

Peripheral and Central Venous Blood Oxygen Saturation Used To Indicate Systemic Vascular Resistance

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ABSTRACT

Introduction

We used a new index to evaluate Systemic Vascular Resistance (SVR) which included arterial, peripheral and central venous saturations.

$$\frac{\text{peripheral vascular resistance} \times \text{SaO}_2 - \text{Speripheral} \times \text{O}_2}{\text{central vascular resistance} \times \text{SaO}_2 - \text{Scentral} \times \text{O}_2} = \text{SVR index}$$

Method

Twenty candidates for coronary artery bypass surgery were enrolled. SVR was calculated at two different time points (when patient is at pre-pump stage and then on-pump stage). At each time point, SVR was measured conventionally and with this new method. The conventional method utilized echocardiography and pump indices to calculate SVR.

Forty pairs of data were analyzed. Correlation and agreement between conven-

tional SVR measurements and SVR index were assessed.

Result

There was good correlation and agreement between the new and conventional method. Pearson coefficient was 0.83 and 0.93 (pre-pump and on-pump respectively) ($p < 0.001$). Bland-Altman plot of percentage difference in pre-pump and on-pump measurements showed 0.1 and -0.05 unit bias, and limits of agreement were -0.4 to 0.65 and -0.5 to 0.4 units respectively.

Measured SVR can be predicted by SVR index using linear regression.

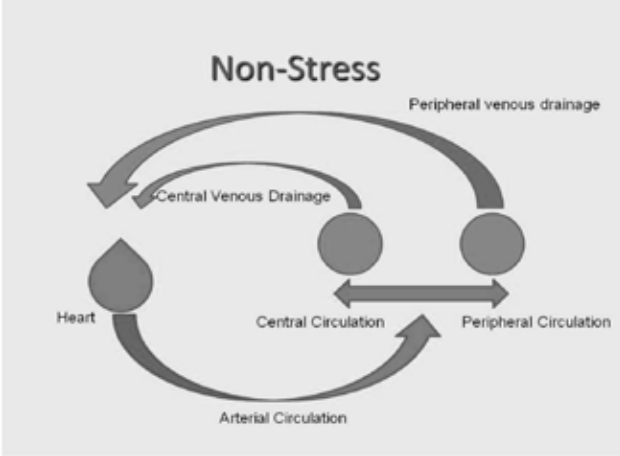
Pre-pump SVR (Dynes.Sec.cm-5.1000-1) = 0.57 (95% CI: 0.2-0.8) × pre-pump SVR Index + 0.9 (95% CI: 0.6-1.2)

On-pump SVR (Dynes.Sec.cm-5.1000-1) = 0.58 (95% CI: 0.3-0.7) × on-pump SVR Index + 0.6 (95% CI: 0.4-0.8)

Conclusion

This novel index had good statistical agreement with the conventional method. It is a simple, less invasive and inexpensive

Figure 1: In non-stress conditions there is no vasoconstriction, therefore venous drainage from the periphery will be saturated.



technique. For general application of this method, further studied are necessary.

INTRODUCTION

In this study we used central (heart and brain) and peripheral venous blood oxygen saturation to assess systemic vascular resistance (SVR). This is a simple, less invasive and inexpensive method. In this paper we will address the agreement between this new technique and measured systemic vascular resistance at two different time points.

During stressful periods catecholamines are released; the associated peripheral vasoconstriction redistributes blood flow to the heart and brain. Stasis of blood within the peripheral system causes greater desaturation compared to central circulation (Figure 1 and Figure 2).

To measure this physiological phenomenon, the Fick equation may be modified mathematically to achieve a new index, as described below. This index consists of peripheral and central venous blood oxygen saturation. It also considers peripheral and central oxygen consumption; which are usually equal, unless

critical levels of hypoxemia are reached.

Adolph Fick described an equation to determine blood flow by measuring overall oxygen uptake and content in blood

Equation 1
$$Q = \frac{VO_2}{(CaO_2 - CvO_2) \times 10}$$

(Equation 1):

Q = cardiac output (L/min)

VO₂ = oxygen consumption (mL O₂/min)

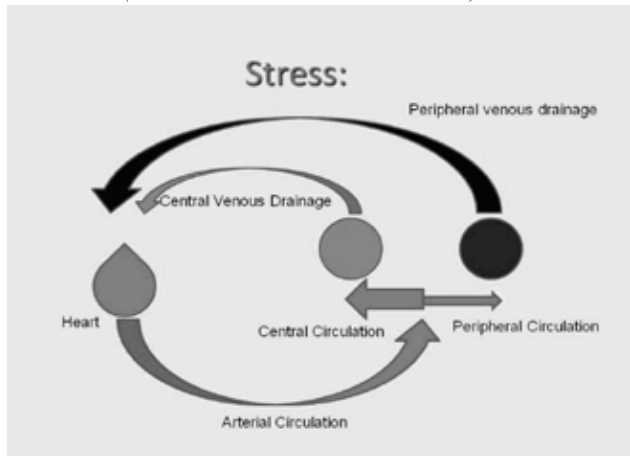
CaO₂ = oxygen content of arterial blood (mL O₂/100 mL blood)

CvO₂ = oxygen content of mixed venous blood (mL

O₂/100 mL blood)

To rephrase, to calculate flow within a circulating system, a substance which has a determined level of consumption needs to be analyzed. The input and output concentration of that substance needs to be considered as well. By dividing the substance consumption in the system by the concentration difference (input-output) of that substance, we would be able to calculate the flow of that circulating system. This equation can be

Figure 2: In contrast, stressful conditions induce vasoconstriction so the venous drainage from periphery will be desaturated. Peripheral vasoconstriction can be estimated by comparing peripheral to central venous saturation (SVR index mentioned in the text).



applied to any circulatory system.

In the Fick equation, oxygen is considered as the substance, and therefore oxygen consumption is divided by O₂ content difference (input to the system-output from the system). Fick's calculation measures the systemic circulation; therefore input into the circulating system is from the aorta and output is from the pulmonary artery.

The O₂ consumption in the above equation equals the total oxygen consumption of the entire body. The same equation can be applied to any other circulating system within the body. Extremities such as hand and leg can be considered a circulating system for which the input and output source of flow should be defined. For example in an upper extremity (periphery), we have the

$$\text{Equation 2} \quad Q_{\text{peripheral}} = \frac{V_{\text{peripheral O}_2}}{(C_{\text{peripheral aO}_2} - C_{\text{peripheral vO}_2}) \times 10}$$

following equation (Equation 2):

$Q_{\text{peripheral}}$ = Flow to the periphery (L/min)

$V_{\text{peripheral O}_2}$ = oxygen consumption by that periphery (mL O₂/min)

$C_{\text{peripheral aO}_2}$ = oxygen content of arterial blood in the periphery (mL O₂/100 mL blood)

$C_{\text{peripheral vO}_2}$ = blood oxygen content of venous side (output) of the periphery (mL O₂/100 mL blood)

This very equation can be applied to central circulation (Equation 3). In this study the right atrium is selected as the output for central circulation (central venous sample); and the aorta as the input. As there is no O₂ consumption in arterial side of circulation, arterial oxygen from the periphery would have nearly the same O₂ content as aorta (we used radial artery saturation instead of aortic saturation). Central circulation includes circulation to the periphery, viscera, heart and brain. However, in periods of stress and catecholamine release, flow to viscera and periphery decreases, so that the circulating system will largely supply the brain and heart. This is referred to as the central circulation in this article.

$$\text{Equation 3} \quad Q_{\text{central}} = \frac{V_{\text{central O}_2}}{(C_{\text{central aO}_2} - C_{\text{central vO}_2}) \times 10}$$

Q_{central} = flow to the central and peripheral parts of the body (L/min)

$V_{\text{central O}_2}$ = oxygen consumption by central and peripheral parts of the body (mL O₂/min)

$C_{\text{central aO}_2}$ = oxygen content of arterial blood (mL O₂/100 mL blood)

$C_{\text{central vO}_2}$ = blood oxygen content of venous side (output) of the central and peripheral parts of the body (mL O₂/100 mL blood)

By dividing the above formulas (Equation 3 divided by Equation 2), and disregarding the dissolved portion of oxygen in the blood (due to its very negligible value), the following equation (Equation 4) can be derived:

$$\begin{aligned} \text{Equation 4} \\ \frac{(Q_{\text{central}})/(V_{\text{central O}_2})}{(Q_{\text{peripheral}})/(V_{\text{peripheral O}_2})} &= \frac{(C_{\text{peripheral aO}_2} - C_{\text{peripheral vO}_2})}{(C_{\text{central aO}_2} - C_{\text{central vO}_2})} \\ &= \frac{(1.39 \times \text{SaO}_2 \times \text{Hb} + \text{PaO}_2 \times 0.003) - (1.39 \times \text{Speripheral vO}_2 \times \text{Hb} + \text{Pperipheral vO}_2)}{(1.39 \times \text{SaO}_2 \times \text{Hb} + \text{PaO}_2 \times 0.003) - (1.39 \times \text{Scentral vO}_2 \times \text{Hb} + \text{Pcentral vO}_2)} \\ \rightarrow \frac{1.39 \times \text{Hb} (\text{SaO}_2 - \text{Speripheral vO}_2)}{1.39 \times \text{Hb} (\text{SaO}_2 - \text{Scentral vO}_2)} &= \frac{\text{SaO}_2 - \text{Speripheral vO}_2}{\text{SaO}_2 - \text{Scentral vO}_2} \end{aligned}$$

This new equation shows that there is a mathematically inverse correlation between perfusion in different parts of circulatory system and their related saturations. Perfusion is also inversely correlated to resistance. Therefore the final part of Equation 4 is used to indicate the ratio of peripheral resistance over central resistance (Equation 5). To rephrase, we want to show that comparison of peripheral and central saturation will indicate peripheral over central vascular resistance.

$$\text{Equation 5} \quad \frac{\text{peripheral vascular resistance} \cdot \text{SaO}_2 - \text{Speripheral vO}_2}{\text{central vascular resistance} \cdot \text{SaO}_2 - \text{Scentral vO}_2} = \text{SVR index}$$

The majority of the resistive forces in circulation affect the peripheral system; therefore "Systemic Vascular Resistance Index (SVR Index)" would be the most suitable title for this novel index.

Method:

The study was approved by the ethical committee of Shahid Beheshti University. The study was commenced in December 2007 in a cardiac operating centre in Tehran. Patients for elective coronary artery bypass graft (CABG) were evaluated to exclude those with pulmonary disease, oxygen saturation less than 90%, body mass index of more than thirty, vascular abnormalities and ejection fraction of less than fifteen percent (exclusion criteria).

Twenty patients were selected; detailed explanations were provided and informed consent attained from all subjects. Also, during surgery, patients with complications such as abnormal bleeding or prolonged pre-pump surgery were to be excluded; fortunately, the twenty selected patients did not have the above complications.

An arterial catheter was placed in the radial artery and anaesthesia was induced with fentanyl 2–5 $\mu\text{g kg}^{-1}$, midazolam 0.05 mg kg^{-1} , thiopentone 2–5 mg kg^{-1} , and cisatracurium 0.15 mg kg^{-1} . Anaesthesia was maintained with isoflurane. Ephedrine was administered when necessary, in order to keep the mean arterial pressure (MAP) above 60 mm Hg, and atropine was given to maintain heart rate (HR) above 45 beats min^{-1} . All patients received an infusion of glycerylnitrate (0.5–1.0 $\mu\text{g kg}^{-1} \text{min}^{-1}$) except when MAP was below 60 mm Hg. The haemoglobin (Hb) concentration was kept above 9.0 g dl^{-1} . A triple lumen Central Venous Catheter was inserted in the right internal jugular vein. It was advanced under radiographic guidance till the tip could be placed 1 cm below the junction of right atrium and superior vena cava. In two dif-

Table 1: Demographic and Hemodynamic Characteristics of Patients Undergoing CABG (pre-pump and on-pump indices included).

Character	Value*
Age(year)	57 \pm 6
Height (cm)	158 \pm 10
Weight (kg)	66 \pm 13
Ejection Fraction (%)	45 \pm 12
Pre-pump Heart Rate (beats/minute)	80 \pm 14
Pre-pump Mean Arterial Pressure (mmHg)	84 \pm 10
Pre-pump Central Venous Pressure (mmHg)	11 \pm 3
Pre-pump Central Venous Oxygen Saturation (%)	87.8 \pm 6.2
On-pump Mean Arterial Pressure (mmHg)	54 \pm 13
On-pump Central Venous Oxygen Saturation (%)	83.9 \pm 9.2
Pump Flow during Cardio-Pulmonary Bypass (L/minute)	4.12 \pm 0.41
Pre-Pump SVR Index	3.2 \pm 1.5
Pre-Pump Estimated SVR (Dynes.Sec/cm5)/1000	2.7 \pm 1
On-Pump SVR Index	1.2 \pm 0.6
On-Pump Calculated SVR (Dynes.Sec/cm5)/1000	1.3 \pm 0.4

*Figures are presented as mean \pm standard deviation

Table 2: Percentage Difference between Pre-Pump SVR Index- Conventional Pre-Pump SVR and On-Pump SVR Index-Conventional On-Pump SVR (Bias). Lower and Upper Limits of Agreement (Bias±2SD) and Coefficient of Correlation between the Measurements during the Procedure. *P<0.0001

	Bias (Dynes.sec/cm5/1000)	95% limits of agreement	r2
Pre-pump SVR index vs. Conventional SVR	0.1	-0.45 to 0.65	0.85*
On-pump SVR index vs. Conventional SVR	-0.05	-0.5 to 0.4	0.9*

ferent time points (pre-pump and on-pump), systemic vascular resistance was measured simultaneously with both methods.

For calculating the new index, blood samples from radial artery, antecubital and central veins were taken at each time point.

Pre-pump SVR was conventionally estimated by employing echocardiography indices, heart rate, central venous, and mean arterial pressures (CVP and MAP) as outlined below:

$$\text{SVR measured from pump indices} = \frac{\text{Mean Arterial Pressure} - \text{Central Venous Pressure}}{\text{pump flow}}$$

When the patient was on cardiopulmonary bypass (CPB) pump, SVR was conventionally calculated as below:

$$\text{SVR estimated by echocardiography indices} = \frac{\text{Mean Arterial Pressure} - \text{Central Venous Pressure}}{(\text{end diastolic volume} - \text{end systolic volume}) \times \text{Heart Rate}}$$

For easier statistical comparison, conventional SVR values were presented in Dynes. Sec.cm⁻⁵.1000⁻¹.

Statistical analysis

The sample size was based on a calculation of power. Clinically relevant mean difference was considered to be 0.20 unit, with an SD of 0.20 unit. Twenty patients were included to ensure power of at least 80%. Variables were normally distributed, and therefore values were presented as mean and standard deviations. A P-value < 0.05 was considered statistically

significant. For the correlation analysis, the Pearson correlation was used and a P-value < 0.01 was considered statistically significant. For the SVR Index and conventional SVR measurements, the agreement was assessed using the Bland–Altman method. The Bland–Altman method could be applied since these variables were normally distributed. Percentage error was calculated as follows: two times the SD of the difference between the two methods, which was then divided by the mean value obtained from both methods {2 x SD (difference between method 1 and method 2)/[(mean of method 1 + mean of method 2)/2]x100}. SVR was obtained simultaneously at each time point for the conventional and new method in all patients.

The statistical analysis was computed with SPSS (Version 16, SPSS Inc., Chicago, IL, USA) and Analyse-it (version 2.2).

RESULTS

Demographic and hemodynamic charac-

Figure 3: Curve fit characteristics of pre-pump SVR index and conventional pre-pump SVR measurement

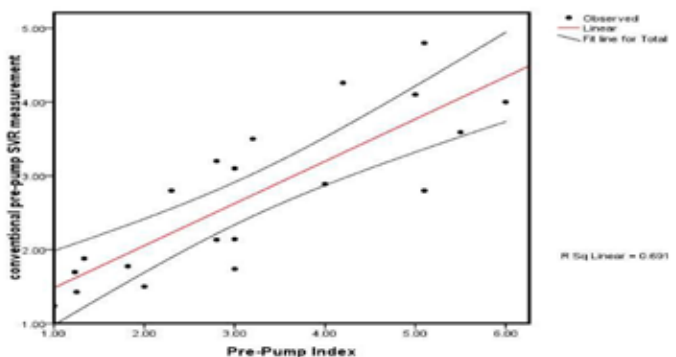


Figure 4: Curve fit characteristics of on-pump SVR index and conventional on-pump SVR measurements.

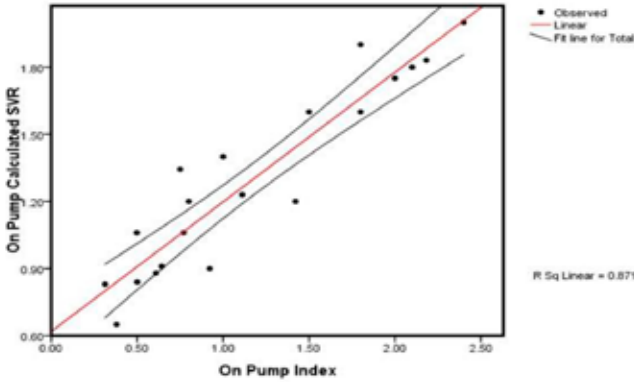


Figure 5: Bland-Altman Level of Agreement Plot with Percent of Difference in Pre-Pump Index and the Estimated Value. Confidence Intervals of Bias And Limits of Agreement are Shown. Bias is not Statistically Significant.

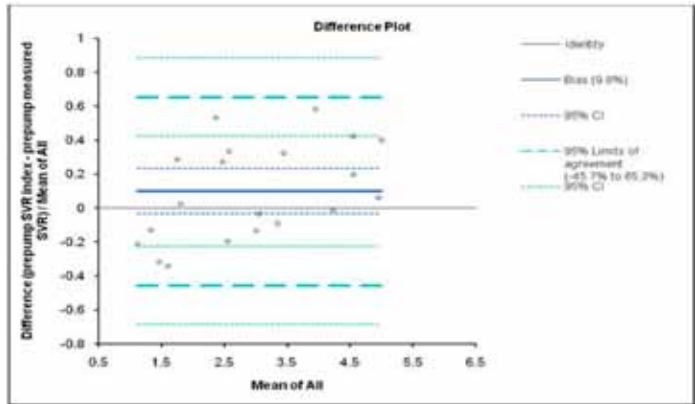
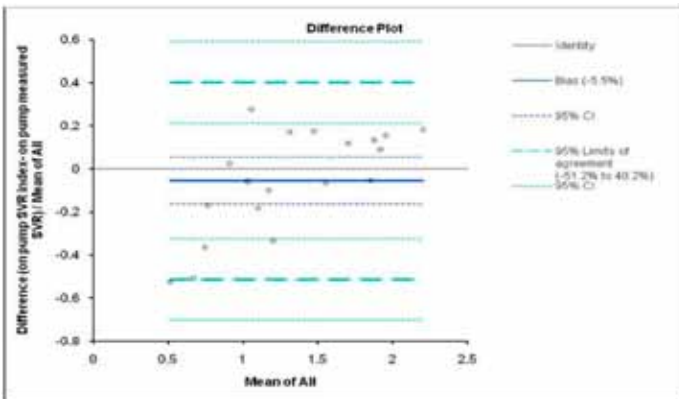


Figure 6: Bland-Altman Level of Agreement Plot with Percent of Difference in On-Pump Index and Measured Value. Confidence Intervals of Bias and Limits of Agreement are shown. Bias is not Statistically Significant.



teristics of patients are illustrated in table 1. The twenty patients enrolled did not have relevant peri-operative complications. No data was rejected. Conventional SVR measurements had a range of 1.2-4.8 and 0.6-2 (Dynes.Sec.cm⁻⁵.1000⁻¹) before and on CPB pump, respectively. The values obtained for the new method were 1-6 and 0.3-2.4 units. There were 40 pairs of comparative measurements performed between conventional SVR and the new method.

Values of SVR Index and conventional SVR are depicted in a scatter plot. Linear fitness was confirmed. Pearson correlation coefficient was 0.83 and 0.93 for pre-pump and on-pump time points (p<0.001) (Figure 3 and Figure 4). The results of agreement analysis and distribution of the observed percentage differences, are shown in Table 2, Figure 5, and Figure 6. Bias was not significantly related to the level of SVR. Linear regression shows that measured SVR can be predicted by SVR index as below:

Pre-pump SVR (Dynes.Sec.cm⁻⁵.1000⁻¹) = 0.57 (95% CI: 0.2-0.8) × pre-pump SVR Index + 0.9 (95% CI: 0.6-1.2)

On-pump SVR (Dynes.Sec.cm⁻⁵.1000⁻¹) = 0.58 (95% CI: 0.3-0.7) × on-pump SVR Index + 0.6 (95% CI: 0.4-0.8)

DISCUSSION

Systemic vascular resistance is a useful hemodynamic index. Pulmonary Artery Catheterization (PAC) is the most precise technique for calculating SVR [1]; however it is expensive, difficult and invasive; and not beneficial for the patient [2].

Previous studies showed good agreement between echocardiography and PAC in SVR evaluation [3]and [4]. Central venous saturation has been used as a guide for hemodynamic change [5], however its relationship with peripheral venous saturation has not been mentioned before.

In this study we calculated a new index (SVR index) using arterial, peripheral and central venous saturation. We showed the agreement of this new index with conventional SVR measurement (echocardiography

and pump indices). This method is easy, inexpensive and is not operator dependent. Collecting samples may seem time consuming therefore easier approaches such as oxymeters can be studied in future [6].

A previous study showed the effect of unstable hemodynamic on this index. However that article did not mention the exact part of circulation that was measured [7]. We have shown that this index can accurately estimate SVR.

Different parts of same body were investigated and compared; therefore external confounding factors such as temperature had minute effect on the results. Imprecise laboratory devices will alter the findings and therefore should be rejected; however minor inaccuracy in laboratory equipment that is repeated each time a measurement is taken, can be tolerated.

Greater agreement was achieved while patients were on-pump (lower percentage difference bias) compared to the values taken with echocardiography at the pre-pump period. This could be due to more accurate measurement of on-pump SVR.

As depicted in table I, vascular resistance was higher than normal in candidates for CABG before CPB, and lower (to normal) while on CPB. This phenomenon may be related to vasodilating mediators release during CPB or more effective flow generation (i.e. the external pump instead of failing heart) and subsequent reduction of SVR [8] and [9].

Instead of Equation 5 a simpler index such as central over peripheral venous saturation seems reasonable in well oxygenated states; however further studies are required.

Limitations

Ideally we would require aortic saturation in equations 3, 4 and 5. However, for practical reasons, the aortic saturation was assumed to be nearly equal to peripheral arteries. This limitation may theoretically overestimate SVR.

In a stable condition (such as in this research) oxygen consumption is constant.

When critical hypoxic point is reached oxygen consumption drops rapidly, both in periphery and central parts. As the peripheral arterial saturation was above 90% in this study, we did not reach that critical point. Therefore the ratio of peripheral over central oxygen consumption (equations 4) is constant in this paper.

We used echocardiography and pump indices to measure SVR, though PAC gives more accurate values. We did not use PAC due to high expense and possible complications [2]. Further study in centres utilizing PAC would be enlightening.

The general application of this index to critically ill patients or those with vasculopathies, sepsis or any other condition that affects vascular resistance non-physiologically, requires additional investigation.

Multicentre studies with larger samples are advocated for the general application of this index. Outcome based designs are required to determine the whether this new index may assist patient management.

CONCLUSION

The following formula provides a good index for estimation of SVR:

This index agrees and has good correlation with the SVR. By utilizing linear regression, SVR can be predicted according to equation below:

$$\text{SVR INDEX} = \frac{\text{SaO}_2 - \text{S peripheral vO}_2}{\text{SaO}_2 - \text{S central vO}_2}$$

On-pump SVR (Dynes.Sec.cm-5.1000-1) = 0.58 (95% CI: 0.3-0.7) × on-pump SVR Index + 0.6 (95% CI: 0.4-0.8)

We advocate further follow up studies with PAC data, larger sample sizes and a

multicentre approach to investigate this innovative approach.

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