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Is Tissue Doppler E/e' A Valid Metric?

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Abstract

The tissue Doppler derived E/e' ratio has been widely promoted as a non-invasive surrogate for left ventricular (LV) filling pressures, yet its scientific validity remains questionable. While early studies reported strong correlations between E/e' and invasively measured diastolic pressures, more recent analyses demonstrate only moderate associations, raising concerns about methodological rigor. The fundamental issue lies in the flawed principles of tissue Doppler measurement. Unlike flow Doppler measurements which can be performed using precise alignment of the ultrasound beam with blood flow, tissue Doppler velocities are subject to multiple, unpredictable vectors at the mitral annulus. This compromises measurement accuracy and introduces spurious correlations when combined with flow Doppler values. Moreover, the magnitude of e' is highly multifactorial, and the empirical relationship between E/e' and LV filling pressures lacks universal applicability. Variability across annular sites further complicates interpretation, with different E/e' values obtained from lateral, septal, and averaged measurements defy the principle of parsimony and risk clinical misclassification. Ultimately, tissue Doppler E/e' measurements compromise established measurement and Doppler conventions, rendering the metric scientifically invalid. Rather than compounding complexity with flawed parameters, diastolic assessment should adhere to accepted Doppler principles and apply Occam's Razor to derive clinically meaningful insights.

Keywords: E/e'; Invalidity; Tissue Doppler; Flow Doppler; Diastology.

Science, my lad, is made up of mistakes, but they are mistakes which it is useful to make, because they lead little by little to the truth. — Jules Verne

The much-hyped E/e' ratio has almost attained the status of the Holy Grail in diastology [1,2]. Although E/e' is a widely used metric, on deeper scrutiny it can be found to be totally unscientific. In any research, it is taken for granted that the measurements are performed using the accepted methodologies – otherwise it becomes a paradigm shift. The concept of a "paradigm shift" was introduced by the philosopher of science Thomas Kuhn and detailed in his landmark book "The Structure of Scientific Revolutions." As he explained, scientific progress requires paradigms (or theoretical models) to guide problem-solving activities—including defining which problems to address, and which methods to address them. While a paradigm can lead to progress, these same advances reveal anomalies that cannot be explained by the paradigm itself [3]. This applies to tissue Doppler and its derivations.

Many earlier papers claimed the clinical application of the E/e' ratio has been consistently found to be more reproducible in daily practice and that spectral tissue Doppler for recording mitral annular velocities have

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produced convincing evidence of a positive, linear relation of E/e' with invasively determined mean left ventricular (LV) diastolic pressure regardless of LV ejection fraction, rhythm and heart rate using conventional statistical method of correlation [4]. The recent papers show the E/e' ratio only moderately correlated with pulmonary capillary wedge pressure or left ventricular end diastolic pressure [5]. But is the data acquisition correct? If not, could these papers be the proof of an ad hoc hypothesis to demonstrate the validity of tissue Doppler?

There are philosophical, methodical and applicational flaws in tissue Doppler [6], so factoring this flawed value to the scientifically valid flow Doppler value would corrupt the latter. In which case, all the correlations produced could be "nonsense" or "spurious" correlations [7,8]. In any research, it is taken for granted that the measurements are performed using the accepted methodologies. Only then we can proceed to deriving correlations. For example, in the measurement of height it is understood that the patients stand erect and the scale is applied in the correct alignment. Measurements taken in a non-erect position and applying the scale without proper alignment are invalid. Producing correlations with these flawed measurements are spurious. The verisimilar Tissue Doppler measurements are akin to this. Apart from compromising on the basic principles of measurement and Doppler, there are various other flaws in the very concept of using Doppler for tissue motion analysis. In any linear measurement we should know the alignment to apply the measurement tool. This is not possible in tissue motion because there are multiple velocities acting at the same point. The longitudinal velocity would have been measurable if it was the sole linear velocity or if the conflicting velocities remained constant.

The importance of knowing alignment in measurement is critical. This is not possible in tissue Doppler measurements. In the American Society of Echocardiography task force recommendation for quantification of Doppler echocardiography, the procedure for flow Doppler measurement is correctly described as "the Doppler sound beam should be oriented as parallel as possible to the flow, guided both by the 2D image (sometimes assisted by color flow imaging) and the quality of the Doppler recording". In the same document the procedure for tissue Doppler measurement is described as "longitudinal velocities within the myocardium can be recorded with tissue Doppler from the apical window with the PW mode. A small (<5 mm) sample volume is placed within a myocardial segment and a spectral recording of velocities within the segment obtained" [9]. They are ambiguous about the alignment of the Doppler beam for the simple reason that you cannot predict the movements! Again, in the recommendations for the evaluation of diastolic function by echocardiography flow Doppler measurement procedure is described as "pulsed-wave (PW) Doppler is performed in the apical 4-chamber view to obtain mitral inflow velocities to assess LV filling. Color flow imaging can be helpful for optimal alignment of the Doppler beam". Tissue Doppler procedure is described as "the sample volume should be positioned at or 1 cm within the septal and lateral insertion sites of the mitral leaflets and adjusted as necessary (usually 5-10 mm) to cover the longitudinal excursion of the mitral annulus in both systole and diastole" [10]. It does not talk about any alignment because we cannot locate the clinically significant velocity vector. Even if we can identify its alignment, we know that the longitudinal excursion is not the sole velocity at the mitral annulus. Since velocity is a vector quantity, the effect of the conflicting velocities should be identified and factored in the result. This would be a daunting task. Measurement of the longitudinal excursion which is a scalar quantity, would be scientifically acceptable.

The magnitude of e' is highly multifactorial, and the relation of E/e' to LV filling pressures is not a hewn-in-granite physical law but an empirical relationship that fortuitously can be used clinically in many cases but fails in others. A similar example would be the inverse relation of transmitral pressure half time to stenotic mitral orifice area. The reason for this problem in mitral stenosis is also similar. We do not know the alignment of the significant velocity due to multiple jets and unpredictable flow [11].

Even if we consider the tissue Doppler values as acceptable, what does E/e' mean? It is the early mitral filling flow velocity divided by early mitral annular tissue relaxation velocity. So, what is derived is early mitral flow velocity per unit of mitral annular tissue relaxation velocity. So far, so good. Does this automatically relate to higher left atrial pressures? It is common knowledge that flow Doppler patterns progress from "E/A normal" to "E/A reversal" with higher left atrial pressures. A higher E velocity in "E/A normal" and a lower E in "E/A reversal" goes against this assumption even after dividing with the usual e' values.

It is assumed that the combination of e' with peak E velocity i.e. E/e' ratio overcomes the influence of ventricular relaxation on peak E velocity and reflect left atrial pressure. The principle may be theoretically correct. It could remove the bias due to different relaxation values in different patients. But what about the application in the same patient? The different points around the mitral annulus ring give different tissue Doppler values. The E value being the same, you will get different E/e' values. It is suggested that values of >10, >12 and >11 for lateral, septal, and average E/e', respectively, can used for predicting pulmonary capillary pressure >15 mmHg in the presence of preserved LV systolic function [12]. So to "overcome the influence of ventricular relaxation on the peak E velocity" multiple values of e' need to be taken

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which would be tantamount to introducing a systematic error. Besides, such an exercise (determination of E/e' ratio) goes against the scientific "principle of parsimony".

The commonly interrogated medial mitral annulus on 2D apical 4-chamber image has an area of about 0.5 cm2 to 1.5 cm^2. In this wide area, where exactly do you place the sample volume? This is considering the fact that the velocities change on minor changes in positioning. Similarly, the medial annulus is common to both the left and right ventricles. How much of an influence the right ventricle has needs to be addressed.

Many papers discuss the limitations of E/e'. But the problem here is beyond limitations. When the measurements are not done according to the accepted conventions the study becomes a blunder. Here the mensuration and Doppler principles are compromised making the measurements invalid. We can accept the tissue Doppler measurements only if we reject the current measurement and Doppler conventions. But such a situation would lead to scientific anarchy. In the case of trans-mitral flow Doppler analysis with its inherent complexities, we do not need to factor in another variable like e' and compound the problem. What is required is the application of the Occam's Razor to derive some meaningful clinical information [13].

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