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Original Article

# Evaluation of the relationship of Delta-$CO_2$ with IVC-CI, IJV-CI, and CVP values in intubated critically ill patients with spontaneous breathing, and who were applied invasive mechanical ventilation in CPAP mode

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**Abstract**

**Aim:** Our aim in this study is to understand whether there is a correlation between IVC-CI, IJV-CI, CVP, and Delta-$CO_2$ values in critical patients in the ICU and whether these values can be used interchangeably in monitoring intravascular fluid status..

**Materials and Methods:** Patients included in this study were selected from critical ICU patients between 18-90 years old with an unknown hypovolemic status that had spontaneous breathing and underwent invasive mechanical ventilation in CPAP mode. Patients' parameters were consecutively measured by USG with the inferior vena cava collapsibility index (IVC-CI), internal jugular vein collapsibility index (IJV-CI), CVP, and Delta-$CO_2$. The results were recorded, and any correlations were checked.

**Results:** There was a statistically significant and moderately negative correlation ($r = -0.428$, $p < 0.001$) between CVP and IVC-CI, and a statistically significant and weakly negative correlation between CVP and IJV-CI ($r = -0.374$, $p = 0.001$). There was a statistically significant and weakly positive correlation ($r = 0.369$, $p = 0.001$) between IVC-CI and IJV-CI. There was no statistically significant correlation between Delta-$CO_2$ and IVC-CI, IJV-CI, and CVP.

**Conclusion:** We think that CVP, IVC-CI and IJV-CI can be used interchangeably in the assessment of the intravascular volume status of critical patients, but Delta-$CO_2$ cannot be used to assess intravascular volume status instead of these parameters.

**Keywords:** Inferior vena cava collapsibility index; internal jugular vein collapsibility index; central venous pressure; delta carbon dioxide; intravascular volume status

## INTRODUCTION

Rapid, earliest, noninvasive, effective and reproducible assessment of intravascular volume status in hemodynamic monitoring is important for critical patients (with polytrauma and/or sepsis) admitted to the intensive care unit (ICU) and it is the duty of the physician responsible for intensive care (1). Early fluid therapy affects mortality and morbidity in patients with sepsis and polytrauma (2,3). The clinical examination is uncertain and unreliable in the assessment of the intravascular volume status (1). Vital signs are poor markers in evaluating fluid response in hemorrhage, shock and trauma (1). Central venous pressure (CVP) measurement is the gold standard in intravascular volume assessment, but it is invasive, time-consuming and requires experienced personnel (1). CVP measurement is not a practical method, it involves complications and risks (1). Inferior vena cava collapsibility index (IVC-CI) measurement is a noninvasive, easily applicable, practical method (1). IVC-CI measurements are correlated with CVP and safely reflect fluid status (1). However, measurement of IVC-CI is impossible in the case of an intra-abdominal surgery, excess intra-abdominal gas, a large amount of intra-thoracic air, over-compression of IVC, increased intra-abdominal pressure, obesity, and certain heart diseases (10-15%) (1). IJV-CI is also a technique used in the assessment of intravascular volume status (4-7). Observing the high IJV pulsation is frequently used in the clinic and provides an indirect measurement of CVP and right atrial pressure, but its sensitivity is poor (1). However, a physical examination showed that only 50% of all these patients correctly reflect the IJV-CI right atrial pressure (1). Although it is indicated in various studies that it shows the volume status of IJV-

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CI, IVC-CI and CVP, there is not enough data on whether there is a correlation between IVC-CI and IJV-CI (7). CVP and mean arterial pressure are important in ensuring tissue perfusion (8). Low-perfusion conditions and non-anaerobic carbon dioxide ($CO_2$) production increase the venous concentration of $CO_2$, and the normal venous-to-arterial CO2 (Delta-$CO_2$) difference increases (8). Delta-CO2 is a parameter that shows tissue perfusion in patients with sepsis. However, it is not included in the 2016 sepsis guideline (8).

We thought that there could be a correlation between IVC-CI, IJV-CI, CVP, and Delta-$CO_2$ values of intubated patients with unknown hypovolemic status who had spontaneous breathing, and invasive ventilation in CPAP mode, and that these values could be used interchangeably. Because CVP measurement requires an invasive procedure and experience. IVC-CI and IJV-CI also require experience. However, there no experience for Delta-$CO_2$ measurament.

Our aim in this study is to understand whether there is a correlation between IVC-CI, IJV-CI, CVP, and Delta-$CO_2$ values in critical patients hospitalized in ICU and whether these values can be used interchangeably in monitoring intravascular fluid status.

## MATERIAL and METHODS

After Gazi Yaşargil University of Health Sciences Training and Research Hospital (TR) local ethics committee approval (19.04.2019 /262), 79 ICU patients over 18 years old who had spontaneous breathing, were intubated for respiratory or hemodynamic reasons, and were followed up in CPAP mode were included in the study. Our study was planned as a prospective observational study. Written informed consent was obtained from the first-degree relatives of the patients included in the study. Our study was planned under the 2008 Helsinki declaration. The correlation between the IVC-CI and CVP values produced r = 0.541value in a pilot study held with 30 patients. Using r value from www.samplesize.net-correlation-sample-size website, it was found to be n = 38 when alpha = 0.05 and test power was 95%. Patients included in the pilot study were also included in the study.

This study included patients randomly selected from ICU patients, aged 18 to 90, with unknown fluid availability, spontaneous breathing and invasive mechanical ventilation in CPAP mode.

**Exclusion criteria:**

1. Patients with serious cardiac disease (cardiac pathology, pulmonary hypertension)

2. Patients with intra-abdominal pressure > 12 mmHg

3. Patients whose IVC and IJV cannot be displayed

4. Patients with a hypotensive course (patients with SAP below 90 mmHg despite noradrenaline infusion greater than 1µg/kg/min)

5. Patients who are not in sinus rhythm

6. Patients with a body temperature >37.5 and < 36 ºC

7. Patients without spontaneous breathing

8. Patients with $CO_2$ > 60 mmHg in arterial blood gas

9. Patients with APACHE II scores below 25.

10. Patients operated on chest and neck and undergoing radiotherapy

11. Patients with deep vein thrombosis of the upper extremity.

12. Pregnant patients

Patient'age, height, weight, gender, body mass index (BMI), APACHE-II score, peak heart rate (PHR), Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), peripheral oxygen saturation (SpO2), Delta-$CO_2$, and body temperature values were recorded.

Electrocardiography (ECG), $SpO_2$, intra-arterial cannulation followed by continuous invasive arterial pressure measurement, skin monitoring of peripheral body temperature and CVP monitoring with central venous catheter were performed with a Philips monitor (Philips, IntelliVueMX550, IntelliBrigde, Netherland) in a supine position, as routinely applied to all patients in the ICU.

Arterial blood gas was taken from the simultaneous intra-arterial cannula and central venous blood gas was taken from the CVP catheter. Delta-$CO_2$ was calculated by 'Delta-$CO_2$= Venous blood gas - artery blood gas' formula. IVC imaging was performed using the convex probe of the USG device (TOSHIBA TA 700, made in Japan), which was used in ICU for imaging patients' IVC. IJV imaging was done with a linear probe.

**CVP Measurement**

The patient was placed in a supine neutral position. CVP monitoring was performed and all fluid infusion from the central catheter was discontinued. The patient was then temporarily disconnected from the ventilator (over several breathing cycles) and the pressure on the monitor was recorded as mmHg.

**IVC-CI Measurement**

The patients were placed in the supine neutral position. Mechanical ventilator PEEP value was set as 5 $cmH_2O$. Via the convex probe of USG, IVC, aorta and vertebra were visualized as out-plane with B-Mode USG from the subxiphoid window (Figure 1). The USG probe was reversed clockwise without changing the point where it was located and the IVC was visualized in the in-plane position (Figure-2). After the visualization of the exit of IVC from the heart and the visualization of the hepatic vein, the USG cursor was placed in the section that is approximately 1 cm below the hepatic vein leaves the vena cava inferior and the M-Mode USG was opened. During several respiration periods, the IVC diameter was monitored and the diameter was measured from where the IVC diameter was the narrowest and widest

by freezing the screen (Figure-3). Screen printouts were taken for each patient separately. For each patient, IVC-CI was calculated using 'IVC-CI = (Vmax – Vmin) / VmaxX 100%' formula.

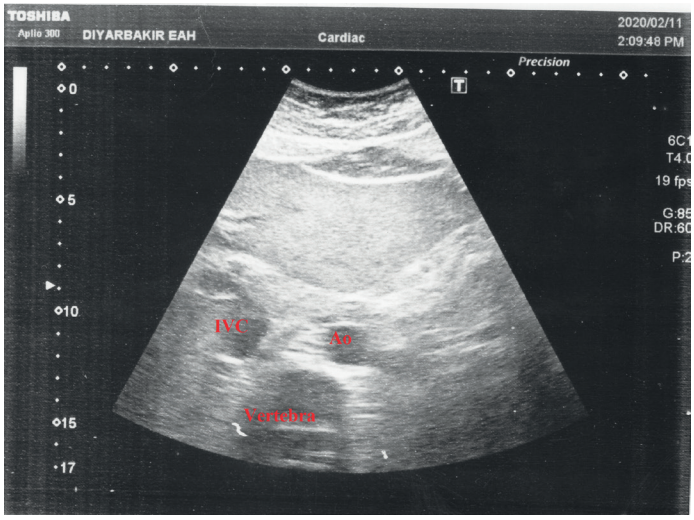


**Figure 1.** View of IVC, Aorta and Vertebra with B-Mode USG

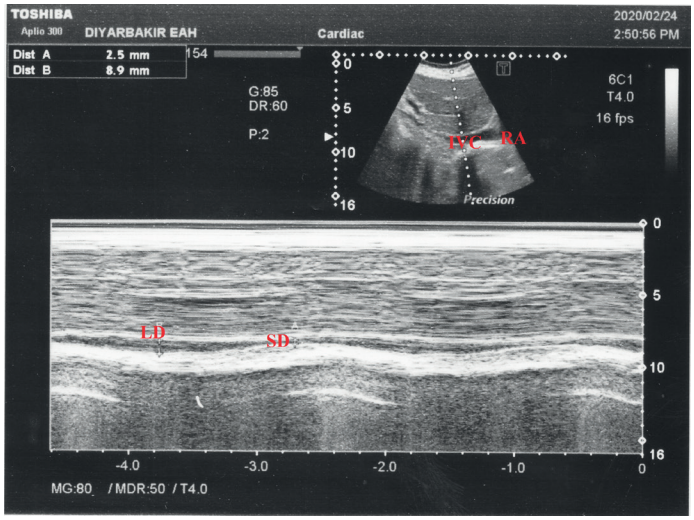


**Figure 2.** B-mode and M-mode view of IVC in in-plane position.

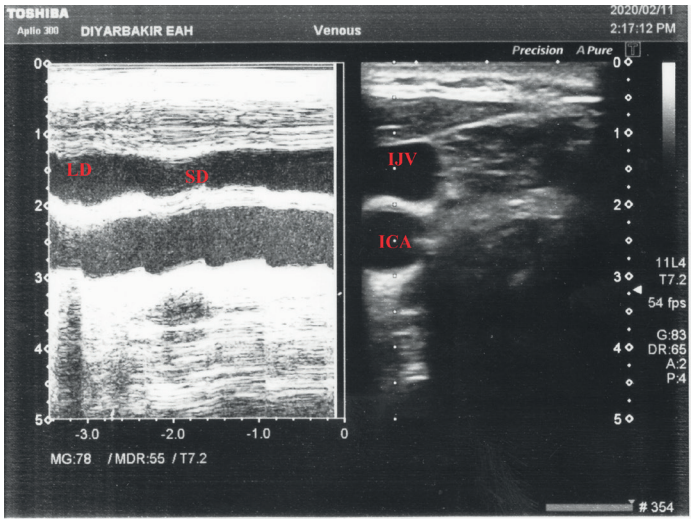


**Figure 3.** B-mode and M-mode view of IJV and ICA in in-plane position

### IJV – CI measurement

When the patient was in the supine position and the head was in 0 degrees position, a linear USG probe was placed 2 cm above the sterno clavicular junction from the right IJV and an IJV image was taken. The USG cursor was placed in a position where it would scan this image vertically and M-Mode USG was opened. Maximum and minimum diameter measurements were made by taking 4 breathing cycles (Figure 3). Measurement was made by applying minimal pressure with the USG probe. The IJV collapsibility index was calculated by 'Maximum Diameter-Minimum diameter / Maximum diameter X 100%' formula.

### Statistical analysis

All data were evaluated with SPSS for Windows 11.5. descriptive statistics of the data were made. Numerical data were defined as Mean ± SD, and categorical data were defined as % n. The relationship between patient data was examined by Pearson correlation test. The degree of relationship between the data was determined according to the Pearson correlation coefficient (r) value.

Interpretation of the Pearson correlation coefficient (r) value:

1. If r <0.2, a very weak correlation or no correlation
2. If 0.2 <r <0.4, a very weak correlation
3. If 0.4 <r<0.6, a moderate correlation
4. If 0.6 <r <0.8, a strong correlation
5. If r > 0.8, a very strong correlation

## RESULTS

Demographic and hemodynamic data of the patients are given in Table 1.

**Table 1. Demographic and hemodynamic values of patients (Mean±SD, %n)**

| | n | Mean | SD |
|---|---|---|---|
| Age (year) | 78 | 62.3077 | 20.39500 |
| Height (cm) | 78 | 166.62 | 10.25928 |
| Weight (kg) | 78 | 74.5641 | 15.68073 |
| BMI (%) | 78 | 26.8758 | 5.47606 |
| APACHE 2 | 78 | 27.1154 | 8.27291 |
| HR (Atım/dk) | 78 | 95.3333 | 22.63755 |
| SAP (mmHg) | 78 | 126.24 | 23.04157 |
| DAP (mmHg) | 78 | 68.4744 | 15.34937 |
| MAP (mmHg) | 78 | 85.2692 | 15.45389 |
| $SpO_2$ (%) | 78 | 97.1282 | 2.51416 |
| Body temperature (°C) | 78 | 36.6705 | 1.25637 |
| CVP(mmHg) | 78 | 5.8718 | 4.62169 |
| IVC-CI (%) | 78 | 42.4784 | 19.09599 |
| IJV-CI (%) | 78 | 38.4030 | 20.60147 |
| Delta-$CO_2$ | 78 | 6.8500 | 5.3753 |
| Gender Female/Male (% n) | 78 | 37-%47.4/ | 41-%52.6 |

There was a statistically significant moderately negative correlation between CVP and IVC-CI (Table 2, Figure 4-9).

There was a statistically significant weakly negative correlation between CVP and IJV-CI (Table 2, Figure 4-9).

There was a statistically significant weakly positive correlation between IVC-CI and IJV-CI (Table 2, Figure 4-9).

Delta-$CO_2$ did not have a statistically significant correlation with VCI-CI, IJV-CI, and CVP (Table 2, Figure 4-9).

**Table 2. Correlation between CVP, IVC-CI, Delta-CO2 and IJV-CI**

| | | CVP (mmHg) | IVC-CI (%) | IJV-CI (%) | Delta-$CO_2$ |
|---|---|---|---|---|---|
| CVP (mmHg) | r | 1 | -,428** | -.374** | .060 |
| | p | | .000 | .001 | .601 |
| IVC-CI (%) | r | -.428** | 1 | .369** | -.125 |
| | p | .000 | | .001 | .274 |
| IJV-CI (%) | r | -.374** | .369** | 1 | -.132 |
| | p | .001 | .001 | | .248 |
| Delta-$CO_2$ | r | .060 | -.125 | -.132 | 1 |
| | p | .601 | .274 | .248 | |

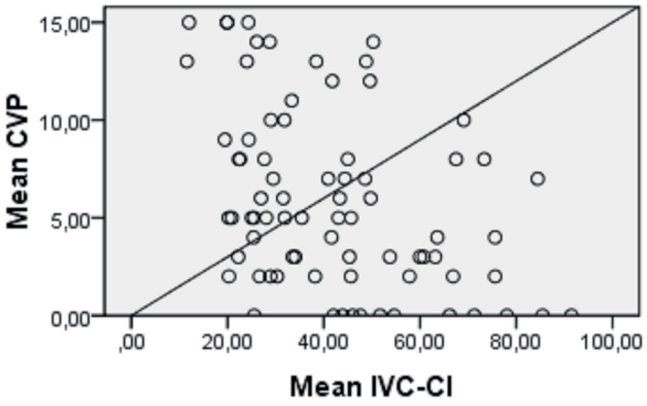


**Figure 4.** Correlation graph between mean CVP and mean IVC-CI

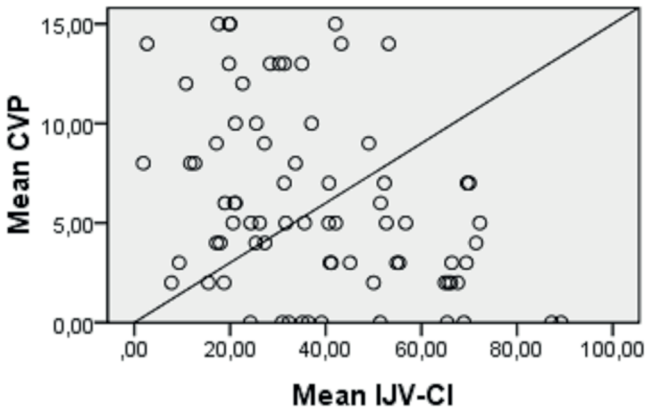


**Figure 5.** Correlation graph between mean CVP and mean IJV-CI

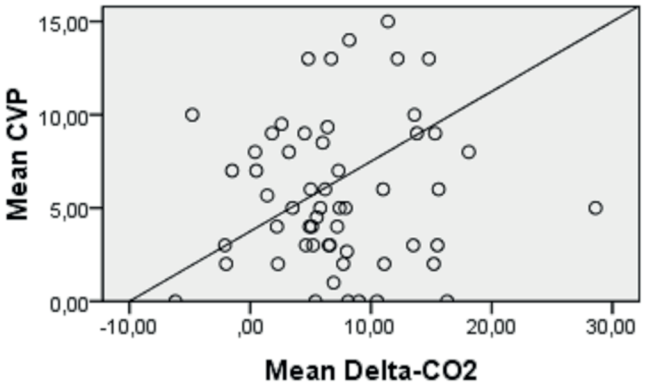


**Figure 6.** Correlation graph between mean CVP and mean Delta-$CO_2$

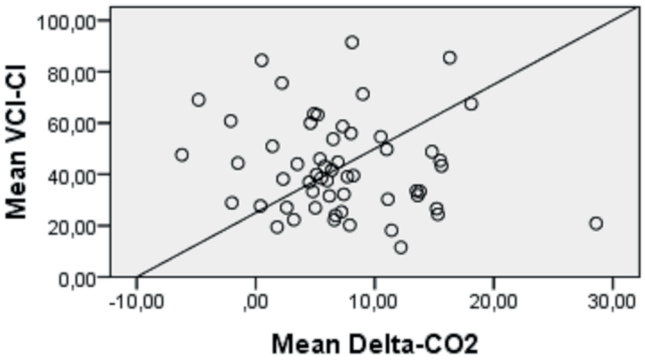


**Figure 7.** Correlation graph between mean IVC-CI and mean Delta $CO_2$

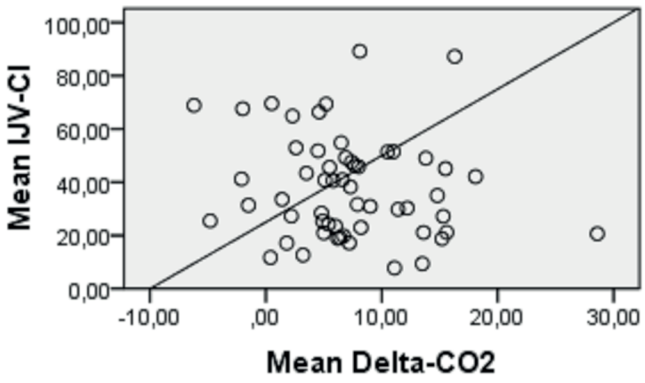


**Figure 8.** Correlation graph between mean IJV-CI and mean Delta-$CO_2$

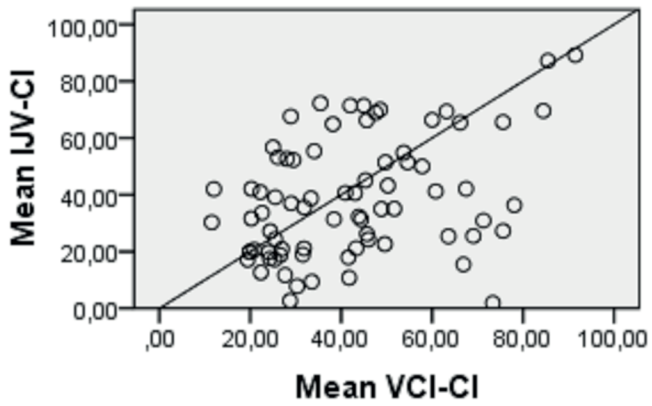


**Figure 9.** Correlation graph between mean IJV-CI and mean IVC-CI

## DISCUSSION

Intravascular volume is extremely important in critical patients in the ICU. Intravascular volume is affected by many factors, such as hypoalbuminemia and sepsis-induced degradation of the glycocalyx. Hypovolemia is still a problem in critically ill patients in ICU. However, in most cases, it continues to be a problem in hypervolemia. Noninvasive and rapid assessment of the intravascular volume status of critical patients is important. It is also important that the intravascular volume assessment is reproducible and low cost. Therefore, in recent years, many studies have been conducted on intravascular volume markers that enable early diagnosis, provide adequate sensitivity and specificity, and are noninvasive, reproducible, and low cost. USG is an imaging method that can be applied at the bedside, is independent of X-rays, and low cost. It can be repeated at any time and enables rapid diagnosis. The only drawback is that it requires experienced practitioners.

In our study, we measured several parameters simultaneously in the same patient for the determination and follow-up of the intravascular volume of critical patients in the ICU and examined whether they are correlated with each other. Each of these methods has its drawbacks and advantages.

The American Society of Echocardiography recommends evaluating the IVC diameter and IVC-CI in assessing the intravascular volume (9). IVC diameter can be a reliable indicator of volume status and IVC-CI can predict the critical ICU patients' response to fluid (9). Doucett JJ et al. (9) concluded that the IVC-CI is reliable in following the resuscitation and fluid status of the trauma patients. In determining and monitoring intravascular fluid status in septic shock, IVC-CI has been determined as a reliable parameter in several publications (10,11). They also evaluated IVC-CI as more specific, sensitive, and easier to apply than CVP in the post-operative hypotension prediction in patients undergoing colonoscopy (12). In patients with cirrhosis, IVC-CI has been used safely in the assessment of volume status and has been found to have a statistically significant negative relationship with CVP (13). It has been stated that the IJV-CI can be used as safely as IVC-CI in the emergency department and ICU (1). It has been reported that in critical patients, intravascular fluid status can be monitored with IVC-CI accompanied by USG (14). However, some publications are reporting that IVC-CI is of little significance in clinical use (15). In noncardiac surgery, preoperative IVC-CI has been evaluated to have high specificity and low sensitivity in predicting postoperative hypotension (16).

In knee arthroscopy, there are also publications indicating that preoperatively increased IVC-CI does not help identify severe hypotension after spinal anesthesia in saline administrated patients (17). IVC-CI can be used safely in the determination of intravascular volume status in patients with sepsis and acute circulatory failure (18). In the literature, many publications indicate that IVC-CI is used in determining and monitoring the intravascular volume status of critical patients. In our study, we used various techniques to determine the volume status and IVC-CI is one of them.

IJV-CI has also been used successfully to reflect the volume status of critical patients rapidly (5). IJV-CI has also been used to determine and monitor the volume status of patients with sepsis (4). However, both IJV-CI and IVC-CI are affected by increased intra-abdominal and intra-thoracic pressure, and this leads to a decrease in their correlation and power in evaluating CVP (7). The IJV-CI can be used quickly in CVP evaluation. Especially when IVC-CI cannot be evaluated and in the absence of a CVP catheter, it is a feasible and reproducible method at the bedside.

CVP is the gold standard in assessing the intravascular volume status (1). However, it may cause complications, it is invasive and requires experienced personnel (1). As vascular collapsibility increases in hypovolemic patients, difficulties may occur in an intervention (1). CVP is correlated with IVC-CI (6). If CVP < 10mmHg, the IVC diameter is < 2 cm and the IVC-CI is > 50% (6). In terms of relationship with CVP, IJV-CI also has the same conditions as IVC-CI (6).

In the literature, we did not find many studies on Delta-$CO_2$. In a study conducted in ICU after cardiac surgery, Delta-CO2 was observed to be an indicator of mortality in ICU patients (19). In another study, delta $CO_2$ increase in infant cardiac surgery was associated with poor clinical results and mortality (20). Delta $CO_2$ has also been associated with poor clinical outcomes and mortality in patients with sepsis (21). Increased Delta-$CO_2$ has been associated with worse clinical outcomes such as lower cardiac index, higher lactate levels, lower venous oxygen saturation, lower lactate clearance, worse hemodynamic parameters, poor tissue perfusion, and higher mortality (8). Again, in a notable study examining the relationship between cardiac output and cardiac index, and Delta-$CO_2$, increased Delta-$CO_2$ has been associated with the $CO_2$ accumulation and low fluid status (8).

However, some studies have indicated the total opposite results (8). Delta-$CO_2$ shows individual variability and its pathophysiology is complex (8). As a result, it was stated that Delta-CO2 is indirectly inconsistent in evaluating cardiac output (8).

In our study, we examined whether there is a correlation between IVC-CI, IJV-CI, and CVP, which we use to determine and monitor intravascular volume, and Delta-$CO_2$ and whether these four parameters can be used interchangeably.

**Limitations**

We planned this study as a prospective observational study. We did not separate patients according to hypovolemic fluid response or hypovolemic status. We tried to embody the patients' measured values with Delta-$CO_2$, but we could not find a relationship between Delta-

$CO_2$ and other parameters. In the future, we recommend looking at the relationship of these values with parameters measured by the thermodilution method in patients who are hypovolemic and respond to fluid.

## CONCLUSION

In our previous pregnancy model, we reported that 5 mg/kg/bw AA dose administration led to oxidative stress in the placental tissue shifted the oxidant/antioxidant balance in favor of oxidants. In the present study, the investigation of the effects of 10 mg/kg/bw AA dose on placental tissues demonstrated that the toxic material filtration potential of the maternal liver and kidney tissues were insufficient based on more detailed biochemical parameters. Thus, we recommend that strong antioxidant substances such as Vit E should be consumed daily to protect the mother and the fetus from permanent damages induced by food-borne AA toxicity.

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