St George's GICU Journal Club Template

Reference of paper:

Monnet X, Rienzo M et al. Passive leg raising predicts fluid responsiveness in the critically ill. Crit Care Med 2006; 34:1402–1407)

Introduction:
What question(s) are the authors trying to answer?

Is the haemodynamic response to passive leg raising predictive of fluid responsiveness in mechanically ventilated patients.

Do the authors provide a rationale to support their investigation / hypothesis?

Yes

Give a detailed explanation of their rationale.

Passive Leg Raising (PLR) is a reversible "self-volume challenge".

Excessive fluid administration in ICU is:

a) Common - only 40 to 72% of critically ill patients have been shown to respond to volume expansion by a significant increase in stroke volume or cardiac output in studies designed to examine fluid responsiveness

b) Detrimental.

    a. In ARDS – conservative fluid strategy improved lung function and shortened the duration of mechanical ventilation and intensive care, without increasing non-pulmonary organ failure

    b. In sepsis – "positive fluid balance may be just a marker of the severity of sepsis, but here a multivariate analysis suggested that it is more than just an indicator of severity and is an independent predictor of outcome

    c. Delaying/denying the correct treatment – i.e. when VL is given to improve haemodynamics but there is no response perhaps another intervention may have been more efficacious.

Volume expansion (VE) is frequently used in critically ill patients to improve haemodynamics.

The expected response to volume expansion is an increase in right ventricular end-diastolic volume (RVEDV), left ventricular end-diastolic volume, stroke volume, and consequently cardiac output. The increase in stroke volume as a result of end-diastolic volume increase depends on both ventricular function and on the partitioning of the fluid into the different cardiovascular compliances organized in series. A patient can be non-responder to a fluid challenge because of high venous compliance, low ventricular compliance and/or ventricular dysfunction.

There is a need for predictive factors of fluid responsiveness in order to select patients who might benefit from volume expansion.

CVP and PAOP are very commonly used but have been found to poorly predict response to fluid challenge. Similarly estimates/measures of preload volume such as RVEDV or LVEDA are limited.

Dynamic parameters (testing the cardiovascular response to respiratory changes in pleural pressure), such as pulse pressure variation (PPV), systolic pressure variation (SPV), and stroke volume variation (SVV) are much better but have limitations – in particular they are of limited value in patients who have any ventilatory effort or arrhythmias

PLR induces a translocation of venous blood from the legs into the intrathoracic compartment – increasing preload. These investigators have previously determined that PLR can predict a response to VE using radial artery pulse pressure variation in mechanically ventilated patients.

This study aims to use aortic blood flow and PPV to measure response to PLR and determine if response to PLR predicts response to VE and which of the two techniques is better in which patient group.

Is the case well presented / argued?

Yes.

Consider the methods used:
What design was used

Prospective clinical study

From what population were the patients recruited

Medical ICU in University hospital in France. Comparable to our patients.

Describe patient numbers / important inclusion criteria / important exclusion criteria / screening & enrolment methods / number screened vs. number enrolled. Was the sample size estimated by performing a power calculation, if so, was this reasonable? Was the estimated sample size achieved? If not, why?

71 patients. No mention of how it selected these particular patients from all others who fulfilled criteria.

Inclusion criteria:

1. Mechanical ventilated patients whom the attending physician decided to perform a fluid challenge due to presence of at least one sign of inadequate tissue perfusion:
    a. SAP <90mmHg or decrease >50mmHg in previously hypertensive patients
    b. Need for vasopressors
    c. UO < 0/5ml/kg/hr for >2 hours
    d. Tachycardia >100bpm
    e. Skin mottling

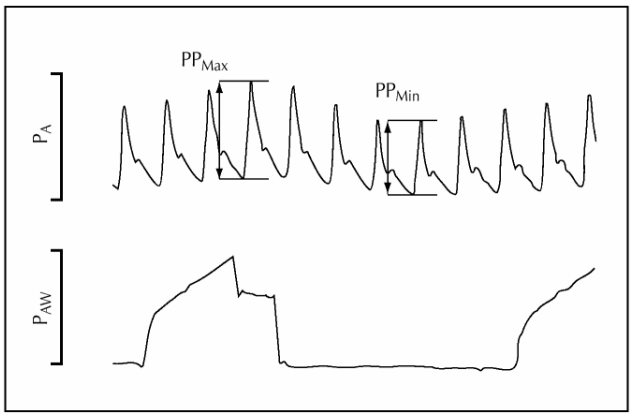
No exclusion criteria. No power calculations. No details on screened vs. enrolled vs. studied. Patients were informed not consent, no assent sought.

Briefly describe control and intervention protocols. Any good ideas? Any concerns? Where all reasonable methods used to minimise the effects of confounding variables? Did the authors measure to what extent their protocols were adhered to? Was there a clinically meaningful difference in intervention actually delivered to the 2 (or more) groups?

All patients were treated the same way and stratified into responders and non responders on the basis of their response to the VE.

PPV was calculated from the arterial pressure trace from a radial arterial line

PPV is PPmax – PPmin divided by the mean of these



Aortic blood flow was calculated using an oesophageal doppler probe that measured aortic diameter and aortic blood velocity.

Measurements were taken at 4 different times:

Base1. Then using automated bed elevation technique the PLR position was reached.

Measurement at PLR took place within 1 minute of this new position

Base 2, after PLR (?how long). Then 500ml N/Saline infused over 10 minutes.

Then Post VE measurements were taken.

No other changes to the patient took place during the study.

What outcome measures were employed (primary and secondary)? How well defined were the chosen endpoints. How reliable were any measurements taken? Would alternative endpoints have been better and if so, how?

The primary endpoint is response of aortic blood flow (ABF) to VE.

<15% increase in ABF = Non responders

>15% increase in ABF = Responders

15% was chosen based on the literature. They acknowledge that a different cut off value would give different results.

Was the method of analysis decided upon during the design and described? Where any subgroup analyses included in the study design?

The stats are described.

Patients with PPV data were divided into two groups: those without ventilatory effort or arrhythmias and those with either.

What follow-up, if any was performed? If so duration / completeness?

N/A

Consider the validity of this study

If randomised, was the method sound? Was the list concealed?

N/A

Where the treatment groups similar at baseline? How was this assessed? Was this assessment adequate? If not, what additional / alternative methods would have enhanced this assessment?

N/A

Are all the patients enrolled in the study accounted for at conclusion?

N/A

Are patients analysed in the groups to which they were randomised?

N/A

Were patients and / or clinicians blinded to treatment?

N/A

Were the groups treated similarly outside of the study intervention? Was there anything about their non-study treatment which was notable? Is there insufficient detail to draw a conclusion?

N/A

Consider the reported results

Are the results well presented? Are any / all statistical analyses properly performed, reported and interpreted?

Yes.

For primary outcome(s) what was the result concluded by authors? Is this justified?

ABF

37 patients had a >15% increase in ABF after VE in (responders) and 34 patients had a less than <15% increase (non-responders)

In responders there was a 28% (+/- 21%) response to PLR and a 40% (+/- 22%) response to VE. The effect of PLR was within 30 seconds.

This compares to non responders who had no significant response to PLR (and by definition none to VE)

For the group as a whole, the increase in ABF induced by PLR correlates well with that induced by VE

An increase in ABF of >10% predicted a VE induced increase in ABF of >15% with a sensitivity of 97% and a specificity of 94%

Authors conclusion: transient haemodynamic changes induced by PLR afford an excellent prediction of preload responsiveness in the critically ill.

I believe this is justified.

For secondary outcome(s) was the result concluded by authors? Is this justified?

PP

Just looking at the pulse pressure (not PPV) they found that if a PLR increase in PP by >12% predicted a significant response to VE with a sensitivity of 60% and a specificity of 85%

PPV

In the 30 patients without ventilatory effort and sinus rhythm – a PPV of >12% pre VE predicted a significant response to VE with a sensitivity of 88% and a specificity of 93% (good)

In those in SR but with ventilatory effort a PPV of >12% pre VE predicted a significant response to VE with a sensitivity of 75% and a specificity of 46% (very poor)

In those with arrhythmias PPV could not be reliably calculated.

Authors conclusions: PPV is of poor value in predicting fluid responsiveness in patients triggering the ventilator.

What was the measured adherence to treatment protocols?

N/A

Where there any adverse events / effects reported?

No

Consider the discussion

What were the strengths and weaknesses of this study?

Strengths: Thorough study of PLR in various patients

Weaknesses: Small numbers, ABF is not very commonly used.

Are the results compared to the literature on this topic and / or the current standard of' care?

Yes

Describe the authors' conclusions. Are they reasonable?

Yes, as above

What conclusions do you draw from this study?

Why aren't we using PLR?

How should this study affect our clinical practice?

We should use a PLR instead of trying a fluid challenge.

What should be the next steps for further study of this area?

Perhaps the GICU could run a study of using PLR vs. standard management

Consider the references
Where all statements of fact appropriately referenced?

Y

Did you read any of the references (please give details)? If so, did you gain any additional insights and what were they?

Yes. Michard F, Teboul JL. A Critical Analysis of the Evidence - Patients Predicting Fluid Responsiveness in ICU. Chest 2002;121;2000-2008 The National Heart, Lung, and Blood Institute. Comparison of Two Fluid-Management Strategies in Acute Lung Injury. NEJM 2006;354:2564-2575 Vincent JL. Sepsis in European intensive care units: Results of the SOAP study. Crit Care Med 2006; 34:344–353

Any additional comments / information / points for discussion.

Who wants to help me design and run a trial in the GICU of standard management vs. using PLR routinely to see if patients have preload responsiveness before giving ‘250 of Gelo’? Patients with LiDCO could be randomised into standard or PLR. Every time there is an indication that they may need VE we should perform a PLR and use a >12% increase in stroke volume to indicate that we should try a VE and if it’s less than 12% we should think again. What outcome measures (apart from cumulative fluid volume) would be best?