Comparison of cardiac output by Fick formula vs. thermodilution, following vasodilator challenge in pulmonary hypertension

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Abstract

Introduction: Cardiac output and index, measured during right heart catheterization are used to define vasoreactivity and predict mortality. The Fick and thermodilution methods are routinely used, but have not been compared following vasoreactivity.

Methods: We retrospectively reviewed the RHC data of 50 patients; that met inclusion criteria, of a right heart catheterization with inhaled nitric oxide challenge and had both methods of CO and CI calculations before and after the challenge. Intra-class correlation was used to demonstrate correlation.

Results: There was a significant correlation between the CO/CI calculated by TD before and after iNO with an ICC of 0.9 (0.83170, 0.94147) for CO and ICC of 0.89 (0.81457, 0.93583.) for CI. There was a weak yet statistically significant correlation between CO/CI calculated by FM before and after iNO with an ICC 0.45 (0.20323, 0.64301) for CO and 0.43 (0.17657 0.62996) for CI. The average pre iNO pulmonary artery (PA) saturation was 67.3% and the average PA saturation post iNO was 79.8%. There was a significant difference between PA saturations of 12.5% (p<0.001).

Conclusion: We found that the CO and CI pre- and post iNO had a stronger correlation by TD method than by FM. The FM is dependent on hemoglobin saturations which is higher in patients with PAH post iNO challenge. The TD is independent of the PA hemoglobin saturations and therefore is not augmented post iNO challenge and should be the preferred method of calculating CO and CI in patients undergoing RHC with iNO challenge.

Introduction

Pulmonary Arterial Hypertension (PAH) is characterized by remodeling of small pulmonary arteries, resulting in increasing pulmonary vascular resistance and ultimately leading to right ventricular failure [1]. Despite all advances in therapy, PAH continues to be a devastating disease and has a poor prognosis if it is not diagnosed and treated early. Unfortunately, most patients are still diagnosed in the late course of the disease [2]. This disorder affects about 15 individuals per million [3]. The diagnosis of PAH is based on hemodynamics obtained during a Right Heart Catheterization (RHC). The current accepted hemodynamic definition of PAH is a mean Pulmonary Artery Pressure (mPAP) equal or greater than 25 mm Hg or a Pulmonary Vascular Resistance (PVR) greater than 3 Wood units along with Left Ventricular End-Diastolic Pressure (LVEDP) or the surrogate measurement of pulmonary capillary wedge pressure (PCWP) when it is less than or equal to 15 mmHg; [4]. The Cardiac Output (CO) and index (CI) are also important measurements during the RHC, they are strong predictors of mortality in patients with PAH and they are used to define “response” to the Vasoreactivity Challenge (VC) [5]. The VC is recommended only for patients with Idiopathic PAH (IPAH) [4]. It involves intravenous or inhaled administration of a rapid acting specific pulmonary vasodilator [6]. Inhaled Nitric Oxide (iNO) is known to vasodilate the pulmonary arteries and thus decreases the pulmonary vascular resistance (PVR) [5,7]. A positive VC is defined as a decrease in mPAP by 20% (about 10 mmHg) and the mPAP should be less than 40 mmHg or into the normal range. The CO must be preserved [5]. The importance of determining acute response is both diagnostic and prognostic. Acute responders typically have better long-term survival and are candidates for initial calcium-channel blocker therapy [8-10].

To calculate the CO and CI we used two accepted methods; the Fick Method (FM) and the Thermodilution method (TD) [11]. Several studies have compared different technologies to measure CO, but only a few studies have tried to answer whether the FM or TD is better in patients with PAH [12]. Recent studies show that there are significant discrepancies between the CO measured by FM or TD [13,14]. We have recently studied and found a good correlation of TD and FM in mild, moderate and severe PAH pre iNO [15]. Rich et al showed that, a Non-Invasive Output Monitor (NICOM) was precise and reliably measuring CO at rest and after vasodilator challenge, and was comparable with FM and TD to detect such changes [16].

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In this manuscript, we retrospectively review the methods of calculating CO and CI via FM and TD and analyze whether these correlated better before and after iNO challenge.

Methods

We conducted a retrospective chart review of patients who underwent RHC for diagnosis or follow up of PAH at a university center and a tertiary referral hospital. All procedures were performed in a cardiac catheterization laboratory guided by fluoroscopy. To be included in the study, patients had to meet the definition for pulmonary arterial hypertension [4], and were non-responders to VC. All patients included in the study underwent a VC with iNO at 40 ppm with 100% oxygen for 5 minutes. Mean Pulmonary Artery Pressure (mPAP), PCWP, CO and CI measurements by both FM and TD were measured pre- and post iNO challenge. Saturation were measured in the inferior vena cava, superior vena cava, right atrium and pulmonary artery. All variables were summarized by means and Standard Deviations (SD). Demographic data and co-morbidities were recorded for each patient. An Intra-class Correlation Coefficient (ICC) was used to demonstrate strength of correlation between CO and CI calculated by FM before and after iNO challenge and similarly by TD before and after iNO challenge. We used student’s “t” test to compare the difference between the mean saturations before and after iNO challenge.

Methods to measure cardiac output

Thermoludiation method: The TD method is based on the principles of dilution uses a room temperature (cold) bolus (10 mL) of sterile solution that is injected into the proximal port of a pulmonary artery catheter. This ends up in the right atrium. Here, the cold saline mixes with the blood and passes through the tricuspid valve. A thermistor within the catheter senses the change in blood temperature as the blood passes the catheter tip located in the pulmonary artery. A curve that shows the change in temperature over time is generated by a computer and converted into a measurement of CO/CI given that CO/CI is inversely proportional to the area under the curve [17]. In other words, the higher the CO/CI the less time the bolus has to warm to body temperature.

Fick method: The FM first described by Adolph Fick in 1870, uses the quotient of the oxygen consumption and the difference of the arterial and mixed venous oxygen content [19].

The used Resting O$_2$ Consumption was 125ml O$_2$ per square meter per minute [18].

Results

One hundred and eighty patient’s charts were reviewed; out of them, 50 (27%) met inclusion criteria matching the diagnosis of PAH and were non-responders to VC. Sixty two percent were females. The most common comorbidities were obstructive lung disease (28%), obstructive sleep apnea (18%) and autoimmune/connective tissue disorder (14%). The hemodynamic parameters before and after iNO are summarized in Table 1. There was a statistically significant and strong correlation between the CO calculated by TD before and after iNO with an ICC of 0.89 (95% CI 0.81, 0.94.) (Figure 1). There was also a statistically significant and strong relationship observed for CI calculated by TD before and after iNO with an ICC of 0.87 (95% CI 0.81, 0.93). There was a statistically significant weak correlation between CO calculated by FM before and after iNO with an ICC of 0.45 (95% 0.20, 0.64) (Figure 2). There was the same statistically significant weak relationship observed for CI calculated by FM before and after iNO with an ICC of 0.43 (95% 0.18, 0.63). The COs by FM and TD before iNO had a difference of the means of 0.19 L/min, with an ICC 0.7 (95% 0.53, 0.82). The average COs by FM and TD after iNO had a difference of means of 1.92 L/min with a statistically significant weak correlation with ICC of 0.49 (95% 0.25, 0.67).

The average pre iNO PA saturation was 67.3% (sd; 8.3%) and the average PA post iNO was 79.9% (sd; 10.1%). (There was a statistically significant difference between saturations of 12.6% (sd; 6.3%) (p<0.001)

Discussion

The FM first described by Adolph Fick in 1870, uses the quotient of the oxygen consumption and the difference of the arterial and mixed venous oxygen content [19].

Table 1. Hemodynamic Parameters before and after Inhaled Nitric Oxide

| PRE - iNO (sd) | POST - iNO (sd) | Difference | p |
|---------------|----------------|------------|----|
| mPAP (mmHg)  | 39.6 (10.7)    | 34.9 (10.9) | 4.7 | 0.55 |
| PCWP (mmHg)  | 11.1 (4.0)     | 13.0 (5.0)  | -1.9 | 0.93 |
| PVR (Woods Units) | 6.09 (4.7) | 7.43 (3.8)  | -1.66 | 0.99 |
| Fick CO (L/min) | 5.77 (2.3) | 3.69 (1.5)  | -0.75 | 0.99 |
| Fick CI (L/min/m²) | 2.94 (1.0) | 2.85 (0.9)  | -0.05 | 0.08 |
| TD CO (L/min/m²) | 5.58 (2.4) | 5.61 (2.4)  | 0.03 | 0.5 |
| TD CI (L/min/m²) | 2.80 (1.1) | 79.9 (10.1) | 12.6 | p<0.001 |
| PA Saturation (%) | 67.3 (8.3) | 79.9 (10.1) | 12.6 | p<0.001 |

iNO: inhaled Nitric Oxide, mPAP: mean Pulmonary Arterial Pressure, PCWP: Pulmonary Capillary Wedge Pressure, PVR: Pulmonary Vascular Resistance, Fick CO: Cardiac Output by Fick method, Fick CI: Cardiac Index by Fick method, TD CO: Cardiac Output by Thermoludiation Method, TD CI: Cardiac Index by Thermoludiation Method, PA: Pulmonary Artery
In conclusion, the CO and CI in patients with PAH predict both prognosis and whether the patients have a positive vasodilatation challenge. The weak correlation of the CO and CI by FM after iNO can be explained by the augmentation of the PA saturation. During the iNO challenge, there is a stronger correlation between CO and CI obtained by TD than by FM. It can be explained by the TD’s independence on the arterial or mPAP hemoglobin saturations. Most of the patients studied were non-responders and no change in the CO and CI were expected. Therefore, for iNO vasoreactivity testing in patients with PAH, the TD measurement of the CO and CI should be used rather than the FM, as TD has a much stronger correlation before and after the iNO challenge.

This study was retrospective study and some patients with chronic hypoxemic respiratory failure were given oxygen before and during the procedure. This may have altered the pre iNO pulmonary artery saturations. A prospective randomized trial would be needed to validate our study.

Authorship

All authors listed on this manuscript made a significant contribution on the Conception and design of the project, data collection analysis and interpretation, rafting of the manuscript and final approval of the version to be published.

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