

CORRELATION OF CARDIAC OUTPUT CALCULATED FROM INVASIVE FICKS PRINCIPLE WITH NON-INVASIVE MEASUREMENT

Cardiology

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ABSTRACT

Background: Estimation of cardiac output has been the cornerstone in understanding and optimizing management of various acute cardiac emergencies not the least heart failure. The contemporary focus of disease management is shifting from symptom management to evaluating hemodynamic performance including CO, left ventricular volumes, systemic vascular resistance(SVR) and ejection fraction(EF). **Methods and results:** Between January 2021 and December 2023, a total of 500 patients were enrolled based on the inclusion criteria established with some form of cardiac disease, who underwent invasive and non-invasive measurement of Cardiac output (CO), Cardiac Index, SVR and VO₂ estimation. The mean age of the study population was 57 years with a male: female ratio of 1.5:1. Mean CO and CI measured invasively (Qi) were 4.07 ± 1.04 and 2.28 ± 0.55 , while mean CO and CI calculated with method 1 (Qn1, non-invasive) were 3.48 ± 0.28 and 1.96 ± 0.11 , method 2 (Qn2, non-invasive) were 2.22 ± 0.55 and 1.2582 ± 0.3008 . Qn1 and Qn2 measured a lower cardiac output by 14.62% ($p < 0.0001$) and 45.45 % ($p < 0.0001$) compared to invasive method. Regression analysis noted a nonlinear correlation between Qi and Qn1 ($r = 0.33$) and a linear correlation between Qi and Qn2 ($r = 0.64$). Qn1 estimated 11.3 % higher SVR(n1) as compared to measured SVR, however there was no statistical difference between values (CO, CI and SVR) derived from LaFarge and Bergstra formula or between measured and estimated RA pressure. **Conclusion:** Cardiac output and cardiac index derived by noninvasive methods have moderate to poor correlation with the standard invasive estimation of CO based on Fick's principle, SVR estimated by non-invasive methods (Uchida K) was statistically overestimated as compared to the SVR obtained by standard invasive technique. VO₂ estimated by Bergstra formula correlates well with VO₂ values of Lafarge formula in all patients irrespective of Killip class and BMI, Bergstra formula can be used as a reliable alternative method for estimation of VO₂ compared to Krovetz-Goldbloom formula. In conclusion, Cardiac output, cardiac index and SVR measurement with currently available noninvasive methods are not reliable in the diseased state.

KEYWORDS

Cardiac Index ■ Cardiac output ■ Fick's principle ■ Systemic vascular resistance ■ Uchida k

Cardiac output (CO) is the amount of blood pumped by the heart per minute, or in other words, cardiac output is the amount of work performed by the heart in response to the body's need for oxygen. Two ways to increase oxygen delivery are through alterations of local blood flow and adjustment of cardiac output by modulating heart rate (HR) and stroke volume (SV). Commonly reported numbers in healthy subjects range from 4 L/min (cardiac index [CI]) = $2.5 - 4.0$ L/min/m² in an at-rest person with a small body habitus to more than 35 L/min in elite athletes during exercise⁽¹⁾.

Heart failure—the inability of the heart to provide sufficient cardiac output (CO) to meet tissue perfusion needs at an acceptable filling pressure—is indisputably a major health care concern. The contemporary focus of disease management is shifting from symptom management to evaluating hemodynamic performance including CO, left ventricular volumes, systemic vascular resistance(SVR) and ejection fraction(EF). Objective, accurate, reproducible, and easy to obtain measurements of physiological parameters which are indicators of hemodynamic function, are essential for managing both predisposing conditions and heart failure itself.

Fick's Method for CO measurement

The **Fick's principle** states that the amount of a substance taken up by an organ (or by the whole body) per unit of time is equal to the arterial level of the substance minus the venous level (**A-V difference**) times the blood flow. Calculation of cardiac output with Fick's formula requires O₂ consumption (VO₂), mixed venous content (CvO₂/MvO₂) and arterial oxygen content (CaO₂).

Direct Fick's cardiac output vs Indirect Fick's cardiac output measurement

For direct Fick's CO determinations, the amount of oxygen extracted in the respiratory cycle is measured from inspired and expired gas as the

“total oxygen consumption.” During the period of time when the oxygen consumption is being measured, a sample of mixed venous blood is withdrawn from the pulmonary artery and, simultaneously, an arterial blood sample is withdrawn from any arterial line. Arterial and venous blood oxygen contents are determined and the arterial-venous oxygen (AVO₂) difference is calculated. The total oxygen consumption (in mL/min X 100) is divided by AVO₂ difference to yield CO in mL/min⁽²⁾.

Accurate CO derived via the direct Fick method is dependent upon the patient being in a steady hemodynamic and metabolic state, stable respiratory rate, heart rate, oxygen consumption, and respiratory exchange ratio. As the AVO₂ difference narrows, small errors in either the collection or analysis of respired gases or blood samples increase the probability of large variations in the CO estimate. Thus, direct Fick CO is more accurate in low output than in high output states. Direct Fick CO determinations are time-consuming, require multiple personnel meticulously carrying out the technique in specialized environments, and produce a onetime only measure of CO. Therefore, use of direct Fick's CO (although considered the “true” gold standard against which other methods are evaluated) is usually confined to the cardiac catheterization lab and research settings only⁽³⁾.

Indirect Fick's cardiac output: Like the direct Fick's method, the indirect Fick's CO determination uses a sample of mixed venous blood drawn from the pulmonary artery. However, rather than using direct measurement of total oxygen consumption and arterial blood oxygen, the indirect Fick uses pulse oximetry devices to derive the arterial oxygen content. The arterial-venous oxygen difference (AVO₂ difference) is calculated using a weighting factor (1.36) times the hemoglobin times the arterial oxygen saturation minus the venous oxygen saturation. Like the direct Fick calculations, small errors in either the collection or analysis of the mixed venous blood sample,

errors in the hemoglobin levels, the unreliability of the oximetry device or errors in calculating BSA will affect the CO accuracy. However, because the indirect Fick procedure is less cumbersome than direct Fick procedure, the indirect Fick can be performed at the patient's bedside by specially trained personnel and can be used serially.

Oxygen Consumption

The metabolic production of carbon dioxide and the consumption of oxygen reflect the fundamental functions of the tissues. Oxygen consumption (VO_2) is the amount of oxygen taken in and used by the body per minute; thus, it is the rate of oxygen use. VO_2 is sometimes expressed in liters of O_2 per minute (mL/min). VO_2 - monitoring can provide information on the adequacy of circulation or oxygen transport, especially when combined with mixed venous oximetry and it can be used to evaluate the causes of arterial hypoxemia.

Methods for measurement of oxygen consumption have included the Douglas bag method, the polarographic method, and the paramagnetic method.

It is common practice to use an estimate of VO_2 instead of measurements. Bergstra, Krovetz-Goldbloom, and LaFarge-Mittiten, using multivariate analysis derived empiric formulas to estimate VO_2 , which remain the most commonly used equations for calculating assumed VO_2 .⁽³⁻⁵⁾

- LaFarge Formula for VO_2 (mL/min) = $138.1 - (X \times \log_e \text{age}) + (0.378 \times \text{Heart Rate}) \times \text{BSA}$ (Men: $X = 11.49$; Women: $X = 17.04$);
- Bergstra formula for VO_2 (mL/min) = $157.3 \times \text{BSA} + X - (10.5 \times \log_e \text{age}) + 4.8$ (Men: $X = 10$; Women: $X = 0$).
- Krovetz-Goldbloom formula for $\text{VO}_2(\text{mL/min})/\text{BSA} = (1.39 \times \text{height} + 0.84 \times \text{weight} - 35.6)/\text{BSA}$

Where BSA is calculated with DuBois Formula i.e. $\text{BSA} [\text{m}^2] = \text{Weight} [\text{kg}]^{0.425} \times \text{height} (\text{cm})^{0.725} \times 0.007184$ ⁽⁶⁾

Arteriovenous Oxygen Difference

The arteriovenous oxygen difference across the lungs must be measured to calculate cardiac output by Fick's principle, and this can be accomplished by the following method.

From appropriately positioned catheters, systemic arterial and mixed venous (pulmonary arterial) blood samples are obtained during the period when oxygen consumption is being measured. Oxygen content (in milliliters of oxygen per liter of blood) can be determined by a variety of methods, the most classic of which (and the one that serves as a standard for all others) being the manometric technique of Van Slyke and Neill⁽⁷⁾.

The major drawback of the Van Slyke and Neill technique is that 15 to 30 minutes are required to run a single blood sample. Devices in widespread use today are of the co-oximeter class and either hemolyzed the blood sample (by ultrasonic or chemical techniques) or use whole blood; both types of co-oximeter depend on spectrophotometric measurement of the percent oxygen saturation of hemoglobin. Using these devices, oximetry of heparinized blood samples is simple, quick and measures the percentage of hemoglobin present as oxyhemoglobin. This percentage, multiplied by the theoretical oxygen-carrying capacity of the patient's blood, yields the calculated oxygen content of that sample

Arterial O_2 content = $\text{CaO}_2 = \text{bound oxygen} + \text{dissolved oxygen} = (1.39 \times \text{Hb} \times \text{SpO}_2) + (0.00314 \times \text{PaO}_2)$

where Hb, SpO_2 and PaO_2 are hemoglobin concentration, oxygen saturation and oxygen partial pressure in arterial blood, respectively.

If mixed venous blood can be taken with a pulmonary artery catheterization/ RA catheterization than Mixed venous O_2 content = $\text{CvO}_2 = \text{bound oxygen} + \text{dissolved oxygen} = (1.39 \times \text{Hb} \times \text{SvO}_2) + 0.00314 \times \text{PvO}_2$ ⁽³⁾, where SvO_2 and PvO_2 are oxygen saturation and oxygen partial pressure in mixed venous blood, respectively.

However, limitations of Fick's principle lie in both oxygen consumption (VO_2) and A-V oxygen content. The accuracy of calculation of flow by the Fick's method is determined, by the accuracy with which VO_2 and arteriovenous oxygen difference can be measured.

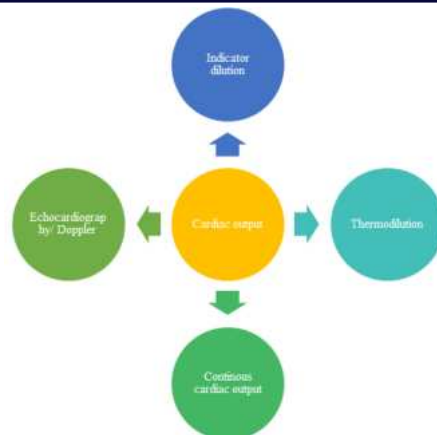


Figure 1. Other methods for calculation of cardiac output.

Systemic Vascular Resistance

Systemic vascular resistance is the quantitative value for left ventricular afterload. The minute-to-minute control of vascular resistance in the systemic bed is under an autonomic nervous system influences and local metabolic factors. Hypotension or reduced cardiac output generally triggers increased systemic resistance through the baroreceptors, adrenergic neural pathways, and release of vasoconstrictor hormones. This circumstance is commonly seen in congestive heart failure or shock. Knowledge of changes in systemic vascular resistance is also important in evaluating the hemodynamic response to stress tests, such as dynamic or isometric exercise⁽⁸⁾. In this regard, there is ample evidence suggesting that normally systemic vascular resistance falls in response to dynamic exercise, but pulmonary vascular resistance remains unchanged (at least with supine bicycle exercise). Transient elevations in systemic vascular resistance have been provoked by infusions of vasopressor drugs to evaluate the left ventricular response to a sudden increase in afterload⁽⁹⁾.

Low systemic vascular resistance may be seen in conditions in which blood flow is abnormally high, such as may occur in patients with an arteriovenous fistula, severe anemia, and other high-output states or conditions associated with peripheral vasodilatation and high output, such as septic shock. It is important to realize that in these circumstances there may well be regional differences in vascular resistance (e.g., very low in the arteriovenous fistula but normal or increased in other vascular beds), and calculations based on mean pressure and flow in the entire systemic circulation must be interpreted with caution.

$$\text{SVR} (\text{dynes} \times \text{s}/\text{cm}^5) = (80 \times \text{MAP})/\text{CO}^{(10)}$$

$\text{MAP} = (1/3) \text{ systolic blood pressure} + (2/3) \text{ diastolic blood pressure}$ in mmHg, (Flame's equation)

$\text{CO} = \text{cardiac output, mL/min}$

Normal SVR is between 900 and 1440 dynes/sec/cm⁵.⁽¹¹⁾

METHODS

We conducted an open label prospective study from January 2021 to December 2023 at U N Mehta institute of cardiology, Ahmedabad and screened over 755 patients for enrollment with 500 patients meeting the inclusion criteria. All patients between 18-80 years of age who had no shunt lesions, serious septic shock, severe anemia, thyrotoxicosis, A-V fistula, or rhythm disorders. U. N. Mehta institute of cardiology is the biggest cardiac hospital of India serving Gujarat and two neighboring states covering over 90.8 million citizens.

Protocol

After careful enrollment of patients, a detailed medical and surgical history was sought, which followed measurement of patient's weight and height. Body surface area was calculated based on Du Bois Formula i.e.

$$\text{BSA} = (\text{W}^{0.425} \times \text{H}^{0.725}) \times 0.007184$$

Baseline vital parameters such as heart rate, blood pressure and saturation were recorded along with Killip class on presentation. All of our Study patients underwent an electrocardiogram and an Echocardiogram. Among these patients, RA pressure was predicted non-invasively, according to IVC diameter and its respiratory

collapsibility as shown in table 1⁽¹²⁾.

Table 1. Estimated RA pressure based on IVC diameter and its respiratory collapsibility

RA pressure(mmHg)	Low (0- 5 mmHg)	Intermediate(5-10 mmHg)		High(15m mmHg)
IVC diameter	<21 mm	<21 mm	>21 mm	>21mm
IVC Collapse with sniff	≥50%	≤50%	>50%	<50%

Central venous access had been taken in all patients to determine RA pressure and mixed venous oxygen which is assumed the same as mixed venous saturation in our study. ABGA obtained from peripheral arterial access.

Cardiac output, Cardiac index, and Systemic vascular resistance had been calculated based invasively and non-invasively obtained data. Cardiac output was calculated at baseline using FICK'S PRINCIPLE. VO2 calculated based on LaFarge, Krovetz-Goldbloom and Bergstra Formulas⁽³⁻⁵⁾.

Arterial O2 content measured with below mentioned formula
 $CaO_2 = (1.39 \times Hb \times SpO_2) + (0.00314 \times PaO_2)$

Mixed venous O2 content measured with below mentioned formula
 $CvO_2 = (1.39 \times Hb \times SvO_2) + 0.00314 \times PvO_2$

According to Fick's equation cardiac output calculated
 $CO = VO_2 / (CaO_2 - CvO_2)$
 $CI = CO / BSA$
 $SVR = 80 * (MAP - RA / CO)$ dynes/sec/cm⁻⁵

Noninvasive estimation of MvO2/ cardiac output

Method 1:

For noninvasive determination of MvO2, the arteriovenous difference was calculated based on the formula derived by Uchida et al i.e.
 $CaO_2 - CvO_2 = -0.265 \times 10^{-3} h^2 + 0.289 \times 10^{-3} h + 7.74$
where h in meter, i.e. 53 meters for U N Mehta Institute of Cardiology and Research, Ahmedabad.

CO and CI calculated based on assumed VO2 calculate from the Bergstra formula.

For SVR calculation assumed RA pressure was used based on echocardiographic parameters
Non-invasively, CaO2 derived from below mentioned,
 $CaO_2 = 1.39 \times SpO_2 \times (Hb/100) + 0.00314 (PAO_2 - 5)$
Than CvO2 calculated by readjusting Fick's equation
 $CvO_2 = CaO_2 - (VO_2 / CO)$

Method 2:

To estimate CvO2 and thereby calculating CO

We estimated VO2/SV from the slope of intercept of a regression line of SpO2 on 1/HR,
Uchida et al derived formula for,
 $SpO_2 = (100/0.201) (VO_2/SV) (1/HR) + CvO_2/0.201 - 0.00314 (PAO_2 - 5) / 0.201$ ⁽²⁴⁾

Where $CvO_2 = 0.201 * [SpO_2 + 0.00314(PAO_2 - 5) - (100/0.0201) (VO_2/SV) (1/HR)]$.
CO calculated based on non-invasively derived CaO2, CvO2 and assumed VO2 based on the Bergstra formula.

RESULTS

Between January 2021 and December 2023, a total of 755 patients were screened for enrollment, 500 patients were certified eligible for enrollment based on the inclusion criteria established. We included a total of 500 patients with some form of cardiac disease. Amongst them, 84% were having ACS and 56/84(67%) were in Killip Class 4. Predominant study subjects were hemodynamically unstable who needed ICU stay and invasive monitoring. The mean age of the study population was 57 years and male: female ratio was 1:1.5. Baseline patient characteristic and parameters are shown in table 2 and table 3 respectively.

Table 2. Baseline Characteristics of study population.

Variables	N=500
Age(yrs.)	57.19±13.49
Sex	

Male	n = 350
Female	n = 150
Height(cm)	165.28 ± 9.19
Weight(kg)	70.46 ± 10.63
BMI	25.68 ± 3.53
<30 kg/m ²	n = 440
>30 kg/m ²	n = 60
BSA	1.78 ± 0.16
Heart rate	103.16±18.97
Blood Pressure	
SBP(mmHg)	90.21±24.22
DBP(mmHg)	63.59±13.14
MAP(mmHg)	72.47±16.32
NYHA class	
NYHA class I	n= 15
NYHA class II	n= 35
NYHA class III	n= 145
NYHA class IV	n= 305
Killip Class	
Killip class I	n= 40
Killip class II	n= 55
Killip class III	n= 30
Killip class IV	n= 285
Hb (g/dl)	11.95±2.14
S. Creatinine(mg/dL)	2.67±9.09

Table 3. Baseline parameters obtained invasively and non-invasively.

Invasive Measures	
Arterial Gas Measurement	
pH	7.33±0.12
HCO3	19.13±4.66
PACO2	30.85±9.51
PAO2	97.89±49.67
SAO2	94.79±2.68
Venous Gas Measurement(RA sampling)	
pH	7.33±0.1
HCO3	20.34±4.55
PVCO2	34.47±10.14
PvO2	73.32±40.19
MvO2	51.97±6.10
CaO2(ml/L)	157.73±28.58
CvO2(ml/L)	86.27±17.25
CVP-RA Pressure(mmHg)	12.05±0.41
Non Invasive Measurements	
RA pressure(based on IVC)mmHg	10.30±3.95
SpO2(%)	94.79±2.69
CaO2(ml/L)	160.34±28.53
CvO2(ml/L)-Method 1	81.41±28.56
CvO2(ml/L)-Method 2	40.01±10.56

After obtaining baseline data, we calculated invasive CO[Qi], CI[CI(i)] and SVR[SVRi] according to Fick's principle. Similarly, we derived non-invasive CvO2 based on method 1 and method 2, i.e. CvO2(n1) and CvO2(n2), respectively. Based on Fick's principle we calculated noninvasive CO, CI and SVR with method 1 and method 2 i.e. CO[n1], CI[n1], SVR[n1] and CO(n2), CI(n2), SVR(n2), respectively.

Table 4. Mean, SD and % error of invasive and noninvasive method 1-Q(n1) cardiac out(CO) and cardiac index(CI) measurement

Group	Invasive	Noninvasive – Method 1	p	% Error
CO (Litre / min)	Q(I) = 4.07 ± 1.04	Q(n1) = 3.48 ± 0.28	<0.0001	(-14.62%)
CI (Litre/min/m ²)	CI(i)2.28 ± 0.55	CI(n1) = 1.96 ± 0.11	<0.0001	(-14.03%)

There was a statistically significant difference in mean Qi and Q(n1) with p < 0.0001 which suggests that noninvasive method 1 measures cardiac output 14.62% lower as compared to invasive method. Similarly, the calculated CI(n1) was 14.03% lower as compared to measured CI(i) (table 4).

Table 5. Mean, SD and % error of invasive and noninvasive

(method 2) cardiac output measurement

Group	Invasive	Noninvasive – Method 2	p	% Error
CO (Litre / min)	4.073±1.0423	2.22 ± 0.55	<0.0001	(-45.45%)
CI (Litre/min/m ²)	2.28 ± 0.55	1.2582 ± 0.3008	<0.0001	(-44.82%)

A statistical significant difference was noted in mean Qi and Q(n1) with $p < 0.0001$ which suggests that non-invasive method 2 measures cardiac output 45.45% lower as compared to invasive method. Similarly calculated CI(n1) was 44.82% lower as compared to measured CI(i) (table 5).

Table 6. Mean, SD and SEM of measured SVR, calculated SVR(n1) and SVR(n2)

Group	SVR(i)	SVR(n1)	p value	SVR(n2)	p value p
Mean	1265.8626	1435.6437	0.0053	2371.068	<0.0001
SD	472.4919	372.8905		888.0465	
SEM	47.2492	37.2891		88.8046	

There was statistically significant difference in mean SVR and SVR(n1) with p -value = 0.0053. Method 1 estimates 11.3 % higher SVR(n1) as compared to measured SVR. Similarly, there was statistically significant difference in mean SVR and SVR(n2) with p -value <0.0001 (table 6).

Table 7. Comparison between obtained various hemodynamic parameters with calculated VO2 with LaFarge and Krovetz-Goldbloom formula

	LaFarge Formula	Krovetz-Goldbloom formula	p value
VO2(ml/min)	274.15	253.33	0.0001
Qi(L/min)	4.05	3.75	0.0351
CI(i)(L/min/m ²)	2.28	2.12	0.0371
SVR(dynes/sec/cm ²)	1274.65	1371.30	0.1847

We calculated CO, CI and SVR based on assumed VO2 with standard LaFarge equation and compare it with the newly suggested Krovetz-Goldbloom formula (table 7). Mean assumed VO2 with LaFarge was 274.15 i.e. 21% higher as compares to Krovetz-Goldbloom formula i.e. 253.33 ml/min. The result showed that measured CO with assumed VO2 based on Krovetz-Goldbloom formula was 3.75 L/min i.e. 7.5% lower as compared to measured CO with assumed VO2 based LaFarge formula. Similarly, calculated CI was also 7.5% lower as compared to invasively measured.

We measured RA pressure with invasive and noninvasive technique in same patients. Mean measured and estimated RA pressure was 11.8 mmHg and 11.3 mmHg, respectively with p -value 0.81. There was no statically significant difference between measured and estimated RA pressure.

We calculated CO, CI and SVR by assuming VO2 with standard LaFarge equation and compared it Bergstra formula. Mean assumed VO2 with LaFarge and Bergstra formula was 274.15 and 274.50 ml/min ($p=0.93$), respectively. It was found that there was no statistical difference between values derived from LaFarge and Bergstra formula (table 8).

Table 8. Comparison between obtained various hemodynamic parameters with calculated VO2 with LaFarge and Bergstra formula

	LaFarge Formula	Bergstra Formula	p value
VO2(ml/min)	274.15	274.50	0.93
CO(L/min)	4.05	4.07	0.87
CI(L/min/m ²)	2.2838	2.3076	0.77
SVR(dynes/sec/cm ²)	1274.65	1265.86	0.9

While on subgroup analysis of patients with Acute coronary syndrome, we found that there was a significant difference in measured Qi and calculated Qn1 irrespective of Killip class as a p -value <0.0001 for each class.

We observed that VO2 calculated with Krovetz-Goldbloom formula was significantly lower as compared to LaFarge formula, with $p < 0.0001$ irrespective of BMI. However, VO2 measurement with Bergstra formula was correlating with LaFarge formula (p -value >

0.05) irrespective of BMI status (table 9).

Table 9. Calculated VO2 with various formulas based on BMI

	No.	LaFarge formula	Krovetz-Goldbloom formula	p value	Bergstra Formula	p value
BMI < 30 kg/m ²	440	273.50±31.61	253.54±18.53	<0.0001	273.10±21.85	0.40
BMI > 30 kg/m ²	60	278.91±35.32	258.75±23.27	<0.03	284.78±23.90	0.63

DISCUSSION

Our aim was to study the correlation between invasive and non-invasive cardiac output measurement techniques based on Fick's principle. The mean age of the study population was 57 years with 70% of subjects being male, mean Hb and Creatinine was 11.95 gm/dL and 2.67 mg/dL respectively.

We had measured non-invasively derived CvO2 thereby CO with two different techniques. In the first method, we calculate the fixed arteriovenous difference based on altitude of our institute (i.e. 53 meters from sea level) by formula derived by Uchida i.e. Arteriovenous difference = $\text{CaO}_2 - \text{CvO}_2 = -0.265 \times 10^{-4} \text{h}^2 + 0.289 \times 10^{-3} \text{h} + 7.74$. (23) CaO_2 was calculated by $\text{CaO}_2 = 1.39 \times \text{SpO}_2 \times (\text{Hb}/100) + 0.00314 (\text{PAO}_2 - 5)$. CvO2 calculated by adjusting the above-mentioned formulas. In our study, mean non-invasively measured CO and CI were 14% low as compared to invasively measure cardiac output which is statistically significant. There was poor correlation between non-invasively and invasively measured CO (Figure 2a).

In the second technique, we had estimated VO2/SV from the slope of the intercept of a regression line of SpO2 on 1/HR i.e. 3.66. Uchida had derived equation for SpO2 calculation i.e. $\text{SpO}_2 = (100/0.201) (\text{VO}_2/\text{SV}) (1/\text{HR}) + \text{CvO}_2/0.201 - 0.00314 (\text{PAO}_2 - 5)/0.201$. CvO2 was calculated by incorporating VO2/SV in this formula. Measured cardiac output and cardiac index were significantly low as compared to invasively measured CO and CI with error percentage ~45% (Figure 2b).

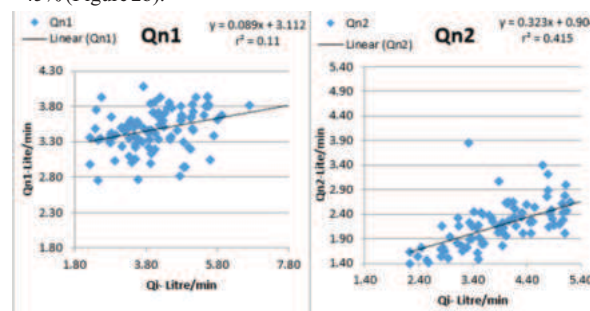


Figure 2. (a) Correlation between Q(i) and Q(n)-Method 1, Pearson Correlation Coefficient (r) = 0.33 and (b) Correlation between Q(i) and Q(n)-Method 2, Pearson Correlation Coefficient (r) = 0.64.

This might be related to the hemodynamically unstable study population. 67% of the study population had a cardiogenic shock. In cardiogenic shock, tissue oxygen delivery (DO2) is reduced as DO2 is directly related to CO⁽¹²⁾. Tissue oxygen extraction also increased. Both of these mechanism leads to a decrease in MvO2 thereby CvO2. In the previous study, the study population was healthy school going subjects. In which they presumed that MvO2 remains constant irrespective of attitude. Their non-invasively derived MvO2 also correlated that of invasively derived MvO2. In our study non-invasively derived CvO2 is not well correlating with invasively derived CvO2.

We estimated RA pressure with the use of an echocardiography machine with IVC measurement and its collapsibility and compare it with RA pressure measured by a central venous catheter placed in RA. Our result showed that there is no significant difference in RA pressure estimation with a noninvasive method. Mandeville et al also showed a similar result⁽¹³⁾. A meta-analysis of 21 studies done by William C et al also concluded that sonographic measurement of IVC diameter and

collapsibility is a valid method of estimating CVP and RAP⁽¹⁴⁾. As IVC measurement was easy to obtain bedside in ICU setup to estimate RA pressure. Elevation of RAP by echocardiography at baseline assessment was associated with increased risk of death or transplant in patients with PAH⁽¹⁵⁾.

We calculated SVR On the basis on non-invasively calculate CO and RA pressure. There was a significant difference between measured SVR and calculated SVR with non-invasive methods. Noninvasively calculated SVR is significantly high. It is primarily related to the difference in measured and calculated CO as SVR is inversely related to cardiac output. We are not recommending noninvasive methods to measure SVR in the diseased state.

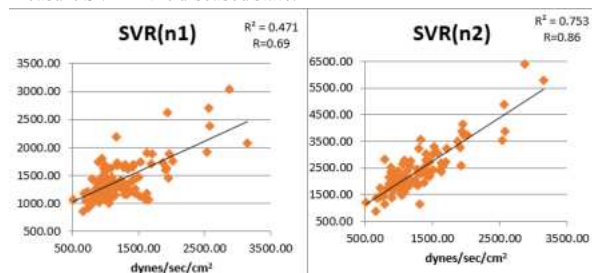


Figure 3, (a) Correlation between SVR(i) and SVR(n1) and (b) Correlation between SVR(i) and SVR(n2).

On regression analysis of invasively calculated SVR in relation to non-invasively calculated SVR(n1), there was some linear correlation between measured SVR and calculated SVR(n1) with correlation equation $SVR(n1) = 0.541 (SVR) + 749.6$, while there was linear correlation between measured SVR and calculated SVR(n2) with correlation equation, $SVR(n2) = 1.631 (SVR) + 306.3$ (Figure 3).

Assumed oxygen consumption (VO₂) is increasingly used as a convenient surrogate for measured VO₂ for the calculation of cardiac out. We compared Bergstra and Krovetz-bloomberg formula with the LaFarge formula. There was no statistical difference between calculated VO₂ with Bergstra and LaFarge formula. Calculated VO₂ with was significantly low as compared to LaFarge formula. Accurate measurement of VO₂ is mandatory for accurate measurement of CO based on Fick's principle. The LaFarge equation was originally generated from a cohort of 879 patients who were mostly children, studied between 1961 and 1966. It was validated by the traditional Douglas Bag method to measure VO₂⁽⁵⁾. Although the LaFarge equation provides the closest estimation of VO₂ among all the predictive equations and remains the most commonly used in cardiac laboratories, it has several limitations in clinical practice⁽¹⁶⁾. Falkner U et demonstrated that there were large errors of greater than 50% that occur in 19.1% (LaFarge-Miettinen) group and 38.5% (Krovetz-Goldbloom) group for VO₂ measurement. Both the formula tends to overestimate VO₂ as compared to measured VO₂. A similarly poor agreement was found when analyzing a subgroup of 25 patients with Fontan-type circulation in the same study⁽³⁾. Bergstra et al assessed VO₂ measurement with their formula in adult patients with a mean age of 39 years which showed it correlates better as compared to LaFarge formula. Wolf et al found that there was significantly higher VO₂ assumed by Bergstra formula as compared to measured V₂ in subjects with a mean age of 57 years. In the same population, the LaFarge formula tends to underestimate VO₂. We found no significant difference in VO₂ calculated with the LaFarge and Bergstra formula in patients with ACS in various Killip class. There was no difference in calculated VO₂ with Bergstra formula as compared to the LaFarge formula in patients with BMI >30 kg/m².

CONCLUSION

- Cardiac output and cardiac index derived by noninvasive methods (Uchida K et al) have moderate to poor correlation with the standard invasive estimation of CO based on Fick's principle (co-efficient of correlation for method 1= 0.33 and method 2 =0.64 respectively).
- SVR estimated by non-invasive methods (Uchida K) is statistically overestimated as compared to the SVR obtained by standard invasive technique with moderate correlation (co-efficient of correlation for method 1= 0.69 and method 2=0.86 respectively).
- Cardiac output, cardiac index and SVR measurement with

currently available non-invasive methods are not reliable in the diseased state.

- VO₂ estimated by Bergstra formula correlates well with VO₂ values of LaFarge formula in all patients irrespective of Killip class and BMI. Thus we conclude that the Bergstra formula can be used as a reliable alternative method for estimation of VO₂ compared to Krovetz-Goldbloom formula.
- VO₂ estimated by Krovetz-Bloomberg had a poor correlation with vo₂ derived by well-established LaFarge formula.

Declarations

None.

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