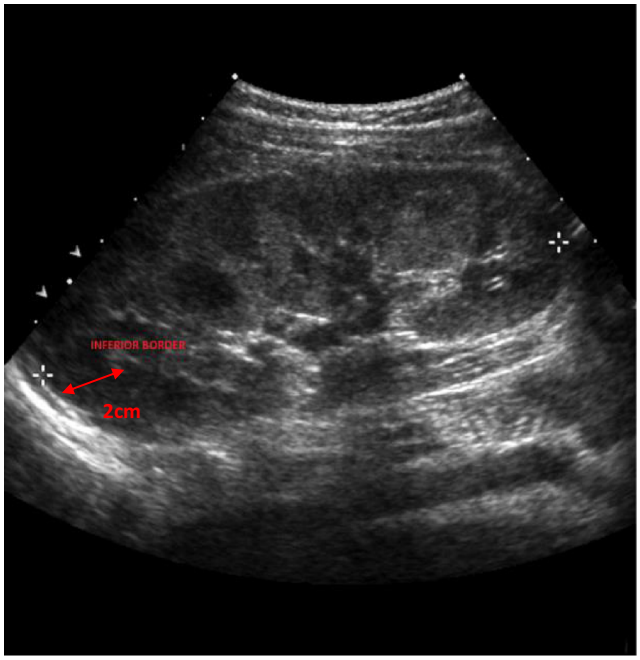

Fig. 1 Longitudinal section of maternal left kidney. The area of insonnation was selected as 2 cm from the inferior border of the kidney

using 3D ultrasound to assess perfusion in other maternal organs has been conflicting [10, 11]. Assessment of the placenta using this method appears reasonable [10], whilst assessment of the maternal liver appears less satisfactory [11].

As there are no other non-invasive methods of assessing maternal renal perfusion, the authors were keen to investigate the use of 3D ultrasound in this area. The hypothesis was that renal perfusion is impaired in patients with pre-eclampsia when compared to those with a normal pregnancy.

Methods

Approval was granted from the Research Ethics committee and Research Governance department (Research Ethics number: 11/NI/0082. Research Governance number: 10113SO-FC).

Fourteen patients with a normal pregnancy and 16 patients with pre-eclampsia were recruited for this study. Informed consent was obtained.

A normal pregnancy was defined as a pregnancy where the mother had no medical conditions, was not on any medication, and was carrying a structurally normal, appropriately grown singleton fetus.

Pre-eclampsia was defined as hypertension of at least 140/90 mmHg on two separate occasions ≥ 4 h apart accompanied by significant proteinuria: urine dipstick 2+ or more, urinary protein:creatinine > 30 mg/mmol or a validated 24-h urine collection result > 300 mg protein, arising de novo after the 20th week of gestation in a previously normotensive woman.

Scanning was conducted by one of two observers who had received identical training in the technique to minimise variation. A Voluson E8 machine (GE Kretz) was used, with a 6-MHz trans-abdominal probe. The Voluson default settings were kept constant at frequency 'mid', dynamic 'set 3', balance '> 150', smooth '4/5', ensemble '11', line density '8', power Doppler map '4', artefact suppression 'off', power Doppler line filter 'off' and quality 'high'. Gain, signal power, pulse repetition frequency and speed of acquisition were controlled for.

When measuring an area of perfusion, colour flow and 3D power Doppler angiography (3D-PDA) were applied, and the depth of insonnation was also recorded. From within the area measured, a constant spherical sample volume was chosen to allow standardisation. The power Doppler signals were then semi-quantified utilising the 'histogram facility', generating the three indices of vascularity: flow index (FI), vascular index (VI) and vascularisation flow index (VFI).

To identify the left kidney, the patient was asked to lie on her right side and the probe was placed between the iliac crest and the lower costal margin to examine in the maternal left kidney in the longitudinal plane. The area of sampling was arbitrarily fixed at 2 cm from the inferior border of the left kidney (Fig. 1). The patient was asked to hold her breath and the sample was taken over 10 s.

Comparison between groups was conducted using Student's *t* test or the Mann-Whitney *U* test as appropriate. Pearson's correlation co-efficient was used to study associations between variables.

Table 1 Patient demographics

	Normal ($n = 14$) Mean (SD)	Pre-eclampsia ($n = 16$) Mean (SD)	p value (Student's t test)
Age (years)	29.5 (7.0)	29.0 (5.9)	0.83
Body mass index (kg/m^2)	23.6 (4.9)	26.3 (5.5)	0.17
Gestation at time of ultrasound (weeks)	35.4 (3.0)	34.6 (2.9)	0.58
Mean arterial pressure (mmHg)	89.2 (6.5)	118.8 (5.0)	< 0.01
Depth of insonnation (cm)	5.3 (1.2)	6.0 (1.3)	0.76

Table 2 Renal perfusion 3D indices

	Normal ($n = 14$) Mean (SD)	Pre-eclampsia ($n = 16$) Mean (SD)	Mann-Whitney U test; value of U ($U = 64$ for statistical significance)
FI	27.9 (7.4)	27.1 (6.5)	99
VI	72.3 (31.6)	79.4 (28.7)	88
VFI	20.8 (10.8)	20.8 (8.1)	107

Results

There were no differences in maternal characteristics between patients with a normal pregnancy and those with pre-eclampsia (Table 1). The mean depth of insonnation was not different between groups. The mean arterial blood pressure (MAP) was significantly higher in patients with pre-eclampsia [mean (SD) for normal vs. pre-eclampsia: 89.2 (6.5) vs. 118 (5.0); $p < 0.01$]. The mean arterial blood pressure at booking was higher in women with pre-eclampsia [mean (SD) for normal vs. pre-eclampsia: 80.7 (8.8) vs. 86.7 98.1); $p = 0.03$].

There was no difference in indices of renal perfusion in women with a normal pregnancy compared to women with pre-eclampsia (Table 2). The Mann-Witney U test was used assuming that the data was not normally distributed. Setting $p < 0.05$, a value of U of 64 was required to determine statistical significance. The mean (SD) for flow index (FI) was 27.9 (7.4) vs. 27.1 (6.5) between women with normal pregnancy vs. women with pre-eclampsia [$U = 99$; not statistically different]. For vascular index (VI), the mean (SD) was 72.3 (31.6) vs. 79.4 (28.7) respectively [$U = 88$; not statistically significant]. For vascularisation flow index (VFI), the mean (SD) was 20.8 (10.8) vs. 20.8 (8.1) respectively [$U = 107$; not statistically significant].

The variability of the indices of perfusion is shown in Fig. 2, clearly showing no differences between groups and showing a high degree of variability.

There was no correlation between FI measurements and maternal creatinine levels (Pearson's R square = 0.04; $p = 0.45$). There was no correlation between FI measurements and urea levels (Pearson's R square = 0.20; $p = 0.10$ (Figs. 3 and 4).

Discussion

Using 3D ultrasound, we failed to demonstrate a difference in maternal renal perfusion in pre-eclampsia compared to normal pregnancy. There was no correlation between maternal urea and creatinine levels and measurements of 3D measurements of perfusion.

The interpretation of the 3D indices of perfusion needs to be performed with caution as these indices are merely a

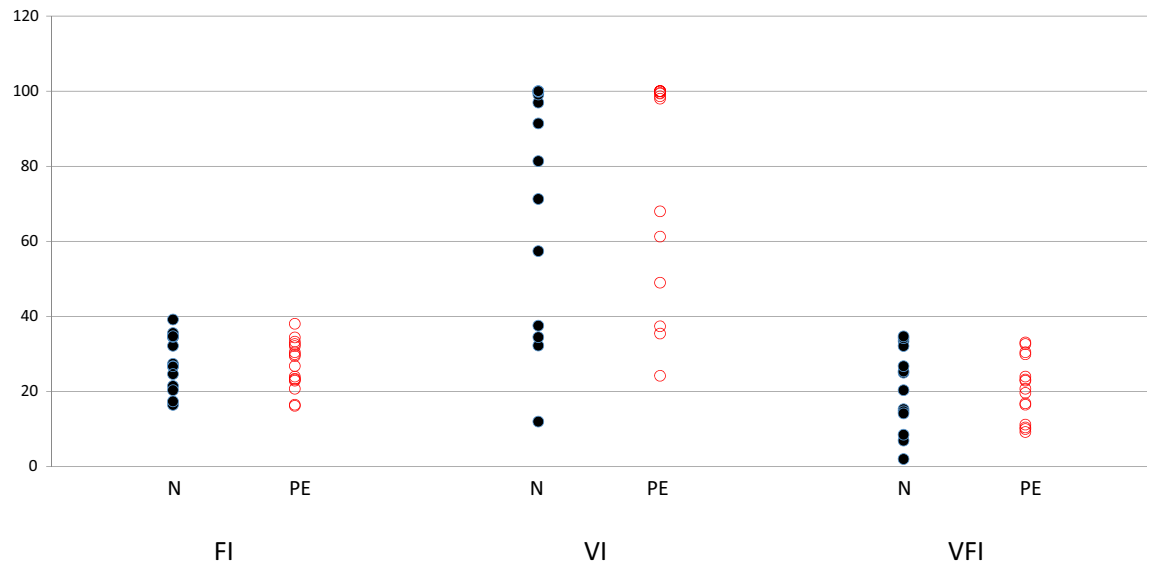

Fig. 2 Data distribution of maternal 3D renal vascular indices

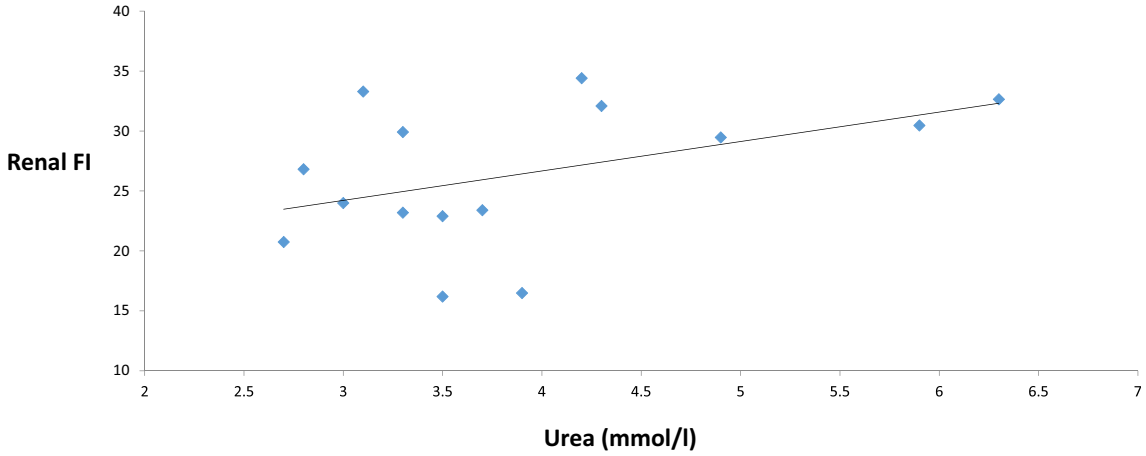

Fig. 3 Correlation between renal FI and urea levels

reflection of vascularity and flow intensity rather than a measurement of perfusion in the classical sense, where perfusion is measured in millilitres per minute per gram of tissue.

The weight of scientific evidence suggests that perfusion to all organs including the maternal kidney is reduced in pre-eclampsia. We were therefore surprised to find no differences between groups in our sample population. Similar to previous work in our unit [10, 11], there may be several reasons why no difference was found. Firstly, our sample size was small. Secondly, the women recruited who had pre-eclampsia mostly did not have severe disease. It would have been difficult to recruit women with more severe disease without compromising maternal safety (in our unit, the ultrasound department is distant from theatres and labour ward).

The index of FI is believed to be the most stable measurement of the three available indices [12]. FI was therefore used to correlate with markers of disease severity such as urea and creatinine levels.

In this study, the position of insonnation was made 2 cm from the inferior border of the kidney. Improvement in accuracy could have been achieved if the position of insonnation was made using two co-ordinates (for example: 2 cm from the lateral border and 2 cm from the inferior border of the kidney).

Given the high variability in the measurements of FI, VI and VFI, it was felt that increasing the sample size in order to show statistical differences between groups would not be worthwhile. A power calculation was conducted: Using data from FI, with an alpha of 0.05 and a power of 80%, in order to show a 10% difference between groups, 107 patients would be required in each group. It may be, that the time is now right, to concentrate efforts on developing other non-invasive methods assessing perfusion and abandoning the use of FI, VI and VFI.

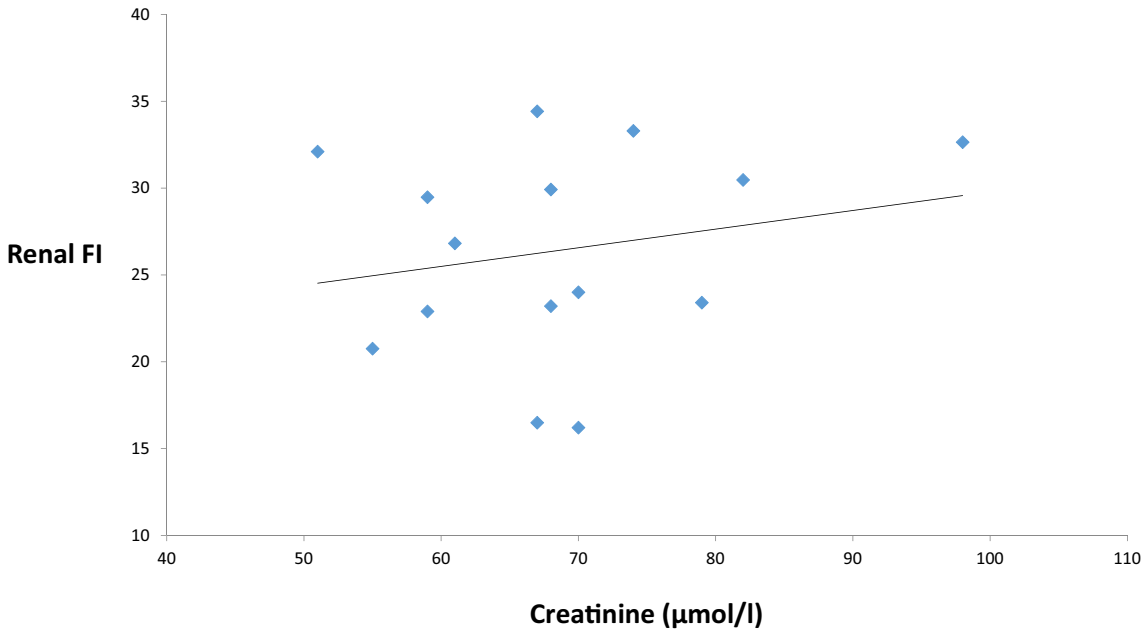

Fig. 4 Correlation between renal FI and creatinine levels

Author contribution AA, SA and SO scanned the patients, performed the analysis of data and wrote the paper.

Compliance with ethical standards

Approval was granted from the Research Ethics committee and Research Governance department (Research Ethics number: 11/NI/0082. Research Governance number: 10113SO-FC).

Conflict of interest The authors declare that they have no conflict of interest.

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