PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Stroke volume variation for predicting responsiveness to fluid therapy in patients undergoing cardiac and thoracic surgery: A systematic review and meta-analysis
AUTHORS	Huan, Sheng; Dai, Jin; Song, Shilian; Zhu, Guining; Ji, Yihao; Yin, Guoping

VERSION 1 – REVIEW

REVIEWER	Deborah Black The University of Sydney, Faculty of Medicine and Health
REVIEW RETURNED	18-May-2021

GENERAL COMMENTS	The abstract should state that it is a meta-analysis to check the reliability of the SVV prediction in the Objectives. The results need to be presented with greater clarity. On page 9 of 37, there is a table with no heading or label. The presentation of the table is quite confusing. One example is column headed endoscope with the paper by Kang having a '/'in the column. There are similar issues in other columns. In the table labelled 'Table 1" sensitivity and specificity appear to be %s for most measure but others are proportions so ther eis a mixture in presentation. Consistent UK Spelling should be applied throughout the paper. The graphic on page 32 of 37 is unlabelled and difficult to interpret.. Maybe use hatching to distinguish high from low. Is there why forest plots are not included.

REVIEWER	Jorge Iván Alvarado Sánchez National University of Colombia
REVIEW RETURNED	24-Jul-2021

GENERAL COMMENTS	Thanks for inviting me to read this study. This study describes the operative performance of SSV in patients undergoing cardiac and thoracic surgery. The authors find a fair operative performance in patients undergoing thoracic surgery (AUC 0.73), a good operative performance in patients undergoing cardiac surgery (AUC 0.80); and, a good operative performance in patients critically ill after cardiac surgery (AUC 0.88). Also, they described changes in operative performance by subgroup analyses (SROC analyses). In patients undergoing thoracic surgery found a change in operative performance: • lateral vs supine position (AUC 0.71 vs 0.82, respectively). • type of fluid used: Colloid vs crystalloid (AUC 0.76 vs 0.47, respectively) • the amount of fluid used: < 250 ml vs > 250 ml (AUC 0.47 vs 0.76, respectively).

	• type of system or technology used: Vigileo vs PiCCO (AUC 0.80 vs 0.43). • for last, tidal volume used: < 8 ml/kg vs > 8 ml/kg (AUC 0.67 vs 0.81). In patients undergoing cardiac surgery they found a change in operative performance of SVV: • type of fluid used: Colloid vs crystalloid (AUC 0.85 vs 0.70). • type of system or technology used: Vigileo vs PiCCO (AUC 0.74 vs 0.70, respectively). • the amount of fluid used: < 250 ml vs > 250 ml (AUC 0.88 vs 0.73, respectively). • PEEP used: non-PEEP vs PEEP (AUC 0.78 vs 0.69, respectively). • If the fluid challenge or passive leg raising were used (AUC 0.75 vs 0.65, respectively) In critically ill patients: • If the fluid challenge or passive leg raising were used (AUC 0.82 vs 0.89, respectively) The main finding of this study is the changes in the operative performance of SVV. Currently, these changes have been assessed by meta-analyses in critically ill patients; these have not been assessed in this clinical setting. Nevertheless, this study has high heterogeneity that would not allow extrapolation of their findings to clinical practice. I have some additional comments: Abstract: • The main aim was to describe the changes in the operative performance of SVV. This may be described. • The authors must describe how were performed the subgroup analyses. Introduction. • The main findings of this study were the changes in the operative performance of SVV. The authors fail to introduce them properly. Methods: • The authors could indicate if a review protocol exists and where can be accessed. • Eligibility criteria must be described before the search strategy. • Were pregnant patients include in this study? This must be clarified. • Usually, the Operative performance is graduated according to Fisher et al: o AUC 0.9-1 excellent operative performance o AUC 0.8-0.9 good operative performance. o AUC 0.7-0.8 fair operative performance. These must be described in methods and results. • The Floc/Trac Vigileo system use pulse contour analysis (PCA) to calculate cardiac output and the PiCCO system can use two methods: PCA and transpulmonary thermodilution to calculate CO. were these systems used to measure SVV or to measure CO? the authors must clarify this point. • The authors categorized some continuous variables; such as PEEP used, Vt used, the amount of fluid used, etc. why were these variables categorized? If can be assessed as continuous variables. • The authors performed a subgroups analysis by SROC. why did

	not the authors perform a meta-regression using as a dependent variable the diagnostic odds ratio? This must be clarified. Results • Figure 1 does not match with the study characteristics claimed. The figure described that 1050 studies were found while the first paragraph described that were found 1371. • In Tables 1, 2, and 3, the authors must describe how the data were presented. Please, include two decimals as well as their confidence intervals. Also, the authors must describe the acronyms used. • The subgroup meta-analyses or metaregresión analyses may be performed used as a variable the diagnostic odds ratio (DOR). Could a metaregresión/subgroup analyses perform using DOR as a variable? • Were the differences found between two AUCs statistically different? Discussion: The authors claimed “it has lower thresholds than the PiCCO system and could predict the insufficiency of blood volume earlier and with greater sensitivity even…” the SVV is a variable used as a predictor of fluid challenge, this is not a variable of Blood volume. • The discussion must be refocused. The authors must describe the relation to previous studies/Why is the different/additions of knowledge. A meta-analysis showed that some technical and variables change the operative performance of some predictors of a fluid challenge.

VERSION 1 – AUTHOR RESPONSE

Response to Review1' Comments:

• We have modified the abstract to specify that it is a meta-analysis for evaluating the reliability of SVV of predicting responsiveness to fluid therapy.

• We optimized the description of the results to make them more concise and easier to understand

• On page 9 of 37, our label is at the bottom of the picture, not the top. We have modified this according to the journal requirements

• We replace all of ‘/’ in Table 1 with NA to ensure consistent descriptions.

• In the Table labeled ‘Table 1’, we revised the data in sure that sensitivity and specificity appear to be %s.

• We’ve asked for help from professional scholar to ensure that consistent UK spelling is included in the article.

• Graphic on page 32 of 37 is the included literature quality assessment according to the QUADAS 2(quality assessment of diagnostic accuracy studies). It is the most recommended diagnostic accuracy test quality evaluation tool at present. Quadas-2 tool mainly consists of four parts (see Table 1): case selection, trials to be evaluated, gold standard, case process and progress. All components would be assessed in terms of bias risk, and the first three components would also be assessed in terms of clinical applicability.

• The forest plot is not included in our original manuscript because it is a diagnostic meta-analysis rather than a conventional meta-analysis (RCT based intervention meta-analysis). The diagnostic value of a technology or an indicator generally depends on pool sensitivity, pool specificity, ODR value and AUC value, while the forest map of sensitivity and specificity is not the main index but just for reference. We pooled the sensitivity and specificity forest plot with Stata V.14.0 and R V.3.6.3 and put them in the supplementary file.

Response to Review2' Comments:

ABSTRACT

• On the basis of ensuring the reliability of SVV in thoracic and cardiac surgery, our modified version clearly describes the effects of different surgical procedures (position, endoscopy,) and different anesthesia management (ventilation, fluid therapy, moments of intervene) on the reliability of SVV.

• In the methodology, we briefly explained the theoretical basis of our subgroup analysis and the software used to conduct subgroup analysis.

INTRODUCTION

• In the revised introduction, we firstly clarified the history and the current situation of SVV, and then pointed out its dispute and changes under different kinds of operative performance.

METHOD

• In fact, we didn't conduct a full PROTOCOL before.

• We describe the eligibility criteria before search strategy.

• We did not include pregnant women. This point has been incorporated into the Eligibility Criteria

• We illustrate in the methods that the operative performance is graduated according to Fisher et al:

  o AUC 0.9-1 excellent operative performance
  o AUC 0.8-0.9 good operative performance.
  o AUC 0.7-0.8 fair operative performance.

• In fact, SVV describes the average variation of SV in a period of time. CO represented for cardiac output per minute, and SV represented for cardiac output per stroke. Therefore, what SVV represent is not just changes of CO or SV, but whether body blood volume is adequate. CO and SV only represent cardiac pump blood volume in a short time and are easily affected by many factors. Oppositely, SVV represents a period time of CO and make mean CO as a control, greatly avoiding the occurrence of false negative result or false negative result.

• Since we're evaluating reliability of SVV in thoracic surgery and cardiac surgery, the intrathoracic condition, mechanical ventilation method, and position of body are very important. In addition, it has

been controversial which liquid is more suitable for rehydration between crystal liquid and colloidal liquid. We wanted to compare them with AUC and screen the better one.

• In my opinion, the purpose of meta regression is to find out which variables the heterogeneity comes from but not to conduct a subgroup analysis. The dependent variables are typically the attributes of each study, such as year of publication, sample size, drug used, age, etc. We cannot understand why DOR could be used as a dependent variable.

RESULT

• We modified the data for Fig1, which may have been due to a lack of careful collation between versions.

• In Tables 1, 2, and 3, we describe how the data were presented. We included two decimals as well as their confidence intervals. Also, we added the abbreviation to the label.

• We thought that DOR could not be used as a variable for meta-analysis or meta regression

• We performed a statistical analysis between AUC with 'MedCalc' software according to Z-test to find out whether significant differences exist. However, since the 'meta4diag' package of R V.3.6.3 could only give the result of mean AUC, the stand error of AUC is difficult to calculate and conduct further Z-test.

DISCUSS

• SVV is actually a variable used to predict fluid challenge rather than variable of blood volume, but we can screen a specific SVV threshold for a particular surgical procedure and anesthesia with optimize sensitivity and specificity. Several included studies reported that FloTrac/Vigileo system has lower thresholds than the PiCCO system. This means on the premise of the same predictive value, smaller change of SV could be determined as hypovolemia and informed anesthesiologists conducted a fluid therapy earlier.

• We revised the discussion and discuss the reason for some previous contradictory conclusions (possibly due to immature technology, old version of device or too few patients). Based on the evaluation of the effectiveness of SVV, the applicability of SVV in thoracic and cardiac patients under different anesthesia and surgical strategy was discussed. Several other indicators for predicting responsiveness to fluid challenges are also involved. In the end, the status and future direction of application of SVV are also mentioned