Hypertension Research (2015) 38, 796–797

www.nature.com/hr

CORRESPONDENCE

Reassessment of data on timing peak flow-mediated vasodilatation confirms that endothelial function returns to normal 11 years after preeclampsia

Hypertension Research (2015) **38,** 796–797; doi:10.1038/hr.2015.70; published online 2 July 2015

Endothelial dysfunction is a key feature of preeclampsia.[1] Impaired endothelial function may contribute to the observed increased risk for future cardiovascular disease in women with a history of preeclampsia.[2] Studies have shown persistent endothelial dysfunction for up to 3 years after a pregnancy with preeclampsia.[3] Whether this endothelial dysfunction eventually resolves has not been well studied. We recently reported in *Hypertension Research* on endothelial function studied by brachial artery flow-mediated vasodilatation assessed 1 and 11 years following a pregnancy with preeclampsia.[4] Compared with women with a normal pregnancy, the initial endothelial dysfunction observed in the preeclampsia group at 1 year had resolved 11 years after the index pregnancy.[4]

Maximal ischemia induced flow-mediated dilatation of the brachial artery occurs 45–60 s after onset of postischemic hyperemia in most young healthy persons, and flow-mediated dilatation has traditionally been assessed by the difference in brachial artery diameter before ischemia and 60 s following the end of the ischemic period. However, it is now recognized that time to maximum vasodilation differs between subjects, and often occurs later in older, diseased persons, and pregnant women.[3] Measuring postischemic diameter at several time points allows researchers to better estimate peak vasodilatation if there are large inter-individual differences in the timing of peak response. In our previous publications, we measured postischemic diameter of the brachial artery at 60 s after cuff release at 1 year postpartum[4] but at 30, 60 and 90 s at 11 years postpartum.[5] We therefore reassessed our results on flow-mediated vasodilatation 11 years postpartum to determine whether there may have been large differences in the timing of peak vasodilation between the preeclampsia group and women with normal pregnancies, as this has not been done before. The results of this analysis will also determine whether the divergent findings at 1 and 11 years postpartum were explained by potential differences in the timing of peak vasodilation between the two study groups.

As described in our initial publication, 18 healthy primiparous women with severe preeclampsia and a control group of 17 women with a normal uncomplicated pregnancy matched for age, parity and date of delivery were investigated 15 ± 3 months following the index pregnancy.[5] All women were again invited for examinations (three were unwilling to attend), which were performed 11.2 ± 0.6 years following the index pregnancy, as previously described.[4] All participants gave their written consent to participate in the study. The Ethics Committee in Stockholm approved of the study, and all procedures followed were in accordance with institutional guidelines.

Endothelium-dependent flow-mediated vasodilatation was assessed by postischemic hyperemia in the non-dominant arm, as described previously.[4,5] Vasodilatation was induced by a pneumatic tourniquet placed around the forearm (inflated to 300 mm Hg for 4.5 min at year; 250 mm Hg for 5 min at 11 years), followed by release. The brachial artery diameter was measured proximal to the cuff by ultrasound (at 1 year by an Acuson XP 128/10c, Siemens, Mountain View, CA, USA, with a 7-MHz linear array transducer; at 11 years by a Vivid 7 Dimension, GE Medical System, Horten, Norway, with a 9-MHz linear array transducer). All images were stored for later off-line analyses. Mean values of 3–4 measurements of arterial diameter at end-diastole were calculated at rest and at 30, 60 and 90 s (only 60 s at 1 year) after cuff release.

Table 1 shows that maximal ischemia-induced flow-mediated dilatation in most women occurs 60 s after onset of postischemic hyperemia, similar in both study groups. A delayed peak in flow-mediated vasodilatation has been reported during pregnancy.[6] Although we did not perform continuous artery diameter measurements during hyperemia, our results do not suggest a markedly delayed peak vasodilatation in women 11 years following preeclampsia. Flow-mediated vasodilatation 11 years following the index pregnancy was similar in both the study groups, whether measured at 30, 60 or 90 s of reactive hyperemia (Table 2). Furthermore, the improvement of endothelial function in the preeclampsia group during long-term follow-up was similar and significant whether measured at 60 s or by use of the maximum value (30, 60 or 90 s) obtained (Table 2). Thus the divergent findings between our studies at 1 and 11 years were not due to methodological differences in the

Table 1 Maximal brachial artery diameter during postischemic hyperemia

	Preeclampsia	*Control*
n	14	16
30 s	2; 14%	2; 13%
60 s	11; 79%	13; 81%
90 s	1; 7%	1; 6%

Time point of maximal brachial artery diameter during postischemic hyperemia in women 11 years after the index pregnancy. There was no difference between the two groups ($\chi^2 = 0.03$; $P = 0.98$).

Table 2 Increase in brachial artery diameter during postischemic hyperemia

	Preeclampsia		*Control*				
	1 year	*11 years*	*1 year*	*11 years*	P *group*	P *time*	P *group×time*
n	15	14	15	16			
30 s	—	5.7±5.0	—	5.6±4.1			
60 s	2.9±3.2	10.5±5.5	9.8±3.1	8.6±4.8	0.018	0.008	0.002
90 s	—	7.5±5.3	—	6.8±4.8			
Maximum of 30–60–90 s		10.7±5.4		9.0±4.7	0.013	0.003	0.002

Mean values±s.d. Two-way repeated-measures analysis of variance was used to assess the difference in flow-mediated dilatation between the preeclampsia and control group (group), the changes from 1 year to 11 years from the index pregnancy (time) and the interaction of group over time (group×time).

timing of the peak vasodilation measurements. With the data available, we cannot show whether the lower flow-mediated dilatation at 1 year in women with previous preeclampsia may have been due to delayed vasodilation at this earlier time point. However, other investigators using continuous diameter measurements have also found lower flow-mediated dilatation in women with preeclampsia approximately 7 months postpartum.[7]

We have reported that preeclampsia is associated with slight but sustained alterations both 1 and 11 years later concerning body size, glucose control, inflammation and blood pressure.[4] These alterations show similarities to the metabolic syndrome, a condition associated with future cardiovascular complications. The present reassessment of our study confirm the results earlier reported by us[4] and others[8] that endothelial dysfunction has resolved approximately 10 years after preeclampsia, and also when the potentially confounding effects of a delayed response in flow-mediated vasodilatation observed by age and in disease, such as the metabolic syndrome, is taken into account.[9,10] This is in line with observations that endothelial dysfunction induced by enhanced oxidative stress is reversible in women with preeclampsia, whereas impaired vascular reactivity may be associated with atherosclerotic changes in pregnant women with chronic hypertension.[11] Preexisting risk factors may be more important than a permanent damage of the endothelium for future cardiovascular disease in women with a history of preeclampsia. These risk factors may be present already before the pregnancy.[12]

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

This work was supported by Karolinska Institutet, Stockholm, Sweden.

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