



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

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**To cite this article:** Bas van den Bogaard, Olav R. de Peuter, Berend E. Westerhof, Hendrik Best, Jasper Truijen, Pieter W. Kamphuisen, Bert-Jan H. van den Born (2011) Does the beta 2 adrenergic receptor influence the wave reflection response to standing?, Artery Research 5:3, 115–117, DOI: <https://doi.org/10.1016/j.artres.2011.07.001>

**To link to this article:** <https://doi.org/10.1016/j.artres.2011.07.001>

Published online: 7 December 2019



SHORT COMMUNICATION

## Does the beta 2 adrenergic receptor influence the wave reflection response to standing?

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Received 26 May 2011; accepted 5 July 2011

Available online 30 July 2011

### KEYWORDS

Wave reflection;  
Hemodynamics;  
Postural change;  
Beta 2 adrenergic  
receptor

### Background

Vasoconstriction either by pharmacological intervention or by stimulation of the sympathetic nervous system increases wave reflection.<sup>1,2</sup> Standing causes a baroreflex mediated increase in sympathetic activity and total peripheral resistance, but paradoxically, wave reflection decreases upon standing.<sup>3</sup> Stimulation of the beta 2 receptor with salbutamol causes vasodilation and a decrease in wave

reflection.<sup>4</sup> Individuals homozygous for the Gly16Glu27 haplotype show increased peripheral vasodilation in response to isoproterenol compared to Arg16Gln27.<sup>5</sup> We hypothesized that the reduction in wave reflection during standing partially depends on beta2 adrenergic receptor (ADRB2) mediated vasodilation and that Arg16Gln27 carriers show a blunted wave reflection decrease upon standing compared to Gly16Glu27 carriers.

### Aims

To assess whether wave reflection decreases upon standing and whether this response differs between subjects with functional ADRB2 haplotypes, we recruited subjects homozygous for Arg16Gln27 or Gly16Glu27 haplotypes.

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doi:10.1016/j.artres.2011.07.001

**Table 1** Supine and standing hemodynamics of all participants.

	All <i>n</i> = 24		<i>p</i> *	Gly16Glu27 <i>n</i> = 15	Arg16Gln27 <i>n</i> = 9
	Supine	Standing		delta	delta
SBP, mm Hg	130 ± 4	138 ± 4	<0.01	5 ± 4	11 ± 4
DBP, mm Hg	67 ± 2	73 ± 3	<0.01	7 ± 3	6 ± 2
MAP, mm Hg	88 ± 3	93 ± 3	<0.01	4 ± 2	6 ± 1
HR, bpm	59 ± 2	68 ± 2	<0.001	9 ± 2	10 ± 2
SV, ml	78 ± 3	67 ± 4	<0.01	-13 ± 4	-8 ± 4
CO, l/min	4.6 ± 0.2	4.5 ± 0.3	0.51	-0.3 ± 0.2	0.1 ± 0.3
TPR, dyn s/cm <sup>5</sup>	1.21 ± 0.4	1.35 ± 0.5	0.06	0.18 ± 0.1	0.07 ± 0.1
RM, %	73.0 ± 1.7	67.7 ± 1.9	<0.001	-6.0 ± 1.4	-4.1 ± 1.8
Pf, mm Hg	36 ± 1	35 ± 1	0.29	-2 ± 1	1 ± 2
Pb, mm Hg	26 ± 1	24 ± 1	0.01	-4 ± 1	-1 ± 2

Data are median±SE for aortic systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), stroke volume (SV), cardiac output (CO), total peripheral resistance (TPR), reflection magnitude (RM), forward pressure wave (Pf) and backward pressure wave (Pb). The differences (delta) in hemodynamic parameters between supine and standing were not significantly different between Gly16Glu27 and Arg16Gln27 carriers.

\**p* for supine versus standing.

## Methods

The study was approved by the local ethics committee and all participants gave written informed consent. Healthy subjects were recruited by public advertising. Blood was drawn for DNA collection to determine beta2-adrenergic genotypes. Persons were included if they were homozygous for the Arg16Gln27 or the Gly16Glu27 haplotype. All measurements were performed in the morning after an overnight fast in a quiet and temperature-controlled room. After instrumentation the subjects rested in supine position for 30 min, before they were asked to rise. Noninvasive finger arterial pressure was recorded with a Nexfin device (BMEYE BV, Amsterdam, the Netherlands).<sup>6</sup> For analysis we selected 20 consecutive beats during the supine and after 5 min of standing. From the beat to beat selection an aortic pressure was constructed with a generalized pressure transfer filter to obtain systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), stroke volume (SV), cardiac output (CO) and total peripheral resistance (TPR). To assess wave reflection the constructed aortic pressure was separated into forward (Pf) and backward (Pb) waves by waveform analysis using software programmed in Mathematica (Wolfram Research Inc., Mathematica, Version 4, Champaign, IL, USA) to calculate the reflection magnitude (RM) as 100× the ratio of Pb and Pf. Data are expressed as median±standard error (SE). We used paired *t*-tests and independent *t*-tests to calculate differences in wave reflection between supine and standing position and between the haplotypes using SPSS software version 16.0.1 (SPSS Inc., Chicago, Illinois, USA).<sup>7</sup>

## Results

Aortic pressure waves were calculated for 24 healthy subjects (mean age 62 ± 8 yrs, 14 [58%] males), 15 subjects had the Gly16Glu27 haplotype (mean age 61 ± 6 yrs, 10 [67%] males) and 9 subjects the Arg16Gln27 haplotype

(mean age 65 ± 11 yrs, 4 [44%] males). Supine and standing hemodynamic data are given in Table 1. In response to standing, SBP, DBP, MAP, HR and TPR increased, while SV and Pb decreased. CO and Pf were not significantly different between supine and standing. The RM decreased from 73.0 ± 1.7% in supine position to 67.7 ± 1.9% while standing (*p* < 0.001). The hemodynamic response to standing was not significantly different between Arg16Gln27 and Gly16Glu27 carriers. The decrease in RM upon standing was not significantly different between subjects homozygous for Gly16Glu27 or Arg16Gln27 haplotype (6.0 ± 1.4% vs 4.1 ± 1.8%, *p* = 0.40).

## Conclusion

Wave reflection, represented by the RM, significantly decreased from supine to standing. Wave reflection and hemodynamic response to standing were not different between subjects homozygous for Gly16Glu27 or Arg16Gln27 haplotype. Small resistance arteries and arterioles are thought to be the major reflection site of arterial pressure waves.<sup>8,9</sup> In most situations an increase in TPR coincides with an increase in wave reflection.<sup>1,2,10</sup> Upon standing, the initial drop in blood pressure is counteracted by a baroreflex mediated increase in vasomotor tone through an increase in sympathetic output accelerating HR and increasing TPR.<sup>11</sup> The decrease in wave reflection upon standing therefore seems counterintuitive. Lower body negative pressure, which mimics the postural change from supine to standing, also causes an increase in TPR and a decrease in wave reflection.<sup>10</sup> The vasoconstrictive response upon standing, however, might differ between arterial beds. We hypothesized that the reduced beta2 receptor mediated vasodilation of Arg16Gln27 carriers might contribute to the smaller decrease in wave reflection, implying a role of the beta2 receptor in the wave reflection response to postural change. We found no significant differences between Gly16Glu27 or Arg16Gln27 carriers. Because of the limited sample size

we cannot exclude however that small differences in wave reflection between ADRB2 haplotypes do exist. Alternatively, the change in body position might have an effect on wave reflection through changes in arterial diameter and function. This needs further study.

### Conflict of interest statement

Part of this study was supported by an unrestricted grant from the Netherlands Heart Foundation [NHF-2006B180].

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