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# 1 How to calculate ventricular–arterial coupling?

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11  
12 Ventricular–arterial coupling (VAC) is a very interesting variable in the field of heart failure  
13 (HF), enabling a more in-depth evaluation of patients' profile. Indeed, “vascular” scenarios  
14 have been mentioned for years as an important entity within the scope of HF, yet without any  
15 practical approach to efficiently identify them. The assesment of VAC can fill in this gap.

16 A consensus document was published in the European journal of Heart failure in January  
17 2019 presenting the assessment, clinical implications and therapeutic perspectives related to  
18 VAC in a clinical HF setting<sup>1</sup>. To show the clinical usefulness of VAC, this viewpoint  
19 presents the assessment of VAC in various clinical scenarios such as systemic hypertension  
20 and heart failure with reduced and preserved ejection fraction (HFrEF and HFpEF)  
21 respectively. In order to facilitate the utilization of VAC into everyday clinical practice, a  
22 simplifying Excel sheet for the VAC calculation is provided.

23 The interplay between the heart and the arterial system has recently gained much attention  
24 since interventions that improve both myocardial and vascular functions may delay the  
25 progression to HF, valvular heart disease and possibly even improve prognosis<sup>1,2</sup>. Today, the  
26 assessment of VAC in clinical practice is being facilitated by advances in the non-invasive  
27 assessment of cardiac imaging. Traditionally, VAC has been defined as the combined marker  
28 of arterial and myocardial function, expressed as  $E_a/E_{es}$  ratio, where  $E_a$  reflects arterial  
29 elastance (an index of arterial load on the left ventricle) and  $E_{es}$  ventricular elastance (an index  
30 of the contractility of the left ventricle)<sup>3</sup>. The  $E_a/E_{es}$  ratio has shown to be a key determinant of  
31 HF and increased arterial stiffness, both independently associated with impaired  
32 microcirculation causing damage to the end organs such as the kidneys.

33  
34 The arterial elastance ( $E_a$ ) is defined as the ratio of end-systolic pressure (ESP) and stroke  
35 volume (SV) ( $ESP/SV$ )<sup>4</sup> which is influenced by the vascular resistance, pulsatile load and  
36 heart rate. In contrast,  $E_{es}$  is a load-independent measure of the left ventricular (LV)  
37 contractility and reflects the slope of the end-systolic pressure-volume relationship (ESPVR),  
38 originated from the principles of pressure-volume curve as the ratio of ESP and end-systolic  
39 volume:  $ESP/ESV$ <sup>5</sup>. Subsequently,  $E_a/E_{es}$  ( $ESP/SV$ )/( $ESP/ESV_i$ ) can be further simplified as  
40  $ESV/SV$ , after removing ESP in the equation.  $E_{es}$  is affected by LV chamber stiffness and  
41 geometry and has an inverse correlation with LV mass.

1 ***In order to calculate***  $E_{es}$ , invasive multi-beat intraventricular catheterization has been  
2 regarded as the golden standard method. However, the non-invasive method by *Chen et al.* is  
3 commonly used where  $E_{es}$  can be calculated by the formula:  $E_{es} = (DBP - [End (est) \times SBP \times$   
4  $0.9]) / End (est) \times SV$  where DBP and SBP are diastolic and systolic arm-cuff BPs, End(est) is  
5 the estimated normalized ventricular elastance at the onset of ejection, and SV is Doppler-  
6 derived stroke volume (**Figure 1**).

7 To elicit VAC results in routine practice, this viewpoint presents the assessment of VAC in  
8 various archetypal clinical scenarios such as systemic hypertension and heart failure with  
9 reduced and preserved ejection fraction (HFrEF and HFpEF). We hope these examples will  
10 promote the use of this formula among physicians managing patients with HF. In addition, an  
11 excel sheet providing embedded calculations is provided as a **supplementary file**. Within  
12 routine care, physicians will only have to enter key variables from their echocardiographic  
13 exams (namely SBP, DBP, LV ejection fraction, stroke volume, pre-ejection time and ejection  
14 time) and the sheet will provide correct calculations of  $E_{es}$ ,  $E_a$  and VAC. This simplified sheet  
15 is more easily usable than the previous iOS based VAC calculators (iElastance); it reaches a  
16 wider audience as it is not tied to a platform/operating system and also allows decimals for the  
17 included variables<sup>6</sup>.

18 Previous studies have shown that the optimal value of VAC derived from the  $E_a/E_{es}$  ratio  
19 should range from 0.5 to 1 reflecting the state when the stroke work of left ventricle is ideal<sup>7,8</sup>.  
20 **Patient 1 (figure)** consequently corresponds to a “normal” situation, as both BP, EF, stroke  
21 volume, and their interplay are within normal range.

22 When arterial load ( $E_a$ ) increases to the point when  $E_a/E_{es} > 1$ , a VAC mismatch appears with  
23 subsequent lower left ventricle contractile efficiency<sup>9</sup>. This mismatch in VAC is often seen as  
24 the effect of increasing age and development of hypertension. Yet, the increase of  $E_a$  is met by  
25 a simultaneous increase of  $E_{es}$  (i.e. LV contractility) which preserves the VAC despite the  
26 presence of hypertension observed in **patient 2**. In the example of patient 3 with HFrEF,  $E_{es}$   
27 is decreased as expected whilst  $E_a$  is slightly increased resulting in  $E_a/E_{es} > 2$ . It should be  
28 acknowledged that  $E_a/E_{es}$  ratio has some limitations: i.e. it does not characterize the LV  
29 loading sequence<sup>10</sup>. Also, in HF with preserved ejection fraction (HFpEF), it may be normal  
30 because both  $E_a$  and  $E_{es}$  are increased (**patient 4**). We would consequently like to emphasize  
31 that the use of Pulse wave velocity (PWV)/ Global Longitudinal strain (GLS) ratio may be  
32 more appropriate in a number of settings to characterize VAC since it incorporates the gold  
33 standard methods to assess arterial load (PWV) and LV contractility (GLS). Importantly,  
34 PWV/GLS has been shown to be better correlated with subclinical target organ damage  
35 (TOD) compared with the traditional echocardiographic method ( $E_a/E_{es}$ )<sup>11</sup>. Further,  
36 PWV/GLS might also help predicting response to resynchronization therapy and the benefit  
37 from sodium glucose transporter 1 inhibitor (SGLTi), glucagon-like protein 1 inhibitor  
38 (GLP1i) and anti-inflammatory treatment in patients with rheumatoid arthritis<sup>12-14</sup>. Yet, even  
39 if PWV/GLS is likely more appropriate in a research setting, we can already use VAC in  
40 routine practice, only using simple echocardiographic measurements.

41 We hope that the figure presented herein (along with the provide online calculator)<sup>15</sup> will  
42 promote the adequate calculate  $E_a/E_{es}$  ratio and prompt the use of VAC in patients with HF  
43

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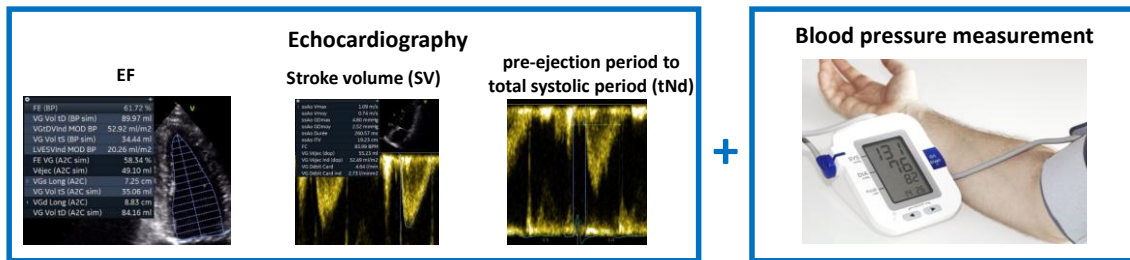
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1 **Figure 1. How to measure VAC in routine practice**

2

## How to measure VAC in routine practice



### Ventricular -arterial coupling = Arterial elastance/End-systolic elastance

Where

- **Arterial elastance ( $E_a$ )** =  $(SBP \times 0.9) / SV$
- **End systolic elastance (Ees)** =  $[DBP - (E_{Nd} (est) \times SBP \times 0.9)] / E_{Nd} (est) \times SV$

With

- **Estimated normalized ventricular elastance at onset of ejection  $E_{Nd} (est)$ :**

$$End (est) = 0.0275 - 0.165 \times EF + 0.3656 \times (DBP / (SBP \times 0.9)) + 0.515 \times E_{nd} (avg)$$

$$E_{Nd} (avg) = 0.35695 - 7.2266 \times tNd + 74.249 \times tNd^2 - 307.39 \times tNd^3 + 684.54 \times tNd^4 - 856.92 \times tNd^5 + 571.95 \times tNd^6 - 159.1 \times tNd^7$$

### Examples

Patient	Age	SBP (mmHg)	DBP (mmHg)	EF	SV (ml)	Pre Ejection time (ms)	Systolic period (ms)	tNd	End(Avg)	Ea	End(Est)	Ees	VAC
Patient 1: Normotensive	60	113	64	0,57	91,87	108,42	440,98	0,25	0,35	1,11	0,34	0,92	<b>1,20</b>
Patient 2: Hypertensive	60	141	68	0,52	57,38	116,77	441,19	0,26	0,37	2,21	0,33	1,37	<b>1,61</b>
Patient 3: HFpEF	61	94	56	0,39	69,05	137,19	393,45	0,35	0,46	1,23	0,44	0,60	<b>2,03</b>
Patient 4: HFpEF	69	95	50	0,55	48,73	98,36	301,12	0,33	0,44	1,75	0,38	0,95	<b>1,84</b>

3

DBP/SBP: Cuff blood pressure; SV: Stroke volume from 4 cavities pulsed Doppler; tNd: ratio of the pre-ejection period to the total systolic period measured on the aortic pulse Doppler; EF: Left ventricular ejection fraction.