Graphing causation: getting a clearer picture or fuzzy logic? Comment on *Br J Anaesth* 2020: 125: 393–97

Nick Barnett

Royal Free Hospital, London, UK

E-mail: trickib@hotmail.com

Keywords: causal inference; evidence-based medicine; graphical causal model; real-world evidence; statistics

Editor—Krishnamoorthy and colleagues[1] present an enlightening introduction to graphical causal models and the field of causal inference in perioperative medicine. However, it merits several additional observations.

The first is contextual. Causal inference is very much *du jour* in the social sciences. Evidence-based medicine created a similar buzz in clinical medicine 20 yr ago and remains for better or worse our *de facto* mental model for assessing causes and treatments. The rhetorical question most associated with evidence-based medicine is 'What is the evidence for improving patient outcomes?' The answer, insofar as graphical causal models are concerned, would have to be substantively none at this point. Graphical causal models are certainly conceptually attractive, and it might seem unfair to judge them by criteria designed to answer questions from another paradigm such as evidence-based medicine. However, this is how medicine operates, and even the best theories must fall or die by the evidence supporting them.

The second is that the authors tend to present causal inference as a binary between statistics (and by implication probability and algebra) on the one hand and graphical causal models on the other; going on to state 'unfortunately statistics often does not have the tools to handle systematic bias', and again 'the grammar for causality abandons algebra and probability for a theory of graphs'. Graphical causal models are not an isolated technique. They are part of a much larger set of techniques available to the causal inference practitioner. These include techniques derived from statistics and economics such as regression, instrumental variables, and or regression discontinuity[2]; evidence-based medicine (randomisation), computer science (graphical causal models), and statistics again, notably the potential outcomes approach.[3]

Graphical causal models, themselves, derive from path analysis and structural equation modelling[4] so clearly have a basis in algebraic manipulation. Pearl and colleagues[5] introduce a novel notation, the do operator, to set the initial conditions of an intervention (present or absent) and circumvent the symmetry of an equation $a=b$ or equivalently $b=a$ from allowing causal claims such as *a causes b* to be inferred. This work and its mathematical expression is at the cusp of logic, computer science, and probability theory. Graphical causal models are the graphical counterpart to these models; they are not separate entities.

The third point: causal inference rightly attempts to apply a direction to causality rather than merely identifying associations. But as has been argued elsewhere in relation to machine learning,[6] does it not simply displace biases from their structural/mathematical formulation to the humans who create the causal diagrams? Causation is not a fixed *a priori* quality; it is set *a posteriori* by the humans who specify their causal models.

The final drawback of graphical causal models and the work of Pearl and colleagues in general is their highly technical, non-trivial nature, despite Krishnamoorthy and colleagues' noble efforts at simplification and explication.

Graphical causal models will undoubtedly find a place in the medical firmament. But for now, the tangible benefits of randomisation we have seen during the pandemic,[7] the true 'magic of randomisation', still trumps 'the myth of real-world evidence'.[8]

Declaration of interest

The author declares that they have no conflicts of interest.

References

1. Krishnamoorthy V, Wong DJN, Wilson M, et al. Causal inference in perioperative medicine observational research: Part 1. A graphical introduction. *Br J Anaesth* 2020; **125**: 393–7
2. Angrist JD, Pischke J-S. *Mostly harmless econometrics*. Princeton, NJ: Princeton University Press; 2009
3. Blakely T, Lynch J, Bentley R. Commentary: DAGs and the restricted potential outcomes approach are tools not theories of causation. *Int J Epi* 2016; **45**: 835–7
4. Streiner DL. Building a better model: an introduction to structural equation modelling. *Can J Psychiatr* 2006; **51**. 31–24
5. Pearl J, Glymour M, Jewell N. *Causal inference in statistics*. Chichester, UK: Wiley Press; 2016

6. Mullainathan S, Obermeyer ZK. Does machine learning automate moral hazard and error? *Am Econ Rev* 2017; **107**: 476–80
7. The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19 – preliminary report. *N Engl J Med* July 17 2020. https://doi.org/10.1056/NEJMoa2021436
8. Collins R, Bowman L, Landray M, Peto R. The magic of randomization versus the myth of real-world evidence. *N Engl J Med* 2020; **382**: 674–8

doi: 10.1016/j.bja.2020.12.014
Advance Access Publication Date: 6 January 2021

Pitfalls in the assessment of ventriculo-arterial coupling from peripheral waveform analysis in septic shock. Comment on *Br J Anaesth* 2020; 125: 1018–1024

Lorenzo Giosa[1,*], Mattia Busana[2] and Didier Payen[3]

[1]Department of Surgical Sciences, University of Turin, Turin, Italy, [2]Department of Anesthesiology, University Medical Center of Göttingen, Göttingen, Germany and [3]University of Paris 7, Denis Diderot, Paris, France

*Corresponding author. E-mail: lorenzo.giosa@gmail.com

Keywords: arterial waveform analysis; cardiovascular efficiency; dicrotic notch; esmolol; sepsis

Editor—We read with interest the paper by Morelli and colleagues[1] on the ability of the systolic-dicrotic notch pressure (SDP) difference to predict the response to esmolol infusion in septic shock patients with persistent tachycardia despite 24 h of haemodynamic optimisation. The message delivered by this *post hoc* analysis[2] is that since ventriculo-arterial (V-A) coupling is a function of both arterial elastance (Ea) and contractility ($_{art}dP/dt_{max}$), and the former decreases with HR, the effects of beta-blockade on cardiovascular efficiency depend essentially on the behaviour of contractility. On this basis, the authors divided patients according to the response of $_{art}dP/dt_{max}$ to esmolol infusion (preserved *vs* decreased); they found that the SDP difference calculated from a *peripheral* arterial waveform (i.e. the radial artery) was the only variable capable of differentiating the two groups both before and after beta-blockade. This parameter was consequently proposed for an overall assessment of cardiovascular efficiency.

The authors should be congratulated for their effort in bringing rather complicated concepts such as V-A coupling to the bedside. We believe that adding a more physiological point of view to the limitations listed in their papers[1,2] may facilitate the external applicability of their findings. While the time-dependency of elasticity in arteries (especially large elastic arteries) is not a novel finding,[3] the use of peripheral SDP difference as a marker of V-A coupling has received little attention so far and definitely deserves further discussion.

Morelli and colleagues[1] claim that '*…a delayed aortic valve closure is indicated by lower dicrotic notch pressure, thus increased SDP difference…*'. While this is certainly true at the aortic level, caution should be paid when analysing peripheral arterial waveforms: the dicrotic notch on a peripheral arterial wave is often considered a surrogate of the *aortic incisura*, but more than mere terminology separates the two.[4] The *incisura* and the following dicrotic wave reflect, respectively, aortic valve closure and rebound of the aortic root at the termination of retrograde flow; they both become less evident distally from the ascending aorta and disappear on arterial signals recorded 35–40 cm from it.[4] The appearance of one (sometimes multiple) late dicrotic notch and wave on peripheral arterial waveforms may not represent aortic valve closure, but rather the impact of backward waves reflected at the arterio-arteriolar junction.[4,5] In young healthy individuals, the timing of wave reflection almost coincides with the beginning of diastole to facilitate coronary perfusion (Fig. 1). Recent animal models have shown that the effect of reflected waves on V-A coupling is actually negligible in normal conditions.[6] If, however, the physical characteristics of the arterial system are altered by aging or disease, reflected waves may change in both amplitude and position,[7] reaching the aortic root during systole and adding complexity to the model[6] (Fig. 1). The architecture of the arterial tree of the fluid-resuscitated septic shock patient (as in Morelli and colleagues[1]) has been investigated in animal models[8] and it is characterised by peripheral vasodilation, aortic wall stiffness with oedema, and low compliance of muscular arteries. In such a deranged arterial tree, propagation of backward waves to the aorta is not predictable from analysis of a peripheral arterial waveform, thus we believe that conclusions about V-A coupling should be drawn with caution under these circumstances.

The authors suggest that '*…increased SDP difference reflects a lower afterload, increased myocardial contractility, or both…*' thus '*…the SDP difference can be proportional to the degree of V-A coupling*'.[1] We were surprised by this statement since it is

DOI of original article: 10.1016/j.bja.2020.05.058.