Reply: Medical science is based on facts and evidence

heterogeneous components [4]. Consequently, for such segments, it cannot be stated that $CAVI_0$ is superior to CAVI. In fact, CAVI is deemed to be more suitable in actual human patients over the heart to ankle pathway. A recent study by Wohlfahrt *et al.* [5] of a total of 2160 white individuals shows that no clear benefit of $CAVI_0$ was seen.

Soon, we will disclose some further aspects of CAVI, including the coefficients *a* and *b* contained in the CAVI formula, in a scientific publication.

Supplement:

P_s: SBP, P_d: DBP, ΔP: $P_s - P_d$

P_m: mid-pressure [defined as $P_m = (P_s + P_d)/2$]

Then, $P_s = P_m + \Delta P/2$, $P_d = P_m - \Delta P/2$

$$\begin{aligned}
\frac{\ln P_s - \ln P_d}{P_s - P_d} &= \frac{\ln(P_m + (\Delta P/2)) - \ln(P_m - (\Delta P/2))}{(P_m + (\Delta P/2)) - (P_m - (\Delta P/2))} \\
&= \frac{\ln(P_m + (\Delta P/2)) - \ln(P_m - (\Delta P/2))}{(P_m + (\Delta P/2)) - (P_m - (\Delta P/2))} \\
&= \frac{\ln(P_m + (\Delta P/2)) - \ln(P_m - (\Delta P/2))}{\Delta P} \\
&= \frac{\ln(P_m(1 + (\Delta P/2P_m))) - \ln(P_m(1 - (\Delta P/2P_m)))}{\Delta P} \\
&= \frac{\ln(1 + (\Delta P/2P_m)) + \ln P_m - \ln(1 - (\Delta P/2P_m)) - \ln P_m}{\Delta P} \\
&= \frac{\ln(1 + (\Delta P/2P_m)) + \ln P_m - \ln(1 - (\Delta P/2P_m)) - \ln P_m}{\Delta P} \\
&= \frac{1}{\Delta P}\left\{\ln\left(1 + \frac{\Delta P}{2P_m}\right) - \ln\left(1 - \frac{\Delta P}{2P_m}\right)\right\}
\end{aligned}$$

By applying the second order Maclaurin expansion to $\ln(1 + \Delta P/(2P_m))$ and $\ln(1 - \Delta P/(2P_m))$

$$\begin{aligned}
&\approx \frac{1}{\Delta P}\left\{\frac{\Delta P}{2P_m} - \frac{1}{2}\left(\frac{\Delta P}{2P_m}\right)^2 + \frac{\Delta P}{2P_m} + \frac{1}{2}\left(\frac{\Delta P}{2P_m}\right)^2\right\} \\
&= \frac{1}{\Delta P}\left\{\frac{\Delta P}{2P_m} - \frac{1}{2}\left(\frac{\Delta P}{2P_m}\right)^2 + \frac{\Delta P}{2P_m} + \frac{1}{2}\left(\frac{\Delta P}{2P_m}\right)^2\right\} \\
&= \frac{1}{\Delta P}\left(\frac{\Delta P}{2P_m} + \frac{\Delta P}{2P_m}\right) \\
&= \frac{\Delta P}{\Delta P \;\; P_m} \\
&= \frac{\Delta P}{\Delta P \;\; P_m}
\end{aligned}$$

ACKNOWLEDGEMENTS

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Spronck B, Avolio AP, Tan I, Butlin M, Reesink KD, Delhaas T. Reply: physics cannot be disputed. *J Hypertens* 2017; 35:1523–1525.
2. Shirai K, Shimizu K, Takata M, Suzuki K. Independency of the cardio-ankle vascular index from blood pressure at the time of measurement. *J Hypertens* 2017; 35:1521–1523.
3. Spronck B, Avolio AP, Tan I, Butlin M, Reesink KD, Delhaas T. Arterial stiffness index beta and cardio-ankle vascular index inherently depend on blood pressure but can be readily corrected. *J Hypertens* 2017; 35: 98–104.
4. Nichols WW, O'Rourke MF. Charalambos Vlachopoulou 2011: *McDonald's blood flow in arteries*, 6th edn. Hodder Arnolds 2011, 99–105.
5. Wohlfahrt P, Cífková R, Movsisyan N, Kunzová Š, Lešovský J, Homolka M, *et al.* Reference values of cardio-ankle vascular index in a random sample of a white population. *J Hypertens* 2017; 35:2238–2244.

Journal of Hypertension 2018, 36:957–965

[a]Mihama Hospital, Mihama-Ku, Chiba Prefecture, [b]Toyama Teishin Hospital, Toyama, Toyama Prefecture, [c]Department of Pharmacology and Therapeutics, Faculty of Pharmaceutical Science and [d]Cardiovascular Center, Sakura Hospital, Toho University, Chiba, Japan

Correspondence to Kohji Shirai, MD, PhD, Mihama Hospital, Mihama-Ku 261-0013, Chiba Prefecture, Japan. E-mail: kshirai@kb3.so-net.ne.jp

DOI:10.1097/HJH.0000000000001661

Reply: Medical science is based on facts and evidence

Bart Spronck[a,b,c], Alberto P. Avolio[b], Isabella Tan[b], Mark Butlin[b], Koen D. Reesink[a], and Tammo Delhaas[a]

We appreciate and read with great interest Shirai *et al.*'s addition [1] to the discussion involving our study on the pressure dependence of arterial stiffness index β and cardio–ankle vascular index (CAVI) [1–4]. In the present letter, we wish to point out that Shirai *et al.*'s [1] statement that CAVI represents arterial stiffness at the 'mid pressure' requires further consideration so as to clarify the underlying logical reasoning. Furthermore, we propose that the presented clinical data [1] neither support CAVI's use of 'mid pressure', nor provide evidence for or against CAVI's or $CAVI_0$'s *acute* blood pressure (BP) (in)dependence.

First, we appreciate that Shirai *et al.* acknowledge the mathematical correctness of stiffness index β_0. Stiffness index β has indeed been widely used with significant clinical impact. However, to our knowledge, no clinical study has directly compared β and β_0 in terms of acute BP dependence. Therefore, we can only conclude that *theoretically* – but based on Hayashi's *experimental* findings of an exponential arterial pressure–diameter relationship [5] – β_0 should show *less* pressure dependence than β [2].

Second, Shirai *et al.* introduce 'mid pressure' (P_m, not to be confused with *mean* BP) as a novel BP-related quantity. They show mathematically that CAVI's correction approximately corresponds to using P_m as a pressure reference point.

Subsequently and moreover, they state that P_m is the appropriate pressure metric to correct CAVI's underlying and essential measurement, the heart-to-ankle pulse wave velocity (haPWV). We respectfully disagree with this statement. haPWV is PWV measured by a foot-to-foot time delay. As we detailed in our previous letter [4] – and as already shown by Bramwell *et al.* [6] – a foot-to-foot PWV is, *by definition*, dependent on DBP [diastolic blood pressure (P_d)] [7–9]. It is the (diastolic) BP dependence of haPWV for which CAVI aims to correct. Therefore, the difference between CAVI and $CAVI_0$ is not strictly a judgement on '...whether arterial stiffness is measured at the point of P_m or of P_d'. $CAVI_0$ uses the pressure at which the essential measurement of PWV is taken (P_d), whereas CAVI uses a pressure (P_m) that is approximately related to the pressure at which the measurement is taken without consideration for the theoretical or experimental evidence for the relationship of foot-to-foot measured PWV with P_d.

Shirai *et al.* [1] present Fig. 3 of their letter as evidence for their claim that haPWV depends on P_m. However, cross-sectional data cannot be reliably used to assess an acute relationship between PWV and BP [10] for reasons which we have previously discussed [11]. In fact, Shirai *et al.* themselves previously warned that 'Several reports showed that CAVI is less dependent on BP than PWV, but these results *do not necessarily mean that CAVI is independent of BP at the time of measurement*' [12]. Although a *P*-value is found wanting, the figure suggests that *between patients*, haPWV relates more strongly to P_m than to P_d. This is plausible and is probably due to patients with a higher P_m having an intrinsically stiffer wall. The latter is the reason that studies on reference values commonly report stiffness measures as a function of *mean* BP [13,14], which is closely related to the '*mid* pressure' (P_m) as introduced by Shirai *et al.* [1]. Mean BP is the pressure that is thought to be the one more closely related to arterial (hypertensive) *remodelling*. CAVI, however, aims to correct for the confounding effect of *acute* BP changes on PWV – not for intrinsic changes in arterial stiffness due to hypertensive arterial remodelling, which is the subject of interest rather than the confounder *per se*.

Third, we fully acknowledge that clinical data sets are sometimes small. However, a small data set should not be used to 'prove' that there is no change in a variable (CAVI in this case), a statement for which the data in this example [15] was statistically underpowered (footnote on p. 108 in [11]). Nevertheless, we would like to compliment Shirai *et al.* [15] with the design of this study, which – with a larger number of patients – would be appropriate to investigate the *acute* BP dependence of CAVI and $CAVI_0$. The (large) epidemiological dataset that Shirai *et al.* refer to (Fig. 2 in [3]) on the contrary only illustrates the *cross-sectional* relationship of CAVI/$CAVI_0$ and age/hypertension.

In conclusion, we propose that there is no need to introduce 'mid pressure' as yet another BP-related quantity, and we hold that the clinical data provided by Shirai *et al.* cannot be used to fully assess the acute BP (in)dependence of CAVI or $CAVI_0$. We would like to emphasise that we have no issue at all with the use of CAVI or the use of the VaSera device (Fukuda Denshi Co., Ltd., Tokyo, Japan). Rather, our article [2] aimed to propose slightly modified stiffness indices – β_0 and $CAVI_0$ – that (unlike β and CAVI) are theoretically independent of BP, but similarly easy to calculate and therefore still clinically applicable. $CAVI_0$ can be directly calculated from existing CAVI values or from underlying variables provided by the VaSera system [16] – the $CAVI_0$ equation could indeed be easily implemented into the VaSera system itself. We look forward to the publication announced by Shirai *et al.* on further aspects of CAVI.

ACKNOWLEDGEMENTS

The current study was supported by an Endeavour Research Fellowship awarded by the Australian Government to B.S.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Shirai K, Takata M, Takahara A, Shimizu K. Medical Science is based on evidence (answer to Spronck *et al.*'s refutation: physics cannot be disputed). *J Hypertens* 2018; 36:958–960.
2. Spronck B, Avolio AP, Tan I, Butlin M, Reesink KD, Delhaas T. Arterial stiffness index beta and cardio–ankle vascular index inherently depend on blood pressure but can be readily corrected. *J Hypertens* 2017; 35:98–104.
3. Shirai K, Shimizu K, Takata M, Suzuki K. Independency of the cardio–ankle vascular index from blood pressure at the time of measurement. *J Hypertens* 2017; 35:1521–1523.
4. Spronck B, Avolio AP, Tan I, Butlin M, Reesink KD, Delhaas T. Reply: physics cannot be disputed. *J Hypertens* 2017; 35:1523–1525.
5. Hayashi K, Handa H, Nagasawa S, Okumura A, Moritake K. Stiffness and elastic behavior of human intracranial and extracranial arteries. *J Biomech* 1980; 13:175–184.
6. Bramwell JC, McDowall RJS, McSwiney BA. The variation of arterial elasticity with blood pressure in man (Part I). *R Soc Lond Proc Ser B* 1923; 94:450–454.
7. Nye ER. The effect of blood pressure alteration on the pulse wave velocity. *Br Heart J* 1964; 26:261–265.
8. Nichols W, O'Rourke M, Vlachopoulos C. *McDonald's blood flow in arteries: theoretical, experimental and clinical principles*. London, UK: CRC Press; 2011.
9. Gao M, Cheng H-M, Sung S-H, Chen C-H, Olivier NB, Mukkamala R. Estimation of pulse transit time as a function of blood pressure using a nonlinear arterial tube-load model. *IEEE Trans Biomed Eng* 2017; 64:1524–1534.
10. Benetos A. Assessment of arterial stiffness in an older population: the interest of the cardio–ankle vascular index (CAVI). *Eur Heart J Suppl* 2017; 19:B11–B16.
11. Spronck B, Delhaas T, Butlin M, Reesink KD, Avolio AP. Options for dealing with pressure dependence of pulse wave velocity as a measure of arterial stiffness: an update of cardio–ankle vascular index (CAVI) and CAVI0. *Pulse* 2017; 5:106–114.
12. Shirai K, Hiruta N, Song M, Kurosu T, Suzuki J, Tomaru T, *et al.* Cardio–ankle vascular index (CAVI) as a novel indicator of arterial stiffness: theory, evidence and perspectives. *J Atheroscler Thromb* 2011; 18:924–938.
13. Wohlfahrt P, Cifkova R, Movsisyan N, Kunzova S, Lesovsky J, Homolka M, *et al.* Reference values of cardio–ankle vascular index in a random sample of a white population. *J Hypertens* 2017; 35:2238–2244.
14. Reference Values for Arterial Stiffness' Collaboration. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: establishing normal and reference values. *Eur Heart J* 2010; 31:2338–2350.
15. Shirai K, Song M, Suzuki J, Kurosu T, Oyama T, Nagayama D, *et al.* Contradictory effects of beta1- and alpha1-aderenergic receptor blockers on cardio-ankle vascular stiffness index (CAVI) – CAVI is independent of blood pressure. *J Atheroscler Thromb* 2011; 18: 49–55.

16. Spronck B, Mestanik M, Tonhajzerova I, Jurko A, Jurko T, Avolio AP, Butlin M. Direct means of obtaining CAVI0 – a corrected cardio–ankle vascular stiffness index (CAVI)-from conventional CAVI measurements or their underlying variables. *Physiol Meas* 2017; 38: N128–N137.

Journal of Hypertension 2018, 36:957–965

[a]Department of Biomedical Engineering, CARIM School for Cardiovascular Diseases, Maastricht University, Maastricht, The Netherlands, [b]Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, New South Wales, Australia and [c]Department of Biomedical Engineering, School of Engineering & Applied Science, Yale University, New Haven, Connecticut, USA

Correspondence to Bart Spronck, PhD, Department of Biomedical Engineering, School of Engineering & Applied Science, Yale University, 55 Prospect Street, New Haven, CT 06511, USA. Tel: +1 203 432 6678; e-mail: bart.spronck@yale.edu

DOI:10.1097/HJH.0000000000001660

Facebook advertising for disseminating hypertension knowledge to older Chinese adults

Phillip H. Dunn and Benjamin K.P. Woo

With great interest, we read the original article by Nash *et al.* [1] discussing the use of Facebook advertising for the recruitment of patients into a blood pressure clinical trial in Australia. The study was the first to determine whether Facebook may be a useful tool to enhance blood pressure clinical trial recruitment and to ascertain the effectiveness of recruiting middle to older aged study participants through intermittent broadcast of Facebook advertisements. Participant recruitment successfully increased at two of three sites where Nash's team conducted the study. The study also found that Facebook advertising could be useful in recruiting a cohort of older participants typical of cardiovascular-related clinical trials [1]. Nevertheless, the authors suggest that the success of Facebook advertising may be location-dependent. To expand upon the study, we demonstrated similar results in a Facebook advertising for disseminating hypertension knowledge to older Chinese adults.

Health disparities facing the Chinese community can be reduced through effective health education and outreach [2]. Although e-health education has enormous potential, in-person workshops are more effective at disseminating knowledge to target older Chinese-speaking population [3,4]. In our study, we created a Facebook campaign to raise awareness and knowledge on hypertension in the Chinese community. Our advertisement included a video link, a five-character title and 26-character text body both in traditional written Chinese. Advertisements were able to be targeted towards Chinese-speaking men and women aged older than 44 years as these details were included as part of registering for Facebook. We then separated the participants into three age brackets: (1) 45–54 years, (2) 55–64 years, or (3) 65 years or older. Our study tracked the click-through rate (clicks/impressions), as defined by the ratio of users who clicked on the video link to the number of total Facebook users who viewed the hypertension awareness and knowledge advertisements. The click-through rates for the three age groups were 3.57, 8.04, and 14.71% for the age brackets 45–54 years, 55–64 years, and 65 years or older, respectively.

Our results lend support to the Nash *et al.* [1] study. Facebook advertising could be useful in outreaching to older adults in different locations. These results encourage using Facebook advertisements, in Australian or Chinese older adults, to increase participations in hypertension health-related studies. Although Facebook was successful in recruiting a cohort of participants in an older age bracket typical of developing cardiovascular diseases, our study showed that the advertisement was most effective in the 65 years or older group, with a click-through rate of 14.71%. Nevertheless, success in recruiting participants in further hypertension education may not translate into success in clinical trial recruitment. Future prospective studies should be designed to determine the effects of Facebook advertising on recruiting older Chinese for blood pressure clinical trials. Given the limited sources of language and culturally appropriate health information for older Chinese [5], future studies should also be designed to determine how to effectively promote quality e-health information online.

ACKNOWLEDGEMENTS

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Nash EL, Gilroy D, Srikusalanukul W, Abhayaratna WP, Stanton T, Mitchell G, *et al.* Facebook advertising for participant recruitment into a blood pressure clinical trial. *J Hypertens* 2017; 35:2527–2531.
2. Woo BK. Dementia health promotion for Chinese Americans. *Cureus* 2017; 9:e1411.
3. Zheng X, Woo BK. E-mental health in ethnic minority: a comparison of youtube and talk-based educational workshops in dementia. *Asian J Psychiatr* 2017; 25:246–248.
4. Zheng X, Woo BK. Exploring the impact of a culturally tailored short film in modifying dementia stigma among Chinese Americans: a pilot study. *Acad Psychiatry* 2016; 40:372–374.
5. Tsiang JT, Woo BK. Comparison of online dementia information in Chinese and in English languages. *Ccureus* 2017; 9:e1808.

Journal of Hypertension 2018, 36:957–965

Asian Pacific Health Corps, University of California, Los Angeles, California, USA

Correspondence to Benjamin K.P. Woo, MD, Department of Psychiatry and Biobehavioral Sciences, Olive View – UCLA Medical Center, Sylmar, CA 91342, United States. Tel: +1 747 210 4433; fax: +1 747 210 3554; e-mail: bkpwoo@gmail.com

DOI:10.1097/HJH.0000000000001668