

# Agreement and Correlation between Arterial and Central Venous Blood Gas Following Coronary Artery Bypass Graft Surgery

MASOUMEH ESMAELIVAND<sup>1</sup>, ALIREZA KHATONY<sup>2</sup>, GHOLAMREZA MORADI<sup>3</sup>, FARID NAJAFI<sup>4</sup>, ALIREZA ABDI<sup>5</sup>

## ABSTRACT

**Introduction:** Arterial blood sampling, used to assess patients in acute conditions, may result in complications such as thrombosis and embolism. However, it can be replaced by venous blood sampling, but there is a dearth of information on this.

**Aim:** To assess the correlation and agreement between the arterial and central venous blood gases analyses in patients undergoing elective Coronary Artery Bypass Graft (CABG) surgery.

**Materials and Methods:** In this cross-sectional study, 100 ICU patients undergoing elective CABG surgery were recruited. 2 mm arterial and a 2 mm venous blood samples were obtained from each patient's arterial and central venous lines, respectively. To predict Arterial Blood Gas (ABG) values based on central Venous Blood Gas (VBG) values, the linear regression analysis was used and for evaluating their agreement Bland–Altman method was used.

**Results:** In total of 200 samples were obtained. The mean

and Standard Deviation (SD) of age was 58.9±9.1 years and 51% of the participants were female. There was a strong correlation between ABG and central VBG values regarding pH, partial Pressure of Carbon Dioxide (PCO<sub>2</sub>), Bicarbonate (HCO<sub>3</sub>) and Base Excess (BE) (r= 0.73, r=0.74, r=0.67 and r=0.71, respectively; p<0.001); however, the correlation between the arterial and venous Partial Pressure of Oxygen (PO<sub>2</sub>) and Oxygen Saturation (SO<sub>2</sub>) was moderate (r=0.29, p=0.005 and r=0.27, p=0.006, respectively). The Bland–Altman analysis showed an excellent agreement between all the variables (p<0.001).

**Conclusion:** Central VBG analysis cannot replace ABG analysis in measuring exact PO<sub>2</sub> status, necessitating arterial sampling in some matters, but with respect to the accuracy of pulse oximetry measurements in determining the exact PO<sub>2</sub> status, for the rest of the indices a central VBG rather than an ABG can be utilised for determining patient's acid-base status. Particularly in patients who are hospitalised for a long time and have a central venous catheter in place like patients who have undergone CABG, thus reducing the risk and need for invasive arterial sampling.

**Keywords:** Arterial blood gas, Blood gas analysis, Venous blood, Venous blood gas

## INTRODUCTION

ABG is an effective method of estimating PO<sub>2</sub>, PCO<sub>2</sub>, bicarbonate and pH, usually for the purpose of assessing ventilation and/or acid-base status [1]. However, the procedure of obtaining a blood sample for ABG analysis is invasive and painful and maybe associated with complications such as thrombosis, embolism, haematoma, aneurism, distal limb ischemia and infections. In addition, for the medical staff, this procedure entails needle-stick injuries and subsequent exposure to infections such as HIV and hepatitis [1].

ABG indices such as the pH, PCO<sub>2</sub> and HCO<sub>3</sub> offer a tool to evaluate the patient's perfusion status and give the physician the chance to resuscitate the patient [2]. VBG is an alternative and safe method of estimating systemic carbon dioxide and pH [3,4]. Some recent studies have documented no significant difference between arterial and venous pH in some special settings; therefore, these studies recommended venous, instead of arterial, blood sample for pH analysis. Studies also revealed a significant correlation between the arterial and venous bicarbonate levels [5-8]. Moreover, Partial Pressure of Venous Carbon Dioxide (PvCO<sub>2</sub>) can be considered as a screening method in the diagnosis of arterial hypercapnia [9]. Some of these studies are not extensively generalizable due to their small sample size [3,10] and most of them have not examined the correlation between all six blood gas indices. To date, most of the studies conducted were in patients with respiratory distress or ketoacidosis and a few studies have been done in patients in the ICU which have shown somewhat contradicting results [3,11-16]. A lack of evidence, in terms of the precision of VBG in the assessment of the patients in different conditions like postoperative, does exist.

The purpose of this study was to assess the correlation and agreement between the arterial and central VBG analyses in patients undergoing elective CABG surgery.

## MATERIALS AND METHODS

The study population consisted of all patients undergoing CABG in a large-scale university-affiliated hospital in Kermanshah, Iran from June 2011 to June 2012. The study protocol was approved by both the Institutional Review Board and the Ethics Committee of Kermanshah University of Medical Sciences. Patients' confidentiality of data was maintained throughout the study. All the patients gave their written and informed consent.

Excluding criteria were any known histories of renal, hepatic and respiratory failure, recent history of cigarette smoking, undergoing intra or postoperative cardiopulmonary resuscitation, experiencing postoperative hypothermia or hyperthermia, haemodynamic instability, severe bleeding, or aged < 30 years or > 75 years.

After the patients underwent CABG operation, they usually have an arterial and a central venous line in place; therefore, obtaining an arterial and venous blood sample in these patients is an easy process. Four to six hours after extubation from a ventilator, we measured and documented the patients' body temperature using an oral glass thermometer. Thereafter, we obtained a 2 mm arterial and 2 mm venous blood sample from each patient's arterial and central venous line, respectively. Blood samples were drawn into tubes which were covered with heparin.

Using an ice-filled container we immediately transferred the samples to the hospital's laboratory and the blood was analysed with a blood

gas analyser (Nova Biomedical®, Waltham, US). The analyser was standardised daily for prevention of miscalculation on a daily basis using a quality control assurance protocol. At the time of blood sampling, the patients were receiving nasal oxygen at a rate of 4–6 litre per minute.

The data collection tool consisted of a demographic questionnaire and a data sheet for documenting the ABG and VBG values.

The normal ranges for the ABG indices were considered as: pH = 7.35 to 7.45; PCO<sub>2</sub>, 35–45 mmHg; HCO<sub>3</sub>, 21–28 mmol/L; PO<sub>2</sub>, 83–108 mmHg; SO<sub>2</sub>, 95–98% and BE, -2 to +3 mmol/L.

### STATISTICAL ANALYSIS

To calculate the sample size, we employed the Power and Sample Size (PS) calculation software (Vanderbilt). PS is a user-friendly mini-program for sample size calculation. With presumption of the minimum value of correlation coefficient for oxygen pressure as 0.29 [10] and a confidence interval of 95%, the PS output for sample size was 100. Accordingly, we recruited a convenient sample of 100 patients undergoing elective CABG. We employed the Stata software (version 12; Stata Corporation, College Station, TX) for data analysis. The Bland-Altman method was employed to assess the agreement between the arterial and venous values. To examine the correlation between ABG and VBG indices we employed the Pearson's correlation test. On the other hand, to predict the ABG values based on the VBG values we employed the linear regression analysis. The significant level for the tests was 0.05.

### RESULTS

In total, 200 blood samples were obtained from 100 patients (100 for ABG and 100 for VBG). Patient's mean age was 58.9±9.1 (mean±SD) years. Total 51% of the participants were female. None of the patients were febrile (ranging from 36.8°-37.5°).

Based on the arterial blood samples, only 45 patients had normal pH values. According to the ABG samples, 23 patients had acidosis and 32 patients had alkalosis. The mean arterial and venous pH was 7.40±0.08 and 7.36±0.07, respectively. In our study the mean (95% CI) difference between the arterial and venous pH, HCO<sub>3</sub> and PCO<sub>2</sub> were 0.046 (0.025-0.067), -1.41 (-2.42 to -0.41) and 6.59 (4.58-8.34), respectively.

The results of the Pearson's correlation test showed a strong and positive correlation between ABG and VBG values regarding pH, partial PCO<sub>2</sub>, bicarbonate (HCO<sub>3</sub>) and BE r=0.73, r=0.74, r=0.67, r=0.71, respectively; p<0.001 for all the variables); however, the correlation between the arterial and venous partial PO<sub>2</sub> and SO<sub>2</sub> was moderate (p=0.005 and p=0.006, respectively) [Table/Fig-1].

The linear regression model for estimating the arterial values based on the venous variables showed the following relationship:

$$\begin{aligned} \text{pHa} &= 1.33 + (0.83 \times \text{pHv}) \\ \text{PaCO}_2 &= 4.63 + (0.73 \times \text{PvCO}_2) \\ \text{HCO}_3\text{a} &= 6 + (0.70 \times \text{HCO}_3\text{v}) \\ \text{BEa} &= -0.7 + (0.71 \times \text{BEv}) \end{aligned}$$

The letters 'a' and 'v' in the indices stand for arterial and venous, respectively.

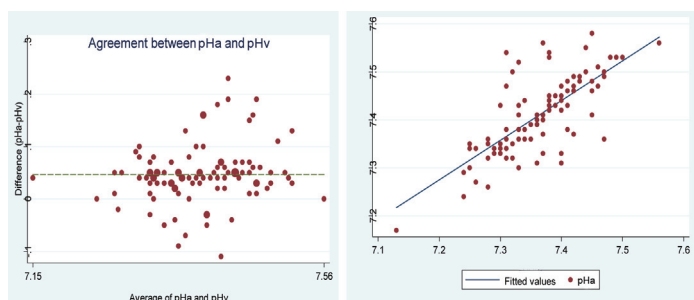
| Blood gas indices        | Arterial    | Venous      | Mean difference (95% CI)* | Pearson's r (95% CI) | R square | p-value | β slop (95% CI)  |
|--------------------------|-------------|-------------|---------------------------|----------------------|----------|---------|------------------|
| pH                       | 7.40±0.08   | 7.36±0.07   | 0.046 (0.025 to 0.067)    | 0.73 (0.66 to 0.98)  | 0.53     | < 0.001 | 0.83 (0.67–0.97) |
| PCO <sub>2</sub> -mmHg   | 35.75±6.24  | 42.35±6.27  | 6.59 (4.85 to 8.34)       | 0.74 (0.60 to 0.82)  | 0.55     | < 0.001 | 0.73 (0.60–0.89) |
| HCO <sub>3</sub> -mmol/L | 23.00±0.68  | 24.40±3.54  | -1.41 (-2.42 to -0.41)    | 0.67 (0.53 to 0.85)  | 0.45     | < 0.001 | 0.70 (0.54–0.85) |
| PO <sub>2</sub> -mmHg    | 86.92±24.20 | 47.55±8.31  | 39.36 (34.32 to 44.41)    | 0.29 (0.15 to 0.82)  | 0.08     | 0.005   | 0.83 (0.28–1.39) |
| SO <sub>2</sub> (%)      | 95.42±2.85  | 76.37±10.56 | 19.03 (16.88 to 21.19)    | 0.27 (0.14 to 0.35)  | 0.07     | 0.006   | 0.07 (0.02–0.12) |
| BE-mmol/L                | -1.30±4.18  | -0.85±4.20  | -0.44 (-1.61 to 0.72)     | 0.71 (0.57 to 0.85)  | 0.50     | < 0.001 | 0.71 (0.57–0.85) |

[Table/Fig-1]: Results of the Pearson's correlation test and linear regression analysis in terms of the arterial and venous blood gas indices\*. \* All the mean±values are means±standard deviations unless stated otherwise. The differences are arterial values minus venous values.

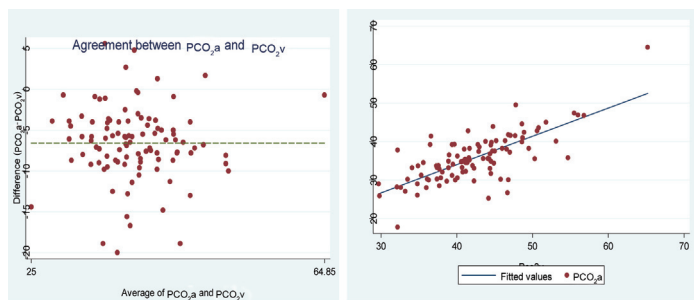
The results of Bland-Altman showed a good agreement between ABG and VBG indices, however, this agreement was more about HCO<sub>3</sub> and pH and less agreement was found in term of SO<sub>2</sub> and PO<sub>2</sub> [Table/Fig-2]. [Table/Fig-3-6] expresses Bland-Altman plot of arterial and central venous blood and fitted linear regression of ABG and VBG indices.

| Blood gas indices         | Agreement coefficient | p-value | 95% CI       |
|---------------------------|-----------------------|---------|--------------|
| pH                        | 0.60                  | < 0.001 | 0.50 to 0.70 |
| PCO <sub>2</sub> - mmHg   | 0.47                  | < 0.001 | 0.37 to 0.57 |
| HCO <sub>3</sub> - mmol/L | 0.62                  | < 0.001 | 0.50 to 0.73 |
| PO <sub>2</sub> - mmHg    | 0.05                  | < 0.001 | 0.01 to 0.08 |
| SO <sub>2</sub> (%)       | 0.03                  | < 0.001 | 0 to 0.05    |
| BE - mmol/L               | 0.70                  | < 0.001 | 0.61 to 0.80 |

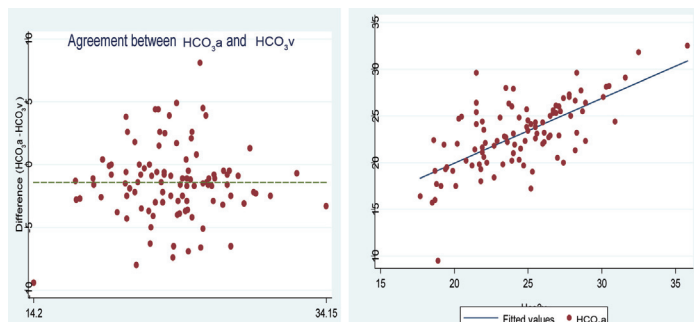
[Table/Fig-2]: The results of the Bland-Altman method for examining the agreement between the arterial and venous blood gas indices.



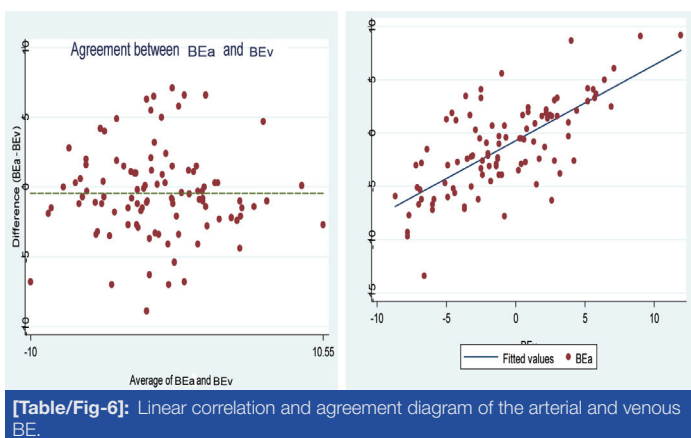
[Table/Fig-3]: Bland-Altman plot of arterial and central venous blood pH fitted linear regression.



[Table/Fig-4]: Bland-Altman plot of arterial and central venous blood PCO<sub>2</sub> fitted linear regression.



[Table/Fig-5]: Bland-Altman plot of arterial and central venous blood HCO<sub>3</sub> fitted linear regression.



**[Table/Fig-6]:** Linear correlation and agreement diagram of the arterial and venous BE.

## DISCUSSION

The aim of this study was to examine the correlation and agreement between the arterial and central VBG in patients undergoing CABG. The study findings showed a strong and significant correlation and agreement between the ABG and VBG related variables.

Treger R et al., studied the agreement and correlation between ABG and VBG variables among 40 ICU patients [3]. Among the 190 samples that were analysed, similar to our study, they found that venous  $PO_2$  cannot replace arterial  $PO_2$  in patients receiving acute care, although this group of patients probably have a pulse oximetry which decreases the need for evaluation of  $SO_2$  and  $PO_2$  using an arterial blood sample. It is notable that the patients mostly had sepsis, which might not have been a good representative of ICU patients.

In their Bland-Altman analysis for agreement between ABG and VBG, they also found an excellent agreement between arterial and venous pH and  $HCO_3$ . They documented that in regression models, multivariate analysis in determining arterial pH, does not change the  $R^2$  considerably, showing that a univariate linear regression equation is a good predictor of arterial pH.

Rudkin SE et al., in their study in 2012 among 346 trauma patients, found that their regression model was able to predict 72% of the arterial pH [11], although their equation was very similar to ours, their's had a higher predictive power ( $R^2=0.70$  vs  $R^2=0.52$ ) and concluded that it was not appropriate for use among patients who need acute intensive care since the management of this group is sensitive and requires more consistency. Regarding BE they also had a similar regression model compared to ours but still had a higher predictive power ( $R^2=0.75$  vs.  $R^2=0.50$ ).

In a study in 2010, they found that among patients that were undergoing lumbar disk surgery, arterial and VBG values correlated strongly regarding pH,  $PCO_2$ ,  $HCO_3$ , BE and  $SO_2$  ( $r=0.93$ ,  $r=0.89$ ,  $r=0.88$ ,  $r=0.86$ ,  $r=0.34$ ;  $p<0.001$ ) but did not correlate very strongly regarding  $PO_2$  ( $p = 0.394$ ) [8]. They documented different linear regression models when compared to our study.

This could be due to some factors like the setting of our study as our patients were patients who underwent CABG operation and our samples were obtained during the postoperation period, whereas, their samples were obtained two hours after induction of anaesthesia and during operation, which might have caused a fluctuation in the blood gas variables, furthermore their samples were obtained from a peripheral vein unlike our study which was obtained from a central vein source. The difference between central and peripheral samples might be attributed to some difference between the results of the two studies, as one study by Toftegaard M et al., in 2008 [20], found that ABG was more compatible with VBG obtained from a central line rather than a peripheral line in term of  $PCO_2$ , however about pH both types of veins (peripheral and central veins) have more acceptable coherency with ABG.

In a meta-analysis in 2014 by Bloom BM et al., evaluated the differences between ABG and VBG variables [17]. They found a pooled mean difference of 0.033 (vs. 0.046 in our study) and 1.03 (vs. 1.41 in our study) for pH and bicarbonate between arterial and venous samples, respectively. Regarding  $PCO_2$  they found a mean difference of 4.41 (vs. 6.59 in our study) mmHg among studies. Overall they found venous pH and bicarbonate were good representative of ABG, although for  $PCO_2$  it was not the same.

The Bloom BM et al., study was also indicative to using VBG in some parameters such as pH, although their review only included studies that had patients with stable circulatory status [17].

In a review published in 2010, Kelly AM et al., evaluated the consistency between arterial and venous blood gas variables among studies published between 1966 and 2010 [18]. They reported that among 12 studies that met their inclusion criteria, regarding pH, studies that evaluated patients with ketoacidosis in comparison to those that evaluated patients with COPD, reported more consistency between their arterial and venous pH (weighted difference of 0.02 vs. 0.03). Regarding  $PCO_2$ , the review showed that among three studies that evaluated arterial hypercarbia with laboratory based testing [5,9,19], all reported a 100% sensitivity for a cut-off of 45 mmHg in venous samples. For bicarbonate, when they pooled the data of seven studies, they found a weighted difference of 1.41 mmol/L between arterial and venous values.

For base excess, Toftegaard M et al., showed that the difference between ABG and VBG was 0.089 mmol/L [20].

One study in 2005 showed that VBG is not a good replacement for ABG, when evaluating blood gas variables in post-trauma patients receiving treatment in intensive care unit [21].

In a recent study by Shirani F et al., they found that low blood pressure (systolic blood pressure less than 90) can increase the difference between arterial and venous related variables in the blood gas analysis [22]. It may be clinically notable that some special conditions should be considered when using a venous blood gas for patient evaluation and management. On the other hand, some studies [20] have indicated that agreement between ABG and VBG variables may be maintained in haemodynamic instability.

Middleton P et al., also reported a significant correlation and agreement between the arterial and venous pH, bicarbonate and base excess and suggested the use of venous pH instead of arterial pH for ICU patients [10].

In our study, the agreement and correlation between the arterial and central venous  $PCO_2$  was also strong and significant. However, the results of the study by Parvizi R et al., revealed a weak correlation between arterial and venous  $PCO_2$  and  $PO_2$  in patients undergoing cardiac surgery [13]. They found a significant difference between arterial and venous blood gas variables and concluded that these two cannot be interchangeably used. They made this conclusion based on the difference between ABG and VBG variables before, during and after operating room, that the patients have taken some medications, in compared to our study in which, we evaluated the changes and the correlation among the blood gas indices at least one day after surgery. So their findings may not have been a good indication for this conclusion.

In terms of BE, our findings also showed a strong and significant correlation between arterial and central venous values. However, the correlation and agreement between the arterial and central venous  $PO_2$  and  $SO_2$  was weak.

## LIMITATION

We recruited a convenience sample for the study. Convenience sampling entails a low generalizability. Since, only patients undergoing CABG were studied, the findings may not be generalizable to all patients and settings. Our patients were postoperative and they all had a central line in place which is not applicable for every patient setting.

Since the peer management of patients based on their VBG indices would be unethical, our study, like previously conducted studies, did not allow an absolute clinical evaluation of patients based on VBG.

## CONCLUSION

Central VBG analysis cannot replace ABG analysis in measuring exact PO<sub>2</sub> status, necessitating arterial sampling in some cases, but with respect to the accuracy of pulse oximetry measurements in determining the exact PO<sub>2</sub> status, for the rest of the indices a central VBG rather than an ABG can be utilised for determining patient's acid-base status. Particularly in patients who are hospitalised for a long time and who have a central venous catheter in place like patients who have undergone CABG, thus reducing the risk and need for invasive arterial sampling.

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## REFERENCES

- [1] O'Connor TM, Barry PJ, Jahangir A, Finn C, Buckley BM, El-Gammal A. Comparison of arterial and venous blood gases and the effects of analysis delay and air contamination on arterial samples in patients with chronic obstructive pulmonary disease and healthy controls. *Respiration; international review of thoracic diseases*. 2011;81(1):18-25.
- [2] Trauma ACoSoc. *Advanced Trauma Life Support for Doctors*.: American College of Surgeons. Chicago, IL. 1997.
- [3] Treger R, Pirouz S, Kamangar N, Corry D. Agreement between central venous and arterial blood gas measurements in the intensive care unit. *Clin J Am Soc Nephro*. 2010;5(3):390-94.
- [4] Walkey AJ, Farber HW, O'Donnell C, Cabral H, Eagan JS, Philippides GJ. The accuracy of the central venous blood gas for acid-base monitoring. *J Intensive Care Med*. 2010;25(2):104-10.
- [5] Ak A, Ogun CO, Bayir A, Kayis SA, Koylu R. Prediction of arterial blood gas values from venous blood gas values in patients with acute exacerbation of chronic obstructive pulmonary disease. *Tohoku J Exp Med*. 2006;210(4):285-90.
- [6] Kelly AM. The case for venous rather than arterial blood gases in diabetic ketoacidosis. *Emerg Med Australasia*. 2006;18(1):64-67.
- [7] Kelly AM, McAlpine R, Kyle E. Venous pH can safely replace arterial pH in the initial evaluation of patients in the emerg department. *Emerg Med J*. 2001;18(5):340-42.
- [8] Khan ZH, Samadi S, Sadeghi M, Alemohammad MG, Zanjani AP, Adine-Hashtjin S, et al. Prospective study to determine possible correlation between arterial and venous blood gas values. *Acta anaesthesiologica Taiwanica: Official Journal of the Taiwan Society of Anesthesiologists*. 2010;48(3):136-39.
- [9] Kelly AM, Kerr D, Middleton P. Validation of venous PCO<sub>2</sub> to screen for arterial hypercarbia in patients with chronic obstructive airways disease. *J Emerg Med*. 2005;28(4):377-79.
- [10] Middleton P, Kelly AM, Brown J, Robertson M. Agreement between arterial and central venous values for pH, bicarbonate, base excess, and lactate. *Emerg Med J*. 2006;23(8):622-24.
- [11] Rudkin SE, Kahn CA, Oman JA, Dolich MO, Lotfipour S, Lush S, et al. Prospective correlation of arterial vs venous blood gas measurements in trauma patients. *Am J Emerg Med*. 2012;30(8):1371-77.
- [12] Razi E, Moosavi GA. Comparison of arterial and venous blood gas analysis in patients with exacerbation of chronic obstructive pulmonary disease. *Saudi Med J*. 2007;28(6):862-65.
- [13] Parvizi R, Safaai N, Neghargar S, Rasouli S. Comparison of arterial and venous blood gas values in cardiac surgery. *Rawal Med J*. 2008;33(1):30-33.
- [14] McCanny P, Bennett K, Staunton P, McMahon G. Venous vs arterial blood gases in the assessment of patients presenting with an exacerbation of chronic obstructive pulmonary disease. *Am J Emerg Med*. 2012;30(6):896-900.
- [15] Lim BL, Kelly AM. A meta-analysis on the utility of peripheral venous blood gas analyses in exacerbations of chronic obstructive pulmonary disease in the emergency department. *Eur J Emerg Med*. 2010;17(5):246-48.
- [16] Kelly AM. Can VBG analysis replace ABG analysis in emergency care? *Emerg Med J*. 2014;1-3.
- [17] Bloom BM, Grundlingh J, Bestwick JP, Harris T. The role of venous blood gas in the emergency department: a systematic review and meta-analysis. *Eur J Emerg Med*. 2014;21(2):81-88.
- [18] Kelly AM. Can venous blood gas analysis replace arterial in emergency medical care. *Emerg Med Australasia*. 2010;22(6):493-98.
- [19] Kelly AM, Kyle E, McAlpine R. Venous PCO<sub>2</sub> and pH can be used to screen for significant hypercarbia in emergency patients with acute respiratory disease. *J Emerg Med*. 2002;22(1):15-19.
- [20] Toftegaard M, Rees SE, Andreassen S. Correlation between acid-base parameters measured in arterial blood and venous blood sampled peripherally, from vena cavae superior, and from the pulmonary artery. *Eur J Emerg Med*. 2008;15(2):86-91.
- [21] Malinoski DJ, Todd SR, Slone S, Mullins RJ, Schreiber MA. Correlation of central venous and arterial blood gas measurements in mechanically ventilated trauma patients. *Arch Surg*. 2005;140(11):1122-25.
- [22] Shirani F, Salehi R, Naini AE, Azizkhani R, Gholamrezaei A. The effects of hypotension on differences between the results of simultaneous venous and arterial blood gas analysis. *J Res Medical Sci*. 2011;16(2):188-94.

### PARTICULARS OF CONTRIBUTORS:

1. Lecturer, Department of Nursing, School of Nursing and Midwifery, Kermanshah University of Medical Sciences, Kermanshah, Iran.
2. Associate Professor, Department of Nursing, Nursing and Midwifery School, Kermanshah University of Medical Sciences, Kermanshah, Iran.
3. Assistant Professor, Department of Anesthesiology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran.
4. Professor, Department of Epidemiology, Research Center for Environmental Determinants of Health (RCEDH), Kermanshah University of Medical Sciences, Kermanshah, Iran.
5. Assistant Professor, Department of Nursing, School of Nursing and Midwifery, Kermanshah University of Medical Sciences, Kermanshah, Iran.

### NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Alireza Khatony,  
Dolat Abad Street, Kermanshah-6714634698, Iran.  
E-mail: akhatony@gmail.com

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