How to calculate ventricular–arterial coupling?

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

A consensus document was published in the European journal of Heart failure in January 2019 presenting the assessment, clinical implications and therapeutic perspectives related to VAC in a clinical HF setting¹. To show the clinical usefulness of VAC, this viewpoint presents the assessment of VAC in various clinical scenarios such as systemic hypertension and heart failure with reduced and preserved ejection fraction (HFrEF and HFpEF) respectively. In order to facilitate the utilization of VAC into everyday clinical practice; a simplifying Excel sheet for the VAC calculation is provided.

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

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

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

To elicit VAC results in routine practice, this viewpoint presents the assessment of VAC in various archetypal clinical scenarios such as systemic hypertension and heart failure with reduced and preserved ejection fraction (HFrEF and HFpEF). We hope these examples will promote the use of this formula among physicians managing patients with HF. In addition, an excel sheet providing embedded calculations is provided as a **supplementary file**. Within routine care, physicians will only have to enter key variables from their echocardiographic exams (namely SBP, DBP, LV ejection fraction, stroke volume, pre-ejection time and ejection time) and the sheet will provide correct calculations of E_{es} , E_a and VAC. This simplified sheet is more easily usable than the previous iOS based VAC calculators (iElastance); it reaches a wider audience as it is not tied to a platform/operating system and also allows decimals for the included variables⁶.

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

When arterial load (E_a) increases to the point when $E_a/E_{es} > 1$, a VAC mismatch appears with subsequent lower left ventricle contractile efficiency⁹. This mismatch in VAC is often seen as the effect of increasing age and development of hypertension. Yet, the increase of E_a is met by a simultaneous increase of E_{es} (i.e. LV contractility) which preserves the VAC despite the presence of hypertension observed in **patient 2**. In the example of **patient 3** with HFrEF, E_{es} is decreased as expected whilst E_a is slightly increased resulting in $E_a/E_{es} > 2$. It should be acknowledged that E_a/E_{es} ratio has some limitations: i.e. it does not characterize the LV loading sequence¹⁰. Also, in HF with preserved ejection fraction (HFpEF), it may be normal because both E_a and E_{es} are increased (**patient 4**). We would consequently like to emphasize that the use of Pulse wave velocity (PWV)/ Global Longitudinal strain (GLS) ratio may be more appropriate in a number of settings to characterize VAC since it incorporates the gold standard methods to assess arterial load (PWV) and LV contractility (GLS). Importantly, PWV/GLS has been shown to be better correlated with subclinical target organ damage (TOD) compared with the traditional echocardiographic method (E_a/E_{es})¹¹. Further, PWV/GLS might also help predicting response to resynchronization therapy and the benefit from sodium glucose transporter 1 inhibitor (SGLTi), glucagon-like protein 1 inhibitor (GLP1i) and anti-inflammatory treatment in patients with rheumatoid arthritis¹²⁻¹⁴. Yet, even if PWV/GLS is likely more appropriate in a research setting, we can already use VAC in routine practice, only using simple echocardiographic measurements.

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

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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 (E_{es})** = $[DBP - (E_{Nd} (est) \times SBP \times 0.9)] / E_{Nd} (est) \times SV$

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	1,20
Patient 2: Hypertensive	60	141	68	0,52	57,38	116,77	441,19	0,26	0,37	2,21	0,33	1,37	1,61
Patient 3: HFrEF	61	94	56	0,39	69,05	137,19	393,45	0,35	0,46	1,23	0,44	0,60	2,03
Patient 4: HFpEF	69	95	50	0,55	48,73	98,36	301,12	0,33	0,44	1,75	0,38	0,95	1,84

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.