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Cardiac Index Predicted Factors for Shock Patients

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ABSTRACT

The report aims to formulate an appropriate cardiac index (CI) model with 19 explanatory variables for 113 shock patients. Determinants of CI are focused from the fitted model. There is little study for the predicted factors of CI based on probabilistic modeling. CI model has been developed in the report with 19 explanatory variables for 113 shock patients, and the data site is: http://www.umass.edu/statdata/statdata/data/shock.txt Statistical method of joint generalized linear models (JGLMs) is adopted. Mean CI is negatively associated with age (P = 0.0044), shock type (SHOCKT) at level 3 (P = 0.0586), diastolic blood pressure (DBP) (P = 0.0032), mean circulation time (MCT) (P<0.0001), hemoglobin (HG) (P = 0.0053), while it is positively with mean arterial pressure (MAP) (P<0.0001), heart rate (HR) (P<0.0001), body surface index (BSI) (P<0.0001), appearance time (AT) (P<0.0001), plasma volume index (PVI) (P<0.0001). Variance of CI is negatively associated with age (P = 0.0020), height (P = 0.0255), sex (P = 0.0582), SHOCKT at level 2 (P = 0.0356), MAP (P = 0.0664), AT (P = 0.0080), hematocrit (HCT) (P = 0.0039), card sequence order (CSO) (P<0.0001), while it is positively associated with systolic blood pressure (SBP) (P = 0.0241) and MCT (P = 0.0039). CI is high if MAP, or HR, or BSI, or AT, or PVI rises, or age, or DBP, or MCT, or HG decreases. Variance of CI depends on many explanatory factors. These findings are completely a new addition in medical literature.

***Keywords*:** Body surface area, Cardiac index, Ejection fraction, Cardiac output, Heart rate, Joint gamma models

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1. INTRODUCTION

An important physiological parameter is cardiac output (CO) which reflects the entire organism metabolism. The sum of the systemic blood flow per minute is known as CO which is measured by the product of heart rate (HR) and stroke volume (SV), and it is related with ejection fraction (EF) [1, 2]. In practice, EF denotes the blood percentage that is ejected (or pumped) out of the ventricles per heartbeat. Therefore, CO can be defined as the amount of blood (in liters) that is ejected by the left ventricle into the circulation system per minute (l/min) [3, 4]. Note that the cardiac index (CI) is measured as the ratio of CO to the body surface area (BSA), and is given by CI = CO/BSA = HR*SV/BSA [1-4]. It is observed that CI is a composite function of HR, SV and BSA. Consequently, CI is a very complex function of HR, SV, EF and BSA. Therefore, CI should be associated with HR, SV, EF, BSA and many others.

CI is a fundamental clinical parameter which is applied in the diagnosis of patients with cardiovascular disease (CVD), under anesthesia as well as critically ill, and it is also used for the patients in cardiac & medicine intensive care [5-7]. Specially, CI is used as a marker of judging the heart functioning as a pump by associating the blood volume pumped by the heart with an individual's body surface area. The normal range of CI in rest is 2.6 - 4.2 L/min per square meter. Lower value of CI is associated with CVD, and if CI falls below 1.8 L/min/m^2, the patient may be in cardiogenic shock [8-12].

Best of our knowledge, the determinants of CI are studied a little in medical literature. Therefore, the following queries arise. What is the relationship of CI with other cardiac parameters? What are the factors that increase or decrease CI? How are they identified? These responses are very little known in cardiology literature. Recently an Editorial [13] focuses the determinants of CI without any derivation. The present report aims to focus these queries with the help of statistical modeling.

2. MATERIAL & STATISTICAL METHODS

2. 1. Materials

The report considers a data set of 113 shock patients with 20 explanatory factors/variables, and the data site is displayed in the Abstract. The source, description, and the data collection method are given in [14]. These are not repeated herein. For the necessary use of the factors/ variables in the report, they are restated as sex (SEX) (male = 0, female = 1), height (HEIGHT), age (AGE), diastolic blood pressure (DBP), systolic BP (SBP), shock type (SHOCKT) (non-shock = 1, hypovolemic = 2, cardiogenic, or bacterial, or neurogenic or other = 3), mean arterial pressure (MAP), heart rate (HR), mean central venous pressure (MCVP), survival status (SURVIV) (survived = 1, death = 2), body surface index (BSI), appearance time (AT), cardiac index (CI), mean circulation time (MCT), urinary output (UO), plasma volume index (PVI), hemoglobin (HG), hematocrit (HCT), red cell index (RCI) and card sequence order (initial = 1, final = 2) (CSO).

2. 2. Statistical Methods

The report focuses the determinants of CI based on probabilistic modeling. Therefore, it considers CI as the dependent variable, which is non-normally, heteroscedatic, positive continuous random response, and it may be properly modeled by JGLMs with Log-normal and

Gamma distribution. These models are well illustrated in [15-19], and their illustrations are not redisplayed herein. For CI, it is noted that Gamma JGLMs fit is better than Log-normal JGLMs. Therefore, Gamma JGLMs are presented herein very shortly. For more details about JGLMs, readers may go through [15, 18].

2. 3. Gamma JGLMs

Let y_i be a continuous positive random variable (or response) with $E(y_i) = \mu_i$ and $Var(y_i) = \sigma_i^2 V(\mu_i)$, where σ_i^2's and μ_i's are respectively, dispersion & mean parameters, and $V(\cdot)$ presents the variance function having two components (in GLM) such as $V(\mu_i)$ (depends on the mean changes) and σ_i^2 (free of mean changes). Generally, GLM family distribution is recognized by $V(\mu_i)$. For example, if $V(\mu) = \mu$, it is Poisson, and it is Gamma or Normal according as $V(\mu) = \mu^2$, or $V(\mu) = 1$, etc. The mean and variance models of Gamma JGLMs 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 respectively, the GLM link functions connected to the mean & variance linear predictors, and x_i^t, w_i^t are the vectors of independent factors/ variables, associated with the mean & dispersion parameters respectively. Generally, the maximum likelihood (ML) and the restricted ML (REML) method are used respectively, for estimating the mean and dispersion parameters [15].

3. STATISTICAL & GRAPHICAL ANALYSIS

CI has been modeled using both JGLMs with Log-normal and Gamma distributions, considering CI as the response variable, and the rest others are independent variables. Final model has been selected according to the Akaike information criterion (AIC) rule, which selects the appropriate model based on its lowest value (within each class) by minimizing both the squared error loss and predicted additive errors [20, p. 203--204]. AIC value concludes that, Gamma JGLMs fit (AIC=416.509) is more better than Log-normal (AIC = 425.3). The derived analysis results of CI is displayed in Table 1. Three partially significant effects such as SHOCKT (in mean model), and SEX & MAP (in variance model) are included in the model for better fitting [20, 21]. In epidemiology, partially significant effects are called confounder.

The data generated model always to be verified with model checking tools, as all the valid interpretation are drawn from the derived model assuming that it is an approximate estimate of the true unknown model. The present Gamma fitted CI model has been verified by Figure 1.

In Figure 1(a), Gamma fitted (Table 1) absolute residuals are plotted with respect to fitted values. It is nearly a straight line, concluding that variance is constant with the running means. Figure 1(b) displays the normal probability plot for the Gamma fitted mean model of CI (Table 1), which does not present any lack of fit. Both the plots show that there is no discrepancy in the fitted models. Thus, the fitted Gamma models (Table 1) may be considered as the approximate true CI models.

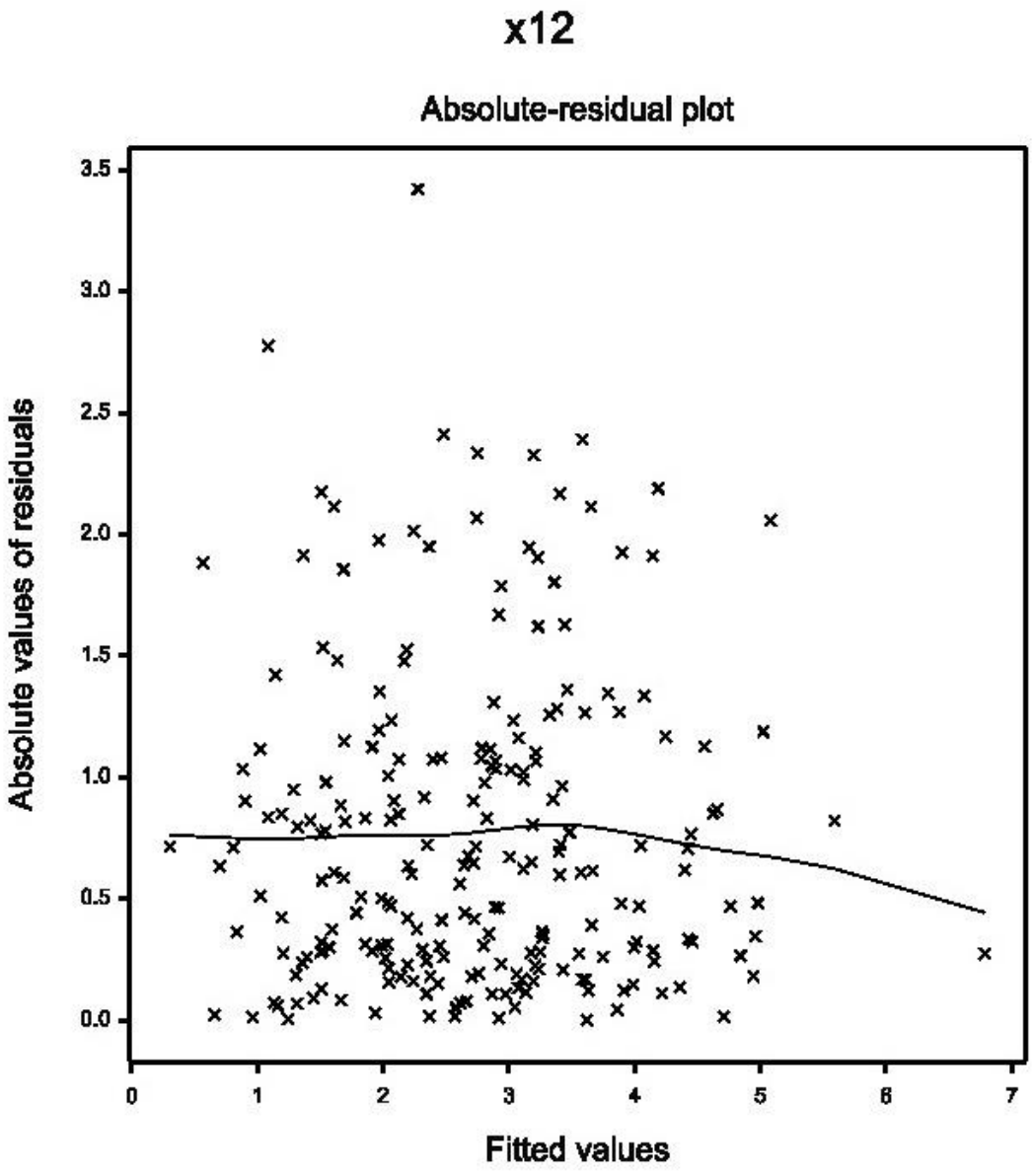
x12
Absolute-residual plot
Absolute values of residuals
Fitted values
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
0
1
2
3
4
5
6
7

Fig. 1(a)

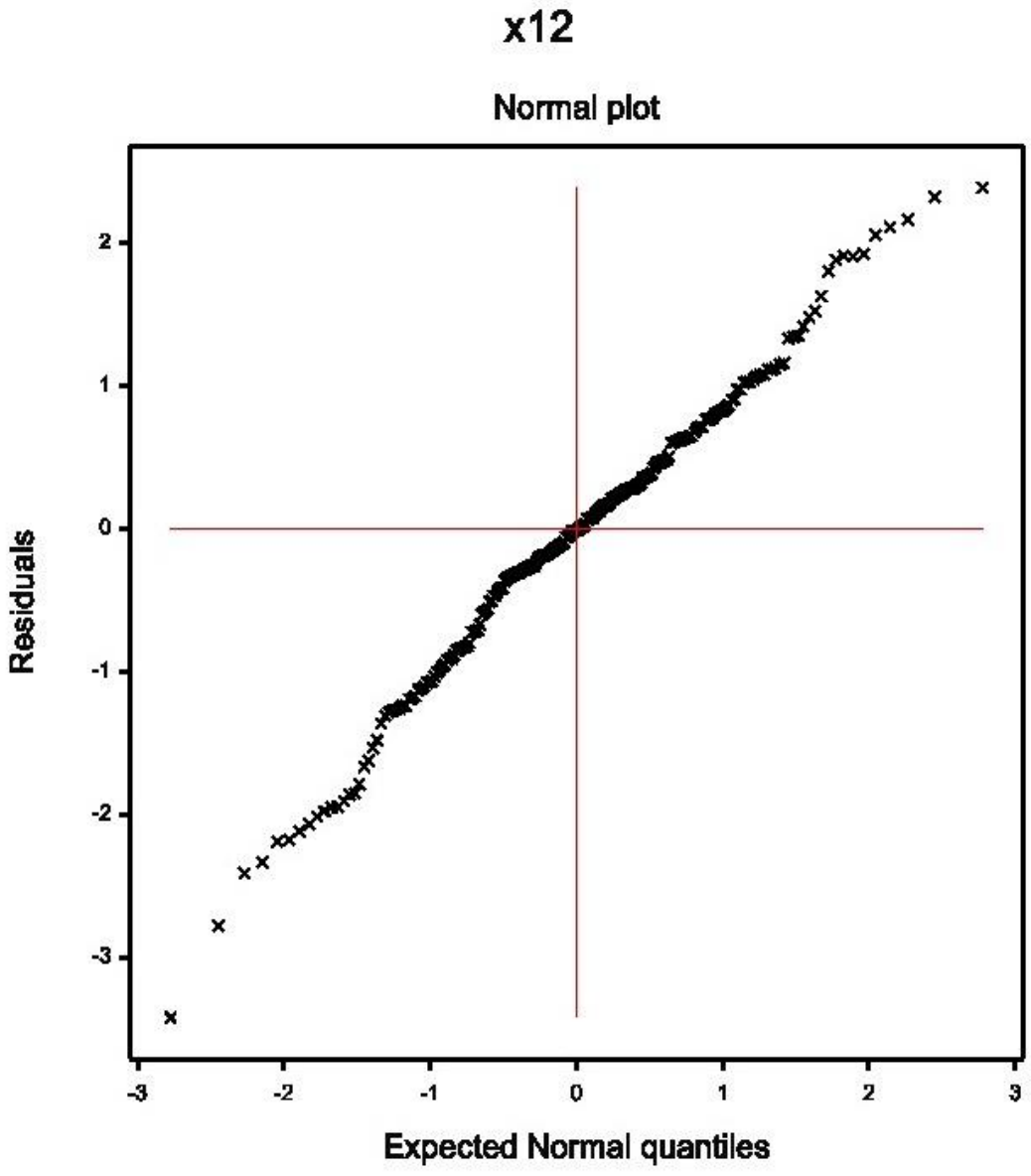

Fig. 1(b)

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

4. RESULTS

Joint generalized Gamma fitted analysis results of CI have been displayed in Table 1. From the fitted mean model of CI, it is observed that mean CI is positively associated with MAP (P<0.0001), HR (P< 0.0001), BSI (P< 0.0001), AT (P< 0.0001), PVI (P < 0.0001), while it is negatively associated with AGE (P = 0.0044), SHOCKT at level 3 (P = 0.0586), DBP (P =

0.0032), MCT (P<0.0001), HG (P = 0.0053). Variance of CI is negatively associated with AGE (P = 0.0020), HEIGHT (P = 0.0255), SEX (P = 0.0582), SHOCKT at level 2 (P = 0.0356), MAP (P = 0.0664), AT (P = 0.0080), HCT (P = 0.0039), CSO (P<0.0001), while it is positively associated with SBP (P = 0.0241) and MCT (P< 0.0001).

Table 1. Results for mean and dispersion models of Cardiac Index from Gamma fit

Model	Covariate	Estimate	Standard error.	t-value	P-Value
Mean Model	Constant	0.16154	0.20349	0.794	0.0613
	AGE (x1)	- 0.00335	0.00117	- 2.874	0.0044
	Shock type (SHOCKT) (Fx5;2)	0.00737	0.04243	0.174	0.8620
	Shock type (SHOCKT)(Fx5;3)	- 0.08095	0.04257	- 1.901	0.0586
	Mean arterial pressure (MAP) (x7)	0.01189	0.00293	4.064	<0.0001
	Heart rate (HR) (x8)	0.00295	0.00063	4.702	<0.0001
	Diastolic pressure (DBP) (x9)	- 0.01133	0.00380	-2.980	0.0032
	Body surface index (BSI) (x11)	0.40120	0.08737	4.592	<0.0001
	Appearance time (AT) (x13)	0.03704	0.00886	4.183	<0.0001
	Mean circulation time (MCT) (x14)	-0.04506	0.00467	-9.651	<0.0001
	Plasma volume index (PVI) (x16)	0.01173	0.00122	9.575	<0.0001
	Hemoglobin (HG) (x18)	-0.02194	0.00779	-2.814	0.0053
Dispersion Model	Constant	5.9025	2.9129	2.026	0.0440
	AGE (x1)	-0.0252	0.0081	-3.121	0.0020
	HEIGHTT (x2)	-0.0356	0.0158	-2.248	0.0255
	SEX (Fx3)	-0.5709	0.2998	-1.904	0.0582
	SHOCKT (Fx5;2)	-0.6366	0.3012	-2.114	0.0356
	SHOCKT (Fx5;3)	-0.3659	0.2838	-1.289	0.1987
	Systolic blood pressure (SBP) (x6)	0.0178	0.0078	2.271	0.0241
	MAP (x7)	-0.0205	0.0111	-1.845	0.0664

	AT (x13)	-0.1619	0.0605	-2.674	0.0080
	MCT (x14)	0.1150	0.0266	4.326	<0.0001
	HCT (x19)	-0.0491	0.0169	-2.910	0.0039
	RSO (Fx20)	-1.0377	0.2335	-4.443	<0.0001

Gamma fitted CI mean ($\hat{\mu}$) model (from Table 1) is

$\hat{\mu}$ = exp. (0.16154 – 0.00335 AGE + 0.00737 SHOCKT2 – 0.08095 SHOCKT3 + 0.01189 MAP + 0.00295 HR - 0.01133DBP + 0.40120 BSI + 0.03704 AT – 0.04506 MCT + 0.01173 PVI – 0.02194 HG),

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

$\hat{\sigma}^2$ = exp. (5.9025 – 0.0252 AGE – 0.0356 HEIGHT - 0.5709 SEX - 0.6366 SHOCKT2 – 0.3659 SHOCKT3 + 0.0178 SBP – 0.0205 MAP - 0.1619 AT + 0.1150 MCT - 0.0491 HCT – 1.0377CSO).

5. DISCUSSION

The Gamma fitted mean & variance models of CI have been presented above (Table1). From these two CI models, the following valid conclusions can be drawn.

- Mean CI is directly associated with MAP (P<0.0001), interpreting that CI rises as MAP increases.
- Mean CI is directly associated with HR (P<0.0001), concluding that CI increases as HR rises.
- Mean CI is directly associated with BSI (P<0.0001), implying that CI rises as BSI increases.
- Mean CI is directly associated with AT (P<0.0001), denoting that CI increases as AT rises.
- Mean CI is directly associated with PVI (P<0.0001), interpreting that CI rises as PVI increases.
- Mean CI is inversely associated with AGE (P = 0.0044), concluding that CI increases at younger ages.
- Mean CI is inversely associated with SHOCKT at level 3 (P = 0.0586), implying that CI is higher at SHOCKT levels 1 & 2 than level 3.
- Mean CI is inversely associated with DBP (P = 0.0032), interpreting that CI increases as DBP decreases.
- Mean CI is inversely associated with MCT (P<0.0001), denoting that CI rises as MCT decreases.

- Mean CI is inversely associated with HG (P = 0.0053), concluding that CI rises as HG decreases.

From the fitted CI variance model, the following can be concluded.

- Variance of CI is negatively associated with AGE (P = 0.0020), concluding that CI variance is higher at younger ages.
- Variance of CI is negatively associated with HEIGHT (P = 0.0255), interpreting that CI variance is higher for shorter shock patients than taller.
- Variance of CI is negatively associated with SEX (male = 0, female = 1 (P = 0.0582), concluding that CI variance is higher for male shock patients than female.
- Variance of CI is negatively associated with SHOCKT at level 2 (P=0.0356), concluding that CI variance is higher for patients with shock type level 1 than level 2.
- Variance of CI is negatively associated with MAP (P=0.0664), denoting that CI variance rises as MAP decreases.
- Variance of CI is negatively associated with AT (P = 0.0080), interpreting that CI variance rises as AT decreases.
- Variance of CI is negatively associated with HCT (P = 0.0039), denoting that CI variance rises as HCT decreases.
- Variance of CI is negatively associated with CSO (initial = 1, final = 2) (P<0.0001), implying that CI variance is higher at initial recoding time than final.
- Variance of CI is positively associated with SBP (P = 0.0241), interpreting that CI variance rises as SBP rises.
- Variance of CI is positively associated with MCT (P < 0.0001), concluding that CI variance rises as MCT rises.

Interpretations of the derived outputs of CI analysis have been presented above. It has been derived that mean CI has been explained by AGE, SHOCKT, MAP, HR, DBP, BSI, AT, MCT, PVI, HG, while variance of CI has been explained by AGE, HEIGHT, SEX, SHOCKT, SBP, MAP, AT, MCT, HCT, RSO (Table 1). The derived results support the practical situation & earlier results that mean CI is negatively associated with age, indicating that CI is lower at older ages [22]. In addition, the derived results support the definition of CI that is mean CI is directly related with HR (Table 1). Best of our knowledge, there is little study about the determinants of CI in the medical literature. So, these results may not be compared with any earlier published results. The present results are the first detailed explanatory factors of CI.

6. CONCLUSIONS

The report has developed probabilistic mean & variance models of cardiac index (Table 1). The models have been selected based on model diagnostic plots (Figure 1) checking, smallest AIC value, very small standard error of the estimates (Table 1), and also verifying the distribution of the response CI. Based on these derived models, many determinants of CI mean and variance have been derived. The report has derived that CI value will be increased if MAP, or HR, or BSI, or AT, or PVI rises, or at younger ages, or patients at shock type levels 1 & 2, or DBP, or MCT, HG decreases.

Variance of CI will be smaller if SBP, or MCT decreases, or at older ages, or for female shock patients, or shock patients at final recording time, or MAP, or AT, or HCT rises.

The derived models (Table 1) are based on the data set given in [14], but they may be different (with respect to regression coefficients) for different data sets. Even though the models will be different for different data sets, but the interpretations of the explanatory variable of CI will not be changed. It has not been examined herein, as we have not enough data. In addition, we have not included many other explanatory cardiac parameters such as basal HR, peak HR, maximum HR, ejection fraction, maximum BP, basal BP, etc., as these are not considered in the given data set [14].

In future medical research, investigators may consider these covariates to derive many explanatory factors of CI. All the above interpretations regarding CI have been derived based on the derived models. Derived models have been verified for their correctness in different ways. Hence, the conclusions that have been drawn herein seems to be correct, best of our knowledge.

Hope that these conclusions are observed in practice. Medical practitioners can justify these conclusions in real situations. But there are a little study regarding the determinants of CI. So, it is not possible to compare these findings with the earlier findings. Biological explanations of these conclusions are not displayed herein, as these are unknown to us. Hope that these explanations will be focused in future research articles.

Medical practitioners always try to increase CI value, and to decrease variance of CI for shock patients, for better treatments. It is noted from Table 1, that if MAP, or AT rises, or MCT decreases, or DBP & SBP are at normal level, both will be achieved. If HR, or PVI is high, mean CI value will be high. Medical practitioners need care on other factors such as HR, BSI, HG, HCT, age, height, shock types etc. of shock patients to increase their CI value. The report may give some ideas to the medical practitioners how to improve the shock patients.

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