The Determinants Of Mean Central Venous Pressure For Shock Patients

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Abstract

Objectives: The determinant of mean central venous pressure (MCVP) has been derived in the report with 113 shock patients containing 20 characters.

Background: The determinants of MCVP for shock patients has not been derived explicitly.

Material & methods: The current study has included113 shock patients containing 20 characters. The data site is: http://www.umass.edu/statdata/statdata/data/shock.txt Statistical analysis has been done by joint generalized linear models (JGLMs).

Results: From the mean model of MCVP, it is found that MCVP is positively associated with survival status (SURVIVE) (P=0.0009), mean arterial pressure (MAP) (P<0.0001), body surface index (BSI) (P=0.0001), mean circulation time (MCT) (P<0.0001), plasma volume index (PVI) (P=0.0333), while it is negatively associated with diastolic blood pressure (DBP) (P<0.0001), appearance time (AP) (P=0.0016), urinary output (UO) (P=0.0120). Variance of MCVP is negatively associated with BSI (P=0.0024), MCT (P=0.0236), red cell index (RCI) (P=0.0183), and it is positively associated with UO (P=0.0316), PVI (P=0.1228), hemoglobin (HG) (P=0.0008).

Conclusion: The report concludes that MCVP increases as MAP, or BSI, or MCT, or PVI increases, or DBP, or AP, or UO decreases. These information is a new addition in medical literature.

 Keywords: Blood biochemical parameters; Cardiac index; Mean arterial pressure; Mean central venous pressure; Plasma volume index; Joint generalized linear models (JGLMs)

Introduction

The predicted or estimated right artrial pressure (RAP) is known as central venous pressure (CVP), and it is calculated in the central veins closely to the heart. The CVP is used to assess the volume status and cardiac preload in critically ill patients [1, 2]. It guides right-side heart failure patient's diagnosis and fluid resuscitation. It doesn't directly calculate blood volume, but it is always used for this purpose. It is measured by the interaction between venous return and cardiac function [1, 3]. Generally, CVP is not only activated by intravascular volume and venous return, but it is also by venous tone and intra-thoracic pressure, including right heart function and myocardial compliance [4-6]. In practice, CVP is applied for the hypotension cardiac patients who are unable to respond primary clinical management [1, 7and 8].

CVP is an indicator of right ventricular and, to a lesser extent, left ventricular preload. It also shows the limit to venous return and reflects about right ventricular function [9, 10]. It measurements may be necessary to guide fluid management. However, it is also influenced by thoracic, abdominal, and pericardial pressures, which makes its prediction more complicated. As a result, the CVP measured does not reflect always the true loading conditions of the right ventricle.   It represents the back pressure of all extra thoracic organs and the limit to venous return. Specifically, the risk of renal, ascites, peripheral edema, and liver impairment is associated with the absolute CVP value [11, 12].

Generally, CVP has very complex association with vascular system and cardiac outputs which is difficult to interpret [13, 14]. In veterinary and human clinical practice, CVP is mostly applied to obtain information regarding intravascular volume and cardiac function [15, 16], but its clinical applications and physiological meaning are frequently misunderstood [17, 18]. Many research articles have agreed that the CVP is affected by many factors [19, 20]. We need to know which factors affect the CVP measurement and how. Based on this knowledge, it may be possible to use them optimally in order control CVP. This may be easily understood from some probabilistic models. Best of our knowledge, there is not any probabilistic or statistical model of CVP with its explanatory variables [21]. In the report, we are interested to identify the explanatory factors of CVP for some shock patients. Therefore, the report seeks the following queries. What are the statistical significant components of CVP? How are the components related with the CVP? How do they act on CVP? What is the probability model of CVP with its component? These answers are little known in the cardio vascular literature, which are focused in the present report.

Materials

The used data site in the report is given in the Abstract. A

clear description of 113 shock patients with 20 study characters and the data collection procedure is displayed in [22]. These data were collected at the Shock Research Unit at the University of Southern California, Los Angeles, California. Data on many physiological variables were collected successively in time on each patient. The present data set is a special subset of the extracted data for the purpose of exercise. For each critically ill patient (total 113 patients), measurements upon admission, and just before death or discharge were taken. For our requirements, the 20 study characters are reproduced as: height (HEIGHT), age (AGE), survival status (SURVIV) (survived=1, death=2), sex (SEX) (male=0, female=1), mean arterial pressure (MAP), body surface index (BSI), shock type (SHOCKT) (non-shock=1, hypovolemic=2, cardiogenic, or bacterial, or neurogenic or other=3), mean circulation time (MCT), systolic blood pressure (SBP), diastolic blood pressure (DBP), appearance time (AP), urinary output (UO), red cell index (RCI), plasma volume index (PVI), hematocrit (HCT), mean central venous pressure (MCVP), heart rate (HR), hemoglobin (HG), card sequence order (initial=1, final =2) (CSO).

Statistical Methods

The stated above hypotheses in Introduction Section can be examined clearly by a probabilistic model of MCVP with its explanatory characters. Note that MCVP is a positive, continuous, non-normally distributed heteroscedastic random variable which is exactly modeled by JGLMs under Log-normal and Gamma models that are clearly & explicitly given in [23-26]. These are not repeated explicitly in the report. Interested readers may go through [23-26]. For the response MCVP, it is found that Gamma JGLMs fit is better than Log-normal fit, so very shortly Gamma JGLMs are displayed herein.

Gamma JGLMs

For a continuous positive random response y_i, if $E(y_i) = \mu_i$ and $Var(y_i) = \sigma_i^2 V(\mu_i)$, where μ_i's and σ_i^2 's respectively, mean & dispersion parameters, and V (**.**) reveals the variance function with two parts (in GLM) such as σ_i^2 (free of mean changes) and $V(\mu_i)$ (depends on the mean changes). It is noted that the GLM family distribution is located by $V(\mu_i)$, as it is Poisson if V (μ) = μ, Gamma if V (μ) = , and Normal if V (μ) = 1, etc. So, the Gamma JGLMs of mean & dispersion (when V (μ) = μ^2) are

$$\eta_i = g(\mu_i) = x_i^t \beta \text{ And } \varepsilon_i = h(\sigma_i^2) = w_i^t \gamma ,$$

where $g(\cdot)$ and $h(\cdot)$ are GLM link functions related to the mean & variance linear predictors respectively, x_i^t and w_i^t, are the vectors of explanatory factors/ variables, connected to the mean & dispersion parameters respectively. Practically, the maximum likelihood (ML) and the restricted ML (REML) method are used respectively, for estimating the mean and dispersion parameters [23].

MCVP analysis, results & interpretation

MCVP Analysis

JGLMs of MCVP have been derived under both Log-normal and Gamma models, considering MCVP as the response variable, and all the rest factors and variables are considered as the explanatory variables. The smallest value (within each class) of Akaike information criterion (AIC) selects the appropriate model by minimizing both the squared error loss and predicted additive errors [27, p. 203--204]. According to AIC rule, Gamma JGLMs fit (AIC=1284.034) shows better fit than Log-normal (AIC=1320). Summarized MCVP analysis results are shown in Table 1. Two partially significant effects RCI (mean model) and PVI (variance model) are included for better fitting [27, 28], which are called as confounder in epidemiology. As a model checking tools, the absolute residuals plot & normal probability plot are shown in Figure 1.
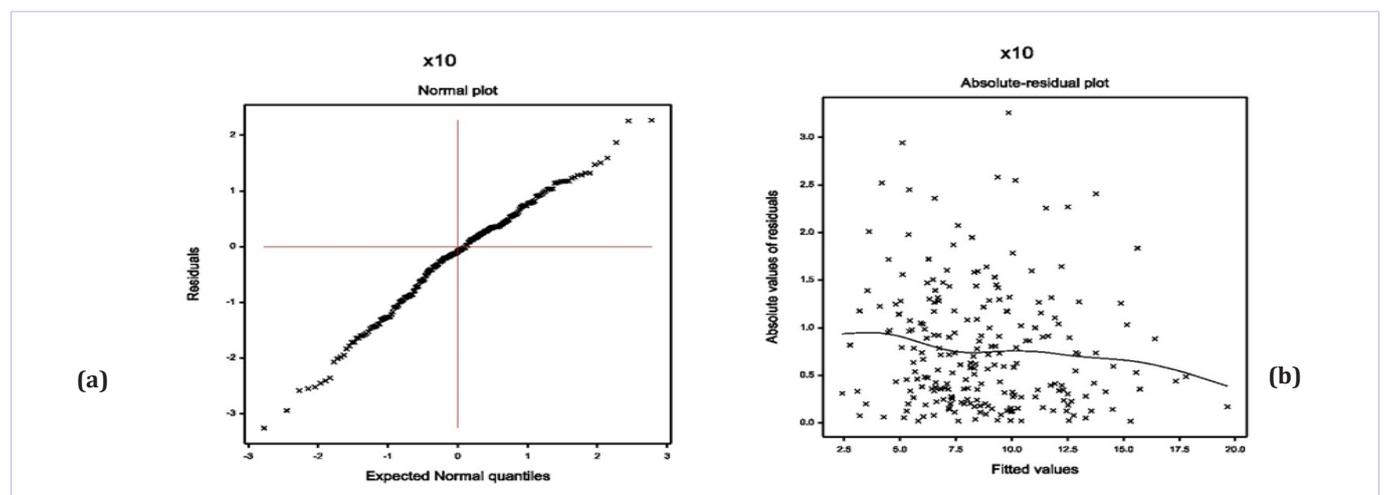

Figure 1: For the joint gamma fitted models of MCVP (Table 1), the (a) absolute residuals plot with respect to the fitted values, and (b) the normal probability plot for the mean model

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Table 1: Results for mean and dispersion models of mean central venous pressure from Gamma fit

Model	Covariate	Estimate	Standard error	t-value	P-Value
Mean Model	Constant	-0.0111	0.47165	-0.024	0.9808
	SURVIV (Fx42)	0.3313	0.0985	3.363	0.0009
	Mean arterial pressure (MAP) x7	0.0293	0.00648	4.52	<0.0001
	Diastolic blood pressure (DBP) x9	-0.0369	0.00814	-4.528	<0.0001
	Body surface index (BSI) x11	0.8039	0.20753	3.874	0.0001
	Appearance time (AT) x13	-0.0468	0.01466	-3.195	0.0016
	Mean circulation time (MCT)x14	0.0344	0.00731	4.702	<0.0001
	Urinary output (UO) x15	-0.0013	0.00049	-2.532	0.012
	Plasma volume index (PVI) x16	0.0064	0.003	2.142	0.0333
	Red cell index (RCI) x17	0.002	0.00201	1.006	0.3155
Dispersion Model	Constant	0.119	1.4544	0.082	0.9347
	BSI (x11)	-1.7843	0.5821	-3.065	0.0024
	MCT (x14)	-0.0256	0.0112	-2.279	0.0236
	UO (x15)	0.0019	0.0009	2.163	0.0316
	PVI (x16)	0.0141	0.0091	1.549	0.1228
	RCI (x17)	-0.034	0.0143	-2.377	0.0183
	Hemoglobin (HG) (x18)	0.2062	0.061	3.381	0.0008

From Table 1, the Gamma fitted mean ($\hat{\mu}$) model of MCVP is

$\hat{\mu}$ = exp. (-0.0111 + 0.3313 SURVIV + 0.0293MAP - 0.0369DBP + 0.8039BSI - 0.0468AP + 0.0344MCT -0.0013UO + 0.0064PVI + 0.0020RCI),

And the fitted variance ($\hat{\sigma}^2$) model is

$\hat{\sigma}^2$ = exp. (0.1190 - 1.7843BSI - 0.0256MCT + 0.0019UO + 0.0141PVI - 0.0340RCI + 0.2061HG).

Gamma fitted (for MCVP in Table 1) absolute residuals are plotted in Figure 1(a), with respect to fitted values, which is approximately straight line, indicating constant variance. Figure 1(b) shows the normal probability plot for the mean model (Table 1), which does not reveal any lack of fit. Both the plots do not show any inconsistency in fitting.

MCVP Analysis Results

Joint Gamma fitted mean & variance models of MCVP are displayed above and their summarized forms are presented in Table 1. From the fitted mean model (Table 1), it is noticed that MCVP is positively associated with SURVIVE (P=0.0009), MAP (P<0.0001), BSI (P=0.0001), MCT (P<0.0001), PVI (P=0.0333), while it is negatively associated with DBP (P<0.0001), AP (P=0.0016), UO (P=0.0120). Variance of MCVP is negatively associated with BSI (P=0.0024), MCT (P=0.0235), RCI (P=0.0183), and it is positively associated with UO (P=0.0316), PVI (P=0.1228), HG (P=0.0008).

Interpretations Of The Derived Results Of MCVP (Table 1)

Mean model of CVP (Table 1) concludes the following:

- MCVP is positively associated with SURVIV (survived=1, death=2) (P=0.0009), concluding that MCVP is higher for shock patients who are close to death than living patients.

- MCVP is directly associated with MAP (P<0.0001), indicating that MCVP increases as MAP rises.

- MCVP is negatively correlated with DBP (P<0.0001), interpreting that MCVP decreases as DBP increases.

- MCVP is directly associated with BSI (P=0.0001), concluding that MCVP increases as BSI rises.

- MCVP is negatively correlated with AP (P=0.0016), concluding that MCVP decreases as AP increases.

- MCVP is directly associated with MCT (P<0.0001), indicating that MCVP increases as MCT rises.

- MCVP is negatively correlated with UO (P=0.0120), concluding that MCVP decreases as UO increases.

- MCVP is directly associated with PVI (P=0.0333), indicating that MCVP increases as PVI rises.

- MCVP is directly partially associated with RCI (P=0.3155), indicating that MCVP increases as RCI rises.

From variance model (Table 1) of MCVP, the following conclusions can be noted.

- Variance of CVP (VCPV) is negatively associated with BSI (P=0.0024), concluding that VCPV decreases as BSI increases.

- VCPV is negatively associated with MCT (P=0.0236), implying that VCPV decreases as MCT increases.

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- VCPV is directly associated with UO (P=0.0316), implying that VCPV increases as UO rises.

- VCPV is directly partially associated with PVI (P=0.1228), implying that VCPV increases as PVI rises.

- VCPV is negatively associated with RCI (P=0.0183), implying that VCPV decreases as RCI increases.

- VCPV is directly associated with HG (P=0.0008), implying that VCPV increases as HG rises.

The above derived joint mean & variance models of MCVP have been selected based on examining the lowest AIC, model checking plots, small standard errors of the estimates (Table 1), and appropriate distribution of the response MCVP. Therefore, the data generated models of MCVP are assumed to be true. Based on the true derived models all the above interpretations have been drawn. Interpretations of all the derived results are clearly described in the above.

Concluding Remarks

The explanatory factors of central venous pressure have been derived in the report based on joint Gamma modeling. Fitted joint Gamma models (Table 1) have been accepted based on lowest AIC, model diagnostic plots, small standard error of the estimates (Table 1), and along with the underlying distribution of CVP. The report has presented very shortly Introduction, Materials, Statistical method, Data analysis sections, as these are available in many articles [1-3, 29, 30]. Many factors such as SURVIV, MAP, DBP, BSI, AP, MCT, UO, PVI and RCI have been derived as the mean predicted variables of CVP (Table 1), while BSI, MCT, UO, PVI, RCI and HG have been derived as the variance predicted variables of CVP (Table 1). Note that SURVIV, MAP, BSI, MCT, PVI and RCI have direct association with mean CVP, while DBP, AP and UO have inverse association with mean CVP. Again, BSI, MCT and RCI have inverse association with the variance of CVP, while UO, PVI and HG have direct association with the variance of CVP.

The above models are related only with the given data set [22]. If the data set is changed, model will be changed, but the association nature of MCVP with the other parameters may be same, even though the data set will be changed. We have not examined it for different data sets, as we have not more data sets. In our future research, we will examine these points. Here the considered data set does not contain many covariates related to blood components and cardiac parameters. Future researchers may consider many more covariates.

The current note may introduce some new information in the medical literature regarding the explanatory factors/ variables of central venous pressure through statistical modeling. From the beginning of medical literature, interpretation about CVP are frequently misunderstood [1, 2, 17 and 18]. Best of our knowledge, the above information and the fitted models of MCVP are not clearly introduced in any previous article based on statistical modeling. From the present results, medical practitioners can be able to know that CVP of a shock patient increases if MAP, or PVI, or BSI, or RCI, or MCT increases, or AP, or DBP, or UO decreases. Accordingly, necessary steps may be taken to control CVP.

Conflict Of Interest

The authors confirm that this article content has no conflict of interest.

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References

1. Reems MM, Aumann M. Central Venous Pressure: Principles, Measurement and Interpretation. Compendium. 2012; 34: E1-E10.

2. Vellinga NAR, Ince C, Boerma EC. Elevated central venous pressure is associated with impairment of microcirculatory blood flow in sepsis: a hypothesis generating post hoc analysis. BMC Anesthesiology. 2013; 13: 17. doi: 10.1186/1471-2253-13-17

3. Boerma EC, Ince C. The role of vasoactive agents in the resuscitation of micro vascular perfusion and tissue oxygenation in critically ill patients. Intensive Care Med. 2010; 36(12):2004–2018. doi: 10.1007/s00134-010-1970-x

4. Thooft A, Favory R, Ribeiro Salgado D, Taccone FS, Donadello K, De Backer D, etal., Effects of changes in arterial pressure on organ perfusion during septic shock. Crit Care. 2011; 15(5):R222. doi: 10.1186/cc10462

5. Dobbe JGG, Streekstra GJ, Atasever B, vanZijderveld R, Ince C. Measurement of functional microcirculatory geometry and velocity distributions using automated image analysis. Med Biol Eng Comput. 2008; 46(7):659–670. doi:10.1007/s11517-008-0349-4

6. Dubin A, Pozo MO, Casabella CA, Pálizas F, Murias G, Moseinco MC, et al., Increasing arterial blood pressure with nor epinephrine does not improve microcirculatory blood flow: a prospective study. Crit Care. 2009; 13(3):R92. doi: 10.1186/cc7922

7. De Backer D, Hollenberg S, Boerma C, Goedhart P, Büchele G, Ospina-Tascon G, etal., How to evaluate the microcirculation: report of a round table conference. Crit Care. 2007; 11(5):R101. doi:10.1186/cc6118

8. Boyd JH, Forbes J, Nakada TA, Walley KR, Russell JA. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. Crit Care Med. 2011; 39(2):259–265. doi: 10.1097/CCM.0b013e3181feeb15

9. Michard F, Boussat S, Chemla D, Anguel N, Mercat A, Lecarpentier Y, et al., Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. Am J Respir Crit Care Med. 2000; 162(1):134–138. doi:10.1164/ajrccm.162.1.9903035

10. Heenen S, De Backer D, Vincent JL. How can the response to volume expansion in patients with spontaneous respiratory movements be predicted? Crit Care. 2006;10(4):R102. DOI:10.1186/cc4970

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11. Legrand M, Dupuis C, Simon C, Gayat E, Mateo J, Lukaszewicz AC, et al. Association between systemic hemodynamics and septic acute kidney injury in critically ill patients: a retrospective observational study. Crit Care. 2013;17(6):R278. doi: 10.1186/cc13133

12. Chen KP, Cavender S, Lee J, Feng M, Mark RG, Celi LA, et al., Peripheral edema, central venous pressure, and risk of AKI in critical illness. Clin J Am Soc Nephrol. 2016;11(4):602–608. doi: 10.2215/CJN.08080715

13. De Backer D, Ortiz JA, Salgado D. Coupling microcirculation to systemic hemodynamics. CurrOpinCrit Care 2010; 16(3):250–254. doi: 10.1097/MCC.0b013e3283383621

14. Jhanji S, Stirling S, Patel N, Hinds CJ, Pearse RM. The effect of increasing doses of norepinephrine on tissue oxygenation and micro vascular flow in patients with septic shock. Crit Care Med. 2009; 37(6):1961–1966. doi: 10.1097/CCM.0b013e3181a00a1c

15. Steele AM. Under pressure: ABP, CVP, what are the number really telling us? Proc 12th IVECCS 2006; 815-818.

16. Fleming E, Ettinger S, DVM, Dacvim. Pulmonary hypertension. Compend Contin Edu Pract Vet. 2006; 28(10): 7720-7732.

17. Magder S. Central venous pressure: a useful but not so simple measurement. Crit Care Med 2006; 34(8): 2224-2227. doi:10.1097/01.CCM.0000227646.98423.98

18. Clayton DG. Inaccuracies in manometric central venous pressure measurement. Resuscitation. 1988; 16(3): 221-230.

19. Cecconi M, Hofer C, Teboul JL, Pettila V, Wilkman E, Molnar Z, et al., Fluid challenges in intensive care—the FENICE study: A global inception cohort study. Intensive Care Med.2015; 41(9):1529–1537. doi:10.1007/s00134-015-3850-x

20. Eskesen TG, Wetterslev M, Perner A. Systematic review including re-analyses of 1148 individual data sets of central venous pressure as a predictor of fluid responsiveness. Intensive Care Med. 2016; 42(3):324–332. doi: 10.1007/s00134-015-4168-4

21. Das RN. The Central Venous Pressure Causality Factors. Journal of General Practice (Los Angel)2017;5(3):e116. doi:10.4172/2329-9126.1000e116

22. Afifi AA, Azen SP. Statistical analysis: A computer oriented approach, 2nd ed. Academic Press, New York. 1979.

23. Lee Y, Nelder JA, Pawitan Y. Generalized Linear Models with Random Effects (Unified Analysis via H–likelihood). New York: 2006. Chapman & Hall.

24. Das RN and Lee Y. Log-normal versus gamma models for analyzing data from quality-improvement experiments. Quality Engineering. 2008; 21(1): 79-87. doi: 10.1080/08982110802317372

25. Das RN and Lee Y. Analysis strategies for multiple responses in quality improvement experiments. International Journal of Quality Engineering and Technology. 2010; 1(4): 395-409. doi: 10.1504/IJQET.2010.035585

26. Das RN. Robust Response Surfaces, Regression, and Positive Data Analyses. Chapman & Hall. London. 2014. 336.

27. Hastie T, Tibshirani R, Friedman J. The Elements of Statistical Learning. Springer-Verlag. 2009.

28. Das RN. Discrepancy in fitting between log-normal and gamma models: An illustration. Model Assisted Statistics and Applications. 2012; 7 (1): 23–32. doi: 10.3233/MAS-2011-0198

29. Das RN. Systolic & Diastolic Blood Pressure Determinants of Shock Patients. J Heart Cardiol. 2017; 3(2): 12-30. doi: 10.15436/2378-6914.17.1740

30. Das RN. Shock patients heart rate variability factors. Journal of Cardiovascular Medicine and Therapeutics. 2017; 1(2):19-23.

Citation: Rabindra Nath Das, Lee Y, Seungyoung Oh (2018) The Determinants Of Mean Central Venous Pressure For Shock Patients. J Clin Trial Cardiol 5(2): 1-5.

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